Jianren Mao
Editor

Spine Pain Care

A Comprehensive Clinical Guide

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Preface

Spine pain refers to pain conditions resulting from spine pathologies including disease, trauma, degeneration, and tumor. Spine pain can also result from changes in the structures adjacent to the spine such as sacroiliac joints and musculoskeletal origins. Spine pain is a primary and significant cause of loss of productivity and high cost of expensive healthcare. Care for spine pain involves multiple medical specialties and is a major focus of contemporary pain management. The issue of spine pain care may also be directly linked to the current nationwide crisis of opioid use and misuse.

Although there have been publications and book titles on the topic of spine pain and its management, most of these publications and book titles focus on a singular aspect of spine pain management such as surgery, interventional procedures including imaging books, medication management, psychotherapy, etc. While these publications and book titles may serve individual groups of professionals, these materials lack integration among various specialties involved in spine pain care. The objective of this book is to present multifaceted perspectives regarding spine pain care by breaking the barriers between different specialties, thereby providing the readers with a comprehensive guide to spine pain care in a single book.

This book is written by specialists in the field of spine pain care, including pain specialists, spine surgeons, neurologists, physiatrists, radiologists, psychologists, psychiatrists, and researchers. The book is divided into six sections: Epidemiology and Economic Impact; Anatomy, Pathophysiology, and Etiology; Clinical Evaluation; Spine Pain Conditions; Treatment of Spine Pain; Challenges and Future Directions.

I sincerely thank my colleagues for their valuable contributions to this important book project. I also would like to thank Springer, including Ms. Diane Lamsback, for the tireless effort and support. I hope that this book will provide healthcare providers (physicians, nurses, physician assistants, physical therapists, radiology technicians, etc.) with much-needed, comprehensive materials about spine pain care.

Boston, MA, USA
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Part I

Epidemiology and Economic Impact

Spine Pain Care: Clinical Challenges and Unmet Research Needs

1

Jianren Mao

Key Points

- Spine pain care requires multidisciplinary and interdisciplinary collaboration and coordination.
- There are unresolved clinical issues related to spine pain care including the development of optimal clinical treatment pathways (algorithms).
- There are unmet research needs to improve spine pain care through better understanding the underlying mechanisms and disease entities of spine pain.
- A paradigm shift in spine pain research is needed to accelerate the development of new drugs and new treatment modalities for spine pain care.

Overview

Spine pain refers to pain conditions resulting from spine pathologies including disease, trauma, degeneration, and tumor. Spine pain also includes etiologies related to changes in the structures adjacent to the spine such as sacroiliac joints, musculoskeletal origins, etc. Spine pain is a primary and significant cause of loss of productivity and high cost of expensive healthcare. Care for spine pain involves multiple medical specialties and is a major focus of contemporary pain management. The issue of improper spine pain care may be directly linked to the current nationwide crisis of opioid use and misuse. Unfortunately, current paradigms of spine pain treatment guided primarily by symptoms and signs, aided with radiological (e.g., X-ray, MRI) findings, are often ineffective due to the complexity and interplay of multiple etiologies of spine pain conditions (e.g., spinal stenosis, disc herniation, joint arthritis, myofascial origin, referred pain). Ineffective treatment prolongs the course of spine pain, which contributes to the genesis of chronic spine pain and comorbidities and has a significant impact on healthcare cost and worker productivity.

Although acute pain treatment has been rather successful, chronic pain remains difficult to manage [1]. Chronic pain is a significant health and economic burden, affecting over 25 million adults daily [2, 3]. The point prevalence of chronic pain is estimated to be 30.7% [4]. It has been reported that annually 266 million individuals worldwide present with degenerative spine diseases and chronic low back pain [5]. The lifetime prevalence of chronic low back pain, a major subcategory of spine pain, is 49–70% [6], and that of radicular back pain (sciatica) can be up to 40% [7].

The annual prevalence of disc-related spine pain [a major cause of radicular pain with inflammatory irritation of spine nerve root and/or dorsal root ganglion (DRG)] in the general population is about 2.2% [6]. Annual cost for caring patients with spine pain and radiculopathy is over $1 billion, and the annual cost for surgical discectomy alone exceeds $300 million in the USA. An analysis of over 6.5 million patients found that back pain (74.7%) and radiating leg pain (50%) are among the most common pain complaints [3].

Indeed, chronic pain is a significant health and economic burden and remains difficult to manage. Spine pain is a major category of chronic pain conditions. For example, patients' description of radiating back pain is often vague and indiscriminative, so are radiological findings, to differentiate between radicular spine pain due to inflammatory irritation or compression of spinal nerve and/or DRG and pseudo-radicular pain that are not caused by such changes. For example, epidural steroid injection (ESI) is the most commonly performed interventional procedure for radiating spine pain treatment, in addition to non-procedural modalities such as physical therapy, costing $743 million per year for Medicare plans only [8]. While ESI often works well for patients with radicular pain, at least temporarily, it is much less effective or ineffective for those with pseudo-radicular

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pain [9–15]. Severe complications can occur with ESI as well [16, 17]. For patients with pseudo-radicular spine pain, other interventions such as lumbar facet or sacroiliac joint injections might be more effective. Indeed, clinicians often find it difficult to predict response to current modalities of spine pain care, particularly interventional procedures [18].

Unresolved Clinical Issues

A frequent challenge of spine pain management comes from a large group of patients who have pain radiating to extremities. The overall prevalence of disc herniation (bulging, protrusion) is estimated at 4.8% among men over 35 years of age and 2.5% among women of the same age group [19], and the rate of disc herniation progressively increases with age [20]. A substantial percent of patients continues to have pain after 1 year with nonsurgical treatments [6]. For example, up to 22% patients have ongoing pain and disability at 12–24 months even after an initial successful lumbar discectomy surgery [21]. A good number of patients (16%) undergo post-lumbar discectomy reoperations within 2 years of the original surgery [22]. Recent studies have also shown that unfavorable outcomes, including chronic pain, are present in about 50% patients at 18–24 months [23] and as high as 60% patients at 6 years [19], after an uncomplicated lumbar disc surgery.

Moreover, a large population of spine pain patients are older adults, and their spine pain conditions are typically of degenerative origins, such as spinal stenosis and degenerative joint arthritis (facet joints, sacroiliac joints). Spine pain conditions persist and often progress over time in this patient population. As such, a significant portion of spine pain patients will experience transition to chronic pain despite active treatments. For example, patients with chronic back and radiating leg pain are often treated with interventional procedures, in addition to physical therapy, pharmacologic therapy, mind-body interventions, acupuncture, and chiropractic manipulation [24]. Despite these treatments, transition to chronic pain is estimated to affect up to 40% of patients with back pain conditions [7, 25, 26].

A major deficiency in the field of spine pain management is the lack of meaningful treatment pathways (algorithms). This issue is particularly significant in deciding which interventional procedure or surgery would be appropriate for spine pain treatment because (1) multiple etiologies (causes) often coexist in spine pain patients, (2) clinical symptoms and signs of spine pain often overlap with different etiologies, (3) the effectiveness of interventional procedures remains unclear due to the complexity and interplay with multiple etiologies, and (4) interventional procedures are expensive to perform and also associated with complications [16, 17].

For example, the cause of radicular back pain due to inflammatory irritation of spine nerve root and/or DRG is mechanistically different from that of referred pain from lumbar facet joint or sacroiliac joint arthritis. However, patients with either pain condition can present with "radiating pain" to lower extremities. Inflammatory radiating pain due to disc herniation or spinal stenosis (i.e., radicular pain) responds well, at least temporally, to ESI, whereas radiating pain due to lumbar facet or sacroiliac joint arthritis (i.e., pseudo-radicular pain) is less likely to benefit from ESI [10–15]. Delayed treatment of spine pain due to an inappropriate choice of treatment modality contributes to the transition to chronic pain and development of comorbidities such as depression, anxiety, and medication overprescribing (e.g., opioid). Delayed treatment of spine pain also causes loss of productivity, loss of income, and disability claims, as discussed earlier. Indeed, poor phenotyping of spine pain patients leads to poor clinical outcome. Therefore, there is a tremendous interest, both for patient care and research purposes, to develop meaningful clinical algorithms of spine pain treatment. This is an under-investigated research area given the high prevalence of spine pain conditions and detrimental economic and societal consequences due to unresolved spine pain conditions.

Unmet Research Needs

As mentioned earlier, opioid and non-opioid pain medications, physical therapy, chiropractic manipulation, acupuncture, psychotherapy, mind-body interventions, and interventional and surgical procedures are integral components of the current multidisciplinary strategy for chronic spine pain management. Non-opioid pain medications include nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, α_2-adrenergic receptor agonists, antidepressants, antiepileptics including gabapentinoids and ketamine, and topical agents [27, 28].

While analgesics such as NSAIDs and acetaminophen are effective for acute spine pain relief, their use for chronic spine pain treatment is limited by gastrointestinal, renal, and hepatic side effects. Topical agents are not useful to treat many chronic pain conditions such as radicular pain. The long-term effectiveness of antiepileptics, α_2-adrenergic receptor agonists, and antidepressants remains unclear [28]. Ketamine has its own side effects and addiction properties. With few exceptions, new drug development for chronic spine pain treatment has not been fruitful despite extensive research efforts over five decades [1]. The reality is that clinicians often need to use opioids as a treatment option despite the known side effects and risk of addiction [29, 30], which contributes to the current opioid use epidemic including overdose and abuse in the setting of chronic pain man-

agement. Therefore, early, targeted, and effective treatment of spine pain patients, guided by scientifically developed treatment pathways (algorithms), would be highly significant to reduce healthcare cost and opioid prescribing, deter the transition to chronic pain, minimize the loss of productivity, and improve quality of life of spine pain patients.

Despite the subjective nature of spine pain, pain is traditionally regarded as a sensory modality. Over more than five decades, basic science research has largely focused on understanding the transduction, transmission, and modulation of nociceptive signals. This research focus has led to the proposal of numerous molecular targets for the development of new analgesics. However, few of these new targets have been successfully brought to clinical use [1]. In the wake of this reality, some in the field question the effectiveness of pain research using animal "pain" models. Indeed, it appears that a paradigm shift in pain research may be needed to move toward studying pain as a system-based integral response that includes psychosocial comorbidities.

In this regard, translational pain research may play a unique role in developing innovative experimental paradigms aimed at understanding the multifaceted interaction of nociception, pain perception, and pain reaction at the system level. There are at least seven areas of research interests that may be of particular significance in advancing translational pain research:

1. Developing a variety of new animal models of nociception and "pain"
2. Transforming the current nociception-oriented conceptual framework of pain research into a system integration conceptual framework of pain research
3. Developing meaningful assessment tools for preclinical and clinical pain research and developing "objective" clinical pain assessment in spine pain patients
4. Identifying biomarkers and genotypes of nociception and pain, particularly those related to disease entities that are responsible for the genesis and progress of spine pain conditions
5. Enhancing pragmatic clinical pain research projects that could directly lead to improvement in spine pain management, including the development of clinical algorithms
6. Selecting targets for new drug development and improving interventional and surgical devices/tools for better management of spine pain
7. Studying the effectiveness of multidisciplinary and interdisciplinary spine care models for improved clinical management of spine pain

The above-listed ideas are further elaborated in this book. It can be anticipated that the advancement of both preclinical and clinical research will further improve spine pain care in the near future.

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The Epidemiology and Economic Impact of Spine Pain

2

Meghan Saxen and Richard W. Rosenquist

Key Points

- Chronic pain is a significant financial burden to the US healthcare system, and spine pain is the primary complaint in the majority of patients.
- The prevalence of spine pain has not changed over the last 18 years despite technological and medical advancements.
- Spine pain is more prevalent in older individuals, women, and American Indian as well as Alaskan Native populations.
- Low socioeconomic status and low level of education are associated with increased prevalence of spine pain.
- There is a compelling need for the development of improved methods of pain management due to the rising costs of current treatment approaches and their lack of sustainability.
- The direct costs of spine pain relate to incurred medical spending.
- Indirect costs relate to loss of productivity, often broken down into absenteeism and presenteeism.
- The indirect cost of presenteeism contributes the most to loss of productivity.
- Significant decreases in quality of life are significant, but unquantifiable, measures of loss of potential.
- There is a need to advance education and promote cultural transformation so that we can improve the outcomes in both our patients and our country.

The mechanics of the US economy are convoluted and circuitous. It is a unique machine that is ever changing and affects us both locally and globally. A particularly influential component of this entity is healthcare. Healthcare spending in the United States is higher than in any other country in the world [1]. In 2015, healthcare spending amounted to $3.2 trillion, which accounted for 17.8% of the US economy and averaged $9990 per person [2]. Despite being of significant concern, this extraordinary value does not appear to be decreasing. In fact, from 2014 to 2015, spending increased by 5.8%, and from 2015 to 2016, it increased to another 4.8%, resulting in an expenditure of $3.4 trillion. According to the Centers for Medicare and Medicaid Services (CMS), this rate is expected to grow at an average rate of 5.6% each year until 2025 [3]. In light of the role of healthcare in both the physical and financial well-being of our population, it is critical that we are knowledgeable about its influence and conscious of our impact as providers. Spine pain plays a particularly significant role in the cost of our healthcare system due to its high incidence. The goal of this chapter is to review the epidemiology of spine pain and its economic impact in the United States.

To gain a true understanding of any topic within the healthcare field, it is important to examine its past, present trends, and future directions. As a whole, an estimated 100 million American adults live with chronic pain [4]. This figure is likely an underestimate, as it does not include acute or pediatric pain. However, even at this underestimated rate, chronic pain is more common than the total estimated number of adults suffering from diabetes, coronary heart disease, and cancer combined [4–8]. Because the scope of chronic pain is so boundless, multiple studies have been conducted in attempt to narrow the focus to the most prominent conditions within this category. The National Institutes of Health conducted a study in which adults, 18 years old and over, were interviewed and asked a series of questions regarding pain during the 3 months prior to their interview. Their attention was directed to four different types of pain, and they were instructed to report any pain that lasted 24 h or more, excluding minor aches. Low back pain was the most commonly reported type of pain in each age group, involving 27% of respondents [9]. This was followed by severe headache or migraine (15%), neck pain (15%), and facial pain (4%).

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Similarly, the Institute of Medicine reports that low back pain is the most common type of pain reported in US adults at a rate of 28.1% of respondents, followed by migraine (16.1%) and neck pain (15.1%) [4]. Correspondingly, data published from the 2002 National Health Interview Survey (NHIS) demonstrated that low back pain was reported by 26.4% of adults and neck pain by 13.8% [10]. These surveys each demonstrate complementary data supporting the notion that spine pain plays a major role in the vast field of chronic pain and, therefore, our field of healthcare as well.

The societal impact of spine pain has been estimated in epidemiological studies evaluating the incidence and prevalence of these conditions. Scientifically speaking, the term incidence refers to the number of new episodes of pain experienced within a specified time period, divided by the size of the population at risk. According to data extracted from the National Electronic Injury Surveillance System, the incidence of back pain is 139 per 100,000 person-years in the United States [11]. While this is a significant number, perhaps one of the most alarming features of spine pain is its sheer prevalence. Prevalence indicates the number of people who have pain at one defined point, or period of time, divided by the total population at that time. In a report released by the Centers for Disease Control and Prevention (CDC) and National Center for Health Statistics (NCHS), 29.1% of adults over age 18 had experienced low back pain in the previous 3 months during the year 2015, and 15.4% of them experienced neck pain. This prevalence was similar to that of low back and neck pain in 1997 (28.2% and 14.7%, respectively) as well as in 2010 (28.4% and 15.4%, respectively) [12]. During a similar time period, despite the lack of progress in treatment outcomes, utilization and cost of pain-related care increased. From 2000 to 2008, there were a 240% increase in cost and a 229% increase in interventional pain procedures performed in the Medicare population. From 2003 to 2006, the number of claims for zygapophyseal joint injections alone increased by 78%. This data supports the notion that the prevalence of spine pain has remained practically unchanged over the span of 18 years despite increased spending and utilization of care [13, 14]. To put this into perspective, let us consider that in 1997 we saw the invention of wireless internet. In 2001, the first USB device was created, allowing transfer and storage of data on a compact device. Six years later, an influential smartphone was created giving us handheld internet connection, communication, and data storage. And by 2014, we had created a device that accomplished all of these previous advancements and fit into a 38 mm device that attached to our wrist. During that same time period in the medical world, we accomplished the sequencing of the human genome, the development of a vaccine to prevent a cancer, and started using stem cells to artificially grow organs. As a population, we broke barriers in both the technological and medical fields. However, despite advancements in technology and medical knowledge throughout those 18 years, we were unable to decrease the prevalence of spine pain by even 1%. This lack of progress is profound and indicative of stagnation in our treatment approach and success in addressing this condition.

It is important to highlight the demographic characteristics of this phenomenon, such as age, gender, race, and socioeconomic status. With respect to age, the CDC found that the highest rate of spine pain was consistently reported in those from the ages of 55–64 [12]. In 2007, Devon Rubin analyzed a large number of manuscripts examining demographic data and concluded that the highest rates of spine pain were in those aged 20–59 [15]. Similarly, a separate systematic review determined that the prevalence of low back pain is lowest in those aged 20–35 with a progressive rate increase through the 60–65 year range, after which there is a decline in the frequency of pain [16, 17]. The genesis of this trend has been theorized to be due to a multitude of changes in one's habits as they age, such as diet, activity, occupation, and changes in comorbidities.

When referencing the relationship between gender and spine pain, the literature appears to favor a higher prevalence in women. According to Bressler et al., women in the older age population have a higher rate of spine pain than men [18]. It has been hypothesized that this could be related to a higher risk of osteoporosis in this population. This gender-specific data is consistent with CDC data, which shows that women as a whole experienced more low back and neck pain than men from the years 1997–2015 [12]. Additionally, it has been noted in several studies that women are more likely to utilize healthcare for their pain, miss more work, have a worse outcome after a single episode of pain, and are more likely to develop persistent, chronic pain lasting more than 3 months [15, 19–21]. Three theories have been hypothesized to explain the differences in pain experienced by women. One theory assumes that it is socially more acceptable for women to report pain [4]. Another theory suggests that women are exposed to greater numbers of risk factors for pain [4]. A final theory suggests that women are more vulnerable to developing musculoskeletal pain [22]. Whatever the cause may be, it is evident that women experience higher rates of spine pain than men.

Race and ethnicity are two other demographic factors that have been well studied in the fields of pain and epidemiology. Over the past several decades, an expanding body of research has identified dissimilitude in health across different ethnicities and has highlighted the incongruity of the prevalence, treatment, progression, and outcomes of pain-related conditions in various ethnicities. However, it is important for one to consider the weaknesses of such data due to cultural perspectives that may strongly influence reporting of pain as well as disparities in quality and access to care. According to the CDC report, the highest rate of both

low back and neck pain were experienced in the cultural categories of American Indian or Alaskan Native. People identifying as White were second in both categories [12]. According to the National Health Interview Survey in 2009, Asian adults were less likely to have lower back pain than White, Black, American Indian, or Alaskan Native adults [23]. The research regarding the etiology of interethnic differences in pain is ongoing; however some factors such as disparities in treatment, sociocultural differences, and genetic variability have been proposed.

Finally, socioeconomic status and level of education have also demonstrated an imbalance when it comes to the prevalence of spine pain. According to the CDC report, those with no high school diploma or GED consistently reported higher rates of pain each year [12]. These results also held true in the population of those at the lowest level of poverty as well. These outcomes are mirrored by the National Health Interview Survey that demonstrated that those with a bachelor's degree or higher were less likely to have spine pain compared to those who did not graduate from high school. Furthermore, those in poor and near poor families were more likely to experience spine pain than those families who were not considered to be poor by economic standards [23]. Similarly, in a systematic review performed by Dionne et al., there was a consistent association with increased rates of spine pain and low educational status [24]. While socioeconomic status is a difficult mark to quantify precisely, it is evident that it is associated with significant health consequences and that health has significant socioeconomic consequences as well.

In 2011, the Institute of Medicine (IOM) compiled an influential report entitled, *Relieving Pain in America*. This report was intended to "increase the recognition of pain as a significant public health problem in the United States" [4]. The report was the product of a congressional mandate and was created at the direction of the Department of Health and Human Services (HHS), who recognized the severity of chronic pain in America and sought recommendations from the IOM regarding pain research, care, and education. The information compiled by the IOM highlighted the need for the development of improved methods of pain management due to the rising costs of current treatment approaches and their lack of sustainability. According to their report, the annual economic cost of chronic pain is in the range of $560–$630 billion in the United States [4]. This number can be broken down into direct and indirect costs. Direct costs were those that were due to the total incremental cost of healthcare and ranged from $261 to $300 billion. The indirect costs incurred were those due to loss of productivity as a result of absent days at work, inadequacy of work performed, and disability. This cost ranged between $297 and $336 billion [4]. As evidenced by this data, both direct and indirect costs of low back pain have a significant economic impact.

In 2016, Dieleman et al. published an estimate of US spending on personal and public health from the year 1996–2013. In their results, they estimated that in those 17 years, the United States spent approximately $30.1 trillion on personal healthcare. They attempted to disaggregate these costs by delineating 155 conditions responsible for the greatest overall spending. The top three conditions were diabetes, ischemic heart disease, and low back and neck pain [25]. Compared to the other conditions during that time period, spending increased the most on low back pain, neck pain, and diabetes. Spending on low back and neck pain increased by an estimated $57.2 billion. These estimates, though daunting in nature, do not account the additional burden of indirect costs.

Typically, in reference to spine pain, indirect costs refer to the loss of productivity within the American workforce due to disability. This loss of productivity can come in two different forms. One is absenteeism, where a person completely misses a portion or period of work, while the other is presenteeism, where a person is in attendance at work, but not performing to their full capabilities. According to the economic analysis performed in the IOM report, people with severe pain missed an average of 5–5.9 more days of work per year than people with no pain [4]. This equated to a loss of approximately $95.2–$96.5 billion due to hours of work lost and $190.6–$226.3 billion due to lost wages [4]. According to a study performed by Ricci et al., significant functional limitation was observed in 72.3% of US workers with spine pain [26]. They estimated that 16.8% of US workers ages 40–65 years old had clinically meaningful back pain with reported loss of productivity, and the majority of this loss of productivity was due to presenteeism (79.6%) [26]. If we are to improve the financial burden of spine pain in America, we need to be aware of its disabling features and seek alternative means to prevent both absenteeism and presenteeism.

Disability and limitations of activity should not only be quantified in dollars but should also be measured according to their impact on quality of life. In 2006, a survey was conducted by the American Pain Foundation to evaluate the impact of chronic pain in over 300 patients. They found that almost two-thirds (59%) reported an impact on overall enjoyment of life with 77% having feelings of depression, 70% having trouble concentrating, 75% having decreased energy levels, and 86% having inability to sleep well [8]. The effects of pain can encompass an array of psychological and social consequences such as fear, depression, anxiety, and inability to fully participate in one's social roles as a family member, friend, or employee [4]. All of these factors contribute to the unquantifiable costs of lost potential and decreased quality of life. For example, when people cannot fully participate in their social roles, it is common for significant stress on personal relationships to occur. Family members often find their relationships and social dynamics changing in the setting of

chronic pain. They may need to take on new roles such as caregiver and take on a greater burden of responsibility within the family infrastructure. These strained relationships may further impact the patient's recovery. For instance, it has been demonstrated that patients who reported having unsupportive families were more likely to have work-related injuries, rely on medication, and report more pain sites, more pain behavior, and more emotional stress [27]. In contrast to this, those with supportive families reported significantly less pain intensity, needed less medication, and were more active [27]. Though it is difficult to precisely measure the psychological and social significance of these effects, it is an important consideration for providers to take into account when developing a treatment plan for patients.

Given the epidemiology and overall economic impact of spine pain, it is important to utilize this information to further the education and future direction of spine pain in America. Even without personal contributions of technological advancements or novel approaches to physical treatment, we as individuals can reduce its societal impact through enhanced education and necessary cultural transformation. As highlighted in the IOM report, there are multiple barriers to the advancement of our education in this field. Our healthcare institutions and their research infrastructures are most commonly separated by specialty, whereas pain does not belong to any one specific field and instead belongs to every field. This leads to barriers in communication and bisects research funding, outcomes, and ideas that when used conjunctively, could potentially benefit the greater population of pain patients. The flaws of our systematic approach to advancement of knowledge are vast and beyond the scope of this chapter. However, it is necessary to recognize the existence of such weaknesses and make attempt to overcome these obstacles.

Additionally, we need to promote a cultural transformation to change the stigma attached to chronic pain patients in our society. A 3-year campaign in Australia in the 1990s utilized mass media to promote the concepts that disability can be improved by positive attitudes, that people with back pain should continue to participate in their usual activities, and that much can be done to help themselves. These ideas were aimed at both healthcare providers and the general public. The results of this campaign produced dramatic improvements in clinician beliefs regarding back pain and demonstrated a decline in related workers' compensation claims and healthcare utilization during the campaign [22]. This campaign should serve as motivation to promote a healthy mindset when it comes to chronic pain and give us the determination to change our outcomes.

The identification of systematic flaws with a proposed set of recommendations by the IOM was just a first step toward the goal of improved pain management. Following this report, the Department of Health and Human Services developed the Interagency Pain Research Coordinating Committee who teamed with the NIH in 2012 to develop a National Pain Strategy. This report was intended to construct a long-term plan for transformation of the perception, assessment, and treatment of pain. It outlines six key areas of concern such as population research, prevention and care, disparity, service delivery and payment, professional education and training, as well as public education and communication. For each category, it proposes short-term, medium-term, and long-term strategies for improvement. This report provides us with a clear outline for action, and the hope is that we take the necessary next steps to contribute to its progress and success.

In conclusion, spine pain plays an enormous role in both the physical and financial well-being of our population. Despite an incredible financial investment, our current approaches to treatment have failed to decrease its prevalence and are not sustainable. As providers, it is our responsibility to recognize the barriers of education, to work to increase communication, and to promote cultural transformation to improve outcomes for our patients and our country. If we are able to produce a decrease in the prevalence of spine pain by even 1%, we will have accomplished more than we have in the past 18 years, and this should serve as motivation for dynamic change.

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Current and Emerging Payment Models for Spine Pain Care: Evidence-Based, Outcomes-Based, or Both?

3

Kayode Williams and Daniel B. Carr

Key Points

- Payment for spine care is moving toward "value-based care" models.
- "Value" is defined as best outcomes at optimum cost.
- This chapter explores currently available models used by policymakers to define best outcomes.
- The Patient-Reported Outcomes Measurement Information System (PROMIS) is among the latest and most influential tools to assess ongoing population-based responses to treatment. Its limitations include lack of granularity with regard to specific treatment provided for each patient.
- "Evidence-based" medicine as a foundation of health policy including payment faces challenges with regard to generalizability of literature-based findings to guide treatments at the level of each individual.
- The US Federal insurance system has recently introduced a merit-based payment system (MIPS) requiring physicians to document specific treatment outcome and quality measures to justify a payment bonus or incur a payment penalty.

Introduction

In contrast to the numerous workshops and handbooks describing methods to optimize payment for care rendered, virtually all academic texts, curricula [1], and monographs [2] about pain consider "translation" of basic findings to end with their clinical application. Rarely do they consider that interventions must be supported in a stable economic context, including paying for the time and effort of clinicians implementing them, if the interventions are to survive [3]. Other chapters in this volume present comprehensive accounts of the neuroscience of pain insofar as they help clinicians understand conditions affecting the spine and guidance as to patient selection when translating preclinical findings and clinical trial results into daily practice. However, none of these advances will persist as therapeutic options if the processes to ensure that they are paid for when applied appropriately fail to do so in an economically sustainable way. Many academic and tertiary pain care settings in which scientific advances are translated into clinical care already struggle to maintain profitability if not viability as healthcare payment evolves from fee-for-service to shared financial risk [4].

The present chapter reviews current and emerging payment models that, presently and in the near future, will provide economic support for the practice of spine care. Some general familiarity with the concepts of outcomes assessment and medical evidence is expected of the reader, not a high barrier, given the pervasiveness of both concepts throughout current medical training and practice [5]. We describe payment models based upon clinical outcomes achieved during the everyday care of real patients, as assessed by generic and specialized instruments such as the Patient-Reported Outcomes Measurement Information System (PROMIS) [6]. We describe other payment models based upon evidence-based methods that consolidate findings in prior published studies of previous cohorts or populations exposed to the same treatment [7]. We indicate that ongoing mandates aimed to contain ever-increasing costs of care are

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likely to result in a convergence of the two approaches as framed through Medicare payment models such as MACRA (see below). We conclude with a glimpse into how emerging technology may accelerate the routine collection of "big" data on a large scale to inform value-based care, including the application of blockchain methodology to aggregate detailed, individual patient data to inform population-based outcomes assessment while maintaining the security and confidentiality of individual records.

Outcomes-Based Care and Payment

Efforts to heal disease and overcome the effects of trauma have been an integral part of civilization since before recorded history [8]. For those cultures with historical records of their approach to sickness, health, and healing, there is clear documentation that some healers and treatments were felt to produce better outcomes than others [9]. Well-regarded healers were accorded a higher status and in many cases paid more, than others. For example, Hammurabi's Code (c. 1695 BCE) stipulated the fee allowed for surgical procedures according to their complexity, the social and economic standing of the patient, the skill of the provider, and whether special equipment was employed [10]. However, this code punished surgeons whose operations were followed by the patient's death by amputation of both hands. Plato's dialogues contain many references to the practice of medicine in ancient Greece, including its two-tiered medical system. Citizens received time-consuming, individualized assessment and care, but slaves were treated in an empirical, hurried fashion in crowded clinics [9]. Physicians who treated citizens were state appointees with an annual term and high socioeconomic status. Their reappointment depended upon citizens' satisfaction with their results in the prior year, as voiced in a community gathering convened annually for this purpose. Socrates made reference to outcomes-based reappointment when he asked, "If you and I were physicians, and were advising one another that we were competent to practice, should I not ask you, and would you not ask me, well, what about Socrates himself, has he not good health? And was anyone else ever been known to be cured by him, whether slave or freeman?" [9].

Yet despite the foundational importance of health, sickness, and treatment to the human condition and references to illness or well-being for millennia not only in medical texts [10] but also in religion [11], systematic approaches to deciding upon the merit and value of specific interventions have been absent until recently. The term "outcomes movement" has been applied in many ways. Broadly, it refers to the use of prespecified measures to assess the effectiveness of medical care, often with an emphasis upon the patient's perspective and preferences as opposed to the function of one or another organ system [12]. Until the late twentieth century, results of medical interventions were as a rule reported in ad hoc, frequently intuitive ways. This approach was suitable for dramatic single cases or small series reporting prevention or cure of the fatal conditions such as diabetic ketoacidosis or scurvy [13], therapies whose real-world benefit was readily confirmed by some easily measured secondary function or physiological outcome or a vaguely phrased result such as returning to one's previous health (or in an Old Testament clinical trial of rich versus simple diets, displaying "fairer countenances") [14].

Multiple factors led to the introduction and now embedding of prespecified outcomes into medical research and health care [5]. These include the growing need to compare different treatments according to a common yardstick or yardsticks; the need to decide whether a treatment has a partial effect that falls short of being lifesaving but is nonetheless clinically significant, such as return to work; the cost of the treatment; and as above mentioned, the rise of consumer empowerment [15]. Consumer empowerment is manifest in medical care as patient-centeredness, reflected in part by the introduction of outcomes particularly important to patients such as quality of life, functional capacity, the medical condition's interference with daily life, mood, satisfaction with care, out-of-pocket costs to patients and families, or readmission to hospital [5, 16–18].

Outcomes assessment instruments have proliferated in recent years, owing to the increasing ease of capturing relevant data in real-world settings (e.g., by smartphones or activity monitors) [19] and the multiple purposes for which such measures may be applied. Such purposes include individual or population-based clinical or health services research, payment "for performance" in a cohort of insured patients treated in a single practice or health-care system, and monitoring the results of individual patients' care. There are generic outcome measures designed to capture health-related quality of life in a population without any single overriding health problem, and supplemental or condition-specific instruments relevant to a specific pathology or cluster of pathologies such as chronic pain or spine conditions [20–22]. Generic measures (particularly when compressed into as few questions as possible to reduce the burden of data capture) may lack the sensitivity to discern changes in outcomes of a patient cohort defined by having a specific pathology and often must be supplemented by questions relevant to that specific pathology [18–20, 23–26]. Alternatively, an adaptive testing instrument such as the Patient-Reported Outcomes Information System (PROMIS; see below) may be programmed to present supplemental questions exploring health-related quality of life and function in greater depth if the patient's initial responses indicate significant impairment. An idea of the range of chronic pain-related outcomes is reflected in consensus recommendations from conferences

Table 3.1 Core domains for clinical trials of chronic pain treatment efficacy and effectiveness

Pain
Physical functioning
Emotional functioning
Participant ratings of global improvement
Symptoms and adverse events
Participant disposition (including adherence to the treatment regimen and reasons for premature withdrawal from the trial)

Adapted from [27]
Note that the first five listed domains are also relevant to outcomes that assess the quality of clinical care

Table 3.2 Recommended research standards prepared by an NIH task force on chronic low back pain ("cLBP")

Define the chronicity of the cLBP
Stratify the cLBP according to its intensity, interference with normal activities, and functional status
Report at least a minimum dataset: history and demographics such as employment status; physical examination; imaging studies; and self-report domains such as can be captured using the PROMIS measures
Measure outcomes drawn from the minimum dataset (among other sources)
Conduct research to refine the research standard
Disseminate the research standards through the National Institutes of Health Pain Consortium and the pain research community

Adapted from [28]
Note: Many of the above proposed standards are also relevant to data obtained to document quality and value of clinical care outside of research

convened by the ACTION/IMPACT group [27] (Table 3.1) and a separate working group to identify a core set of outcomes for clinical research on spine-related conditions [28] (Table 3.2).

With regard to outcome measures as a driver of payment, a major impetus for this approach was the emphasis upon "value-based care" under the Affordable Care Act, where "value" is defined as improved clinical outcomes delivered "cost-effectively" (meaning reduced cost for similar outcomes or similar cost for improved outcomes). A current, widely used instrument for capturing outcomes in a variety of disorders including pain-related conditions relies upon computerized adaptive testing that as mentioned earlier minimizes the number of questions posed to respondents by having the choice of later questions depend upon the severity of symptoms and impairment revealed in the responses to earlier questions.

PROMIS was developed in 2004–2009 with funding from the National Institutes of Health [6, 29]. The self-reported outcomes for adults include measures of global, physical, mental, and social well-being. With the exception of global health status, the same measures for children are reported by proxy. Pain-specific domains include intensity, interference, behavior, and quality. Additional domains (e.g., fatigue or sleep disturbance) often associated with pain are also assessed. Initially, the validity and other psychometric properties of the PROMIS questions were categorized in longitudinal studies of six widespread, burdensome, and costly clinical conditions: congestive heart failure, chronic obstructive pulmonary disease, rheumatoid arthritis, cancer, back pain, and major depression. These initial studies characterized the responsiveness of the PROMIS measures to changes in health-related quality of life and function during treatment of each of these conditions [6, 29].

For example, the back pain study evaluated the impact of "spinal injections" on individuals with back and/or leg pain as assessed by the PROMIS pain measures. Similarly, the depression study examined the impact of standard treatments (medication, psychotherapy, or the combination of both) in a sample of individuals with clinical depression and evaluated their responses using the PROMIS measures of emotional distress (depression, anxiety, and anger). Such validation and outcomes studies of the PROMIS measures provide an initial framework for standardized, precise, and continuous measurement and improvement of outcomes. However, the information provided will require further comparative effectiveness studies (CERs) to provide practitioners, policymakers and third-party payers specifics with regard to treatment modalities that deliver the best outcomes in various cohorts of patients with chronic diseases. This is because the PROMIS dataset lacks the granularity of CER, e.g., to document which specific treatment was provided or what criteria drove the medical decision-making process. Thus, though we have made great strides in collecting data on outcomes, we have still not addressed the most important question for value-based care: "Which treatment or combination of treatments provide the best outcomes for this patient at the optimum cost?"

In summary, the rationale for outcomes-based payment lies with the opportunity to collect and monitor uniform, normative data, increasingly in real time, captured under real-world conditions of life and medical care. On the other hand, if an outcome instrument is used that is insensitive to the specific population and pathologies treated, a false-negative conclusion may be reached indicating that the treatment did not produce significant benefit. If one asks a greater number of questions to enhance the sensitivity of monitoring outcomes, this approach increases the burdens upon the respondent and clinician. Opportunities associated with routine outcomes assessment include the intuitively fair approach to care of paying for what works – as in Hammurabi's Code [30, 31] – and the prospect of collecting "big data" so as to refine care of populations by identifying opportunities for improvement. Threats and dangers to applying outcomes-based payment include incorrect or incomplete application of the primary sources dictating what the preferred outcomes are, for example, in misinterpreting the CDC Guidelines for

Opioid Treatment of Chronic Noncancer Pain [32] as stating in a blanket fashion that long-term use of opioids is necessarily a poor outcome. Further, any standardized instrument measuring health-related quality of life runs the risk of failing to assess personal abilities such as preparing a meal for a loved one, sitting through a religious service, or playing with a pet that may hold great meaning for the patient.

Evidence-Based Versus Outcomes-Based Medical Care and Payment: "Chicken or Egg"?

A 1996 bellwether definition of evidence-based medical care was offered by David Sackett: "Evidence-based medicine is the conscientious use of current best evidence in making decisions about the care of individual patients or the delivery of health services" [33]. Others have offered similar definitions, sometimes explicitly mentioning that the reduction of bias is one of EBM's (evidence-based medicine's) fundamental goals. To reduce bias in estimates of treatment efficacy, proponents of EBM have relied heavily upon randomized controlled trials, a method introduced into clinical investigation after the Second World War. Sackett's definition continued: "Current best evidence is up-to-date information from relevant, valid research about the effects of different forms of health care, the potential for harm from exposure to particular agents, the accuracy of diagnostic tests, and the predictive power of prognostic factors."

As pointed out above, prospective appraisals of individual outcomes of medical treatment date back at least as early as the Old Testament [14] and likely antedate the historical record. Yet until valid outcome measures were developed to capture the salient features of the disorder being treated, medicine's ability to predict the likely result of a treatment, assess its side effects, judge whether its cost is justified, and compare the effectiveness of one treatment versus another was quite limited. Arguably, the relationship between outcomes-guided care and evidence-based care is one of chicken and egg. The collection of valid, relevant outcomes is a foundation of clinical research, the aggregated results of which constitute "current best evidence." Awareness of current best evidence allows clinicians to prepare evidence-based guidelines, adherence to which is assumed to improve outcomes. Systematic collection of outcomes during clinical practice provides evidence to support continuous quality improvement [34]. Indeed, advances in outcomes assessment and clinical evidence have taken place concurrently in recent years.

Regarding the aggregation of data from multiple patients and sources, a fundamental stumbling block in translating clinical trial evidence to clinical care is that "the physician serves as advocate for the personal goals and subjective preferences of individual patients, not for classes of patients or for society as a whole" [13]. Decades ago, Louis Lasagna recognized that results obtained during everyday care of patients may not reflect the results of RCTs conducted to receive marketing approval [13]. The latter are typically conducted in artificially homogeneous populations without significant comorbidities, with few, if any concurrent medications, recruited and followed attentively – "hothouse medicine," in Lasagna's words. Therefore, he urged evaluation of new medications in the setting of everyday clinical practice, in what he termed a "naturalistic" fashion akin to what we now call "comparative effectiveness research." Critiques of the application of EBM to medical decision making have continued to appear in the subsequent decades [15, 35, 36].

Apart from questions regarding the generalizability of RCTs or their aggregated results reported in systematic reviews or meta-analyses, there are other reasons to question the use of this form of structured evidence as the basis for insurers' reimbursement for specific treatments [37]. Statistical methods for combining the results of clinical trials to reach a conclusion based upon the clinical literature were developed in postwar United Kingdom to help its government estimate resources required to support its newly declared policy of free health care for all [38]. Archie Cochrane was a public health physician who was instrumental in this early assembling of clinical trial evidence to support policymakers' decisions in the United Kingdom's National Health Service; the Oxford-based worldwide collaboration in EBM is named in his honor. The statistical decision support methods that Cochrane and colleagues introduced were population-based and by design decreased the weighting ascribed to results of individual outliers. On the other hand, patients referred for evaluation and treatment at specialized pain treatment centers are de facto outliers in that they have not responded adequately to efforts of their primary care providers. Therefore, prior approval or denial of payment based upon a systematic review or meta-analysis of the literature, showing no aggregate benefit for the experimental intervention compared with the control, may limit access by subgroups or individual patients who may respond to the treatment, albeit insufficient numbers to produce group differences in published outcomes between the active and control groups. For decades, clinical and health services researchers have recognized the merit of multiple sources of evidence beyond RCTs to aid in the evaluation of health effects, patient preferences, and costs of treatments [39] including novel technologies [13]. Examples of these non-RCT sources of evidence include case series, case studies, epidemiologic surveillance, cohort studies, decision analyses, mathematical modeling, group judgment methods, and administrative data. See Tables 3.3 and 3.4.

Table 3.3 Technology assessment methods for evaluating safety and efficacy of proposed treatments, risks, costs, preferences, and current practice

Randomized clinical trial
Receiver-operating characteristic curve, relating true positive rate to false positive rate
Series of consecutive cases
Case study of a procedure, program, institution, or decision
Registers and databases
Sample surveys
Administrative data
Epidemiological methods: cohort studies, case-control studies, cross-sectional studies
Surveillance
Quantitative synthesis methods, including meta-analysis
Group judgment methods (Delphi, consensus conferences, etc.), sometimes incorporating literature reviews
Cost-effectiveness and cost-benefit analysis
Mathematical modeling
Decision analysis
Examination of social and medical issues

Adapted from [13]
Note: Although presented in the context of technology assessment, the above methods and those in Table 3.4 are also relevant to evaluating the quality and value of clinical care

Table 3.4 Examples of studies with effects on policy or practice

Randomized, controlled trials
Meta-analyses, systematic reviews, decision analyses
Prospective cohort studies
Retrospective cohort studies
Case-control studies
Cross-sectional studies
Ecologic studies
Pragmatic trials and large observational studies
Program-based evidence
Case reports and series
Registries

Adapted from [39]

Variation in study designs of the available RCTs in clinical pain research, including interventions or outcomes measured and the timing of both, limits the strength of conclusions drawn from their pooled findings (meta-analysis). Except for a limited number of conditions, it has taken an inordinate amount of time to develop consensus treatment recommendations relevant to pain medicine, following EBM methodology [40–47].

Applying Outcome Measures in Routine Clinical Care

There has been some move to address the gap between patient-reported outcomes and clinical recommendations. The acute pain arena lends itself to such detailed reporting of specific perioperative treatment provided while collecting outcome measures data [48]. This is exemplified in the PAIN OUT initiative [49, 50] under the auspices of the European Pain Federation (also designated as "EFIC"). Other initiatives apply tools specifically developed for patients undergoing total knee arthroplasty (TKA) or benchmarking of patients post hip surgery [51, 52]. Efforts are now under way to adapt the PROMIS measures into a 1-day timeline so as to develop a modified instrument suitable for acute pain outcomes studies (Kent M, 2018, personal communication). In the chronic pain arena, the Pain Assessment Screening Tool and Outcomes Registry (PASTOR) developed by the Veteran's Administration [53] allows for routine data collection to guide clinical care, according to a framework that supports longitudinal outcomes assessment and comparison against a representative sample of the US population from the 2010 Census. PASTOR is based upon the PROMIS measures but extends them by adding problem screening questions to elicit (a) opioid abuse/misuse, (b) post-traumatic stress disorder, (c) health utilization – patient report of providers seen by type (primary care provider or pain specialist) – and (d) self-reported treatment history and effectiveness evaluation. The inclusion of the section in health utilization with self-reported treatment and effectiveness evaluation helps provide the information that closes the gap between actual treatment provided and changes in outcomes observed.

How Do Policymakers Currently View the Issue of Physician Payment Models for Chronic Pain (Spine Pain Care)?

With the rising cost of health care globally, regulators and insurers worldwide are implementing policies to lower the cost of health care while maintaining quality and effectiveness or capping costs while improving health-related outcomes. In the United States, the efforts of the Congress illustrate the magnitude of the challenge. In October 2016, the Centers for Medicare and Medicaid Services (CMS) published a final rule for implementing the Medicare Access and Children's Health Insurance Plan Reauthorization Act of 2015 (MACRA). MACRA extended the efforts of the 2010 Affordable Care Act (ACA) that focused on physician payment reform as a mechanism for managing cost while realigning incentives to enhance health-related outcomes. The ACA expanded access to health care through insurance subsidies and Medicaid expansion and addressed health-care cost through delivery reform. In the lay media, the ACA's efforts to expand coverage have received greater attention than its impact upon delivery/payment reform although the latter is crucially important for clinicians providing care for spinal conditions [54]. MACRA established two new pathways for

Medicare payments to physicians and other health-care providers based on quality and value, superseding the prior traditional fee-for-service model in which physicians are paid for services rendered to patients. Policymakers' desire to move beyond the fee-for-service model was motivated by the aging of the population, driven by the baby boomers: the cost of care was outstripping the sustainable growth rate, a mechanism put in place earlier by the Congress to control cost of care for Medicare patients. The "game-changing" provision of MACRA is its mandate to implement a structured mechanism to report outcomes data. This standardized data is factored into a new payment model that provides a bonus for meeting target outcomes or, if they are not met, a risk for being paid less than under the current fee-for-service model. The new payment model is termed the "Quality Payment Program," within which MACRA has defined two main categories of physicians based on the size and location of the practice. Physicians who practice within an Accountable Care Organization will receive payment under the Advanced Alternative Payment Model (APM) pathway, and physicians who practice independently either solo or in varying sized group practices (urban, suburban, or rural) will receive payment under the Merit-Based Incentive Payment System (MIPS) [4, 55, 56].

Merit-Based Incentive Payment System (MIPS)

MIPS-Eligible Clinicians

Under the statute, physicians, physician assistants, nurse practitioners, clinical nurse specialists, and certified registered nurse anesthetists are all considered "eligible clinicians" and must participate in MIPS during 2017 and 2018 performance years (2019 and 2020 payment years).

Physicians are eligible to receive payment under MIPS as calculated by CMS according to performance in four main areas: (1) quality of care, (2) cost of care, (3) improvement activities, and (4) advancing care information (related to the use of the electronic health record (EHR) and information sharing practices). Stipulations have been made for how eligible physicians are to report the information in each of the categories, over what period, and what targets are to be met. The system is designed to provide CMS a 2-year lead time to evaluate the data reported by the eligible physicians so, for example, the initial reporting period started in 2017 and will affect payment made in 2019, and results from 2018 will be applied to payments of 2020. The system provides an adjustment that ranges from +/− 4% in 2019 to +/− 9% in 2022 and all future years based on performance measures in all the 4 areas outlined above [56]. CMS has reserved the right to modify these adjustments moving forward according to newly gathered information.

Quality of Care

Of all the four areas, this has the most direct impact on patient outcomes. Key provisions include:

Data Submission Requirements For both solo physicians and group practices using the EHR, data must be submitted to a Qualified Clinical Data Registry (QCDR) and a Qualified Registry. Group practices will be able to use CMS's Web Interface (for groups of 25 or more physicians) and a CMS-approved survey vendor for Clinician and Group Consumer Assessment of Healthcare Providers and Systems (CAHPS) data for MIPS.

Minimum Data Submission Eligible physicians are required to report at least six measures among which are at least one "cross-cutting" measure and one "outcome" measure. These measures are to be chosen from a list of all MIPS and specialty-specific measures provided by CMS. Specialist physicians may select outcomes from a specialty-specific measure set with no requirement to report a cross-cutting measure.

Patient Experience Measure The CAHPS survey counts as one patient experience measure and also meets the requirement to report a high priority measure. Of broader relevance to the issue of payment for treatments to relieve pain of spinal origin, in 2017 CMS announced that as of January 2018, all institutions' responses to the three HCAHPS questions related to in-hospital pain control were to be delinked from quality-based payment adjustments. The basis for this change lays in a suspicion (admittedly without supporting evidence, according to CMS) that asking inpatients to rate their pain intensity might ultimately result in greater quantities of prescription opioid analgesics being available with consequences such as substance abuse and overdoses. Regardless of the impact of this change for payment, it illustrates how pain treatment and payment for it have been affected by the recent epidemic of substance use disorder, particularly opioid abuse including overdoses.

Global and Population-Based Measures CMS requires group practices of 16 or more clinicians to report on all-cause readmissions (ACRs) within 30 days. Compliance with this measure is particularly important for multispecialty practices in which spine surgeons, physiatrists, and other physicians practice together, but between whom communication may not always be optimal. Patients managed surgically who are readmitted for poorly controlled pain or infection will adversely affect such scoring for all members of the practice. Alternatively, multispecialty practices that can demonstrate that patients move seamlessly from the primary care physician to the physiatrist or pain physician and then to the surgeon and back to the primary care physician in

the most expeditious manner will score highly for population health management and coordination of care. A minimum of 200 cases are to be reported to meet this requirement for reporting these 2 measures.

Cost

CMS will evaluate physicians only on those cost measures relevant to their practice (where there are a minimum of 20 patients that can be ascribed to a specific physician or group). Two main value-based modifier measures are required for reporting cost measures: total cost per capita and the Medicare Spending Per Beneficiary. In addition, CMS included ten clinical conditions for which episode-based cost measures can be reported. These include (in the sequence as announced by CMS):

- Mastectomy
- Aortic/mitral valve surgery
- Coronary artery bypass graft
- Hip/femur fracture or dislocation treatment, inpatient-based
- Cholecystectomy and common duct exploration
- Colonoscopy and biopsy
- Transurethral resection of the prostate for benign prostatic hyperplasia
- Lens and cataract procedures
- Hip replacement or repair
- Knee arthroplasty

The episode measures include Medicare Part A (hospital, other health facility, or home care) and B (preventive or medically necessary services) payments for the reported treatment or procedure. Attribution of treatment or performance of a procedure to a clinician requires that the clinician bill for the procedure. For acute care, attribution is to the clinician billing for at least 30% of the inpatient billing codes. Individual clinicians or groups require a minimum of 20 cases to meet the reporting requirement for this measure.

Improvement Activities Performance

CMS defines improvement activities as activities that an eligible clinician or group identifies as improving clinical practice or care delivery which ultimately enhances outcomes. These activities are to be reported with the same mechanisms for reporting quality measures. Such improvements include organizational activities designed to enhance care coordination to ensure that the patient has access to care and can navigate between primary care and specialist care seamlessly, minimizing waste due to unnecessary or dis-coordinated care. These activities also include changes in clinical practice through introduction or design of enhanced clinical pathways that improve patient outcomes.

How Do Insurance Companies (Third-Party Payers) Currently View the Issue of Physician Payment Models for Chronic Spine Pain Care?

Precedents for payment set by CMS will ultimately be mirrored by other third-party payers. Unlike the MIPS-eligible clinicians, those practicing in large hospital settings meet the criteria for, and hence may elect to receive payment according to, the Advanced Alternative Payment Model (Advanced APM). CMS under the MACRA statute requires that participants "bear financial risk for monetary losses under the APM that are in excess of a nominal amount" [56]. CMS has further categorized financial risk into (1) the financial risk standard and (2) the nominal risk standard. Under the former, CMS can (1) withhold payments for services to the APM entity's eligible clinicians, (2) reduce payment rates to the APM entity and/or the APM entity's eligible clinicians, or (3) require the APM entity to owe payments to CMS. Regarding the latter (nominal) risk standard, CMS provided a three-part test for an APM to determine if risk for losses is "in excess of a nominal amount," which includes the following: (1) the specific level of marginal risk must be at least 30% of losses in excess of expenditure; (2) a minimum loss rate (MLR) must not exceed 4% of expected expenditures, and (3) total potential risk must be at least 4% of expected expenditures. As of the time of writing this chapter (mid-2018), MACRA is in the second year of performance; the APM as outlined herein will be applied in year 3 (2019).

Although there is no spine-specific model, by examining the next closest surgery (Comprehensive Care for Joint Replacement, CJR) one can gain insight into the APM process. Under the mandatory CJR model, CMS holds hospitals participating as Accountable Care Organizations (ACOs) under the APM financially accountable for the quality and cost of CJR episode of care for elective hip and knee surgery. The episodes start at admission and follow through till 90 days after hospital discharge. The episode includes all medical care and services billed to Medicare Part A and Part B for all Medicare fee-for-service beneficiaries. Between 2019 and 2024, hospital performance will be assessed each year for quality-adjusted spending targets, and the hospital with either receives a bonus for spending below target or pays a penalty for spending that exceeds the quality-adjusted target. Thus, in order to adapt to evolving expectations by CMS and by extension, private payers, ACOs must develop and implement value-based care delivery models in which well-designed clinical operation-provided care is coordinated throughout the hospital system to ensure that the right patient gets to the right provider at the right time for the best outcome at optimum cost.

Meeting the Mandate for Value-Based Care Delivery Models that Are Evidence-Guided and Outcomes-Driven

An illustration of coordinated care that potentially meets the requirements for Advanced APMs and Medicare Bundled Payments for Care Improvements (BPCI) is the growth in musculoskeletal (MSK) service lines in most ACOs. These MSK service lines are complex, coordinated, multidisciplinary/interprofessional, outpatient/inpatient, value-based care delivery models that span the continuum of care. They include physical medicine and rehabilitation (PM&R) specialists on the front end to address acute/acute on chronic low back pain (duration <12 weeks), working with physical therapy and medication management. For patients who experience pain beyond 12 weeks, the above triage is supplemented by referral to an interventional pain medicine specialist. Some patients will also require care from a behavioral medicine specialist for treatments to enhance coping strategies and resilience. If necessary, then according to the triage protocol, the next step will include specialized imaging and referral to a spine surgeon for evaluation and possible surgery.

If surgery is required, protocolized care involving enhanced recovery after surgery (ERAS) and novel acute pain service-outpatient programs (APS-OP), transitional pain programs (perioperative surgical homes), and perioperative pain programs will facilitate patient progress through the continuum of care. For these novel models of care, value is measured by reduced length of stay, reduced inpatient complication rate, reduced acute readmission rates, and reduced post-acute care complications.

As of the time of writing this chapter (mid-2018), most ACOs are in the process of implementing these novel value-based care delivery models. There is abundant published evidence illustrating the efficacy and effectiveness of elements of these protocols, e.g., multimodal pain control. However, specific data on outcomes and cost-effectiveness of their implementation within CMS's MIPS framework of care delivery models is yet to accrue because the first year of data-based payment adjustment will be in 2019. MIPS-eligible physicians practicing solo or whose practices are not able to support participation in service line models (e.g., MSK service line) have been called on by CMS to propose measures that would meet similar quality performance goals. CMS suggests that such proposed measures should include but not necessarily be limited to (1) measures that are outcomes-based; (2) measures that address the domain for care coordination; (3) measures that address efficiency, cost, and resource use; (4) measures that identify appropriate use of diagnostics and therapeutics; (5) measures that address patient safety; and (6) measures that include submission methods beyond claims-based data submission. These measures should in theory enable MIPS-eligible clinicians to develop models of care comparable to those of ACO-based clinicians.

The assessment of the value of and ultimately future reimbursement for these models will be determined by how data is collected and analyzed. The data should demonstrate that improvements in patient outcomes and concurrent reductions in cost of care have to be readily attributed to enhancements in the care delivery models adopted. The challenge is that CMS has provided many options for data submission methods for both MIPS-eligible clinicians and ACS-based clinicians; the databases are varied and range from claims databases to QCDRs, electronic health records, and CMS Web Interfaces (for groups of 25 clinicians or more) to the use of a CMS-approved vendor for CAHPS for MIPS. These databases do not share the same architecture (compatibility or interoperability) so the data pooling necessary to decide upon population-wide, normative values or to stratify individual clinicians' results specifically will be a complex and ongoing challenge. Such challenges, however, represent opportunities for medical and surgical spine specialists to drive innovative solutions as to which outcomes are gathered and when and how best to collect, pool, and report such data.

Coordination of MIPS Data Collection: Blockchain Technology?

Data will be accepted from MIPS-eligible clinicians, who may submit it using a wide variety of disparate systems. CMS will have access to this data and will analyze it and provide feedback regarding payment status, i.e., whether or not the physician meets the bonus payment criteria for the payment period. Current registries and reporting database systems meeting CMS requirements are not uniform in terms of format and compatibility, i.e., interoperability, and therefore additional work will be needed to achieve comprehensive population-based outcomes data to inform best practices.

Among the many creative solutions to overcoming the gap between the voluminous collection of data and its aggregation and analysis to improve outcomes, blockchain technology has been advanced as a partial solution. Blockchain technology can be defined as a "distributed peer-to-peer system of ledgers that utilize a software unit that consists of an algorithm which negotiates the informational content of ordered and connected blocks of data together with the cryptographic and security technologies to achieve and maintain its integrity" [57]. The technology was proposed in 2008 under the pseudonym Satoshi Nakamoto [58]. Bitcoin, the peer-to-peer electronic cash system, is the most popular current application of blockchain technology. Biomedical applications potentially include detailed analyses of comprehensive

data acquired from individual patients while maintaining the anonymity of the patients and the practices in which they are treated (except for those MIPS-eligible clinicians who are authorized access to such information).

The foundation for the transformational power of block-chain technology is its capacity to employ underutilized computers and harness their computational power by linking them within a peer-to-peer system. Two types of architectures have been described: (a) distributed, in which component computers are connected to one another without having a central element, and (b) centralized, in which all the component computers are connected to one central component [57]. Hybrid systems have been described, such as multiple distributed systems of computers that connect with a central node. Another hybrid variation is a centralized system in which all the peripheral computers are connected to a central node, within which lies a network of highly interconnected computers. The value of block chain is based on its ability to serve as a tool for achieving and maintaining integrity and anonymity in a distributed peer-to-peer system due to disintermediation (elimination of middleman CMS vendors). Specific examples include payment (managing ownership and creation of digital fiat currencies), cryptocurrencies (managing ownership and creation of digital instruments of payment that exist independently from any government or central bank), and records management (creation and storage of medical records that meet MACRA reporting requirements).

Blockchain technology using the appropriate software has the potential for using all the computing power computer of MIPS-eligible and advanced APM-eligible entities without the need for expensive registries or the use of middlemen vendors to transfer, store, analyze, and report outcome measures to and receive reports from CMS [59].

Summary and Future Considerations

The answer to the question posed at the beginning of this chapter, "should evidence-based medicine or outcomes drive payments for spine pain treatment?" is "yes," i.e., both criteria together should drive payment! Both are two sides of the same coin. Evidence-based medicine is developed through rigorously designed clinical trials in carefully selected, often homogeneous cohorts. Outcome studies are driven by implementation of evidence-based clinical pathways aimed at achieving the desired health-related improvement in the patient population served. Despite steady improvements in both approaches to improving health care, the lead time from inception of an innovation until its acceptance as a new standard of clinical practice is significantly longer than in other industries (e.g., aerospace). Further, the standards for determining and updating optimum outcome measures for each diagnosis in spine care are yet to be fully developed and agreed upon by all stakeholder subspecialties and payer groups. For example, the outcome measures for two patients with post-laminectomy pain could be very different if one is a 70-year-old male with coronary artery disease and diabetes and the other is a 55-year-old otherwise healthy female with moderately severe osteoarthritis and osteoporosis presenting for care 6 months after her second spine surgery. Ongoing engagement with CMS by subspecialties involved in spine care will help shape future quality and outcome measures. Analyses of data that accrues from the measurement of outcomes of well-defined care will help reduce knowledge-practice gaps and identify areas for future research. Through the reorganization of practice engendered by the implementation of MACRA, one theme has become clear: the time has come to coordinate resources in care delivery and reporting of outcomes to ensure that value-based care can be delivered and quantified. As a practical matter, the issue of coordination of care may be more readily addressed by ACOs through internal structural changes (e.g., development of MSK service lines) and more difficult for individual or group-based MIPS-eligible clinicians.

This chapter has provided a glimpse at key concepts related to health care, with an emphasis on applicability to the treatment of painful conditions affecting the spine. The health-care industry is fast moving, and how payment is organized significantly changes. The key to survival (let alone success) lies in our ability as a specialty to improve care delivery models and outcomes through data-driven improvement in clinical operations: value-based care delivery models that leverage advances in health information technology.

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Part II

Anatomy, Pathophysiology, and Etiology

Functional Anatomy of the Human Spine

4

Daniel Gray Trujillo, Krishnan Chakravarthy, and Gary Jay Brenner

Key Points

- Cranial nerves carry sensory information to the brainstem, while spinal nerves carry sensory information to the spinal cord and may bear axons for neurons that synapse within the spinal cord or brainstem.
- The ability to localize painful stimuli depends on the topographic organization of the nervous system.
- There are significant differences in the clinical presentation of visceral pain and somatic pain.
- The central nervous system (CNS) is both the processing center for the perception of noxious stimulation and the primary regulator of adaptive and modulatory mechanisms to produce a pain behavior.
- Synaptic transmission by nociceptive afferent neurons at the level of the dorsal horn is mediated primarily by the excitatory neurotransmitter glutamate.
- Central pain (CP) is initiated by a lesion that interferes with the pathway of nociceptive signals within the CNS from the spinothalamic tract to the parietal somatosensory areas and is a common sequela of spinal cord injury.
- Sympathetic preganglionic neurons are located in the T1 through L2 spinal segments. Parasympathetic preganglionic neurons are located in the brainstem and the S2–S4 spinal segments.

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Introduction

This chapter will describe the specific anatomic structures within and related to the spine that are involved in the transduction of physical stimuli into sensory responses, the conduction of sensory information to the CNS, and the modulation of this sensory information within the spinal cord and brain. It will also discuss some of the major perturbations in these structures as related to clinical pain phenomena.

Organization of the Central and Peripheral Nervous System

To appreciate the role of human spinal anatomy, one must have an understanding of the general organization of the peripheral and central nervous system as they relate to both the somatic and autonomic systems. There are several major anatomic units involved in pain sensation. First, primary sensory neurons whose peripheral terminals respond to physical energy conduct action potentials along long axons bundled into peripheral nerves from the site of sensory stimulus to the spinal cord [2]. Next, nociceptive synaptic relay occurs at the dorsal horn of the spinal cord, where substantial integration and modulation of sensory information occur [3–5]. Ascending fiber tracts carry this information to the brainstem and, from there, diverse brain regions. Descending fiber tracts project from the brainstem and brain to the dorsal horn of the spinal cord and regulate the processing of incoming sensory information [6].

The peripheral nerves that carry sensory information from visceral organs, bone, muscle, joint, or skin to the CNS may be either cranial nerves or spinal nerves. Cranial nerves carry sensory information to the brainstem [7], while spinal nerves carry sensory information to the spinal cord and may bear axons for neurons that synapse within the spinal cord or brainstem [8, 9]. Spinal nerves are mixed nerves that carry general somatic afferent fibers, general visceral afferent

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fibers, general somatic efferent fibers, and general visceral efferent fibers. Somatic afferents primarily carry information from skin, muscle, tendon, and joint, whereas visceral afferents carry information from the other tissues. The cell bodies of both the somatic and the visceral afferent fibers carried by spinal nerves reside in the dorsal root ganglia (DRG) of the spinal cord, whereas those carried by cranial nerves reside in the brainstem cranial nerve nuclei [12].

The ability to localize painful stimuli depends on the topographic organization of the nervous system. The somatic afferent system and the visceral afferent system are strikingly different in this regard, with precise stimulus position detected and encoded by the somatic nervous system but only relatively diffuse information coming to conscious awareness from the visceral afferent system [1]. In the clinical setting, precise localization of pain is often considered evidence that the pain is detected by somatic afferents rather than visceral afferents. For example, knife-like well-localized pain associated with inspiration is likely detected by somatic fibers innervating the parietal pleura [10]. In the abdomen, well-localized lower right quadrant pain occurring late in the course of acute appendicitis is likely due to spread of the periappendiceal inflammation that irritates the somatic nerves innervating the abdominal wall overlying the appendix [11].

In the somatic system, the spinal cord is segmentally organized, such that each spinal segment receives afferent information about a specific cutaneous band or dermatome (Fig. 4.1) [12]. This organization arises during embryonic development when the embryonic neural tube and adjacent mesodermal tissues segment into a series of rostro-caudally adjacent somites [13]. Each spinal nerve innervates tissue developing from a single somite [14]. Spinal nerves from several different spinal segments, such as axons from neurons with cell bodies located in several different DRG, join to give rise to peripheral nerves with cutaneous fields of innervation that span multiple dermatomes (Fig. 4.2) [15].

Although there are many anatomical similarities between the somatic and autonomic afferent fibers, there are significant differences in the clinical presentation of visceral pain and somatic pain. Visceral pain is perceived as deep and is typically not well spatially localized. Pain symptoms resulting from visceral afferents are felt in a location different than the organ itself, such as the experience of arm pain with myocardial infarction [16]. A possible explanation for the clinical symptoms of referred pain is that peripheral nociceptors from somatic and visceral origin converge on a single projection neuron in the dorsal horn. As a result, higher levels of the CNS cannot distinguish the source of the signal input and attribute the sensation to somatic structures by default because somatic sensory representation predominates in the CNS. Convergence occurs in the dorsal horn neurons in lamina I, IV, and V as well as in the intermediate gray matter in lamina X (Fig. 4.3) [17–19] as well as other areas of the CNS including the brainstem, basal forebrain, thalamus, and cerebral cortex [20]. Functional neuroimaging studies have shown that regions of the cortex that are activated by noxious stimuli can also be activated by visceral stimuli [21]. In the thorax, substernal chest pain may be due to any of the visceral sensory afferents from the T1 to T6 spinal segments and may arise from the heart and great vessels, esophagus, lungs, or chest wall. Visceral pain in the abdomen tends to follow the structure of endodermal embryonic development with pain due to foregut structures (stomach, proximal duodenum, liver, biliary system, and pancreas) perceived in the epigastrium or upper abdomen, pain due to midgut structures (distal duodenum, small bowel, cecum, appendix, ascending colon, and proximal transverse colon) perceived in the periumbilical region, and pain due to hindgut structures (distal transverse colon, descending colon, sigmoid, rectum, and urinary bladder) perceived in the lower abdomen [11].

The central processes of the visceral fibers synapse extensively above and below the segment where they entered, thus activating spinothalamic cells at multiple levels, a process referred to as arborization. Clinically, noxious stimulation of the viscera elicits an autonomic spinal reflex reaction, with sympathetic activation that causes symptoms such as excessive sweating and pronounced changes in circulatory system resulting in increased blood pressure. This reflex reaction tends to be more pronounced than what is seen with noxious stimulation of the skin. Noxious visceral stimulation can also result in hypotension and bradycardia by either reflex inhibition of sympathetic outflow or activation of the parasympathetic nervous system [22]. These reactions may be mediated by the periaqueductal gray matter (PAG) and the nucleus of the solitary tract. There are also protective reflexes that are directed toward reducing pain, such as the inhibition of visceral motility. Deregulation of this reflex as well as aberrant response by vagal afferents in the enteric system is thought to contribute to the pathophysiology of irritable bowel syndrome [23]. Coordination centers at higher levels of the CNS, such as the PAG, also mediate nausea and vomiting as well as complex somatic responses in the context of visceral pain.

Functional Anatomy of the Central Nervous System

The CNS is both the processing center for the perception of noxious stimulation and the primary regulator of adaptive and modulatory mechanisms to produce a pain behavior. Pain may be categorized by duration of symptoms (acute vs. chronic), the origin of the pain (visceral vs. somatic), and the nature of the pain (nociceptive, inflammatory, neuropathic).

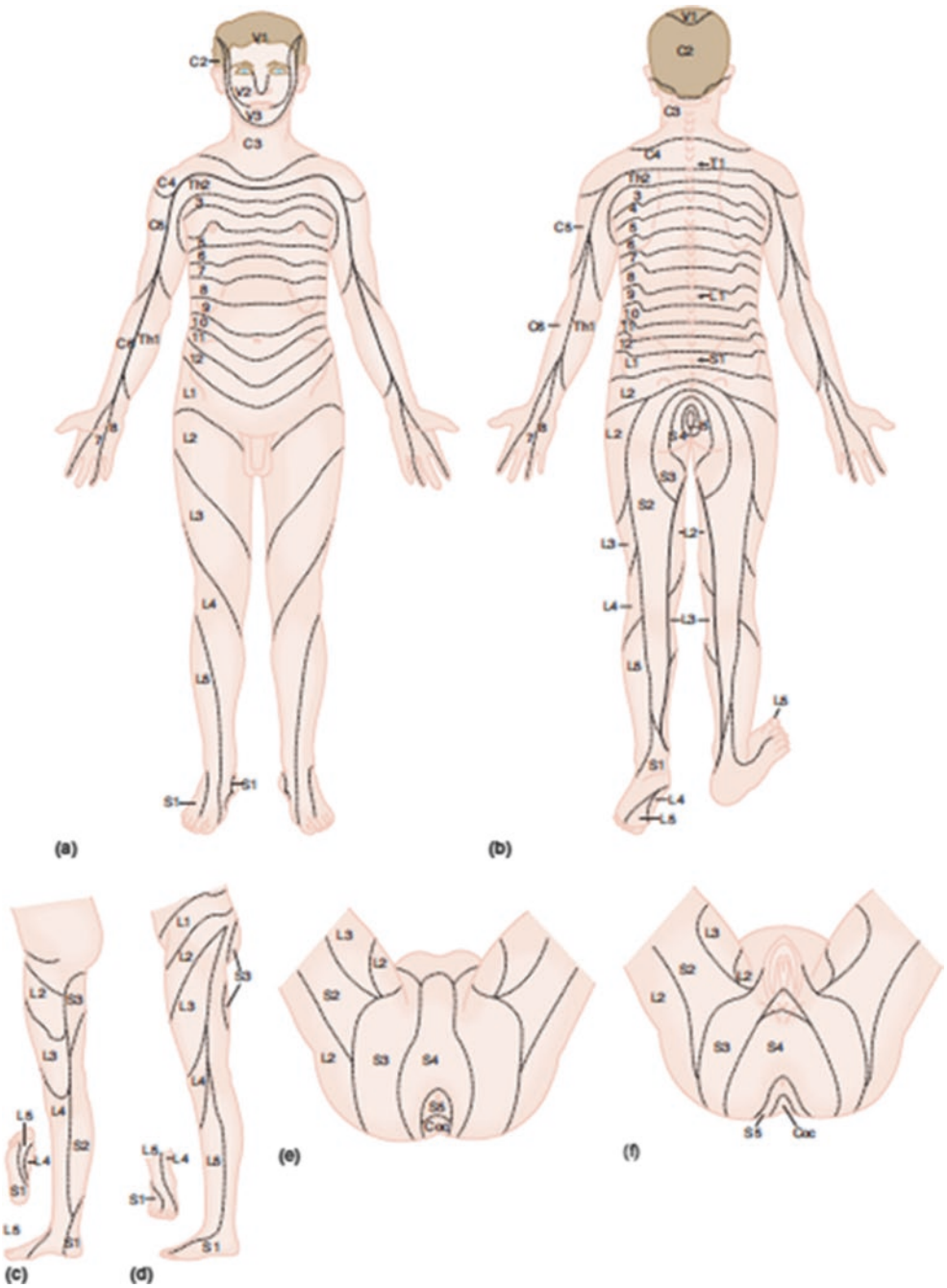

Fig. 4.1 The dermatomes developed by Bonica on the basis of personal observation and data published by others. See text for description. (Reprinted with permission from Fishman et al. [74])

Understanding the anatomy and function of CNS nociceptive pathways and centers is essential to understanding and managing pain.

Dorsal Horn

The dorsal horn of the spinal cord represents the termination point of the dorsal root in the CNS. There is a correspondence between the functional and anatomical organization of the dorsal horn. It is arranged into ten laminae and distinct sensory modalities from the periphery terminate in distinct laminae (see Fig. 4.3) [24]. Signals conducting nociceptive signals (Aδ and C-fibers) terminate in the superficially located laminae I (also called the marginal layer) and II (also called the substantia gelatinosa). Many neurons from lamina I respond exclusively to noxious stimulation and project to higher levels of the CNS. Some neurons called wide dynamic range neurons respond in a stepwise fashion to peripheral stimulation. The neurons of lamina II are mostly interneurons and modulate nociceptive responses at the level of the dorsal horn. The Aδ fibers also terminate in lamina V which

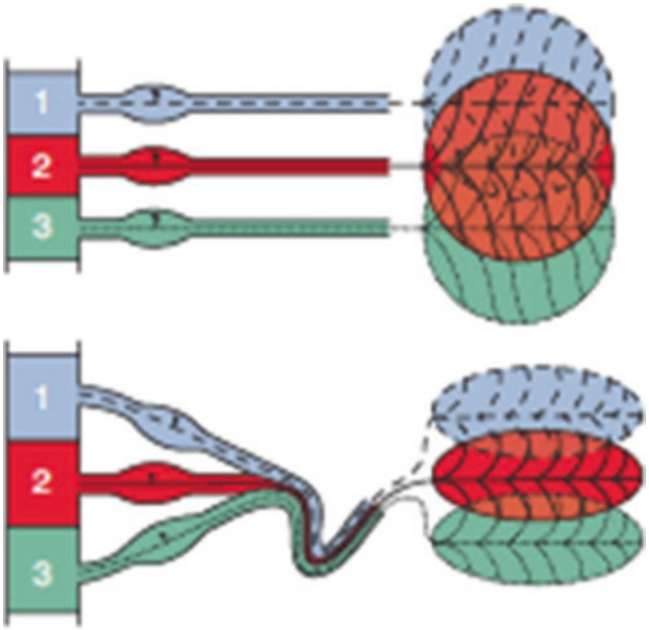

Fig. 4.2 Simple diagrams to illustrate the overlap of cutaneous fields of segmental and peripheral nerves. In the upper figure, three intercostal (segmental) nerves extending from the periphery to the spinal cord are represented. The lower figure illustrates a somewhat analogous but less extensive overlap in the peripheral nerves. (Reprinted with permission from Fishman et al. [74])

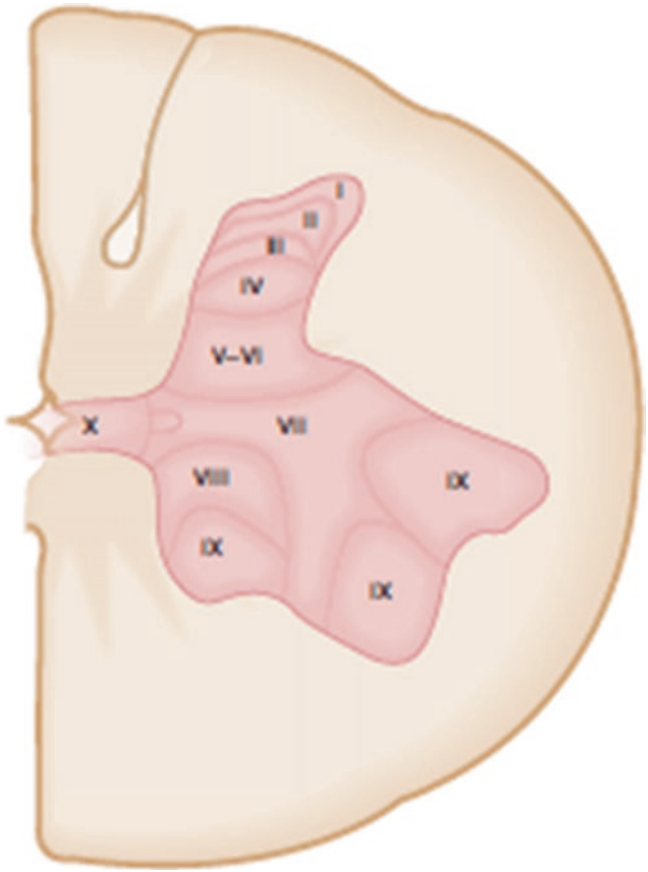

Fig. 4.3 Schematic drawing of a cross section of the cervical spinal cord highlighting the lamina. (Reprinted with permission from Fishman et al. [74])

contains wide dynamic range neurons that project to higher levels of the CNS including the thalamus [25]. There is some convergence of somatic and visceral nociceptive input within lamina V, which may explain referred pain from visceral structures [26]. Single axons of all receptors give off ascending and descending branches after entering the spinal cord. In addition to synapsing at the level they enter, these branches give off multiple collaterals that end in the gray matter of the dorsal horns at one to two levels above and below where the axon entered the spinal cord [27]. Integration of signals from the periphery and higher levels of the CNS occur at the level of the dorsal horn through the dense network of dendrites and interneurons.

Synaptic transmission by primary nociceptive afferent neurons within the dorsal horn is mediated primarily by the excitatory neurotransmitter glutamate. Both ionotropic and metabotropic glutamate receptors are present in high concentration in the substantia gelatinosa [28]. Many neuropeptides (e.g., substance P, vasoactive intestinal polypeptide, cholecystokinin, and CGRP [calcitonin gene-related peptide]), which are theorized to modulate synaptic action, are present in the neurons in the dorsal horn. The receptors for most of these neuropeptides are concentrated in the substantia gelatinosa which suggests that they are involved in the transmission of pain. Among the neuropeptides, substance P and its receptor, neurokinin-1, are likely to be involved in the processing and modulating of pain signals in the dorsal horn. Substance P may increase the excitation from incoming sensory fibers by enhancing and prolonging the actions of glutamate. This has been demonstrated experimentally: substance P and CGRP have been found to increase the release of glutamate; substance P induces the N-methyl-D-aspartate (NMDA) receptors to become more sensitive to glutamate. This unmasks normally silent interneurons and sensitizes second-order spinal neurons [29]. Blocking the neurokinin-1 receptors can prevent many of these effects. Substance P can also extend long distances within the spinal cord and sensitize dorsal horn neurons several segments away from the initial nociceptive signal. This results in an expansion of receptive fields and the activation of wide dynamic neurons by non-nociceptive afferent impulses [30].

Sustained noxious stimulation or high-intensity nociceptive signals to the dorsal horn neurons may lead to increased neuronal responsiveness, sometimes termed central sensitization [31]. The factors that contribute to these hyperexcitable states appear to include altered function of neurochemical and electrophysiological systems as well as changes in the anatomy in the dorsal horn [32].

"Summation" refers to a clinical observation in which repetitive noxious stimulation results in a crescendo of increasing pain and is thought to suggest a state of central sensitization [33]. In experimental pain models in rodents, what is believed to be the correlate of clinical summation is referred to as "windup" [73]. The amplification of the pain signal occurs in the spinal cord when nociceptive C-fibers

synapse on the dorsal horn nociceptive neurons activating the NMDA receptors [34]. A cascade of events ensues with the activation of nitric oxide synthase [35]. This ultimately leads to enhancing the release of sensory neuropeptides, including substance P, from presynaptic neurons, contributing to the development of hyperalgesia and maintenance of central sensitization [36]. Windup can be elicited if identical nociceptive stimuli are applied at a frequency of 3 per second or greater [37].

Spinothalamic Tract

Prior to synapsing in the dorsal horn of the spinal cord, C-fibers and Aδ fibers may ascend or descend one to two spinal levels, forming a tract dorsal to the dorsal horn called the tract of Lissauer (Fig. 4.4). Lissauer's tract also contains axons of interneurons that may travel for several spinal segments. Following synapsing of the central projections of C- and Aδ-afferents, the axons of many of the second-order neurons cross the midline, forming the lateral spinothalamic tract which ascends without interruption from the dorsal horn through the brainstem to the thalamus. This somatotopically organized tract carries information from neurons about the location, intensity, and duration of nociceptive stimuli. This tract is also responsible for relaying the sensation of temperature, and, to a lesser extent, it transmits touch and pressure sensation. A large proportion of the neurons that contribute fibers to the lateral spinothalamic tract originate in lamina I. There is also a dorsally located spinothalamic tract arising ipsilaterally from lamina I neurons, though this projection of second-order nociceptive neurons is less well described.

Lamina V also contributes a large group of neurons to the spinothalamic tract mostly comprised of Aδ fibers. The anterior spinothalamic tract, which conveys information about the location of nociception, is largely composed of fibers from lamina VII and VIII. Conversely, lamina II sends very few fibers to the spinothalamic tracts despite being the destination for many C-fibers. The fibers from lamina II modulate the spinothalamic cells in lamina I, V, VII, and VIII at the level of the nociceptive input as well as at spinal segments above and below via spinal interneurons that travel in the tract of Lissauer. This complex mesh of interneurons plays a significant role in determining whether signals from nociceptors will be propagated to higher levels of the nervous system or be inhibited. Spinal interneurons modulate the intensity of a stimulus and also establish connections with other spinal neurons to form somatic and autonomic reflex arcs at the level of the spinal cord. While interruption of the spinothalamic tract results in immediate loss of pain and temperature perception in the contralateral side of the body, injuries of the spinothalamic tract can develop into central pain syndromes.

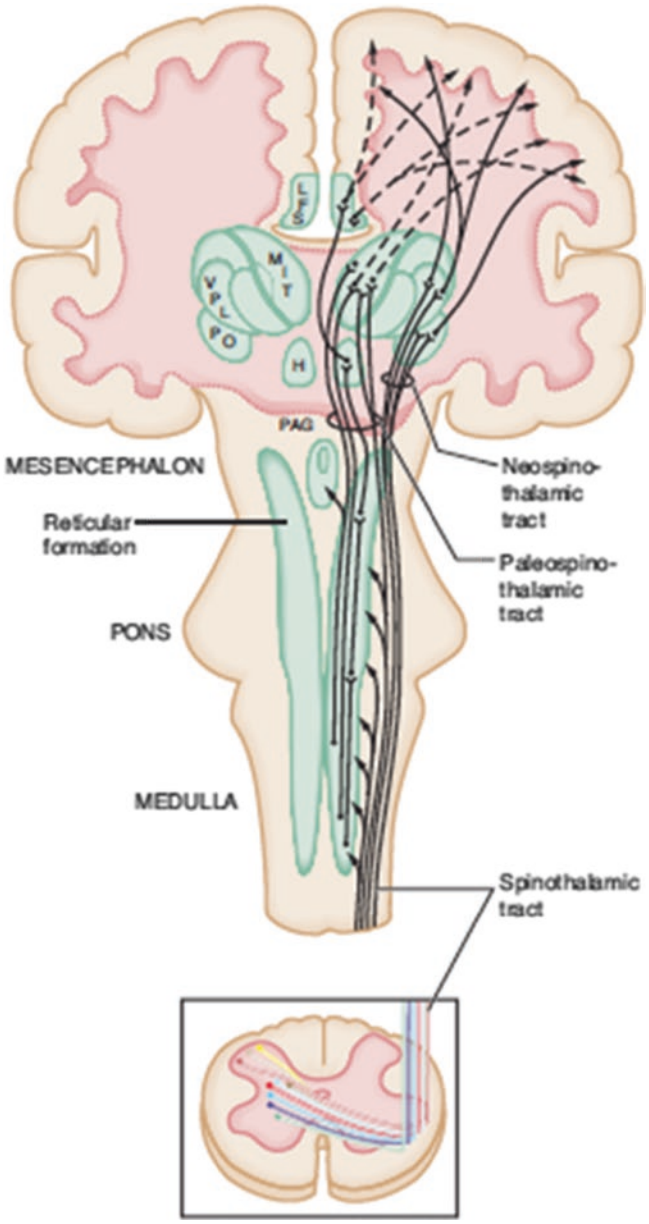

Fig. 4.4 Simple diagram of the course and termination of the spinothalamic tract. Most of the fibers cross to the opposite side and ascend to the brainstem and brain, although some ascend ipsilaterally. The neospinothalamic part of the tract has cell bodies located primarily in laminae I and V of the dorsal horn, whereas the paleospinothalamic tract has its cell bodies in deeper laminae. The neospinothalamic fibers ascend in a more superficial part of the tract and project without interruption to the caudal part of the ventroposterolateral thalamic nucleus (VPLc), the oral part of this nucleus (VPLo), and the medial part of the posterior thalamus (POm). In these structures, they synapse with a third relay of neurons, which project to the somatosensory cortex (SI, SII, and retroinsular cortex) (*solid lines*). Some of the fibers of the paleospinothalamic tract pass directly to the medial/intralaminar thalamic nuclei, and others project to the nuclei and the reticular formation of the brainstem and thence to the PAG, hypothalamus (H), nucleus submedius, and medial/intralaminar thalamic nuclei. Once there, these axons synapse with neurons that connect with the limbic forebrain structure (LFS) via complex circuits and also send diffuse projections to various parts of the brain. (Reprinted with permission from Fishman et al. [74])

Nociceptive afferents from visceral organs and somatic structures terminate in the same population of spinothalamic cells in the spinal cord, which in turn synapse in the thalamus. The convergence of nociceptive signals in the spinal cord is segmentally arranged and may account for pain from visceral organs being referred to somatic structures; this topic is discussed in more detail later in the chapter. There are several other ascending tracts that supply nociceptive signals to higher levels of the CNS. The spinoreticular tract transmits nociceptive signals on the ipsilateral side of the spinal cord. This tract is clinically important as it may explain the persistence of pain after anterior cordotomy.

Central Pain After Spinal Cord Injury (SCI)

Central pain (CP) is a term that includes dysesthesias, paresthesias, and even pruritus initiated by a lesion that interferes with the pathway of nociceptive signals within the CNS from the spinothalamic tract to the parietal somatosensory areas [39]. CP remains an underdiagnosed condition that occurs with damage to the CNS. Studies suggest that up to 10% of all individuals who experience cerebrovascular accidents [40], up to two-thirds of spinal cord injury (SCI) patients [41], 18% of patients with multiple sclerosis, and an undefined number of patients with other neurologic conditions suffer CP [42].

Central pain is a complex clinical phenomenon with several subtypes of pain that can be moderate to severe in intensity. Patients may complain of a constant pain often described as aching, burning, pricking, dysesthesias, paresthesias, or pruritus in isolation or in combination. Most of these patients also complain of stimulus-evoked pain. Patients may complain of spontaneous episodic pain superimposed on their chronic symptoms that is most commonly characterized as lancinating [38]. These painful and other unpleasant sensations are difficult to treat and are often poorly tolerated, which leads to a decrease in quality of life.

Chronic pain is a major complication of SCI, with approximately two-thirds of all SCI patients experiencing some type of chronic pain and up to one-third complaining that their pain is severe [43]. The prevalence of pain after SCI often increases with time after injury [43]. There are an estimated 40 cases per million population in the United States, or approximately 11,000 new individuals with SCI pain each year [44]. Research suggests that chronic pain in SCI patients significantly interferes with their rehabilitation and activities of daily living and therefore reduces quality of life. Attempts to manage these pain symptoms are costly and success is often limited [45].

In addition to central pain, there are multiple types of pain that develop after SCI including musculoskeletal, visceral, and peripheral neuropathic pain. The etiology of pain in SCI is multifaceted, and the various types of SCI pain differ regarding clinical findings, pathophysiology, and therapy. The mechanisms involved in the development of CP after SCI are not fully elucidated, but continuing research has identified possible mechanisms for pain generation. CP has been reported with injury to all levels of the spinal cord [46].

Central pain (CP), a common sequela of SCI, has many descriptors. It is often characterized as a continuous burning, shooting, aching, and tingling. The distribution of pain is usually bilateral and can involve multiple adjacent dermatomes or be regional in nature. In addition, many patients with SCI report feeling the phantom phenomenon of their body below the lesion, and it is described in a distorted fashion. This occurs despite most patients having no conscious appreciation of sensory input below the spinal cord lesion [47]. Central neuropathic pain after SCI has been categorized based on the location of the complaint as either at the level of the injury or below the level of the injury. Although it may be difficult to distinguish the two clinically (and both may be present in the same patient), CP that occurs at the level of injury is due to segmental spinal cord damage, not nerve root damage. CP that occurs at the level of injury can be within two dermatomal levels either above or below the level of injury [48]. CP associated with SCI may also be caused by syringomyelia [47].

Physiologic changes occur to the nociceptive neurons in the dorsal horn following SCI, including an increase in abnormal spontaneous and evoked discharges from dorsal horn neurons [49, 50]. Noxious stimulation causes primary afferent C-fibers to release excitatory amino acid neurotransmitters in the dorsal horn. Prolonged high-intensity noxious stimulation activates the NMDA receptors, which induces a cascade that may result in central sensitization [51]. The cascade includes upregulation of neurokinin receptors and activation of the intracellular cyclo-oxygenase-2, nitric oxide synthase, and protein kinase C enzymes [52]. Other neuroanatomic and neurochemical changes thought to impact CP in SCI include alteration in the activity of the neurotransmitter glutamate [53], interruption of descending inhibitory pathways [54], and dysfunction of the inhibitory GABAergic interneurons [55], all at the level of the dorsal horn. On a molecular level, abnormal sodium channel expression within the dorsal horn (laminae I–VI) bilaterally has been implicated as a major contributor to hyperexcitability.

Thalamic neurons appear to undergo changes after SCI in both human and animal models. In animal modeling of this pain, enhanced neuronal excitability in the VPL (ventroposterolateral) has been demonstrated directly [56] as well as indirectly; enhanced regional blood flow has been found in the rat VPL after SCI, suggesting increased neuronal activity [57]. Magnetic resonance spectroscopy studies have demonstrated changes in metabolism of the neurons in human thalamus associated with pain in SCI [58]. Much like the neurons

in the dorsal horn, the thalamic neurons after SCI show increased activity with noxious and non-noxious stimuli. VPL neurons are spontaneously hyperexcitable following SCI without receiving input from the spinal cord neurons suggesting that the thalamus may act as a pain signal generator in CP accompanying SCI [47].

There is emerging evidence that cortical reorganization may play a role in the development of phantom symptoms after loss of limbs, but little evidence of the cortical mechanisms at work with the development of phantom phenomena after SCI [59]. The full spectrum of anatomical, chemical, and physiologic changes contributing to central neuropathic pain after SCI is still being elucidated.

Spinal Components of the Autonomic Nervous System (ANS)

The ANS is composed of peripheral and central elements which are integrated into the neuroanatomy of the spine. We will focus on the central components of the system. At the turn of the twentieth century, the Cambridge physiologist John Newport Langley coined the term "autonomic nervous system" to describe the portion of the nervous system that mediated the unconscious function of the internal organs [60]. Soon afterward, the concept of two distinct components of the ANS, the sympathetic and parasympathetic systems, which antagonize each other to maintain homeostasis, was developed. In addition to regulating the activity of visceral organs, vessels, and glands, the ANS has been found to play an active role in many pain states.

Autonomic Centers in the CNS

As opposed to the peripheral ANS, distinctions between the somatic and autonomic structures and pathways are often difficult in the CNS. The spinal cord is a central area of integrating the somatic and autonomic functions. Through spinal reflexes, somatic nociception can exert a major impact on the autonomic system. Noxious stimulation to the skin induces a cascade of sympathetic responses, including increased sweat production and skin vasomotor responses [72].

The location of the preganglionic neurons for the sympathetic and parasympathetic nervous systems in the CNS differs. The sympathetic preganglionic neurons are localized to the T1 through L2 spinal segments. The parasympathetic preganglionic neurons reside in the brainstem and the S2–S4 spinal segments (Figs. 4.5 and 4.6). The locations of the cell bodies of preganglionic sympathetic and parasympathetic neurons, which mediate their function in various parts of the body, are listed in Table 4.1. There are essential differences between the ganglia these neurons form. The sympathetic ganglia are distributed widely throughout the body, are located close to the CNS, and use epinephrine as the primary neurotransmitter. In contrast, the parasympathetic ganglia largely innervate visceral organs, which they are in close proximity to, and use acetylcholine as a neurotransmitter. Figure 4.5 depicts the autonomic pathways that connect the preganglionic neurons in the intermediolateral horn of the spinal cord with the hypothalamus and other brainstem structures.

Sacral Parasympathetics

The sacral portion of the parasympathetic system consists of preganglionic neurons which have their cell bodies in the intermediolateral column of the gray matter of the S2–S4 spinal segments (see Figs. 4.5 and 4.6). The preganglionic fibers travel via the ventral roots to the corresponding spinal nerves for a short distance and then form the pelvic splanchnic nerves. These nerves form the pelvic plexuses which are in close proximity to the target organs (rectum, bladder, prostate gland in the male, cervix in the female). Many of these preganglionic fibers synapse in the plexus, while other fibers pass through the plexus without interruption and terminate in intramural ganglia of their target organs (e.g., urinary bladder, descending colon, sigmoid colon and rectum, and genital organs). All of the pelvic organs are innervated by postganglionic parasympathetic fibers. These fibers play an essential role in eliminating waste products from the bladder and rectum [61].

Sympathetic Thoracolumbar Division

The peripheral sympathetic nervous system is composed of efferent and afferent fibers. The efferent portion of the sympathetic division of the ANS consists of preganglionic neurons, the two paravertebral (lateral) sympathetic chains, prevertebral and terminal ganglia, and postganglionic neurons (see Figs. 4.5 and 4.6) [62, 63].

Sympathetic Preganglionic Neurons

The cell bodies of the efferent preganglionic neurons reside in the intermediolateral column in the spinal cord from T1 to L2. The efferent fibers of these preganglionic neurons travel from the spinal cord into the periphery through the ventral roots accompanying the somatic fibers at these levels at the thoracolumbar spine. From this point, the preganglionic neurons diverge to provide inputs to ganglia in multiple locations. Each preganglionic fiber synapses on multiple postganglionic cells, thus serving to amplify the sympathetic

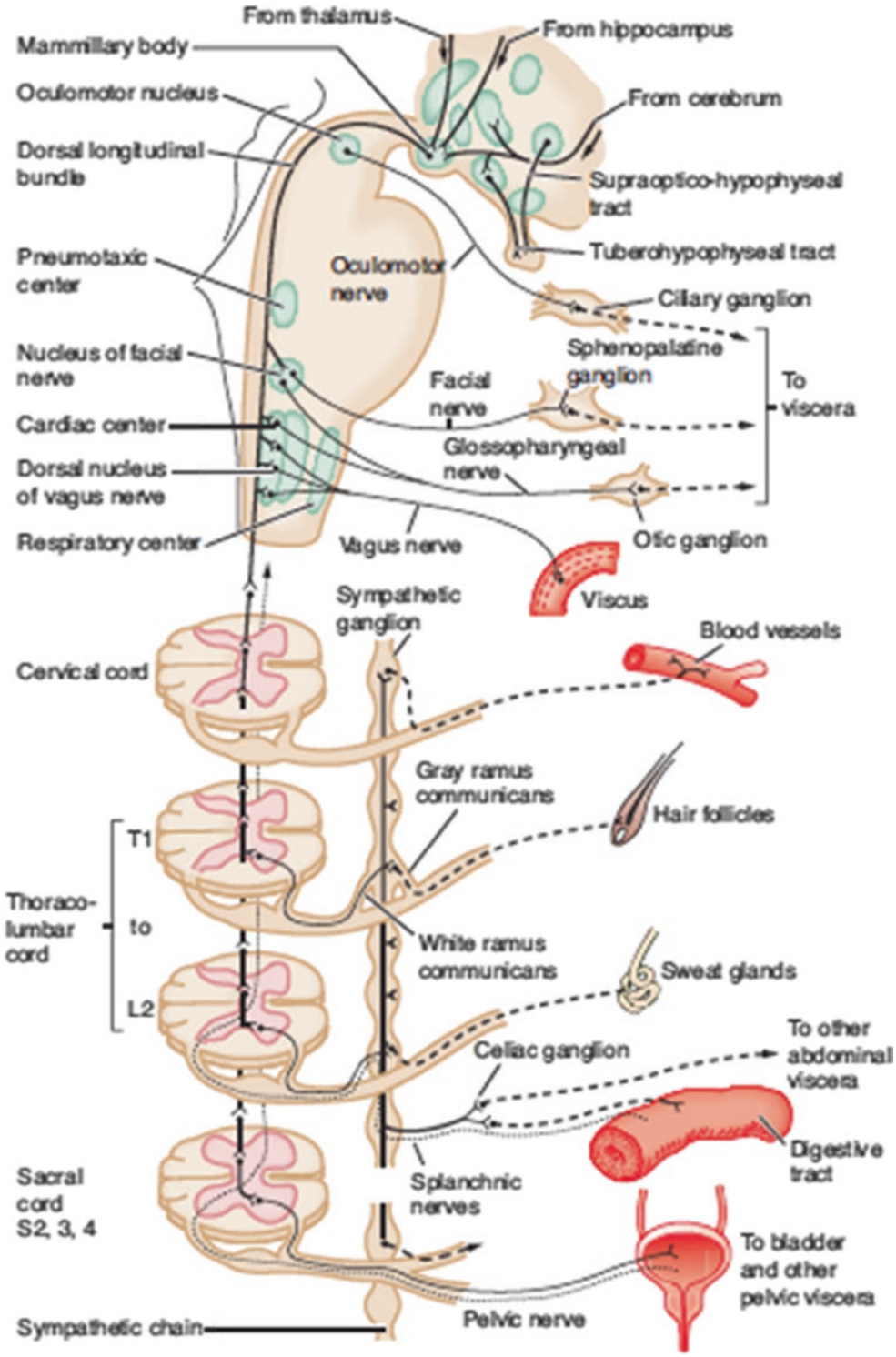

Fig. 4.5 Schematic representation of autonomic pathways in the neuraxis and the efferent peripheral pathways. Note the connection among the various hypothalamic nuclei and between these structures and the nuclei and important autonomic centers in the brainstem and spinal cord. The dorsal longitudinal fasciculus (DLF) passes from the hypothalamus caudad through the central and tegmental portion of the mesencephalon and the tegmental portion of the pons to terminate in the reticular formation, the autonomic centers and cranial nerve nuclei in the brainstem, and in the intermediolateral cell column of the spinal cord. The DLF is composed of both crossed and uncrossed fibers, including some long ones and an extensive system of short fibers, which are arranged in the gray matter in frequent relays. Note also that the cell bodies of preganglionic sympathetic neurons are located only in spinal cord segments T1 through L2, whereas the parasympathetic neurons are located in cranial nerves and in S2, S3, and S4. The solid lines represent preganglionic fibers, the dashed lines represent postganglionic fibers, and the dotted lines are afferent (sensory) fibers. Not shown are the sensory fibers contained in the facial, glossopharyngeal, and vagus nerves, which transmit nociceptive and other somatosensory information from the head. (Reprinted with permission from Fishman et al. [74])

outflow from the CNS [64]. Some of the sympathetic fibers leave the spinal nerve immediately after the ventral and dorsal roots fuse to form the white communicating ramus which synapses with postganglionic neurons in the sympathetic ganglia outside the neuraxis (see Fig. 4.6). The white rami are usually present only in the thoracic and upper two or three lumbar segments corresponding to the location of the intermediolateral column in the spinal cord (see Fig. 4.6). The white color of the rami is a result of the sympathetic fibers being myelinated.

The peripheral ganglia of the sympathetic nervous system are located close to the CNS. These paravertebral ganglia are segmentally arranged in two sympathetic trunks, each of which is a vertical row along the anterior margin of the ver-

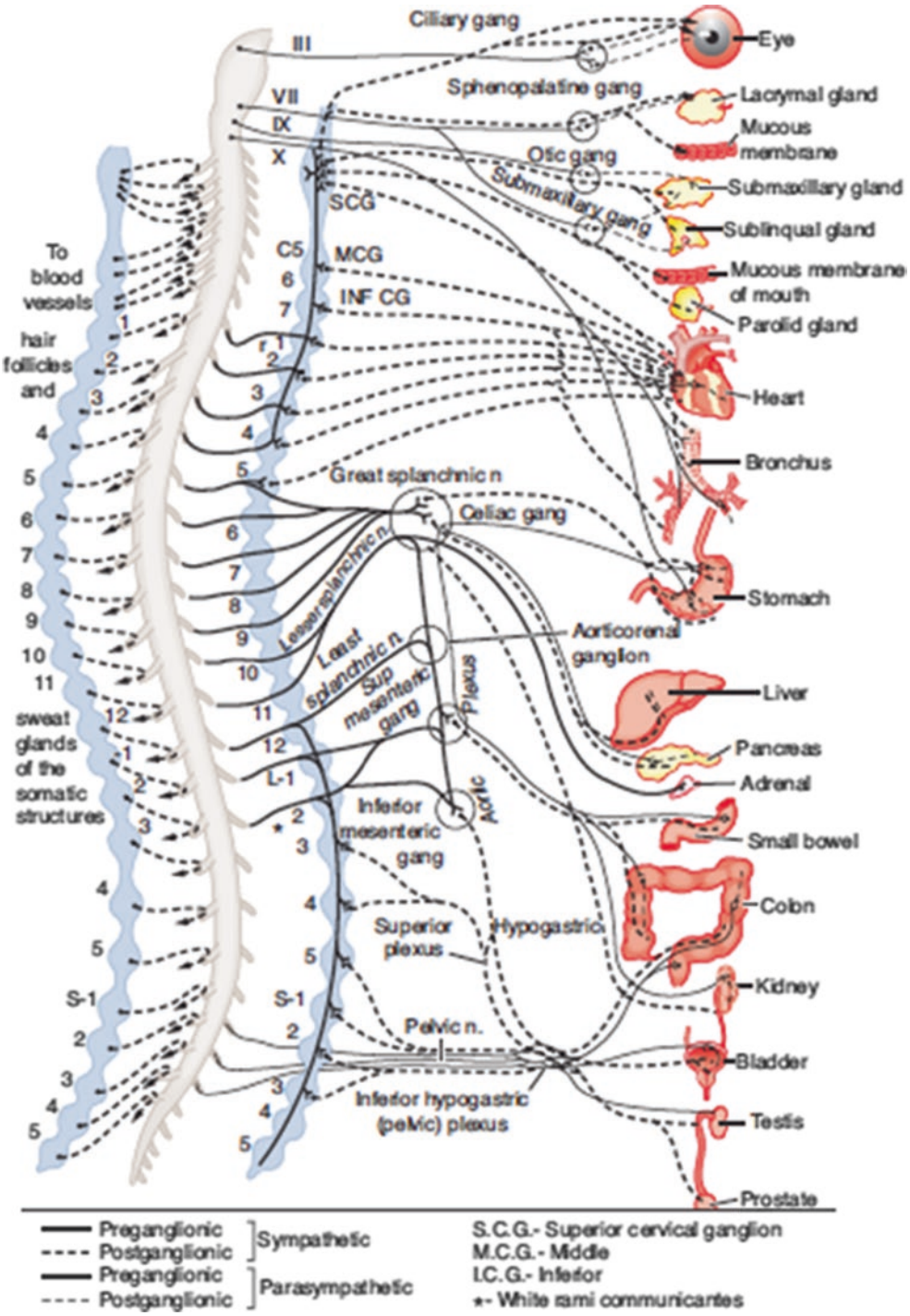

Fig. 4.6 Distribution of peripheral autonomic nervous system to various structures of the body. On the reader's right are shown (from above downward) the four cranial nerves which contain preganglionic parasympathetic fibers, the axons of preganglionic sympathetic fibers (which pass from the anterior root to the paravertebral sympathetic chain), and the parasympathetic preganglionic axons in S2, S3, and S4. Note that the axons of all of the preganglionic sympathetic neurons pass via the white rami communicantes into the paravertebral chain, in which some synapse with postganglionic neurons, whereas others pass to the prevertebral sympathetic ganglia, in which they synapse with postganglionic fibers. On the reader's left are depicted the gray rami communicantes, containing postganglionic sympathetic fibers, which originate in the paravertebral chain and then pass to each of the spinal nerves to innervate blood vessels, hair follicles, and sweat glands in various parts of the body. (Reprinted with permission from Fishman et al. [74])

tebral column. Each trunk is comprised of a longitudinal network of ganglia connected to each other by ascending and descending nerve fibers that extend the entire length of the spinal column. As each spinal segment develops in the embryo, one sympathetic ganglion is formed for every level on each side. Some of these ganglia fuse, so the final number of ganglia is usually less than the number of spinal segments [65]. This is most prominent in the cervical region where only the superior, middle, intermediate, and inferior cervical ganglia are present for seven cervical vertebrae. The middle cervical ganglion is often not present, and the inferior cervical ganglion commonly fuses with the upper thoracic ganglion forming the stellate ganglion. The cephalic end of the paravertebral ganglia continues beyond the cervical spine, traveling along the carotid nerve to eventually distribute sympathetic fibers within the head. The caudal end of the two trunks converges and terminates in front of the coccyx as the ganglion impar [62].

Table 4.1 Summary of sympathetic and nociceptive nerve supply to more important body structures

		Sympathetic nerve supply			Nociceptive pathways
Region, structure	Location of cell body in spinal cord and course of preganglionic neurons	Site of synapse of preganglionic with postganglionic neurons	Course of postganglionic axons	Location of primary afferent pathway	Entrance into central nervous system
Head and neck					
Meninges and arteries of brain	T1, T2 (3)[a] To and through cervical sympathetic chain	All cervical sympathetic ganglia	Plexuses around internal carotid and vertebral arteries	Cranial nerves (CN) V, IX, X C1–C3	Trigeminal subnucleus caudalis C1–C3 spinal segments
Eye[b]	T1, T2, T3 (4) To and through cervical sympathetic chain	Superior cervical ganglion and ganglia in internal carotid plexus	Internal carotid and cavernous plexuses → ciliary ganglion or nasociliary nerve → ciliary nerves or along ophthalmic artery	Ophthalmic branch of CN V	Trigeminal subnucleus caudalis
Lacrimal gland[b]	T1, T2 To and through cervical sympathetic ganglia	Superior cervical sympathetic ganglion	Internal carotid plexus → vidian nerve → sphenopalatine ganglion → maxillary nerve → zygomatic/lacrimal nerves	Lacrimal nerve → ophthalmic branch of CN V	As above
Parotid gland[b]	As above	All cervical sympathetic ganglia	External carotid plexus → internal maxillary and middle meningeal plexus → to auriculotemporal nerve and plexus and to the parotid arterial plexuses	Parotid nerve → auriculotemporal nerve of mandibular division of CN V	As above
Submandibular and sublingual glands[b]	As above	As above	External carotid plexus → facial plexus → submandibular ganglion → direct glandular filaments or via lingual nerves or directly to glands along vessels	Submandibular branch of lingual nerve → mandibular division of CN V	As above
Thyroid gland	As above	Middle and inferior cervical sympathetic ganglia	Perivascular sympathetic plexuses accompanying superior and inferior thyroid arteries	Afferents accompanying sympathetic pathways	T1 and T2 spinal cord segments
Blood vessels of skin and somatic structures sweat glands hair follicles	T1–T4 To and through cervical sympathetic chain	All cervical sympathetic ganglia	In perivascular plexuses accompanying various branches of external and internal carotid arteries	Afferents accompanying sympathetic nerves CN V, IX, X C2–C4	Tl–T4 spinal cord Subnucleus caudalis C2–T4 spinal cord segments
Thoracic viscera					
Heart	T1–T4 (5) To upper thoracic and cervical sympathetic chain	All cervical and upper four (5) thoracic ganglia	Superior, middle, and inferior cervical cardiac nerves and the four (5) thoracic cardiac nerves → cardiac plexuses	Afferents in middle and inferior cervical cardiac and the thoracic cardiac nerves	T1–T4 (5)
Larynx	T1, T2 To and through cervical sympathetic chain	Superior cervical ganglion	Laryngeal branch of superior cervical ganglion → superior laryngeal nerve	Superior laryngeal nerve	Trigeminal subnucleus caudalis
Trachea, bronchi, and lungs	T2–T6 (7) To upper thoracic sympathetic chain	T2–T6 (7) Sympathetic ganglia	Pulmonary branches from sympathetic trunk → pulmonary plexuses	Afferents with sympathetics Afferents with vagus	T2–T6 (7) Nucleus tractus solitarius (medulla)
Esophagus cervical	T2–T4 To and through upper thoracic sympathetic chain	All cervical sympathetic ganglia and pharyngeal plexus	From cervical ganglia to recurrent laryngeal nerve	Afferents in vagus Afferents with sympathetics	N. tractus solitarius T2–T4 (?)

Table 4.1 (continued)

		Sympathetic nerve supply			Nociceptive pathways
Thoracic	T3–T6 To and through upper thoracic sympathetic chain	Stellate and upper thoracic ganglia	Direct esophageal branches and through cardiac sympathetic nerves	Afferents with vagus Afferents with sympathetics	N. tractus solitarius T3–T6 (?)
Abdominal	T5–T8 To thoracic sympathetic chain—superior thoracic splanchnic nerve	Celiac ganglia	Via plexuses around left gastric and inferior phrenic arteries	Afferents with sympathetics Afferents with vagus	T5–T8 N. Tractus solitarius
Thoracic aorta	T1–T5 (6) To thoracic sympathetic chain	Synapse upper five (6) thoracic sympathetic ganglia	Branches from cardiac sympathetic nerves and direct fibers from thoracic sympathetic chain	Afferents with sympathetic pathways	T1–T5 (6)
Abdominal viscera					
Abdominal aorta	T5–L2 Some through splanchnic nerves and direct branches	Celiac ganglia and paravertebral sympathetic chain	Fibers that contribute to the aortic plexus	Afferents associated with sympathetics	T5–L2
Stomach and duodenum	T(5) 6–9 (10) (11) Superior (greater) and middle (lesser) thoracic splanchnic nerves and celiac plexus	Celiac ganglia	Right and left gastric and gastroepiploic plexuses	Afferents with sympathetics	T(5) 6–9 (10) (11)
Gallbladder and bile ducts	T(5) 6–9 (10) Superior thoracic (greater) splanchnic nerves and celiac plexus	Celiac ganglia	Hepatic and gastroduodenal plexuses	Afferents associated with sympathetics	T(5) 6–9 (10)
Liver	T(5) 6–9 (10) Superior thoracic (greater) splanchnic nerves and celiac plexus	Celiac ganglia	Hepatic plexus	Afferents associated with sympathetics	T(5) 6–9 (10)
Pancreas	T(5) 6–10 (11) Superior thoracic (greater) splanchnic nerves and celiac plexus	Celiac ganglia	Direct branches from celiac plexus and offshoots from splenic, gastroduodenal, and pancreaticoduodenal plexuses	Afferents associated with sympathetics	T5–T10 (11)
Small intestines	T8–T12 right T8–T11 left To superior (greater) and middle (lesser) thoracic splanchnic nerves to celiac plexus	Celiac and superior mesenteric ganglia	Superior mesenteric plexus → nerves alongside jejunal and ileal arteries	Follow sympathetic pathways through celiac and inferior mesenteric plexuses	T(8) 9, 10 T10, T11
Cecum and appendix[b]	T10–T12 Superior (greater) and middle (lesser) thoracic splanchnic nerves → celiac and superior mesenteric plexuses	Celiac and superior mesenteric ganglia	Nerves alongside ileocolic artery	Accompanying sympathetic pathways	T10–T12
Colon to splenic flexure[b]	T10–L1 Middle (lesser) and inferior (least) thoracic and first lumbar splanchnic nerves	Superior and inferior mesenteric ganglia	Mesenteric plexus → nerves alongside right, middle, and superior left colic arteries	Associated with sympathetics, pass through superior and inferior mesenteric plexuses and splanchnic nerves and to spinal cord	T10–L1

(continued)

Table 4.1 (continued)

		Sympathetic nerve supply			Nociceptive pathways
Splenic flexure to rectum[b]	L1, L2 (left side) S2–S4 Lumbar and sacral splanchnic nerves → inferior mesenteric and inferior hypogastric pelvic plexuses	Inferior mesenteric ganglion and ganglia in superior and inferior hypogastric plexuses	Nerves alongside inferior left colic and rectal arteries	Afferents with parasympathetic nerves and pudendal nerves	S2–S4
Suprarenal (adrenal) glands[b]	T(7) 8–L1 (2) Superior (greater), middle (lesser), and inferior (least) thoracic splanchnic nerves and first (second) lumbar splanchnic nerves	Chromaffin cells of adrenal medulla	Within the gland		
Kidneys[b]	T10–T12, L1 (2) Middle (lesser) and inferior (least) thoracic splanchnic nerves and first (second) lumbar splanchnic nerves → celiac and renal plexuses	Celiac and aorticorenal ganglia	Along renal plexus	Accompanies sympathetic pathways	T10–T12 (L1, L2)
Ureters[b] Upper two-thirds	T(10), T11, T12, L1, L2 Middle and inferior thoracic splanchnic and upper two lumbar splanchnic nerves	Celiac and aorticorenal ganglia	Superior mesenteric and renal plexuses → superior and middle ureteric nerves	Associated with sympathetics	T10–T12 (L1, L12)
Ureters Lower one-third	T11–L1, S2–S4	Aorticorenal ganglion and sacral sympathetic ganglia	Aortic, superior hypogastric, and inferior hypogastric (pelvic) plexuses and sacral splanchnic nerves	Accompany sympathetic and parasympathetic nerves	T10–T12
Pelvic viscera					
Bladder	T(11), T12, L1, L2 Middle and inferior thoracic splanchnic nerves	Inferior mesenteric ganglion and sacral paravertebral ganglia	Superior and inferior hypogastric plexuses and sacral splanchnic nerves to vesical plexus	Predominantly afferents of parasympathetic nerves; also some sympathetic afferents	S2–S4
Uterus	T(6–9) 10–12, L1 (2) Splanchnic nerves to aortic and ovarian plexuses and superior and inferior hypogastric plexuses	Celiac ganglion and various paravertebral ganglia	Lumbar and sacral splanchnic nerves; superior, middle, and inferior hypogastric plexuses → uterine plexus	Accompanying sympathetic pathways	T11–L2
Testes, ductus deferens, epididymis, seminal vesicles, prostate	T10–L1 inclusive Splanchnic nerves → aortic and superior hypogastric plexus	Prevertebral ganglia and inferior mesenteric ganglion	Follow various vascular plexuses in sacral splanchnic nerves	Testes (ovaries) Prostate Parasympathetic afferents	T10 S2–S4
Trunks and limbs (innervation of vessels, sweat glands, and hair follicles)					
Trunk	T1–T12	T1–T12 paravertebral sympathetic ganglia	Gray rami communicantes → thoracic spinal nerves	Primary afferents in spinal nerves	T2–L1

Table 4.1 (continued)

		Sympathetic nerve supply			Nociceptive pathways
Upper extremities	T2–T8 (9) To and through upper thoracic and lower cervical sympathetic chain	Middle and stellate ganglia; T2 and T3 ganglia	Gray rami communicantes to roots of brachial plexus → brachial plexus and its major nerves; some directly to plexuses around subclavian, axillary, and upper brachial arteries	Brachial plexus and its branches	C5–T1
Lower extremities	T10–T12, L1, L2 To and through lumbar and upper sacral sympathetic chain	L1–L5, S1–S3 paravertebral ganglia	Gray rami communicantes → lumbosacral plexus and its major nerves; direct branches to perivascular plexuses as far as upper femoral artery	Lumbosacral plexus	L1–S3

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[a]Segments in parentheses are inconstant
[b]Unilateral innervation

The paravertebral sympathetic ganglia are connected by interganglionic fibers forming the lateral sympathetic chain which extends from the skull to the coccyx. On entering the sympathetic chain, some preganglionic axons synapse in the ganglia at the spinal level they exited the neuraxis. Other preganglionic fibers pass uninterrupted cephalad or caudad within the sympathetic trunk before they synapse to ensure that preganglionic fibers synapse at all levels of the sympathetic trunk.

Some preganglionic sympathetic fibers pass uninterrupted through the sympathetic chain to form splanchnic nerves that synapse within one of the prevertebral ganglia that are found at the junction of the celiac and mesenteric arteries and the abdominal aorta. The postganglionic fibers that travel from the prevertebral ganglion tend to follow arteries within the abdomen to their target organs. The greater and lesser splanchnic nerves are formed from preganglionic fibers from the T6 to T10 levels, pass through the sympathetic chain without synapsing, and terminate in ganglia that innervate the abdominal viscera in the upper and middle part of the abdomen. Splanchnic nerves also contribute preganglionic fibers to the adrenal medulla. These fibers synapse within chromaffin cells, which are homologous to postganglionic neurons but release epinephrine into the bloodstream with sympathetic stimulation [66, 71].

Sympathetic Postganglionic Neurons

The axons of the postganglionic neurons travel via multiple pathways into the periphery. Some of the postganglionic neurons which have their cell bodies in the paravertebral chain reenter the spinal nerves via the gray communicating ramus, which, in distinction to the white rami, has a gray color because most of these postganglionic fibers are unmyelinated. Postganglionic sympathetic neurons from gray rami communicantes travel in all spinal nerves. These postganglionic sympathetic fibers follow the spinal nerves into somatic areas innervating various somatic, sudomotor, and pilomotor structures, such as the sweat glands and smooth muscle fibers in hair follicles in the skin. The axons of other postganglionic neurons, which have their cell bodies in the paravertebral chain, travel largely along arteries to pass to the thoracic and pelvic viscera. This is in contrast to the preganglionic neurons that pass uninterrupted to the prevertebral ganglia via the greater and lesser splanchnic nerves and are distributed to the viscera in the upper and middle part of the abdomen. The visceral organs in the lower abdomen receive their sympathetic innervation from the lumbar splanchnic nerve which also synapses in prevertebral ganglia. The celiac ganglia are the largest of the prevertebral ganglia and surround the celiac artery at its juncture with the aorta. The sympathetic innervation of the heart originates in the cervical and thoracic ganglia and travels via the cardiac nerves to the heart. Table 4.2 summarizes the autonomic and nociceptive pathways to various body structures.

In addition to the gray rami, the sympathetic trunks give off postganglionic rami that supply the viscera of the head, chest, and abdomen. These rami include the carotid nerve; the superior, middle, and inferior cardiac nerves; the superior, middle, and inferior thoracic splanchnic nerves; and the lumbar and sacral splanchnic nerves.

Some preganglionic fibers synapse in the intermediary ganglia in the white communicating rami, ventral nerve roots,

Table 4.2 Autonomic centers (AC) in spinal cord

Structure	Location of AC in spinal cord
Head and neck	T1–T4
Upper limb	T2–T8/T9
Upper trunk	T2–T8
Lower trunk	T9–L2
Lower limb	T10–L2
Viscera	
Thoracic (sympathetic)	T1–T5 (8)
Abdominal (sympathetic)	T5–L2
Pelvic (parasympathetic)	S2–S4

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or the spinal nerves outside of the sympathetic chain [62, 63]. These anomalous sympathetic pathways are most commonly found in the sympathetic trunk at the cervicothoracic juncture and the thoracolumbar juncture [67–69]. These pathways explain why surgical interruption of the sympathetic chain may not completely block sympathetic outflow. Conversely, these anatomic variations often respond to sympathetic blockade with a local anesthetic solution because it diffuses locally to affect these pathways [67]. A sympathetic block can therefore be a poor predictor of the efficacy of surgical sympathectomy. In cases of incomplete sympathectomy, a postsurgical sympathetic block that produces complete interruption of sympathetic outflow and pain relief in sympathetically dependent pain syndromes may suggest the presence of anomalous sympathetic ganglia [67, 68].

Sympathetic postganglionic neurons may be involved in the generation of pain, hyperalgesia, and inflammation in disease. Depending on the extent of the peripheral nerve lesion, plastic changes can occur at multiple levels of the ANS. Release of mediators (e.g., epinephrine, norepinephrine) from efferent sympathetic nerves both locally and systemically and upregulation of adrenoreceptors in nociceptive afferents contribute to the increased excitability of nociceptors and changes in local vasomotor and sudomotor activity [70]. This reorganization of the peripheral neurons may lead to chemical coupling between sympathetic and afferent neurons. This may be responsible for sensitization and/or activation of primary afferent neurons by the sympathetic neurons [71].

Summary

An understanding of anatomy and physiology of spinal cord nociceptive systems is essential for the optimal practice of pain medicine. Clear breakdown of pain as visceral or somatic and further characterization of pain as central, peripheral, or mixed in origin play a critical role in evaluation and treatment. Thus, optimal evaluation of pain is dependent on a thorough understanding of anatomy of nociceptive systems as well as anatomic localization of the lesions for the initiation and maintenance of pain.

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Pathophysiology of Spinal Pain

5

Annie W. Hsu, Steven P. Cohen, and Yian Chen

Key Points

- Spine pain is a costly and prevalent problem in the United States and worldwide.
- Risk factors for back pain include age, obesity, smoking, and workplace stress and dissatisfaction.
- Disc herniations occur anywhere in the spine but mostly in the lower lumbar and cervical spine leading to radicular symptoms in the distribution of the affected nerve root(s).
- Discogenic pain derives from injury to the intervertebral disc but has complex molecular underpinnings that involve changes in vascularization and innervation.
- Spinal stenosis occurs most commonly in the lumbar region and secondary to degeneration, causing extremity paresthesias, weakness, and neurogenic claudication.
- Facet joints can be a common source of spine pain that typically develops after cumulative lifetime stress, leading to inflammation.
- The sacroiliac joints are richly innervated, both in the joint capsule and the extra-articular ligaments; sacroiliac joint pain can be associated with leg length differences, low-grade trauma, and pregnancy.
- Cancer and inflammatory conditions are unique pathophysiological states which can produce spinal pain.

Epidemiology of Spinal Pain

Disorders of the spine constitute a majority of chronic pain complaints, with the lifetime prevalence of spinal pain reported to range from 54% to 80% [1]. Among spinal pain conditions, annual prevalence estimates range from 30% to 50% for neck pain, 15% to 45% for chronic low back pain, and 3% to 23% for thoracic pain [1]. The socioeconomic burden of spinal pain, and in particular back pain, is tremendous, cutting across developed and developing countries alike. In the United States, spinal pain is the leading cause of activity limitation in people younger than 45 years of age and the fifth most common cause for all physician visits, at an estimated annual cost of $86 billion in 2005 [2–5]. National expenditures for spinal pain have steadily increased an average of 7% per year from 1997 to 2006 [2]. Further, it appears that the prevalence of low back pain may be increasing. In one study, the prevalence of low back pain was found to have increased from 3.9% in 1992 to 10.2% in 2006 [6]. Calculated at roughly 1% of the gross domestic product in 1998, health-care expenditures for back pain are astounding [7].

Several risk factors for back pain have been reported. Age is one of the more common risk factors. The incidence of back pain is highest in the third decade, increasing with age until 65 years, before gradually decreasing [8]. Other factors such as obesity, smoking, and lack of exercise and workplace

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factors such as job dissatisfaction, monotony, lack of social support, and stress have also been reported to be associated with an increased incidence of back pain [9–11].

Brief Anatomy of the Human Spine

The human spine is a complex structure comprised of 7 cervical, 12 thoracic, 5 lumbar, 5 (fused) sacral, and 4 coccygeal bony units termed vertebrae. These vertebrae are arranged in a linear column, connected by ligaments, intervertebral discs (IVDs), cartilage, and muscles. The fundamental anatomical unit of the spine is composed of paired facet joints and the intervertebral disc, referred to as the three-joint complex. Each of the elements contributes to strength and function of the spine but is also a potential source of pain in the event of injury or pathology. Each of these general regions (cervical, lumbar, etc.) is exposed to different insults and disturbances, thus having predilections for different pathological states. Common causes of lumbar back pain include radicular pain due to disc herniation or spinal stenosis, discogenic pain, facet joint pain, myofascial pain, and sacroiliac joint pain. Table 5.1 summarizes features of these clinical syndromes.

Disc Herniation

Intervertebral discs (IVDs) are complex structures, composed of a central nucleus pulposus (NP) that is encased by the annulus fibrosus (AF) and bordered superiorly and inferiorly by cartilaginous endplates (EP) (Fig. 5.1). The NP is a gelatinous structure that is composed of proteoglycans con-

Table 5.1 Clinical evaluation of lumbar pain [77, 97, 106, 133–144]

Source of pain	Risk factors	History	Clinical signs	Physical exam
Radicular				
Disc herniation	Advanced age Genetics Obesity Diabetes Smoking Strenuous labor	Acute onset	Back pain Radiating LE pain, weakness, paresthesias in dermatomal and myotomal distribution Exacerbated by bending forward, sitting, coughing, straining Relieved by lying down, walking	Straight leg raise (SLR) test: 92% sens, 10–100% spec for lower lumbar and sacral pathology Crossed SLR test: 28% sens, 90% spec Femoral nerve stretch test: 50% sens, 100% spec for L2–L4 (mid to upper lumbar radiculopathy)
Spinal stenosis	Advanced age Congenital narrowing Trauma (e.g., fractures or post-surgical)	Insidious onset	Back pain LE sensory loss, weakness Neurogenic claudication Exacerbated by walking, standing Improved by forward bending	Neurological exam often normal, unless severe or prolonged course Wide-based gait, positive Romberg in setting of LBP has 90% spec
Axial				
Facet joint	Motor vehicle accident Trauma (e.g., sports, fall) Advanced age Obesity Female sex	Insidious or acute (less frequent) onset	Localized back pain Referred pain does not typically extend past knee	Paraspinal tenderness Pain worsens with various movements including lateral flexion, flexion and extension No neurological deficits
Sacroiliac joint	Leg length discrepancy Scoliosis Gait abnormalities Persistent low-grade trauma Pregnancy	More likely to be associated with an inciting event than other sources of axial pain	Variable presentation Buttock pain extending into posterolateral thigh most typical referral pattern Pain radiating to groin	Numerous exam maneuvers, individual utility debatable >3 positive provocative tests have reasonable sens (77–94%) and spec (57–100%) in identifying positive response to diagnostic joint injections
Intervertebral disc	Smoking Advanced age Trauma	Insidious onset	Localized back pain Paraspinal muscle spasms	Midline tenderness, reduced ROM Centralization phenomenon 64% sens, 70% spec; bony vibration test utility debated
Myofascial pain	Postural habits Sleep disorders Exercise deficiency or overuse injury Trauma	Chronic, localized symptoms	Can mimic other conditions due to heterogeneity of symptoms Muscle tightness and imbalance which can be associated with stress, anxiety	Imbalance, gait abnormalities Palpation: taut bands and tender points in muscles of interest Imaging: ultrasound with Doppler flow, magnetic resonance elastography

Abbreviations: *sens* sensitivity; spec, specificity, *LE* lower extremity, *LBP* lumbar back pain, *ROM* range of motion

tained in a loose network of type II collagen and is primarily responsible for the ability of the IVD to withstand substantial axial loading. The AF is a thick and dense outer ring that is commonly divided into the inner and outer annulus. The outer annulus is made of highly organized, concentric lamellae that are composed of fibroblast-like cells that make type I collagen, giving it high tensile strength. The inner annulus is a transitional zone between the AF and NP, which consists of different proteoglycans and both type I and type II collagen. The EP is made of a 0.6-mm-thick layer of hyaline cartilage and has a capillary network that may extend into the outer AF, providing nutrients to the otherwise avascular IVD [12, 13].

The IVD functions to stabilize the spine, absorb shock, and allow for movement and flexibility of the otherwise rigid spine. It must withstand the biomechanical demands of the spectrum of human movement, including axial and rotational forces, flexion, extension, and lateral bending motions. These demands, coupled with its relatively avascular composition and limited ability to remodel, contribute to the natural degenerative process of IVDs and predispose it to pathologies such as disc herniations [12].

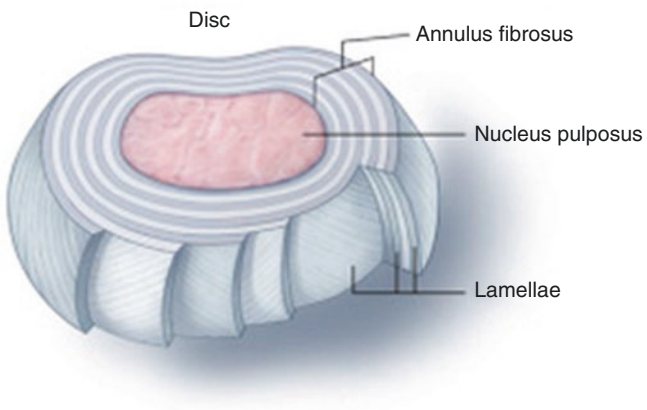

Fig. 5.1 Intervertebral disc structure. (Reprinted with permission from Hooten and Cohen [145])

According to the recommendations of the North American Spine Society, American Society of Spine Radiology, and American Society of Neuroradiology, the consensus definition of a disc herniation is a "localized or focal displacement of disc material beyond the limits of the intervertebral disc space" [14]. Disc herniations can be divided into three classifications, based on structural damage. *Protrusions* are wide-based herniations in which the outer annulus remains intact. *Extrusions* are narrow-based herniations with rupture of the outer annulus. Lastly, sequestrations are herniations that are completely detached from the rest of the IVD [12]. Figure 5.2 shows the potential consequences of disc protrusion on traversing and exiting nerve roots.

Whereas disc herniations can occur anywhere along the spine, the majority occur in the lumbar spine (L4–L5 or L5–S1), followed by the cervical spine (C5–C6 or C6–C7) [15, 16]. Lumbar disc herniations have highest prevalence among people aged 30–50 years and are more common in men. Several risk factors have been identified, including obesity, diabetes, hyperlipidemia, and smoking [12]. The mechanisms by which these comorbidities increase the risk for disc herniation is unknown, although it has been proposed that they may promote annular degeneration through altering microcirculation and cytokine expression [17, 18]. Other risk factors include strenuous labor, especially that requiring a combination of axial load with flexion or torsion [19, 20]. Lastly, positive family history (i.e., genetics) appears to impart an increased risk of developing lumbar disc herniation [21].

Disc herniations can result from acute trauma or progressive degenerative changes. Degenerative changes start early in life and include small clefts in the AF, decreased cell density of the NP, and decreased capillary supply to the AF [22, 23]. Changes to the AF play a crucial role in the development of disc herniations. With age, the number and severity of

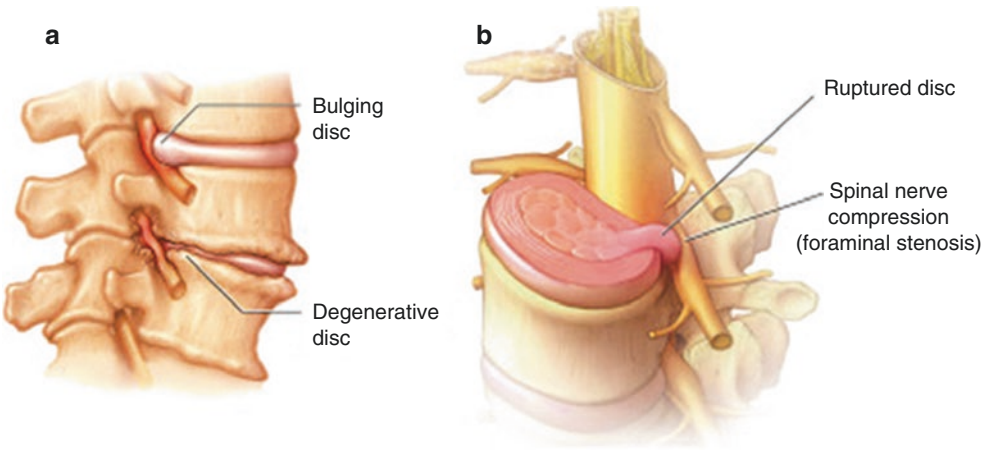

Fig. 5.2 (**a**) Lateral view of the potential effects of disc herniation and degenerative changes on spinal nerve roots. (**b**) Axial view of a ruptured lumbar intervertebral disc. (Reprinted with permission from Hooten and Cohen [145])

annular clefts increase, the boundary between the AF and NP fades, and the integrity of the outer layer of the AF becomes compromised [24]. Lumbar disc herniations most often occur posterolaterally, where the AF is relatively thin and not reinforced by the posterior or anterior longitudinal ligament [12]. In contrast, herniations in the cervical spine are more likely to occur laterally.

Pain is often characterized as sharp and stabbing, with a radicular component. Radicular pain is commonly attributed to either mechanical compression of the traversing nerve root or spinal canal or to chemical irritation [25]. Mechanical compression not only deforms the nerve root but can impinge on the microcirculation and lead to ischemia and radicular symptoms [12]. Further, studies have demonstrated that while disc herniation stimulates an inflammatory cascade that has a role in stimulating the resorption of the disc, this same cascade can also lead to chemical irritation of the nerve root and radicular symptoms, even in the absence of compression [26–29]. The observations that over 10% of patients who undergo discectomy for refractory pain experience unsatisfactory results months or years after and that there is no apparent correlation between lumbar decompression outcomes and radiological evidence of persistent herniation point to an underlying pain mechanism that is not purely related to mechanical compression but rather perpetuated by upregulation of inflammatory mediators such as TNF-alpha [30, 31].

Discogenic Pain

Approximately 39% of patients with mechanical lower back pain suffer from primary pathology of the intervertebral disc [32], with the proportion of individuals with positive discograms varying widely based on selection criteria (i.e., more liberal criteria will result in a lower proportion of positive results). Discogenic pain can be difficult to diagnose, and the pathophysiological components of disc degeneration have molecular, anatomical, and physiological aspects. As previously discussed, the intervertebral disc is composed of a tough and ring-like annulus fibrosus surrounding a gelatinous nucleus pulposus [33]. The annulus fibrosus is composed of concentric rings (lamellae); there are 15–25 layers depending on the location of the disc within the spine [34]. The annulus fibrosus surrounds the gelatinous nucleus pulposus [24, 33]; both of these structures are flanked superiorly and inferiorly by cartilaginous endplates. The innervation of the disc is complex but is thought to be composed of sinuvertebral nerves which derive from the dorsal roots [33, 35] and from sympathetic fibers ventrally. Normally, there is only minimal neural penetration of the annulus fibrosus [36].

The pathophysiology of discogenic pain can be viewed from the perspective of distinct pathological lesions which are found to correlate with painful symptoms or from the molecular and histological changes which have been found in tissue. The physiological causes of discogenic pain are commonly divided into torsion injury, internal disc disruption, and infection [37]. Internal disc disruption is the most common attributed cause of discogenic pain, resulting from radial tears to the disc and degradation of the nucleus pulposus. Radial fissures extend from the nucleus pulposus outward to the annulus fibrosus; other types of fissures include transverse fissures, which extend horizontally outward and involve the peripheral annulus and circumferential fissures, which resemble separation between the concentric rings of the annulus. These can form from compression injury or endplate deficits. Additionally, painful symptoms have been reported to occur more frequently in patients with high-grade annular disruptions.

Torsional injuries to the disc can result from forcible rotation about the zygapophyseal (facet) joint and lateral stress to the annulus fibrosus [37]. Based upon ex vivo studies, Farfan et al. showed how torsion could produce tears of the annulus [38]. Subsequent study has shown that torsion has a greater propensity to produce damage when combined with flexion [39].

More mechanistic details regarding discogenic pain have also been ascertained by ex vivo studies of degenerated discs. Changes in innervation and vascularization seen in harvested intervertebral discs from patients with discogenic pain and disc degeneration have shown more extensive spread of nerve fibers and granulation, which extend further into the annulus fibrosus and even into the nucleus pulposus [35, 40]. Freemont et al. showed that nerve growth factor (NGF) expression correlated with microvascular and nerve fiber ingrowth into the annulus fibrosus and nucleus pulposus, suggesting how molecular signaling reflects histological changes [41]. Increased expression of inflammatory markers such as TNF-alpha has also been found to be enriched in cadaveric samples of intervertebral discs from patients with clinical symptoms [42].

Spinal Stenosis

Spinal stenosis is a clinical entity defined by narrowing of the spinal canal, leading to cord or nerve root impingement that can result in radiculopathy and neurogenic claudication. Spinal stenosis can occur throughout the spine, but at an estimated annual incidence of 5 cases per 100,000 individuals, lumbar spinal stenosis (LSS) is 4 times more common than cervical spinal stenosis [43]. LSS is often classified by etiology and anatomy. Primary LSS results from congenital abnormalities (e.g., short pedicles) that narrow the spinal canal, while secondary LSS results from an acquired insult, most commonly from progressive

degenerative changes [44]. Other etiologies of secondary LSS include metabolic causes such as epidural lipomatosis, infectious causes such as osteomyelitis and discitis, rheumatologic conditions, cancer, and post-traumatic stenosis such as with fractures or surgeries [45]. Anatomically, LSS can be classified as involving the central canal, lateral recesses, neural foramina, or any combination of the three. Attempts have also been made to classify LSS based on the anterior-posterior diameter of the spinal canal, although this has not been clinically validated. A spinal canal diameter <10 mm is considered absolute LSS and is often symptomatic, while a spinal canal diameter of 10–12 mm is considered relative LSS and is usually asymptomatic. LSS most commonly affects the lower three levels, with L4–L5 most frequently affected, followed by L3–L4, L5–S1, and then L1–L2 [45]. In the cervical region, C5–C6 is the most frequently affected segment.

Degenerative LSS, the most common form of LSS, develops through multifactorial processes that can act in concert to propagate the disease. Thickening of the ligamentum flavum (LF), which covers a significant portion of the posterior and lateral walls of the spinal canal, is believed to play a major role in the pathogenesis of LSS. Whether thickening occurs by "buckling" of the LF into the spinal canal due to loss of intervertebral disc height or by hypertrophy of the LF in the absence of disc space narrowing, the diameter of the spinal canal is reduced, causing mechanical compression of the nerve root, cauda equina, or dural sac, leading to a variety of symptoms that may include back pain, leg pain, and gait disturbance [46]. LF hypertrophy is believed to be a multifactorial process, associated with aging, mechanical stress, activity level, and genetics. It is postulated that stress-induced tissue damage triggers an inflammatory response that causes scarring, the repeated accumulation of which results in the development of LF hypertrophy [47, 48]. Spinal instability has also been postulated to play a role—increased segmental range of motion has been shown to be an independent risk factor for LF thickening [46]. Whereas normal LF is composed primarily of elastic fibers, hypertrophied LF is characterized by disorganized and decreased elastic fibers as well as increased fibrosis, especially along the dorsal aspect of the LF, which is subject to higher stress [49]. Hypertrophied LF is thus stiffer and more vulnerable to the constant flexion-extension movements required, potentially leading to a feed-forward cycle of further scarring and repair [46]. The molecular mechanisms of LF hypertrophy are not fully understood, but LF hypertrophy has been shown to be associated with increased expression of matrix metalloproteases (MMPs), tissue inhibitors of matrix metalloproteases (TIMPs), connective tissue growth factor (CTGF), bone morphogenetic protein (BMP), platelet-derived growth factor-BB (PDGF-BB), and various inflammatory cytokines, including TGF-β [49–57].

In addition to LF hypertrophy, other degenerative processes occur that predispose to the development of LSS. As the intervertebral disc degenerates, disc protrusions can develop that cause ventral narrowing of the spinal canal, resulting in central stenosis. Disc degeneration also results in a loss of height of the intervertebral space, resulting in not only potential buckling of the LF into the dorsal spinal canal as aforementioned but also narrowing of the lateral recesses and foraminal stenosis. Disc degeneration also adds increased strain on the facet joints. This increased load can result in facet arthrosis, joint capsule hypertrophy, and joint cysts, leading to lateral and foraminal stenosis as well as increased spinal instability, which promote further deleterious hypertrophic changes [45]. These degenerative changes ultimately result in potential compression of nerve roots, dura, intraspinal vessels, and the cauda equina, leading to a heterogeneous array of symptoms.

Common symptoms of LSS include lumbago, neurogenic claudication, leg hypesthesias and paresthesias, ataxia, and leg weakness or heaviness. Neurogenic claudication is considered the classic clinical presentation. This term was coined by Dejerine in 1911 and first defined by von Gelderen in 1948 as "localized, bony discoligamentous narrowing of the spinal canal that is associated with a complex of clinical signs and symptoms comprising back pain and stress-related symptoms in the legs (claudication)" [45]. Neurogenic claudication is comprised of lumbar back pain that radiates toward the gluteal region, groin, and legs, often in a radicular pattern, with associated sensorimotor deficits such as paresthesias, weakness, and cramping. It is typically exacerbated by activities like standing and walking that transiently extend the spine, increasing lordosis and the degree of stenosis. Conversely, pain is eased by activities like stooping and sitting that cause flexion of the spine, opening the spinal canal. Means to distinguish neurogenic from vascular claudication include longer time to offset, pain relieved by sitting, a positive "shopping cart sign" or pain not worsened when walking uphill, more prominent neurological symptoms (e.g., numbness or neurological weakness), and a normal ankle brachial index [58].

The reproducibility of symptom onset and offset with postural changes highlights the importance of dynamic factors in the pathogenesis of neurogenic claudication. Epidural pressure has been shown to vary significantly with lumbar flexion and extension, increasing with walking and decreasing immediately after stopping [59]. Although these pressure variations, ranging from 15 to 18 mmHg during flexion to 80–100 mmHg during extension, are not enough to interrupt arterial flow, they may play a significant role in the development of venous congestion, as well as intermittent compression of nerve roots that results in impairment of nerve conduction. Indeed, neurogenic claudication is believed to result from either direct mechanical compression of nerve

roots or indirect vascular insufficiency from reduced arterial blood flow or venous congestion. With spinal extension, exacerbation of the stenosis occurs, causing mechanical compression of the cauda equina and nerve roots, leading to tissue injury and degeneration of nerve fibers. In addition, there is occlusion of the subarachnoid space, leading to venous stasis. The relationship between extensor postures, increased intraspinal pressure, vascular engorgement, and decreased venous drainage has been demonstrated in multiple studies [60–63].

Venous stasis is deleterious in several ways. Venous stasis has been shown in a rat model of LSS to elicit ectopic firing, which is thought to emanate from the dorsal root ganglia, with propagation in both directions, potentially playing a role in the origination of radicular pain as well as the development of paresthesias [64]. Further, venous stasis results in elevated capillary pressures, which can lead to intraradicular edema. Intraradicular edema is also thought to result from mechanical compression, which has been shown to increase permeability of the endoneurial capillaries, causing an inflammatory response with macrophage and mast cell infiltration [65]. Intraradicular edema is thought to be closely related to the development of radiculopathy.

Facet Joint Pain

Facet, or zygapophysial, joints are important sources of acute and chronic spine pain, due to their rich innervation. The facet joints form the posterolateral articulations between adjacent vertebral arches, with the superior articular facet facing upward and articulating with the inferior articular facet of the above vertebra (Fig. 5.3). This three-joint complex formed by the intervertebral disc and the paired facet joints functions to stabilize the spine and limit excess motion [66]. The facet joints also assist the intervertebral discs with weight-bearing, with the percentage of axial burden increasing with aging, disc generation, and facet arthritis [67]. Structurally, facet joints are true synovial joints, comprised of hyaline cartilage overlying subchondral bone, a synovial membrane, a fibrous joint capsule, and a joint space that can accommodate 1–2 mL of fluid [68]. Each facet joint receives dual innervation from the medial branch of the posterior primary rami at that level and from the level above. Thus, the L4–L5 facet joint receives innervation from the L4 medial branch (corresponding segment) and the L3 medial branch (the level above). The medial branches of the L1–L4 dorsal rami travel across the top of the transverse process, through the dorsal leaf of the intertransverse ligament at the base of the transverse process. Each nerve then travels in the groove between the transverse process and superior articular process, before curving medially around the base of the superior articular process. As it crosses the lamina, it then divides into multiple branches that innervate not only the facet joints but also the multifidus muscle, the interspinous muscle and ligament, and the periosteum of the neural arch [66, 69]. Although unproven, some studies suggest that the facet joints may also receive additional innervation from the dorsal root ganglion, the medial branch below the facet joint, and the paravertebral sympathetic ganglia [70–73]. Histologic studies of facet joints demonstrate the presence of encapsulated and free nerve endings, as well as nerves containing substance P and calcitonin gene-related peptide [74, 75]. Nerve fibers have also been found in structures outside the joint capsule, including subchondral bone, which may contribute to pain [76]. This rich innervation of the facet joint capsule and surrounding structures makes it an important pain generator.

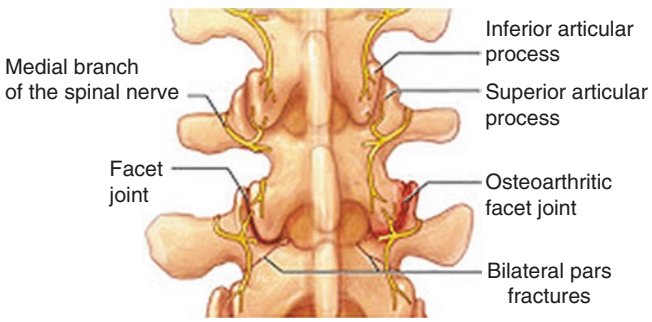

Fig. 5.3 Anatomy and innervation of the lumbar facet joint. Also depicted are bilateral fractures of the pars interarticularis (pars defect) and an osteoarthritic facet joint. (Reprinted with permission from Hooten and Cohen [145])

Although the development of facet joint pain can sometimes be traced to an inciting event [77], the majority of cases are the result of cumulative stress over a lifetime [66]. Studies have shown that the upper three lumbar facet joints are maximally strained with lateral bending, while the lower two lumbar facet joints are maximally strained during forward flexion [78]. Further, disc degeneration can alter the biomechanics of the three-joint complex, resulting in increased stress on the facet joint and hypertrophic changes in the capsule [79]. Repetitive stress is associated with synovial release of inflammatory mediators, leading to facet joint effusion and subsequent capsular distension. This capsular distension activates synovial and capsular nociceptors, resulting in pain [80]. The mechanism by which this can lead to persistent pain has been demonstrated in several animal studies. In goats, excessive capsular strain activates nociceptors and can lead to persistent neural after-discharges [75]. This persistent nociceptive input leads to peripheral sensitization, which may lead to central sensitization and neuroplasticity [81]. At even higher degrees of capsular strain, signs of capsular axonal injury were present, as demonstrated by axonal swelling and retraction balls, which can lead to

axonal hyperexcitability and spontaneous firing and hence may play a role in the generation of neuropathic pain [75]. In a series of other animal studies, the application of inflammatory mediators such as substance P and phospholipase A_2 was shown to lead to vasodilation, venous congestion, and polymorphonuclear leukocyte aggregation in the lumbar facet joint and surrounding tissues [82–84]. Inflammation also resulted in neuronal sensitization, as demonstrated through decreased thresholds of nerve endings, increased basal discharge rates, and recruitment of previously silent units [85].

In addition to capsule distension, other mechanisms of pain generation have been postulated. Chronic inflammation can lead to facet hypertrophy and foraminal narrowing, which can cause impingement of nerve roots, leading to radicular symptoms [86, 87]. Nerve entrapment can also occur with calcification of the mamilloaccessory ligament and is especially common at L5 (20%) and L4 (10%) [88]. Lastly, irritation of the facet joint capsule may result in reflex spasm of the paraspinal muscles [89, 90].

Sacroiliac Joint Pain

The sacroiliac joint (SIJ) is the largest axial joint in the body and is estimated to be the source of approximately 15–25% of axial lumbar back pain cases in carefully screened patients (i.e., non-neuropathic pain predominantly below L5) [91–93]. Although the SIJ is often characterized as a diarthrodial synovial joint, the posterior two-thirds of the joint interface lacks a capsule and is connected through an extensive network of ligaments [94]. The SIJ is also reinforced by numerous myofascial attachments that impart joint stability and influence movement, including the thoracolumbar fascia, gluteus maximus, piriformis, and biceps femoris [95, 96]. Innervation to the SIJ is complex and the subject of debate. The posterior joint is believed to receive its major innervation from the lateral branches of the dorsal rami of S1–S3, with variable contributions from L5 to S4 in some individuals [97, 98]. Innervation to the anterior joint is even less well understood, with studies suggesting innervation from the L5 to S2 ventral rami, with possible contributions from L4 [99, 100].

Numerous histological studies have suggested that the SIJ is capable of transmitting proprioception and nociception [101–103]. In cadaver studies, substance P and calcitonin gene-related peptide (CGRP)-positive nerve fibers have been found to be present in the superficial layers of sacral and iliac cartilage, as well as the surrounding ligamentous structures, supporting the idea that the SIJ is capable of nociception [104]. Furthermore, as several pathways of communication have been demonstrated between the SIJ and nearby neural structures, it is possible that inflammatory mediators extravasate in the setting of capsular disruption, leading to symptoms of sciatica. In one study, ventral capsular tears were observed in 21% of patients based on contrast injection patterns [92]. On post-arthrography CT, the most common patterns of extracapsular contrast extravasation from the SIJ to nearby neural structures include posterior spread into the dorsal sacral foramina, superior recess spread into the L5 nerve root sheath, and ventral spread into the lumbosacral plexus [105]. Thus, injuries to the various components of the SIJ and surrounding structures, whether by distension, compression, shearing forces, altered mechanics, or inflammation, can all be sources of pain [106]. Mechanistically, these can be simplified into intra- and extra-articular sources of SIJ pain. Extra-articular causes include enthesopathies, ligamentous and muscular injuries, and fractures. Intra-articular causes are less common and include arthritis and infection [106].

Several predisposing factors for developing SIJ pain have been reported [106]. These include factors that increase SIJ burden, such as leg length discrepancy and scoliosis, which can both increase pelvic obliquity, leading to abnormal bilateral alignment of the SIJ and increased stress through the joint [107, 108]. In a finite element model of SIJ loading, as little as 1 cm of leg length discrepancy increases the load across the SIJ during lateral bending by almost five-fold [109]. Other factors that increase SIJ burden include gait abnormalities, vigorous exercise, and other forms of persistent low-grade trauma [110, 111]. Lumbar and lumbosacral fusion have also been shown to increase the risk of SIJ pain, especially as the number of operative segments increases, presumably through ligamentous weakening, disruption of the joint cavity, and postoperative hypermobility [112–115]. Lastly, pregnancy increases the risk of SIJ pain through a combination of weight gain, increased lordosis, hormone-induced ligamentous laxity, and trauma associated with parturition [116]. MRI changes of the SIJ during the peripartum period include bone marrow edema, capsulitis, and enthesitis [117].

Compared to facetogenic and discogenic pain, which tend to be more insidious in onset, SIJ pain is more likely to be associated with an inciting event [97, 118]. In one study evaluating patients with injection-confirmed SIJ pain, most (44%) recalled a specific traumatic event (e.g., motor vehicle accident, fall, or pregnancy), while 35% had idiopathic onset, and 21% were considered to have had cumulative trauma [118]. The mechanism of SIJ injury is described as a combination of axial loading with abrupt rotation [106]. Specific mechanisms of acute injury include direct fall on the buttocks, sudden heavy lifting, rear-end motor vehicle accident with the ipsilateral foot on the brake, and stepping into an unexpected hole [95, 106, 119, 120]. Other chronic mechanisms include repetitive shear or torsional forces, such as with golfing and bowling [121] .

Inflammatory Disorders and Cancer

There are a number of less common conditions that can also cause spinal pain. Inflammatory disorders such as ankylosing spondylitis and metastatic disease can contribute to spinal pain, involving complex mechanisms that deserve special mention. Their pathophysiological involvement of the elements of the spine can often present a mixed pain syndrome with both nociceptive and neuropathic features.

Ankylosing spondylitis is a seronegative spondyloarthropathy with a strong association with HLA-B27, which can lead to a syndrome of sacroiliitis, thoracolumbar, and even cervical pain [122, 123]. Inflammatory back and pelvic pain that is dull and deep, with nocturnal exacerbations, is the most common clinical presentation [124], although studies have also suggested that some patients report neuropathic pain and sensorimotor symptoms [125]. Pathogenesis of this arthropathy involves aggregation of inflammatory T-cells, B-cells, macrophages, and osteoclasts at the insertions of ligaments (entheses) [122]. Gradually, patients develop dysregulation of cytokines such as TNF-alpha or IL-17, also considered important in the genesis of this disease; as a useful corollary, disease-modifying agents targeting TNF-alpha have been helpful in the amelioration of symptoms. At a structural level, damage through bone erosion followed by bone formation [126] and gradual fusion and loss of mobility of joints [127] contribute to disability and loss of mobility. Thus, a complex and poorly understood process with immunological overtones presents a unique syndrome of spine pain.

Metastatic cancer represents another important cause of spinal pain with up to 70% of cancer patients showing signs of tumor infiltration to the axial spine on postmortem examination. Spinal metastases occur most commonly in the thoracic spine (60–80%), followed by the lumbar spine (15–30%), and finally the cervical spine (<10%). The most common cancers to metastasize to the spine are breast, lung, and prostate cancers, although renal, thyroid, and gastrointestinal sources of malignancy are also observed [128]. Additional information will be provided in other chapters in this book.

Cancer-associated bone pain is complex, has been found to involve unique mechanisms on molecular and physiological levels, and can demonstrate aspects of both nociceptive and neuropathic pain. Studies have shown that patients with cancer-associated bone pain frequently describe neuropathic symptoms [129], which can result from direct compression on nervous structures or central sensitization [130]. Pain can result from tumor cell-driven infiltration, compression of peripheral nerves, or stretching of bone. Central sensitization also occurs from chronic inflammatory or neuropathic injury from bone cancer, with studies revealing neurochemical changes which can be seen in the spinal cord as demonstrated in animal models of cancer pain [131, 132]. Thus, there are multiple mechanisms that can contribute to the uniquely devastating symptoms caused by metastatic spread of cancerous disease to the axial spine.

Summary

There is a wide range of pain syndromes that affect the spine, each with distinct molecular, cellular, and anatomic abnormalities, leading to their respective symptoms. It is crucial for the pain practitioner to understand the underlying pathophysiology of spinal disease in order to efficiently utilize helpful therapeutic approaches. Perhaps most important, continued study into the basis of a specific syndrome may guide development of more beneficial future therapies.

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Clinical and Research Tools for Pain Assessment

6

Myrella Paschali, Asimina Lazaridou, and Robert R. Edwards

Key Points

- There is no single best tool for pain assessment; the appropriate measure should be chosen depending on the needs of the study or the clinical setting.
- Pain is a subjective and private experience. Although there is no "objective" measure of pain, numerous self-report pain assessment tools have been shown to be valid and reliable.
- Specialized pain assessment scales are available for special populations (e.g., children, cognitively impaired patients).
- Behavioral and functional neuroimaging-based assessing methods may provide valuable data on pain responses but cannot substitute self-reported pain experience.
- Pain is not synonymous with quality of life or disability; other assessment tools for these important outcome dimensions are recommended.

Introduction

Pain is a subjective experience and a complex, multidimensional perceptual phenomenon. It is nearly ubiquitous, familiar to everyone, and pain remains one of the most common reasons why US patients are likely to seek medical consultation [1]. Pain associated with tissue damage, inflammation, or a disease process of brief duration is referred to as acute pain, whereas pain that persists for extended periods of time (e.g., >3 months), accompanies an ongoing disease process, or is the result of an injury not resolved within an expected period of time is referred to as chronic pain [2]. In the case of chronic recurrent pain, patients experience episodes of acute pain interspersed with pain-free periods [3]. Recent reviews and a recent AAAPT taxonomic proposal highlight the difficulty of specifying a temporal cutoff for acute pain, noting that it can last from seconds to a period of weeks [4].

Pain has several important dimensions: a sensory-discriminative dimension (including location, intensity, and temporal aspects of pain); an affective-motivational dimension (including the emotions and aversive aspects of pain); and a cognitive-evaluative dimension (the interpretation of the situation and the possible consequences of the pain) [5]. By its nature (as a private sensory and emotional experience), pain cannot be directly observed by others; therefore, its assessment relies largely on patient's self-report or behavioral observation (e.g., evaluation of facial expressions). At present, there is no formal consensus on an optimal tool for pain assessment; while the 0–10 numeric rating scale is likely the most widely used tool in clinical practice in the USA, many instruments and methods are available. The purpose of this chapter is to provide an overview of pain assessment tools by providing a critical analysis in an effort to assist clinicians and researchers in selecting the pain assessment methods best suited to serve their purposes.

Pain Assessment

Comprehensive, individualized, and ongoing pain assessments are an essential part of chronic pain management. Pain intensity is one of the most important dimensions of pain, the most common outcome in clinical trials of chronic pain treatments, and great efforts have been invested in developing assessment tools that are valid and reliable. However, pain is a rich multidimensional experience, and pain report is associated with an array of multimodal factors such as cultural background, emotional processes, and past experiences.

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Therefore, assessing solely a single dimension of pain intensity can be insufficient as it fails to capture other important dimensions of pain [3].

Self-report assessments have been shown, in many cases, to have a significant level of concordance with disease characteristics and objective functional performance. Despite their limitations they have many advantages such as low cost, direct reference to the individual experiencing pain, and the potential assessment of a wide range of psychosocial and behavioral processes and functions [6]. A great deal of research has also been conducted for the development of pain assessment measures that do not rely on self-report. For example, assessment of pain based on nonverbal communication may be of crucial importance for patients with limited or no ability to communicate [3]. Many of the numerous challenges in pain measurement are discussed later (see Pain Assessment in Special Populations and Other Challenges of Pain Management). Recent reviews note that current frameworks for guiding pain assessment do not adequately tackle issues such as how to understand quantitative data as a proxy for subjective individual experience and how to prioritize different methods of pain assessment (e.g., if verbal report of pain and behavioral indices of pain do not align) [7]. The newly proposed multimodal assessment model of pain (MAP) is a framework that aims to address these gaps.

Self-Report Measures of Pain

Assessing Pain Intensity

Pain intensity can be defined as *how much* pain an individual is feeling. A number of clinically tested and well-validated pain intensity scales are being used. Most of them are strongly related to one another; however, each demonstrates strengths and weaknesses which should be taken into consideration while selecting the suitable measure.

Visual Analogue Scales (VAS)

A VAS consists of a line, often 10 cm long; its ends are generally labeled with verbal pain anchors (e.g., "no pain" and "pain as bad as it could be"). Patients are asked to indicate the point along the line that best reflects their pain intensity (Fig. 6.1). There is good evidence supporting the validity of the VAS for pain intensity; measured differences represent actual differences in pain magnitude [3]. Furthermore, VAS is sensitive to treatment effects [8], and VAS scores correlate with pain behaviors. One limitation of the VAS is the fact that it can be a relatively time-consuming assessment. Therefore, the mechanical and the computer-based VAS scales were created. The mechanical VAS uses a sliding scale superimposed on a horizontal VAS drawn on a ruler. It can be easily scored from the back and includes numbers for each marker placement [9].

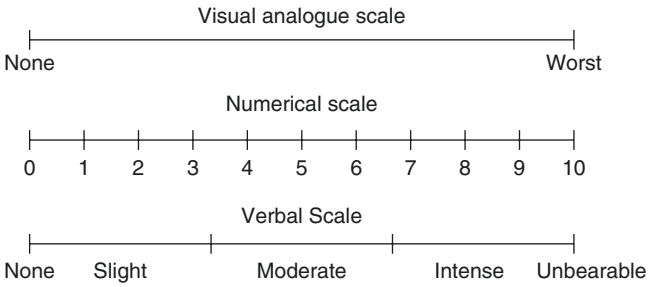


Fig. 6.1 The Visual Analogue Scale (VAS), the Numerical Rating Scale (NRS), and the Verbal Rating Scale (VRS). (Reprinted with permission from Sadaf and Ahmad [85])

Numerical Rating Scales (NRS)

An NRS most often consists of a line with a series of numbers representing the possible range of pain intensity. Patients are asked to rate their pain from 0 to 10, 0 to 20, or 0 to 100 with the instruction that 0 represents "no pain" and 10, 20, or 100 represents a maximal value for pain such as "pain as bad as it could be" (see Fig. 6.1). The NRS can be administrated in a written format or orally. It is an easily administrated, understood, and scored scale with well-documented validity and positive correlation with other pain intensity measures, which has led to its adoption as the most commonly used measure of pain intensity [3, 10].

Verbal Rating Scales (VRS)

A VRS consists of a series of adjectives listed from the least to most intense or unpleasant. The scale should span a maximum possible range of the pain experience (e.g., from "no pain" to "extremely intense pain") and sufficient intervals to capture the many possible gradations in the pain experience. Patients are asked to select the adjective best describing their pain level (see Fig. 6.1). A VRS is scored quantitatively by assigning each adjective a number according to its rank (e.g., 0–3: 0, no pain; 1, mild pain; 2, moderate pain; 3, severe pain). The strengths of VRS include simplicity of administration and scoring, good reliability, and established validity. Despite its significant strengths, the VRS also has some weaknesses, for example, its scoring method assumes equal intervals between the adjectives, even though it is unlikely that equal perceptual intervals exist. This property of the VRS poses difficulties in the interpretation and analysis of VRS-derived data [3].

Picture or Face Scales

Picture or face scales uses photographs or line drawings illustrating facial expressions of different levels of pain severity (Fig. 6.2). Patients are asked to indicate which photograph or drawing best depicts their pain experience. Each face is associated with a number representing the pain intensity score, so that the response can be converted into a

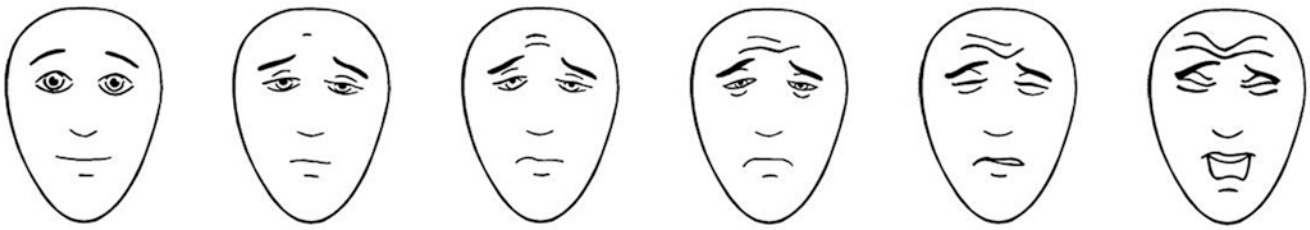


Fig. 6.2 Faces Pain Scale – Revised, ©2001, International Association for the Study of Pain. This Faces Pain Scale-Revised (www.iasp-pain.org/fpsr) has been reproduced with permission of the International Association for the Study of Pain® (IASP). The figure may *not* be reproduced for any other purpose without permission

numeric pain score. The scales provide an option for patients who have difficulty with written language and for pediatric populations. For both adults and children, the scale has demonstrated divergent and convergent validity with other measures of pain [11, 12].

Assessing Pain Affect

Pain affect is a distinct pain dimension; it is more complex than pain intensity and can be defined as the unpleasant emotional arousal and disruption caused by the pain experience. The most widely used measure of pain affect is the affective subscale of the McGill Pain Questionnaire (MPQ). Some additional methods of assessing pain affect are VRSs, VASs, and the affective scale of the Pain-O-Meter (POM) [3]. Similar to pain intensity, affective pain VRSs consist of adjectives describing increasing amounts of discomfort and suffering (e.g., from bearable to excruciating) [13]. The advantages and disadvantages of the VRSs are similar to those for pain intensity. Although the validity of the scale has been confirmed [4], investigations among patients with chronic or postoperative pain indicated that VRSs measuring pain affect are not always distinct from pain intensity [10]. VAS measures of pain affect generally consist of a line bounded by anchors such as "not bad at all" and "the most unpleasant feeling possible for me" as endpoint descriptors. A great deal of evidence supports the validity of VAS affect measures, which appear to be sensitive to treatment effects [14]. The disadvantages of the VAS affect measures are similar to those of VAS intensity measures. VRSs may be able to better distinguish between pain intensity and pain affect than VASs, perhaps because verbal descriptors are more suitable for describing an emotional reaction [15]. The POM includes a mechanical VAS and two lists with pain descriptors (11 affective descriptors, of which 3 are selected from the MPQ). Patients indicate which of the words may be used to describe their pain; each word is associated with an intensity score (1–5), and the sum of these values gives the total POM affective score. The POM affective scale has been shown to be a reliable measure that is sensitive measure to analgesic treatment effects [16].

Assessing Pain Quality

Assessment of pain quality involves the evaluation of distinct, specific physical sensations associated with pain (e.g., burning pain, stabbing pain, etc.). Pain quality can be assessed with measures such as the McGill Pain Questionnaire (MPQ), the short-form MPQ, and the Neuropathic Pain Scale (NPS). The NPS, designed for use in patients with specifically neuropathic pain conditions, begins with an introduction that describes how people may experience sensations differently and how unpleasantness differs from intensity. The scale itself includes two items that assess the global dimensions of pain intensity and pain unpleasantness and eight items that assess specific qualities of neuropathic pain: "sharp," "hot," "dull," "cold," "sensitive," "itchy," "deep," and "surface" pain. The NPS possesses the ability to discriminate between groups of patients with different neuropathic pain diagnoses [17].

The painDETECT questionnaire is another assessment tool that was specifically developed to detect neuropathic pain components in adult patients [18]. More recently, researchers have developed the Spine painDETECT questionnaire (SPDQ) and its short-form version (SF-SPDQ) as valid screening tools for neuropathic pain caused by spinal disorders. Both have moderate utility as screening tools, with the SF-SPDQ perhaps being preferable for clinical use in samples of patients with chronic spinal pain conditions [19]. For the assessment of pain quality in patients with musculoskeletal or other non-neuropathic pain conditions, the MPQ or the short-form MPQ is recommended. Both have very good evidence for their reliability and validity in the assessment of pain qualities [3].

Assessing Pain Location

The assessment of pain location determines the perceived location of the patient's pain sensation. The most widely used instrument to assess pain location is the pain drawing, which usually involves a line drawing of the front and back of the human body [3]. Patients are requested to mark or shade the location of their pain on the drawings. The score is calculated according to the number and "weight" of regions that were shaded (Fig. 6.3, [20]). This score has

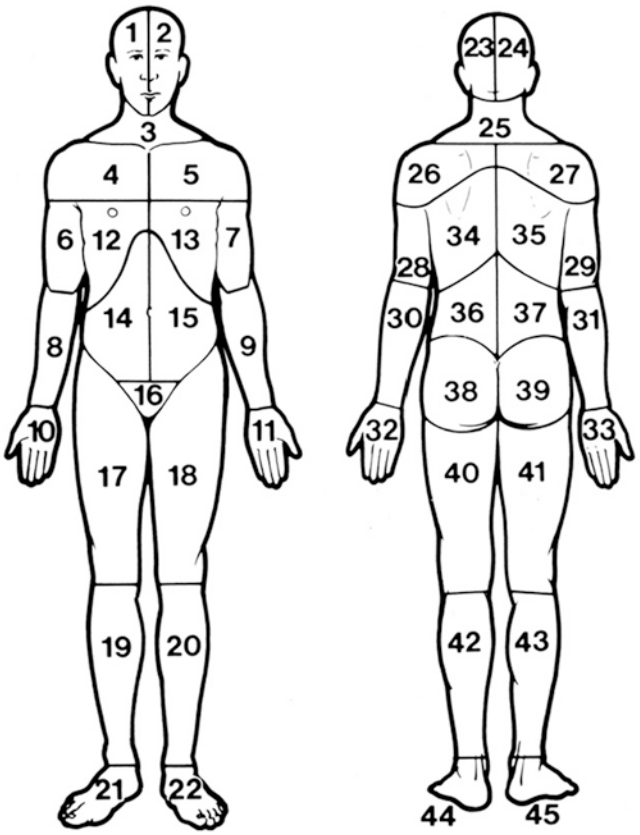


Fig. 6.3 Scoring template for pain drawing. (Reprinted with permission from Margolis et al. [20])

been shown to be related to several important pain-related constructs such as dimensions of the MPQ and interference of pain with basic activities such as walking, working, and recreation. The number of body regions in which pain was endorsed was unrelated to pain intensity and duration, suggesting that pain location or the "widespreadness" of pain is an independent dimension of the pain experience [21].

The McGill Pain Questionnaire (MPQ)

The MPQ and its brief analog, the short-form MPQ, are among the most widely used measures of pain. The MPQ was created to assess the multiple dimensions of pain (sensory-discriminative, affective-motivational, and cognitive-evaluative). It consists of 20 sets of verbal descriptors, from lowest to highest intensity. These descriptors are divided into sets assessing the sensory (10), affective (5), evaluative (1), and miscellaneous (4) dimensions of pain. Patients are asked to select the words that describe their pain; their selections are then converted into a pain-rating index. In addition, the MPQ contains a present pain intensity (PPI) VRS, ordered from "mild" to "excruciating." The MPQ provides quantitative information that can be used for statistical analysis, and it is sufficiently sensitive to detect differences among various pain relief methods [22].

The short form of the MPQ is more frequently used; it consists of 15 descriptors including the sensory (11 items) and affective (4 items) categories of the original MPQ. A PPI and a VAS are also included (Fig. 6.4). The short form correlates highly with the original scale [23].

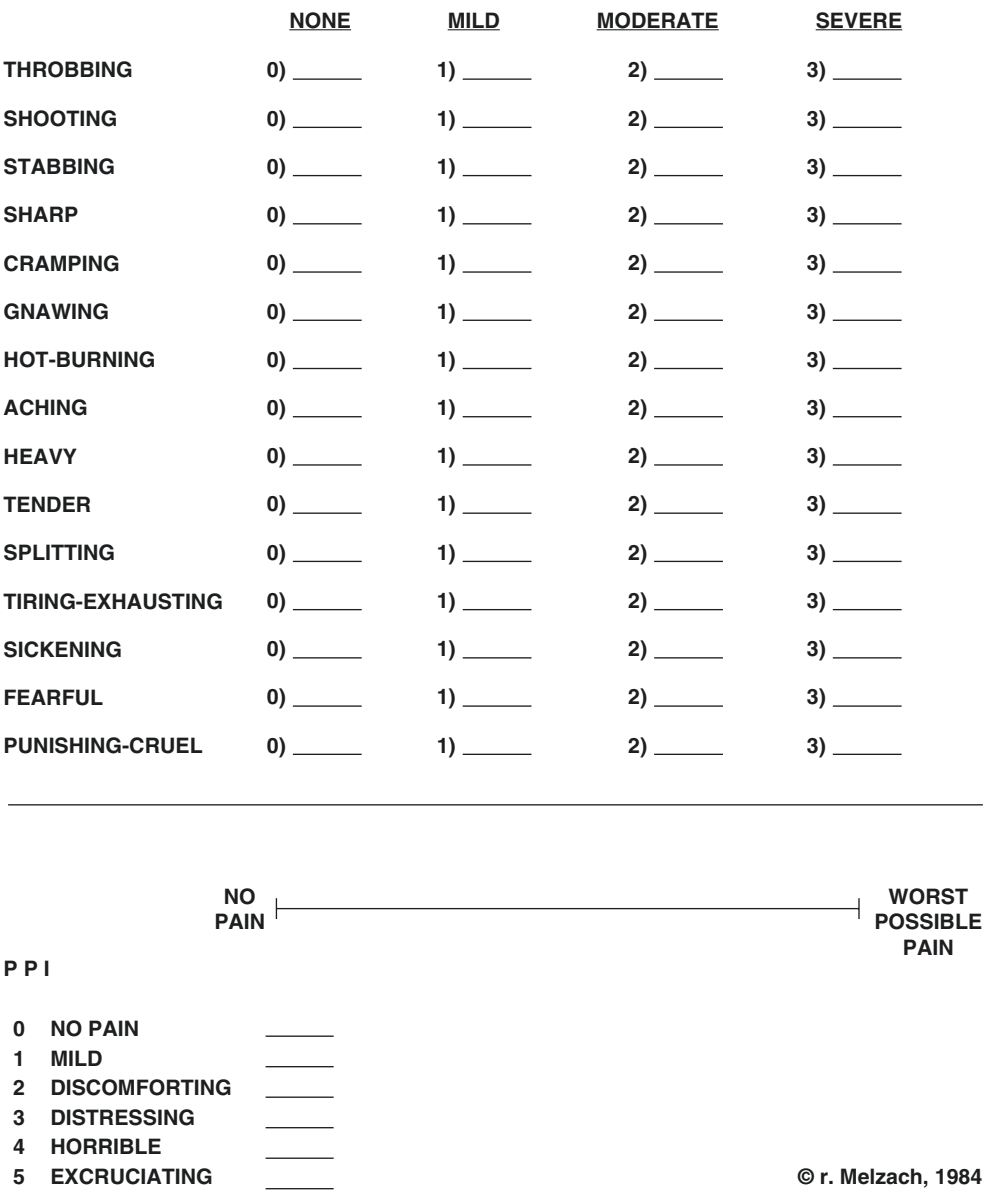
Behavioral Observation-Based Measures of Pain

Patients in pain exhibit a variety of behaviors that serve to communicate the fact that pain is being experienced. Pain behaviors can be verbal (including vocalizations of distress; moaning or complaining) or nonverbal (facial expressions, body postures, withdrawing from activities, taking pain medication). These behaviors have been termed pain behaviors [24]. Their assessment is particularly valuable when the capacity of speech is unavailable or limited, such as in infants or small children or people with intellectual disabilities, acquired brain damage, or dementia. Nonverbal expression is nonetheless valuable information from people who *can* use the language; patients' verbal reports of pain are only modestly correlated with behavioral indices of pain (e.g., a patient may be exhibiting severe pain behaviors while indicating that "I'm fine"), and some research suggests that behavioral appraisals of others' distress and pain are more often more credible to observers than patients' verbal self-reports [25, 26].

Facial expressions are complex and difficult to describe and quantify. The evaluation of pain-related facial expression requires a comprehensive and controlled assessment method, minimizing inference and maximizing objectivity. Ekman and Friesen's Facial Action Coding System (FACS) provides the most satisfactory approach. It is anatomically based and entirely descriptive and identifies 44 discrete facial expressions produced by individual facial muscles or muscle combinations [27, 28]. Numerous elements of facial expressions like lowering the eyebrows, narrowing the eyes, raising the upper lip, or dropping the jaw have been identified as pain-related actions. These facial expressions have been described as "universal" and are found to be consistent across different social groups and across different pain modalities; these expressions also show consistent relationships to patients' pain ratings [29].

Experimental Pain Assessment

Quantitative sensory testing (QST) is a noninvasive method of assessing sensory and pain perception that has been used widely in the past 30 years to study pain mechanisms as well



	NONE	MILD	MODERATE	SEVERE
THROBBING	0) _____	1) _____	2) _____	3) _____
SHOOTING	0) _____	1) _____	2) _____	3) _____
STABBING	0) _____	1) _____	2) _____	3) _____
SHARP	0) _____	1) _____	2) _____	3) _____
CRAMPING	0) _____	1) _____	2) _____	3) _____
GNAWING	0) _____	1) _____	2) _____	3) _____
HOT-BURNING	0) _____	1) _____	2) _____	3) _____
ACHING	0) _____	1) _____	2) _____	3) _____
HEAVY	0) _____	1) _____	2) _____	3) _____
TENDER	0) _____	1) _____	2) _____	3) _____
SPLITTING	0) _____	1) _____	2) _____	3) _____
TIRING-EXHAUSTING	0) _____	1) _____	2) _____	3) _____
SICKENING	0) _____	1) _____	2) _____	3) _____
FEARFUL	0) _____	1) _____	2) _____	3) _____
PUNISHING-CRUEL	0) _____	1) _____	2) _____	3) _____

Fig. 6.4 The short-form McGill Pain Questionnaire. Descriptors l–11 represent the sensory dimension of pain experience, and 12–15 represent the affective dimension. Each descriptor is ranked on an intensity scale of 0 = none, 1 = mild, 2 = moderate, and 3 = severe. (Reprinted with permission from Melzack [23])

as individual differences in pain perception. There have been numerous published studies that have demonstrated the importance of QST in the analysis of the pathogenesis, classification, and differential diagnosis of musculoskeletal and neuropathic disorders. Several modalities of noxious stimulation, administered in a calibrated manner, are commonly used to induce pain (e.g., thermal, mechanical, electrical, chemical, ischemic); typical parameters that are measured include pain threshold, pain tolerance, and ratings of suprathreshold noxious stimuli using an NRS, VAS, or VRS. The clinical relevance of experimental pain assessment is rapidly being established; quantitative sensory testing can be used to subtype patients with chronically painful conditions, to identify mechanisms of chronic pain, and to prospectively predict postoperative pain [30]. Recent studies in patients with neuropathic pain have also noted that phenotyping of patients using QST (sometimes termed sensory profiling) can predict responses to different classes of analgesic medications, which represents a potentially exciting development for personalized pain medicine [31].

Opioid-Treated Patients

There is evidence that strongly indicates that chronic opioid administration leads to a progressive and lasting reduction of the baseline nociceptive threshold, which is referred to as opioid-induced hyperalgesia. Prolonged opioid treatment not only results in the reduction of the opioid antinociceptive effect (desensitization) but also triggers activation of a pronociceptive system that reduces the nociceptive threshold (sensitization) [32]. QST has an important role in the assess-

ment of opioid-induced hyperalgesia. The use of standardized noxious stimuli patterns allows quantification of changes in pain sensitivity as a result of pharmacologic treatment. Many studies have used QST to investigate long-term effects of opioid treatment on pain perception. For example, individuals maintained on methadone show reduced pain tolerance and high sensitivity to a variety of modalities of painful stimuli [33, 34]. QST is expected to become an increasingly common pain assessment tool; future studies may, for example, investigate whether it can be used as a preoperative testing, in order to predict individual variability in the need for postoperative opioids following painful surgical procedures [35].

Functional Neuroimaging

Over the past 20 years, brain imaging techniques have provided critical insights into cortical, subcortical, and spinal mechanisms involved in pain perception and pain modulation in humans. Pain neuroimaging has been increasingly used as a biomarker in clinical trials with a greater focus on diagnostic properties, serving as a tool for understanding the mechanisms involved in generating and sustaining chronic pain. For example, reduced gray matter volume and white matter alterations have been found in individuals with chronic pain conditions compared to healthy controls [36]. Moreover, the use of imaging in the early phases of clinical drug evaluation is increasing, with the potential of making central nervous system (CNS) drug development more efficient [37]. Below we briefly describe some of the pain neuroimaging approaches:

Proton magnetic resonance spectroscopy (1H-MRS) can assess the relative concentrations of neurotransmitters such as gamma-aminobutyric acid (GABA), which may be beneficial in evaluating analgesic compounds thought to work on a specific class of neurotransmitters. Functional neuroimaging methods such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) allow noninvasive assessment of the neurophysiology of pain processing in the brain and the spinal cord. Most of these studies have been based on measurement of brain responses to acute pain stimuli, and brain activity is measured during periods of pain and pain-free periods. The difference between these two measurements is considered an index of pain-related neurophysiologic processes in the brain. Positron emission tomography (PET) can analyze the binding capacity of endogenous opioids to μ-opioid receptors by using radioactively labeled molecules. Furthermore, PET imaging may contribute to a better understanding of the consequences of pharmacologic opioid use such as habituation, desensitization, and opioid-induced hyperalgesia [38].

Additional applications of functional neuroimaging include neurofeedback techniques such as the real-time fMRI (rt-fMRI). This technique gives an individual feedback on activation of single or multiple brain areas involved in specific functions, training patients to cognitively manage their own pain [39]. Unfortunately, MRI-based methods have limited use in daily clinical assessment of pain because of the restrictions posed by the expensive equipment and the challenging logistics of MRI scanning, as well as the potential for artifacts influencing data specificity and sensitivity [40].

Pain Assessment in Special Populations

Children

Distress behaviors and pain expression vary depending on the child's age, cognitive development, and sociocultural background. Children between ages 2 and 4 are typically able to indicate the presence of pain verbally. By the age of 5, children can differentiate a wide range of pain intensities and can use quantitative pain scales. Several pain measurement tools have been designed for children; the most common measures are pain intensity scales. A recent systematic review by Pediatric Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (Ped-IMMPACT) indicated the following recommended self-report pain scales: Faces Pain Scale-Revised, Poker Chip Tool, the Visual Analogue Scale (VAS), and the Oucher Photographic and Numerical Rating Scale (NRS) in children with acute and persisting pain [41].

For the assessment of pain in children below 3 years old (and in children who are developmentally impaired), the most suitable approach for pain assessment is the observation of pain-related behaviors. Typical acute pain indicators include facial expressions, body movements and posture, the inability to be consoled, crying, and groaning. Some indicators of chronic pain can include abnormal posturing, fear of being moved, lack of facial expression and interest in surroundings, increased irritability or anger, low mood, sleep disruption, changes in appetite, and poor school performance [42]. The Neonatal Infant Scale (NIPS) can be named as an example of a widely used behavior pain rating scale [43].

Elderly Patients

Pain assessment in the elderly poses a challenge for clinicians because of several unique characteristics of aging. Older individuals tend to under-report pain, perceiving pain as a normal part of aging or fearing the consequences of reporting pain, such hospitalization. Stoic attitudes toward

pain appear to be more commonly endorsed in older samples relative to younger samples [44]. Sensory and cognitive impairments as well as multiple comorbidities also affect the pain presentation. The abovementioned demonstrates the multidimensionality of pain assessment in older adults and highlight the need for a multidisciplinary approach [45]. Many multidimensional pain assessment tools for use with older adults are available; the short-form McGill Pain Questionnaire (SF-MPQ), the Brief Pain Inventory (BPI; [46]), the Pain Disability Index (PDI; [47]), the Functional Pain Scale (FPS; [48]), and the Multidimensional Pain Inventory (MPI; [49]). The Geriatric Pain Measure (GPM) is a recently developed assessment option specifically for use with older adults [50]. The BPI, the PDI, and the GPM are relatively short and easy to complete, providing information on the impact of pain. They can be used to assess changes in pain, as well as the treatment response in the clinical setting [51]. A comprehensive pain assessment in the elderly must moreover include the assessment of functional limitations (e.g., impairment in performance of activities of daily living (ADL), mobility, sleep, and appetite), psychosocial function (e.g., mood, interpersonal interactions, beliefs about pain, fear of pain-related activity), and cognitive function (e.g., dementia or delirium) [51].

Cognitively Impaired Patients

The assessment of pain in the cognitively impaired elderly population poses additional challenges to those mentioned above, as memory and language impairments may impede pain report. As an effect of mild to moderate cognitive impairment, high failure rates in the completions of pain scales have been reported. Ferrell et al. found the highest completion rate for the Present Pain Intensity Scale of the McGill Pain Questionnaire (a VRS) and the lowest for a horizontal VAS [50]. LaChapelle et al. report in their study with persons with intellectual disabilities that 35% of the participants were unable to provide valid self-report, as they were unable to understand the nature of queries about characteristics of their pain [52]. Similar findings were shown in patients with dementia [50]. Despite the difficulties associated with the use of self-report scales in this population, self-report assessment should be attempted and only rejected after it becomes clear that the patient cannot use the measure reliably [3]. Especially in patients with dementia, observational tools for pain, such as the Pain Assessment In Advanced Dementia Scale (PAINAD), should be used in combination with self-report tools in order to achieve a multidimensional assessment of pain [53, 54]. Other pain assessment tools for cognitively impaired patients are the Facial Action Coding System (FACS) [55] and the Pain Assessment Checklist for Seniors with Limited Ability to Communicate-II (PACSLAC-II) [56]. These observer-based behavioral pain assessment measures have an extremely important place in the toolkit of assessment measures for individuals with cognitive limitations and impairments.

Mentally Ill Patients

In patients with schizophrenia, a decreased or impaired pain sensitivity has been reported since the early works of Bleuler and Kraepelin. The mechanism underlying this effect is poorly understood, as hypoalgesia in these patients cannot be solely explained by the effects of antipsychotic drugs [57]. One explanation for the denial of pain and low pain ratings might be the fact that the disease overwhelms the patients' thought processes (e.g., hallucinations, intrusive thoughts), thus shifting their focus away from pain. Negative symptoms of schizophrenia including lack of drive could consequently lead to failure to seek medical help. It remains unclear whether hypoalgesia is present in both stable and acute phases of psychosis [58]. Another explanation is that hypoalgesia constitutes a trait or endophenotype which is associated with the conditions independent of psychotic symptoms [59]. The pain assessment in patients with schizophrenia should not differ from mentally healthy individuals, although one should always bear in mind that patients could deny pain even in obviously painful situations or diseases [60]. Pain reports should be always taken seriously as pain is almost never experienced as a hallucination [61].

In patients with posttraumatic stress disorder (PTSD), various studies have reported both decreased and increased pain sensitivity [60]. The presence of high peritraumatic pain levels is associated with the development of PTSD [62]. Therefore, after traumatic events, a comprehensive pain assessment should be carried out. Chronic pain and PTSD often coexist, with PTSD commonly being underdiagnosed in this setting. Screening individuals with chronic pain for PTSD is therefore recommended [60]. Patients with both diagnoses tend to have increased pain sensitivity. The most often proposed mechanisms for this comorbidity are shared vulnerability (e.g., elevated anxiety sensitivity may be a predisposing factor for both conditions) and mutual maintenance (chronic pain maintains or exacerbates symptoms associated with PTSD) [63].

Other Challenges of Pain Measurement

Gender-Specific Aspects of Pain

Several large-scale epidemiological studies have consistently revealed a higher prevalence of several chronic pain conditions in women. These include migraine, chronic

tension-type headache and temporomandibular disorders, fibromyalgia, irritable bowel syndrome, and interstitial cystitis. Women report higher levels and longer duration of pain, as well as more frequent pain in more areas of the body than men. The underlying mechanisms for those differences have not yet been elucidated completely; it has been suggested that an interaction of biological, psychological, and sociocultural factors probably contributes to these differences [64, 65]. Multiple studies have also examined sex differences in experimentally induced pain, concluding that women display greater sensitivity to most forms of experimentally induced pain (with the exception of ischemic pain) compared with men [64, 66, 67].

A broad array of mechanisms likely contributes to the observed sex differences in the prevalence and experience of pain. Estrogens have been shown to play an important role in the observed differences between males and females; estrogen plasma level changes (i.e., during the menstrual cycle) may be associated with increased pain [68]. Exogenous estrogens have also been associated with clinical pain; postmenopausal women using hormone replacement have shown increased risk for back pain [69]. Sex differences could furthermore result from differences in the distribution, expression, or sensitivity of opioid receptors in brain regions involved in nociceptive processing. Men demonstrated larger magnitudes of μ-opioid system activation than women in the anterior thalamus, ventral basal ganglia, and amygdala; during pain, women showed reductions in the basal state of activation of the μ-opioid system in the nucleus accumbens, an area previously associated with hyperalgesic responses in animal studies. These discrepancies in pain-related μ-opioid receptor binding may not only depict sex differences in basal pain perception but also contribute to variations in sensitivity to opioid medications [64, 70].

Cultural Considerations

Various ethnic groups clearly express pain and suffering in their own unique language for pain; different social and cultural groups have specific methods for signaling pain both verbally and nonverbally. Pain expression in a given culture appears to depend, for example, on whether the culture approves or disapproves the display of emotions or verbal expressions in response to pain or injury. Some cultural groups expect an intense display of emotion in the presence of pain, but others value stoicism, restraint, and playing down the pain [71]. When a language barrier is present, pain assessment and providing good quality of care can be challenging. This correlates with the finding that minority populations receive inadequate care in comparison to the general population, including being less likely to receive pain medications including opioids, receiving lower doses of pain medications, and having longer wait times in the emergency department [72].

Some of the assessment tools covered here have been evaluated cross-culturally and are currently in broad use around the world. For example, the reliability and validity of the Faces Pain Rating Scale (FPS-R) have been established in many different cultural groups; the test is available in approximately 30 languages. The Brief Pain Inventory (BPI) has also been shown to have a high degree of validity and reliability in cancer patients from outside the USA [60]. Although pain expression may differ substantially among cultures, the impact of pain on life quality appears to be quite similar. Therefore, clinicians are strongly encouraged to seek information about the cultural background of their patients both through exploration with the patients and using the available literature. Giger and Davidhizar provide information about the health- and illness-related beliefs of different cultures [60, 73].

Pain Memory

Research demonstrates that memory for pain experiences is systematically influenced by a number of cognitive heuristics and biases that appear to be nearly universal in humans. Pain memories appear to rather relate most strongly to specific aspects of the experience; memories for the severity of pain are highly influenced by the single most intense or severe experience of pain and by the last portion of the pain experience. This is known as the "peak-end" phenomenon, and it has been observed across a number of settings, such as surgical procedures [74]. Additionally, it has been suggested that pain-related negative affect influences both pain recall and future pain reporting [75]. Furthermore, it has been shown that present pain levels affect memory and may function as a point of reference when averaging pain [76]. One way to overcome these memory biases is the use of electronic pain assessment, such as the "painometer," a recent smartphone app for pain assessment for different pain intensity scales [77]. Another method may be by asking patients about their average pain on "good days" (for pain at its least), which might be a good reflection of typical pain experiences. Pain-related memory appears to be a valuable target for interventions in clinical practice, as it appears to contribute in the maintenance of chronic pain [78].

Disability Assessment

Disability according to the International Classification of Functioning Disability and Health (ICF) serves as an "umbrella term for impairments, activity limitations, or par-

ticipation restrictions" [79]. Chronic low back pain is an extremely common condition with global significance that influences the levels of activities and participation, therefore potentially leading to disability. A recent review indicated that in patients with chronic pain, the noted self-reported levels of physical activity were significantly lower than those objectively measured [80]. Therefore, quantitative assessment of physical activity appears to be necessary as an adjunct to disability questionnaires. Movement registration seems to be preferred because of its higher objectivity in comparison with self-report assessments [81]. In order to provide a brief overview, we selected two self-reported questionnaires that are specific to low back pain and that have been evaluated for their relevant psychometric properties in patients with low back pain [82].

The Roland Morris Disability Questionnaire (RDQ) The RDQ was developed in 1983 for use in primary care research to assess physical disability due to low back pain (LBP). It contains 24 items that represent the execution of daily physical activities and functions that may be affected by LBP, such as housework, sleeping, mobility, dressing, appetite, irritability, and pain severity. The total score is calculated by adding up the "yes" answers or the items checked by the patient. The RDQ is the most comprehensively validated measure in low back pain. Other strengths of the Roland Morris Disability Questionnaire include its ease of use and acceptability by users and its availability in a variety of different languages, many of which have been validated [82, 83].

The Quebec Back Pain Disability Scale (QBPDS) This self-completed questionnaire measures the level of functional disability. It contains 20 items representing elementary daily activities that patients with back pain might perceive difficult to perform. Items can be classified into six domains of activity affected by back pain: bed/rest, sitting/standing, ambulation, movement, bending/stooping, and handling of large/heavy objects. The total score is calculated by adding up the scores of each item. Scores range from 0 (no disability) to 100 (maximal disability). The QBPDS is short, is easy to use, and has good clinimetric properties (reliability, validity, ability to detect changes) and is available in several validated translated versions [84].

Summary and Recommendations

Pain assessment is a crucial step in pain management. In this chapter we attempted to provide essential information on pain assessment tools and methods. Any assessment of pain should include at least one self-report measure, and it is often beneficial to use either multiple measures or a multidimensional measure of pain (e.g., the short form of the MPQ, which includes both verbal descriptors and a VAS). Pain is a multifactorial experience rather than a simple physical sensation, which makes the use of multiple measures or a multidimensional measure of pain (e.g., MPQ or the SF-MPQ) necessary, especially in the elderly. Behavioral observations can also be very helpful in the pain assessment of nonverbal patients (e.g., evaluating pain-related facial expression using the FACS) and infants (e.g., using the NIPS scale). In other patient populations, observational tools should serve as adjunctive measures and should not be used as a substitute for self-report measures. In children the use of the Faces Scale, the Oucher Scale, or a quantitative scale, e.g., a VAS (for children older than 5 years) is recommended. In addition, cultural differences, gender, memory biases, cognitive function, and psychiatric comorbidities should be taken into consideration when assessing pain. Alongside these factors, a pain assessment should be selected after carefully considering its strengths and limitations. Work still continues in this area, with ongoing evaluation of more sophisticated measurement approaches or biomarkers of pain assessment.

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Part III

Clinical Evaluation

History and Physical Examination

7

Gary I. Polykoff and Jaleesa Jackson

Key Points

- Obtaining a careful history and physical examination is essential to the diagnosis of spine pain.
- It is important not to ignore potential red flags of spine pain, which can have serious consequences.
- A thorough knowledge of neuroanatomy is an invaluable tool when determining the etiology of spine pain.

Case Presentation

A 37-year-old right-handed healthy female with complaints of left-sided neck and low back pain (LBP) suffered a motor vehicle accident (MVA) 6 months ago. The patient was a restrained driver alone in a sedan at a full stop on traffic light and car was rear-ended by another sedan. No loss of consciousness reported at that time. She remembers being pushed forward and backward with no direct impact on the body. Within the next few days, she reported pain on the left side of neck and lower back without radiation. She was seen by her primary care physician (PCP) and received a prescription for ibuprofen and cyclobenzaprine with some relief. In 2 weeks she started reporting additional symptoms of tingling in left hand fingers and low back pain radiating to posterior thigh. She had no history of neck or low back pain in the past. She was seen again by her PCP with referral for cervical and lumbar spine X-rays, which were done and reported with minimal degenerative changes in the spine and straightening of cervical lordosis. During a follow-up, the patient was referred by the PCP for physical therapy (PT). After 8 weeks of PT, she had some improvement in the neck and LBP, still with intermittent tingling in left hand fingers and pain to the left posterior thigh. She also reported sleeping problems secondary to pain.

Patient is back to work as a legal secretary and has a legal representation for injuries after her MVA.

Pertinent physical exam: Posture with the neck and shoulders protracted forward. Palpation of the neck notable for tenderness over cervical paraspinal, upper trapezius, and levator scapulae muscles on the left with active trigger points and reproducible tingling to the left hand. The active ROM in the neck is close to functional with pain to right-side rotation and left-side bending.

Examination of the lumbar spine with mild tenderness over the lower lumbar paraspinal muscles on the left, extending to the sacroiliac (SI) joint. Palpation of the left SI joint with tenderness and reproducible pain to left posterior thigh. Patrick's test is positive. Neurologic examination is intact. Spurling's sign is negative, though reproduces pain radiation to the left scapula.

Assessment: A 37-year-old right-handed female with chronic neck pain with facetogenic and myofascial components, same as chronic LBP with facetogenic and SI joint dysfunction components on the left. The condition is exacerbated with sleeping problems secondary to pain.

Her condition appears to be related to a whiplash-related injury, sustained during the described above MVA.

Introduction

A careful history and physical examination are of primary importance in the evaluation of a patient with spine pain and related symptoms. It can be the difference between sending a patient home with a conservative treatment plan and admitting the patient for an immediate evaluation and possible surgery. The history and physical examination can determine if an expensive evaluation is necessary immediately or whether conservative treatment is appropriate first.

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Spine pain is a common problem throughout the world and is a significant cause of pain and loss of function. Lifetime prevalence estimates are as high as 84% for back pain and 67% for neck pain. Low back pain (LBP) is a leading cause of disability, with lost wages estimated at over $200 billion in 2002–2004. At any one time, about 5% of the US population has sufficient neck pain to cause disability [1].

Although the likelihood of defining a precise cause of neck and back pain is low, if the etiology and structural source can be determined, they may be valuable in directing treatment [2]. Patient history serves to identify red flags and yellow flags, whereas the physical examination, guided by the history, serves primarily to confirm those suspicions. Careful history and physical examination are essential in the diagnostic evaluation of patients with spine pain. During the history and physical examination, the clinician must be cognizant of signs or symptoms that may indicate a more serious disorder by attending to red flags and yellow flags. The differential diagnosis of neck and back pain is extensive, and although most of the pain is benign and self-limiting, the real challenge to the clinician is to distinguish serious spinal pathology or nerve root pain from nonspecific spine pain. The etiology is usually multifactorial with involvement of muscles, ligaments, discs, nerve roots, and zygapophyseal (facet) joints.

Cervical Spine

History

When taking a history, the presence of multiple red flags should raise suspicion and indicate the need for further investigation (Table 7.1).

Although red flags listed below have not been specifically formulated for patients with neck pain, low back pain red flags are commonly applied. Red flags and yellow flags identified by history or physical findings indicate the need for further evaluation with laboratory tests or imaging. These flags are listed in Tables 7.2 and 7.3. In any given patient, associated social, psychological, and emotional factors must be considered in addition to, and sometimes more than, organic factors.

Table 7.1 Possible risk factors and promoters for chronic neck pain

Number of children
Poor self-assessed health
Poor psychosocial status
Past history of chronic low back pain
Past history of neck injury (even a remote)
Dissatisfaction with work
Work-related stress
Workers' compensation disability

Based on materials and data from Croft et al. [3–5]

Table 7.2 Red flags for occurrence of lower back pain (also applicable to neck pain)

Fever
Unexplained weight loss
History of cancer
History of violent trauma
History of steroid use
Osteoporosis
Aged younger than 20 years or older than 50 years
Failure of pain to improve with treatment
History of alcohol or drug abuse
History of HIV
Lower extremity spasticity
Loss of bowel or bladder function

Based on materials and data from Haldeman [7]

Table 7.3 Yellow flags for occurrence of lower back pain (also applicable to neck pain)

Individual factors
Age
Physical fitness
Strength of neck muscles
Smoking
Psychosocial factors
Stress
Anxiety
Mood/emotions
Pain behavior
Occupational factors
Manual labor
Bending and twisting
Whole-body vibration
Dissatisfaction with job and work relationships

Based on materials and data from Haldeman [7]

When taking a history from patients complaining of neck pain, a few basic qualities of the pain should be elicited, including location, radiation, severity, alleviating factors, aggravating factors, onset, and associated symptoms.

Location

Is the pain in the upper, middle, or lower cervical spine? Is the pain over the spinous processes or over the paravertebral muscles? Is the pain unilateral or bilateral?

Radiation

Does the pain radiate, and if so, where does it radiate? Not only can cervical radiculopathy cause radicular pain but muscle irritation and facet-mediated pain may also cause referred pain in the upper extremities [6].

Severity
Extremely severe pain could be associated with several conditions, including neuralgic amyotrophy, radiculopathy, or cancer.

Alleviating Factors
What makes the pain better? A little known clinical sign is the abduction relief sign, in which abduction of the ipsilateral arm over the head may improve the pain in cervical radiculopathy (patients may even say they sleep in that position) [8]. Neck pain is typically reduced when patients are recumbent, but if the pain is not reduced by recumbency, then vertebral column infections and metastatic cancer should be considered [9].

Aggravating Factors
What makes the pain worse? Pain that worsens when patients turn and look ipsilateral to the pain can be associated with facet-mediated pain or radiculopathy. Pain with contralateral neck motion can be the result of muscle strain or other myofascial pain. Pain that worsens with coughing, sneezing or straining may be associated with discogenic or radicular pain, as a result of increase in the intrathecal pressure.

Associated Symptoms
Is there also numbness or tingling in an arm or hand? The presence of arm or hand paresthesias along with neck and upper extremity pain may be indicative of cervical radiculopathy, neuropathy, or brachial plexopathy. However, it is common for patients to have mechanical neck pain with coexisting carpal tunnel syndrome. Patients with brachial plexopathy can present with severe shoulder and upper extremity pain, which is then followed by significant weakness and atrophy. These patients do not frequently present with neck pain or worsening of symptoms with head/neck movement. On the basis of history alone, it can be difficult to distinguish brachial plexopathy from cervical radiculopathy [5].

Onset
When did the pain start? Details about the onset may help determine any sentinel events associated with the pain. Identifying the onset will also help determine the acuteness of the pain and its relationship to trauma (e.g., within 24 hours of a motor vehicle accident). Trauma, heavy lifting, repetitive lifting, or long automobile rides may cause radiculopathy [5].

Nighttime Symptoms
Does the pain awaken patients at night and do patients wake up with neck pain in the morning? Any of the possible causes of pain can awaken patients at night, but neck position during sleep must be carefully considered. Do patients use a pillow with good neck support?

Is there pain in the thoracic and lumbar spine? Patients with ankylosing spondylitis may present with nighttime neck and back pain with reduced lateral mobility and an elevated erythrocyte sedimentation rate. Is there stiffness, especially in the morning? Excessive morning stiffness can be present with ankylosing spondylitis as well as rheumatologic conditions, such as polymyalgia rheumatica.

Is there weakness, and if so, where? Potential neurologic causes of weakness include cervical radiculopathy, neurologic amyotrophy, and spinal cord tumor. Weakness in the lower extremities may indicate cervical spondylosis associated with spinal cord compression, tumor, syrinx, or other causes of myelopathy.

Is there bladder or bowel dysfunction, which would also be consistent with cervical spinal cord involvement [10]?

Is there pain in the lower limbs? Diffuse aching or burning pain may be associated with cervical cord compression [10]. Differentiating peripheral neuropathy, cauda equina syndrome, and cervical myelopathy purely on the basis of the history can be difficult if not impossible.

Previous Testing and Treatment
Which diagnostic tests have been performed? Which treatments have been completed and were they helpful? This information helps determine which diagnostic tests may still be indicated and provides a basis for a treatment plan.

What pain medications are patients taking now and in the past, and are they helping relieve the pain? Have patients been evaluated and treated with a physical therapist?

Past Medical History and Review of Systems
Do patients have a history of coronary heart disease, gastroesophageal reflux disease, or hypertension? If the neck pain radiates to the left arm, is worsened with activity, and improves with rest, then have patients had a cardiac workup? A history of hypertension may preclude the use of some medications such as nonsteroidal anti-inflammatories (NSAIDs) or bisphosphonates. Gastrointestinal conditions may also preclude use of NSAIDs.

Have patients experienced weight loss or decreased appetite, which could be caused by cancer or a metastatic disease? Are patients taking any lipid-lowering medications, which could cause aching as a complication? If patients are women of childbearing age, then are they pregnant or breastfeeding? This information is crucial in defining testing and treatment limitations. Are patients suffering from depression or anxiety that could be exacerbating symptoms or making treatment difficult? Home or occupational stress is often associated with disability from neck pain [2].

Social History
Do patients have a history of illicit drug abuse or addiction to prescription medications? Are patients currently working or on disability? Neck pain is commonly encountered in jobs requiring prolonged posturing either at a desk or on an

assembly line [11]. Is this a job-related injury? Is legal action pending? If this is a worker's compensation case, then is the case still open? In patients whose accident or injury occurred several months before the initial visit, the consultation may be motivated by legal purposes rather than by desire for diagnosis and treatment. Prospective studies have demonstrated that psychosocial factors are important in patients with whiplash injuries [11].

Smoking cigarettes is associated with an increased risk of spine pain [12]. It is also important to inquire about patients' social support network, including family and friends.

Physical Examination

The basic elements of the physical examination of the neck include inspection, palpation, range of motion, and a neuromuscular examination.

General Appearance

Do patients seem to be in pain? Do patients seem calm, in no distress, and yet reporting terrible pain (possible nonorganic origin of the pain) [10]?

Inspection

The muscles of the neck, upper back, and arms should be inspected for atrophy. Is the neck laterally flexed and rotated, as in torticollis? Examine the shoulder for medial or lateral winging or drooping, which may occur with neuralgic amyotrophy, C6 or C7 radiculopathy, or long thoracic neuropathy. Posture is an important factor in causing neck pain. An exaggerated dorsal kyphosis (round back) places the head in front of the center of gravity, increasing the cervical lordosis. The weight of the head in this position is borne by the zygapophyseal (facet) joints and can cause pain [13].

Range of Motion

Range of motion of the cervical spine should be evaluated actively and passively. Is there any loss in range of motion with lateral bending or lateral rotation asymmetric? Is pain associated with neck movement?

Palpation

Examine for tenderness in the cervical area muscles. Is there tenderness at the base of the skull near the insertion of the cervical spine muscles? Potential causes are tendonitis or occipital neuritis. Palpation and percussion of the neck/cervical spine typically have low yield with regard to identifying a specific process.

Neurologic Examination

The traditional neurologic examination for patients with neck pain includes individual muscle group testing of the upper (and at times lower) extremities, a sensory examination concentrating on the dermatomes of the upper extremities, an assessment of deep tendon reflexes in the upper (and at times lower) extremities and special tests.

Manual Muscle Testing

Manual muscle testing should be performed, at least, in the upper extremities in the antigravity position using techniques described by the Medical Research Council (MRC) to allow detection of minimal weakness [14].

One commonly accepted scale is the 0–5 grading system outlined in the MRC guidelines, with 0 being no movement, 3 representing antigravity strength, and 5 representing normal strength [13]. The examiner should try to determine if the patient is applying full effort; ratcheted, give-way weakness is suggestive of less than full effort. It may be helpful to test the asymptomatic side first to avoid pain and to help the patient understand the motion before testing the painful extremity. In cervical radiculopathy, manual muscle testing is thought by some to be the most important component of the examination to localize the involved nerve root [15]. Upper extremity weakness could be caused by cervical radiculopathy, brachial plexopathy, peripheral nerve entrapment neuropathy (e.g., median neuropathy, radial neuropathy, or ulnar neuropathy), poor patient effort, or pain from a tendinopathy (e.g., shoulder impingement or lateral epicondylitis).

Reflexes

As with much of the physical examination, symmetry of muscle reflexes implies normalcy. The biceps reflex may be absent or diminished in a C6 (or C5) radiculopathy, a brachial plexopathy, or a musculocutaneous neuropathy. The triceps may be absent or diminished in a C7 radiculopathy, a brachial plexopathy, or a proximal radial neuropathy. The brachioradialis reflex may be absent or diminished in a C5 or C6 radiculopathy, a brachial plexopathy, or a radial neuropathy. Lower extremity reflexes may be considered, as well as the Hoffman and Babinski reflex. Increased reflexes and the presence of a Hoffman or Babinski reflex suggest myelopathy, and the examiner should evaluate further for upper and lower extremity weakness, bowel or bladder incontinence, spasticity, and ataxia.

Sensation to Light Touch and Pin Prick

If peripheral neuropathy is suspected, both the upper and lower extremities should be examined. If cervical myelopathy is suspected, the upper extremities and torso should be evaluated for a level of diminished or absent sensation. Decrease or alteration of sensation with sensory testing can suggest radiculopathy, brachial plexopathy, peripheral neuropathy, peripheral nerve entrapment, or myelopathy. When testing sensation in the hand, the cervical dermatomal map

reveals that the tip of the thumb is C5 innervated, the thumb and index finger are C6 innervated, the index and long finger are C7 innervated, and the ring finger and little finger are C8 innervated. Each numbered cervical root passes through the foramen above the numbered cervical vertebra (e.g., the C6 spinal nerve exits through the foramen between the C5 and C6 vertebrae). As such, a C5–C6 intervertebral lateral disc protrusion may encroach on the C6 spinal nerve emerging through the C5–C6 intervertebral foramen, potentially causing radiating pain from the neck to the thumb [13]. Peripheral nerve sensory innervation in the hand includes median nerve innervation of the palmar aspect of the thumb, index finger, and long finger; ulnar innervation of the lateral half of the ring finger and little finger; and radial nerve innervations of the dorsum of the thumb index finger and long finger [2].

Several other tests, such as the Spurling maneuver, can be particularly helpful in evaluating patients with neck pain. It involves passively tilting the head toward the side of the painful upper extremity, extending the neck, and then applying a downward compressive force [16]. If this induces radiating pain and paresthesia into the symptomatic extremity (not just in the neck), then cervical radiculopathy is suggested. A positive Spurling maneuver has a high specificity for cervical radiculopathy, but unfortunately, it has a low sensitivity [10, 15].

Shoulder Pathology

Patients commonly perceive shoulder impingement as neck pain, so an evaluation of the shoulder can be helpful in determining the pain generator. A basic evaluation of the shoulder includes testing the passive and active range of motion of the shoulder in flexion, extension, abduction, adduction, internal rotation, and external rotation; examining for tenderness in the biceps tendon, rotator cuff tendons, subacromial bursa, and acromioclavicular joint; and testing resisted shoulder abduction.

Provocative shoulder tests, such as the Empty can test, the Drop arm test, the Hawkins-Kennedy test, the O'Brien test, and the apprehension and relocation tests, may be helpful in distinguishing shoulder pain, but the diagnostic accuracy of each maneuver to evaluate for a specific shoulder pathology is limited [17]. A more comprehensive discussion of shoulder versus neck pain requires a more detailed discussion.

Isolated strength testing of the cervical spine can also be performed. Previous studies have shown decreased cervical flexor strength in subjects with neck pain compared with healthy controls [18]. Cervical flexion strength can be determined in the sagittal, right-rotated, and left-rotated positions with the chin tucked and subject in the supine position [18, 19]. Extensor strength can also be determined with patients in the prone position [18].

Neuromechanical special tests, as with low back and lower extremity pain, are useful in the assessment of patients with neck and upper extremity pain:

- *Spurling test*: The head is inclined toward the side of the painful upper extremity and then compressed downward by the examiner. Pain and paresthesia that radiate into the symptomatic extremity strongly suggest nerve root compression, usually secondary to disc herniation. (It should be noted that lateral head movement away from the symptomatic extremity sometimes can accentuate pain and paresthesia in the symptomatic upper extremity, secondary to stretching a compressed nerve root.)
- *Traction ("distraction") test*: Lifting (traction) on the head may relieve cervical spinal nerve compression and reduce upper extremity pain and paresthesia.
- *Valsalva test*: As with low back pain, the Valsalva maneuver with resultant increased intrathecal pressure can accentuate neck and upper extremity symptoms.
- *Lhermitte's test*: In patients with myelopathy that affects the posterior columns, neck flexion can produce paresthesia, usually in the back but sometimes into the extremities. As is familiar to neurologists, Lhermitte's sign is most commonly associated with an inflammatory process, such as multiple sclerosis, but it is sometimes noted with spinal cord compression.
- *Adson's and hyperabduction tests*: Long used in the evaluation of suspected thoracic outlet syndrome, these tests are nonspecific and unreliable. With the patient sitting erect and the upper extremities at the side (Adson) or the symptomatic upper extremity abducted and extended (hyperabduction), the radial pulse is palpated. The test results are positive if the pulse disappears and paresthesia develops in the hand of the symptomatic extremity.

Cervical Spine Conditions

Cervical Radiculopathy

Cervical radiculopathy is any dysfunction of a nerve root emerging at the level of the cervical spine, most often but not always associated with disc herniation. Radiculopathy is a very wide term, nonspecific, but some authors use this term to talk about pain, weakness, or numbness in a specific radicular pattern.

Dysfunction of the nerve root can be secondary to:

- Internal (non-compressive) causes (inflammation, nerve tumors like schwannomas or neurofibromas)
- External causes (compression due to a herniated disc, neuroforaminal narrowing, tumors, fibroproliferation,

hematomas, and trauma; irritation due to inflammatory mediators such as substance P, bradykinin, potassium, and histamine; or changes in vascular supply)

Heavy lifting, neck trauma (sports, motor vehicle accidents, etc.), and smoking have been associated with an increased risk for cervical radiculopathy [19–21]. Adopting good sleep postures, good sleep habits, stress reduction skills, as well as good ergonomic postures are paramount in treating active symptoms and reducing chance of recurrent symptoms.

History

History taking is an important component of evaluation of cervical radiculopathy as this is still largely a clinical diagnosis. Information regarding characteristics of the pain, its distribution, and aggravating and relieving factors is important, in addition to ruling out less common causes of radiculopathy. The symptoms may have a specific pattern depending on the nerve root compromised (Table 7.4). However, sometimes the pain is not limited to just the innervated skin (dermatome) and can be perceived in other innervated structures including muscles, joints, ligaments (sclerotome), as well as the affected nerve root (dynatome) [20–22]. While history taking, it is of utmost importance to evaluate for symptoms of myelopathy, such as subtle loss of hand dexterity, balance dysfunction, bowel or bladder incontinence, or sensory/motor deficits in upper and/or lower extremities. Should history (and then physical examination) indicate involvement of more than one root level, cervical polyradiculopathy should be suspected. The most common cause of it is degenerative cervical spondylosis (which again would prompt an assessment of spinal cord dysfunction). Other causes are spinal cord tumors (ependymoma, leptomeningeal metastases, etc.), inflammatory disorders (such as cervical radiculoplexus neuropathy, Lyme disease, etc.), or root avulsion (in the setting of trauma).

Common differential diagnosis for cervical radiculopathy includes the following:

- Brachial plexitis
- Cardiac pain
- Cervical myelopathy
- Cervical disc injury
- Cervical facet syndrome
- Complex regional pain syndrome
- Herpes zoster
- Intraspinal and extraspinal tumors
- Myofascial pain syndrome, cervical
- Nerve entrapment syndromes
- Parsonage-Turner syndrome
- Pancoast syndrome
- Rotator cuff injury
- Thoracic outlet syndrome
- Vasculitis

Physical Examination

Physical examination involves observation and posture evaluation, cervical range of motion evaluation, musculoskeletal palpation, neurological exam, and special testing. Neurological exam includes strength testing, sensory exam, and reflex testing including evaluation of upper motor neuron signs. Red flags that would point toward myelopathy include sensory and motor deficits in multiple root levels, bilateral upper extremity or upper and lower extremity involvement, as well as positive upper motor neuron signs (upgoing toes with Babinski sign testing, positive Hoffman's sign, hyperactive reflexes). The pattern of dermatomal and myotomal changes based on the root level is as follows:

- C5 radiculopathy: pain in the medial scapular border and lateral upper arm; weakness of the deltoid, supraspinatus, and infraspinatus; sensory loss in the lateral upper arm; and changes in the supinator reflex.
- C6 radiculopathy: pain in the lateral forearm, thumb, and index finger; weakness of the biceps, brachioradialis, infraspinatus, and wrist extensors; sensory loss of the thumb and index finger; and changes in the biceps and/or brachioradialis reflex.

Table 7.4 Cervical radiculopathy symptoms

Root	C5	C6	C7	C8
Pain	Neck, shoulder, interscapular	Neck, shoulder, interscapular, radial forearm	Neck, interscapular, forearm, chest, hand	Neck, medial forearm, ulnar hand
Motor weakness	Shoulder abductors, elbow flexors, external shoulder rotators	Elbow flexors, external shoulder rotators, forearm supinators, forearm pronators, shoulder abductors, wrist extensors, shoulder protractors	Elbow extensors, forearm pronators, finger extensors	Wrist flexors, finger and thumb abductors, adductors, extensors, and flexors
Decrease in sensation	Tip of thumb, lateral shoulder	Thumb and index finger	Thumb, index, middle, ring fingers in some combination	Little and ring fingers
Reflex (diminished or absent)	Deltoid	Biceps, brachioradialis	Triceps	Finger flexor

Based on materials and data from Honet and Ellenberg [2]

- C7 radiculopathy: pain in the medial scapula, posterior arm, and dorsum of forearm and third finger; weakness of the triceps, wrist flexors/extensors, and finger extensors; sensory loss in the posterior forearm and third finger; and changes in the triceps reflex.
- C8 radiculopathy: pain in the ulnar side of the forearm and fifth finger; weakness of thumb flexors, abductors, and hand intrinsics; and sensory loss in fifth finger [20, 21]. While this distribution of findings is generally accurate, Slipman et al. have shown that the pain referral patterns are highly variable from person to person [23].

The most common special test used in evaluation of cervical radiculopathy is the Spurling's maneuver, which includes end-range neck extension, rotation, side bending, and axial compression. Wainner et al. found that with the cluster of involved cervical rotation less than 60°, positive distraction test, positive Spurling's test, and positive upper limb tension test (ULTT), the posttest probability of cervical radiculopathy is 90% [24]. ULTT is performed with the patient supine and the examiner introducing scapular depression, shoulder abduction, forearm supination, wrist and finger extension, shoulder lateral rotation, elbow extension, and contralateral then ipsilateral cervical side bending. This is also known as the brachial plexus tension or Elvey test with median nerve bias. While not applicable to testing for cervical radiculopathy, it is important to keep in mind that by changing the positions of the shoulder, elbow, and wrist, the ulnar and radial nerves can also be assessed. A note should be made that if sensory examination reveals allodynia, hyperalgesia, or sensory after effects in the setting of chronic radicular pain, a component of central and peripheral sensitization should be considered.

Cervical Spinal Stenosis

Acquired cervical stenosis results from age-related degenerative disc and facet disease with associated uncinate process hypertrophy, ligamentum flavum thickening, and buckling of the posterior longitudinal ligament. Congenital spinal stenosis is associated with short pedicles and bony anomalies of the lateral masses and laminae.

Cervical spondylosis is a frequent finding in asymptomatic adults with prevalence rates of 25% of adults <40 years, 50% of adults >40 years, and 85% of adults over 60 years being reported [25]. The prevalence rate of cervical stenosis in the US adult population, as derived from one large cadaveric study, was estimated to be 4.9% [26].

Risk factors for developing cervical stenosis include athletic participation in American football, soccer, rugby, and horseback riding, as well as major trauma and dystonic cerebral palsy.

History

In addition to asking questions regarding pain and numbness, the physician should query patients on subtle changes in gait, balance, and loss of fine motor skills, which may suggest myelopathy. Bowel and bladder dysfunction are typically late manifestations. Physicians caring for collision sport athletes need to inquire about cervical spine range of motion and tackling technique, because early loss of cervical extension and shoulder depression during tackling are associated with an increased risk for cervical neuropraxia and/or nerve root and plexus injury.

Physical Examination

Cervical spine range of motion, muscle stretch reflexes, and strength should be routinely tested in all patients suspected of having cervical stenosis. The Spurling maneuver may reproduce radicular pain and/or paresthesias, which may be relieved by asking the patient to elevate the affected arm overhead (i.e., Bakody sign). A Babinski sign, Hoffman sign, ankle clonus, and Lhermitte phenomenon should be documented, if present. Sensory ataxia secondary to posterior column dysfunction is assessed by performing a Romberg test.

Cervical (and Thoracic) Facet/Zygapophyseal Joint Arthropathy

Cervical and thoracic zygapophyseal joint arthropathy refers to degenerative changes in the zygapophyseal joints (facet joints, z-joints) of the spine, which may result in facet-mediated head, neck, and back pain. It results from osteoarthritis of the z-joints, and it is a component of spondylosis, spondylolisthesis, trauma, and whiplash. Z-joints are considered part of the third or posterior column of the spine and usually deteriorate after the first or anterior column, involving the intervertebral discs. The facet joints are often referred to as part of the "posterior elements." There are no symptoms specific/unique to facet-mediated neck/back pain. Patients may present with nonspecific symptoms which include deep/achy pain localized to paravertebral region (unilateral or bilateral) that may be exaggerated by hyperextension, twisting, side bending, and torsional loads. Rarely is the pain axial or central. Patients may also report headaches or morning neck stiffness. Facet arthropathy pain is largely progressive, except when caused by trauma or whiplash injuries (Fig. 7.1).

History

Patients may present with specific referral patterns to the occiput, neck, and upper back, which may correlate to specific facet joints. Published sclerotomal pain maps identify these common referral areas; however nonspecific in terms of pathology and are substantially variable in spinal-level

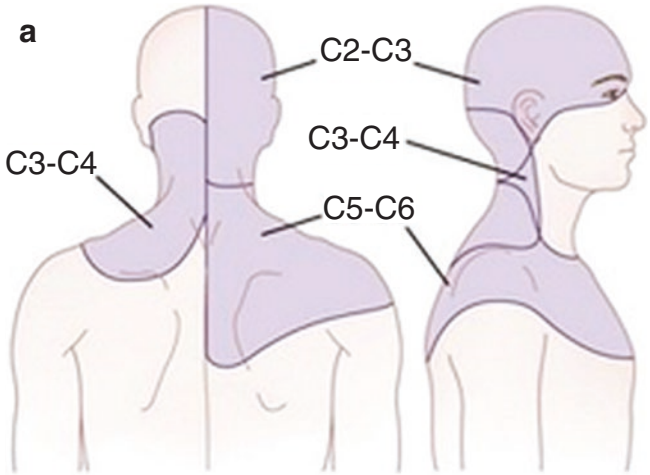

Fig. 7.1 Cervical facet pain referral patterns. The upper cervical facets are a common source of occipital pain and headache, while pain from the lower cervical facets tends to be felt in the lower neck and trapezius region. (Reprinted from Bogduk and Marsland [27], with permission from Wolters Kluwer)

overlap [28]. These findings should be interpreted with caution as other pathologies such as discogenic pain can produce similar pain patterns.

Physical Examination

Facet-mediated neck/back pain is largely a diagnosis of exclusion. There are no specific signs or special examination maneuvers/movements to aide in the diagnosis. Diagnosis is often guided by the absence signs that may suggest alternate etiologies, such as neurological impairment or radicular symptoms [29]. Numerous quality studies consistently fail to demonstrate a correlation between the popularized "facet-loading" maneuver (*pain upon extension and ipsilateral rotation*) and facet-mediated pain [30]. The only physical exam finding that appears to consistently correlate with facet arthropathy, and later successful treatment, is paraspinal tenderness, which has been shown to distinguish facet pain from discogenic back pain [30]. Manual spine examination, when used in conjecture with paraspinal tenderness, may also be a useful clinical tool [31]. Additional examination findings may include range of motion restrictions (specifically in flexion, extension, and rotation), cervical kyphosis (loss of normal lordotic curvature), and hypertonicity of anterior/middle scalenes, trapezius, and sternocleidomastoid.

Patients may assume a forward flexed kyphotic posture to alleviate pain and will likely have limited mobility in all planes [28]. Pain may be exacerbated by going from a sitting to standing position [32]. Upper cervical spine z-joint arthropathy can limit head rotation, causing difficulty with driving, and can hinder conversations in social situations. These impairments may lead to decreased quality of life and can contribute to depression, especially in elderly patients.

Cervical Whiplash Injury

Cervical whiplash is an injury to the cervical spine and supporting structures resulting from an acceleration-deceleration force.

Cervical whiplash injury has been reported with various impact mechanisms but most frequently occurs as the result of a rear-end or side-impact motor vehicle collision (MVC) typically caused by a rapid acceleration of the body with respect to the head, which results in a horizontal translation at the neck. Subsequently, a rapid correction causes compression, shearing, or tension forces on the cervical spine. Less often whiplash is associated with falls, violent collisions in contact sports, or diving. Experimental model suggests that "limit of harmlessness" for velocity change after rear-end collision is between 5 and 10 MPH. Photographs of involved vehicles are helpful in determining velocity change, although no correlation has been made between type of collision, velocity change, and prognosis [33, 34].

Cervical whiplash injuries are the most common injury observed after motor vehicle collisions. The annual incidence of acute symptoms due to a cervical whiplash varies across different countries and is estimated to be between 1 and 6 cases per 1000 population [35]. The prevalence of chronic whiplash pain is estimated to be 1% [35]. One case-control study across nine US states found that 45% of patients with chronic neck pain attributed their pain to a motor vehicle collision [36]. Cervical whiplash injuries have led to a significant socioeconomic cost in many countries leading to numerous attempts to discredit its existence [37]. Head restraints have significantly reduced the number of whiplash injuries related to rear-end collisions with integral (nonadjustable) headrests more effective than adjustable [38].

During the initial 100 ms after impact, the cervical spine is compressed from below, causing the lower cervical segments to extend, while the upper cervical segments are relatively flexed. This results in the cervical spine initially assuming an S-shaped curve prior to all of the cervical segments being forced backward into extension [39]. Multiple anatomical structures along the cervical spine are potentially injured as the result of a cervical whiplash event, including bones, ligaments, muscles, tendons, discs, and zygapophyseal joints (z-joint). Injury to the z-joint is widely believed to be the most common source of chronic pain after a cervical whiplash event [40].

History

Disease progression including natural history, disease phases or stages, and disease trajectory (clinical features and presentation over time):

- Up to two-thirds of people involved in MVCs will report neck pain and related symptoms immediately (within sev-

eral hours post-injury) with another third having a delayed symptom onset of up to 48 hours.
- Initial complaints often include neck and upper back pain. A constellation of other symptoms such as headache, dizziness, concentration and memory disturbances, upper limb weakness and paresthesias, and blurred vision are also frequently seen and have been called "whiplash-associated disorders."
- Subacute and chronic symptoms may also include fatigue, sleep disturbances, depression, and anxiety.
- Most injured patients experience rapid recovery after the acute event.
- After 12 months, 20–25% of patients remain symptomatic [41, 42].
- Detailed history of the collision including patient as driver versus passenger, side of vehicle that was involved, seat belt use, headrests, deployment of airbags, and involvement in litigation.
- Detailed history of initial injury including presence or absence of head injury, loss of consciousness, emergency department evaluation with images, and initial treatments.
- History of present illness and treatments including medications, injections, therapies, modalities, and trials of acupuncture and/or osseous manipulation.
- Determination of associated symptoms including referral of pain down an arm, new numbness or tingling in an arm, weakness, headache, or new gait abnormality.

Assess pre-injury functional status, pain symptomology, and psychological status as pre-accident whole body pain and general psychological distress have been associated with neck pain chronicity [42].

The Neck Disability Index [43] is a functional outcome measure designed as a checkbox questionnaire scored out of 50 and reported as a percentage. It is often used clinically and in research for acute and chronic neck pain. It has acceptable reliability with minimum detectable change of 5/50 for uncomplicated neck pain and up to 10/50 for cervical radiculopathy. It is interpreted as an interval measurement and has an inconsistent clinically important difference [44].

Physical Examination

Acute phase will most often demonstrate guarded range of motion in all planes, generalized neck, occipital and upper back tenderness, and a positive Spurling maneuver if nerve root irritation/injury is present. The presence of strength deficit, reflex asymmetry, or sensory abnormality should be assessed. Chronic whiplash without nerve root or spinal cord involvement will generally reveal more localized tenderness in the neck or upper back, cervical extension and rotation pain, and no focal neurological deficits.

Thoracolumbar Spine

History

The history is of critical importance in assessing patients with symptoms believed to be secondary to cervical and lumbar spine disorders, especially in persons with a nonfocal neurologic examination. The differential diagnosis is frequently based solely on the history in these patients.

Pain Profile

Onset In most instances, patients who present with a history of acute onset of low back pain have a history of preceding pain, often for weeks or months or longer. This is also the case in patients with the acute onset of radicular pain. The acute onset of lumbosacral radicular pain in the absence of any prior history of low back pain is the exception rather than the rule.

Quality Variable, nonradiating musculoskeletal back pain is often described as being deep and aching, whereas radicular pain is usually described as sharp, jabbing, or lancinating in quality.

Location Musculoskeletal pain is usually localized to the paraspinous regions. Lumbosacral pain tends to be maximal in the paraspinal regions, spreading at times to the flanks and into the buttocks. When lumbar roots are involved, the pain generally radiates into the lower extremity. In the case of lumbosacral radiculopathy, the pain usually radiates into one or both lower extremities. The distribution of the pain also can occasionally point to the specific root involved. For example, "high" lumbar (L2, L3) radiculopathic pain does not radiate distal to the knee, whereas the pain of an L4 radiculopathy can radiate to the medial leg distal to the knee. L5 and S1 radiculopathies tend to produce pain that radiates into the posterolateral thigh and posterolateral leg and often involves the foot. Pain may be maximum in the medial (L5 radiculopathy) or lateral aspect of the foot (S1 radiculopathy).

Duration Mechanical low back pain generally has a duration of days to weeks. Radicular pain often resolves more gradually over 6–8 weeks. An extensive neurodiagnostic evaluation is generally not necessary in this setting. A patient who presents with a history of chronic low back pain, however, requires a careful history to rule out a new problem superimposed over chronic symptoms that, in the proper setting, may require an immediate neurodiagnostic evaluation.

Severity As all clinicians recognize, the severity of pain is often difficult to interpret because it can be colored by several factors, including a patient's personality. Severe low back pain that is not relieved when the patient is recumbent

suggests metastatic cancer, pathologic vertebral fracture, or infection of a vertebra, disc, or the epidural space.

Time of Day Lumbar radiculopathy frequently present upon awakening in the morning. Nonradiating pain that tends to be dull during the day is often the result of mechanical disorders (e.g., muscle strain, degenerative disc disease, spondylosis). Tumors of the spine and spinal cord often produce pain that persists and occasionally increases in the supine position; patients with lumbar tumors may have increased pain in bed at night.

Associated Symptoms In the case of low back pain, the patient should be questioned about abdominal pain and intestinal or genitourinary symptoms.

Triggers Valsalva maneuvers (e.g., coughing, sneezing, and bearing down at stool) often transiently aggravate lumbosacral pain. Low back radicular pain is generally made worse by sitting and standing and often is relieved by lying supine. If pain persists or increases in the supine position, the possibility of spinal metastatic cancer or infection must be considered. In the case of lumbar canal stenosis, neurogenic claudication can be brought on by standing erect and walking.

Motor Symptoms In the face of pain, distinguishing between weakness and guarding by the history alone can be difficult. In the case of low back and lower extremity pain, however, weakness is suggested by a history of a foot slap when walking or of falls secondary to a lower extremity "giving way."

Although weakness is usually best appreciated on a neurologic examination, the history is a useful adjunct in helping to separate weakness from guarding secondary to pain.

Sensory Disturbances Patients with radiculopathy often report numbness, tingling, and even coolness in the involved extremity. At times, symptoms suggest dysesthesia and allodynia. The distribution of a sensory disturbance by history, particularly of numbness and tingling, may be even more useful in determining the presence and localization of a radiculopathy than the sensory examination itself.

Bladder and Bowel Disturbances Symptoms of a hypertonic bladder (i.e., urgency, frequency, nocturia, and incontinence of bladder [or occasionally of bowels]) are often found in association with cervical myelopathy. Sphincter disturbances also may appear with cauda equina compression and, when acute, always must serve as a warning of the need for urgent surgical intervention.

Risk Factors Although various risk factors have been associated with an increased incidence of low back pain, knowledge of these risk factors is not necessarily helpful in evaluating individual patients. Risk factors are better established for low back pain than neck pain, but many risk factors are common to both, including the following:

- Increasing age
- Heavy physical work, particularly long static work postures, heavy lifting, twisting, and vibration
- Psychosocial factors, including work dissatisfaction and monotonous work.
- Depression
- Obesity
- Smoking
- Severe scoliosis (80%)
- Drug abuse
- History of headache

Several other factors are commonly thought to increase the risk of low back pain but probably do not, including:

- Anthropometric status (height, body build)
- Posture, including kyphosis, lordosis, and scoliosis
- Gender
- State of physical fitness (although not a predictor of acute low back pain, fit individuals have a lower incidence of chronic low back pain and tend to recover more quickly from episodes of acute low back pain than unfit individuals)

The Pain Patient at Risk Although most patients who present with back pain do not need immediate diagnostic evaluation and initially should be treated conservatively, certain historical features should lead to the consideration of an immediate and thorough study of the patient with new-onset back pain with or without radiating pain into extremity. These historical features include the following factors:

- Age >50
- Body temperatures >38° C
- Neuromuscular weakness
- Significant trauma before the onset of pain
- History of malignancy
- Pain at rest in the recumbent position
- Unexplained weight loss
- Drug and alcohol abuse (increased risk of infection and possibly unremembered trauma)

Physical Examination

The experienced neurologist knows that the neurologic examination of the patient with low back pain can be altered by the pain itself. For example, when testing strength, guarding must be taken into account. Tendon reflexes may be sup-

pressed as a result of poor relaxation of a limb as a consequence of pain. Preparing the patient by explaining each step of the examination in advance may reduce anxiety and encourage relaxation, thereby reducing guarding and enhancing the reliability of the examination itself.

General Examination

The necessity for a general physical assessment in the patient who complains of back pain cannot be underestimated. The presence of a low-grade fever, for example, may signal infection that involves the vertebral column, the epidural space, or the surrounding muscle (e.g., psoas abscess). Inspection of the skin for lesions may yield diagnostic information. Changes in the rectal examination, including sphincter tone, anal "wink," and the bulbocavernosus reflex, may reflect changes in the spinal cord or cauda equina, whereas an abnormal prostate may lead to a diagnosis of prostate cancer with spinal metastases.

The abdominal examination may be particularly important. The presence of abdominal tenderness, organomegaly, or a pulsatile abdominal mass with a bruit in a patient with low back pain should immediately direct an urgent diagnostic evaluation, which may lead to a potentially lifesaving diagnosis, such as a leaking abdominal aortic aneurysm. In patients with low back pain and claudication, evaluation of the peripheral pulses in both lower extremities is essential to help distinguish neurogenic claudication from vascular claudication.

Musculoskeletal/Neurologic Examination

Inspection of the low back can be of value. The presence of a tuft of hair over the lumbar spine suggests diastematomyelia/spina bifida occulta. Percussion may produce pain over an infected area or at the site of a malignancy.

Palpation of the paraspinous muscles may demonstrate spasm as a cause, or accompaniment, of acute low back pain. The concept of spasm itself as a cause of back pain has been challenged.

Posture while standing may be altered by a herniated lumbar disc. Splinting with list away from the painful lower extremity is seen with lateral lumbar disc herniation, whereas list toward the painful side can be seen with medial herniation. Tilting the trunk to the side opposite the list can cause additional nerve root compression, with resultant accentuation of radicular distribution pain. Patients with neurogenic claudication secondary to compression of the cauda equina may tend to stand and walk with the trunk flexed forward, which reduces compression by widening the anterior posterior dimension of the lumbar canal. Walking with the trunk extended may accentuate the symptomatology. Lumbar spine mobility is usually reduced in patients with low back pain, but because there is such wide variability as a result of conditioning and age, a measurement of degrees of mobility is usually not useful. Evaluation of the gait is of fundamental importance to seeking, for example, evidence of:

- An antalgic gait that favors the side of a lumbar radiculopathy
- "Foot slap" (i.e., foot drop) secondary to weakness of dorsiflexors of the foot, found with an L5 radiculopathy
- Trendelenburg gait ("drop" of ipsilateral side of pelvis as foot is lifted), which signals proximal (unilateral or bilateral) lower extremity weakness

Neuromechanical special tests are an important adjunct to the traditional neurologic examination in patients with low back pain and sciatica. They include the following:

Straight leg raising test With the patient in the supine position, the symptomatic lower extremity is slowly elevated off the examining table. The spinal nerve and its dural sleeve, tethered by a herniated disc, are stretched when the lower extremity is elevated between 30° and 70°. This movement accentuates the radiating pain ("sciatica"). Increased pain at less than 30 and more than 70° is nonspecific.

Lasegue test A variation of the Straight Leg Raising test, with the patient in the supine position, the symptomatic lower extremity is flexed to 90° at the hip and knee. The knee is then slowly extended, which produces radiating pain with L5 and S1 nerve root compression.

Bragard's sign (test) After a positive Straight Leg Raising test, the elevated extremity is lowered to the point of pain resolution. The foot is then dorsiflexed by the examiner. If this movement recreates the pain, the test is positive.

Contralateral ("well") straight leg raising test Performed on the asymptomatic lower extremity, this test has specificity but low sensitivity for disc herniation.

Prone straight leg raising test With the patient in the prone position, the symptomatic lower extremity is slowly extended at the hip by the examiner. Accentuation of pain in the anterior thigh suggests a "high" lumbar (L2, L3) radiculopathy.

Valsalva test This maneuver increases intrathecal pressure, which accentuates radicular pain in the presence of spinal nerve compression and inflammation. Deep coughing produces the same effect under like circumstances.

Brudzinski test With the patient supine, the head is flexed by the examiner, which aggravates radicular pain in the presence of spinal nerve compression.

Patrick's (FABERE) test [45] The lateral malleolus of the symptomatic lower extremity is placed on the patella of the opposite extremity, and the symptomatic extremity is slowly externally rotated. Again, the thigh is flexed (F), abducted (AB), externally rotated (ER), and extended (E). This test also helps to confirm a suspicion of hip joint pathology. Accentuation of pain favors a lesion of the hip or sacroiliac joint as the cause for the pain.

Gaenslen's test With the patient supine and the symptomatic extremity and buttock slightly over the edge of the examination table, the asymptomatic lower extremity is flexed at the hip and knee and brought to the chest. The symptomatic lower extremity is extended at the hip to the floor. Increased nonradiating low back and buttock pain indicates sacroiliac joint disease.

Lumbosacral root testing It is the essence of the neurologic examination in patients with back pain and a suspected lumbosacral radiculopathy. Each myotome and dermatome must be carefully evaluated. There are several pitfalls to be avoided in this portion of the examination. Guarding secondary to pain may simulate weakness, but this is usually diffuse and not specific to a given myotome. Reflexes may be suppressed secondary to poor relaxation. The sensory examination is usually less useful than the history of the distribution of paresthesia, particularly early in the course of a radiculopathy.

Heel/Toe walk test Walking for several steps on the base of the toes with the heels raised will normally produce no discomfort to the patient. Except for a localized forefoot disorder (e.g., plantar wart, neuroma) or an anterior leg syndrome (e.g., shin splints), an inability to do this because of low back pain or weakness can suggest an S1–S2 lesion. Heel walk test may help with diagnosis of L5 radiculopathy with a "foot drop" presentation.

Yeoman's test The patient is placed prone. With one hand, firm pressure is applied by the examiner over the suspected sacroiliac joint, fixing the patient's anterior pelvis to the table. With the other hand, the patient's leg is flexed on the affected side to the physiologic limit, and the thigh is hyperextended by the examiner lifting the knee from the examining table. If pain is increased in the sacroiliac area, it is significant of a ventral sacroiliac or hip lesion because of the stress on the anterior sacroiliac ligaments. Normally, no pain should be felt on this maneuver.

Leg length discrepancy

- True leg length: ASIS to medial/lateral malleolus – *Bony* landmarks.
- Apparent leg length: Umbilicus to medial malleolus *Soft tissue* landmarks. Greater than ¼ inch difference is considered a discrepancy and associated with increased risk of developing a radiculopathy or LBP [46–48].

Thoracolumbar Conditions

Thoracic Radiculopathy

History and Physical Examination

Thoracic radiculopathy most commonly presents with a burning or shooting pain, which can present as back, scapular, chest, or abdominal wall pain depending on the level affected. The most common presenting complaint is "band-like" chest pain, present in 67% of patients [49]. The pain of radiculopathy tends to follow a dermatomal distribution and is worsened by coughing or straining. Figure 7.2 demonstrates the various dermatomes, with the T1–T12 distributions having the potential to be affected by thoracic radiculopathy.

Myelopathy may manifest only by gait abnormalities and increased tendency to fall. It may run in course with orthostasis or autonomic dysreflexia (lesions over T6), bowel/bladder dysfunction, sexuality issues, sensory impairment (dysesthesia or anesthesia), and/or motor deficits [50–52]. An asymmetric band-like dermatome sensory anomaly in the chest or abdominal wall is suggestive of thoracic radiculopathy, usually associated with neuropathic pain symptoms exacerbated by trunk movements.

The neurologic involvement of myelopathy can be classified and followed according to the American Spinal Injury Association (ASIA) impairment scale [53]. Gait abnormalities, sensory deficits, weakness, hyperreflexia, increased muscle tone, bowel and bladder incontinence, and upgoing toes are generally seen in myelopathy, although subtle myelopathy may not provide definitive findings. In complete spinal cord injury, there will be no rectum sensation and increased rectal tone with no volitional sphincter contraction [50, 51].

Thoracolumbar Junction (TLJ) Syndrome

The role of the thoracolumbar junction (TLJ) in common spinal disorders is frequently overlooked. This may be due to a number of reasons:

- The patients virtually never complain of pain at the level of the TLJ. Pain caused by a disorder at this site is invariably referred to a different site.
- Only rarely will there be radiographically demonstrable degenerative disease at the level of the TLJ (T11–T12–L1).
- The diagnosis can be made only in the light of a detailed and systematic clinical examination, which will show a tender spinal segment at this level.

The usual cause is often termed painful minor intervertebral dysfunction (PMID), most commonly at *T12/L1*. In some very rare cases, the problem may be due to a prolapsed intervertebral

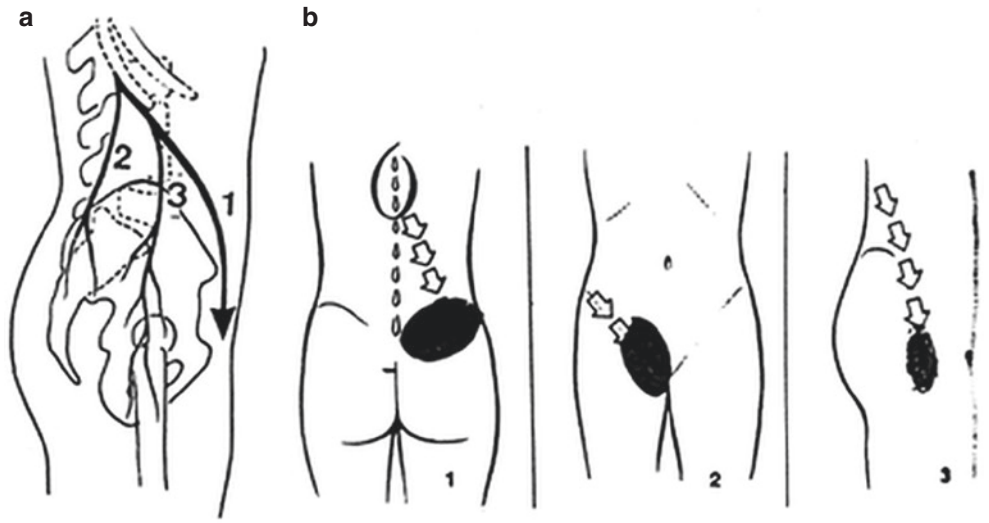

Fig. 7.2 (**a**) Distribution of the spinal nerves T12 and L1. (1) Anterior ramus; (2) posterior ramus; and (3) perforating lateral cutaneous branch. (**b**) Referred pain from the TLJ is felt in the cutaneous distribution of these nerves; the skin and subcutaneous tissues are the site of reflex cellulalgia. However, the pain is felt as deep pain. (1) Low back pain (posterior ramus); (2) pseudovisceral pain and groin pain (anterior ramus); and (3) pseudotrochanteric pain (lateral perforating branch). Usually, the cause is painful minor intervertebral dysfunction of TLJ segment. (Reprinted with permission from Maigne [54])

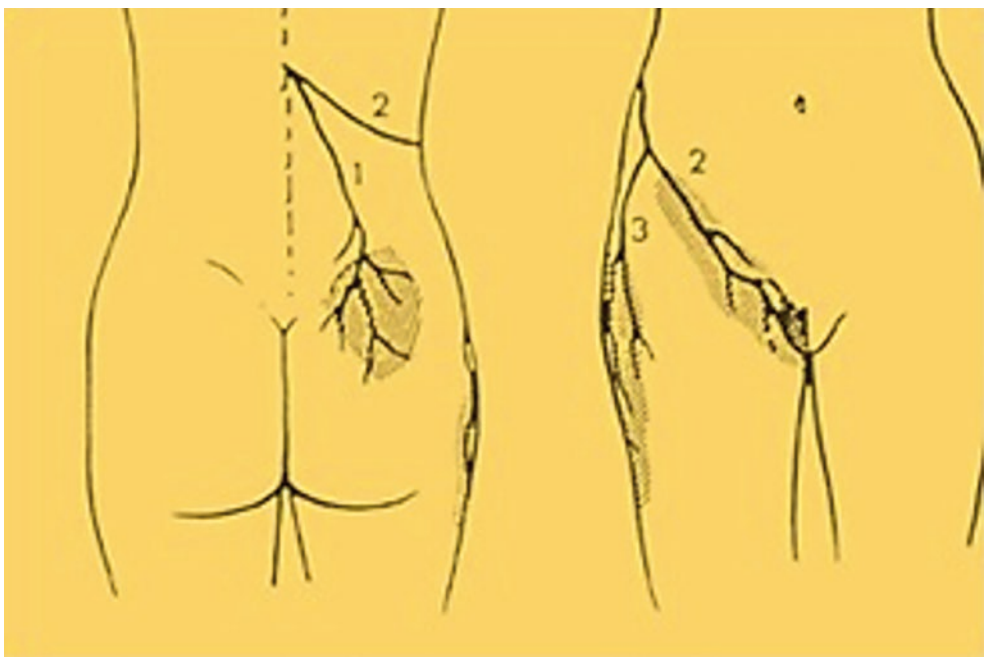

Fig. 7.3 Skin territories innervated by T12 and L1. These two nerves have a similar distribution: (1) territory of the posterior ramus; (2) territory of the anterior ramus; and (3) territory of the lateral cutaneous branch of the anterior ramus. (Reprinted with permission from Maigne [54])

disc. The most frequent manifestation of this thoracolumbar junction syndrome is *low back pain*, which is exactly like low back pain of lumbosacral or sacroiliac origin. This pain was the first feature to which our attention was drawn. However, there may also be *lower abdominal pain* mimicking visceral problems or *pain mimicking trochanter bursitis*; in an even smaller number of cases, there may be *pubic pain*. These symptoms may occur by themselves or in association [54].

The pain pattern coincides with the distribution of the corresponding spinal nerves (T12, L1). It is due to reflex tissue disturbances as a result of a celluloperiosteomyalgic syndrome of spinal origin [54] shown by the clinical examination of the patient (Fig. 7.3).

The T12 and L1 spinal nerves emerge at the level of the thoracolumbar junction. These nerves have a similar course (see Fig. 7.3).

The anterior rami supply includes:

- The skin of the lower abdomen, the medial aspect of the upper thigh, and the labia majora or the scrotum

- The lower part of the rectus abdominis and transversus abdominis muscles
- The pubis

History

Low back pain is the most frequent complaint. It may be associated with one or more of the following symptoms: abdominal pain mimicking visceral disease (pseudovisceral pain), hip pain, or pubic pain. It may be overshadowed by one or other of these symptoms.

The pain, which is generally unilateral, is always felt in the sacroiliac or low lumbar region; sometimes, it may radiate posteriorly or laterally into the thigh. It is exactly like low back pain of lumbosacral or sacroiliac origin and is, in fact, invariably, mistaken for that kind of pain. The patient never complains of anything wrong with his or her thoracolumbar junction.

In the chronic form, which is the most commonly encountered pattern, the pain is mechanical, i.e., it is made worse by exertion and by certain positions. It is always felt as a deep, not as a superficial, pain. It is more common in the over-50s than in younger subjects; however, it may occur at any age. It may be isolated or associated with low back pain of lumbosacral origin.

In the acute form, the pattern is that of acute low back pain after exertion or a false movement (usually a rotational movement). The spine will be found to be stiff and painful, very immobile, but usually without the antalgic position commonly found in low back pain originating at L4/L5 or L5/S1. The condition is most frequently seen in subjects over 50 years of age.

Physical Examination

Tenderness in one or two segments of the TLJ can be demonstrated only by a careful and detailed examination, segment by segment. This segmental pain is most commonly a manifestation of PMID at this level. For the examination, the patient is positioned prone across the couch, with a cushion under the abdomen. The examination must be performed with meticulous attention to detail. The examination is performed segment by segment, using maneuvers that directly stress the vertebrae, in order to provoke pain and to show the involvement of the particular segment. In a healthy segment, these maneuvers will not cause pain. Two maneuvers are particularly useful at this level:

1. *Lateral pressure on the spinous processes*. The search is conducted from T9 to L3, exerting pressure on each spinous process, slowly but firmly, and tangentially to the skin. The test should be done with one thumb or, preferably, with one thumb on top of the other. The test is performed from left to right and then repeated from right to left. In the case of PMID, pain will usually be felt in one direction only; in right-sided low back pain, right-to-left compression will provoke pain; left-to-right tenderness is rarely seen.
2. *Compression-friction of the facet joints*. The tip of the middle finger (preferably with the index finger placed on top of the middle finger for bracing) is used to exert firm, slow pressure, and friction along a line paralleling the spinous processes, at a distance of 1 cm from the midline, on either side. This maneuver must be performed with firm and constant pressure and up-and-down movements along the spine. At the healthy levels, it will be painless; at the affected level, however, it will provoke pain at the level of the involved facet joint either on the right or on the left, depending on the affected side.

Two other signs may be found in the same segment, although they are less consistently encountered: tenderness of the spinous process on PA compression exerted with one thumb placed on top of the other and tenderness of the interspinous ligament of the segment concerned, elicited by pressure with the bow end of a key [54].

Lumbar Spinal Stenosis

History

The most common presentation of lumbar spinal stenosis (LSS) is low back pain, followed by intermittent neurogenic claudication, variably felt in the buttocks, posterior thigh, calf, and groin [55]. Additionally, patients may have paresthesias, weakness, cramping, or fatigue affecting the lower limbs. Symptoms of a central stenosis are usually bilateral and worsen with lumbar extension and walking, particularly downhill for progressively shorter distances. There may be improved pain while sitting or with lumbar flexion as when one leans on a shopping cart [56]. Subarticular, lateral recess and foraminal stenosis present typically with a unilateral radiculopathy based on the affected level.

Physical Examination

A complete lumbar spine examination should be performed, including: inspection, palpation, range of motion (ROM), muscle strength, sensation, reflexes, Romberg maneuver, and special tests (straight leg raise, crossed straight leg raise, slump test, femoral nerve stretch test, Kemp's test). Neurological examination and straight leg raising test may be normal or may demonstrate focal weakness, sensory loss, diminished muscle stretch reflexes, or radiating leg pain. The patient may demonstrate a slow, wide-based gait or unsteadiness during the Romberg maneuver [57]. Peripheral pulses, skin, and hair exam should be performed to assess for signs of vascular insufficiency. Lumbar extension may worsen pain.

Diminished walking distance is a significant functional limitation in patients with lumbar stenosis and may be used as a functional outcome measure [58]. In addition, functional assessment may be accomplished using functional tools (VAS score, Oswestry Disability Index, FIM score, Brief Pain Inventory, Medical Outcomes Survey 36-Item Short-Form Health Survey (SF-36), McGill Pain Questionnaire).

Lumbar Radiculopathy

Lumbar radiculopathy refers to any pathologic condition affecting the lumbar nerve roots. In practical terms, radiculopathy is spinal nerve-related symptoms such as pain, with variable presence of paresthesias, weakness, reflex changes, and secondary interference of normal activities.

Lumbar radiculopathy is usually caused by mechanical compression in combination with inflammatory biochemical and immunological insult to a nerve root or roots. Though disc herniation (DH), synovial cysts, and spinal stenosis account for nearly all cases, rarer causes include a multitude of musculoskeletal, vascular, rheumatologic, neurologic, infectious, iatrogenic, and other etiologies.

History

Lumbar radicular pain is usually described as any combination of throbbing, aching, sharp, dull, burning, pressure, numbness, tingling, tearing, stretching, or shooting. Though back pain is usually present, leg symptoms (including buttock) predominate. Limb pain and paresthesias may fit a distinct dermatomal distribution (90% of the time will involve the S1 or L5 root) [59]. History must include questions to rule out cauda equine syndrome (CES), progressive weakness, and red flag questions for possible occult process: tumor, infection, fracture, inflammatory arthritis, and nonmechanical visceral diseases. The practitioner should ask for exacerbating and alleviating factors and symptom intensity on a numerical rating scale, as well as precipitating factors. Social history should include questions on substance use and abuse, including tobacco and opiate use or abuse. Other particular points to emphasize include how the pain impacts lifestyle and previous exercise history.

Physical Examination

1. Neurologic exam: strength, reflexes, and sensory testing (sacral segments if CES suspected, with rectal examination). Lower motor neuron signs
2. Functional strength tests: repeated single heel lift or toe walking (S1), heel walking (L5), and single leg sit to stand or squat/rise (L3, L4)
3. Root tension signs: supine straight leg raise (SLR) and variations, slump test, crossed SLR (low sensitivity high specificity), and femoral nerve stretch test (upper lumbar radiculopathy)
4. General musculoskeletal screening and inspection to rule out soft tissue or joint pains mimicking or superimposed with radicular pain:
   A. Hip range of motion, hip provocative maneuvers such as flexion, adduction, and internal rotation.
   B. Sacroiliac joint maneuvers (Gaenslen's, FABER, shear tests, hip hyperextension, etc.)
   C. Other diseases: screen for ischial or trochanteric bursitis, facet, IT band or knee joint dysfunction, myofascial trigger points, Piriformis syndrome, plantar fasciitis, etc.

Lumbar Disc Herniation

History

The onset of lumbar disc disease is frequently after inciting event, which required flexion and rotation. Some patients may not have an identifiable event. The character of the pain is described as aching, sore, and stabbing. The location is most likely midline lower back pain [60] but can refer to groin, genitals, buttocks, and extremities. Pain is frequently worse with flexion, sitting, twisting, lifting, vibration, coughing, and sneezing. Patients will often endorse frequent position change or extension to alleviate pain [61, 62]. The patient's medical history may be notable for prior spine surgeries (lumbar arthrodesis, discectomy, or laminectomy make remaining discs susceptible) [61], history of cancer, steroid/drug use, and recent systemic or local infections. Because psychosocial factors also play a role in pain, it is important to review psychiatric and social history.

Red flags during the historical assessment include bowel or bladder issues (retention/incontinence), saddle anesthesia, and motor weakness, which are concerning for myelopathy or cauda equina syndrome. Fevers/chills should raise suspicion for infectious etiology. Night sweats, constant pain that is worse at night, unintentional weight loss, and pain not improved with conservative therapy should raise suspicion for malignancy. Low back pain in older adults or the immunosuppressed merit workup for fracture.

Physical Examination

The physical examination should include evaluation of vital signs to evaluate for fever, tachycardia, or blood pressure abnormalities, which may indicate systemic pathology. While examining the patient with suspected lumbar disc disease, five key components of the exam must be performed:

- Inspection: the examiner may note need for repositioning, preferred position (standing or sitting in extension decreases disc load), body habitus (excess weight may

add load to discs), surgical scars, mood, and reaction to exam maneuvers.
- Range of motion: lumbar range of motion may be limited, particularly in flexion.
- Palpation: the paraspinals may be tender or tight, and spinous tenderness or step deformity may indicate spondylolisthesis.
- Neurologic exam: sensation, strength, reflexes, and gait may be full and symmetric. Impaired sensation, focal weakness, or hyperreflexia may localize associated radiculopathy. It is important to evaluate tandem, heel, and toe walking, which may assist in identifying associated radiculopathy or myelopathy.
- Provocative maneuvers: seated and supine straight leg raise and femoral nerve stretch test [61, 63].

Lumbar Spondylolisthesis

History

Lumbar spondylolisthesis is the forward or backward slip of one vertebra relative to another. In lumbar spondylolisthesis (LS), patients typically complain of diffuse and dull axial lower back pain with or without lower limb radiation [64, 65]. Patients with nerve or cord involvement may have sensory disturbances and/or weakness. Radiculopathy develops insidiously because of a combination of vertebral subluxation and associated disc degeneration, causing foraminal and/or central stenosis. System review should assess for symptoms indicating neurologic deficits, CES or cord injury such as stool and urinary continence, and other pathologic conditions. Sexual dysfunction may be observed in patients with LS but is frequently underreported [66]. Activity-related pain or specific traumatic event should be queried and include a detailed sports-specific history in athletes.

Physical Examination

Inspection may reveal paraspinal hypertrophy, increased lumbar lordosis, or postural changes, such as a shortened waistline or flattening of the buttocks [64, 65]. Evaluate spinal range of motion and alignment. A palpable lumbar step-off is a very specific finding but is more often seen with Grade 3 and Grade 4 LS. Dural tension signs are typically negative although approximately half of adult patients with symptomatic IS will have a positive straight leg test [67]. Focal neurologic deficits, such as weakness, sensory loss, or diminished reflexes, may be seen secondary to radiculopathy. If there is clinical concern for CES secondary to LS, perform a rectal exam for sensation and tone and always evaluate for upper motor neuron signs.

Gait evaluation may reveal a compensated extended lumbar spine position to relieve symptoms, although hyperextension and rotational motions may cause pain, especially during single-limb stance [64, 68]. Measures for assessing LS include the Oswestry Disability Index, Short Form of Medical Outcomes, and visual analog scale [67]. The Meyerding classification is generally used for grading lumbar spondylolisthesis. Grade I is 0–25% slippage of one vertebra forward over the vertebral body below. Grade II is 26–50%. Grade III is 51–75%, and Grade IV is 75–100%. Grade V is greater than 100% and is also known as spondyloptosis [64].

Lumbar Spondylosis Without Myelopathy

History

Lumbar spondylosis is a radiographic finding that does not rely on clinical symptoms for diagnosis. It is the result of degeneration of the spine, which can result in bony overgrowths also known as osteophytes. However, in some patients with acute or gradual onset of low back pain, lumbar spondylosis is present and could potentially be a cause of the pain. Pain may refer unilaterally or bilaterally to the buttock, hip, groin, and thigh regions, although, typically, it does not extend past the knee [69, 70]. The pain tends to worsen with extension, rotation, and standing; it is better with lying and lumbar spine flexion [70]. By definition, lumbar spondylosis exhibits no neurologic deficits; however, because of its association with conditions that can affect the neurologic function of the lower limbs, it is imperative to ask about weakness, balance, gait, and bowel/bladder function.

There are several validated outcome measures for grading functional limitations, including the following: McGill Low Back Pain Scale, Oswestry Disability Index, and the Medical Outcomes Study 36-Item Short-Form Health Survey [71]. These should typically be administered at every office visit for following the patient's progression.

Physical Examination

A systematic review revealed that most physical exam maneuvers have limited or no diagnostic validity for spondylosis [69]. Paraspinal tenderness is the only physical exam maneuver that seems to correlate with z-joint arthropathy, but not with high diagnostic confidence. Although classically felt to diagnose z-joint pain, joint loading with pain on extension and ipsilateral rotation has not been shown to consistently correlate with spondylosis [72, 73]. Because the pain distribution may overlap with other clinical entities, a comprehensive exam including radiculopathy, hip, and sacroiliac joint provocative maneuvers should be performed routinely. Associated neurologic conditions should be ruled out through thorough strength, sensation, reflexes, gait, and balance testing.

Lumbar Zygoapophyseal (Facet) Joint Arthropathy

History

There are no symptoms specific/unique to facet joint arthropathy (FJA). Common causes of acute and chronic low back pain (LBP) can have similar presentations [74]. History is most useful in excluding alternative etiologies, in particular, radiculopathies, fractures, infections, neoplasms, or rheumatologic conditions [30, 75]. "Typical" facetogenic LBP is progressive [30]. Referred pain is predominantly in the buttock and thigh, rarely radiating past the knee (Fig. 7.4) [28]. The pain is typically described as a nearly constant dull ache with episodic stabbing pain. It tends to be associated with morning stiffness, worsened by spinal extension. Pain from the lower lumbar facet joints presents with referred pain to the groin.

Physical Examination

There are no specific signs or special tests to aid in FJA diagnosis, which is often guided by the absence of signs that suggest alternate etiologies. The only exam finding that correlates with facetogenic LBP is paraspinal tenderness, which has been shown to distinguish facet from discogenic back pain [30, 77]. "Facet loading," or pain upon extension and ipsilateral rotation, was popularized in a small retrospective study; however, larger, higher-quality studies have consistently failed to replicate this finding.

Inspection of posture is essential because increased or decreased lordosis, muscle atrophy, postural asymmetry, and alignment are diagnostic elements. Palpation of tender points along paravertebral regions and transverse processes as well as any pain referral patterns from trigger points adds to the formulation of a focused treatment plan. Perform range-of-motion evaluation to include limits and pain evoked with flexion, extension, rotation, and lateral flexion.

Lumbar Strain

History

In lumbar strain, patients present with axial, nonradiating low back pain due to an inciting injury or event. Lower limb symptoms such as pain, numbness, tingling, or weakness are usually absent. Pain is usually worse with movement and better with rest. Screening questions for "red flags" exclude the suspicion

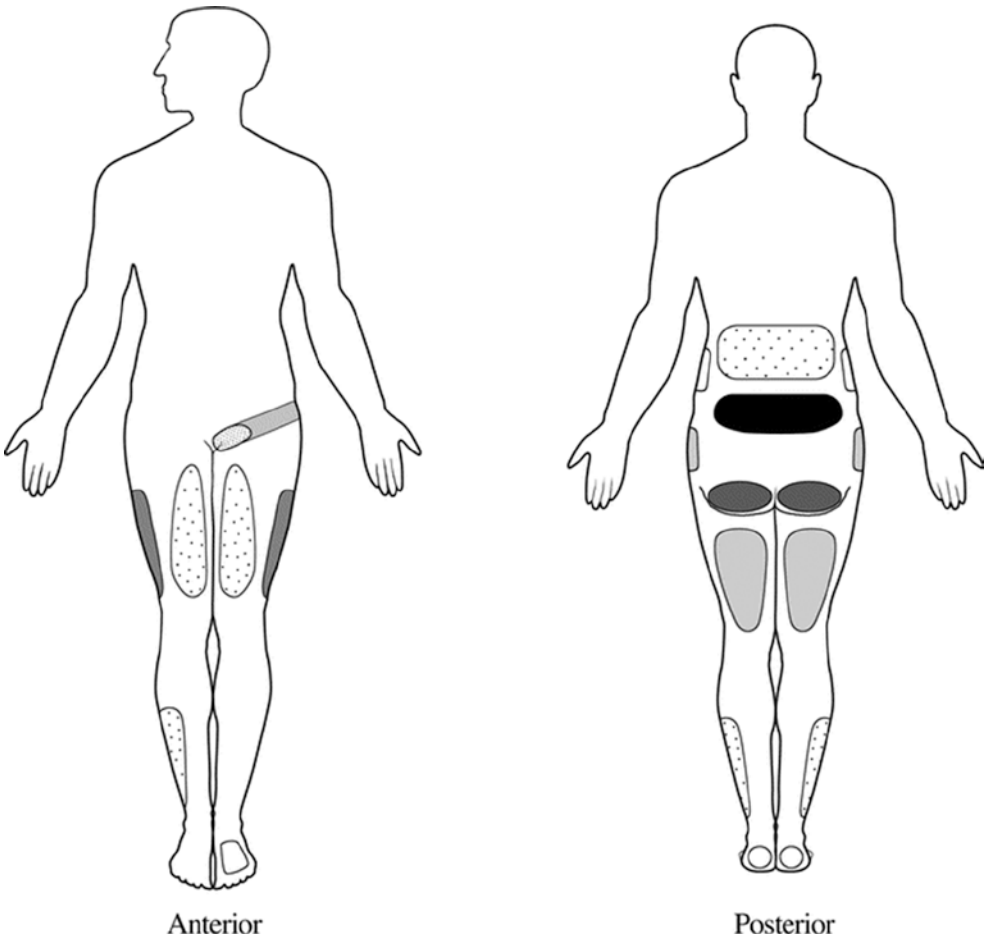

Fig. 7.4 Lumbar facet pain referral patterns. The most common areas of referred pain from the lumbar facets are noted in black (low back) in descending order to the lightest regions (foot is least common). Each facet joint can refer pain to a number of locations, with a great deal of overlap between the different levels. Although there are trends, there are no direct associations between specific joints and referral pain regions. (Reprinted from Cohen and Raja [76], with permission from Wolters Kluwer)

for the presence of cancer or infection, fracture, cauda equina syndrome, inflammatory arthritis, or nonmechanical visceral disease. Psychosocial factors and emotional distress should also be assessed, as they are strong predictors of poor outcomes [78].

Physical Examination

Physical examination includes inspection of the lower back and extremities. In standing, a postural shift may be present. Lumbar range of motion may be limited and painful in any plane. There is typically tenderness over the lumbar paraspinal muscles or quadratus lumborum muscle, with absence of spinous process tenderness. Straight leg raises may provoke axial back pain, but should not elicit radicular pain (therefore a negative test). Strength, reflex, and sensory testing should be normal. Hip examination and special tests, including FABERE's (flexion/abduction/external rotation/extension) and Gaenslen's maneuver, can help rule out other sources of pain. Advanced physical exam assessment may include evaluation of core strength such as ability to perform a plank or bridge exercise.

Functional evaluation of lumbopelvic core strength can be assessed during the clinical exam through observation of trunk and hip control during single-limb stance, presence of Trendelenburg gait, and assessment of ability to perform core exercises such as bridge, plank, and one leg step down. Mobility and function may be impaired by pain. The Oswestry Low Back Pain Disability Index is a questionnaire that assesses the impact of low back pain on ten aspects of daily life (such as lifting, walking, self-care, and work). On occasion, assessment of function relative to work demand is needed. A functional capacity evaluation (FCE) consists of a battery of standardized assessments that offers results in performance-based measures and offers predictive value about the individual's return to work.

Sacroiliac (SI) Joint Pain

History

There is no specific history which suggests SI joint pain. However, patients often report pain with sitting or getting out of bed movement.

Physical Examination

Exam should include inspection (asymmetry, shift, leg length discrepancy), palpation, and a combination of at least three provocative manuevers, including: Patrick's/FABERE test, Lateral pelvic compression or distraction maneuver, Fortin sign/test (point tenderness within 1 cm inferomedial to the posteriorsuperior iliac spine), or other. Gait assessment is also important in evaluating abnormal SI joint motion. However, other studies suggest that the only way to diagnose SI joint pain is after a diagnostic injection [79].

Posture, pelvic balance, mobility, transfers, gait assessment, and functional assessment of proper body mechanics are important to assess, as is the recognition of signs of inappropriate illness (behavior, depression, or anxiety.)

Seronegative Spondyloarthropathy

History

Individuals with spondyloarthropathies (SpAs) commonly relate morning stiffness and low back pain that improves with exercise and NSAIDs. Inflammatory low back pain is the hallmark of SpAs, and recognizing this is critical for early diagnosis. Morning stiffness lasts more than 30 minutes. Low back pain radiates into the buttocks, and nocturnal back pain only occurs during the second half of the night [80–82]. Chronic LBP lasting greater than 3 months with an age of onset before age 45 should raise suspicion of an autoimmune disorder.

In addition, other common symptoms to look for are those that include enthesitis (e.g., of the heel or ischial tuberosity) and unilateral or symmetrical arthritic-type pain, along with the common extra-articular manifestations of SpA such as uveitis, iritis, skin rash, constitutional symptoms, dactylitis, and aortitis. Reactive arthritis usually presents 2–4 weeks after a urogenital (including sexually transmitted diseases) or gastrointestinal infection [82].

Physical Examination

Findings on physical examination in patients with SpA include restricted spinal range of motion, tenderness of the sacroiliac and peripheral joints to palpation, swelling, warmth and erythema (synovitis) in the peripheral joints, enthesitis (edema, warmth, tenderness, erythema at tendon insertion points), dactylitis, and pertinent skin rashes (such as psoriasis).

Functional difficulties due to spine pain and peripheral joint arthritis should be assessed in patients suspected of SpA. Functional assessment should be tailored to the individual's disease. All patients with ankylosing spondylitis should have their cervical spine range of motion assessed. This group of patients is at risk of developing a progressive spinal flexion deformity which can be measured with the occiput to wall test. Involvement of a patient's thoracic spine can be measured by the degree of chest expansion. Lumbar spine range of motion is measured in the sagittal and coronal planes. Lumbar flexion is assessed using the modified Schober test [83, 84]. Functional assessment tool such as the Bath Ankylosing Spondylitis Functional Index (BASFI) should be used [85].

Post Laminectomy Pain Syndrome

History

History should include pain location, pattern, quality, and temporal factors. Location of pain in the lower back (axial)

vs. the lower extremity (radicular) or both can help to differentiate etiology. Evaluation of red flags (nocturnal pain, weight loss, trauma, infection, saddle anesthesia, and acute bladder and/or bowel incontinence or retention) and yellow flags (attitude that back pain is severely disabling, kinesiophobia, depression or anxiety, social withdrawal, and financial problems) should also be undertaken. Prior pain treatments (pharmacological and non-pharmacological), along with their efficacy, should be established. Validated low back pain scales, like the Pain Catastrophizing Scale, can be useful to quantify pain experiences [86].

Physical Examination

Vital signs and examination of abdominal, pelvic, and vascular systems may be important. A focused spinal physical examination should include observation of scars, posture, spinal alignment, balance, and gait. Spinal range of motion must be evaluated. A complete motor and sensory neurologic examination should be included. Evaluation of the sacroiliac joints (SIJ), hips, and knees should complement the examination. Special tests to assess for nerve root tension signs must be performed (seated/straight leg raising test, femoral nerve stretch test). Nonorganic findings that deviate from anatomic patterns of injury pathology, such as Waddell signs, should also be addressed. Some of the signs include disproportionate pain behavior, regional weakness, altered sensation (whole-leg weakness or sensory loss), change in straight leg raising test result after distraction, superficial or nonanatomic tenderness, and pain while simulating examination tests such as axial pressure in the skull. Presence of two or more signs may be indicative of psychological distress and is associated with poor outcome after surgery [87].

If presence of significant yellow flags includes coexistent mood disorder or signs of chronic pain syndrome, consider psychological consultation including a detailed neuropsychological assessment battery to ensure accurate diagnosis and help with subsequent treatment planning.

Pain might result in functional limitations such as diminished walking tolerance. Change in biomechanics and resultant mobility restriction may lead to an inability to perform daily activities, depression, or anxiety which impairs quality of life. The generic WHOQOL-BREF questionnaire can be used to evaluate quality of life, which studies have found to be directly related to postoperative recovery in FBSS patients [88].

Compression Fractures of the Spine

Vertebral compression fractures (VCF) are defined as a loss of height of a vertebral body resulting from a failure of the structural osseous components of the vertebrae [89].

VCFs may result from osteoporosis, malignancy, infection, or trauma. Among these, osteoporosis is the most common cause of VCFs [90]. Benign insufficiency VCFs occur as a result of a natural decrease in bone density related to osteoporosis and aging. By definition, there is no infiltration into bone by any extraosseous process. On the other hand, pathologic insufficiency VCFs are due to weakening of bone density as a result of a bony destructive factor such as primary or metastatic bone cancer or osteomyelitis.

Traumatic VCFs may result from high-energy trauma such as a motor vehicle accident, fall from height, violent act, or gunshot wound.

For the spinal column, traditional teaching is that the column can be divided into three sections: (1) anterior column (anterior longitudinal ligament, anterior annulus, the anterior portion of the vertebral body), (2) middle column (posterior vertebral body, posterior annulus, and posterior longitudinal ligament), and (3) the posterior column (ligamentum flavum, neural arch, facets, posterior ligamentous complex). If two of these three columns are compromised, the injury is considered unstable, and the patient potentially needs surgery.

Compression fractures typically only involve the anterior column and, therefore, are considered stable. When they progress to the middle and/or posterior column, they become burst fractures.

About 50% of all spine fractures occur at the thoracolumbar junction, and an additional 30% occur at the L2–L5 region (Fig. 7.5). About 50% of spine fractures are due to motor vehicle collisions with another 25% being due to falls. Osteoporosis is another mechanism that can result in vertebral compression fractures. It is estimated that 44 million Americans have osteoporosis and that 50% of Caucasian females will have an osteoporotic compression fracture at some point.

History

Disease progression including natural history, disease phases or stages, disease trajectory (clinical features and presentation over time).

New onset/acute The majority of VCFs are asymptomatic and never cause a patient to seek medical attention. Over 50% of benign VCFs will go undiagnosed in their acute phase. A small number of VCFs are initially diagnosed during a work-up for unrelated complaints [92]. Symptomatic VCFs can be excruciatingly painful requiring medical intervention, ranging from conservative measures to invasive interventional procedures.

Subacute Pain typically improves substantially, and as it does, the patient's mobility likewise increases.

Chronic/stable Pain typically resolves. Function returns to pre-fracture levels in many instances.

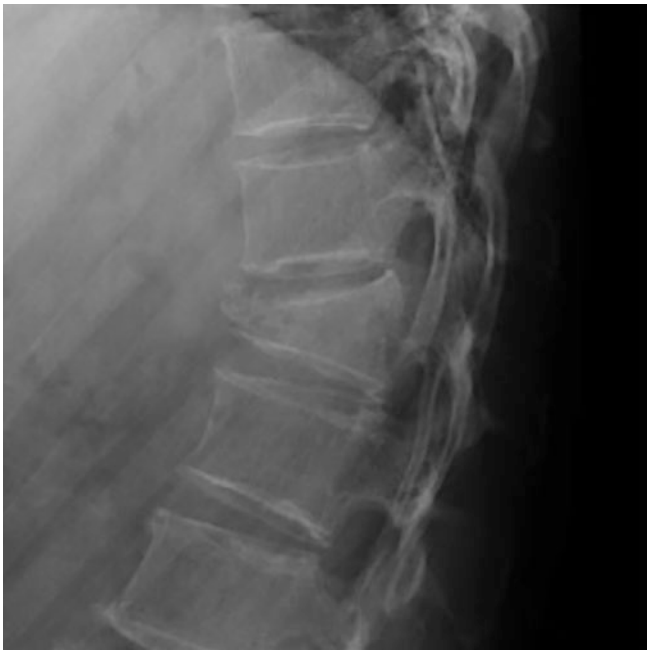

Fig. 7.5 Sagittal T2-weighted MRI of the lumbar spine showing L2 compression fracture. (Reprinted from Image Quiz: Lumbar Burst Fracture [91], with permission from Wolters Kluwer)

Preterminal Some vertebral fractures are caused by metastatic malignancy and may be associated with kyphosis, deconditioning, respiratory difficulty, or antalgic gait. Seventy-five percent of people with painful compression fractures complain of chronic axial pain [92–94].

The risk of future fractures is elevated after an initial vertebral compression fracture. Nineteen percent of individuals will develop another compression fracture within a year [92–94].

Physical Examination

Initial evaluation of spine fractures, once the patient has been stabilized, includes evaluation of the neurologic function of the arms, legs, bladder, and bowels. The keys to a thorough exam are organization and patience. Of note, many high-energy compression fractures have associated abdominal, cerebral, and extremity injuries, and these all should be evaluated. One should not only evaluate strength but also sensation and reflexes. It is also important to inspect the skin along the back and document the presence of tenderness to compression. Documentation is paramount as these initial findings will likely be used as a baseline for all future evaluations.

Physical examination will reveal tenderness directly over the area of acute fracture, and an increased kyphosis may be noted. In cases of uncomplicated compression fractures, straight leg raise will be negative, and neurologic examination will be normal. An ileus, or decreased bowel sounds, may be present. The diagnosis can be confirmed if plain radiographs show the classic wedge deformity correlating with the area of tenderness found on physical examination.

About one-third of vertebral fractures are actually diagnosed [95, 96], because many patients and families regard back pain symptoms as “arthritis” or a normal part of aging. Therefore, compression fracture should be suspected in any patient older than 50 years with acute onset of sudden low back pain. Most patients will remember a specific injury as the cause [97]; however, fractures may occur without any history of increased force on the spine. Lying in the supine position generally relieves some of the discomfort. Standing or walking exacerbates the pain.

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Radiological Evaluation of the Lumbar Spine

8

Jad S. Husseini, Connie Y. Chang, and William E. Palmer

Introduction

Radiography, computed tomography (CT), and magnetic resonance imaging (MRI) are the primary modalities used in the imaging assessment of the lumbar spine. This chapter will discuss these imaging modalities with a focus on the fundamentals of imaging technique and the normal and abnormal imaging appearance of the lumbar spine.

Radiography

The standard radiographic examination of the lumbar spine consists of frontal and lateral views. Images are typically obtained with the patient standing, although supine or seated radiographs may also be performed if the patient is unable to stand. Standing radiographs, unlike cross-sectional imaging which is performed with the patient in a supine or prone position, provide information on weight-bearing spinal alignment. In addition to alignment, radiographs allow assessment of the vertebral bodies but are of limited value in evaluation of the bone marrow, posterior elements, soft tissues, and the spinal canal.

Computed Tomography (CT)

CT is ideal for assessment of the osseous structures of the spine. Unlike radiographs, areas of interest can be assessed without being obscured by superimposed structures. Although CT can show abnormalities of the intervertebral discs, the paraspinal muscles, and other soft tissues, these structures are typically better assessed by MRI. Tools such as metal artifact reduction techniques make CT useful for characterizing structures adjacent to hardware (Fig. 8.1). Volume-rendered three-dimensional reconstructions made from source data are not typically used for diagnostic purposes but may be helpful for presurgical planning.

Magnetic Resonance Imaging (MRI)

MRI is the best modality to assess marrow, intervertebral discs, soft tissues, and the structures within the spinal canal (nerves and meninges). As a result, MRI is the modality of choice for imaging back pain and radiculopathy. A complete MRI examination of the lumbar spine includes a T1-weighted sagittal, T2 fat-suppressed or short tau inversion recovery (STIR) sagittal, and T2-weighted sagittal and axial sequences. Additional T1-weighted image obtained following the administration of intravenous gadolinium should be considered in patients with low back pain, radiculopathy, or cauda equina syndrome when there is concern for malignancy as post contrast images may accentuate bone marrow abnormalities and allow for better delineation of extraosseous metastatic disease. Intravenous contrast should also be used when infection is suspected because post contrast images better assess the extent to which infection involves the discs, vertebral bodies, epidural space, and paravertebral soft tissues and allow for the distinction between phlegmon and abscess [1–3].

Systematic Approach to Imaging

A common imaging approach can be applied to all imaging of the lumbar spine, regardless of the modality used. The following elements should be assessed on each study: alignment, vertebral bodies, discs/end plates, posterior elements, and other structures. Adherence to a systematic approach to image interpretation is crucial for ensuring that the appropriate diagnosis is made and abnormalities are not overlooked.

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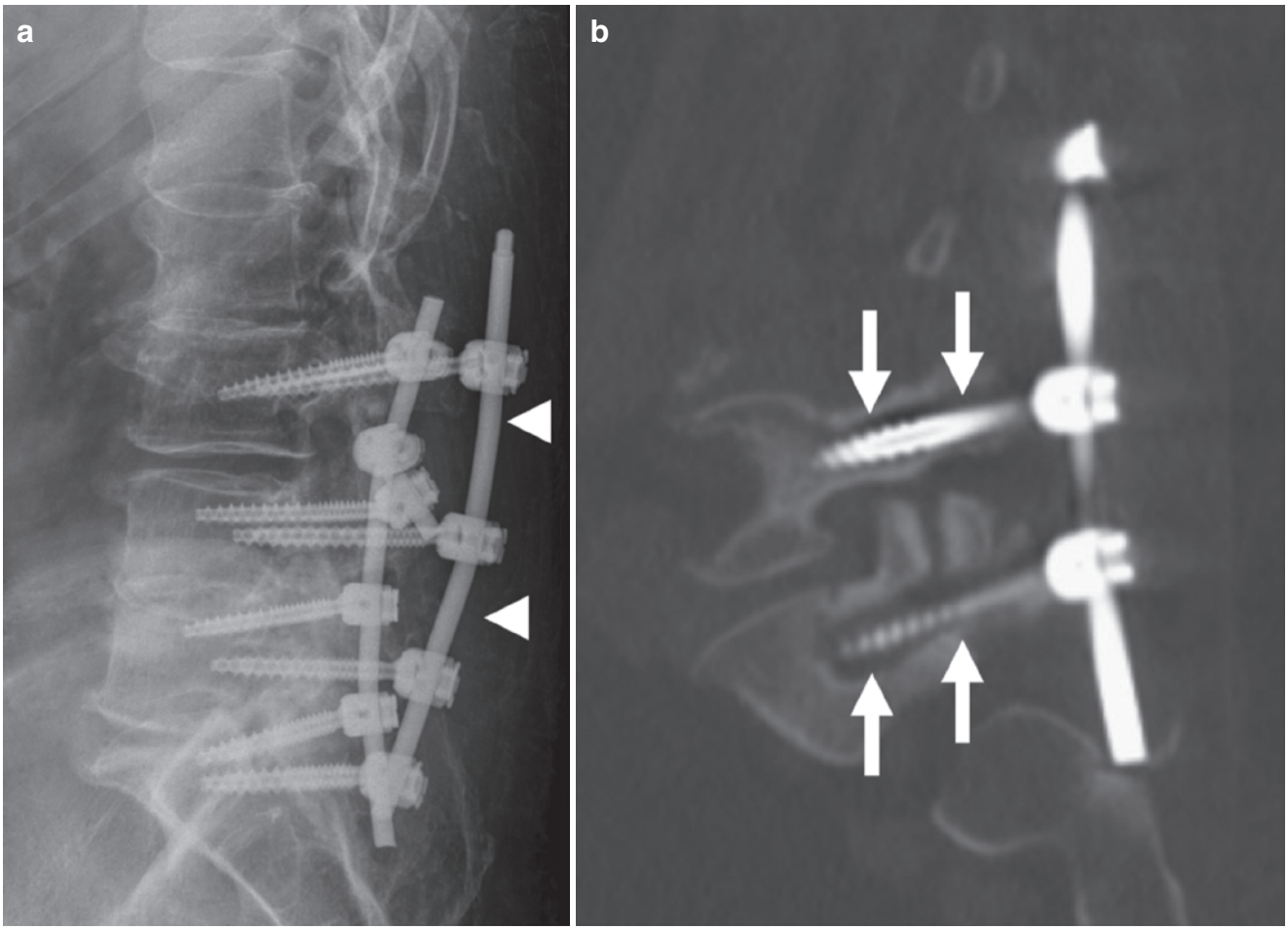

Fig. 8.1 A 57-year-old male with back pain for 2 years following posterior decompression and instrumented fusion of the lumbar spine. (**a**) Lateral radiograph of the lumbar spine demonstrates postoperative changes related to posterior lumbar decompression and instrumented fusion spanning from L3 to S1. The left rod and screw construct is displaced posteriorly suggesting hardware loosening (arrows). (**b**) Sagittal image from a non-contrast CT employing metal artifact reduction demonstrates lucency surrounding the left L5 and left S1 pedicle screws (arrows) consistent with hardware loosening

Alignment

Scoliosis

Standing frontal radiographs of the spine including the head and pelvis are typically performed as the initial study for assessing scoliosis. The most widely used measurement technique for scoliosis is the Cobb method, in which the most angled superior and inferior vertebrae of the scoliotic segment are identified and the angle between their respective superior and inferior end plates is measured [4] (Fig. 8.2). Although Cobb angle measurements on frontal radiographs can be performed reliably, patient positioning on frontal views is important because differences in positioning on serial studies can result in substantial differences in Cobb angle measurements [5–7]. Lateral bending views can be obtained to show segments of the scoliosis that result in reduced mobility. CT and MRI are often performed if there is a complex scoliosis and suspicion for congenital bony anomalies or if there are abnormal neurological exam findings. MRI is of particular utility in infantile or juvenile idiopathic scoliosis, which is associated with high rates of neural axis abnormalities not well assessed by radiographs or CT, such as Chiari malformations, syringomyelia, and tethered cord [8–11].

Anterolisthesis

Anterolisthesis, the anterior displacement of one vertebral body relative to the level below, is commonly seen in the lumbar spine. This alignment abnormality can be detected on lateral views on radiographs and in the sagittal plane on cross-sectional imaging by measuring offset of the posterior end plates of consecutive vertebral bodies. Standing radiographs are superior in detecting and determining the severity of anterolisthesis as the alignment abnormality

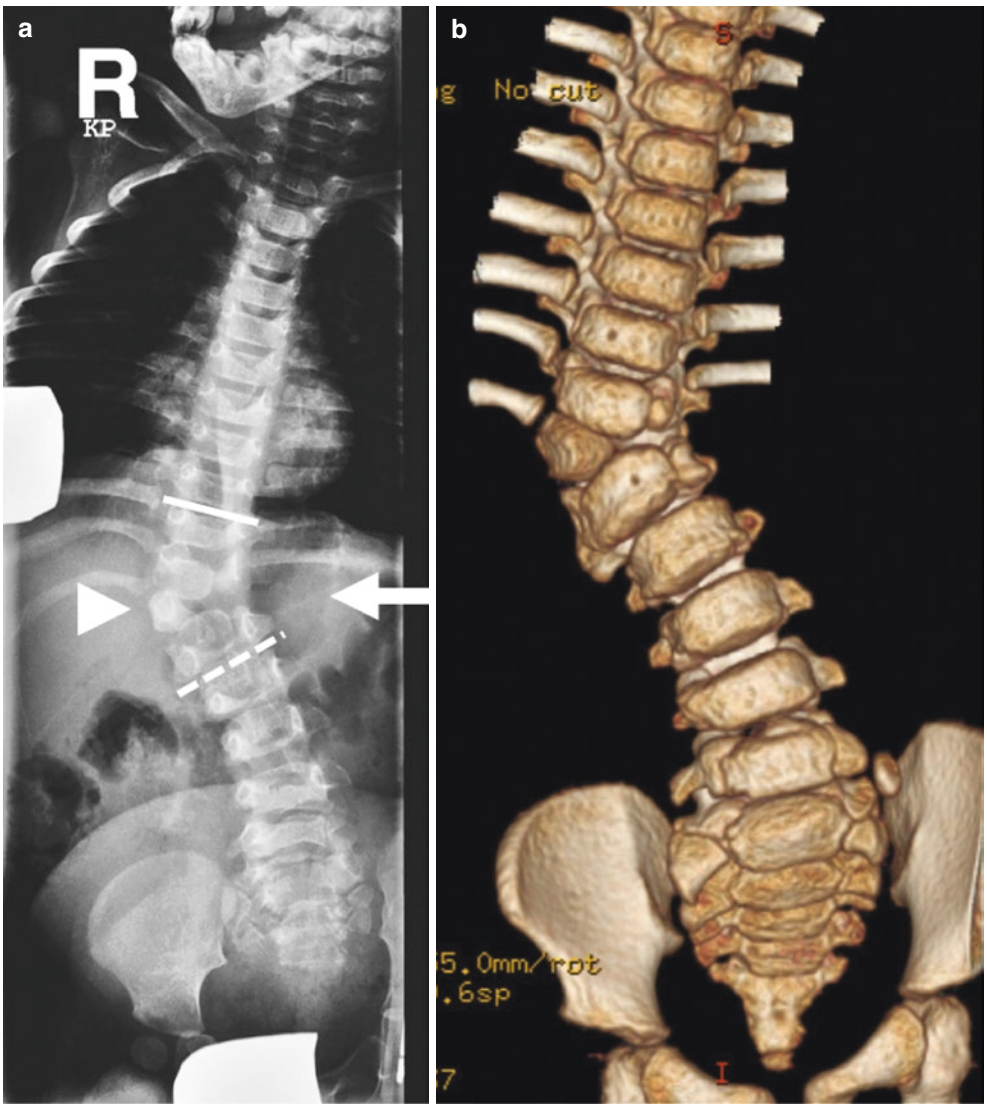

Fig. 8.2 A 6-month-old girl with scoliosis. (**a**) Frontal radiograph of the entire spine demonstrates dextro-convex scoliosis centered at T12, where there is a right lateral hemivertebra (arrowhead) and associated absence of the left 12th rib (arrow). The cobb angle of 41% is measured as the angle made by lines at the superior end plate of the superior-most tilted vertebra (line) and the inferior end plate of the inferior-most tilted vertebra (dashed line) in the scoliosis. (**b**) Image from a three-dimensional volume-rendered CT demonstrates dextro-convex scoliosis. The scoliosis is centered at the T12, where there is a right lateral hemivertebra (arrowhead) and associated absence of the left 12th rib (arrow), as illustrated in (**a**)

may be less apparent or absent in the supine position in which CT and MRI are obtained [12]. Standing flexion and extension radiographs are commonly used to quantify the degree of associated segmental instability by measuring the differences in sagittal alignment with movement [13–15].

In patients under the age of 50, defects in the pars interarticularis are the most common cause of anterolisthesis. These defects most commonly occur at the L5 level and result in anterolisthesis of L5 on S1 [16]. This alignment abnormality does not typically result in spinal canal narrowing, as the disruption of the neural arch prevents the lamina from translating anteriorly with the vertebral body [17]. On radiographs, pars interarticularis defects are best seen on lateral radiographs and on oblique radiographs, where the pars defect will correspond to the collar of "Scottie dog" formed by the vertebral posterior elements (Fig. 8.3). CT has a high sensitivity for detection of pars interarticularis defects and should be considered if radiographs are indeterminate [18]. MRI may show increased signal within the pars interarticularis on T2-weighted sequences reflecting bone marrow edema, a finding that can indicate early-stage spondylolysis when radiographs or CT is negative [19]. CT and MRI will best assess for resulting neural foraminal stenosis, which can result from a combination of disc degeneration due to segmental instability and elongation of the neural foramen (Fig. 8.4).

In patients over the age of 50, anterolisthesis due to facet degenerative changes is more common and is most frequently seen at the L4–L5 level [16, 20, 21]. Imaging will show anterior translation of both the vertebral bodies and the posterior elements and associated disc and fact degenerative changes. Because the neural arch remains intact, the anterior translation of the entire vertebra can result in spinal canal narrowing [17] (Fig. 8.5).

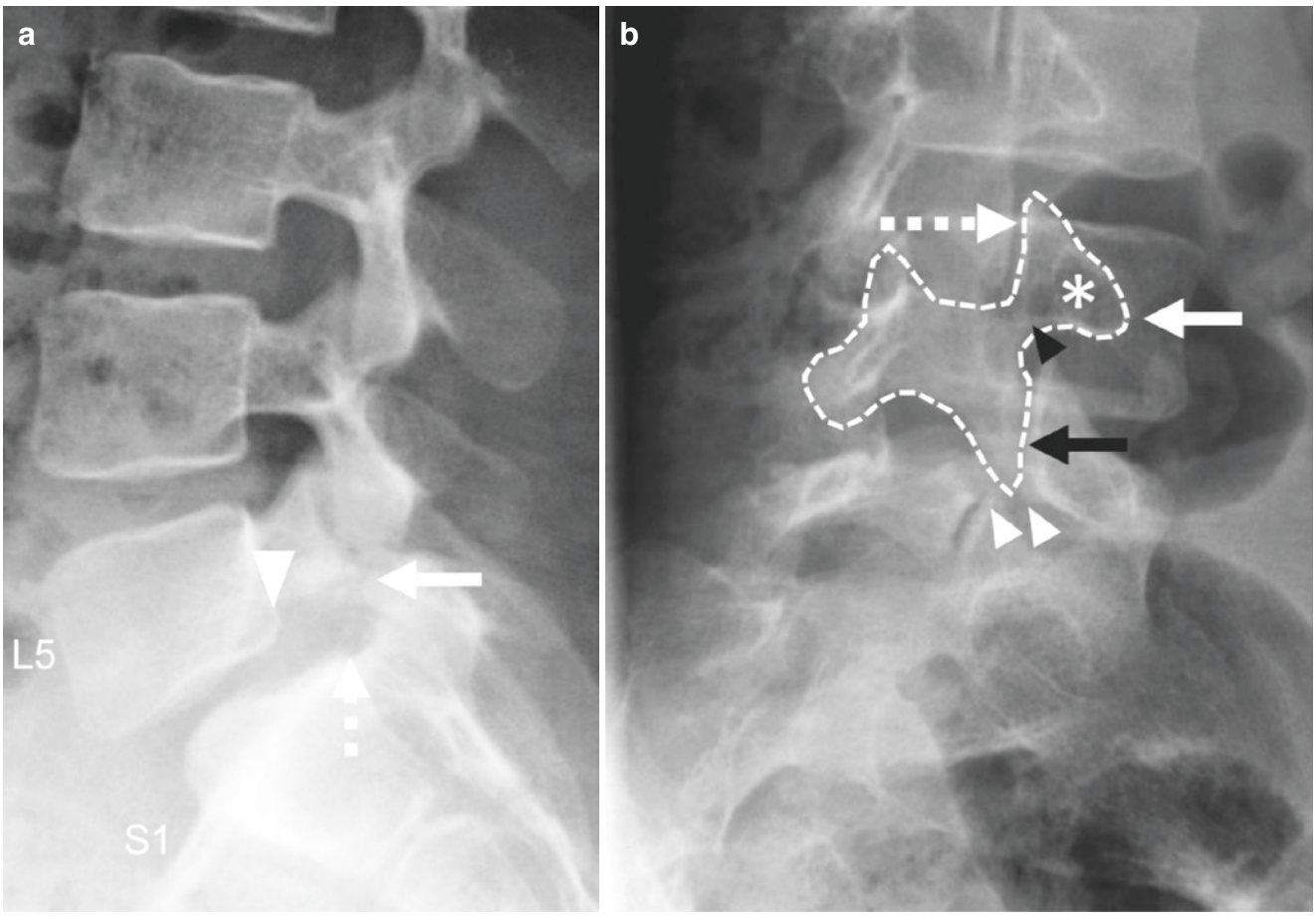

Fig. 8.3 A 14-year-old girl with L5–S1 spondylolytic spondylolisthesis. (**a**) Standing lateral radiograph of the lumbar spine demonstrates anterolisthesis of L5 on S1 with offset of the posterior margin of L5 (arrowhead) with respect to the posterior margin of S1 (dashed arrow). There is a defect in the L5 pars interarticularis (arrow). (**b**) Oblique radiograph of the lumbar spine shows the "Scottie dog" appearance of the L4 posterior elements created in this projection (dashed line). The transverse process forms the nose (white arrow). The pedicle forms the eye (∗). The inferior articular facet forms the front leg (black arrow). The superior articular facet forms the ear (dashed arrow). The pars interarticularis forms the collar (black arrowhead). There is a break in the collar of the "Scottie dog" formed by the L5 posterior elements (white arrowheads) consistent with a pars interarticularis defect

Bone Marrow

Normal bone marrow consists of yellow and red marrow. The relative amounts of each of these components can be dictated by many factors including age, gender, and medical conditions [22, 23]. In general, there is a relative predominance of red marrow in infants and children which progressively decreases with age as red marrow is converted to yellow marrow. By adulthood, yellow marrow predominates.

MRI is the preferred modality for assessment of the bone marrow. On T1-weighted sequences, yellow marrow will appear relatively hyperintense owing to the presence of fat. Red marrow signal on T1-weighted images is higher than that of the intervertebral disc or skeletal muscle but is relatively hypointense when compared to yellow marrow. In infants and children, the red marrow predominance will make the vertebral bodies appear T1-hypointense relative to the intervertebral discs [24, 25] The conversion of red to yellow marrow with aging results in a progressive increase in the T1-hyperintensity of the vertebral bodies such that they will appear hyperintense compared to the intervertebral disc [26] (Fig. 8.6).

Tumors of the spine can result in single or multiple focal marrow abnormalities. Radiographs are insensitive for detection of osseous metastases, because approximately 50% of normal bone must be destroyed in order for a lesion to be clearly identifiable [27]. Although CT is more sensitive than radiography for detection of lytic and blastic osseous metastases, MRI is the best modality due to both high sensitivity for detection of marrow-replacing lesions and the ability to characterize the relationship between the extraosseous tumor and the spinal cord, cauda equina, and nerve roots [28–30] (Fig. 8.7). Metastases or other marrow-replacing lesions will appear hypointense on T1-weighted sequences. Metastases are often difficult to see on T2-weighted images because both metastases

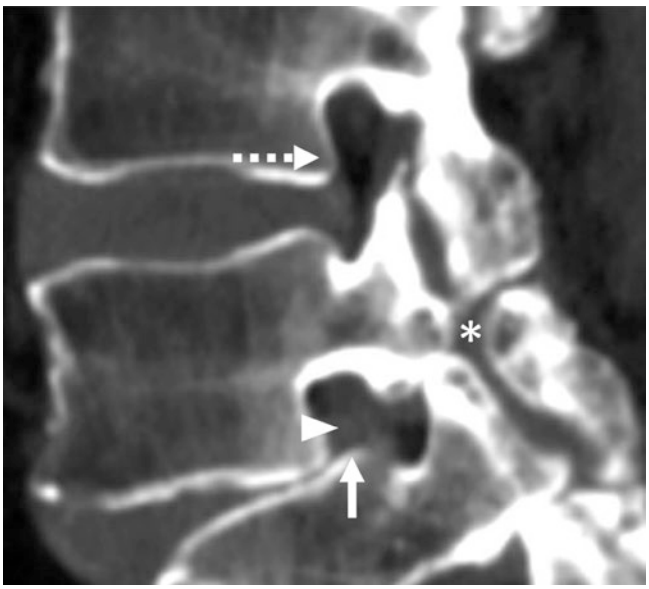

Fig. 8.4 A 48-year-old man with back pain and radiculopathy. Sagittal image from a non-contrast CT of the lumbar spine through the left L4–L5 pedicle demonstrates a defect in the left L4 pars interarticularis (∗) with anterior translation of the L4 vertebral body with respect to L5 consistent with anterolisthesis (arrow). There is narrowing of the left L4–L5 neural foramen due to elongation of the neural foramen and disc uncovering (arrowhead). In contrast, the left L3–L4 neural foramen is patent (dashed arrow)

and the adjacent bone marrow are T2-hyperintense and can appear similar in signal. When fatty marrow signal is suppressed on T2-weighted fat-saturated or STIR sequences, metastases will be more apparent and should appear hyperintense relative to the adjacent bone [31]. Suspicion for metastatic disease is an indication for obtaining images following the administration of intravenous contrast because most metastases are hypervascular and will be hyperenhancing compared to adjacent bone marrow [32, 33].

Intraosseous vertebral hemangiomata are common benign lesions of the spine which should be differentiated from metastases [34]. Although hemangiomata often appear lucent on CT and can at times be indistinguishable from lytic metastases, the presence of coarsened trabeculae traversing the lesion is characteristic of hemangiomata and can give a "polka dot" appearance to the lesion on axial images [35]. On MRI, both hemangiomata and metastases are typically T2-hyperintense and enhance on post contrast images. The appearance of hemangiomata on T1-weighted sequences varies with the amount of internal fat. When high fat content results in intrinsic T1-hyperintensity, hemangiomata can be easily distinguished from metastases [36] (Fig. 8.8).

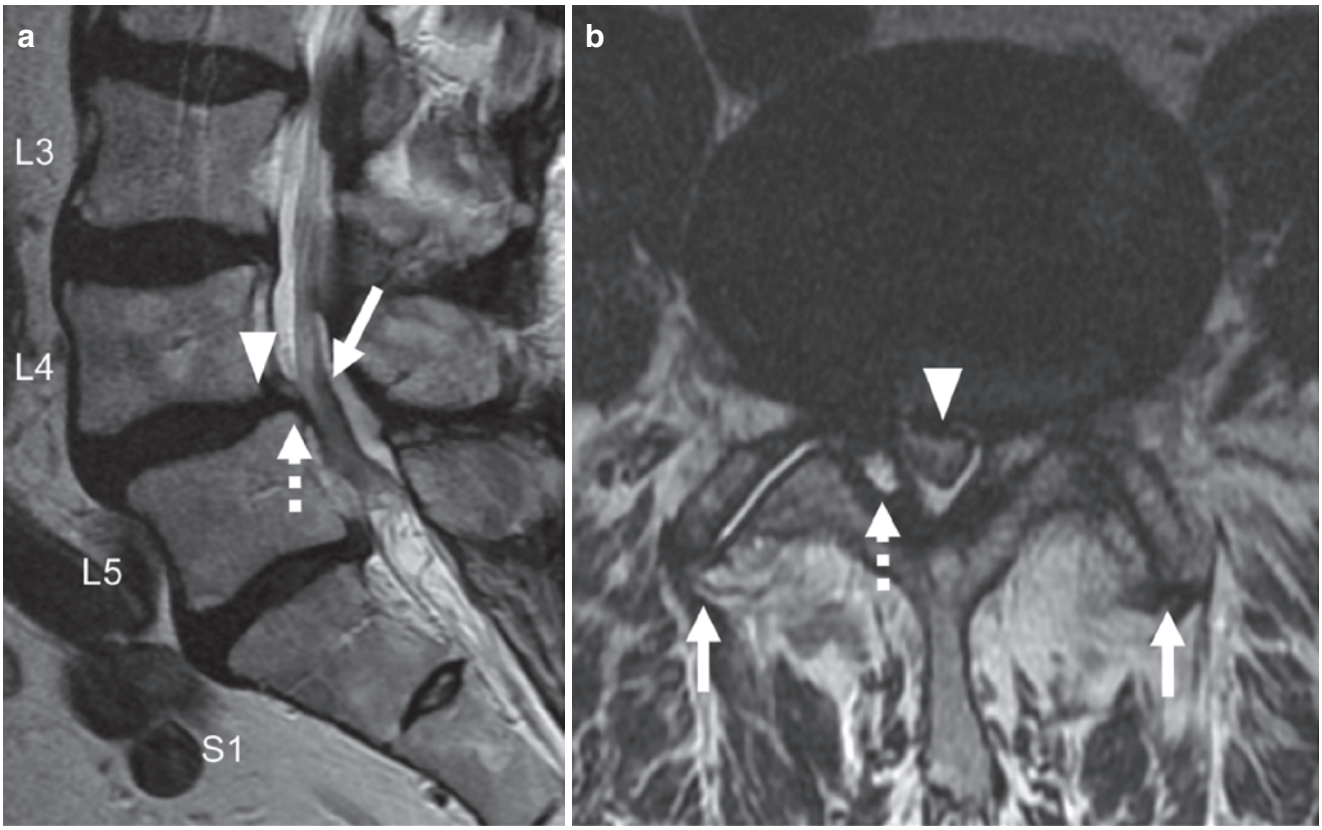

Fig. 8.5 A 68-year-old woman with low back pain and a degenerative anterolisthesis of L4 on L5. (**a**) Sagittal T2-weighted image of the lumbar spine shows anterolisthesis of L4 on L5 with offset of the posterior end plate of L4 (arrowhead) with respect to the posterior end plate of L5 (dashed arrow). (**b**) Axial T2-weighted image through the L4–L5 intervertebral disc demonstrates prominent bilateral L4–L5 facet degenerative changes with joint space narrowing, bony proliferative changes, and a right facet joint effusion (arrows). A rounded, T2-hyperintense structure in the right ligamentum flavum represents a degenerative cyst (dashed arrow). Degenerative changes in combination with anterolisthesis result in severe spinal canal stenosis (arrowhead)

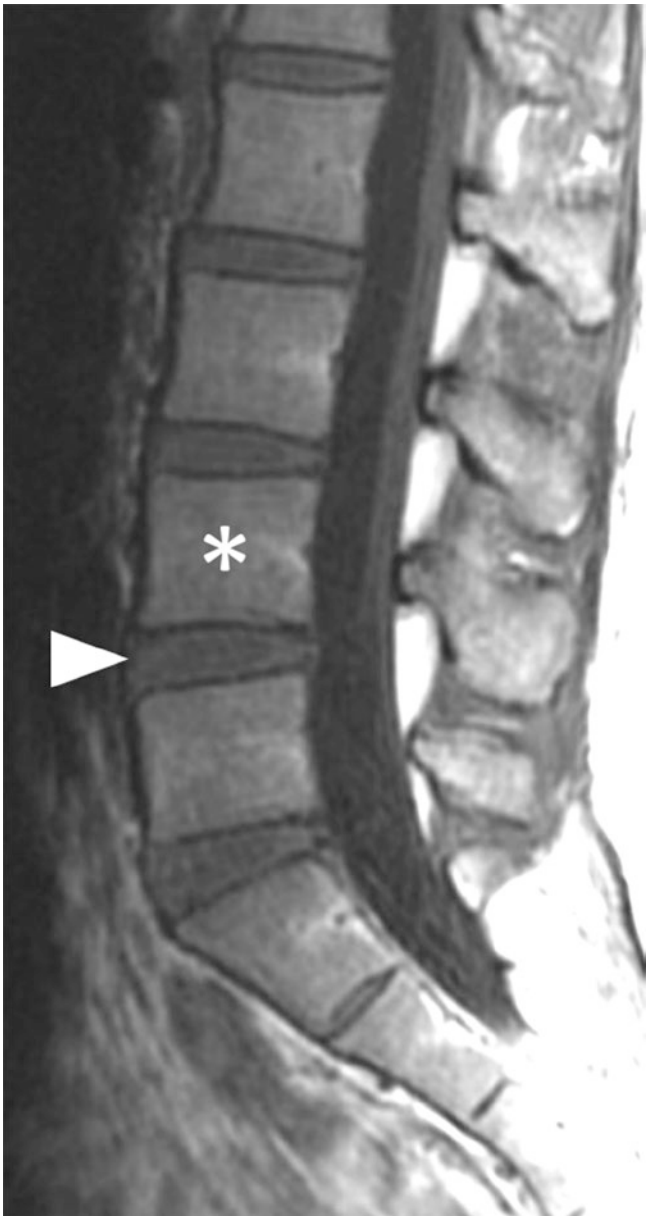

Fig. 8.6 A 37-year-old asymptomatic woman with a normal-appearing bone marrow. Sagittal T1-weighted MRI image of the lumbar spine demonstrates normal T1 marrow signal. The bone marrow (∗) is T1-hyperintense with respect to the intervertebral discs (arrowhead)

Vertebral Fractures

CT is the modality of choice in the setting of acute trauma [37]. CT images are acquired rapidly and with the patient in a supine position, features that are particularly helpful when the patient's clinical status is tenuous or when an unstable spine injury is suspected. CT can demonstrate acute fractures, characterize the extent to which fractures involve the different columns of the spine, and reveal the degree of bony retropulsion into the spinal canal (Fig. 8.9). If there is clinical concern for a ligamentous injury, spinal cord injury, or epidural hematoma, MRI should be considered as these injuries may not be detected on CT [38, 39].

Patients with suspected osteoporotic compression fractures are often referred for imaging. Fractures can be seen on radiographs as loss of vertebral body height or loss of the parallel alignment of the end plates [40, 41]. MRI can be helpful in further characterizing the morphology and acuity of osteoporotic compression fractures. In acute and subacute fractures, MRI will show surrounding T1-hypointense signal and increased T2-hyperintense signal indicating bone marrow edema (Fig. 8.10). As the fracture heals, the associated bone marrow edema will resolve (Fig. 8.11). MRI can also assess the degree to which retropulsed fracture fragments result in spinal canal or neural foraminal stenosis.

Authors report a high sensitivity of MRI for distinguishing benign osteoporotic fractures from pathologic fractures due to underlying malignancy [42, 43]. Characteristics of benign fractures include absence of marrow signal abnormality in the posterior elements, preservation of the cortex of the posterior end plate of the vertebral body, a well-defined fracture line or cleft, the absence of extraosseous soft tissue mass, and fluid or gas within the fracture [44] (see Fig. 8.11).

Degenerative Disc Disease

Radiographs do not directly image the intervertebral disc. Instead, secondary evidence of disc degenerative changes must be identified by assessing the disc space and adjacent vertebral end plates. Radiographic evidence of degenerative disc disease includes a decrease in the space between the vertebral end plates, intradiscal calcifications, and intradiscal gas. Degenerative end plate changes include end plate sclerosis, end plate irregularity, vertebral apophyseal osteophytes, and intravertebral disc herniations or Schmorl's nodes [45, 46] (Fig. 8.12). Disc and end plate changes appear similar on CT as on radiographs. However, CT is not as useful as MRI in showing soft tissue structures within the spinal canal including disc material, the thecal sac, and nerve roots.

MRI is the modality of choice for assessing degenerative changes of the intervertebral disc [37]. Disc degenerative changes are best assessed on T2-weighted sequences [47]. The normal disc has a T1-intermediate signal and T2-hyperintense nucleus pulposus with a surrounding annulus fibrosus that demonstrates a low signal on all sequences

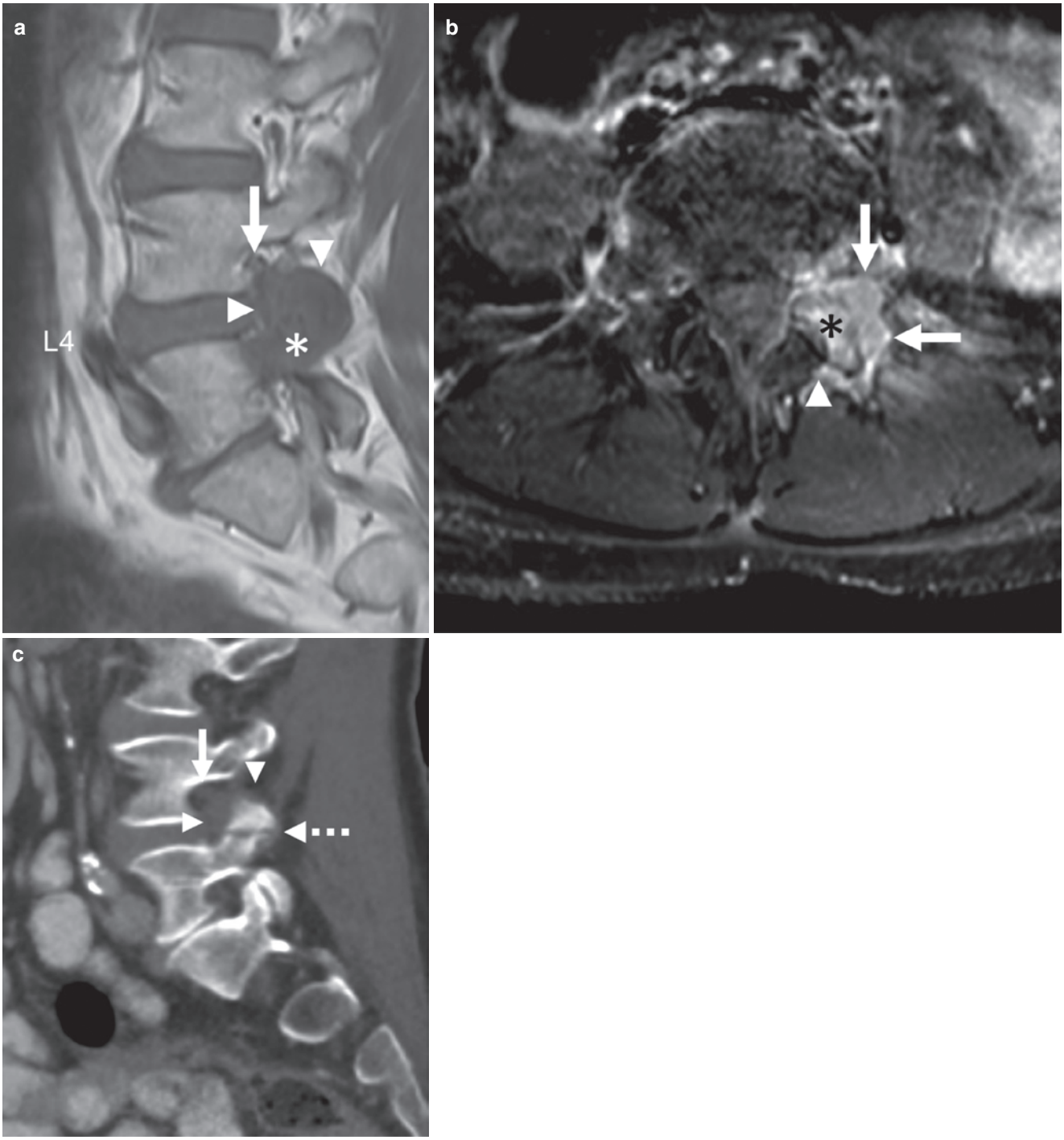

Fig. 8.7 A 76-year-old woman with a history of lung cancer presenting with back pain and radiculopathy and osseous metastatic disease. (**a**) Sagittal T1-weighed MRI image of the lumbar spine demonstrates a hypointense, marrow-replacing lesion centered the left superior articular process of L5 (∗). There is extraosseous tumor extension anteriorly and superiorly (arrowheads) which results in narrowing of the left L4–L5 neural foramen, where the mass contacts the exiting left L4 nerve (arrow). (**b**) Axial T1-weighted fat-saturated post contrast image of the lumbar spine through the L4–L5 level demonstrates an enhancing lesion involving the left L4 superior articular process (∗). There is extraosseous extension of tumor anteriorly and laterally (arrows). There is also tumor extending into the inferior articular facet of L4 (arrowhead). (**c**) Sagittal image from a CT of the lumbar spine with intravenous contrast demonstrating a transversely oriented pathologic fracture through the left L4 superior articular process (dashed arrow). There is extraosseous tumor extension anteriorly and superiorly (arrowheads) which results in narrowing of the left L4–L5 neural foramen, where mass contacts the exiting left L4 nerve (arrow)

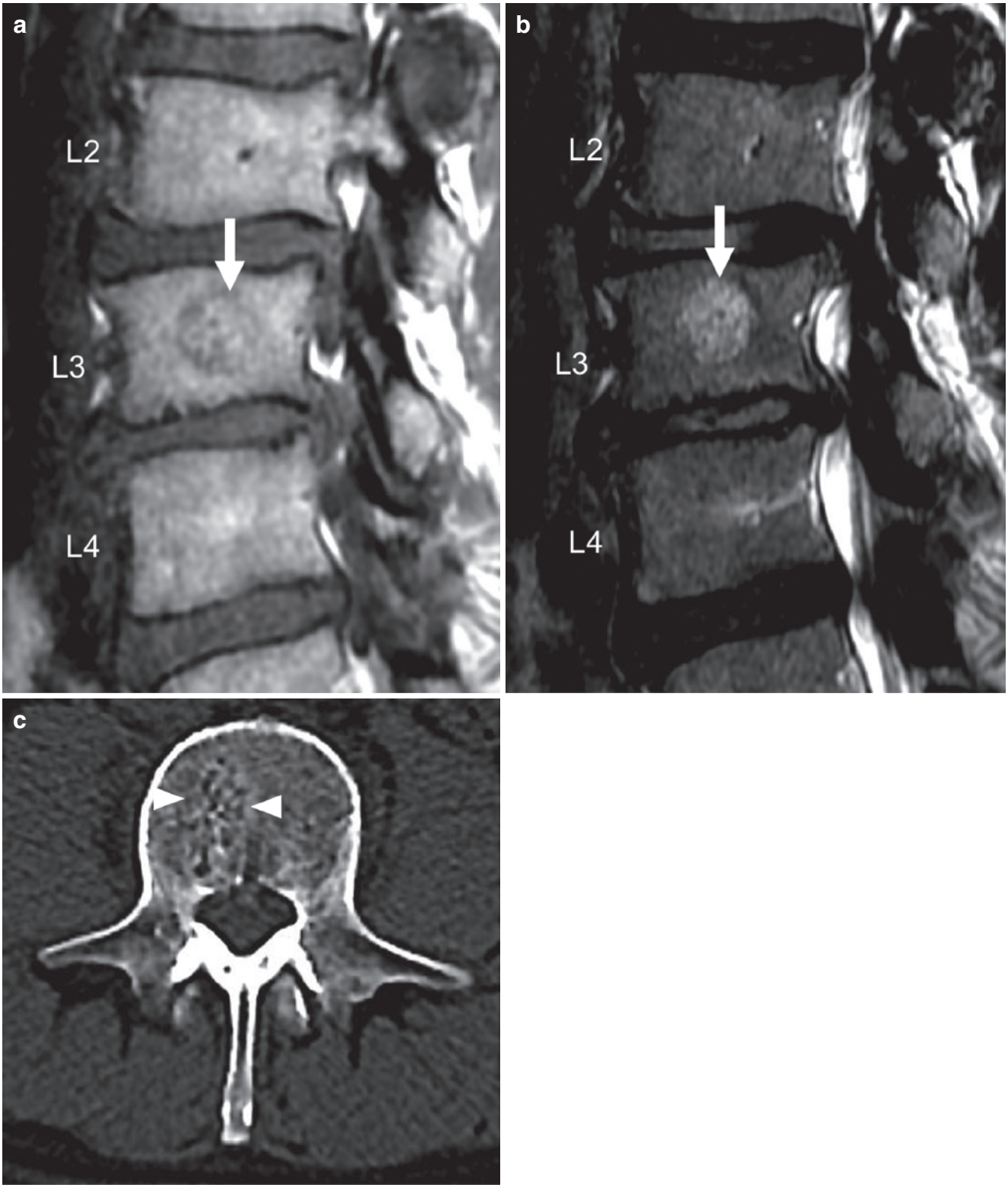

Fig. 8.8 A 50-year-old asymptomatic man with an intraosseous hemangioma in the L3 vertebral body. (**a**) Sagittal T1-weighted image of the lumbar spine demonstrates a rounded lesion in the L3 vertebral body with internal T1-hyperintense signal (arrow). (**b**) Sagittal STIR image of the lumbar spine demonstrates a hyperintense rounded lesion in the L3 vertebral body (arrow) without surrounding bone marrow edema. (**c**) Axial CT image without intravenous contrast demonstrates a lucent lesion containing coarsened trabeculae (arrowheads)

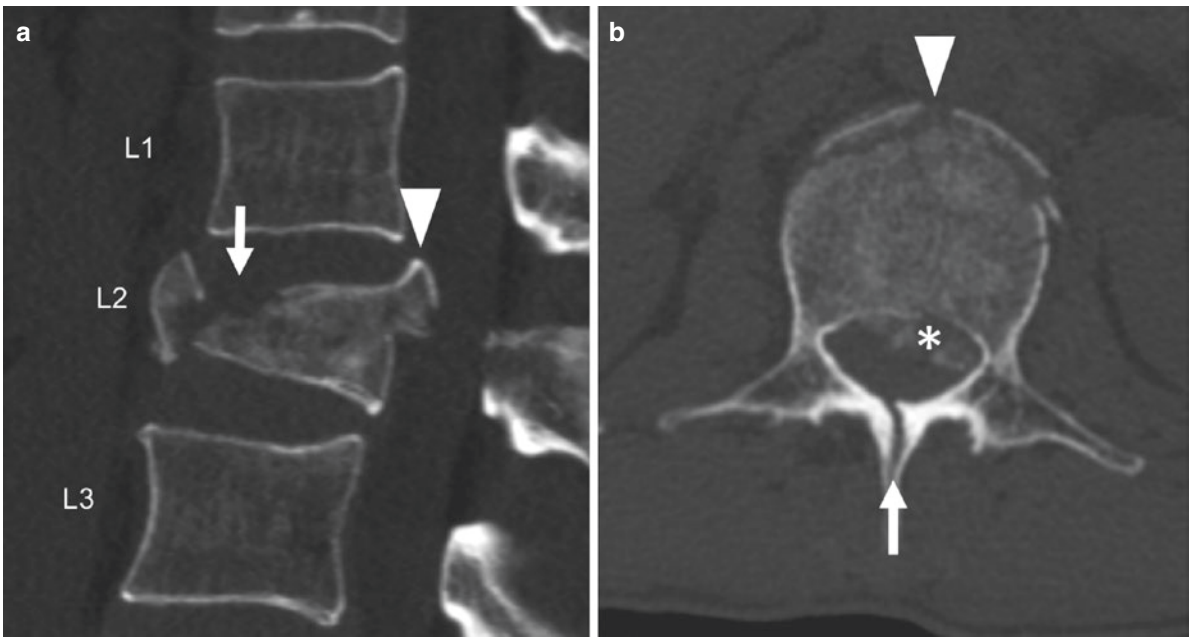

Fig. 8.9 A 55-year-old man with back pain following a fall from 8 feet and an L2 burst fracture. (**a**) Sagittal image from a non-contrast CT of the lumbar spine body demonstrates loss of L2 vertebral body height most pronounced at the anterior aspect (arrow). There is retropulsion of a fracture fragment into the spinal canal (arrowhead). (**b**) Axial image from a non-contrast CT of the lumbar spine through the L2 vertebral body demonstrates a fracture line through the anterior portion of the vertebral body (arrowhead) and retropulsion of a fracture fragment onto the left subarticular zone of the spinal canal (∗). A sagittally oriented fracture through the spinous process is also present (arrow)

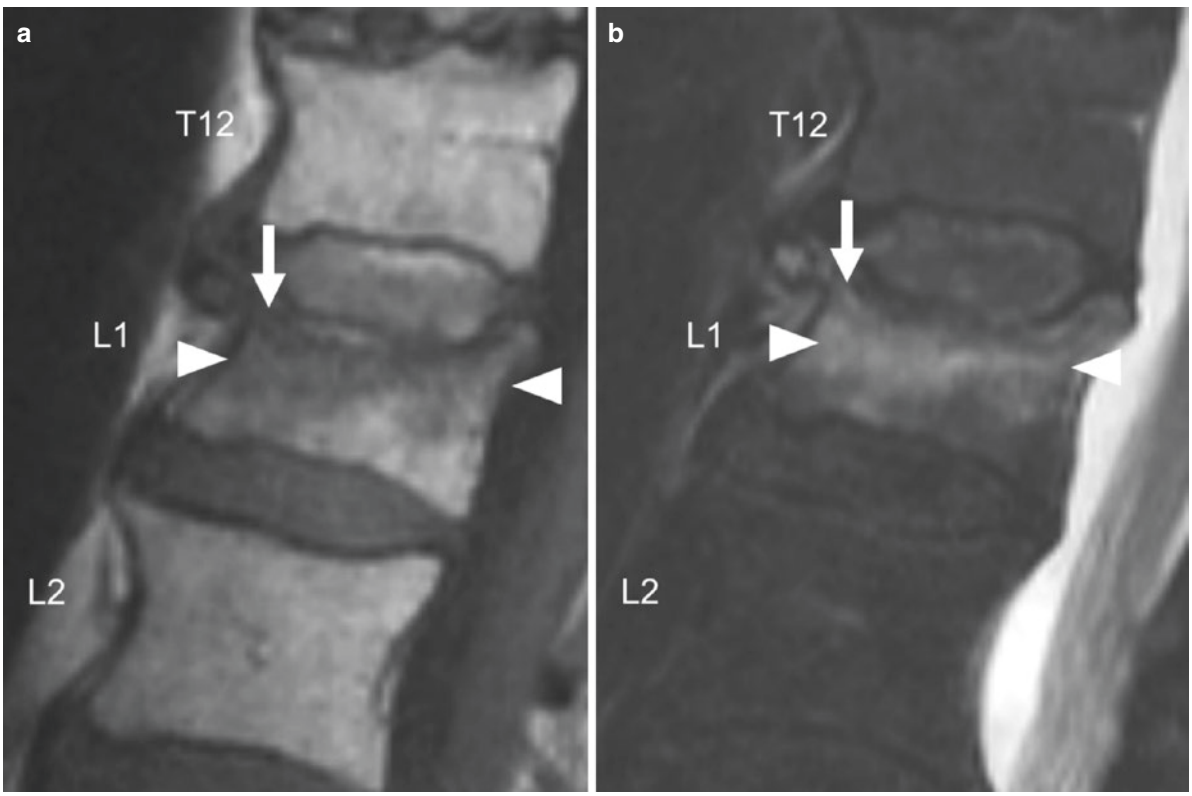

Fig. 8.10 A 63-year-old women with osteopenia and back pain with a compression fracture at L1. (**a**) Sagittal T1-weighted MRI image of the lumbar spine demonstrates approximately 30% loss of vertebral body height at the anterior aspect of L1 (arrow) and a horizontal low-signal band through the superior portion of the vertebral body (arrowheads). (**b**) Sagittal STIR image of the lumbar spine demonstrates approximately 30% loss of vertebral body height at the anterior end plate of L1 (arrow) with a horizontal high-signal band through the superior portion of the vertebral body (arrowheads)

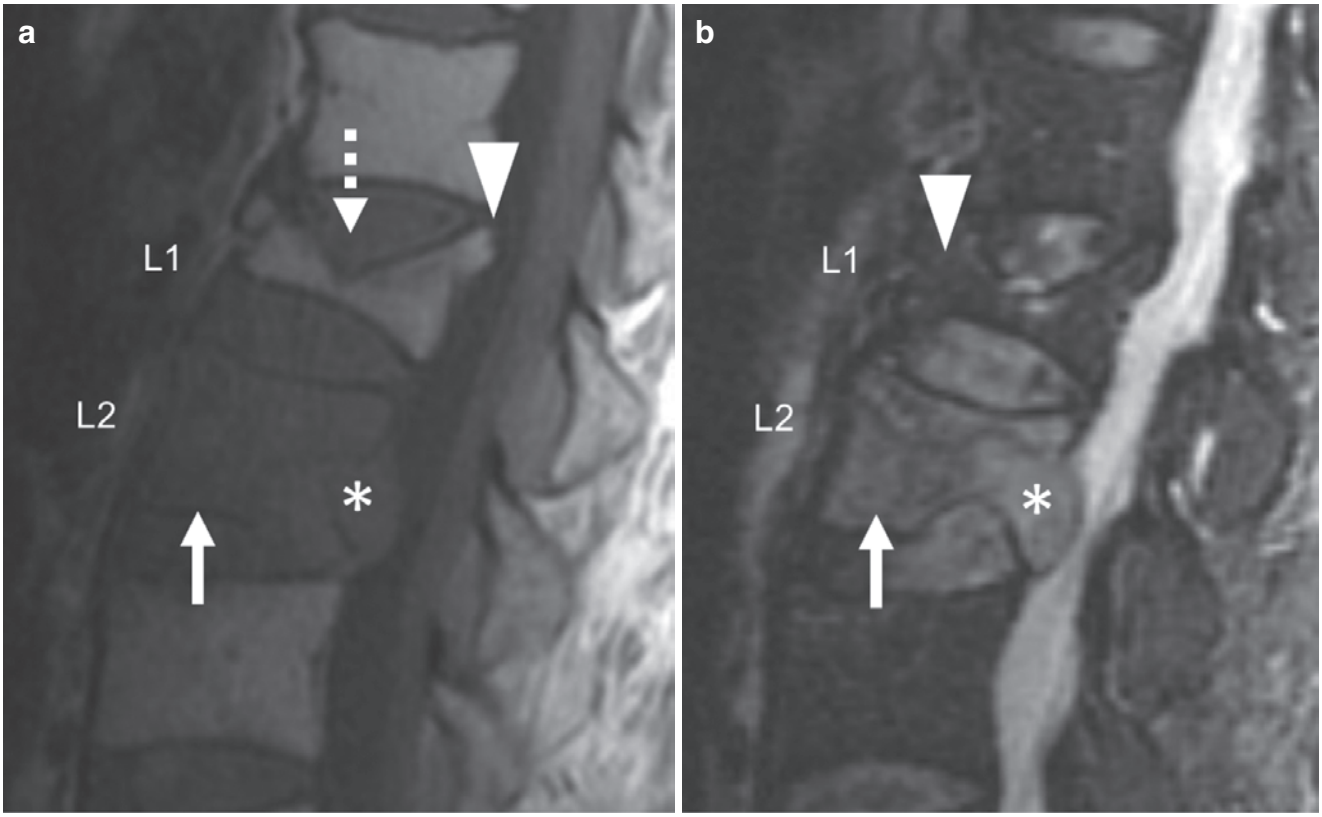

Fig. 8.11 A 67-year-old female with back pain and a chronic osteoporotic compression fracture at L1 and a pathologic compression fracture at L2. (**a**) Sagittal T1-weighted image of the lumbar spine demonstrates a severe compression deformity of the L1 vertebral body with near complete loss of vertebral body height at the mid-vertebral body (dashed arrow) and minimal bony retropulsion into the spinal canal (arrowhead). The normal T1-hyperintense marrow signal at L1 is preserved. There is a compression deformity of the L2 vertebral body with mild loss of vertebral body height. There is T1-hypointense mass extending beyond the posterior margin of the L2 vertebral body into the ventral epidural space (∗). Diffuse T1-hypointense signal involving the remaining vertebral body is consistent with associated marrow edema or inflammation. (**b**) Sagittal T1 fat-saturated post-contrast images of the lumbar spine image of the lumbar spine show no significant enhancement at the L1 vertebral body indicating that the fracture is chronic (arrowhead). The mass at the posterior inferior end plate of L2 enhances (∗), with extraosseous tumor extension beyond the posterior margin of the vertebral body into the ventral epidural space. Enhancement of the remaining L2 vertebral body likely reflects surrounding marrow edema or inflammation (arrow)

(see Fig. 8.12). The loss of T2-hyperintensity in the nucleus pulposus is the earliest indication of disc degenerative changes and can be followed by the loss of intervertebral disc [48]. In 1988, Modic and colleagues described three stages of degenerative end plate changes as seen on MRI which remain in common clinical use [49] (Figs. 8.13, 8.14, and 8.15).

Degenerative changes to the intervertebral disc frequently result in extension of disc material beyond the contour of the adjacent vertebral end plates. In 2014, a combined task force of the North American Spine Society, the American Society of Spine Radiology, and the American Society of Neuroradiology proposed updated standardized nomenclature for describing disc abnormalities [50]. Disc bulge refers to the extension of disc material beyond the margin of the vertebral end plate by greater than 25% of the disc circumference (Fig. 8.16). Disc herniation, in contrast, refers to extension of disc material beyond the margin of the vertebral end plate by less than 25% of the disc circumference. Herniation can be further characterized as a disc protrusion, extrusion, or sequestration, depending on the morphology of the herniated disc material (Fig. 8.17). Consensus nomenclature has also been applied to the description of the location of posteriorly oriented herniated disc material as it relates to the spinal canal and neural foramina (Fig. 8.18).

Annular fissures are degenerative linear defects in fibers of the annulus fibrosus of the intervertebral disc. Although these can be associated with back pain, they are also commonly seen in asymptomatic individuals [51–54]. Annular fissures are not seen on radiographs or CT but will manifest as a "high-intensity zone" on MRI. This term refers to hyperintense signal on T2-weighted sequences at the peripheral margin of the posterior intervertebral disc [55] (Fig. 8.19).

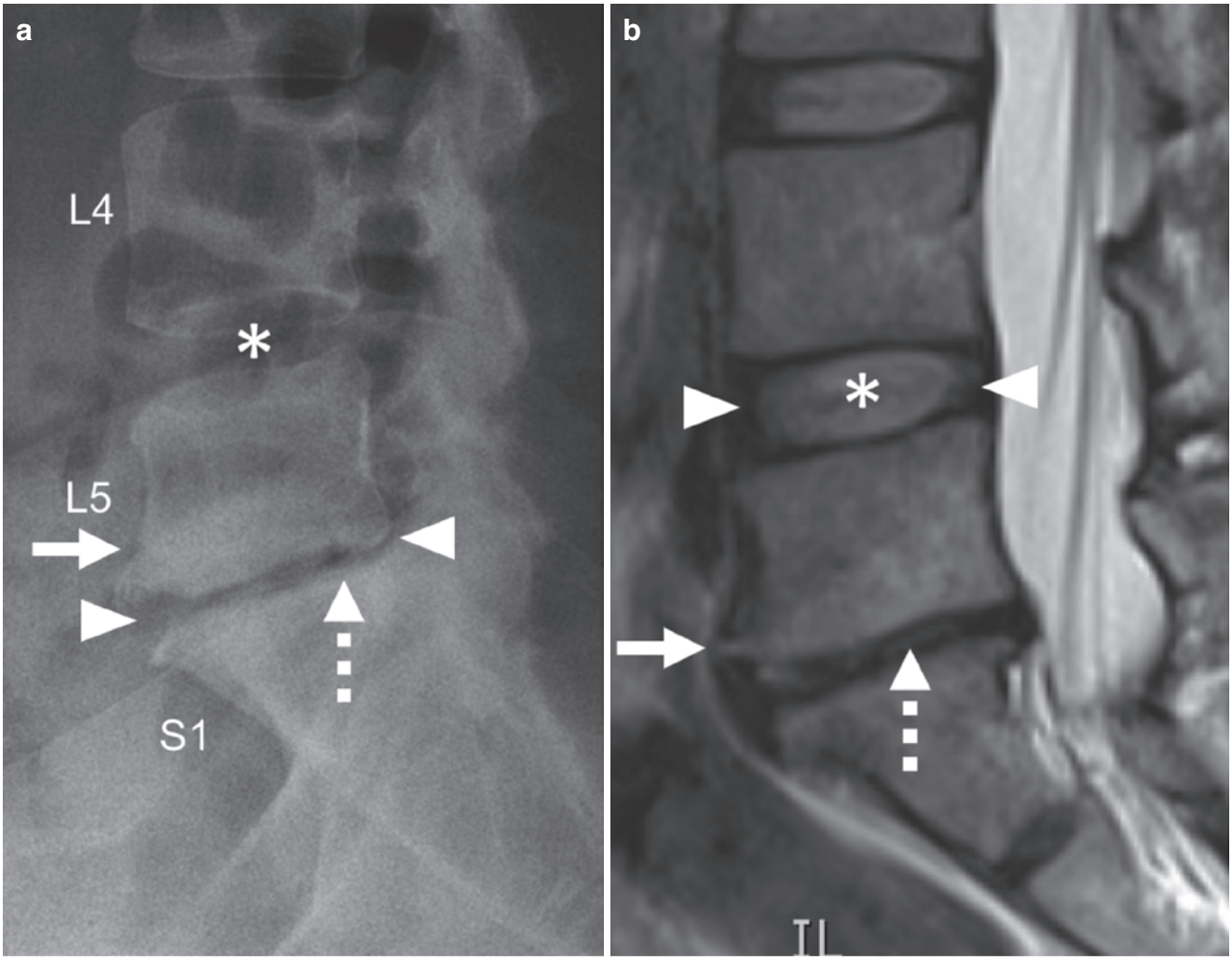

Fig. 8.12 A 47-year-old woman with back pain and disc degenerative changes at L5–S1. (**a**) Lateral radiograph of the lumbar spine demonstrates disc degenerative changes at L5–S1 with disc space narrowing (arrowheads), sclerosis of the adjacent L5 end plate (arrow), and vacuum phenomenon in the disc space (dashed arrow). The L4–L5 disc space (∗), in contrast, is preserved. (**b**) Sagittal T2-weighted image of the lumbar spine demonstrates disc degenerative changes at L5–S1 with loss of height and T2-hypointensity of the disc compatible with dessication (dashed arrow). There is apophyseal osteophytosis at the inferior end plate of L5 (arrow). The L4–L5 intervertebral disc is normal, with normal disc height, a low signal annulus fibrosus along the periphery of the disc (arrowheads), and a T2-hyperintense nucleus pulposis (arrowheads)

Post contrast images may show avid enhancement of the adjacent annulus and adjacent extradural space indicating inflammation [56, 57].

Infection

Vertebral discitis-osteomyelitis refers to infection of the intervertebral disc and its adjacent end plate. This most commonly occurs as a result of hematogenous dissemination of infection to the vertebral end plate which spreads to the intervertebral disc [58]. Radiographs are typically normal in early discitis-osteomyelitis, with findings of end plate irregularity and loss of disc height appearing after the first 2–4 weeks of infection [59] (Fig. 8.20). However, initial radiographs are frequently positive, as patients are not typically imaged until symptoms have been present for weeks or months [60]. On CT, the findings of discitis-osteomyelitis are similar to those seen on radiographs, although the superior bone detail provided by CT allows for earlier detection of end plate irregularity. CT can show soft tissue findings such as collections in the paravertebral musculature and epidural space, particularly if intravenous contrast is administered.

MRI performed with and without intravenous contrast is the imaging study of choice for assessment of discitis-

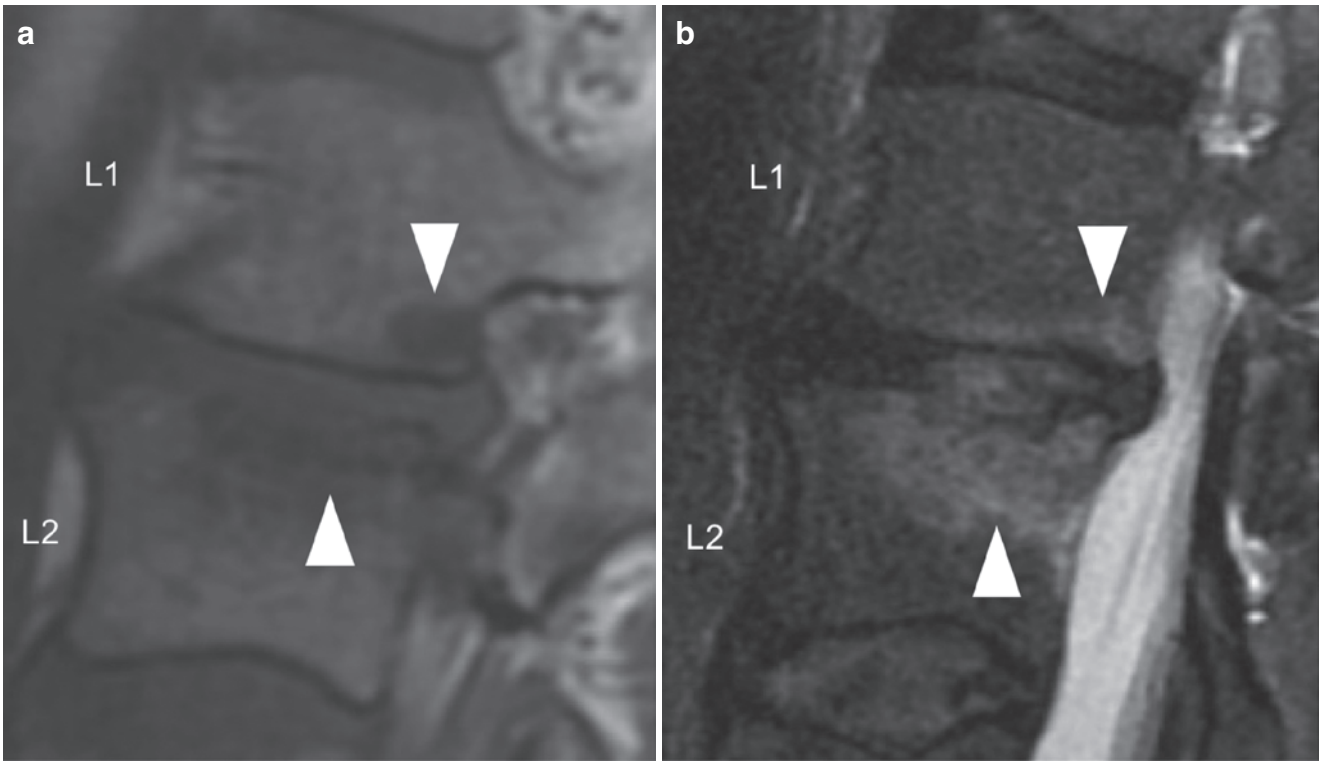

Fig. 8.13 A 67-year-old male with Modic type 1 end plate changes at L1–L2. (**a**) Sagittal T1-weighted image demonstrates low T1 signal at both the inferior end plate of L1 and the superior end plate of L2 (arrowheads). (**b**) Sagittal STIR image demonstrates hyperintense signal at both the inferior end plate of L1 and the superior end plate of L2 (arrowheads). These signal abnormalities indicate end plate marrow edema

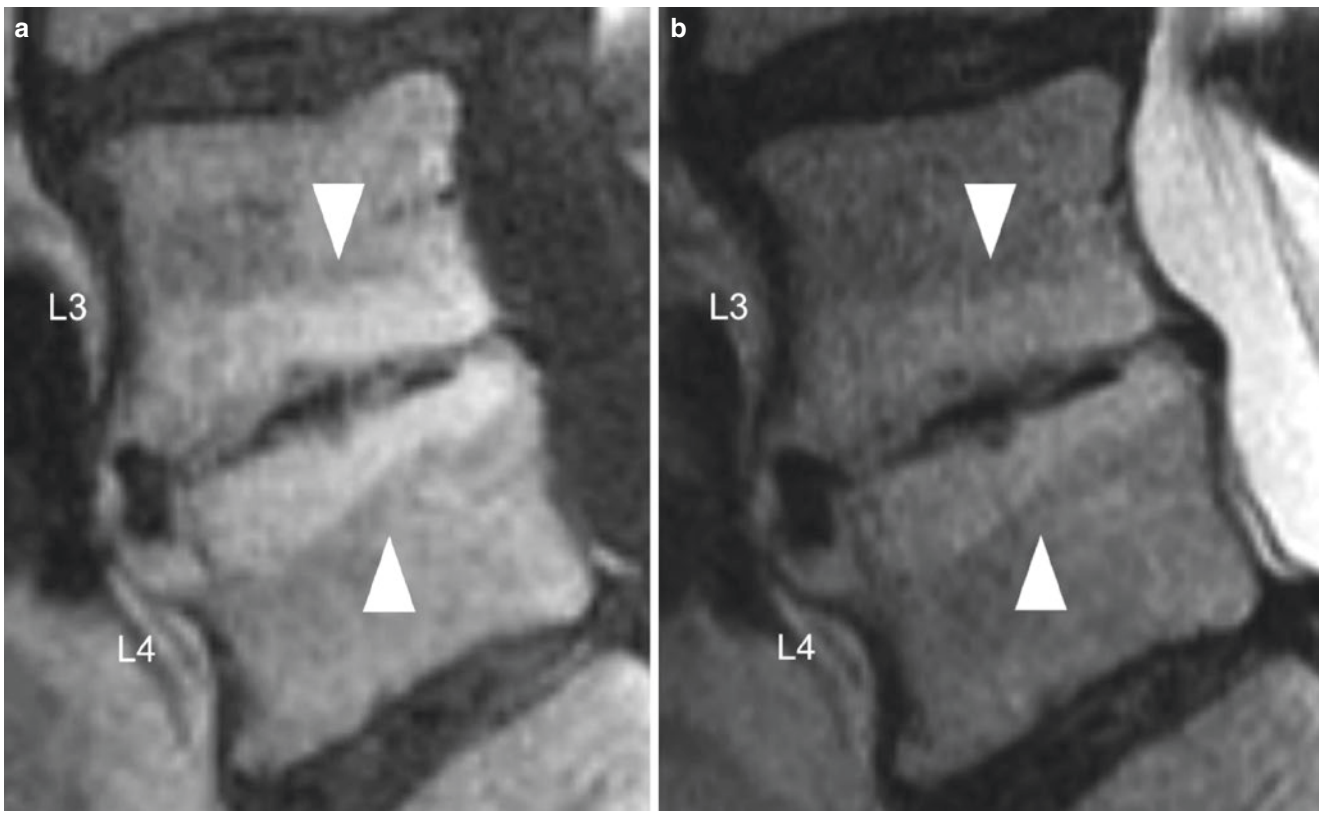

Fig. 8.14 A 55-year-old woman with Modic type 2 end plate changes at L3–L4. (**a**) Sagittal T1-weighted image demonstrates increased T1 signal at both the inferior end plate of L3 and the superior end plate of L4 (arrowheads). (**b**) Sagittal T2-weighted image demonstrates T2-hyperintense signal at both the inferior end plate of L3 and the superior end plate of L4 (arrowheads). These signal abnormalities reflect fatty replacement of the bone marrow at the vertebral end plates

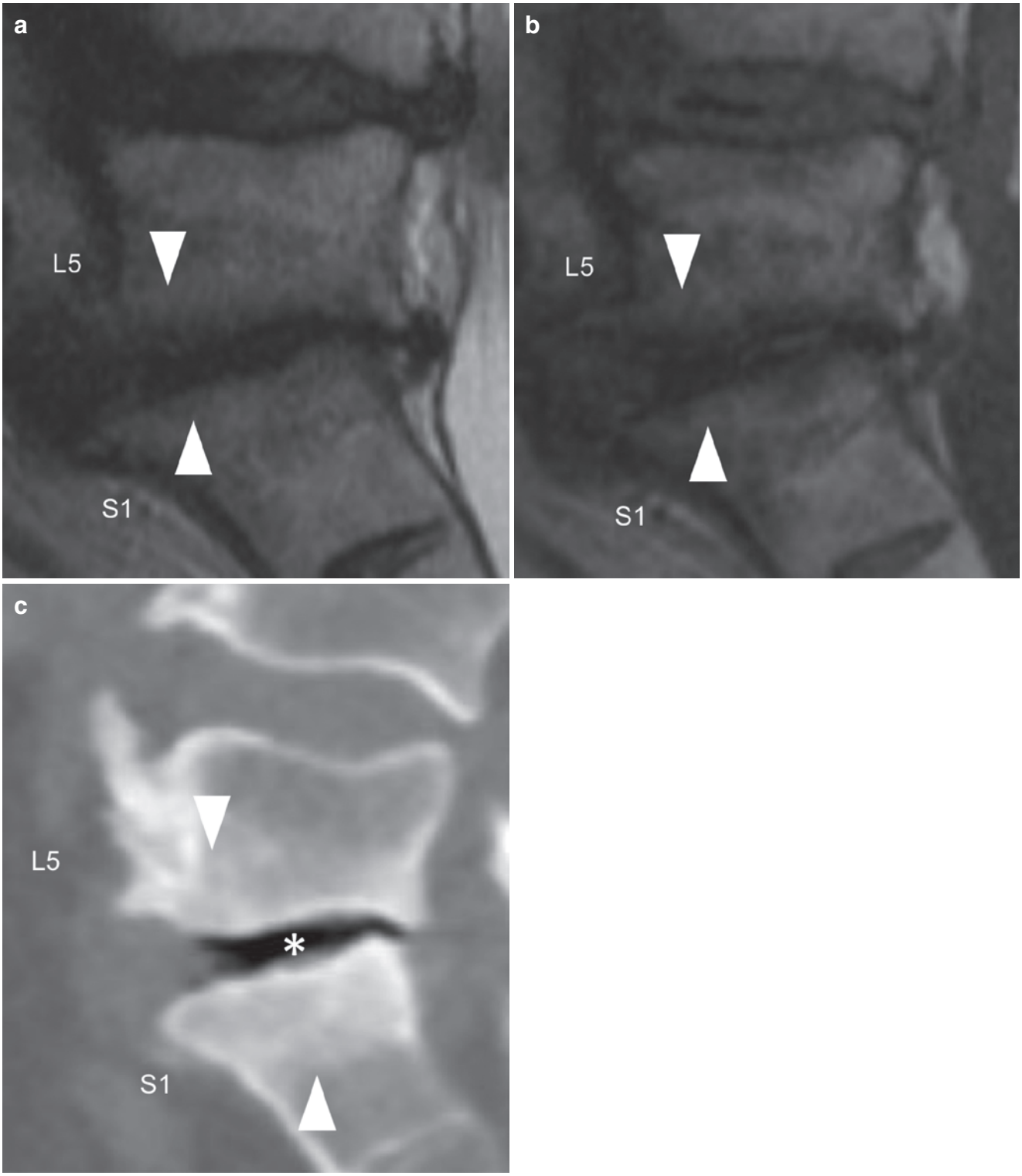

Fig. 8.15 52-year-old man with Modic type 3 end plate changes at L5–S1. (**a**) Sagittal T1-weighted image demonstrates low T1 signal at both the inferior end plate of L5 and the superior end plate of S1 (arrowheads). (**b**) Sagittal T2-weighted image demonstrates low T2 signal at both the inferior end plate of L5 and the superior end plate of S1 (arrowheads). (**c**) Sagittal image from a CT without intravenous contrast shows sclerosis of the inferior end plate of L5 and the superior end plate of S1 end plates (arrowheads). There are also degenerative changes of the intervertebral disc with disc space narrowing and intradiscal gas (*)

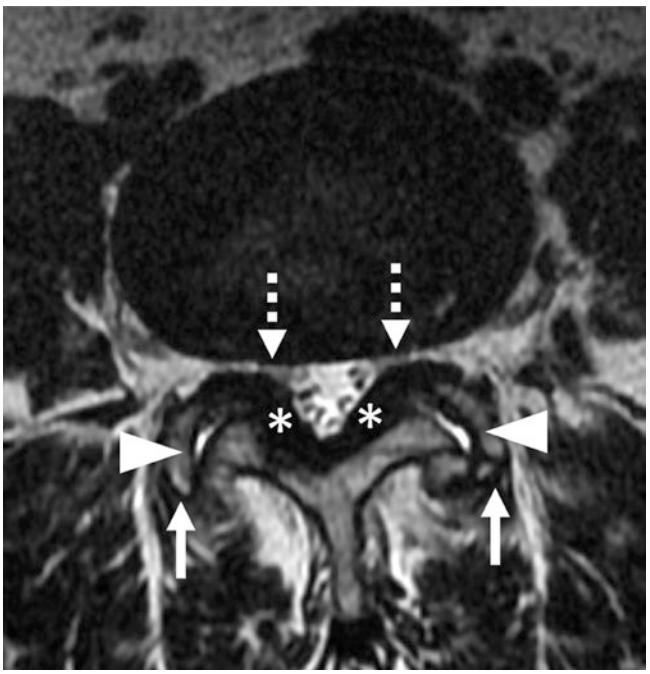

Fig. 8.16 A 44-year-old man with bilateral lower extremity radiculopathy and bilateral L3–L4 subarticular zone narrowing. Axial T2-weighted image through the L3–L4 intervertebral disc demonstrates concentric disc bulge. There is also bilateral facet arthropathy as evidenced by bony proliferative changes (arrows) and bilateral facet joint effusions (arrowheads). Ligamentum flavum hypertrophy is also present (∗). Together, disc and facet degenerative changes combine to result in bilateral subarticular zone narrowing with impingement of both descending L4 nerve roots (dashed arrows)

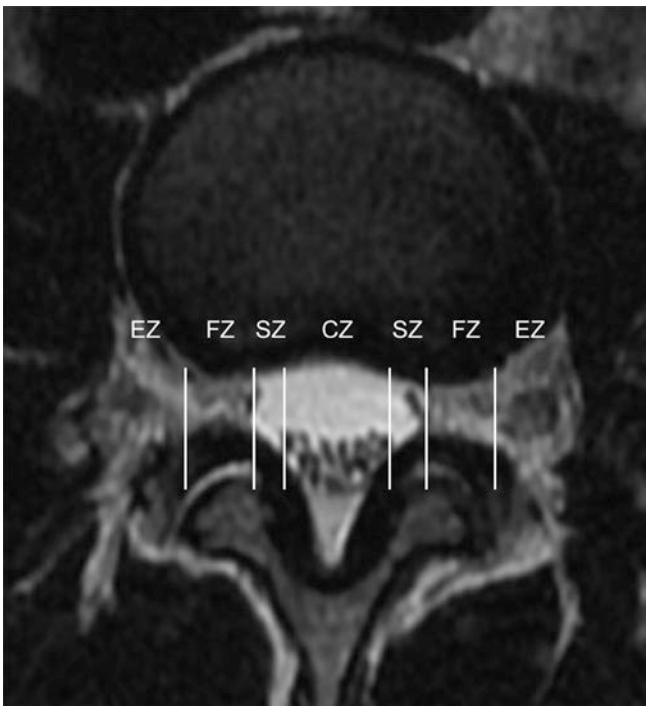

Fig. 8.18 A 25-year-old asymptomatic man. Axial T2-weighted image through the L3–L4 intervertebral disc shows no disc bulge or herniation. The central zone (CZ) describes to the center of the spinal canal bounded by the medial edges of both facet joints. The subarticular zone (SZ) describes the space bounded medially by the central zone and laterally by the medial margin of the pedicles. The foraminal zone (FZ) describes the space between the medial and lateral margins of the pedicles. The extraforaminal zone (EZ) refers to the space beyond the lateral margin of the pedicles

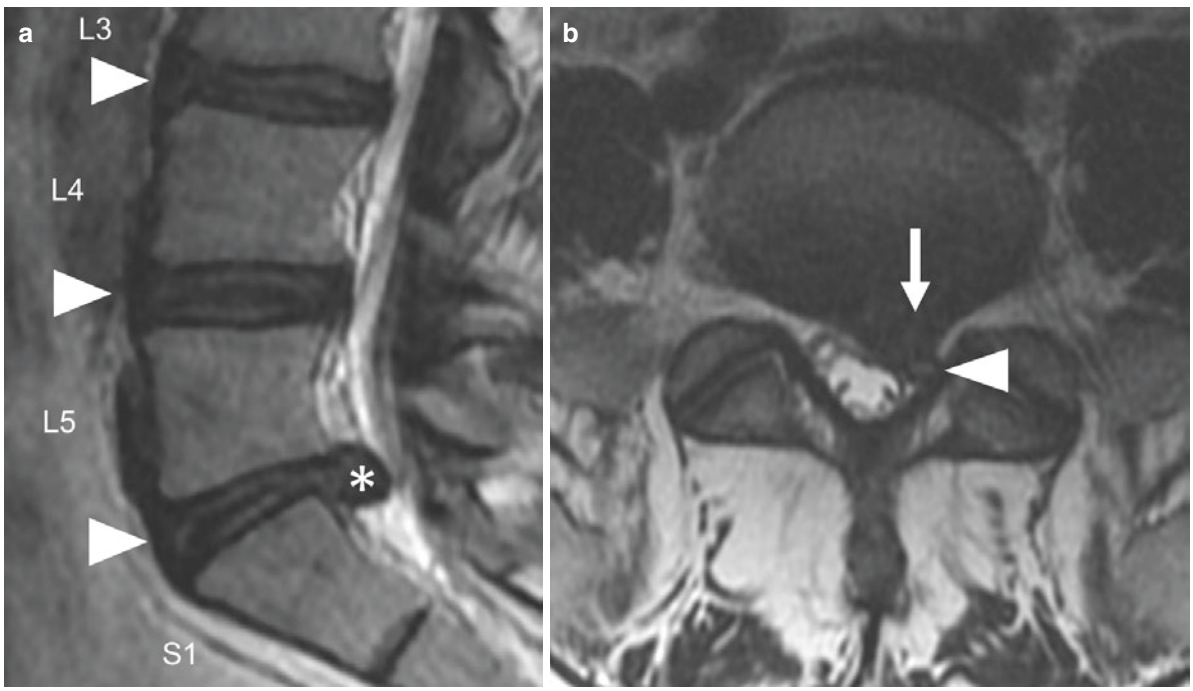

Fig. 8.17 A 31-year-old woman with low back pain and a disc extrusion at L5–S1. (**a**) Sagittal T2-weighted image demonstrates an abnormal contour of the posterior aspect of the L5–S1 intervertebral disc (∗). The herniated disc material involves less than 25% of the circumference of the disc and has a narrow neck near where it contacts the remainder of the disc and is therefore consistent with an extrusion. The L3–L4, L4–L5, and L5–S1 intervertebral discs all show decreased T2-hyperintense signal indicating disc desiccation (arrowheads). (**b**) Axial T2-weighed image through the level of the L5–S1 intervertebral disc demonstrates disc herniation (arrow) which narrows the left subarticular recess and results in mass effect on the descending left S1 nerve root (arrowhead). Enlargement and increased T2 signal of the descending S1 nerve root indicate edema and inflammation

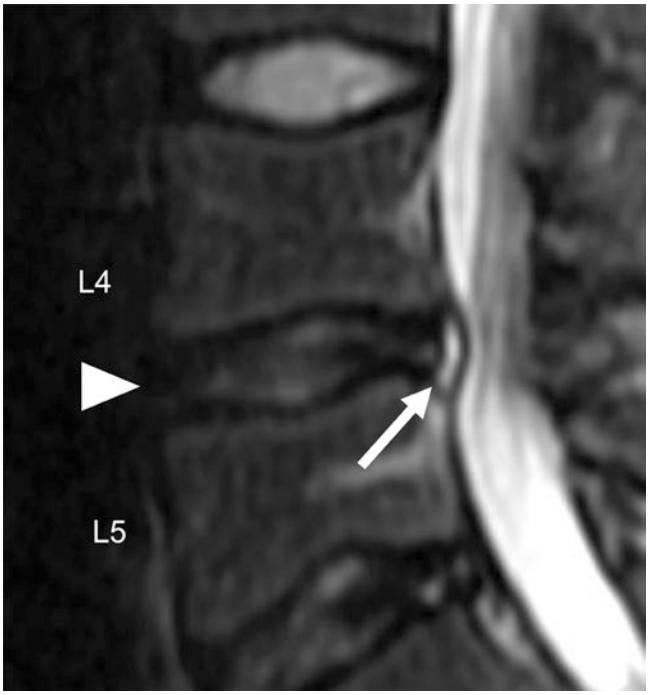

Fig. 8.19 A 54-year-old man with back pain and an annular fissure at L4–L5. Sagittal T2-weighted image of the lumbar spine demonstrates disc desiccation at L4–L5 (arrowhead). There is focally increased T2-hyperintense signal at the peripheral posterior margin of the L4–L5 intervertebral disc indicating an annular fissure (arrow)

osteomyelitis [59]. Early findings include T1-hypointense and T2-hyperintense signal of the vertebral end plates which can appear similar to type 1 Modic changes. However, unlike the T2-hypointense signal typically seen in desiccated disc material, infected disc typically demonstrates T2-hyperintense signal [1]. Post contrast images can show enhancement of the disc, the adjacent vertebral bodies, and surrounding paravertebral soft tissues indicating phlegmon (Fig. 8.21). Post-contrast images are necessary to distinguish paravertebral or epidural phlegmon from abscess. Both phlegmon and abscess will appear as hyperintense signal on T2-weighted sequences. However, while phlegmon will enhance, diffuse abscess will show peripheral rim enhancement with an internal non-enhancing component [2, 3] (see Fig. 8.20). Routine MRI follow-up of spine infection is not recommended, as imaging findings can persist or worsen despite clinical improvement on appropriate antimicrobial therapy [61–64].

Posterior Elements

The normal facet joint articular surfaces should appear smooth on all imaging modalities. The space between the bony articular surfaces of the articular processes should measure 2–4 mm [65]. Degenerative changes at the facet joint are the same as those in other synovial joints, where imaging findings include joint space narrowing, marginal osteophyte formation, subchondral sclerosis, and subchondral cystic changes [65–67]. Although these can be seen on radiographs, facet joints are better assessed by cross-sectional imaging. Additional findings on MRI include join effusion, synovial thickening, bone marrow edema of the superior and inferior articular processes, and periarticular edema [67] (Fig. 8.22).

Hypertrophy of the ligamentum flavum is commonly associated with facet degenerative changes [68, 69]. The ligamentum flavum, normally a thin structure of soft tissue attenuation on CT and low signal on all MRI sequences, will appear thickened and may have accompanying areas of internal mineralization or ossification. This thickening can contribute to spinal canal narrowing, particularly in the subarticular zones where there can be resulting mechanical impingement of the descending nerve roots (see Fig. 8.16). Mineralization and thickening of the ligamentum flavum may also be due to diffuse idiopathic skeletal hyperostosis, ankylosing spondylitis, renal failure, calcium pyrophosphate deposition disease, and hemochromatosis [68].

Cystic lesions associated with the posterior elements of the spine can develop as a result of degenerative changes to the facet joints and the surrounding ligamentous structures. These are most commonly seen at the L4–L5 level [70]. Although not typically well assessed on radiographs or CT unless they contain gas or foci of calcification, degenerative cysts are heterogeneously T2-hyperintense with a rim that is low in signal intensity on all sequences [70–72]. Post-contrast images will show peripheral but no central enhancement [73]. Cysts that extend into the extradural spinal canal or the neural foramen can result in spinal canal or neural foraminal stenosis (see Fig. 8.22).

Spondyloarthropathies

The seronegative spondyloarthropathies are a class of inflammatory diseases that share common clinical and imaging features. Although this group includes psoriatic arthritis, reactive arthritis, and arthritis related to inflammatory bowel disease, ankylosing spondylitis is most likely to demonstrate axial skeletal manifestations. Abnormalities in the lumbar spine typically precede abnormalities in the cervical or thoracic spine [74, 75]. Early findings on radiographs or CT are erosions with surrounding sclerosis at the corners of the vertebral bodies [76]. MRI will show T2-hyperintensity and enhancement on post-contrast images in a similar location suggesting edema and inflammation [77]. Inflammation of the ligaments surrounding the

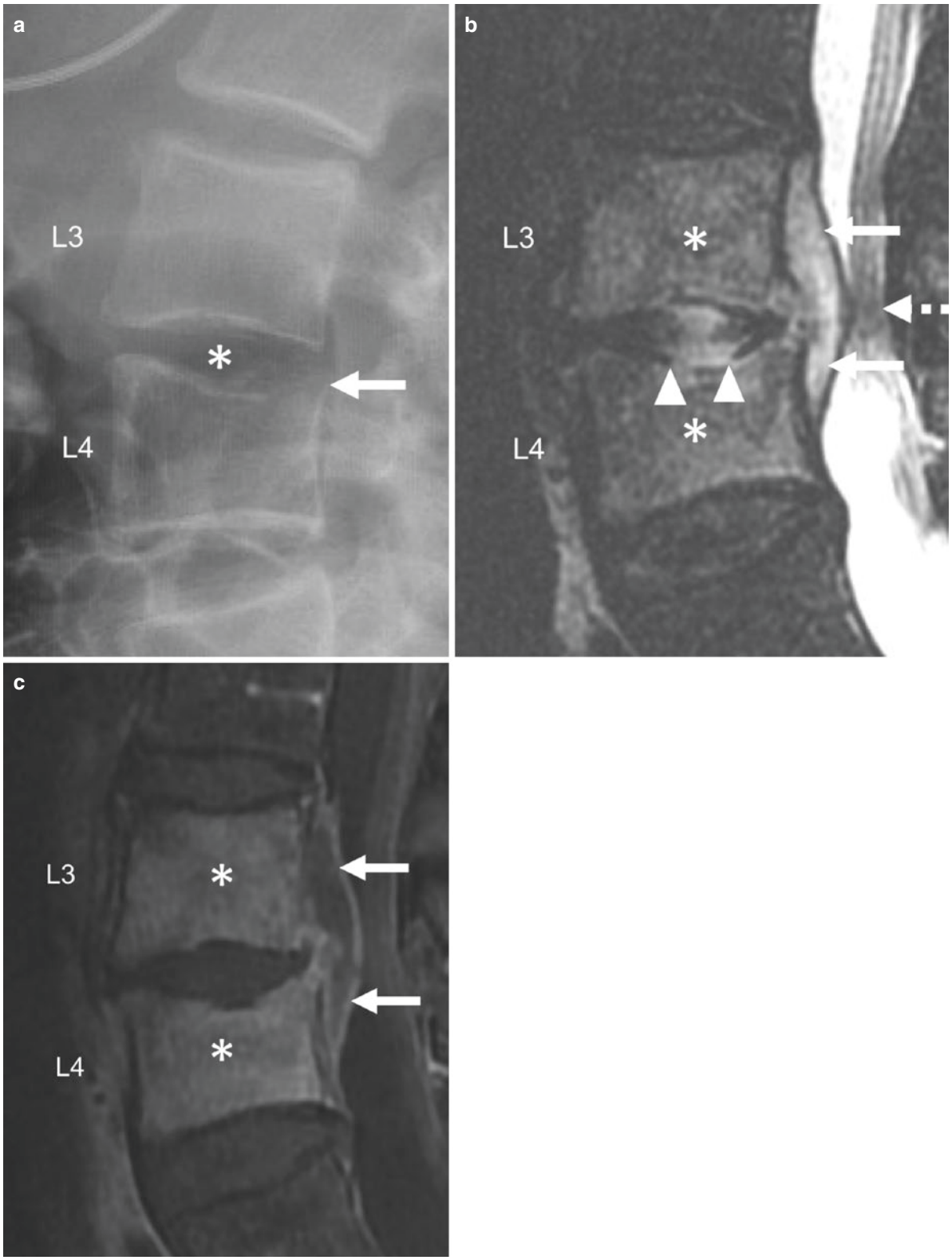

Fig. 8.20 A 34-year-old male intravenous drug user with discitis-osteomyelitis and epidural abscess. (**a**) Lateral radiograph of the lumbar spine demonstrates a preserved L3–L4 disc space (∗). There is an ill-defined appearance of the posterior aspect of the superior end plate of L4 (arrow). (**b**) Sagittal STIR image of the lumbar spine demonstrates increased STIR signal involving entire L3 and L4 vertebral bodies (∗). There is loss of the linear low along the superior L4 vertebral end plate suggesting destruction of the end plate (arrowheads). A lenticular T2-hyperintense structure extends into the ventral epidural space along the posterior end plates of L3 and L4 (arrows) consistent with phlegmon or abscess and results in compression of the cauda equina (dashed arrow). (**c**) Sagittal T1 post-contrast image of the lumbar spine demonstrates enhancement of the entire L3 and L4 vertebral bodies (∗). The lenticular structure in the ventral epidural space extending along the posterior end plates of L3 and L4 demonstrates peripheral enhancement with central non-enhancement and is consistent with epidural abscess

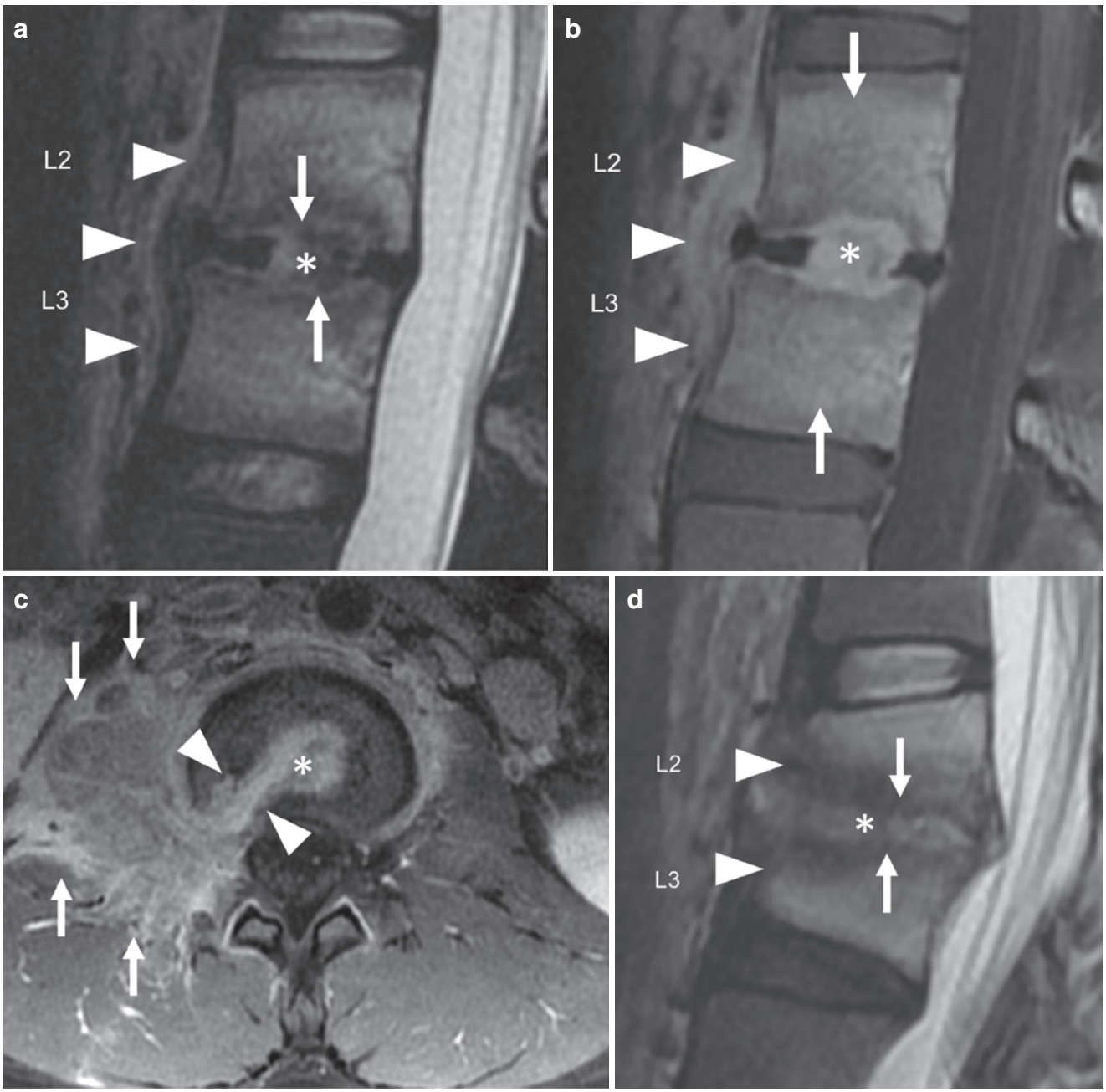

Fig. 8.21 A 27-year-old female intravenous drug user with back pain and discitis-osteomyelitis. (**a**) Sagittal T2-weighted image of the lumbar spine shows increased T2 signal in the central portion of the L2–L3 intervertebral disc (∗) with associated irregularity of the adjacent end plates (arrows). Thickening and increased T2 signal of the anterior longitudinal ligament and surrounding prevertebral soft tissues are also present indicating paravertebral inflammation (arrowheads). (**b**) Sagittal T1-weighted fat-saturated post-contrast image of the lumbar spine shows enhancement of the central L2–L3 intervertebral disc (∗) as well as of nearly the entire L2 and L3 vertebral bodies (arrows). Thickening and enhancement of the anterior longitudinal ligament and surrounding prevertebral soft tissues are also present indicating paravertebral inflammation (arrowheads). (**c**) Axial T1-weighted fat-saturated post contrast image through the L2–L3 intervertebral disc demonstrates enhancement of the central disc (∗) with a defect in the right posterolateral annulus fibrosis (arrows). Enhancing material extends beyond the annular defect with enlargement and enhancement of the right psoas and quadratus lumborum muscles consistent with phlegmon (arrowheads). (**d**) Sagittal T2-weighted image of the lumbar spine performed 8 months later after noncompliance with the antimicrobial regimen demonstrates progressive changes of discitis-osteomyelitis with loss of the L2–L3 intervertebral disc height (∗), worsening end plate destructive changes (arrows), and loss of vertebral body height resulting of a focal kyphosis (arrowheads)

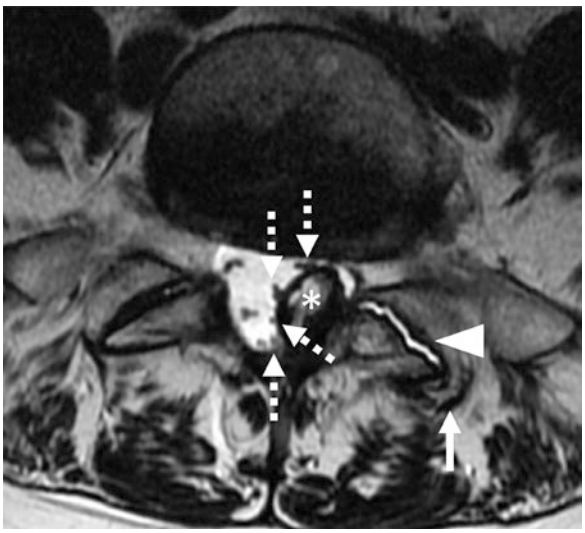

Fig. 8.22 An 81-year-old woman with back pain and radiculopathy and prominent left L5–S1 facet degenerative changes and a degenerative cyst. Axial T2-weighted image through the L5–S1 intervertebral disc demonstrates bilateral facet degenerative changes which are more severe on the left, where there are prominent bony proliferative changes (solid arrow) and a joint effusion (arrowhead). A heterogeneously T2-hyperintense rounded structure (∗) with a low signal rim extends into the spinal canal and contacts the descending sacral nerve roots (dashed arrows) consistent with a degenerative cyst

posterior elements will not be seen on radiographs or CT but can be seen on MRI as T2-hyperintense signal and enhancement, most commonly involving the supraspinal and interspinous ligaments [78, 79] (Fig. 8.23). In more advanced disease, bridging syndesmophytes at the vertebral end plates can cause ankylosis across the intervertebral spaces and a resulting "bamboo spine" appearance. Chronic facet joint arthritis and enthesitis at bony attachments of the spinal ligaments may also result in ankylosis of the posterior elements [80]. Biomechanical changes due to ankylosis of the spine predispose individuals to serious spinal injury, even in the setting of minimal trauma (Fig. 8.24). As these fractures can be difficult to detect on radiographs, there should be a low threshold for ordering cross-sectional imaging if there has been a history of prior trauma or if symptoms are severe [78, 81].

Other Structures

Lumbar spine imaging, while tailored for assessment of the lumbar vertebrae and their supporting structures, often includes other anatomic structures including portions of the sacrum, the retroperitoneum, and abdominopelvic viscera.

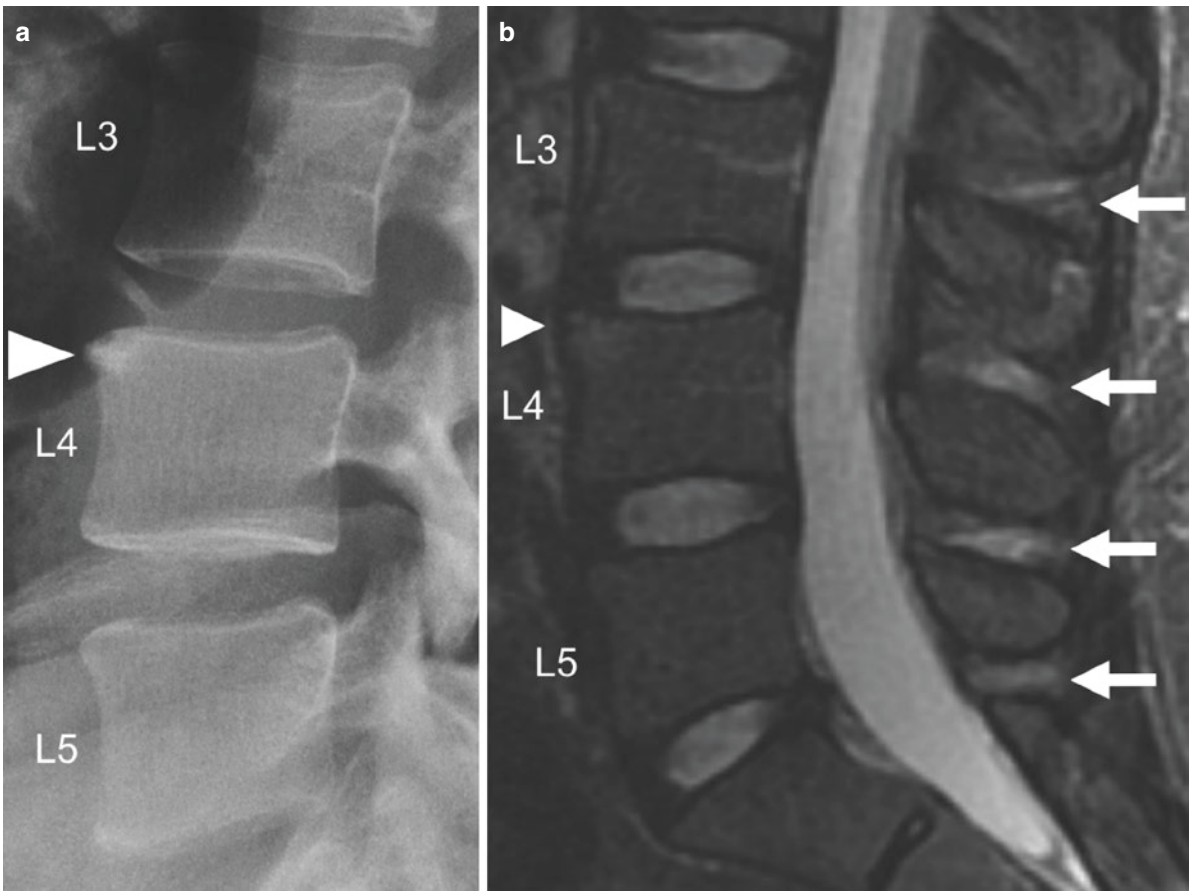

Fig. 8.23 A 37-year-old man with chronic back pain and ankylosing spondylitis. (**a**) Lateral radiograph of the L4 vertebral body demonstrates an irregularity at the anterior superior end plate with surrounding sclerosis (arrowhead) compatible with an inflammatory erosion. (**b**) Sagittal STIR image the lumbar spine demonstrates edema at the anterior superior end plate of the L4 vertebral body (arrowhead) suggesting active inflammation. Increased signal involving the interspinous ligaments at all the imaged levels (arrow) is consistent with enthesitis

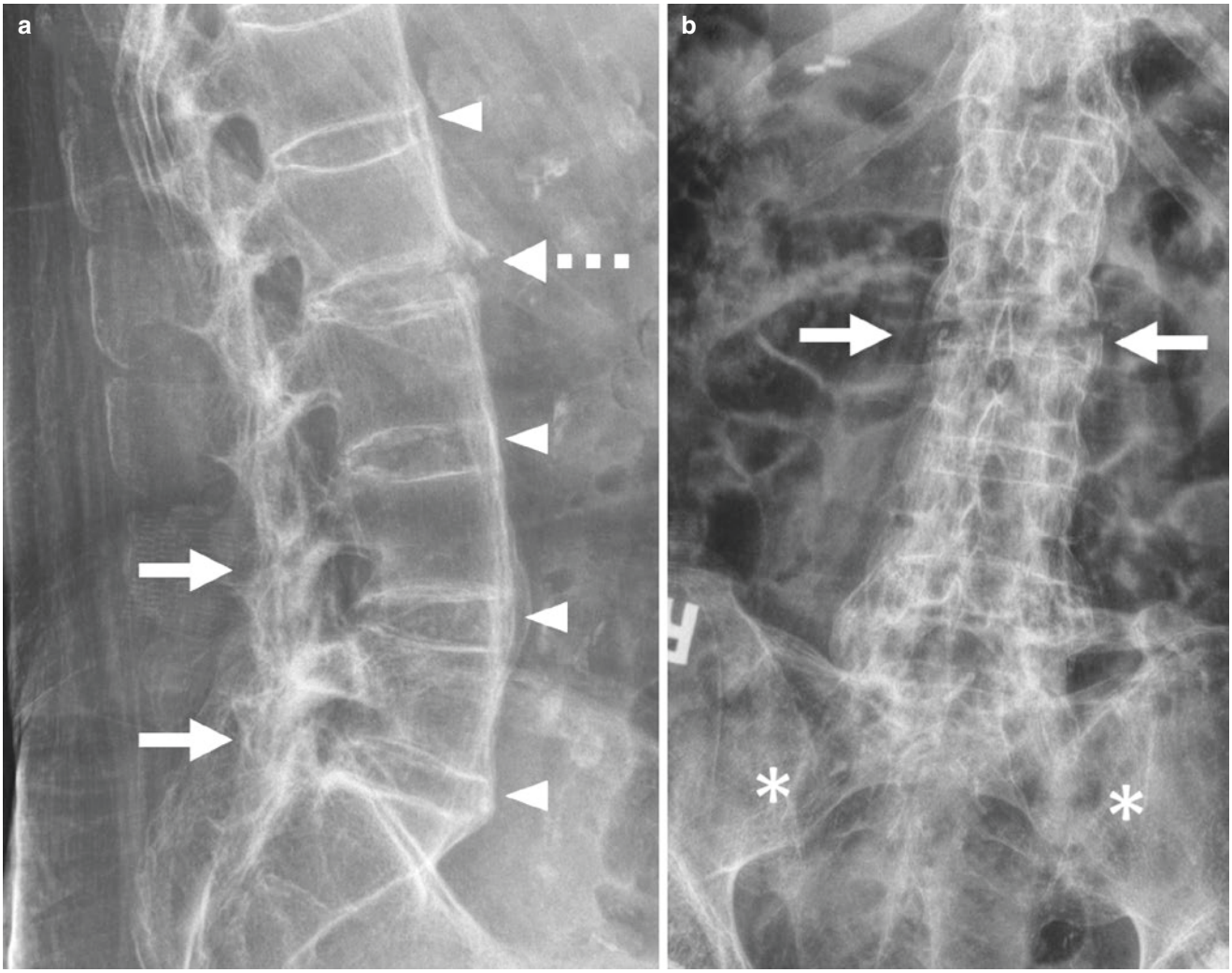

Fig. 8.24 A 95-year-old man with history of ankylosing spondylitis and pain after a mechanical fall from standing. (**a**) Lateral radiograph of the lumbar spine shows multilevel intervertebral syndesmophytes resulting in a "bamboo spine" appearance (arrowheads). Osseous fusion of the facet joints is also seen (solid arrows). A mildly displaced fracture extends through the L2 syndesmophyte (dashed arrow). (**b**) Anteroposterior radiograph of the lumbar spine shows the fracture extending through the L2–L3 disc space (arrows) with mild rightward displacement of the L2 vertebral body with respect to the L3 vertebral body. These fractures are unstable and may lead to severe deformity, neural injury, and pseudarthrosis. There is also ankylosis of both sacroiliac joints due to chronic sacroiliitis (∗)

Although abnormalities involving these structures are often incidental findings, they may also account for the patient's presenting symptoms.

Portions of the sacrum are normally imaged on radiographs, CT, and MRI. Sacral insufficiency fractures may be detected on radiographs but are often difficult to identify. Insufficiency fractures will appear as a sclerotic vertical line parallel to the sacroiliac joint on frontal radiographs. A transverse component through the sacral vertebral body can be detected as offset and sclerosis of the anterior sacral end plates on the lateral view [82, 83]. CT can better detect the fracture lines and the degree of displacement and can show surrounding sclerosis [84] (Fig. 8.25). MRI is more sensitive than radiographs or CT and can show bone marrow edema of the sacral ala suggesting an early insufficiency fracture, even before a fracture line is apparent [85].

The sacroiliac joints are at least partially visualized on dedicated lumbar spine imaging and can account for low back or pelvic pain. Sacroiliac joint degenerative changes are common and will manifest joint space narrowing, sclerosis, and osteophyte formation [86]. Sacroiliitis, a manifestation of a large number of inflammatory disease processes, is characterized by erosive changes that are best evaluated on MRI [35, 87]. Long-standing sacroiliitis can result in complete ankylosis of the joint [86] (Fig. 8.26). Degenerative changes of the sacroiliac joint and inflammatory sacroiliitis should be distinguished from septic arthritis. Septic arthritis of the sacroiliac is typically unilateral and characterized by joint effusion, synovial thickening, bone marrow edema, and

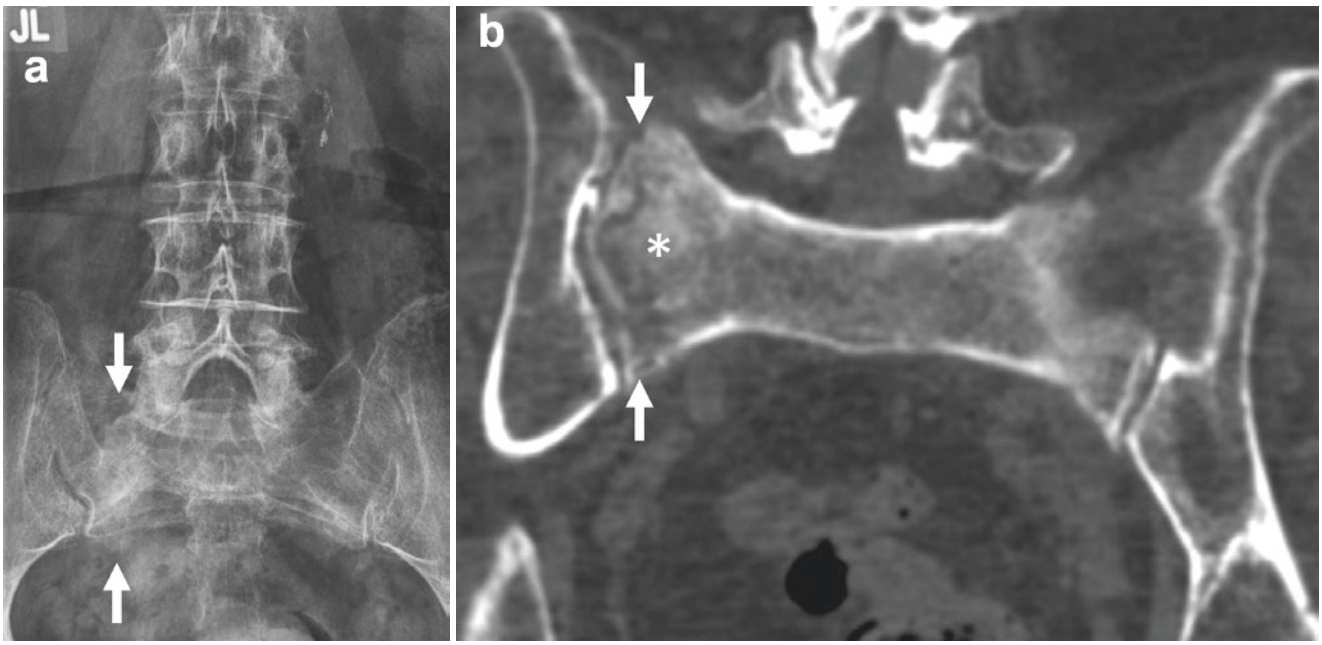

Fig. 8.25 A 73-year-old woman with osteopenia presenting with low back and pelvic pain with an insufficiency fracture of the right sacral ala. (**a**) Frontal lumbar spine radiograph demonstrates a vertical sclerotic band involving the right sacral ala. A distinct fracture line is not clearly identified. (**b**) Coronal CT image without intravenous contrast through the pelvis shows a nondisplaced sagittally oriented fracture through the right sacral ala near the sacroiliac joint with surrounding sclerosis (∗)

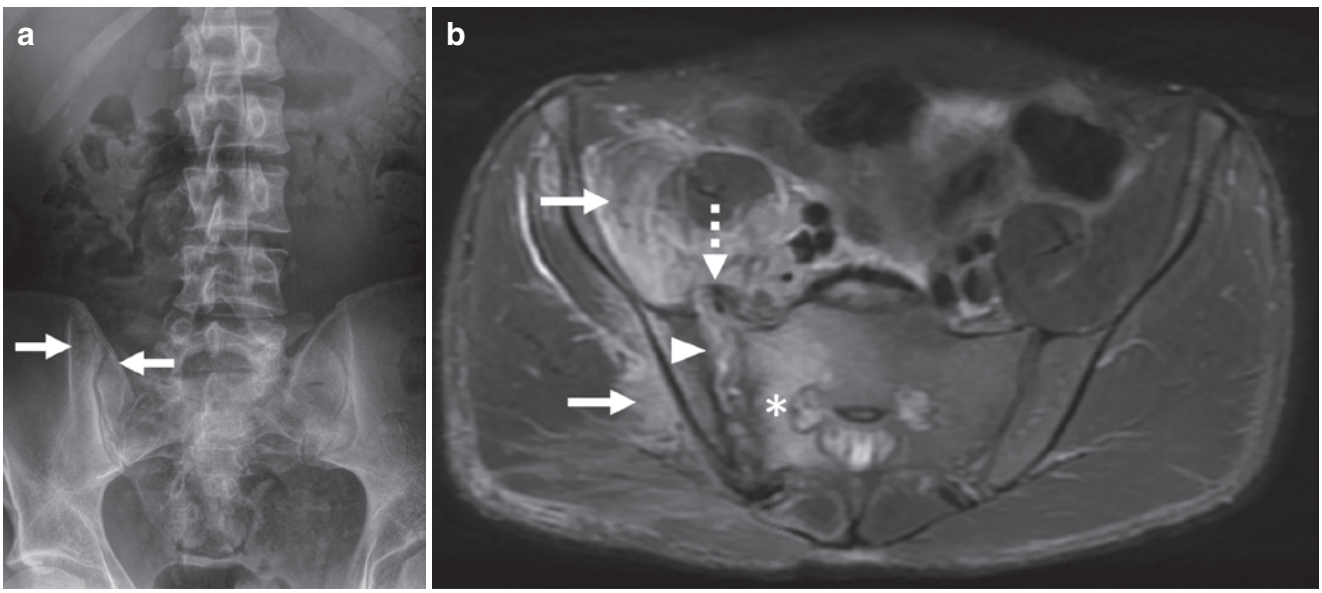

Fig. 8.26 A 27-year-old male intravenous drug user with right low back pain and fever and septic arthritis of the right sacroiliac joint. (**a**) Frontal lumbar spine radiograph demonstrates mild irregularity of the cranial portion of the right sacroiliac joint with surrounding periarticular osteopenia. (**b**) Axial T2-weighted fat-saturated image of the pelvis demonstrates irregularity of the right sacroiliac joint (arrowhead) and a right sacroiliac joint effusion (dashed arrow). There is adjacent bone marrow edema involving the sacrum (∗). T2-hyperintense signal and enlargement of the right iliacus, right psoas, and right gluteus medius muscles (arrows) reflect inflammation

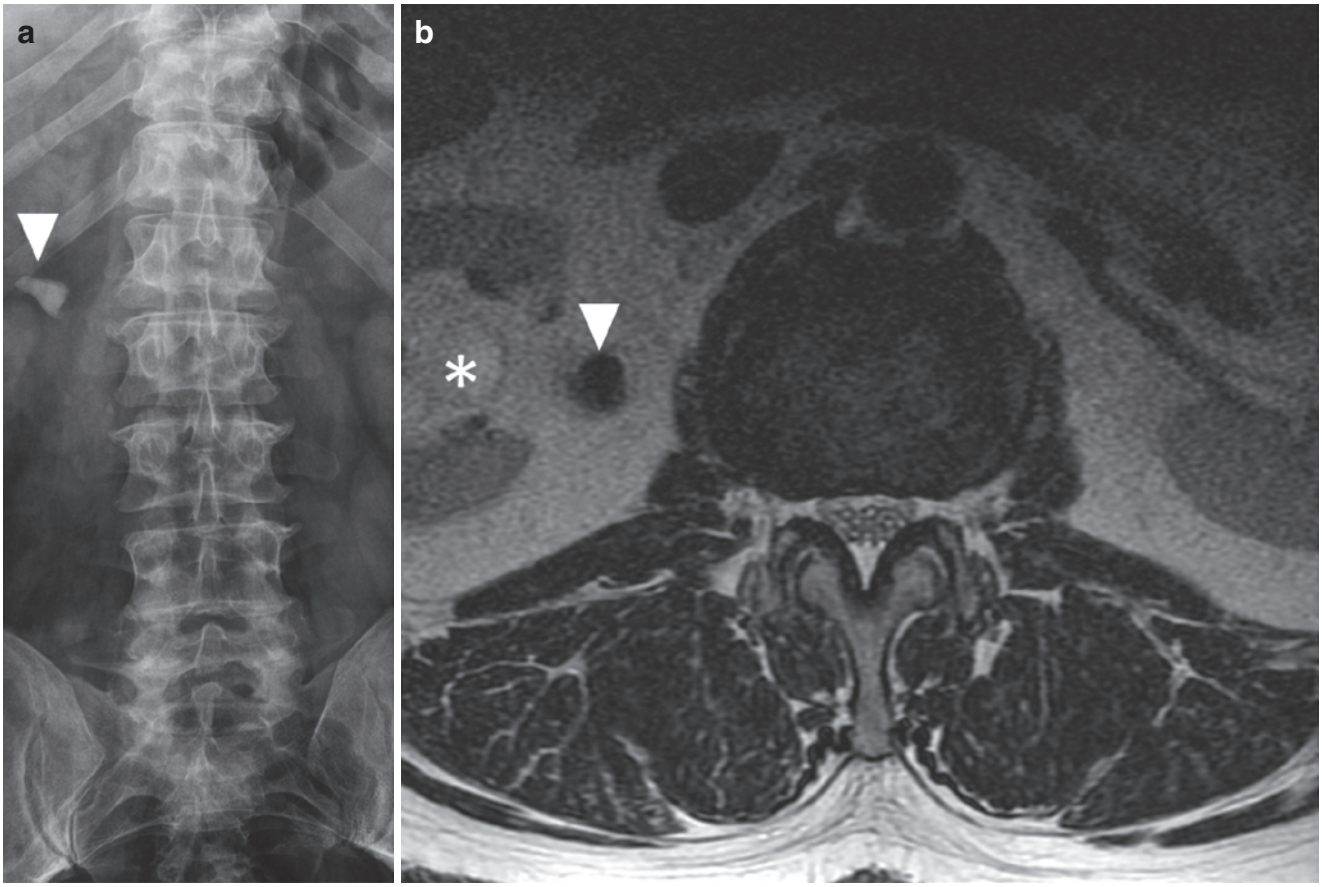

Fig. 8.27 A 60-year-old woman with right back and flank pain with hydronephrosis resulting from a stone in the right proximal ureter. (**a**) A frontal lumbar spine radiograph demonstrates a calcification lateral to the spine at the level of the L1–L2 intervertebral disc. (**b**) An axial T2-weighted image of the lumbar spine through the L1–L2 intervertebral disc demonstrates a low signal structure in the right retroperitoneum (arrowhead) which represents a stone in the right ureter. The stone is obstructive and results in right hydronephrosis (∗)

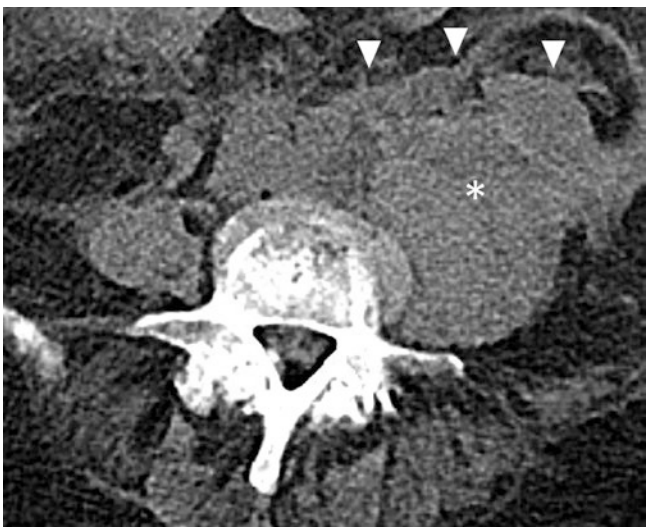

Fig. 8.28 A 82-year-old man on systemic anticoagulation with atraumatic flank pain and a left psoas hematoma. An axial CT image without intravenous contrast through the lumbar spine at the L3 level shows expansion of the left psoas muscle (∗) with surrounding retroperitoneal fat stranding (arrowheads). There was no acute lumbar spine fracture

destructive changes to both the sacral and iliac sides of the joint with adjacent periarticular edema or soft tissue fluid collections [88, 89] (Fig. 8.27).

Retroperitoneal abnormalities seen on lumbar spine imaging can account for symptoms of low back or pelvic pain. Renal calculi can be identified on radiographs as radiopaque structures lateral to the lumbar spine. These can also be seen on CT or MRI, where calculi can be localized and resulting hydronephrosis detected (see Fig. 8.27). Retroperitoneal hematomas occur in the psoas or iliacus muscle and can result in back or flank pain. These will not be seen on radiographs but are often included in the field of view on both CT and MRI (Fig. 8.28).

Radiography, CT, and MRI are important modalities for assessing the lumbar spine. Each provides different and at times complementary information about spinal abnormalities. An understanding of the strengths and weaknesses of each modality as well as a familiarity with the normal and abnormal imaging appearance of the spine is necessary for proper image interpretation.

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Neurological Exam and Neurophysiologic Evaluation for the Pain Patient

9

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Key Points

- The neurophysiological tests of nerve conduction studies (NCS) and electromyogram (EMG) are considered an extension of the neurological exam.
- NCS measure thickly myelinated Aβ fibers of the somatic motor and sensory nerves but not the nociceptive Aδ and C fibers. Thus, NCS is expected to be normal in primarily painful small fiber neuropathy.
- Axonal injury NCS features include significantly reduced amplitude with no more than mild slowing of conduction velocity.
- Demyelinating lesions NCS features include prolonged distal latency, significant slowing of conduction velocity, and conduction block.
- A single-isolated radiculopathy generally does not result in severe or dense numbness due to overlapping dermatomes.
- Sensory NCS are typically normal in radiculopathy because the lesion is proximal to the dorsal root ganglion.
- Motor NCS and EMG are abnormal and demonstrate neuropathic pattern of injury in radiculopathy.
- EMG findings of "acute denervation," including positive sharp waves and fibrillation potentials, can take several weeks to develop on account of time necessary for Wallerian degeneration to occur.
- NCS and needle EMG cannot diagnose discogenic pain and facetogenic pain and are usually unhelpful in the diagnosis of spinal stenosis.

Case Presentation

A 62-year-old man presents with 6 weeks of lower back pain. He reports the pain radiates from his lower back down his left buttock, to the left lateral thigh and calf, and into the dorsum of his left foot. He shares that he has trouble walking and has fallen a few times due to ankle weakness. The neurological exam demonstrates mild sensory impairment in the left L5 dermatome with light touch, temperature, and vibration. He has clinical weakness with ankle dorsiflexion and eversion. A nerve conduction study/electromyography (NCS/EMG) study demonstrates normal compound muscle action potentials (CMAPs) and sensory nerve action potentials (SNAPs). EMG shows positive sharp waves and fibrillation potentials. The motor unit action potential (MUAP) morphology is normal, but reduced recruitment is recorded. Clinically and neurophysiologically, he presents with subacute L5 radiculopathy with active denervation.

How can this precise neurological assessment, both by examination and neurodiagnostic studies, inform the pain physician? First, the tests can help establish a diagnosis, providing valuable information to the patient and practitioner alike. Second, the test can help guide treatment and interventional procedures. Third, the results can help with prognosis and monitoring clinical progression, potentially helping inform decisions on when patients may be most likely to benefit from surgery. This chapter will help the reader become familiar with the performance and interpretation of neurological evaluation of the pain physician using clinical examination and neurodiagnostic testing.

The basic approach of the neurological examination is first to identify the pathology and second to determine the etiology. Neurophysiologic tests complement the physical examination by providing more objective, quantitative functional data and depending much less on patient effort. Primarily, the most utilized electrophysiologic tests are nerve conduction studies (NCS) and needle electromyography (EMG). NCS/EMG interrogate the peripheral nervous system and can be useful in distinguishing radiculopathy, plexopathy,

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mononeuropathies, and polyneuropathies. Painful small fiber neuropathies can be investigated with quantitative sensory testing (QST) and quantitative sudomotor axon reflex testing (QSART) [1–3]. Additional neurophysiologic tests include somatosensory evoked potentials (SSEP) [4] and magnetoencephalography (MEG) [5], which record cortical responses to peripheral stimulation. This chapter will focus on how the neurological examination and NCS/EMG together serve to localize and determine the pathology.

Neurological Exam

How does a practitioner efficiently but comprehensively evaluate the broad spatial localizations and etiologies of neurological dysfunction and pain? One answer is that a thorough history and screening exam will help identify other symptoms and signs that suggest a particular anatomical location. For example, in the case of a left foot drop, one would pay particular close attention to relevant cortical signs that would implicate the right (non-dominant in the majority of people) cortical hemisphere. One would focus on difficulty recognizing numbers drawn on the hand (agraphesthesia), impaired two-point discrimination, or problems identifying objects by feel (astereognosia). On the cranial nerve exam, one would emphasize the assessment of the left visual field and left facial movements. On the motor exam, in addition to upper motor neuron signs, one would focus on signs of subtle weakness in the left upper extremity (pronator drift and rapid finger movements). Any such identified abnormalities would strongly suggest a cortical or subcortical location of pathology, as opposed to the frequently seen and even more frequently presumed radiculopathy. Because always anticipating in advance what particular locations one should focus on can be difficult, particularly in the real-time environment of a clinical visit and examination, one should instead perform a "screening exam." Such an exam should be sufficiently broad so as to identify abnormalities that would help both identify and localize particular pathologies. At the same time, the exam must be brief enough that it can be completed within the appropriate timeframe of a typical outpatient encounter.

Furthermore, a thorough screening exam will help identify a group of symptoms that when identified initially are not specific with regard to etiology but when identified as a group can point strongly toward a particular diagnosis. For example, both ataxia and neuropathy can be due to a wide range of causes. However, the combination of the two may suggest a specific etiology, such as in this case, Friedreich's ataxia.

While a reliable screening exam is an essential tool, often further meticulous detail is required. Clinicians should use the chief complaint and history to generate a hypothesis that can be tested during the examination. As appropriate for evaluating the hypothesis, the examiner may delve into certain components of the examination in more detail. For example, in evaluating a patient with wrist drop (which when due to peripheral injury often localizes to C6 or the radial nerve), one should investigate a C6 muscle that is not innervated by the radial nerve, such as the pronator teres (C6 but innervated by the median nerve), even though routine assessment of that muscle is not included in most screening examinations. Indeed, this expansive assessment of myotomes, components of the brachial and lumbar plexi, and individual nerve roots embodies the strategy used by neuromuscular physicians during the NCS/EMG evaluation.

One should pay particular emphasis to the identification of "upper motor neuron signs" versus "lower motor neuron signs." Distinguishing the two can be of critical importance in the practice of pain medicine. Upper motor neuron injury can masquerade as many of the common lumbar pain syndromes. As a general rule, spine injury thought to occur at a particular level, for example, pain involving the front of the thighs (L2 distribution), can be due to injury at any more cephalad level. One should pay particular attention to cervical spine injury mimicking pain thought to be due to a more caudal injury.

Mental Status Exam

Undoubtedly the most complex component of the neurological examination is the mental status examination, and a screening exam checks only the most superficial components. The basic components of the mental status exam include the following assessments: level of arousal, attention, orientation, language, memory, integrative sensory function, and integrative motor function.

A number of terms are used, often ambiguously, to define level of arousal. What one means by "sleepy, somnolent, obtunded" is often unclear and varies from physician to physician. Instead, it can be more helpful to simply describe what one sees with regard to whether the eyes are closed or open and what stimulus is necessary for a patient to open the eyes. For example, an ICU level exam might include "Eyes closed. Patient does not open eyes to verbal stimulus but opens eyes to gentle movement of the arms." Attention refers to maintained arousal. It can easily be assessed by asking a patient to count backward from 20 to 1 or in a patient with a high level of education by subtracting serial 7s from 100. As delirium is a common feature of pain patients, particular in the setting of over-medication, testing attention is an important component of the exam. Delirious patients can seem surprisingly normal, in that they can speak fluently and interact appropriately, but simple tests of attention can expose the

deficit. Appearance, mood, and affect can be important to consider in assessing how a patient's psychological state may modulate pain perception.

Language is most commonly assessed based on categorization of aphasias such as those due to receptive and expressive language areas in the brain. Such classification depends on assessing comprehension, naming, fluency, and repetition. Typically, reading and writing are checked as well. Immediate registration, short-term memory, and long-term memory can be evaluated by individual questions. However, often simple questions, such as "what did you eat for dinner last night" or "have we met before," can provide similar information.

Appearance/mood/affect and thought content, both components of the psychiatric mental status examination, are important to include in the assessment of pain patients. Identifying features of depression can alert a provider to potential affective enhancement of pain.

Integrative sensory functions focus on non-dominant parietal signs such as neglect of a particular visual or sensory region, graphesthesia (recognizing a number drawn on the hand), astereognosia (identifying an object by feel alone), two-point discrimination, somatognosia (inability to recognize that a body part is self), and anosognosia (lack of awareness of disease or disability). The most common integrative motor functions include apraxias, which refer to sequences of movements for which all the components are themselves performable but not the entire ensemble. Examples of apraxias include demonstrating how to comb hair or salute.

Cranial Nerve Exam

Although the cranial nerve exam, like the mental status assessment, is often not the focus of a pain practitioner's neurological exam, it is nonetheless critically important. The first cranial nerve, the olfactory nerve, is not routinely assessed. The second cranial nerve, the optic nerve, is evaluated in several ways. First, through fundoscopy, the practitioner visualizes the optic nerve head and can identify pathological processes such as atrophy or papilledema. Second, the pupillary light response assesses afferent fibers in the optic nerve (as well as connections from the pretectal nucleus to the Edinger-Westphal nucleus, which contains the parasympathetic efferent fibers for the reflex). Third, one tests visual fields via confrontational testing as well as visual acuity.

The extraocular muscles are innervated by the oculomotor (III), trochlear (IV), and abducens (VI) nuclei. One should assess the lids and pupils, looking for components of the Horner's syndrome, namely, ptosis, miosis, and anhidrosis. In addition to a Pancoast tumor that affects the apices of the lungs, one should remember that Horner's syndrome can be caused by carotid dissection (which causes neck pain that radiates to the jaw) or a mass lesion involving the cavernous sinus.

The trigeminal nerve (V) provides sensory innervation from the face as well as motor innervation to the muscles of mastication. The facial nerve (VII) innervates the muscles of facial expression. The motor neurons innervating muscles above the forehead generally receive bilateral innervation from the primary motor cortex, so that a peripheral VIIth nerve lesion will affect all the unilateral muscles of facial expression but a central lesion will spare the muscles above the eye. The facial nerve also conveys taste sensation from the anterior tongue, explaining why taste is affected in a Bell's palsy. Finally, the facial nerve mediates secretion from the salivary glands (except the parotid) and the lacrimal gland.

One can coarsely test the vestibulocochlear nerve (VIII) using finger rub. The glossopharyngeal nerve (IV) and vagus nerve (X) serve a number of functions including taste and general sensory inputs from the posterior tongue, pharynx, swallowing, afferent visceral inputs, and parasympathetic innervation to the body. The spinal accessory nerve (XI) provides partial innervation to the sternocleidomastoid and trapezius muscles. The hypoglossal nerve (XII) is responsible for motor innervation to most of the tongue muscles. It too is important for swallowing.

Motor Exam

The motor exam is of primary importance in the assessment of pain patients. The first component of the motor exam is an assessment of the bulk and tone. It is important to observe the patient, often in different positions. For example, scapular winging can be brought out by leaning against a wall with shoulders abducted and the elbows flexed.

In observing the muscles, one also is in a position to identify abnormal movements such as fasciculations, myoclonus (sudden, short contractions), asterixis (sudden, short relaxations), and tremor.

Movements should be assessed as much as by isolating particular joints for investigation. For example, when checking a patient's wrist extensors, one should anchor the wrist with one hand and assess the power of the wrist extensors with the second hand. By stabilizing the wrist, one ensures that only the wrist extensors are used in generating the power and not, for example, more powerful proximal muscles such as the brachioradialis or biceps. Additionally, one must test individual muscles against one's own muscles of comparable strength. For example, one cannot identify subtle weakness in a patient's tibialis anterior when using one's finger flexors.

Power is graded from 0 (no movement) to 5 (full strength). 1/5 represents trace movements, 2/5 movement in a sup-

ported plane, 3/5 movement against gravity, 4−/5 movement against minimal resistant, 4/5 movement against resistance, and 4+/5 trace weakness. One should realize that 4/5 represents an enormous range, from very weak to very strong. Precise and accurate grading of power is important for ensuring agreement among different practitioners and for assessing changes over multiple assessments. Such information is often critical, for example, the urgency for a decompressive surgery is much higher when weakness is progressive as opposed to static.

When evaluating individual muscles, one should keep the innervation of the muscles in mind. On a screening exam, one should not only evaluate muscles innervated by most limb-supplying spinal levels but also compare muscles innervated by the same spinal level but supplied by different nerves. For example, identifying weakness in the abductor pollicis brevis (APB) (a C8/T1 muscle supplied by the median nerve) but preserved strength in the abductor digiti minimi (a C8/T1 muscle supplied by the ulnar nerve) might suggest carpal tunnel syndrome as an explanation.

When assessing power, one should keep in mind that rapid alterations in level of power are usually due either to voluntary changes in effort or to pain. Such "give-way" weakness often results in physicians' "over-calling" weakness. That is, a patient with pain radiating down the leg has pain on straightening the leg. One should focus on the maximum power generated, even if for a very brief period of time (a second or less). Often, encouraging a patient to produce maximum power can be helpful or necessary. However, equally often pain limits full assessment, and one must document this, for example, "pain in the left hip flexor at least 4/5 but full assessment limited by pain."

As mentioned previously, distinguishing upper and lower motor neuron signs is of principal importance in making a correct assessment and pursuing the appropriate diagnostic and treatment strategies. Signs of upper motor neuron injury include preserved bulk with increased tone and hyperreflexia. Additionally, certain patterns of weakness are characteristic of upper motor neuron injury. In the upper extremities, upper motor neuron lesions cause weakness in the extensor muscles out of proportion to weakness in the flexor muscles; in the lower extremities, flexor muscles (including foot dorsiflexion) are more strongly affected. In contrast, lower motor neuron signs include decreased muscle bulk with decreased tone and hyporeflexia. Additionally, fasciculations may be seen in the muscles.

See Table 9.1 for a list of frequently assessed muscles.

Table 9.1 Frequently assessed muscles

Upper extremities
Shoulder abduction: axillary nerve to deltoid C5 (C6), suprascapular nerve to supraspinatus C5 (C6) mediates first 15° of abduction
Elbow flexion: musculocutaneous nerve to bicep C5 (C6)
Wrist extension: radial nerve to extensor carpi radialis longus C6 (C5)
Elbow extension: radial nerve to triceps C7 (C6, C8)
Forearm pronation: median nerve to pronator teres C6–C7
Extension at metacarpophalangeal joint: radial nerve (posterior interosseous branch) to extensor digitorum C7 (C8)
Finger flexion: median nerve to flexor digitorum superficialis C8 (C7, T1) flexes at PIP joints, digitorum profundus (digits 2–3) C8 (C7, T1) (anterior interosseous branch of median nerve) flexes at DIP joints Ulnar nerve to flexor digitorum profundus (digits 4–5) C8 (C7,T1)
5th digit abduction: ulnar nerve to abductor digiti minimi C8, T1
2nd digit abduction: ulnar nerve to first dorsal interosseous T1 (C8)
Thumb abduction: median nerve to abductor pollicis brevis T1 (C8)
Lower extremities
Hip flexion: spinal nerves and femoral nerve to illiopsoas L1–L2 (L3)
Knee extension: femoral nerve to quadriceps L3–L4 (L2)
Dorsiflexion: deep peroneal nerve to tibialis anterior L4 (L5), deep peroneal nerve to extensor hallucis longus L5 (S1)
Plantarflexion: tibial nerve to gastrocnemius S1–S2
Knee flexion: sciatic nerve to hamstrings S1 (L5, S2)
Foot inversion: tibial nerve to tibialis posterior L4–L5
Foot eversion: superficial peroneal nerve to peroneus longus and brevis L5, S1
Hip adductors: obturator nerve L2–L3 (4)
Hip abduction: superior gluteal nerve to gluteus medius and minimus and tensor fasciae latae L4–L5 (S1)
Hip extension: inferior gluteal nerve to gluteus maximus L5, S1 (S2)

Reflexes

Reflexes are a critical and often overlooked component of the neurological exam. Increased reflexes can help identify a "central" etiology, whereas loss of reflexes can help localize to a particular root level or lower motor neuron injury. One should always consider metabolic effects on reflexes such as in diseases that affect levels of calcium or thyroid hormones.

There is less consistency in the grading of reflexes than in the grading of power. One system often used by neuromuscular neurologists is the following:

- 0/4: absent.
- 1/4: obtainable with distraction (such as the Jendrassik maneuver, when the patient is asked to interlace his finger tips and then pull from both sides simultaneously).
- 2−/4: less than normal but obtainable without distraction.
- 2/4: normal.
- 2+/4: brisker than normal but without spreading.
- 3/4: hyperreflexic in that there is spreading from one reflex to a nearby one. For example, stimulation at the bicep causes finger flexion. Alternatively, the presence of crossed adductor reflexes would warrant 3/4.
- 4/4: clonus.

One should keep in mind that reflexes tend to be much more brisk in younger patients than in older ones. While not

strictly considered in the grading, such information must be considered in the interpretation of the findings.

Babinski sign (dorsiflexion of the great toe upon stroking of the plantar lateral foot) typically indicates injury to the corticospinal tract. Hoffman's sign (flexion of the thumb and index finger upon flicking of the distal third digit) indicates hyperreflexia due to a process at the level of the cervical spinal cord or more cephalad.

Sensory

When assessing the sensory system, one should consider what sensory fibers are being assessed. Pinprick, heat, or cold assess nociceptors, the unmyelinated C fibers and thinly myelinated Aδ fibers. Vibration sense and proprioception assess the thickly myelinated Aβ fibers. One should keep in mind the anatomy: the first group of fibers (for nociception) synapse in the ipsilateral dorsal horn, and the second order neurons cross and then ascend contralaterally in the lateral spinothalamic tract; in contrast, the second group of fibers (for vibration and proprioception) ascend ipsilaterally in the dorsal columns and then synapse and cross in the lower brainstem.

One should remember that common peripheral sensory processes can involve particular fiber types. Furthermore, one should look for common patterns of involvement, including the "stocking-glove" pattern of distal symmetric neuropathy, single nerve or root involvement, or mononeuropathy multiplex patterns. As a general rule, because of overlap of sensory dermatomes, complete sensory loss is not expected after a single-level radiculopathy. In contrast, injury to a peripheral nerve would cause complete or near complete sensory loss. For example, injury to the deep peroneal nerve produces more profound sensory loss in the web between the first and second toes than an L5 radiculopathy.

Common signs associated with neuropathic pain should be documented. These include the following: allodynia, pain in response to a stimulus that normally is innocuous; hyperalgesia, increased pain response to a noxious stimulus; summation, increased pain response to repeated innocuous or mildly painful stimulus; paresthesias, abnormal positive sensory phenomena, such as a pins and needles sensation; and dysesthesias, painful paresthesias.

Coordination

Coordination is assessed on finger-nose and heel-shin testing as well as assessment of the truncal posture. Cerebellar injury commonly produces a coarse horizontal wavering present on the entire motion arc between the finger and the nose (dysmetria). In contrast, essential tremor causes higher frequency deviation predominantly at the beginning and end of the trajectory.

Stance and Gait

High-level functions such as stance and gait are particularly important and should be assessed during every visit. The basic characterization of stance should be whether the feet are normally spaced or broadly spaced. Gait can be described as fluid or rigid, with attention to the arm swing and the smoothness of turns. Posture should be noted as normal, or stooped. Walking on the toes and heels assesses the foot dorsiflexors and plantarflexors in a functional manner (and is more sensitive for identifying subtle weakness than confrontational testing). One should assess cerebellar functioning by asking the patient to walk heel to toe "on a tightrope."

A number of terms are used in describing the gate abnormalities due to particular etiologies. For example, a wide-based or "drunken" gait can be associated with cerebellar pathology. A "shuffling" gait is typically due to parkinsonism, whereas a "magnetic" gate – in which the feet do not leave the floor – is associated with normal pressure hydrocephalus. An "antalgic" gait refers to abnormalities due to pain.

One should always assess for Romberg's sign, which primarily reflects interference with proprioceptive signaling. To test for Romberg's sign, ask the patient to stand with the feet together and the eyes open, focused on a distant target. Romberg's sign refers to impairment in balance when visual inputs are removed (by closing the eyes), in a patient who can stand with the feet together when the eyes are opened. Importantly, if a patient cannot stand with the feet together while the eyes are open, this should not be referred to as a positive Romberg sign; rather, it reflects a problem in, for example, the vestibular or cerebellar functioning.

Putting Together an Assessment

In the assessment, one should review key elements of the history and clinical findings. One often depends on combinations of the different components of the exam to help establish as precise as possible the localization of disease, such as in the motor and reflex components of lower motor neuron signs. Based on the localization, one should be familiar with pathological processes that occur at particular locations. For example, with the presenting symptom of foot drop, the lesion could localize to the CNS at the contralateral cortical gray matter, subcortical white matter, brainstem, or ipsilateral spinal cord. However, it could also be an initial presentation of motor neuron disease affecting the anterior horn cells; the foot drop could result from an L4 or L5 radiculopathy, lumbar plexopathy, peroneal neuropathy, disease of the neuromuscular junction (NMJ), or a myopathy. The practitioner can then determine what laboratory, imaging, or neurophysiologic studies might help further distinguish among the proposed possible diagnoses.

NCS/EMG

Nerve conduction study (NCS) and electromyography (EMG) are neurophysiologic studies that evaluate the peripheral nervous system. NCS/EMG acts as an extension of the neurological exam by providing electrophysiologic data of the nerves and muscles. NCS is performed by electrically stimulating a targeted nerve (sensory or motor) and recording the resultant action potential response. These action potentials are conducted through thickly myelinated Aβ fibers of the somatic motor and sensory nerves. Patients will feel a sharp electrical sensation, but the nociceptive Aδ and C fibers are not recorded. EMG is performed by placing a recording needle into the targeted muscle belly and recording the electrical activity. Although any distal peripheral nerve and muscle can theoretically be tested, the approach to NCS/EMG is reliant on the patient's history and clinical exam. By evaluating individual nerves and muscles via NCS/EMG, the clinician can localize the pathology to the level of the nerve root, plexus, peripheral nerve, neuromuscular junction, or muscle. Furthermore, specific electrophysiologic patterns can also distinguish the degree of injury as well as the underlying pathology (e.g., axonal loss vs demyelinating disorders). This is especially helpful in cases where the clinical exam is limited by pain or volition. We will review the terminology required for interpretation of NCS/EMG studies.

Motor Nerve Conduction Study

Motor NCS is performed by stimulating a motor nerve and then recording with an electrode placed over the motor nerve innervated muscle belly. The resultant potential is called the compound muscle action potential (CMAP). The CMAP represents the combined potentials of all underlying muscle fiber action. Important CMAP components include amplitude, duration, latency, and conduction velocity (Fig. 9.1).

CMAP amplitude is directly correlated with the number of muscle fibers that are activated. CMAP duration represents synchrony of individual muscle fibers firing. Latency describes the time between stimulation of targeted nerve and onset of the fastest muscle action potentials. This includes time from stimulus to neuromuscular junction (NMJ), NMJ activation, and depolarization time across muscle. Conduction velocities are defined as the speed of the fastest action potentials [6].

Sensory Nerve Conduction Study

Sensory nerve action potentials (SNAP) are generated by stimulating a sensory nerve and recording the cutaneous response with two recording electrodes. SNAP characteristics include onset latency, peak latency, amplitude, duration, and conduction velocity (Fig. 9.2).

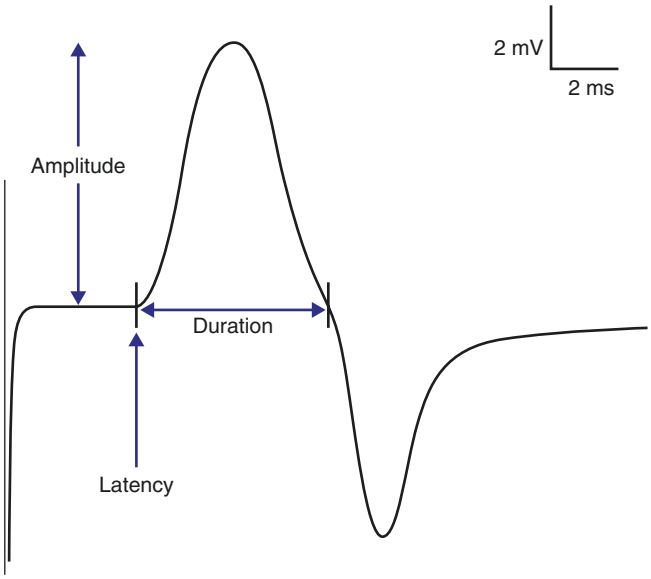

Fig. 9.1 CMAP waveform. Amplitude represents the summation of muscle fibers activated and is calculated from baseline to peak of waveform in millivolts. Latency is the combined time from nerve stimulation, conduction of motor nerve, depolarization across NMJ, and depolarization across muscle. Latency is measured from time of stimulation to initial deflection from baseline. Duration of the waveform represents synchrony of individual muscle fibers firing and is measured from initial deflection to return to baseline. (Reprinted with permission from Preston and Shapiro [6])

Amplitude represents the total depolarization of all individual sensory nerve fibers. Onset latency represents time from stimulus to initial deflection from baseline; this typically represents nerve conduction time from the largest heavily myelinated cutaneous sensory fibers as these are the fastest fibers [7]. Peak latency is the time to peak amplitude on the SNAP waveform. Conduction velocity is the speed of the fastest action potential between the stimulator and recording electrode. Again, an important point related to the use of neurodiagnostic tests in pain medicine is that SNAPs do not reflect the activity of nociceptors, the unmyelinated C fibers and thinly myelinated Aδ fibers. The action potentials from these fibers are too small and too temporally dispersed to contribute to the SNAP amplitude. Thus, SNAPs are typically affected by a "large fiber" neuropathy but not by a "small fiber" neuropathy.

NCS F Response and H Reflex

NCS F response and H reflex are specialized NCS tests for evaluation of the proximal nerve segments including the nerve roots and plexus. Late responses are obtained by stim-

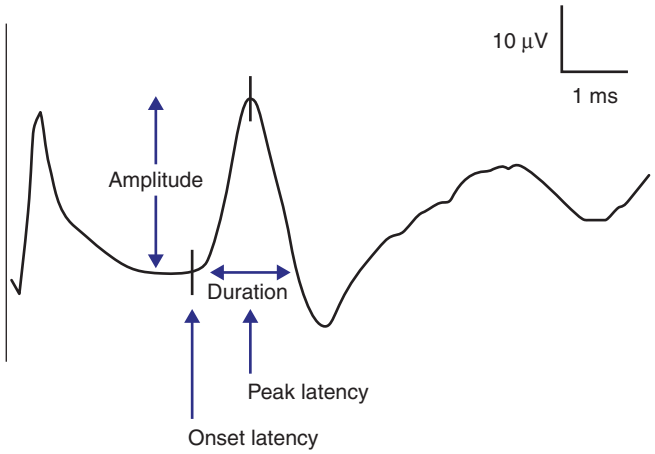

Fig. 9.2 SNAP waveform. Amplitude represents the total depolarization of all individual sensory nerve fibers which is measured in microvolts. Onset latency represents time from stimulus to initial deflection from baseline; this typically represents nerve conduction time of the largest heavily myelinated cutaneous sensory fibers as these are the fastest fibers. Peak latency is the time to peak amplitude on the SNAP waveform. Duration represents the synchrony of action potentials and is measured from initial deflection to return to baseline. (Reprinted with permission from Preston and Shapiro [6])

ulation of the nerve and allowing for antidromic conduction (afferent) toward the spinal cord and recording the following orthodromic conduction (efferent) response toward the axon terminals.

The F response is a late motor CMAP which is obtained by supramaximal depolarization of a motor nerve, allowing for antidromic nerve conduction up to the anterior horn cell followed by orthodromic response down to the recorded muscle. The F response is usually small in amplitude, representing 1–5% of muscle fibers. Of note, the F responses are purely motor and provide no information regarding lesions that only affect sensory nerve fibers. If distal nerve conduction studies are abnormal, a prolonged F response could then be suggestive of proximal neuropathy, plexopathy, or radiculopathy. Unfortunately, utility of diagnostic F response is limited by targetable nerves. In the upper extremities, supramaximal stimulation of the median and ulnar nerve can evaluate F responses in C8–T1. In the lower extremities, supramaximal stimulation of the peroneal and tibial nerves can evaluate F responses in L5–S1.

The H reflex is a late response like the F response. The H reflex differs in that it is a true reflex involving stimulation of sensory afferent fibers, a synapse at the anterior horn cells, followed by efferent motor fibers. The H reflex can only be reliably obtained by stimulating the tibial nerve in the popliteal fossa with an expected response in the gastrocnemius-soleus muscle. It is an NCS correlate to the physical exam's ankle reflex. Therefore, the H reflex will be prolonged in S1 radiculopathy, lumbosacral plexopathy, tibial and sciatic neuropathy, and polyneuropathy. The H reflex is a sensitive early electrodiagnostic test for Guillain-Barre syndrome (Fig. 9.3) [8].

Needle Electromyography (EMG)

The needle EMG study is performed by inserting a recording needle into the target muscle to measure electric potentials of the muscle at rest and during activation. The electrical potentials of the muscle at rest are described as spontaneous activity, and the electrical potentials of voluntary muscle activation are called motor unit action potentials (MUAP). Almost all skeletal muscles can be interrogated; however a priori muscle testing is recommended due to limited tolerance for this invasive test. For example, in suspected L5 radiculopathy with clinical history of back pain and radiating paresthesias to the posterior lateral calf extending to dorsum of foot with concomitant weakness in ankle dorsiflexion, the EMG operator will evaluate myotomes above, below, and at the level of the expected lesion – specifically targeting lumbar paraspinal, proximal muscles (gluteus medius, vastus medius) and distal muscles (tibialis anterior, tibialis posterior, medial gastrocnemius).

Spontaneous Activity

Normal healthy muscle will not generate spontaneous activity at rest. Abnormal spontaneous activity can inform the underlying pathology. Fibrillation potentials and sharp waves represent single muscle fiber depolarization and are electrophysiologic markers of active denervation suggestive of a recent lesion. Complex repetitive discharges represent a group of denervated adjacent muscle fibers that are more typically seen in chronic myopathies than neuropathies. Myokymic discharges are rhythmic, grouped, spontaneous repetitive discharges of the same motor unit. Myokymic dis-

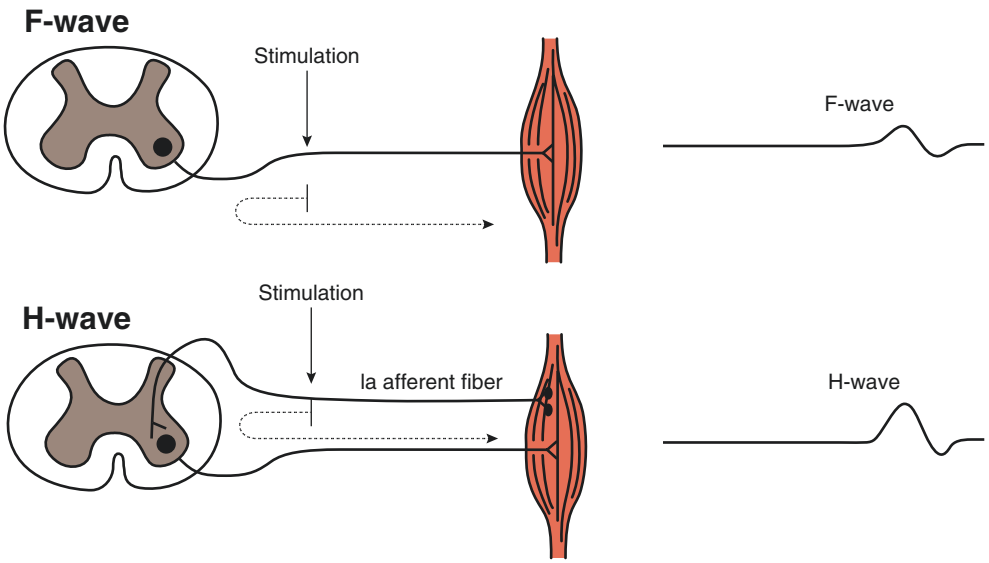

Fig. 9.3 NCS late response. Diagram of the NCS F response test and H reflex test with their resultant waveforms. F waves are produced with afferent conduction of a motor nerve to the anterior horn cell followed by efferent conduction of the same motor nerve to the recorded muscle. H waves represent afferent conduction of a sensory nerve synapsing onto the anterior horn motor neuron followed by efferent conduction of a motor nerve to the recorded muscle. (Adapted from Kai and Nakabayashi [26]. This is an open access peer-reviewed chapter InTech Open, licensed under a Creative Commons Attribution 3.0 Unported License)

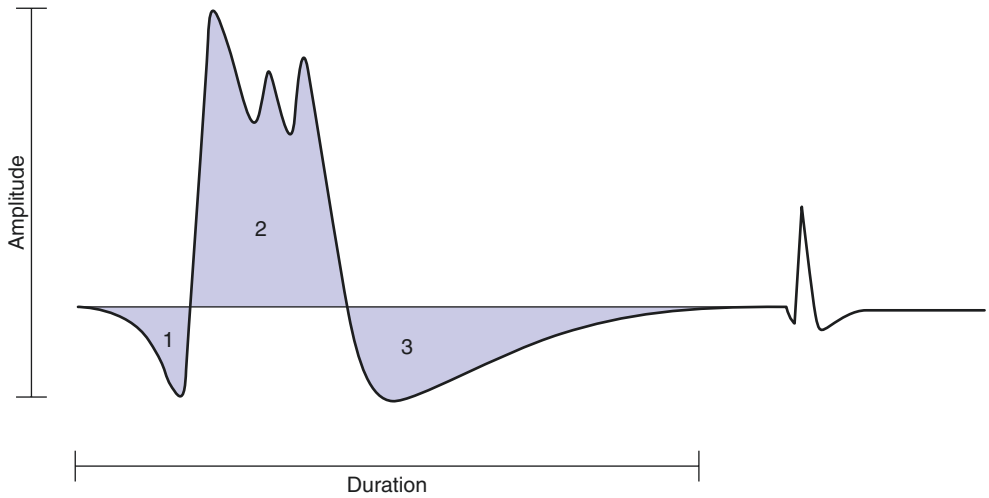

Fig. 9.4 Motor unit action potential (MUAP) measurements. Motor unit action potential amplitude is measured from peak to peak. The duration is measured from the time of initial deflection to when it returns to baseline. Polyphasia is evaluated by the number of phases above and below the baseline (triphasic in this sample) MUAP. (Reprinted with permission from Preston and Shapiro [6])

charges are features strongly suggestive of radiation-induced plexopathy or neuropathy and are rarely seen in spinal cord lesion, radiculopathy, and entrapment neuropathy.

MUAP

Motor unit action potentials (MUAP) are obtained with target muscle activation. A motor unit consists of a motor neuron and its innervated muscle fibers. Muscle strength is a function of the number of motor units and the fire rate of each individual motor unit. MUAP can be defined by two major characteristics: morphology and firing pattern. *Morphology* of MUAP varies by duration, amplitude, and phase. Duration is the length of time from the initial deflection to return to baseline. Duration reflects the number of muscle fibers within a motor unit. Amplitude is measured from lowest peak to highest peak and reflects the overall strength of the motor unit. Phase reflects the number of times the MUAP crosses the baseline, normally two to four, and reflects the synchrony of the muscle fibers firing within the motor unit (Fig. 9.4).

MUAP firing patterns function to increase muscle force through *activation* (the ability to increase the firing rate) and *recruitment* (the ability to add additional motor units). Impaired activation is typically suggestive of a central ner-

vous system lesion but can also be seen in pain limited or noncooperative exams. Reduced recruitment is suggestive of a peripheral neuropathic lesion: because additional motor units are not available, the intact units must fire at high rates to generate increased force.

Electrophysiologic Patterns of Disease

Neuropathies are disorders of the peripheral nerves of which the localization of the pathology could be attributed to the cell body (neuronopathy), axon (axonopathy), or myelin (demyelinating disorders). Clinically, neuropathies can also be defined by their time course, acute, subacute, and chronic, as well as by their primary symptoms: motor predominant, sensory predominant, or mixed. Etiologies are all-encompassing ranging from hereditary, idiopathic, autoimmune, toxic-metabolic, infectious, inflammatory, infiltrative, neoplastic, structural, to postradiation. NCS/EMG can play a pivotal role in diagnosis as pathologies produce specific electrophysiologic patterns of disease.

Axonal Injury

The electrophysiologic pattern of axonal injury is significantly reduced NCS amplitude with only mild reduction in conduction velocity. The major reduction in amplitude with relative preservation of conduction velocity is reflective of the functions of the axon vs myelin in nerve conduction. In hyperacute axonal injury, NCS can sometimes be normal if the lesion is proximal to the nerve that is being evaluated. The abnormal NCS findings are expected to develop after Wallerian degeneration (atrophy of the distal disconnected nerve), which can take days to weeks. EMG in acute axonal injury demonstrates normal spontaneous activity and reduced recruitment of MUAP, which is reflective of the loss of axons and motor units. Denervation occurs in the following weeks, and fibrillation potentials and sharp waves manifest in the subacute period of injury. Nerves have the potential for axonal repair which occurs at a rate of approximately 1 mm/day. If reinnervation is successful in chronic axonal injury, the remaining intact axons will have sprouted and connected with the denervated muscle. The former denervation potentials can resolve, and larger amplitude and polyphasic MUAPs will be recorded. However, if reinnervation is not successful, denervation potentials will persist. Of importance to the pain physician, complex regional pain syndrome type II (causalgia) – and potentially complex regional pain syndrome type I (reflex sympathetic dystrophy) – is thought to be a complication of incomplete or incorrect reinnervation. Please refer to Table 9.2 for common axonal neuropathies.

Table 9.2 Axonal loss neuropathy

Diabetes mellitus
Cryoglobulinemia
Ischemic monomelic neuropathy
Sarcoidosis
Amyloidosis
Lymphoma
Acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN)
Toxins: taxanes, colchicine, lead, alcohol

Table 9.3 Demyelinating polyneuropathy

Charcot-Marie-Tooth
Hereditary neuropathy with liability to pressure palsies (HNPP)
Krabbe disease
Metachromatic leukodystrophy
Acute inflammatory demyelinating polyradiculoneuropathy (AIDP)
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)
Multifocal motor neuropathy
Multifocal acquired demyelinating sensory and motor neuropathy
Distal acquired demyelinating symmetric neuropathy (DADS)
Toxins (diphtheria, buckthorn, amiodarone, n-hexane, arsenic)
Human immunodeficiency virus (HIV)

Demyelination

The hallmark of demyelinating disorders in NCS is slowing of conduction velocity and delayed distal latency. Injury to myelin will impair saltatory nerve conduction producing these results. NCS amplitude is normal in mild to moderate demyelinating disease. However, amplitude can be reduced in cases where demyelination is significant enough to produce conduction block or phase dispersion and loss of signal. EMG is generally normal in demyelinating disorders with the exception of conduction block where MUAP recruitment is reduced. Of note, prolonged and severe demyelination can result in secondary axonal injury and a mixed pattern NCS/EMG. Please refer to Table 9.3 for common demyelinating disorders.

NCS/EMG in Spine Conditions and Mimics

Neck and back pain is one of the most common clinical complaints. It is estimated to be a leading cause of years lived with disability in both developing and developed countries [9].

Spondylosis of the cervical and lumbar spine refers to degenerative structural changes in the spine that can result in compression of the nerve root (radiculopathy) and compression of the spinal cord (myelopathy). Nonspondylotic causes are many including infectious, autoimmune, infiltrating/tumors, ischemic, and toxic-metabolic. Presentation can be variable and involve pain, sensory changes, and motor weakness. The

neurological exam in conjunction with electrophysiologic testing can localize these lesions and provide information in regard to pathophysiology, severity, and chronicity.

Radiculopathy

The clinical presentation of radiculopathy is of pain, paresthesias, and muscle weakness of the associated nerve root. Cutaneous sensory innervation of the nerve root is defined as a dermatome. Anatomically, this is innervated by the dorsal root ganglion at each root level. Muscle innervation of the nerve root is known as a myotome. Anatomically, each myotome is innervated by lower motor neurons in the anterior horn of the spinal cord. The clinical and electrophysiologic diagnosis of radiculopathy relies heavily on the examiner's knowledge of root level dermatome and myotome innervation. Notably, a single root radiculopathy rarely presents as dense numbness or severe weakness as there is overlap in sensory innervation and most skeletal muscles are innervated by more than one nerve root. After a comprehensive neurological exam is performed, the suspected root levels can then be interrogated with NCS/EMG (Fig. 9.5).

In a case of cervical spondylosis resulting in C6 radiculopathy, a patient classically can present with the following clinical syndrome: pain and neck tightness from paraspinal muscle spasm, pain and numbness radiating down the lateral aspect of his arm in the C6 dermatome, and weakness with shoulder abduction, elbow flexion, and elbow pronation in addition to a wrist drop. Physical exam maneuvers such as ipsilateral neck rotation, extension, and downward pressure on the head (Spurling test) may exacerbate his symptoms. Reflexes in radiculopathy are expected to be abnormal and reduced. The brachioradialis and potentially biceps reflexes are likely diminished in isolated C6 radiculopathy. Triceps reflex should be preserved.

NCS/EMG in Radiculopathy

Sensory NCS is normal in radiculopathy because the lesion is proximal to the dorsal root ganglion. Therefore, the nerve cell

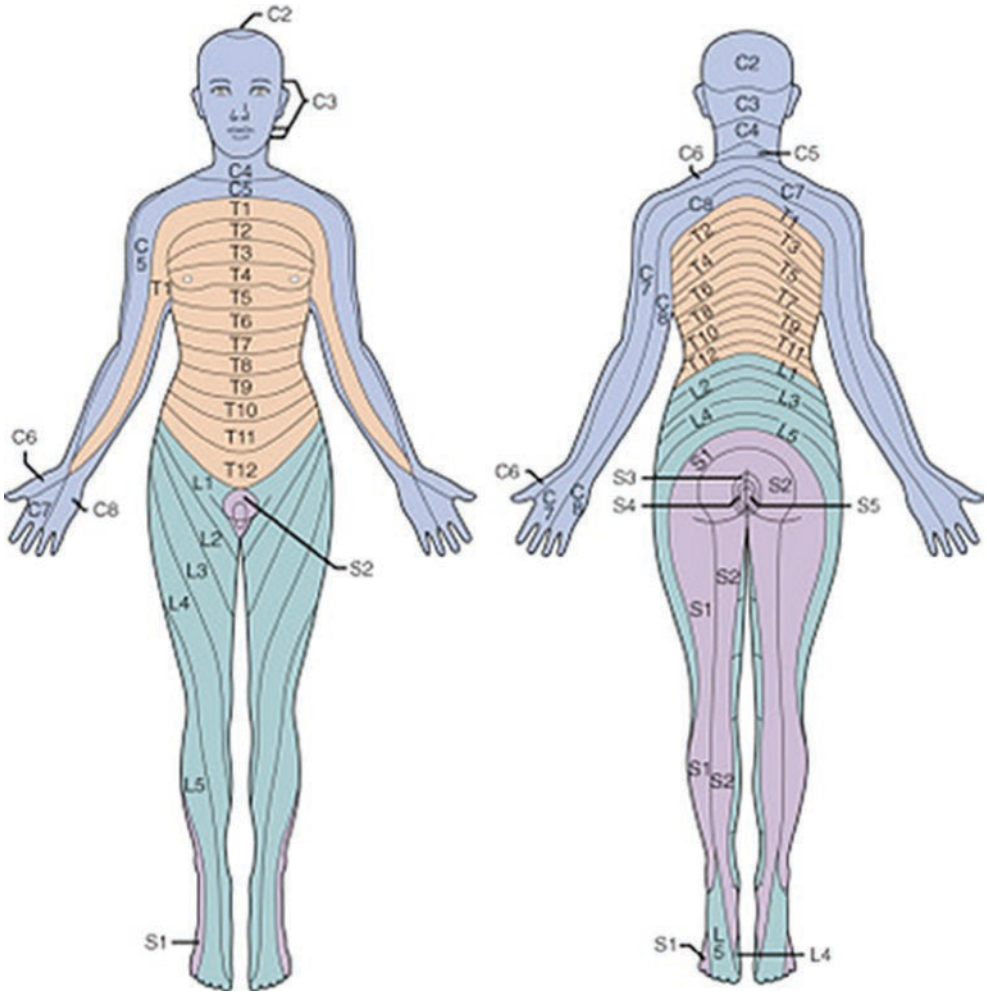

Fig. 9.5 Dermatome map. Dermatome map with anterior and posterior view. (Reproduced with permission from Strakowski et al. [27])

bodies in the dorsal root ganglion are unaffected, and the axons extending to the distal peripheral nerves are likewise normal. If SNAPs were to be abnormal, then this would generate suspicion of a lesion distal to the dorsal root ganglion such as a plexopathy, mononeuropathy, or polyneuropathy (Fig. 9.6). Motor NCS can be abnormal in radiculopathy as the lesion is distal to the anterior horn motor neurons in the spinal cord (Fig. 9.7).

Of note, motor NCS changes are directly related to the time course of injury. To elucidate, for days to weeks after a radiculopathy injury, the interrogated peripheral nerves may have normal CMAP, because the distal portion of the nerves is not yet injured. After several weeks, the motor nerve has undergone Wallerian degeneration thereby resulting in CMAPs with reduced amplitude, increased distal latency, and reduced conduction velocity. Nonetheless, because only a select few motor nerves are assessed by motor NCS, needle EMG is generally better suited for radiculopathy assessment.

Needle EMG findings in radiculopathy are consistent with neuropathic injury. We will describe the time course of radiculopathy needle EMG findings in regard to spontaneous activity, MUAP firing pattern, and MUAP morphology. In acute injury, the clinically weak muscles of the affected myotome will demonstrate reduced recruitment of MUAPs. Reduced MUAP recruitment reflects the loss of axons and motor units. However, the healthy remaining axon and motor units will continue to function with normal MUAP morphology. In the subacute phase of injury, Wallerian degeneration progresses in a proximal to distal fashion where denervation is first noted in the paraspinals (10–14 days), followed by the proximal muscles (2–3 weeks) and later in the distal muscles (5–6 weeks). During this period, abnormal spontaneous activity in the form of fibrillation potentials and sharp waves is observed. MUAP morphology continues to be normal with reduced recruitment. In chronic injury, typically after 2 months, denervated motor units will connect with surviving axons to produce larger motor units which are described as reinnervation. Reinnervation produces large amplitude, extended duration, and polyphasic MUAPs. After successful reinnervation, spontaneous activity normalizes, and fibrillation potentials and sharp waves are no longer detected. MUAP recruitment continues to remain reduced

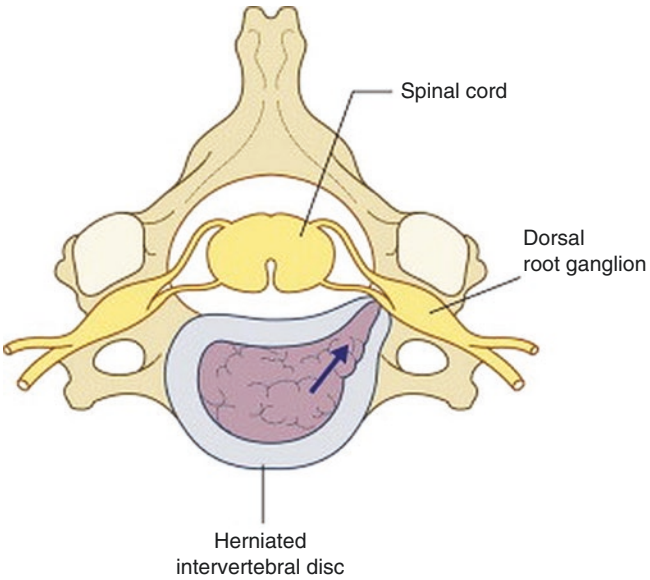

Fig. 9.6 Radiculopathy and sparing of the dorsal root ganglion. Herniated intervertebral discs can cause cervical and lumbosacral radiculopathy. Lateral posterior herniations compress the exiting spinal nerves but spare the dorsal root ganglion. Consequently, sensory NCS of peripheral nerves distal to the dorsal root ganglion are normal in radiculopathy. (Reprinted with permission from Wilbourn [28])

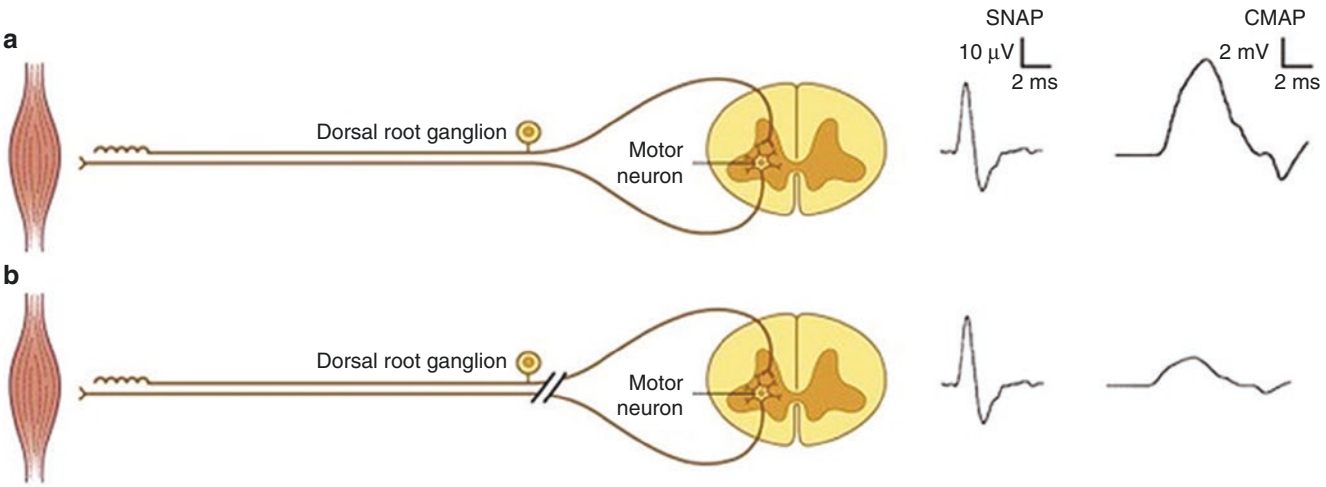

Fig. 9.7 NCS changes in radiculopathy. (**a**) Normal. (**b**) Radiculopathy. The lesion is proximal to the dorsal root ganglion. The sensory nerves distal to the dorsal root ganglion are spared. SNAPs are normal. The motor nerves will be affected. CMAPs are abnormal. (Reprinted with permission from Preston and Shapiro [6])

in chronic radiculopathy. The time course of neuropathic changes witnessed in radiculopathy allows NCS/EMG to describe the chronicity of disease [10].

Cervical Myelopathy

The clinical manifestation of myelopathy is dependent on the extent of cord involvement as well as the level of the lesion. Cervical myelopathy may present with local axial pain, cervicogenic headache, gait impairment, bladder changes, and sensory changes and motor weakness in upper and lower extremities. The neurological exam may demonstrate upper motor signs including positive Babinksi and Hoffman sign, increased muscle tone, and pathologically brisk reflexes. Lhermitte's sign, a radiating electrical shock sensation down the spine and into the extremities, can be generated by flexion of the neck. In chronic disease, there may also be lower motor neuron findings of fasciculations, atrophic muscles, reduced muscle tone, and suppressed reflexes in the setting of damaged anterior horn cells and Wallerian degeneration. "Myelopathic hands" are characterized by muscle wasting, weakness, and spastic dysfunction [11].

NCS/EMG in Myelopathy

Sensory NCS SNAPs are normal in myelopathy because the disease is proximal to the dorsal root ganglion. In chronic myelopathy affecting the lower motor neuron anterior horn cells, there will be reduced CMAP amplitude and slowed conduction velocity and distal latency. Late responses will be abnormal or absent if the affected cord levels are involved. Affected myotomes will present in the same pattern of axonal loss injury as described in radiculopathy (above). NCS/EMG cannot independently diagnose myelopathy; the diagnosis heavily relies on clinical history, physical exam, and neuroimaging. However, NCS/EMG is helpful in evaluating for peripheral nerve pathology which can mimic cervical myelopathy [12, 13].

Lumbar Spinal Stenosis

Lumbar spinal stenosis clinically presents with pain in the buttocks and groin with radiation posteriorly down the leg into the feet. Associated symptoms include lower back pain, weakness, and paresthesias. A distinguishing feature of lumbar spinal stenosis is that lumbar extension worsens symptoms whereas lumbar flexion improves symptoms. Patients may complain of pain and paresthesias with lying flat or standing with improvement of symptoms when sitting or curling up on their side with hips flexed [14]. The underlying pathophysiology is attributed to positional mechanical compression of nerve roots.

NCS/EMG in Lumbar Spinal Stenosis

In early disease, NCS/EMG can be normal due to intermittent neuroclaudication. In advanced disease, NCS/EMG findings are similar to chronic multilevel lumbosacral radiculopathy. NCS /EMG demonstrates axonal pattern of injury with abnormal paraspinal and limb muscle fibrillation potentials that corresponds to the root level of injury. It is important to note, that SNAPs are unaffected, as the lesion is proximal to the dorsal root ganglion. Late responses such as the H-reflex are typically abnormal or absent if the spinal stenosis is present at the S1 level [15–17].

Axial Pathology Mimics

Cervical Spine Disease Mimics

Brachial plexopathy and upper extremity neuropathy can mimic cervical spine disease by presenting with prominent pain, sensory loss, or motor weakness in the upper arm, forearm, and hand. We will review the upper extremity neuroanatomy and describe clinical syndromes with NCS/EMG findings.

The brachial plexus is comprised of the roots, trunks, divisions, cords, and terminal nerves. There are five roots beginning at C5 and continuing to T1. The dorsal scapular nerve arises from the C5 nerve root. The long thoracic nerve arises from the C5, C6, and C7 nerve roots. There are three trunks. The upper trunk is formed by C5 and C6 roots and gives rise to the suprascapular nerve. The middle trunk is formed by the C7 trunk. The lower trunk is formed by the C8 and T1 nerve roots. Each trunk has an anterior and posterior division. The lateral cord is formed by the anterior divisions of upper and middle trunk. The posterior cord is formed by the posterior division of all three (upper, middle, and lower) trunks. The medial cord is formed by the anterior divisions of the lower trunk. The lateral cord gives rise to the lateral pectoral and musculocutaneous nerves. The lateral cord also innervates the median nerve with contribution from the medial cord. The medial cord itself gives rise to the medial pectoral, medial brachial cutaneous, medial antebrachial cutaneous, as well as the ulnar nerve. The posterior cord branches off into the axillary nerve, radial nerve, subscapular nerve, and thoracodorsal nerve (Fig. 9.8). Cutaneous innervation by the brachial plexus is described in Fig. 9.9. Distinguishing dermatomal distribution of symptoms versus a peripheral nerve distribution can be instrumental in diagnosis.

Presentation of brachial plexopathy and upper extremity neuropathy varies from acute to insidious. Etiologies are many including traumatic traction, shearing and compression injuries, neoplastic infiltration, mass lesions, ischemic, brachial plexitis (Parsonage-Turner syndrome), and thoracic outlet syndrome. Iatrogenic causes include delayed postradiation injury and perioperative stretch injuries which typically occur

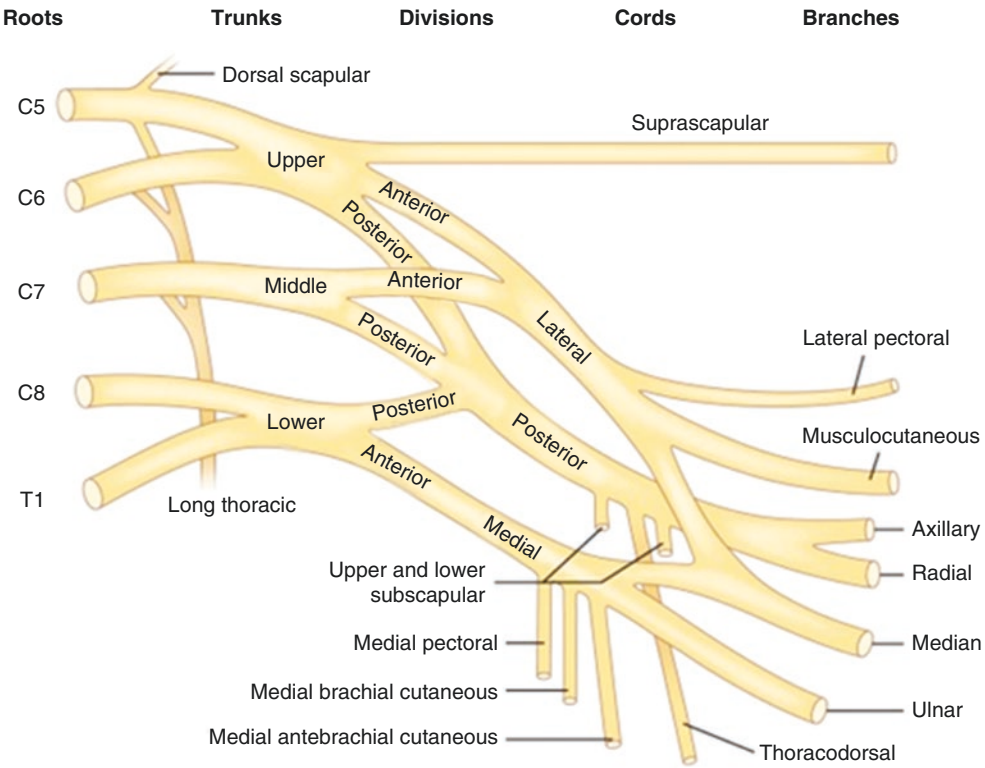

Fig. 9.8 Brachial plexus. Representation of the brachial plexus with depiction of roots, trunks, divisions, cords, and branches. (Reprinted with permission from Bednar and Wurapa [29])

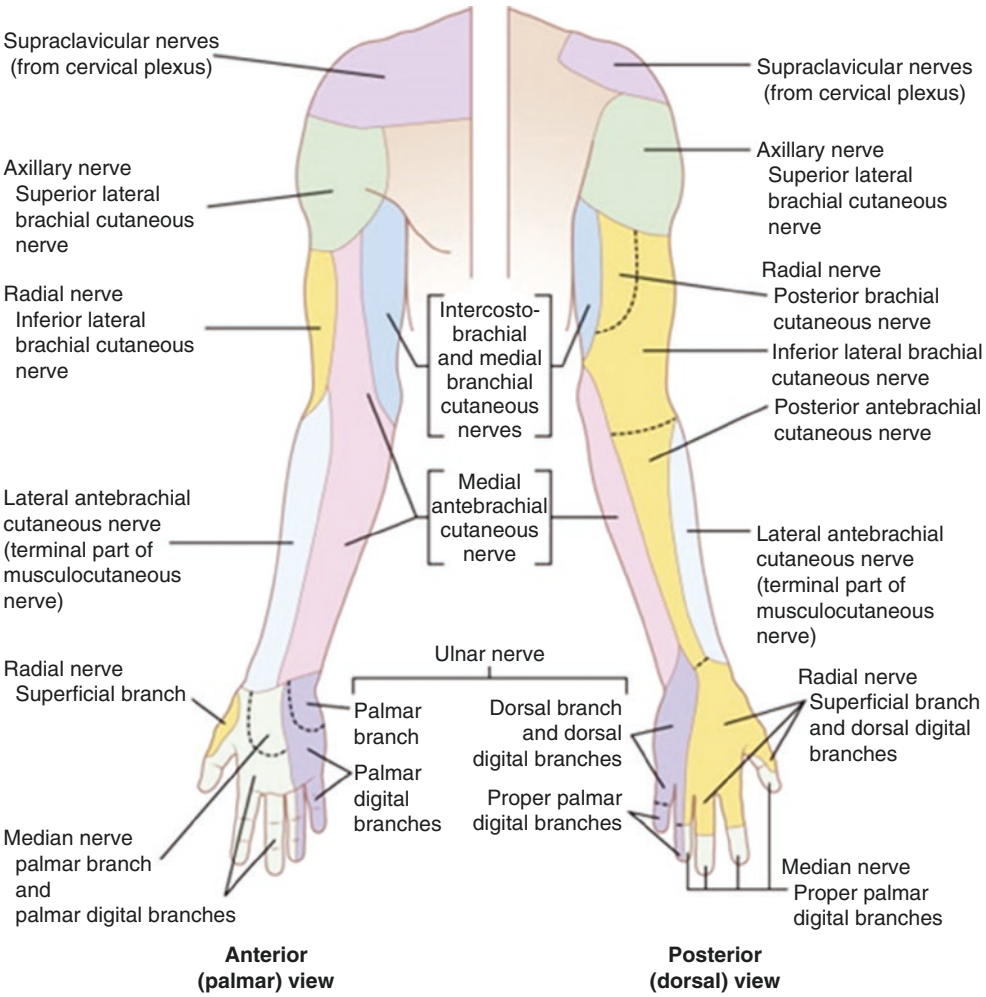

Fig. 9.9 Cutaneous innervation of the upper limb. Anterior and posterior view displayed. (Reprinted with permission from Hooks [30]. © 2012)

with surgeries requiring chest-wall retraction. Brachial plexitis (Parsonage-Turner syndrome), bilateral carpal tunnel, and neurogenic thoracic outlet syndrome are commonly on the differential and will be discussed further [18].

Idiopathic brachial plexitis, known as Parsonage-Turner syndrome, clinically presents with acute onset of severe pain involving the neck, shoulder, and periscapular area followed by weakness and numbness 2–3 weeks later. Clinical prognosis is variable and dependent on severity of injury with functional recovery estimated to occur between months and up to 3 years. The underlying pathophysiology is not well understood but is attributed to an immune-mediated mechanism. Known risk factors include recent infection or vaccination. NCS/EMG of brachial plexitis demonstrates a patchy distribution with neuropathic pattern of injury and can show proximal conduction block [19].

Median nerve entrapment at the wrist (carpal tunnel syndrome) presents as wrist and arm pain with associated hand paresthesia involving the first, second, third, and splitting the fourth digit (Fig. 9.10). Symptoms are aggravated with prolonged wrist flexion or extension. Nocturnal paresthesias are common. Functional hand weakness is typically a delayed finding and is associated with wasting of the thenar eminence. The differential for hand pain, paresthesias, and numbness can also include cervical (C6–C7) radiculopathy especially if the presentation is bilateral. NCS/EMG can distinguish these etiologies. In carpal tunnel syndrome, NCS should demonstrate distal focal slowing or conduction block of the median nerve across the carpal tunnel. EMG may show denervation in the median nerve innervated abductor pollicis brevis (APB) [6]. A cervical radiculopathy would

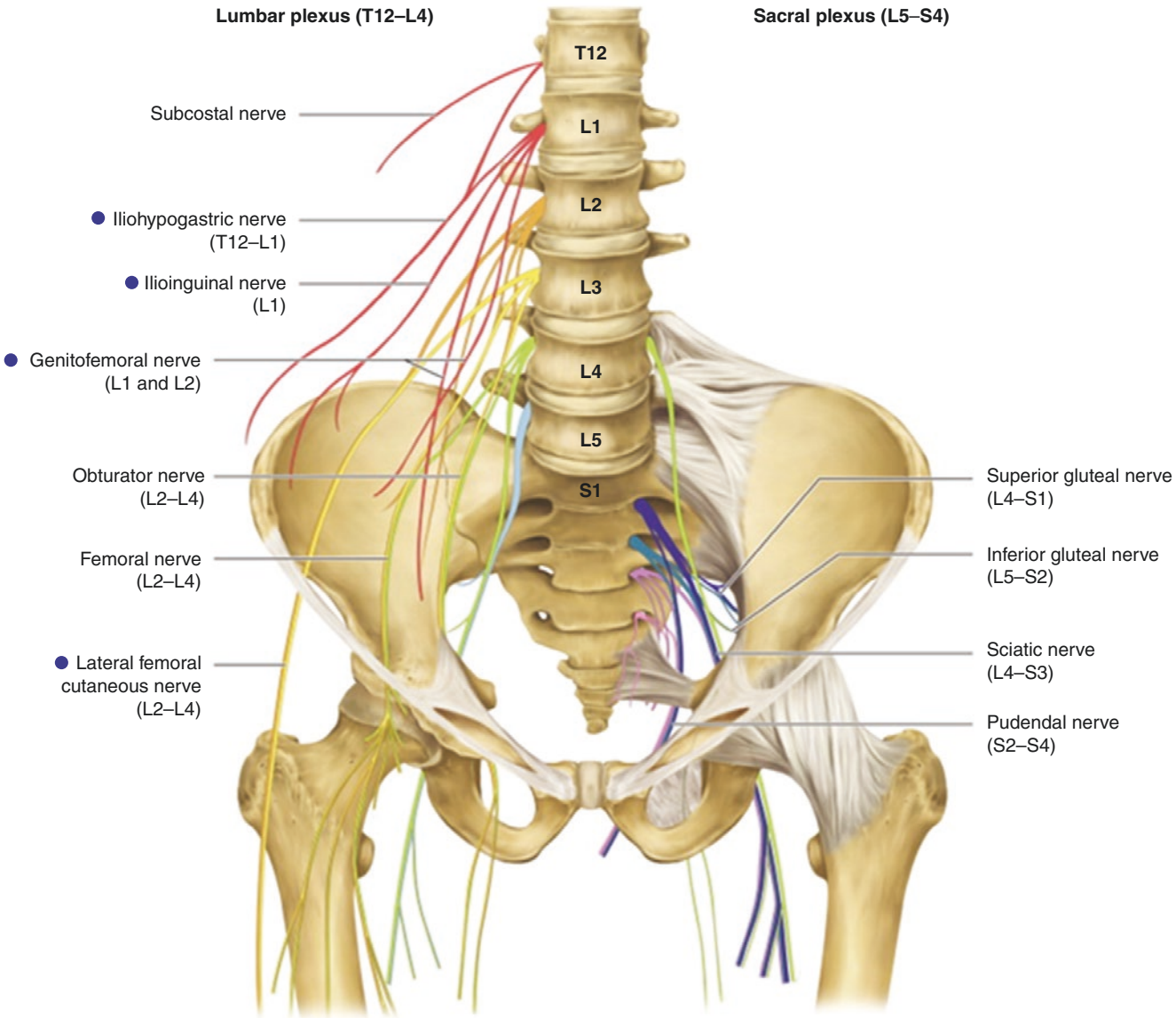

Fig. 9.10 Lumbosacral plexus. (Reprinted with permission from Kim et al. [31])

have normal SNAP (lesion proximal to the dorsal root ganglion) but abnormal CMAP and needle EMG findings in the distribution of the affected myotome and including areas proximal to the wrist [7, 13].

Neurogenic thoracic outlet syndrome is rare condition that can present as neck and shoulder pain with associated limb paresthesias and weakness [20]. Symptoms are worsened or provoked with sustained overhead activity. Neurogenic thoracic outlet syndrome is caused by the entrapment of the lower trunk of the brachial plexus by a fibrous band from a cervical rib. NCS/EMG findings are typically most consistent with a lower trunk plexopathy. Accordingly, sensory NCS studies will have abnormal SNAPs in ulnar and medial antebrachial cutaneous nerves. Motor NCS studies will be abnormal in the median and ulnar innervated muscles. Neuropathic pattern of injury demonstrating denervation, MUAP abnormalities, and reduced recruitment is expected in the median and ulnar innervated muscles.

Lumbar Spine Disease Mimics

Lumbosacral plexopathy and lower extremity neuropathy can mimic lumbar spine disease by presenting with pain, sensory changes, and motor weakness in the lower back and leg. Diagnosing radiculopathy vs plexopathy vs mononeuropathy can be challenging without neurophysiologic testing. We will review the lower extremity neuroanatomy, clinical syndromes, and relevant NCS/EMG findings.

The lumbosacral plexus is divided into the upper lumbar plexus (L1–L4) and lower lumbosacral plexus (L5–S3). The upper lumbar plexus gives rise to the iliohypogastric nerve, ilioinguinal nerve, lateral femoral cutaneous nerve of the thigh, genitofemoral nerve, femoral nerve, and obturator nerve. The lower lumbosacral plexus gives rise to the superior gluteal nerve, inferior gluteal nerve, pudendal nerve, sciatic nerve, and posterior cutaneous nerve of the thigh. The sciatic nerve at the popliteal fossa divides into the tibial nerve and common peroneal nerve, which itself divides into the superficial and deep peroneal nerve (see Fig. 9.10). Cutaneous innervation of the lower limb with branches of the lumbosacral plexus and distal peripheral nerves is described in Fig. 9.11.

Common etiologies in lumbosacral plexopathy include hip or pelvis trauma/surgery, postradiation injury, diabetic amyotrophy (also described as radiculoplexus neuropathy), postpartum plexopathy, and mass lesions including neoplasm, retroperitoneal hematoma, and psoas abscesses [21]. Lumbosacral radiculopathy and lumbosacral plexus lesions can be difficult to distinguish clinically given similarity of symptoms: low back pain, pelvic pain, and lower extremity numbness and weakness. NCS/EMG is helpful in distinguishing these disorders. EMG of the paraspinal muscles is expected to be abnormal in radiculopathy and normal in plexopathy. Sensory NCS is expected to normal in radiculopathy (because the lesion is proximal to the dorsal root ganglion) and abnormal in lumbosacral plexopathy and distal peripheral nerve disorders.

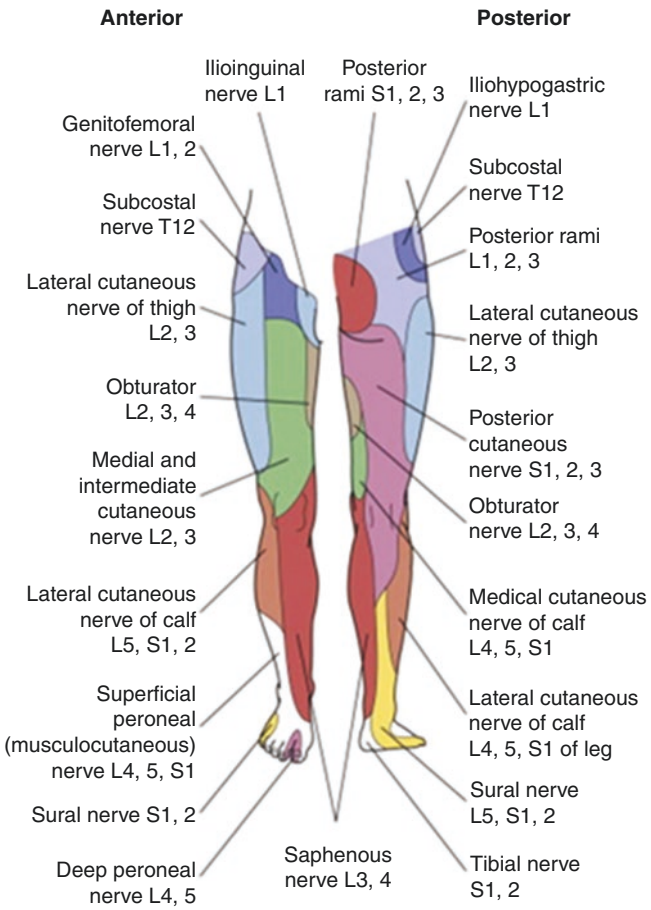

Fig. 9.11 Cutaneous innervation of the lower limb. Peripheral nerve cutaneous innervation of the lower limb. (Reprinted with permission from Harmon et al. [32])

Diabetic amyotrophy presents with unilateral deep pain in the pelvis and hip for 4–6 weeks followed by proximal leg weakness, weight loss, and autonomic dysfunction [22]. Diabetic amyotrophy primarily affects the upper lumbosacral plexus but can also involve the nerve roots and thus is described as a radiculoplexopathy. Clinical weakness primarily involves the obturator and femoral nerve manifesting in hip flexion weakness, hip adduction weakness, and knee extension weakness. The patellar reflex is typically diminished or absent. The pathophysiology underlying diabetic amyotrophy is thought to be chronic microvascular ischemic injury. NCS/EMG in diabetic amyotrophy is consistent with neuropathic pattern of injury predominantly in the L2–L4 myotome which reflects the clinical weakness [6].

Meralgia paresthetica or isolated entrapment of the lateral femoral cutaneous nerve is another clinically important syn-

drome to recognize. The lateral femoral cutaneous nerve arises from L2 to L3 nerve roots and is part of the upper lumbar plexus. Isolated lateral femoral cutaneous nerve entrapment presents with pain, burning, and numbness over the anterior and lateral thigh without focal weakness. Etiology is likely compressive with risk factors of obesity, diabetes, and tight clothing – namely, belts and pants. As discussed above, the lateral femoral cutaneous nerve can be assessed by sensory NCS. Due to technical difficulty, reduced or absent SNAPs should be cautiously interpreted with bilateral comparisons and correlated to clinical history [23].

Limitations of NCS/EMG

NCS/EMG is an important diagnostic tool for radiculopathy, plexopathy, mononeuropathies, and polyneuropathies. It has a limited utility in spinal pathology without associated peripheral nerve or myotome to interrogate. For instance, discogenic pain can clinically present similarly to radiculopathy with radiating pain in the affected dermatomal level with or without associated weakness or paresthesias. The intervertebral disc is innervated by branches of the sinuvertebral nerve and branches of the paravertebral sympathetic trunk which cannot be examined by NCS/EMG [24]. Likewise, facetogenic pain is a source of axial neck and back pain exacerbated with facet loading action such as extension and rotation [25]. Facet joints are innervated by the medial branch nerves dorsal rami at the level of and level above the lesion, and these nerves are not interrogatable by NCS/EMG (Fig. 9.12).

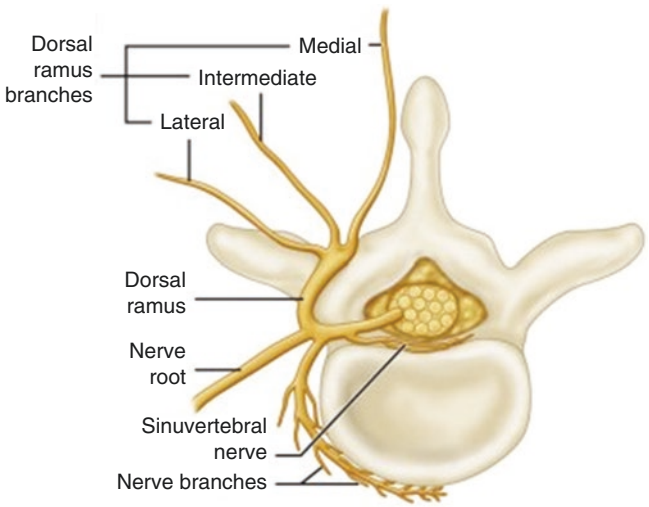

Fig. 9.12 Sensory innervation of the spine. Cross-sectional view of the spine at endplate and disc. Sinuvertebral nerve innervates the dorsal surface of the disc. The medial branch nerves of the dorsal rami innervate the facet joints. (Reprinted with permission from Gardocki and Park [33])

Summary

An understanding of the neurological examination and in continuation the neuromuscular diagnostics tests, EMG and NCS are important tools for the pain physician. Often, pain practitioners play a primary diagnostic role, in addition to treating pain. In such cases, an intimate understanding of neurological assessment is crucial. Performing a screening examination is the best way to make sure that one does not miss a diagnosis or mistake one condition for another. As an unfortunate example, many patients are treated with interventional procedures, including spine surgeries, when the ultimate diagnosis is a progressive neuropathy or even amyotrophic lateral sclerosis. The critical ability to identify upper motor neuron signs can implicate cervical spine stenosis and consequent myelopathy masquerading as lower extremity pain.

Beyond the neurological examination, NCS and EMG are essential for confirming the involvement of specific nerves and muscles or identifying a key pathological process at play in a patient's condition. Important considerations include the timing of injury and whether to expect signs of acute denervation on EMG, namely, fibrillation potentials and positive sharp ways, or whether the main features will reflect chronic denervation and reinnervation, as evidenced by changes in motor unit morphology. For neuropathy, the main features include patterns of axonal loss versus demyelination, as the latter include a smaller group of conditions for which some have specific treatments.

The use of NCS/EMG for pain physicians includes a range of indications, such as diagnosis and prognosis, monitoring disease progression, and evaluating patients for interventions including surgery. While indications for NCS/EMG are at times uncertain, the tests are particularly useful in cases where examination is limited or conclusions uncertain.

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Psychological and Psychiatric Evaluation of the Spine Pain Patient: An Interface of the Mind/Body Dynamic

10

Gregory Acampora

Key Points

- Comprehensive treatment of pain patients involves attention to both primary causes and tributary results.
- The objective and subjective perception of pain are bidirectionally intertwined and influence each other.
- Patients may be confused by this interaction; clinicians who understand the interface will better articulate a treatment strategy.
- Effective empathic communication involves affect more than cognition; at the same time, a clinician should be aware of the risk of personal affective distortion.
- PTSD is a significant co-occurring condition with chronic pain, often misinterpreted as anxiety or depression. The pain clinic encounter may provide a unique opportunity for early treatment of PTSD.
- Substance use disorders and pain influence each other, but there are significant misperceptions about incidence, prevalence, causality, and treatment approaches.
  - Discussing controlled substances can lead to misinterpretations and miscommunication.
  - There are established strategies to best address this comorbidity.
- Suicide risk is increased with chronic pain; it is important to address subtle signs of diminished coping strategies.
- The modern mind-body construct is based on objective observations and should be included in the comprehensive multimodal treatment of spinal pain.

Introduction

Clinicians who are dedicated to treating complex spine pain patients are well aware of the multisystem and interdisciplinary complexity of the cases. Comprehensive treatment of any patient requires awareness and thoughtful considerations of treatment approaches and modalities that extend beyond the idealized scope of management imagined by the provider. The goal of this chapter is to offer the reader practical guidance and insight into some of the behavioral manifestations by patients with a complex pain process including their responses to treatment modalities that are being offered. These behaviors may have primary or secondary mental origins and may or may not fit existing taxonomic or diagnostic criteria according to either the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5) or International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM). As with most co-occurring conditions, there is a confluence of mechanisms at work, and the integration may not be simple. The mind-body dynamic is a subtle construct. This chapter will help define it and apply this to some of the common concerns pain clinicians voice as they deal with the pain/behavior interface during treatment.

Duality

A highly simplified but useful cornerstone to approach the comprehensive evaluation of a patient presenting with pain is summarized in seven words: *Pain affects mood and mood affects pain*. At first this may seem a simplistic dictum; however, it exemplifies a mind-body dynamic. The bidirectionality is partly a result of the brain's highly associational makeup that invariably compares new and past experiences, both physical and emotional. Moreover, the amount of attention given to these experiences can be viewed as occurring in *top-down* "voluntary" (prefrontal, goal oriented, *endogenous*, or sustained) vs. *bottom-up* "automatic/involuntary"

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(parietal, stimulus generated, *exogenous*, or transient) processes. Although there is evidence that the endogenous and exogenous attention pathways operate independently, the "intertwining" with consciousness and response to stimuli are variable both physiologically as well as perceived [1].

Like other complex physiologic homeostatic systems that constantly maintain a tightly balanced steady state (e.g., autonomic, hemostatic, endocrine, and immune), the pain system employs feedforward and feedback mechanisms to achieve a purposeful and protective functional equilibrium. When this advantageous steady state is disturbed, protective homeostatic systems can become disruptive or even dangerous to the individual.

From the behavioral standpoint, chronic pain patients are dealing with a "pain-trap." They experience a shift in the protective signaling function of the pain system. Whereas pain typically signals something that is to be changed or avoided, chronic pain exceeds usual duration limits. The patient begins to find themselves unable to make sufficient changes to escape their physical and psychological discomfort. As the attention shifts from exogenous to endogenous, a new quandary presents itself in the duality of frontal-cortical versus striatal ("limbic") mental processes. Visualize frontal as proactive or executive (judgment, foresight, and planning) and limbic as reactive or reflex. We need both of these systems in order to remain safe and secure as we engage in daily activities. Much of our daytime is spent unconsciously engaged in avoiding harm: we look both ways before crossing, we sidestep suspicious or threatening things, we adhere to rules of the road and sidewalk, and we dress for security with weather appropriate items or bright/reflective sports gear. The limbic system is our early warning system and is very sensitive. The frontal lobes generate managerial oversight for what to do with hazard and are quite specific. *When we are threatened, it interferes with our sense of security, self-esteem, and ambition*. To press on with the concept, chronic pain functionally shifts the density of responses to threats beyond early automatic responses toward more frontal-temporal processing. By recruiting more of our attention pathways, chronic pain interferes with the ideal homeostasis of mind and can influence the physiologic response [2]. The chronic pain process may lead to allosteric compensation in the frontal cortex and influence corticofugal interactions at midbrain and spinal levels [3]. For clinicians who treat pain, understanding this highly encompassing dichotomy manifested by chronic pain will lead to a more sophisticated, comprehensive, and empathic treatment approach.

It is very exciting that there are many recent studies using functional neuroimaging that can illustrate the brain networks responsible for the subjective responses to pain [4]. Neuroimaging studies of psychiatric conditions and observed responses to multimodal treatments are guiding targeted treatments [5]. Our eventual hope is for robust guided advancements in the understanding and treatment to pain incorporating possible individual differences in emotional modulation of pain neural processing including at the level of the spinal cord and brainstem [6].

Just as I have used the expression "pain-trap" as a concept, any number of conditions can produce a similar scenario: COPD-trap, CHF-trap, addiction-trap, etc. The unifying implication is a significant systems disease that consumes many collateral resources and energy.

Empathy and Countertransference

It would not be reasonable to expect a clinician with expertise and focus on pain management to intuitively perceive and understand behavioral dynamics at the level of a behavioral specialty trained clinician. Medical schools attempt to teach empathy as part of the curriculum, but a recent review identified that the historic metrics of empathy in training may be limiting [7]. Most emphasis has been on cognitive empathy which involves an ability to understand another's experience and then communicate and confirm that understanding with someone. Affective empathy has more to do with a sense of emotional congruence or feeling about that person's experience. The blending of cognitive and affective empathy will more likely yield the goal of perceiving a patient's emotional state and couple it with a motivation to address their welfare. Patients often express a wish to feel heard or be understood more than to be investigated. A patient is a complex being with hopes, wishes, and dreams as well as hurts, regrets, and fears. In modern clinical settings with demands to meet relative value units (RVU), see more patients, and attend to the electronic medical record (EMR), trying to "relate emotionally" with a patient sufficiently may seem a tall order. In a twist on the "mind-body dynamic" interface, there are some practical things the clinician can consider in generating a sense of congruence and collaboration in their patient's care including posture and taking short spans of time away from the EMR [8]. Consider taking the time to identify and develop the "soft skills" that will enhance your clinician-patient interaction and conceivably even impact patient outcome positively [9]. Think about this as you complete your next new evaluation, for example.

Psychiatry and psychology training puts a significant emphasis upon self-awareness regarding the impact a clinician has on the patient. One entity that is accentuated in training as a potential problem emotion in the treater is the concept of *countertransference*, which addresses the reactions and responses the treater has toward the patient based on the treater's own background and personal issues. Specifically, the priority here is placed on the trainee understanding *their own* response to the patient, good or bad. This is important to avoid accidentally pursuing a path in which the clinician is

making decisions on behalf of the patient while influenced by their own emotions. If we seek to put emphasis on shared decision-making for patients seeking help with complex medical problems, we have to keep an emphasis on patient-centered "decision quality" [10–12]. Our own mind-body dynamic affects our impact on our patients.

Post-traumatic Stress Disorder (PTSD)

PTSD may be one of the most clinically overlooked co-occurring psychiatric diagnoses in chronic pain management [13]. Although the type of pain linked to PTSD is variable, a large-scale systematic review showed a consistent association between chronic pain and PTSD [14]. From a treatment perspective, it is worthwhile to imagine two types of patient when considering PTSD and pain. Patients who have had PTSD exposure and symptoms *before* the onset of an index pain event have primary PTSD, which I will call PTSD1; those who develop PTSD from an index pain event and the sequelae following pain onset have secondary PTSD, which I will call PTSD2. In either case, there will be clinical presentations that are manifest because the "duality," or interplay (intertwining), of the physical and mental responses to pain and trauma.

In the most recent DSM-5, which is the standard classification of mental disorders used by mental health professionals in the United States, PTSD is now categorized under *trauma and stressor-related disorders* and not under the anxiety disorders [15]. The diagnosis complex includes the exposure event(s) "A" and sequelae "B–E." Exposure (A) includes actual or threatened, death, serious injury, or sexual violence: the previous language that "involves fear, helplessness, or horror" is no longer included acknowledging that dissociation can occur at the time of the event. The requirement of exposure to a stressful event as a precondition for the diagnosis is particular among psychiatric disorders.

The PTSD persisting clinical sequelae (B–E) include:

- B. Intrusion symptoms: involuntary recall, nightmares, flashbacks, distress, and marked physiologic reactivity
- C. Persistent avoidance of stimuli associated with the trauma: reminders, thoughts, or feelings
- D. Negative alterations in cognitions and mood that are associated with the traumatic event: dissociative amnesia (loss of memory of key features), persistent negative self-beliefs and/or distorted blame of self or others for causing the traumatic event or for resulting consequence, loss of interest, detachment/estrangement, and constricted affect
- E. Alterations in arousal and reactivity that are associated with the traumatic event: irritability, aggressivity, recklessness, hypervigilance, startle, poor concentration, and sleep disturbance

DSM-5 spectrum diagnosis allows clinicians more flexibility to account for variations from person to person [15]. Upon review of the above set of diagnostic criteria, the pain clinician will likely recognize any number of these traits in their patients. By becoming more attentive to the mechanism behind what may be perceived as disruptive behaviors by the patient, the clinician can more accurately diagnose co-occurring conditions that produce the patient's pain presentation.

PTSD is associated with high degrees of depression and/or anxiety. It is important to remember that clinicians may be more attuned to recognizing depression and anxiety while overlooking PTSD as the primary diagnosis. Sometimes the presentations of PTSD may even invoke diagnosis such as "bipolar," "borderline," and "psychosomatic." There is ample evidence that patients may respond to treatment modalities to diminish depression and anxiety symptoms, while PTSD symptoms may still linger [16].

It would be propitious to put more emphasis on identifying patients who demonstrate PTSD2. In cases of PTSD2, the Pain Clinic evaluations can serve as an excellent opportunity for a primary, accurate diagnosis that could generate prospects for early and more rigorous treatment of co-occurring PTSD in this group. This may mitigate penetrating and persisting PTSD symptoms that could interfere with comprehensive multimodal pain treatments offered to the patient [17].

Earlier in this chapter, the concepts of duality and attention put emphasis on the response of the chronic pain patient to vulnerability. PTSD symptoms are associated with high catastrophizing (see PTSD symptoms "E") resulting in low self-efficacy. Efforts to overcome fear-related beliefs (kinesophobia and avoidance) by tailoring interventions may motivate patients' perceptions to be more engaging in rehabilitative activities [18]. From a practical standpoint, if the clinician is able to shift thinking from "why is this patient behaving this way?" (possibly pejorative) to "what is behind the patient behaving this way?" (empathic and solution oriented) one may circumvent a clinical lost opportunity.

Controlled Substances and Substance Use Disorder (SUD)

The linkage between chronic pain and SUD is bidirectional [19]. It is beyond the scope of this chapter to address the scientific epidemiology of this confluence; however, in terms of the mind/body dynamic, the interaction of perceived pain vs. sought relief invokes the internal and external neurobehavioral interactions discussed earlier in this chapter.

The rubric of controlled substances prescription (CSRx) arises often with chronic pain patients and can become complex for any number of reasons including historic prescribing patterns, response or failure to attempted treatment modalities, and possible (likely) misinterpretations of treatment

application and results on the part of the patient or clinician. The recent confluence of analgesic prescribing trends and recent focus on the "opioid crisis" [20] has resulted in polarization of attitudes by stakeholders surrounding CSRx. Negotiating this prescribing theme can invoke many prefrontal and striatal neurobehavioral circuits and responses in both clinicians and patients. It is important to be mindful about making conscious or unconscious affiliations of CSRx use to substance use disorder (SUD) with either prophylactic or prejudicial intent. To make matters worse, the language of SUD can be confusing. Notably, clinician CSRx decisions can be influenced by menaces of legal sanction [21].

It will be useful at this juncture to draw out some presuppositions. The history of addictions has been steeped in stigmatic language worldwide [22]; within the modern field of addiction medicine and addiction psychiatry, there is great emphasis placed on the language surrounding addiction so as to avoid stigma. Here are some useful key terms:

I. Tolerance: diminished response to a drug, which occurs when the drug is used repeatedly and the body adapts to the continued presence of the drug
II. Dependence: adaptive changes by the body to a drug that result in *withdrawal symptoms upon cessation of that drug*
III. Addiction: compulsive drug seeking despite negative consequences (NIDA); impaired control, social impairment, risky use, and *craving* leading to problematic pattern of use of an intoxicating substance with clinically significant impairment or distress (2 of 12 DSM V criteria) [15]
IV. Abuse = illegal patterns: selling, forging prescriptions, stealing drugs from others, using by nonprescribed route (e.g., injecting or crushing and snorting), multiple doctor sources or multiple pharmacy fills, repeated losing/running out/self-dosage increases
V. Misuse: nonpatterned use of illicit substances or incorrect use of CSRx

Engaging the patient in a discussion about CSRx while avoiding interactive pitfalls can be a significant challenge. A suggested approach is to avoid dichotomous language and focus on solving any *misinterpretations* that may be had by the patient or the clinicians. If a patient says they took some extra tablets, consider asking an open-ended question such as "how did you decide to do that?" rather than a closed-ended "why did you do that?" (the response will invariably begin with "because…").

Consider trying a spectrum (non-dichotomous) approach to address the subject with the patient (Fig. 10.1).

Focus attention on the colored triangle suggesting it is like a stoplight: Green is *go*, yellow is *proceed with caution*, and red is *stop*. Explain that CSRx is complicated by the fact that these medications may work favorably at low doses, but as one increases dose, unwelcome neurobiological responses including triggering of tolerance and dependence occurs and can lead to reward, addiction [24], or overdose. Keep most of the emphasis on the yellow zone and the word misinterpreted to keep the clinician and patient on a collaborative plane. If the issue is weaning a patient down from a high morphine equivalent (or benzodiazepine) dose, suggest that the patient strive "to move towards the green zone." The Trigger zone is meant to indicate that as doses increase, there is increased risk of invoking anticipation and preoccupation for use. There is ample scientific evidence that CSRx risk can outweigh benefit on many levels [25]; communicating this to a chronic pain patient in a non-shaming way will yield the best results.

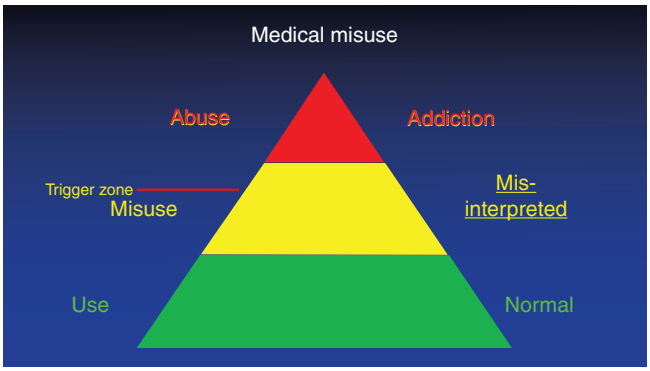

Fig. 10.1 Diagram tool to guide the controlled substances prescription (CSRx) dialogue toward solution and away from confrontation by using an easily recognizable construct (see text) [23]

Note the term trigger zone in the above illustration. This represents a proposed mechanism of shift to increased sensitization ("trigger" or runaway) response to a potent drug [26].

A treatment trap to avoid is concluding a patient with any history of SUD as ineligible for CSRx. Although a previous history of SUD is considered an additive risk for future SUD, it is not exclusive. Assessment of a patient's recovery status by a skilled addictions specialist can provide useful guidance beyond formulaic opioid risk stratification instruments by addressing psychosocial history and generating a more robust assessment, structure, and monitoring program [27]. The US Substance Abuse and Mental Health Services Administration (SAMHSA) produces a series of Treatment Improvement Protocol (TIP) publications that can assist clinicians in comprehensive decision-making in this setting (Fig. 10.2) [28].

Suicide

Suicide was the 10th leading cause of death in the United States with 44,965 deaths in 2016 at a rate of 13/5 deaths per 100,000 people, half of which were by firearms [29]. A

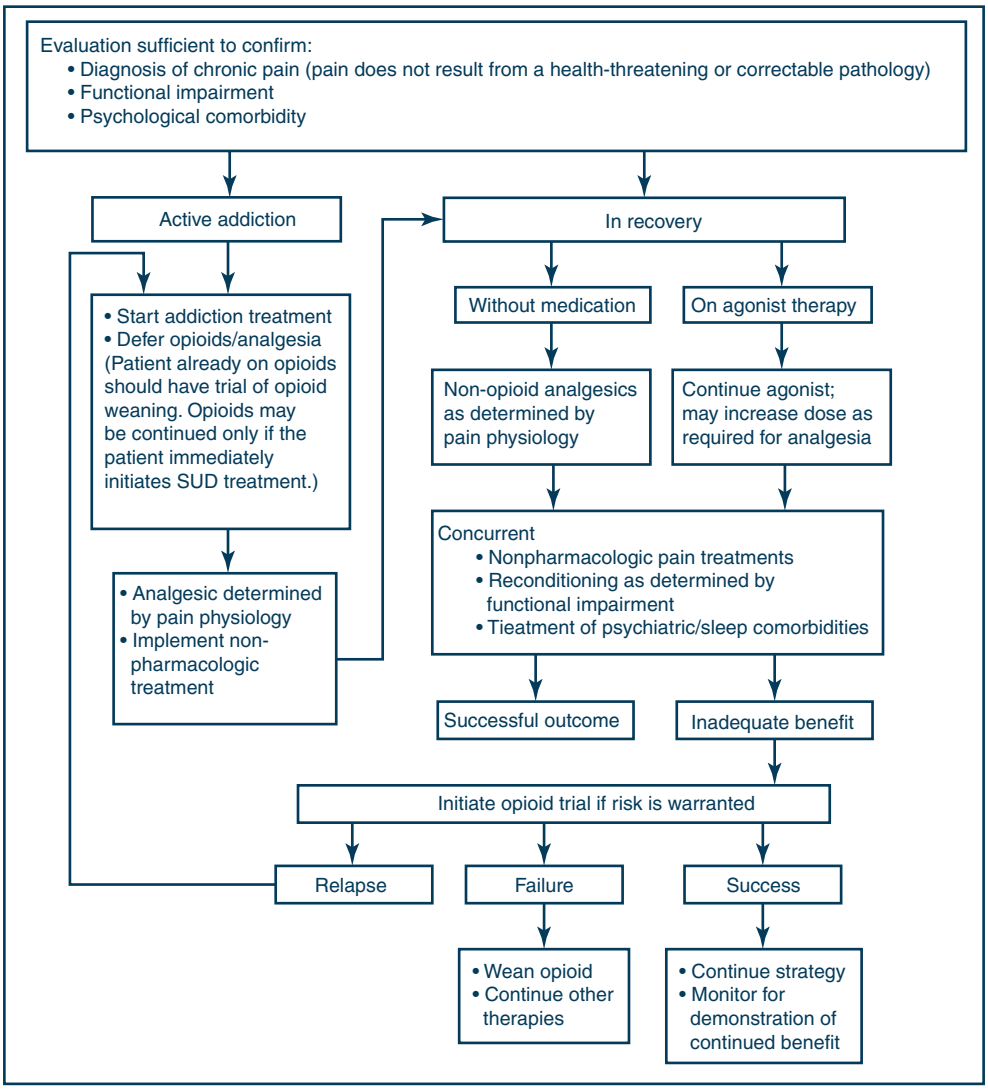

Fig. 10.2 Example of a diagnostic algorithm that guides clinicians who wish to consider opioids in chronic pain patients with SUD history from Protocol (TIP) Series 54. (SMA) 12-4671 Exhibit 4-11 Exit Strategy, p. 62

recent analysis of National Violent Death Reporting System (NVDRS) data from 2003 to 2014 revealed that 8.8% of decedents had chronic pain but was surprising to show an increased death rate trend of those with chronic pain from 7.4% in 2003 to 10.2% in 2014 [30]. A recent comprehensive review of chronic pain and suicide risk corroborated data suggesting that chronic pain is a significant independent risk factor for suicidality [31]. Family history, childhood and adult adverse events, and co-occurring primary mental illness including SUD were considered a general risk with unemployment and disability recognized as an associated risk for suicide for those with chronic pain. Predictors of suicidality included frequent episodes of intermittent pain, sleep problems, and negative perceived mental health, while pain duration, intensity/severity, or type were not related to suicide risk. A note of optimism was generated in the study by identifying psychosocial risks that are known to be amenable to treatment interventions such as belongingness, burdensomeness, catastrophizing, hopelessness, and mental defeat.

From the mind-body dynamic standpoint, there is noteworthy evidence that central pain processing pathways resemble and/or utilize the same reward/anti-reward pathways as with substance use and other mental disorders [32]. Notable negative behavioral hallmarks occurring with extremes of SUD, pain, depression, and anxiety are significant isolation and withdrawal. The result is diminished suitable coping strategies and can lead to apathy, anhedonia, and numbing. These represent neuropsychopathological allostatic results of the illness.

In the clinical domain, pain specialists should not avoid discussing the emotional restrictions experienced by their

patients. Do not be afraid to ask about suicide; use it as a metric of emotional pain intensity. The report of levels of mild passive ("OK if I didn't wake up"), moderate passive ("wish I would die"), active consideration ("hope I don't live) to active (plan, intent and means) is an indication of the burden of emotional hopelessness and mental defeat realizing these are treatable. As the intensity of these negative perceived mental health symptoms intensifies, the clinicians' response should be to increase emphasis on alternative multimodal therapeutic interventions. It may indicate the need for an assessment by a mental health specialist.

Therapeutic Constructs

The mind-body construct has a long history dating back to Buddha, Aristotle, and Plato and has undergone philosophical, theological, metaphysical, and mystical examination and dissertation. The goal of this chapter has been to offer pain clinicians an objective and scientific introduction to contemporary mind-body constructs with clinically applicable examples. The intention is to expand the treaters therapeutic contribution, thus amplifying the likelihood of a favorable outcome. Modern mind-body practice mechanism studies objectively demonstrate recruitment of genetic, neuroplastic, hormonal, and homeostatic effects [33]. The ultimate goal is to identify modalities that demonstrate clear clinical or physiological benefit. A good example of this is a study of modulation of pain through mindfulness meditation using fMRI with the added practical observation of seeing effect within four sessions [34]. A recent and pertinent article that proposes "addiction as learning, not disease" is highly informative and provides a perspicacious angle on how to consider pain behaviors [35].

The benefit of psychiatric and psychological expert evaluation and input cannot be emphasized. Through collaborative exchange of specialty knowledge, predictive assessments can be made in specific pain treatment areas such as the decision tree for spinal cord stimulator placement [36].

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Part IV

Spine Pain Conditions

Spinal Stenosis

11

Julie Petro and Damoon Rejaei

Key Points

- Spinal stenosis is defined as a narrowing of the spinal canal. It can be classified in terms of location (central, foraminal, or lateral recess stenosis) or cause (congenital, acquired, or degenerative).
- Degenerative spinal stenosis most commonly affects individuals in their 60s and is the most common diagnosis for spinal surgery for individuals over 65 years old.
- The diagnosis of spinal stenosis is from a combination of symptoms and their correlation with pathology found on radiology imaging.
- Radiographs provide limited information but are wildly available and low cost and have low radiation exposure. Magnetic resonance imaging is the most commonly utilized imaging modality with high sensitivity for detecting spinal stenosis and soft tissue pathology.
- There are no generally accepted radiologic criteria for diagnosing spinal stenosis. In the anteroposterior (AP) diameter, central canal stenosis is compatible with a bony canal diameter of less than 10 mm in the cervical spine and 12 mm in the lumbar spine.
- Central canal stenosis most commonly presents with neurogenic claudication. Neuroforaminal and lateral recess stenosis most commonly presents with radiculopathy.
- Symptoms of cervical spinal stenosis include impaired gait, numbness of the hands, hyperreflexia, atrophy of the intrinsic hand muscles, positive Hoffmann's test, and positive Babinski reflex. In the thoracic region, fatigue, leg heaviness, loss of proprioception, and pseudoclaudication are more common. Lumbar spinal stenosis stereotypically presents with neurogenic claudication and radiculopathy.
- Degenerative changes contribute to spinal stenosis. These include discal degeneration, disc herniation, facet hypertrophy, hypertrophy of the ligamentum flavum, bone remodeling, and osteophyte formation. Degeneration can furthermore lead to instability, scoliosis, and spondylolisthesis.
- Commonly employed conservative treatment includes physical therapy, exercise, patient education, and medication. Epidural steroid injections may offer some benefit as well. In cases of severe symptoms, surgical decompression may improve symptoms and functional capacity.

Introduction

The terminology of spinal stenosis is derived from the Greek word *stenos*, which is translated as narrow. Spinal stenosis refers to the abnormal anatomic narrowing of the spinal canal and can be classified in terms of location (central, foraminal, or lateral recess stenosis) or cause (congenital, acquired, or degenerative). Degenerative spinal stenosis most commonly begins in the sixth decade of life [1, 2]. Age-related changes result in diminished space for the neural and vascular structures. There are significant variations in the description and reporting of spinal stenosis; however, it has been cited as the most common diagnosis for spinal surgery in patients over 65 years old [2].

Congenital Stenosis is a normal variant in the population as well as a feature of achondroplasia. In congenital stenosis, defects in cellular metabolism lead to retardation of skeletal

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growth and hypoplasia, premature fusion of endplates, and irregular intracartilaginous bone formation. Major contributors to congenital stenosis are shortened pedicles, thickened lamina, and hypertrophied facet joints [2, 3]. These changes result in reduction of the AP (anteroposterior) diameter of the spinal canal, and spinal stenosis commonly occurs earlier in life [4–6]. Stenosis can also be acquired due to trauma, neoplasms, and infection or through disorders such as acromegaly, Paget's disease, fluorosis, or ankylosing spondylitis.

Central Stenosis is defined as a narrowing of the central canal, between the medial edges of the two zygapophysial joints (facet joints), resulting in reduced available space for nerve rootlets within the cerebrospinal fluid (CSF) in the dural sac [7, 8] (Fig. 11.1). In the axial plane, the central canal can be compromised anteriorly by disc protrusions or osteophytes, posterolaterally by facet hypertrophy, posteriorly by ligamentum flavum (LF) hypertrophy and buckling, and, in the cervical spine, anterolaterally by uncovertebral hypertrophy [9].

Foraminal Stenosis Foraminal Stenosis causes encroachment of the exiting neural structures at the intervertebral foramen, defined by the medial and lateral pedicle borders (see Fig. 11.1). Lateral recess stenosis is the impingement of the exiting nerve in the lateral recess or proximal foramen at the level of the facet joints, between the medial edge of the facet joint and the medial pedicle border [4, 7, 10, 11]. In the anteroposterior or craniocaudal orientation, foraminal stenosis can occur as a result of disc herniation, facet hypertrophy, or subluxation [9]. The definition of severity of foraminal stenosis, as well as the differentiation between foraminal and lateral recess stenosis, varies and is often inconsistent. Some definitions focus on deformation or obliteration of the perineural fat portraying an increase in the degree of foraminal stenosis [12], while others focus on direction of perineural fat obliteration or nerve root collapse in the foramen [13, 14].

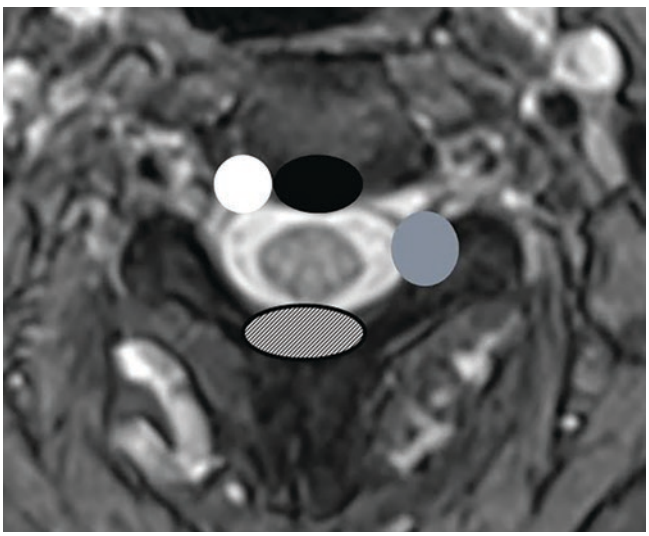

Fig. 11.1 Axial gradient recalled echo image of the cervical spine at the level of the disc space. The canal can be compromised in the following ways: anteriorly by a disc protrusion, osteophytes, or OPLL (black oval); posterolaterally by facet hypertrophy (gray circle); and posteriorly by ligamentum flavum infolding (white and gray oval). Anterolaterally, uncovertebral hypertrophy can narrow the spinal canal in the cervical spine (white circle). (Reprinted with permission of Anderson Publishing LTD. from Talekar et al. [9]. ©Anderson Publishing Ltd.)

Basic Anatomy

A further understanding of spinal stenosis relies on an understanding of the underlying bony and soft tissue anatomy, the physiology of aging, degeneration, and other acquired causes. The spinal column consists of 33 vertebrae, divided into 24 presacral vertebrae (7 cervical, 12 thoracic, and 5 lumbar vertebrae), 5 fused sacral vertebrae which make up the sacrum, and 4 frequently fused coccygeal vertebrae which make up the coccyx. The lumbar vertebrae articulate with the sacrum, which articulates with the five ossicles of the coccyx [15–17]. Each vertebra consists of a vertebral body anteriorly, joining pedicles bilaterally which connect the body to the transverse process, and lamina, which connects the transverse processes to the spinous process bilaterally. Superior articular processes from the vertebrae below articulate with the inferior articular processes from the vertebrae above to form the zygapophyseal, or facet joint [15–17].

The spinal canal is bordered anteriorly by the vertebral body, disc, and posterior longitudinal ligament (PLL), laterally by the pedicles, ligamentum flavum, and neural foramen and posteriorly by the facet joints, lamina, and ligamentum flavum. Anatomic variants exist in the shape of the canal. These include a circular, ovoid, and trefoil shape, the circular and ovoid shapes presenting the largest cross-sectional area [17]. The intervertebral foramen is bounded anteriorly by the posterior wall of the vertebral body and disc, posteriorly by the lateral aspect of the facet joint and ligamentum flavum, and superiorly and inferiorly by the pedicles and vertebral bodies [15–17]. Spinal stenosis can occur due to changes in any of these bordering structures. Descending from the cervical to lumbar vertebrae, characteristic changes occur at the various anatomical bony segments.

Imaging

The diagnosis of spinal stenosis is commonly a combination of symptomatology, imaging, and evidence of neurovascular compromise [4, 9, 18, 19]. In general, radiographs provide limited information. They are insensitive to soft tissue hyper-

trophy and non-osseous causes of spinal stenosis. However, they are rapidly available and low cost and produce low radiation exposure to the patient. Radiographs are able to provide some information on alignment and deformity, degenerative changes, and loss of disc height and aid in ruling out other pathological causes of pain such as fractures [4, 9].

Electromyography is not commonly utilized, and its utility may be limited to differentiating spinal stenosis from peripheral neuropathies, particularly in circumstances where a clear spinal etiology is not found to explain the patient's symptoms of pain or radiculopathy [4]. Computed tomography (CT) is helpful in diagnosing metastasis and infection and visualizing bony anatomy. In a patient with prior back surgery, CT can reduce artifact from metallic hardware. Disadvantages of CT examination include the reduced ability to detect nerve root impingement and the amount of radiation exposure [9, 20–22].

Traditionally, myelography has been used to provide dynamic information about spinal pathology, narrowing of the spinal canal with axial loading and extension. However, this test is invasive, requiring intrathecal injection of contrast and, when CT myelography is utilized, subjects the patient to ionizing radiation. Contrast in the subarachnoid space outlines neural structures for detecting stenosis and impingement and also is useful in diagnosing CSF leak and nerve root avulsion [4, 23].

MRI

Magnetic resonance imaging (MRI) is the most commonly utilized imaging modality for diagnosing spinal stenosis. MRI is noninvasive, has no ionizing radiation, and has high sensitivity in diagnosing spinal stenosis and identifying soft tissue pathology. Contrast may be added to further detect infection, tumor, and postsurgical changes [9, 22, 23]. There is no generally accepted radiologic criteria for diagnosing spinal stenosis [4, 9, 24]; thus, MRIs are usually described qualitatively as mild, moderate, or severe [7, 11]. In the anteroposterior diameter, a bony canal of less than 10 mm in the cervical spine and 12 mm in the lumbar spine is compatible with central canal stenosis. On MRI, a midsagittal diameter of the dural sac less than 10 mm is also compatible with central canal stenosis. Additionally, the cross-sectional area and transverse diameter have also been described [24].

Neuroforaminal stenosis diagnosis requires an AP diameter less than 3 mm on sagittal images and, for lateral recess stenosis, a lateral recess height less than 3 mm or lateral recess angle less than 30°. In the sagittal plane, the combined task force of the North American Spine Society, American Society for Spine Radiology, and the American Society of Neuroradiology recommends defining stenosis as demarcated by the pedicle, defining it, in terms of levels, as supra-pedicle, pedicle, infra-pedicle, and disc level. In the axial plane, they define spinal stenosis with zones of central, subarticular, foraminal, and extraforaminal [9].

Many have proposed alternative grading systems to better describe spinal stenosis. On sagittal images, compromise of neural structures can be inferred by noting degree of CSF obliteration and structural impingement of the spinal cord. Abnormal signal of the spinal cord, crowding of nerve fibers, and redundancy may also provide useful information [9]. Pfirrmann and colleagues created a grading system for disc herniation-related nerve compromise, correlating with intraoperative findings. This scheme uses four grades based on displacement, contact, and compression of neural structures [25]. Schizas and colleagues have described a grading system of CSF-to-rootlet ratio [26], whereas Barz and colleagues have described sedimentation of the nerve roots in the dural sac [27]. However, neither of these two grading systems correlates with functional status, symptomology, or outcomes.

Symptomatology

Lumbar central canal stenosis most commonly results in neurogenic claudication described as pain, dysthesias, paresthesias, or weakness in the back or buttocks radiating to the lower extremities. The abnormal sensations are most commonly bilateral and do not follow a dermatomal distribution. They are worse with extension of the lumbar spine and often relieved by flexion. Patients characteristically can state a duration of walking that brings on the symptoms, and this distance and duration shorten as the stenosis worsens. In comparison to the neurogenic claudication of central canal stenosis, foraminal and lateral recess stenosis typically results in radiculopathy. Radiculopathy is described as pain and paresthesias in a dermatomal distribution of the corresponding nerve root [2, 11, 14, 23].

Many patients have asymptomatic narrowing, with degenerative changes commonly occurring with increasing age, and thus imaging often correlates poorly with symptomatology [28, 29]. This may be, at least partially, due to an individual's ability to compensate for accumulating pathologic changes, which, in turn, is affected by the rate of changes that lead to stenosis. Many studies have looked at compression of the thecal sac leading to increased pressure at the nerve roots [30, 31]. This compression can lead to neural dysfunction, capillary constriction, and venous congestion, which can lead to altered local nutrition, as well as inflammatory chemical mediator accumulation, and electrophysiologic alteration. Mechanical compression and chemical mediators may both affect the experience of symptoms, and, since only the structural anatomy is visible on imaging, this may contribute to the poor correlation [2, 32, 33].

Characteristics of Cervical Spinal Stenosis

Cervical spinal stenosis can have both congenital and acquired causes. Acquired degenerative changes at the disc level are the most common cause of stenosis. These degenerative disc changes such as disc herniations and ossification can cause altered mechanical function and hypertrophy of the posterior elements, such as the facet joints and ligamentum flavum, ultimately leading to cervical stenosis and cord compression. Spondylotic changes of the cervical spine are more prevalent at the C5–C6 segment, followed by the C6–C7 and C4–C5 segments [34]. Symptoms of cervical stenosis can include impaired gait and numbness of the hands, while clinical signs can include hyperreflexia, atrophy of the intrinsic hand muscles, positive Hoffmann's test, and positive Babinski's reflex [35].

The first (atlas) and second (axis) cervical vertebrae are perhaps the most unique spinal segments with a significant portion of forward flexion and rotation occurring at these segments. Characteristics unique to the third to seventh cervical vertebrae are the uncinate processes, transverse foramen, and orientation in the sagittal and transverse planes [15, 16, 36]. An uncinate process is located at the superior lateral edge of the vertebral body where it connects to the transverse process, and the articulation is the joint of Luschka. The transverse processes project laterally with an anterior and caudal tilt. Within the transverse process, the transverse foramen houses the vertebral artery ascending from the sixth to the first cervical vertebrae. The transverse foramen is lateral to the pedicles and medial to the sulcus for the spinal nerves and, descending caudally, becomes more lateral. Anterior disc height is greater than dorsal height, and a slight lordotic curve exists in the cervical spine [15, 16, 36].

The normal AP diameter of the entire cervical spinal canal in adults is 17–18 mm with the spinal cord itself having a diameter of 5–6 mm. Other soft tissue components of the spinal canal such as the posterior longitudinal ligament, dura, and ligamentum flavum occupy another 2 mm of the canal diameter. As such, the common threshold for absolute cervical spinal canal stenosis is 10 mm given that any AP diameter less than this value will cause compression of the spinal cord. There is also an AP diameter threshold for relative cervical stenosis of 12–13 mm given that the AP diameter of the cervical spine reduces by 2–3 mm on neck extension [4, 37]. Furthermore, the intervertebral foramen with the nerve roots becomes smaller in extension and larger in flexion. Defining the parameters of neuroforaminal stenosis in the cervical region is further confounded by the fact that the neuroforamen are at a nearly 45-degree oblique orientation [14].

Cervical canal stenosis has also been defined by the Torg-Pavlov ratio (TPR), which is the ratio of the spinal canal to the vertebral body on conventional radiographs. The TPR is defined by dividing the distance from the midpoint of the posterior aspect of the vertebral body to the nearest point on the corresponding spinolaminar line by the AP width of the same vertebral body [37, 38]. The TPR was originally studied as a parameter to correlate with transient neuropraxia in football players, identifying normal as 1 and congenital cervical stenosis as 0.8 or less [4, 38]. The TPR has a low positive predictive value for compressive myelopathy. Moreover, spondylotic changes commonly occur at the level of the intervertebral disc as opposed to the vertebral body, and conventional radiographs cannot assess canal narrowing by soft tissue. As such, MRI has been deemed the best imaging modality for cervical spinal stenosis as it can provide information on disc and other soft tissue pathology, as well as any changes within the spinal cord itself [4, 37, 39].

Characteristics of Thoracic Spinal Stenosis

The prevalence of thoracic spinal stenosis is much less than that of the cervical and lumbar regions. Thoracic stenosis is radiographically defined as a spinal canal narrowed <10 mm in the AP diameter best measured on MRI or CT imaging. Unlike lumbar stenosis, pain is not the most common symptom of thoracic stenosis. Clinical presentation is mainly one of fatigue, leg heaviness, loss of proprioception, and pseudoclaudication in which symptoms are exacerbated with standing and walking and relieved by rest or forward flexion [40, 41].

The unique anatomy of the thoracic spine leads to its limited range of motion, which protects it from stenosis. Unlike the cervical and lumbar regions, the thoracic spine consists of 12 rib-bearing segments. The first seven ribs are directly connected to the sternum through the costal cartilage; the 8th, 9th, and 10th ribs connect to the sternum through an elongated costal cartilage and are known as false ribs, while the 11th and 12th ribs do not directly connect to the sternum at all and are known as floating ribs. The ribs and sternum provide stability to the thoracic spine along with a decreased range of motion. This stability decreases from higher to lower levels, which in turn affects the level of degeneration seen at various levels. Interestingly, the spinal canal is narrowest at the thoracic spine [41].

A variety of local and systemic metabolic diseases can cause thoracic stenosis. The most common cause is due to degenerative disc disease causing hypertrophy of the posterior elements including the facet joints and the ligamentum

flavum [42]. Posterior compression can also be caused by congenitally short pedicles. Ventral spurs of the uncinate processes, discal intrusions, limbus fractures, and ossification of the posterior longitudinal ligament can also impinge on the canal ventrally [40]. Indeed, these degenerative changes are seen more commonly in the lower thoracic levels where there are greater flexion, extension, and rotation movements and less stability as well as more of a lumbar-like configuration to the vertebrae [40, 43]. Thoracic disc herniations themselves can cause stenosis although this is rare given they account for less than 1% of all disc protrusions. The most common level for disc protrusions is T11/T12 with 75% of all thoracic disc protrusions occurring, again, at the lower levels and below T8 [43]. Systemic metabolic diseases that affect the thoracic spine tend to not only involve longer segments of the spine but also create circumferential narrowing lesions. Examples of these disease processes include acromegaly, achondroplasia, osteochondrodystrophy, Scheuermann's disease, fluorosis, ankylosing spondylitis, and Paget's disease [40, 42]. Space-occupying lesions such as epidural lipomatosis, hematomas, abscesses, and tumors can also cause thoracic stenosis [41].

Characteristics of Lumbar Spinal Stenosis

Due to the increased mechanical load carried by the lumbar vertebrae, lumbar spinal stenosis is more prevalent than cervical or thoracic stenosis. The increased weight supported by the intervertebral discs also renders them more prone to degeneration, resulting in further disc bulging, facet joint hypertrophy, and buckling of the ligamentum flavum (Fig. 11.2). The incidence of lumbar spinal stenosis in asymptomatic individuals aged 60–69 years is estimated to be 47% for relative stenosis and 19% for absolute stenosis [7, 22, 44].

The spinal cord in adults ends at the upper border of the first lumbar vertebral body and continues as nerve roots, the cauda equina. The central canal anteroposterior diameter ranges from 15 to 23 mm. Commonly, the threshold for radiographic lumbar spinal stenosis is an anteroposterior diameter of less than 12 mm, with relative spinal canal stenosis, and less than 10 mm, with absolute spinal stenosis [7, 44]. Alternatively, some clinicians define spinal stenosis not on a specifically quantified diameter but as relative reduction in cross-sectional area with mild as narrowing of the anteropos-

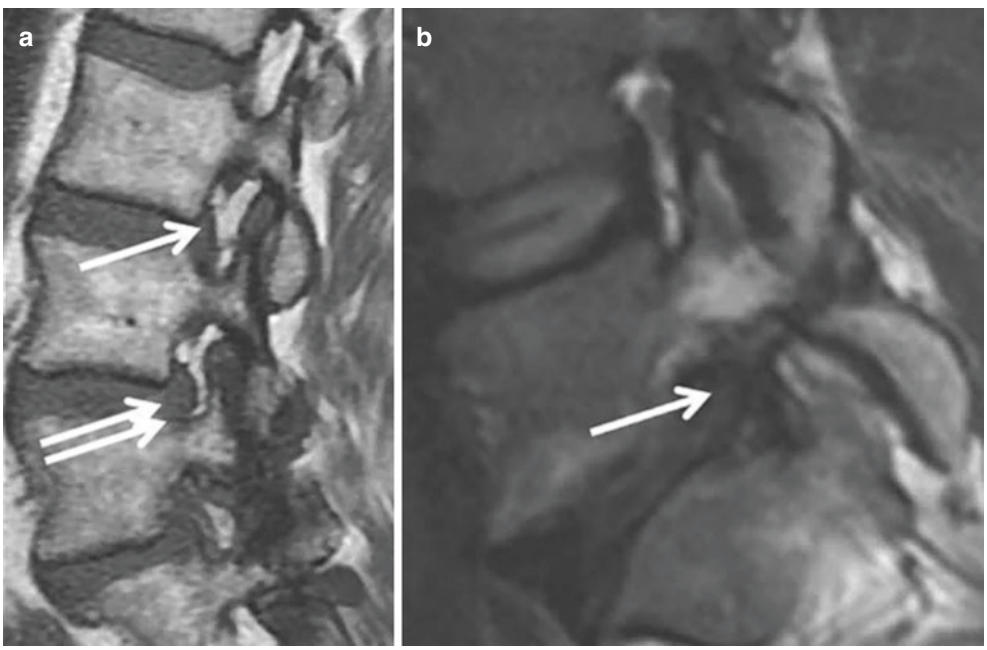

Fig. 11.2 Sagittal, T1-weighted image of the lumbar spine demonstrates intervertebral disc material protruding into the neural foramen, narrowing its inferior portion (single arrow, **a**). There is progressive narrowing extending more superiorly in the neural foramen at the two lower levels due to disc bulge and facet hypertrophy (double arrows, **a**). Foraminal fat is preserved at all these levels. Image (**b**) is a sagittal T2-weighted image demonstrating craniocaudal subluxation as well as disc bulge severely narrowing the neural foramen (arrow). Note the obliteration of the perineural fat. (Reprinted with permission of Anderson Publishing LTD. from Talekar et al. [9]. ©Anderson Publishing Ltd.)

terior canal by one-third or less, moderate by narrowing by one- to two-thirds, and severe as more than two-thirds [7, 11].

The symptoms common to lumbar spinal stenosis, such as neurogenic claudication, can be explained by transient encroachment of structures on the cauda equina with sensory and motor nerve dysfunction. In addition, the symptoms of spinal stenosis may be caused, or exacerbated by, disrupted blood flow and venous congestion [2, 7, 33]. This presents as intermittent low back pain with radiation into the buttock and bilateral legs [2]. A defining characteristic of the pain associated with lumbar spinal stenosis, with high specificity, is that it is triggered by ambulation and relieved by rest or forward flexion [7]. When a patient exhibits forward flexion, the diameter of the spinal canal is increased and the compression of nerve axons is reduced [2, 7].

Weakness is not a prominent symptom but may be present, especially after prolonged walking. If stenosis occurs in the lumbar neuroforamina or lateral recess, symptoms are more commonly radicular. No clear relationship between the severity of symptoms and degree of stenosis exists [2, 14, 23]. The third and fourth lumbar vertebrae exhibit a higher degree of rotational movement, and degeneration at these levels is more common. Anterolisthesis of the L4 on L5 is also more common. Thus, central canal stenosis is more prevalent at L4/L5, followed by L3/L4. Facet joint arthritis is also more prevalent in these locations with the more sagittal orientations of the facets between L4 and L5 exhibiting a predisposition to instability. The iliolumbar ligaments attach the fifth lumbar vertebrae to the iliac crest, creating increased stability in this area, and L5/S1 anterolisthesis is less common than L4/L5 or L3/L4 [10, 45, 46]. In neuroforaminal or lateral recess stenosis, L4/L5 and L5/S1 are the most common locations of narrowing [47].

The Anatomy of Aging (Degeneration)

The spinal degenerative process starts in the first decade of life and progresses throughout an individual's lifetime [48, 49]. In this section, the anatomy of aging and degeneration is briefly discussed. Changes associated with the aging spine can narrow the diameter of the spinal canal, causing spinal stenosis. These changes include disc degeneration, disc herniation, facet hypertrophy and laxity, hypertrophy, and buckling of the ligamentum flavum and can lead to spondylolisthesis or scoliosis [9, 48, 50].

Disc degeneration is considered one of the earliest changes and can predispose to changes of the disc itself as well as deterioration of the bony elements and ligaments [4, 9, 48]. The intervertebral disc is composed of nucleus pulposus confined within the annulus fibrosis. The nucleus pulposus is composed of collagen fibers in a random orientation and radially arranged elastin fibers embedded in an aggrecan rich gel-like matrix. The annulus is composed of concentric collagen fibers with elastin fibers between them. The extracellular matrix and composition of the disc is normally balanced by modeling and enzymatic degradation. The hydrophilicity and gel-like nature of the disc allow it to increase the hydrostatic pressure and handle the axial compressive load. Loss of proteoglycans and water content, alterations in the collagen network, and increase in metalloproteinases result in decreased osmotic pressure in the disc and decreased ability to accommodate compressive forces. The demarcation between the annulus fibrosis and nucleus pulposus also becomes less distinct, predisposing to concentric fissuring and radial tear and disc herniation [48, 51].

The facet joints are the major posterior load-bearing unit of the spine, stabilizing the motion of flexion and extension. As the disc degenerates, it is no longer able to appropriately stabilize the spine anteriorly leading to increased stress on the facet joints. This furthermore leads to subluxation and cartilage degradation, which in turn leads to facet malalignment and hypertrophy, erosions, sclerosis, and osteophyte formation [17, 48]. Healthy ligaments of the spine are highly flexible and restrain motion in multiple dimensions. As ligaments degenerate, elastin increases in concentration, reducing the tensile properties and weakening the ability to stabilize structures. Degeneration of the ligamentum flavum also occurs, leading to increased thickness and buckling [52, 53].

With continued mechanical compression over time, changes in the bony structures can occur. This includes sclerosis and remodeling, formation of osteophytes, and decreased stability. Osteoporosis furthermore weakens the bony elements, predisposing to bone remodeling, rotational deformities, or subluxation. Discal degeneration increases with a reduced blood supply from the surrounding vertebral endplate. This results in tissue breakdown, progressing the degenerative cycle [48].

Ligamentum Flavum Hypertrophy

The ligamentum flavum (LF) is a posterior structure formed during the 10th to 12th week of gestation [54]. It connects the laminae of adjacent vertebrae from C2 to S1 [55]. At each level, the LF inserts on the inferior and anteroinferior aspects of the cranial vertebral arch and on the superior and posterosuperior aspect of the caudal lamina [56]. Thinnest at the cervical and high thoracic levels [57], the histologic characteristics of the LF separate it from other ligaments of the spine in that it consists of 80% elastin and 20% collagen [58]. Indeed, the LF is also called the yellow ligament because of the color given to it by this higher concentration of elastin fibers [59].

It is postulated that this histologic difference assists with the unique function of the LF compared to other ligaments of the spine. One theory is that its elastic nature may help with restoring a flexed lumbar spine back to the extended position. Other theories have focused on the location of the LF rather than its possible biomechanical composition – given its immediate position posterior to the vertebral canal, should the ligament be more collagenous, it would buckle with approximation of the laminae causing encroachment on the spinal cord or nerve roots. An elastic ligament, however, would stretch thin minimizing any buckling during spine flexion and therefore prevent nerve root compromise [60]. Nonetheless, under pathologic conditions, the LF does in fact contribute to spinal stenosis.

Elsberg first reported the hypertrophy of the LF as a possible cause of spinal stenosis in 1913 [61]. Since then, multiple studies have confirmed that thickening of the LF can reduce the diameter of the spinal canal resulting in spinal stenosis [46, 53, 62]. The exact etiology of LF hypertrophy remains poorly understood and is most likely multifactorial. One possible etiology is a disturbance in the ratio of elastin to collagen alluded to before through fibrosis. Fibroblast growth factors play a crucial role in cell proliferation and tissue repair. Several cytokines and growth factors have been reported to play a role in LF hypertrophy including TFG-β, platelet-derived growth factor-BB, and basic fibroblast growth factor [59, 63, 64]. Fibrotic changes can lead to increased levels of collagen and reduced levels of elastin with elastin degeneration [65, 66]. These inflammatory mechanisms may be the result of degenerative processes such as facet arthropathy [67] or from scarring prompted by the accumulation of mechanical stress with the normal aging process [68].

Other studies have proposed the etiology of LF hypertrophy to be secondary to infolding and buckling into the spinal canal as a result of degenerative disc disease as opposed to actual LF thickening. Decreased disc height causes a laxity of spinal column ligamentous tissue leading to LF buckling [66, 69]. As such, factors such as disc bulging, collapsed disc height, mechanical stress, and body mass index may also play a role in the LF's contribution to spinal stenosis. While most studies do show a correlation between increasing age and increasing LF thickening at the L4–L5 level, others have questioned any such association [67].

Disc Herniation

Disc herniation and radiculopathy is covered in detail in another chapter. Here we will briefly review its role in spinal stenosis. The intervertebral discs are the major axial load-bearing structures that absorb compressive forces. The annulus fibrosis consists of concentric fibers that resist tensile forces and confines the gel-like substance of the nucleus pulposus. In healthy discs, axial loads increase hydrostatic pressure within the nucleus pulposus which is resisted by tensile stresses of the annulus fibrosis. Bending and torsion are furthermore resisted by the tensile forces of the annulus [70].

Breakdown of the extracellular matrix and desiccation of the disc result in less distinct demarcation of the annulus and the nucleus, decreased ability to handle a mechanical load, loss of disc height, annular fissure, and eventually herniation [48]. Historically, disc degeneration is thought to be the cornerstone of other degenerative changes with more stress placed on the facet joint leading to degeneration, hypertrophy, and osteophyte formation. Genetic factors may play a role in disc herniation. Genetic mutations in collagen type IX alpha 2 and alpha 3 chains as well as genes involved with cytokines interleukin-1beta and interleukin-6 have been suggested to predispose to herniation [70, 71].

The vertebral endplate, the tissue interface between the vertebral body and the intervertebral disc, is essential in maintaining the integrity of the disc [72]. It balances load distribution, manages metabolite transport, and encases the nucleus within the annulus. Endplate lesions, along with degeneration and desiccation of the disc itself, predispose to herniation of the nucleus pulposus through the annulus fibrosis. Herniated disc materials then result in mechanical narrowing of the space available for the nerve root, causing impingement. Furthermore, chemical mediators and inflammation may play a role in pain symptoms produced [73]. In response to herniated material, increased angiogenesis and microglia and astrocyte can infiltrate the area. An inflammatory milieu is also created, consisting of mediators and cytokines such as IL-1alpha, IL-6, and TNF-alpha which furthermore activate the immune system and upregulate the expression of proteinases [33, 74–76]. The inflammatory mediators themselves can be a chemical irritant to the nerve as well as cause disorganization of the myelin sheath and Wallerian degeneration of the peripheral axons.

MRI allows clinicians to evaluate the relationship between protruding disc material and the nerve roots. Disc herniation is commonly quantified by the Combined Task Force, Jensen, and van Rijn classification systems. The Combined Task Force definition classifies disc bulges as broad based or focal, based on the circumference involved, and as protrusion or extrusion, depending on the shape of material displaced [9, 50]. The classification system by Jensen and colleagues is also commonly used, separating lumbar disc herniation into four grades [77]. Van Rijn further classifies disc bulges by nerve root compression [78].

When the disc herniates, it can lead to a functional narrowing of the spinal canal. In an individual with narrowing of the bony structures of the spinal canal, disc material can further reduce the spinal canal diameter. Posterolateral her-

niations can compress individual nerve roots and lead to radiculopathy, while central herniations can compress the cord or cauda equina and lead to symptoms more consistent with neurogenic claudication [79]. It can also present as muscle weakness or asymmetric reflexes [73, 80]. In absence of underlying stenosis of the bony vertebral canal, disc herniation resulting in symptoms most commonly presents in the fourth or fifth decade of life. The most commonly affected segments are the lower lumbar segments below the third lumbar vertebrae [81].

Spondylolisthesis

Spondylolisthesis is defined as the translational movement of one vertebra on another. The movement can be anterograde or retrograde and most commonly occurs in the middle lumbar spine, rarely in the cervical or thoracic spine. Anatomic and environmental factors can lead to spondylolisthesis, and these are commonly caused by congenital abnormalities, degeneration, trauma, and fracture of the pars interarticularis [82, 83]. Activities that result in repetitive hyperextension of the lumbar spine can also predispose to spondylolisthesis [84].

Commonly utilized classification systems to describe the grade of spondylolisthesis are the Meyerding, the Wiltse, or the Marchetti and Barolozzi classification systems. Meyerding and colleagues grade spondylolisthesis based on percent of slippage [83–85]. Grade 1 is 0–25%, Grade 2 is 25–50%, Grade 3 is 50–75%, and Grade 4 is 75–100% [85]. Wiltse uses the etiologies of dysplastic, isthmic, degenerative, traumatic, and pathological to categorize spondylolisthesis [82]. Marchetti et al. also use an etiology-based system with the categories of iatrogenic, traumatic, and pathologic [83].

Spondylolisthesis of any orientation can cause narrowing of the spinal canal and encroachment of the neural structures. Lower-grade spondylolisthesis more commonly affects the nerve at the subarticular zone and results in radiculopathy, whereas higher-grade spondylolisthesis can reduce the central canal diameter and presents with either radiculopathy or neurogenic claudication [86–88]. Because of weight-bearing mechanics, degenerative spondylolisthesis most commonly occurs between the L4 and L5 or L5 and S1 vertebrae, resulting in an L4 or L5 radiculopathy. In the lumbar spine, facet joints are oriented in a sagittal plane, allowing them to resist rotation but less able to resist flexion and extension. When in extension, they support an axial load. Hyperextension stress as well as hyperflexion and compression can cause excessive force and deformation of the area [89, 90]. At the L5 and S1 junction, a greater lumbosacral joint angle is associated with a greater translational force, and traumatic spondylolisthesis is more common in this location [90].

When spondylolisthesis occurs in the cervical spine, the most common symptom is radiculopathy. However cervical spondylolisthesis can also present with static or dynamic myelopathy [91, 92]. Spondylolisthesis in these areas is rare, with the upper cervical segments more commonly affected. The more coronal nature of the facet joints can predispose to facet dislocations [90, 93]. Traumatic injuries can also cause subluxation when associated with hyperextension injuries on an axial load [91, 92].

Treatment Options-Interventions

Since treatment of spine pain is covered extensively in other chapters, we will briefly touch on intervention options targeting spinal stenosis specifically. Once it is decided that the etiology of back pain is from spinal stenosis, the question of treatment arises. Conservative management, minimally invasive procedures and injections, or surgery may be employed. The most commonly employed conservative treatments for spinal stenosis are physical therapy, exercise, patient education, and nonsteroidal anti-inflammatories, muscle relaxants, or TENS for pain control. Exercise has been shown to improve walking distance, but no specific type of exercise has been shown to be superior [94].

Epidural steroid injections provide analgesia by inhibiting phospholipase A2 as well suppress conduction in C fibers and ectopic discharges of injured fibers. Phospholipase A2 is an inflammatory mediator itself, and its inhibition furthermore reduces the hydrolysis of phospholipids into arachidonic acid and lysophospholipids [95]. Epidural steroid injections may decrease pain and improve walking distance; however, this may be temporary [94, 96]. Evidence for improved efficacy in the long term, beyond 3–6 months, is conflicting [95, 97]. Epidural steroid injections also do not appear to reduce the need for surgery [95].

When symptoms are severe, surgical options are frequently sought, and lumbar spinal stenosis is the most common reason for spinal surgery in patients over 65 years of age [2]. Since the symptoms and functional impairment associated with lumbar spinal stenosis occur secondary to compression of neural structures, surgery aims at decompression techniques [98, 99]. Traditionally a wide laminectomy and open decompressive techniques can create more space to the neural structures. With improved imaging and surgical advances, more directed laminotomy and segmental interlaminar decompression with preservation of the paraspinal musculature and posterior stabilizing structures may be employed [97, 98, 100]. Surgery has been shown to improve symptoms and disability, at least temporarily, with decreased pain and increased function most evident in the first year [99, 101–103].

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Disc Herniation and Radiculopathy

12

Brent Earls and M. Alexander Kiefer

Key Points

- Intervertebral discs are pads of fibrous cartilage located between the vertebrae of the spinal column designed to allow for complex range of motion and withstand mechanical loading.
- These discs undergo changes with aging, which may predispose the disc to prolapse beyond the limits of the intervertebral space.
- Disc herniation as a result of this degenerative process is the most common cause of radiculopathy, which refers to a condition that affects the function of one or more nerve roots as they exit the spinal column.
- Herniations commonly occur in the lower segments of the cervical and lumbar areas and can manifest as pain, paresthesia, sensory deficits, motor weakness, and muscle atrophy along the affected dermatome.
- Pain is generated from two distinct processes: mechanical compression of exiting nerve roots and chemical irritation as a result of the local inflammatory cascade in response to the nucleus pulposus itself.
- Prior episodes of back or neck pain, smoking, certain occupations or recreational activities, and genetics have been associated with an increased risk of developing neck and back radicular symptoms.
- Physical exam will often reveal a sensory deficit, motor deficit, or a combination of both in a dermatomal distribution, diminished deep tendon reflexes, and symptoms increased by provocative maneuvers. The supine straight leg raise (SLR) test has consistently shown the highest specificity for lumbar radiculitis/radiculopathy.
- Advanced imaging with CT or MRI has not been shown to improve outcomes if pain has been present for less than 6 weeks in the absence of red flag symptoms (fever, weight loss, severe or progressive deficits on exam, bowel and bladder dysfunction, etc.).
- Disc herniations have been shown to significantly diminish or fully resolve in almost 80% of patients. This resolution has a strong association with clinical improvement in pain over 6–12 weeks.
- Best evidence supports a stepwise approach to therapy beginning with physical therapy and non-opioid medication management in patients without concerning signs or symptoms.
- Epidural steroid injections have shown clear benefit to reduce acute-to-subacute radicular pain, with a transforaminal approach being superior in the case of unilateral symptoms.
- There is no clearly established consensus regarding surgical indications. However, progressive neurologic deficits, signs of myelopathy, fractures, or signs of instability may warrant surgical evaluation.

Introduction

Intervertebral discs are pads of fibrous cartilage that rest between the vertebral bodies of the spine. With the exception of the articulation between the atlas (C1) and the axis (C2), as well as sacral vertebrae, each vertebra is separated from the others by a disc. Collectively, the intervertebral discs constitute 20–33% of the overall height of the normal vertebral col-

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umn. The function of the intervertebral disc is to provide articulation between the vertebral bodies and stability to the spine. In addition to allowing complex range of motion, the discs transmit and withstand mechanical loads such as axial loading, bending, and twisting. The discs have an overall similar structure throughout the spine with minor variation among the different regions. Three basic components comprise each intervertebral disc. The central nucleus pulposus (NP) is surrounded by the annulus fibrosus (AF). Both of these structures are bound on top and at the bottom by the cartilaginous end plates. The cells of these regions are morphologically distinct; however, major changes take place over time during the aging process. The anatomy of intervertebral discs is also briefly described in another chapter, and the following sections provide a more detailed description of the disc anatomy.

The outer annulus fibrosus is a highly organized cartilaginous structure, which contains elongated and fibroblast-like cells aligned parallel in discs of concentric lamellae [1]. These specialized cells produce both type I and type II collagen with the outer annulus consisting of primarily type I collagen and the inner annulus having a more balanced mixture of types I and II collagen [2]. Cells of the disc are responsive to all types of mechanical loading, including compression or strain, as well as the direction and magnitude of the load [3]. The nucleus pulposus is predominantly made up of cells that synthesize only type II collagen and tend to be more rounded or chondrocyte-like in morphology. Its ground substance is gelatinous and primarily made of proteoglycans in a loose network of collagen [4]. The cumulative hydrophilic nature of these proteins provides the nucleus pulposus with hydrostatic properties used to counteract compressive loading of the spine.

The state of the intervertebral disc is dynamic over its lifetime [5]. Changes in the vascularity, nutrition, and cellular and molecular structure vary from early youth through adulthood [6]. These changes correlate with age as the disc matures; however, early degeneration is frequently seen [7]. The nucleus pulposus is a homogeneous structure that serves a vital role in maintaining the mechanical function and structure of the disc. The healthy disc, with abundant hydration, largely hydrophilic proteoglycans, and a competent annulus, is ideal for absorbing complex loads early in life and in young adulthood (Fig. 12.1). Beginning in the second decade, however, as the nucleus begins to lose its strongly hydrophilic proteoglycans, the disc becomes more solid and less adept at absorbing these loads and dispersing them to its surrounding structures [8].

As a result of this degenerative process, the nucleus becomes heterogeneous and absorbs axial loads in a nonuniform manner, which alters load transfer to the annulus and vertebral end plate [9]. This uneven distribution of forces across the end plate increases as the degenerative process progresses. As a result, compressive and shear forces are

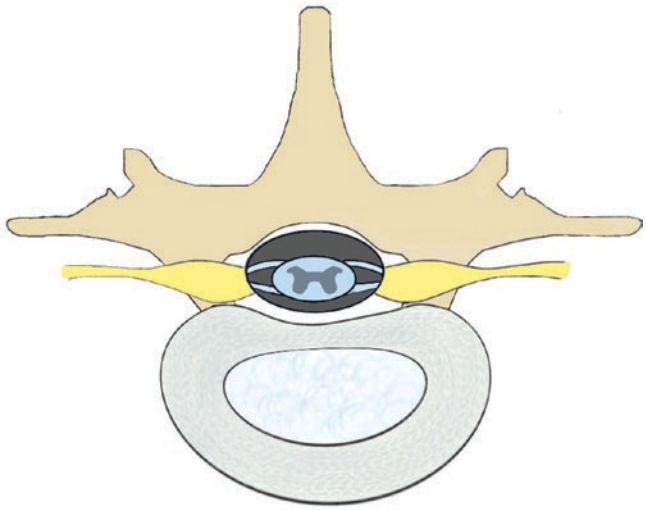

Fig. 12.1 Normal vertebral body and disc

increasingly transmitted to the annulus, stressing its fibers [10, 11]. Continued strain on the annular fibers results in fissuring within and rupture of the annular complex [12, 13]. Stress concentration in the posterior annulus may predispose this region to disc prolapse. Fissuring and concentration of stress to the posterolateral region permit the migration of nuclear fragments to the periphery of the disc and herald the herniation of disc material.

Herniation is specifically defined as a "localized displacement of disc material beyond the limits of the intervertebral disc space." This classification encompasses all of the components of the disc (nucleus pulposus, annulus fibrosus, cartilaginous end plates). The disc space is defined by the end plates of the vertebral bodies and peripherally by the outer edge of the vertebral ring apophyses except osteophytes. Herniations are further classified as localized (<25% disc circumference), broad-based (25–50%), and circumferential (50–100%). The histology of herniated discs is quite variable, as is the degree of structural damage, ranging from protrusions (when the outer annular lamellae remain intact) (Fig. 12.2) to extrusions (when they are ruptured) (Figs. 12.3 and 12.5a) to sequestrations (in which the herniation is completely detached from the body of the disc) [14, 15] (Figs. 12.4 and 12.5b). The morphology of all of these herniations can be very heterogeneous and may include tissue that appears to be from any combination of the three materials that comprise the disc itself.

Radiculopathy refers to a disease process that affects the function of one or more nerve roots as they exit the spinal column. Structural lesions such as disc herniation or degenerative spondylosis are the most common cause; however, inflammatory, infectious or malignant disorders can exist. Radiculopathy can cause dysfunction in any of the three types of axons traveling in the spinal nerve roots. This

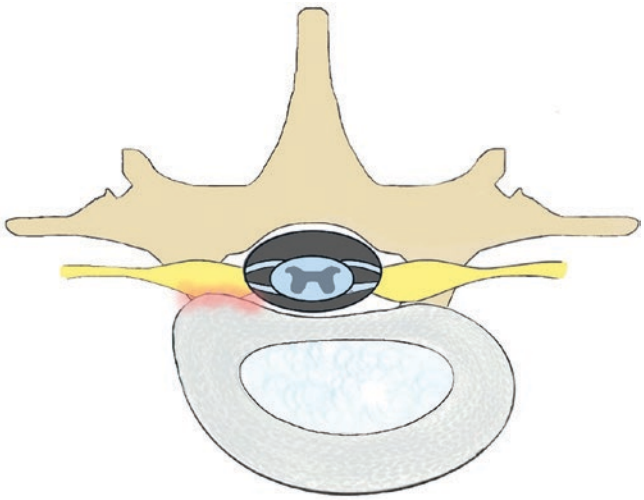

Fig. 12.2 Disc protrusion or "disc bulge"

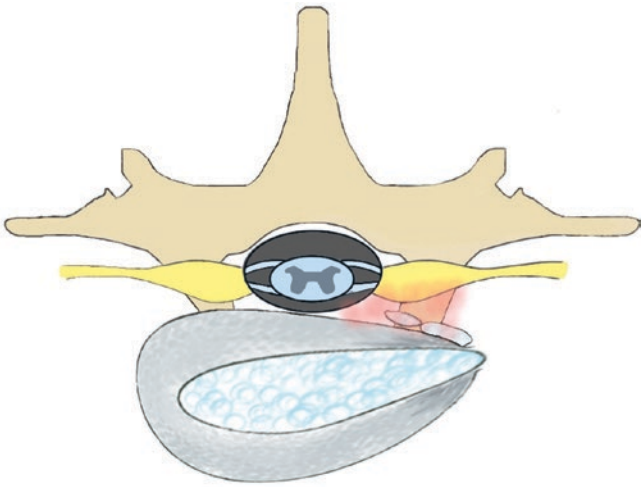

Fig. 12.4 Disc sequestration

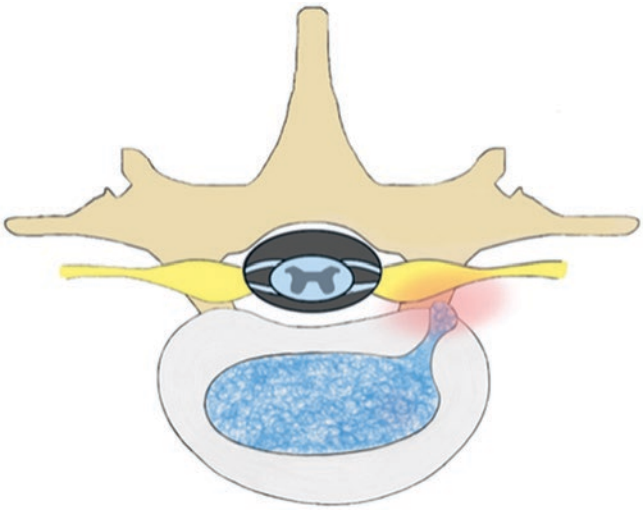

Fig. 12.3 Disc extrusion

includes somatosensory nerves, lower motor neuron nerves, or autonomic dysfunction. Somatosensory abnormality tends to be most prominent with radiculopathy and is described with a characteristic shooting pain along the dermatomal distribution of the affected spinal nerve root [16, 17].

Historic Perspective

While this condition has been described in medical literature dating back to Hippocrates, our understanding and treatment have grown much more sophisticated since the 1930s [18]. Mixer and Barr first introduced the concept of herniated disc material leading to radiculopathy in 1934, and the diagnosis of "ruptured disc" had gained favor in the medical community [19]. This team quickly pioneered a transdural approach for disc removal as the treatment of choice. Love, of Mayo Clinic (1937–1939) [20], introduced the extradural/interlaminar approach, which provides the basis of the standard open procedure performed even today. Caspar and Yasargil [21] applied the concepts of microsurgery to the procedure as early as 1977 through medial facetectomy and extradural dissection [22]. Advancements in lumbar radiculopathy treatment were paralleled by developments regarding cervical radiculopathy. In 1940, Stookey outlined three clinical manifestations that could occur following protrusion of cervical discs, namely, bilateral anterior pressure on the spinal cord, unilateral anterior pressure producing a Brown-Sequard syndrome, and nerve root pressure [23].

Due to the growing knowledge of disc herniations of the lumbar spine, surgeons began using decompression for treating cervical disc herniations [24]. Scaglietti, an Italian orthopedic surgeon, described one such surgery in 1949 for the treatment of cervical radiculopathy which like many of the early surgeries was performed through a posterior approach [25]. By the 1950s, surgeons had begun to shift to the anterior approach with the first being described by Smith and Robinson in 1955 [26]. By the mid-1990s, approximately 200,000 discectomies were performed annually in the United States alone [27]. New techniques are still being developed to reduce incision size, speed up recovery time, and improve long-term results [28–30].

Clinical Presentation

The clinical presentation of a herniated nucleus pulposus varies from no symptoms to rapid paralysis. Symptom severity often correlates with the acuity and degree of com-

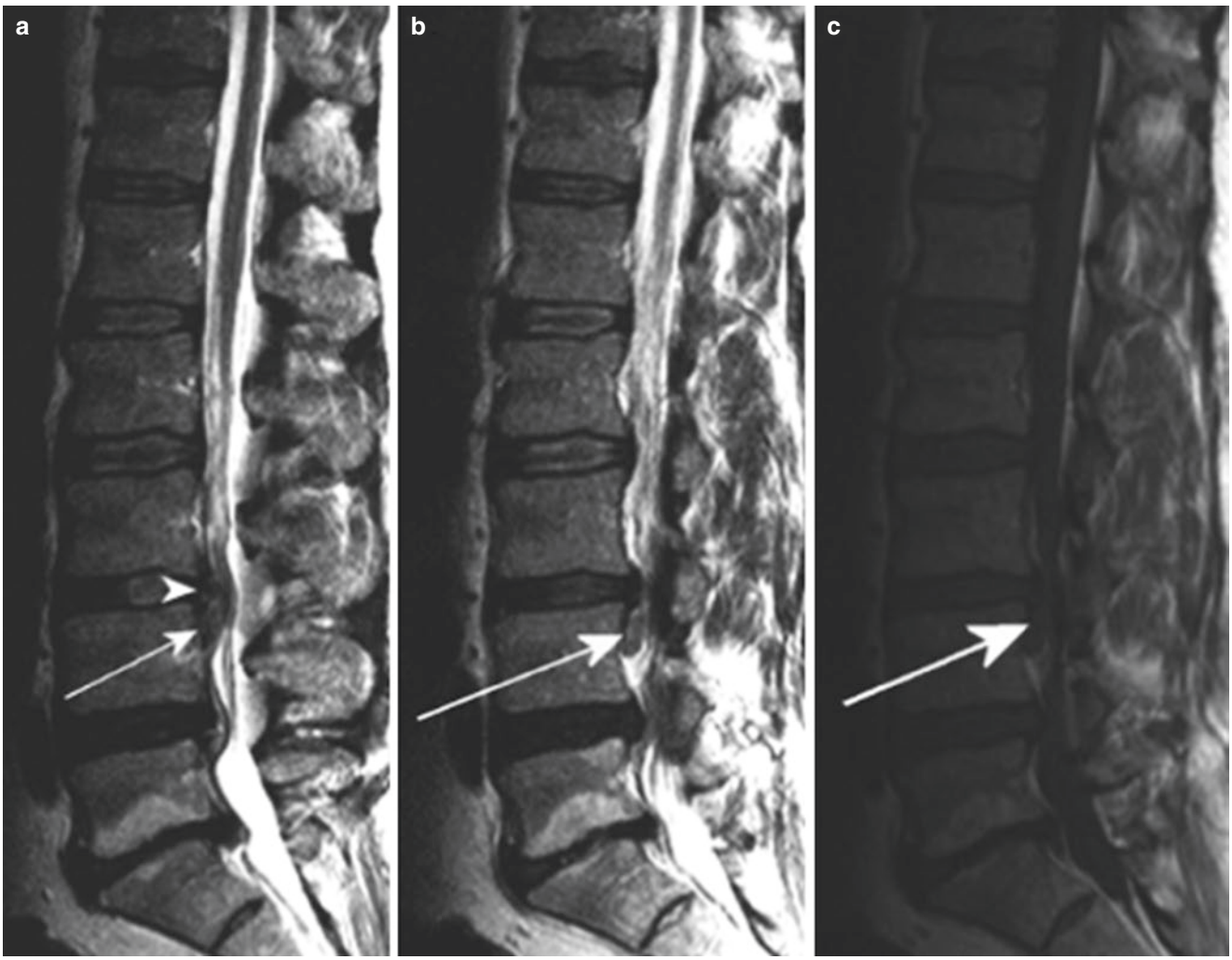

Fig. 12.5 MRI sagittal T2-weighted (**a**, **b**) and T1-weighted (**c**) image of herniated disc. In acute disc herniation, high signal intensity can be seen on T2-weighted MRI; however, with chronic intervertebral disc prolapse, low signal intensity is appreciated on T2-weighted MRI, which can be difficult to distinguish from osteophytes. Nerve root swelling and perineural enhancement can be seen after administration of a contrast agent. (Reprinted with permission from Hattingen et al. [140])

pression to the neural and vascular elements. In the lumbar spine, herniations are most common at L4–L5 and L5–S1. Manifestation of herniated discs ranges from progressive motor weakness along the affected nerve root(s) up to the bladder and bowel to sexual dysfunction from conditions such as conus medullaris and cauda equina syndrome. Fortunately, extreme presentations are rare, with incidence of about 1–2% in lumbar disc herniations and about 4 in 10,000 in all low back pain patients, but should connote immediate further evaluation [31]. Common presenting features of simple disc herniation include radicular pain and numbness, dysesthesias, motor weakness, and even muscle atrophy from prolonged compression or disuse. The lumbar spine is the most common location for symptomatic disc herniations accounting for 80% of all disc herniations. Common symptoms of symptomatic lumbar disc herniations are varied and include lower back and buttock pain, with or without radicular leg pain and sensory dysesthesias. These symptoms may be partially relieved with rest, activity modification, or change in position. Trunk flexion, prolonged standing or sitting, and straining maneuvers (i.e., Valsalva, cough) commonly increase the symptoms of disc herniation.

Risk Factors

Several factors have been investigated and associated with risk of developing neck and back radicular pain, including gender, prior episodes of neck or back pain, and occupational or recreational factors [32, 33]. Although some studies suggest that radiculopathy occurs more frequently in men, others have shown equal rates between genders. Previous history of axial low back pain is a well-established risk factor for

lumbosacral radiculopathy, and a prior history of lumbosacral radiculopathy has been found in patients presenting with cervical radiculopathy [34]. Additionally, prior history of trauma was found in approximately 15% of cases of cervical radiculopathy, but this association has not been documented in the lumbar spine. Although there is a correlation between a higher body mass and low back pain, the same relationship does not appear to exist in radiculopathy [35]. Multiple studies have shown a genetic linkage for spinal canal size as well as occurrence of disc herniation and subsequent radiculopathy [36]. With regard to occupational factors, lumbosacral radiculopathy occurs more frequently in patients who have performed jobs requiring manual labor, who work in positions of sustained lumbar flexion or rotation, and who engage in prolonged driving [37, 38].

In a case-control study of juvenile disc herniation, the estimated risk of developing a herniated disc before the age of 21 was four to five times greater for patients who had a positive family history, as compared to those who did not [39]. Similarly, below 18 years old, the odds ratio of a patient with juvenile disc herniation to have a family history of disc surgery was 5.6 times that of a patient without disc herniation [40]. Clinicians should also consider risk factors for ankylosing spondylitis in this population. Symptoms of morning stiffness, improvement with exercise, alternating buttock pain, and awakening due to back pain during the second part of the night only should prompt immediate investigation [41].

While most factors focus on the risk of structural compromise, there is considerable evidence that psychological and occupational factors can also play a role [42]. Interestingly, evidence supports the idea that psychosocial variables can be more important in the progression to chronic pain and disability than biomechanical variables [43]. Other risk factors identified have also included cigarette smoking, driving, and lifting objects greater than 11.3 kg (25 lbs) while twisting the body [44, 45]. Frymoyer, in a 1992 review of the epidemiology of degenerative disc disease wrote, “Among the factors associated with its occurrence are age, gender, occupation, cigarette smoking, and exposure to vehicular vibration. The contribution of other factors such as height, weight, and genetics is less certain” [46]. A decade later, following a review of the same topic, which incorporated more recent research, Ala-Kokko concluded, “Even though several environmental and constitutional risk factors have been implicated in this disease, their effects are relatively minor, and recent family and twin studies have suggested that sciatica, disc herniation and disc degeneration may be explained to a large degree by genetic factors” [36]. Recent studies have investigated genetic influences of disc degeneration contributing to risk of radiculopathy using twin models that indicate heredity has a dominant role in disc degeneration and subsequent pathology [47, 48].

Evaluation of Radicular Pain

A thorough history and physical exam are the cornerstone in any clinician’s armamentarium for the appropriate diagnosis and treatment of the patient. To develop the best differential diagnosis, one must be aware of correlative signs and symptoms. A key component in the initial evaluation of radicular pain is to rule out serious pathology and non-musculoskeletal diseases as a cause of pain and associated symptoms. Some symptoms that warrant further evaluation would include age less than 20 years old, history of trauma, presence of constitutional symptoms (i.e., fever, chills, weight loss, etc.), history of cancer, recent bacteremia, immunosuppression, unrelenting pain, or presence of cauda equina syndrome [49–51]. A comprehensive physical examination is necessary to aid in determining distributions of symptoms and identify all possible generators of pain. In the diagnosis of a radiculopathy, there is significant clinical utility in understanding the structures in the nervous system responsible for observed sensory deficits over a given area of the skin. Unfortunately, there has been a lack of consensus with regard to the precise localization of specific dermatomes. This variability among dermatomal maps arises from a number of difficulties encountered when attempting to create an accurate representation. Similar to a dermatome, the term myotome is used to describe all of the muscles that receive innervation from a single spinal segment or spinal nerve. Significant overlap in myotomes occurs in a similar fashion to dermatomes. Nearly every muscle receives motor nerve fibers from more than one spinal level [52]. Although many muscles have a dominant innervating nerve root, multiple spinal levels likely contribute to the complete innervation. Similar to dermatomes, there is some disagreement and overlap among varying sources with regard to the spinal levels responsible for the innervation of particular muscles. Despite the challenges present in dermatomal and myotomal mapping, they are very useful in the evaluation and diagnosis of radiculopathy.

Neurologic exam of a patient presenting with radiculopathy secondary to herniated nucleus pulposus will often show a sensory deficit, motor deficit, or combination of both. Sensory modalities including temperature, pinprick, proprioception, and vibration will be reduced in a dermatomal distribution. Deep tendon reflexes are often diminished or absent in the setting of radiculopathy as this causes a lesion of either the afferent or efferent limb of the monosynaptic arc responsible for these reflexes. When examining deep tendon reflexes, signs of upper motor neuron lesions should give the examiner pause. Upper motor neuron lesions will cause hyperreflexia. The Babinski and Hoffman signs may be present in patients with upper motor neuron dysfunction. The Babinski sign is elicited by stroking the lateral aspect of the sole of the foot with a blunt object. A positive test is indi-

cated by dorsiflexion of the great toe. Hoffman sign is tested by briskly flicking the dorsal or palmar aspect of the distal phalanx of the middle finger. A positive result is recorded when the index finger and thumb show reflex flexion [53].

Physical Evaluation of Cervical Radiculopathy

The Spurling test has been described as "almost pathognomonic of a cervical intraspinal lesion" [54]. A study by Shah and Rajshekhar in 2004 evaluated the test on 50 surgical patients with positive herniated nucleus pulposus on magnetic resonance imaging (MRI). The results of the study revealed that the Spurling test was 92% sensitive and 95% specific, with a positive predictive value of 96.4% and a negative predictive value of 90.9%, concluding that the Spurling test is the gold standard for evaluating cervical radiculopathy [55].

The Lhermitte sign, also known as the barber chair phenomenon, is named after Jacques Jean Lhermitte, who described findings in 1920 when evaluating patients with spinal cord concussion and later in other neurologic diagnoses [56, 57]. There are still variations of how the Lhermitte sign is described; however, current description is an electric shock-like sensation that occurs on flexion of the neck that radiates down the spine, often into the legs, arms, and sometimes the trunk [58]. The findings have been described in various pathologic states caused by trauma to the cervical portion of the spinal cord, multiple sclerosis, cervical cord tumor, cervical spondylosis, or even vitamin B12 deficiency. There is limited literature evaluating the effectiveness of the Lhermitte sign in determining cervical radiculopathy. A review by Malanga and colleagues concluded that there is insufficient evidence of the inter-rater reliability, sensitivity, and specificity of the Lhermitte sign specifically. However, the active flexion and extension test described by Sandmark and Nissell resembles the Lhermitte sign and was found to have a high specificity (90%) and low sensitivity (27%) with a negative predictive value of 75% and positive predictive value of 55% [59].

Physical Evaluation of Lumbar Radiculopathy

The straight leg raise (SLR) test, also known as Lasegue sign, is a commonly used provocative test of radicular symptoms for lumbar pathology [60]. The SLR has been described in the literature since the late nineteenth century by numerous investigators, and subsequent eponyms have described the slight variations in testing. Through historical references and descriptions, the consensus of a positive finding using the classic SLR test is the elicitation of radicular pain down the posterior thigh below the knee with the patient supine and the leg, with knee extended, being raised between 30° and 70° [61]. Pain below 30 or beyond 70 is unlikely to be from nerve root irritation and more likely to be secondary to musculoskeletal tension. Overall, a positive SLR was present in 70–98% of patients with a lumbar disc pathology confirmed operatively [62]. The sensitivity of the test ranges from 72% to 97%, whereas specificity is between 11% and 66%. A systemic review and meta-analysis by Deville and colleagues compiled data from numerous studies evaluating the SLR test with surgery as reference standard. The results of the pooled data of these studies revealed the pooled sensitivity for the SLR test was 91% (95% CI 0.82–0.94) and the pooled specificity 26% (95% CI 0.16–0.38) [63].

There have been numerous studies to assess the validity and reliability of the crossed straight leg raise (CSLR). CSLR was compared with SLR to predict the presence of disc herniation on physical examination and found to be strongly reliable. In one study, CSLR was positive in 97% of patients as compared with 64% with SLR alone. When evaluating the presence of herniations at surgery, the study by Kosteljanetz and colleagues revealed that 19 of 20 positive patients had correlative findings [64]. Andersson and Deyo demonstrated that the CSLR had a higher specificity (85–100%) and a lower sensitivity (23–42%) as compared with the SLR when reviewing various studies as well as a high positive predictive value of 79% and negative predictive value of 44% [65]. These findings were confirmed by Deville and colleagues in a meta-analysis, which also revealed a low sensitivity (29%) and high specificity (88%) [63]. A more recent Cochrane review provided a similar conclusion, with CSLR showing high specificity (pooled estimate 0.90, 95% CI 0.85–0.94) with consistently low sensitivity (pooled estimate 0.28, 95% CI 0.22–0.35) [66]. A positive CSLR has been shown to predict poor prognosis of conservative management as well as those who would have positive outcomes with surgical intervention. Until recently there has been very limited evidence-based research on other lumbar provocative tests; however, with these new contributions, there is a better understanding of the utility of these tests.

Electrodiagnostic Evaluation

Electrodiagnostic studies such as electromyography (EMG) and nerve conduction studies (NCS) are common tools employed together in the evaluation of nerve compression or injury. Radiculopathy is suggested when abnormalities are noted in at least two muscles innervated by the same root, but different peripheral nerves, provided that muscles innervated by adjacent roots are normal [67]. While these tests can be a useful adjunct to the history and physical exam, there are

several notable limitations to the various needle electrode exams (NEE), which should be taken into account. These tests can be painful to the patient as well as expensive. The electrodiagnosis of radiculopathy also relies on a myotomal pattern of abnormality; therefore variation in anatomic pattern of nerve roots must be accounted for in the interpretation [68]. EMG targets exclusively motor neurons, and nerve conduction studies are typically normal in radiculopathy; however, the more important reason to perform nerve conduction studies is to exclude other conditions that may mimic radiculopathy, especially entrapment neuropathy and plexopathy. Because most radiculopathies are predominantly sensory in nature, EMG lacks sensitivity in their evaluation.

Sensory nerve action potentials (SNAP) can be useful in the diagnosis of sensory radiculopathy; however, abnormalities on these studies are not part of the diagnostic criteria [69]. SNAPs can also be useful to rule out other potential causes such as peripheral polyneuropathy or entrapment mononeuropathy [70]. It is also difficult to localize a radiculopathy to a single nerve root. This effect is more pronounced when evaluating the brachial plexus in cases of cervical radiculopathy, with the most difficult levels to differentiate being C6 and C7 [71]. If lesions are acute or purely demyelinating in nature, the EMG study may be normal because the effect of fibrillating potentials and signs of axonal loss can take weeks to develop after nerve injury. Based on EMG alone, an abnormality of the nerve root cannot be distinguished from an abnormality of the motor neurons supplying that root. While clear and unequivocal clinical differences exist to allow the distinction, this is an important concept to keep in mind when evaluating results of these exams.

Evaluation of the usefulness of electrodiagnostics has been particularly challenging in the literature. Partially due to the limitations mentioned above, no "gold standard" exists by which to compare these methods. Patient selection in most studies that were reviewed was based on clinical symptoms, signs, or radiological findings. None of these indicators, in isolation or when combined, come close to a gold standard for the diagnosis of radiculopathy. The American Association of Neuromuscular and Electrodiagnostic Medicine published a large literature review in which they evaluated 75 studies to evaluate the utility of electrodiagnostic studies in the diagnosis of radiculopathy. The studies evaluated used various reference standards, which is a great limitation; however, sensitivity for EMG in cervical radiculopathy ranged from 30% to 95% with an abnormality rate of 50–71% in patients with clinical signs or radiological findings. Despite low sensitivity, needle EMG evaluation of 404 clinically normal myotomes revealed abnormality in only 1.5% [72]. Although the EMG study is very sensitive to the presence and approximate localization of a radiculopathy, equivocal or false-negative studies are not uncommon in true radiculopathy.

Imaging Evaluation

Clinicians should consider performing diagnostic imaging and testing for patients with low back pain when severe or progressive neurologic deficits are present [31]. Routine advanced imaging, with computed tomography (CT) or magnetic resonance imaging (MRI), has been discouraged due to several factors including the following: it has not been shown to improve patient outcomes if pain is present for less than 6 weeks with no red flag symptoms, and it identifies many radiographic abnormalities that are poorly correlated with symptoms, which could lead to additional or unnecessary procedures, and, in the case of CT, exposes patients to possibly unnecessary ionizing radiation [73–76]. On a similar note, studies have recognized a high prevalence of abnormalities seen on imaging in asymptomatic patients [77–82].

In patients for whom 4–6 weeks of conservative management has been unsuccessful and continued physical exam signs of nerve irritation exist, imaging should be pursued if they are possible candidates for surgery or other intervention or diagnostic uncertainty remains. MRI has become the initial imaging modality of choice, displacing myelography and CT in recent years. However, CT can be performed if a contraindication to MRI exists in the patient. Additionally, in patients who cannot undergo MRI, x-ray myelography with postmyelography CT of the spine is recommended to assess the patency of the spinal canal and thecal sac and of the neural foramen. The sensitivity of MRI in detecting lumbar nerve root compromise was very low at 0.25 (95% CI), while the specificity, which is the probability of getting a negative MRI test result on a patient with negative findings for nerve root compromise by physical examination, was relatively high at 0.92 (95% CI) [83, 84]. When comparing post-myelographic computed tomography (CTM) to MRI, Song et al. showed utility in diagnosis of foraminal stenosis and bony lesion; however, there was limitation in intra- and inter-observer findings in disc abnormality and nerve root compression [85].

Natural History

The advent of CT and MRI has significantly impacted the ability to diagnose and monitor disc herniations in patients with radiculopathy. These imaging studies have also made it possible to follow the natural course of disc herniations and compare the morphologic changes with symptomatic improvement [86, 87]. Key was the first to document the spontaneous regression of a herniated disc in the lumbar spine by myelography in 1945; however, this phenomenon was not confirmed until the use of follow-up CT scans in the lumbar and cervical spine in 1985 [88]. Saal and colleagues published a subsequent study in 1990 of 12 patients with

documented lumbar herniations on CT. These patients were rescanned at an average of 25 months, and the following findings were documented: 46% of subjects had 75–100% resorption, 36% had 50–75% decrease in herniation size, and 11% had 0–50% regression. They found that the greatest degree of resorption was most frequently seen in the patients who had the largest herniations. However, they did not find a significant correlation between clinical and morphologic improvement [89].

Maigne and Deligne established a similar relationship between greater spontaneous resolutions in larger herniations in the cervical spine [90]. Bush and colleagues performed repeat CT scans on 106 patients 1 year after being diagnosed with lumbosacral radiculopathy [91]. Disc herniations that decreased or fully resolved were seen in 76% of patients. However, only 26% of disc bulges decreased or resolved. Masui and colleagues found that disc herniation size decreased by 95% in 21 patients who had follow-up MRI imaging 7–10 years after being diagnosed with disc herniation and radiculopathy [92]. Cribb and colleagues focused on massive lumbar disc extrusions that obscured greater than 66% of the spinal canal at the time of diagnosis of radiculopathy. They found that after 25 months, 14 out of 15 herniations had completely resolved [93]. Although Komori and colleagues did not find a correlation between clinical symptom and radiological improvement, this finding has been demonstrated in more recent studies [94]. Dellerud and Nakstad followed 92 patients over 14 months with follow-up CT scans and found a strong association between clinical improvement and reduction in the size of the lumbar herniation. They also found that central herniations and disc bulges were less likely to resolve, and the reduction in size of disc bulges was associated with a lesser degree of symptomatic improvement than with disc herniations [95].

Etiology of Symptoms

After a disc has prolapsed, it may affect nerve roots in many ways. The process of pain generation can be broken into two broad categories: mechanical and chemical [96]. The mechanical process may be caused by direct compression of the nerve root from a disc fragment. This may lead to alteration of the function of the nerve and may manifest as pain, weakness, or paresthesias along the nerve's distribution. Foraminal narrowing is another potential result and has been found to correlate with clinical success of intervention [97]. Herniations typically result in impingement of the adjacent, traversing nerve root. The patient may develop discomfort in a radicular, or dermatomal, distribution due to associated inflammation [98]. Classic posterolateral disc herniations characteristically compress the traversing nerve root and produce symptoms along that dermomyotome. Far lateral herniations, on the other hand, characteristically compress the exiting rather than the traversing nerve root. For example, a typical posterolateral herniated nucleus pulposus of the L4–L5 disc would produce symptoms from the fifth lumbar nerve root or L5 dermatome. Symptoms along this nerve root could also be generated from a far lateral herniation of the L5–S1 intervertebral disc [53]. Unlike the lumbar spine, where the traversing nerve root is most commonly irritated, in the cervical spine, disc herniations and spondylosis most often affect the exiting nerve root, so a C6–C7 disc herniation will usually cause C7 symptoms [99, 100]. The cervical spinal nerves exit the spinal cord oriented obliquely toward their respective neural foramen. The most commonly affected levels are C7 (45–60%), C6 (20–25%), and C5 and C8 (10%), possibly due to the normal anatomic finding of the C7/T1 foramina being the most narrow [101].

The chemical effects that generate pain are believed to stem from local inflammation propagated by the inflammatory cascade in response to components of the nucleus pulposus [102]. Several inflammatory markers have been found in herniated discs including IL-1α, TNF-α, TGF-β, and many others [103–109]. Increased levels of these inflammatory cytokines have been correlated with higher levels of pain in patients. After embryonic development is complete, the nucleus pulposus receives no exposure to the immune system due to the lack of blood vessels in direct contact with the NP itself [110]. Herniated disc material, particularly when sequestered, may release substances, which are capable of inducing an autoimmune response [96]. A growing body of evidence has implicated bioactive molecules within the disc as important in sensitizing nerve roots and participating in the pathogenesis of radiculopathy [111]. Along with inflammation and pain, this response has been shown to generate the production of matrix metalloproteinases, which play a crucial role in disc resorption [112].

Prognosis

The prognosis of radicular pain from a herniated nucleus pulposus is very favorable. Studies that look at back and leg pain specifically from a herniated disc have found resolution of symptoms in 6–12 weeks in up to 80% of patients and up to 90% showing improvement in symptoms without significant long-term disability [94, 113, 114]. Disc protrusion in the cervical region has had a much more complex history in terms of outcome with conservative management. Referral center-based studies have shown that cervical radiculopathy can cause persistent pain and incapacity in two-thirds of patients treated conservatively. In a group of 255 patients treated nonsurgically, only 29% obtained complete relief. Gore et al. followed 205 patients with nonoperatively treated neck and referred pain for an average period of 15 years in

the late 1980s. At the end of the study period, only one-third had moderate to severe pain that interfered with their lifestyle [115]. Rothman and Rashbaum observed a similar group of patients for 5 years; 23% remained partially or totally disabled. A more recent study of 563 patients who presented to the Mayo Clinic from 1976 to 1990 also showed that 90% of patients had mild or no symptoms after 4–5 years of follow-up [116]. However, one-fifth of patients did not improve and ultimately underwent surgical treatment. Only one study specifically monitored for recurrent symptoms and found that recurrences occurred in 12.5% of patients during a follow-up period of 1–2 years [117]. The challenge with interpretation of earlier studies is the ever-evolving definition and understanding of the pathologic process associated with the herniated nucleus pulposus and evaluations in which to make an accurate diagnosis. As our understanding and evaluation have improved, so too has our ability to prognosticate in reference to pain caused by this specific pathology. Based on recent review, radiculopathy appears to be self-limiting in the majority of cases with conservative measures only.

Treatment

Medications in several classes have been shown to have moderate, primarily short-term benefits for patients with low back pain [118–122]. While many studies have been performed investigating these medications for efficacy in low back pain, very few have been performed to specifically address radiculopathy. The medication classes will be addressed in more detail; however, acetaminophen, NSAIDs, and skeletal muscle relaxants are popular first-line agents for clinicians [123]. Antiepileptics, such as gabapentin, tricyclic antidepressants, and judicious use of opioid pain medications have also been shown to have a significant but short-term benefit with back pain with or without radiculopathy [124]. Other treatment modalities in an initial conservative approach include physical therapy and low-impact resistance training with or without traction. Remaining active has also been shown to be more effective than resting in bed for patients with acute or subacute low back pain [125, 126]. In addition to medications and physiotherapy, prior to pursuing surgery, many clinicians will recommend less invasive options such as epidural steroid injections. A stepwise approach, in this fashion, has been shown to be therapeutic and cost-effective in those patients suffering from radiculopathy [127, 128]. While epidural corticosteroid injections are associated with early improvements, recent reviews and meta-analyses have shown benefits to be short-lived and have little effect on the natural history of the disease process [129–131]. Because of the inflammatory aspect of the herniated disc, directed anti-inflammatory therapy has been attempted. Transforaminal injection of steroid has shown success in decreasing the symptoms of disc herniation [132, 133]. Efforts to use infliximab, a TNF-blocker, however, have not shown strongly positive results despite success in decreasing inflammation in vitro [134]. Biological therapies including stem cell therapy, nerve growth factor inhibitors, and platelet-rich plasma have been evaluated in other chronic pain conditions and have yielded mixed results.

There is strong evidence to support the use of lumbar transforaminal epidural steroid injection (TFESI) in patients with acute-to-subacute unilateral radicular pain caused by herniated nucleus pulposus or spinal stenosis [135]. Leung et al. showed the technique of TFESI helps give time for better quality of pain relief, but it does not affect the ultimate need of surgery, especially for patients who require spinal fusion for spinal instability, either anticipated preoperatively or after surgical decompression. The patients who received a transforaminal epidural steroid injection for the treatment of symptomatic lumbar disc herniation had significantly better short-term pain improvement and required fewer long-term surgical interventions than patients who were treated with an interlaminar epidural steroid injection [136].

Few nonsurgical treatments have been studied for cervical radiculopathy. Most systematic- and evidence-based reviews have concluded that transforaminal ESI provides more benefit than interlaminar injections, but its use in the neck is limited because of the risk of catastrophic complications such as spinal cord infarction, particularly with depo-steroids [50]. Another randomized study in 169 patients with radicular pain found the combination of ESI and conservative treatment consisting of physical therapy and the adjuvants nortriptyline or gabapentin (or both) provided superior relief compared with either treatment alone (mean reduction in pain score of 3.1 in the combination group versus 1.9 in the others at 1 month; $P = 0.035$) [137]. Several high-quality reviews on the topic of progression to conservative management have led to incomplete or mixed results. Most studies on surgical techniques comparing them to conservative management show a high risk of bias. The benefit of surgery over a more conservative approach is not clear based on current evidence [138, 139].

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Degenerative Spine Joint Disease

13

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Key Points

- Facet joints, also known as zygapophysial joint, are formed from the articulation of the inferior articular process of one vertebra with the superior articular process of the adjacent caudal vertebra. Facet joints are crucial in stabilizing the spine and guiding flexion, extension, and rotation.
- Intervertebral motion can be isolated to the two vertebral bodies and the three-joint complex, consisting of the disc anteriorly and the two facet joints posteriorly. Degenerative change in disc can accelerate the degenerative changes in the facets.
- Spondylosis is defined as age- and stress-related degenerative changes that occur within the articular components of the spine.
- Because of the pars interarticularis' vulnerable position, stress forces make the area prone to fracture, and the vertebral body is then more inclined to forward slippage eventually leading to spondylolisthesis.
- Hyperkyphosis is a fixed and exaggerated convex anterior-posterior curvature of the thoracic spine that develops from age-related muscle weakening, degenerative disc disease, vertebral fractures, and genetic predisposition.
- While arthropathy of the sacroiliac joint can occur in isolation, sacroiliac joint dysfunction occurs more commonly in association with other degenerative syndromes, such as degenerative disc disease, spinal stenosis, and facet syndrome. Spinal fusion and laminectomy may be a significant predisposing factor.
- Hip osteoarthritis describes degenerative and degradative changes of the cartilaginous structures that occur in the hip joint. Primary osteoarthritis of the hip occurs due to normal wear and tear of the cartilaginous structures of the weight-bearing joint, typically becoming symptomatic in adults over the age of 40. Secondary hip osteoarthritis is caused by congenital or developmental etiologies.

Normal Anatomy and Function

Vertebral Column

The spine is composed of 7 cervical (levels C1–C7), 12 thoracic (levels T1–T12), 5 lumbar (levels L1–L5), 5 fused sacral (levels S1–S5), and 4 fused coccygeal segments [1]. The morphology of the first two cervical segments is the most distinctive and specialized to allow for movements of the skull, whereas the other segments are more consistent in appearance.

The C1 vertebra, also known as the atlas, is a ring-like structure, composed of the anterior arch, the posterior arch, and paired lateral masses, each articulating superiorly with the occipital condyles of the skull and inferiorly with the vertebral body of C2. C1 is unique in that it lacks a vertebral body. The C1–C2 junction is unique for the absence of an intervertebral disc. Instead, a bony isthmus, known as the dens or the odontoid process, originates at C2 projecting upward into the anterior arch of C1, thereby forming a bony articulation which confers substantial dynamic stability to the upper cervical spine (Fig. 13.1).

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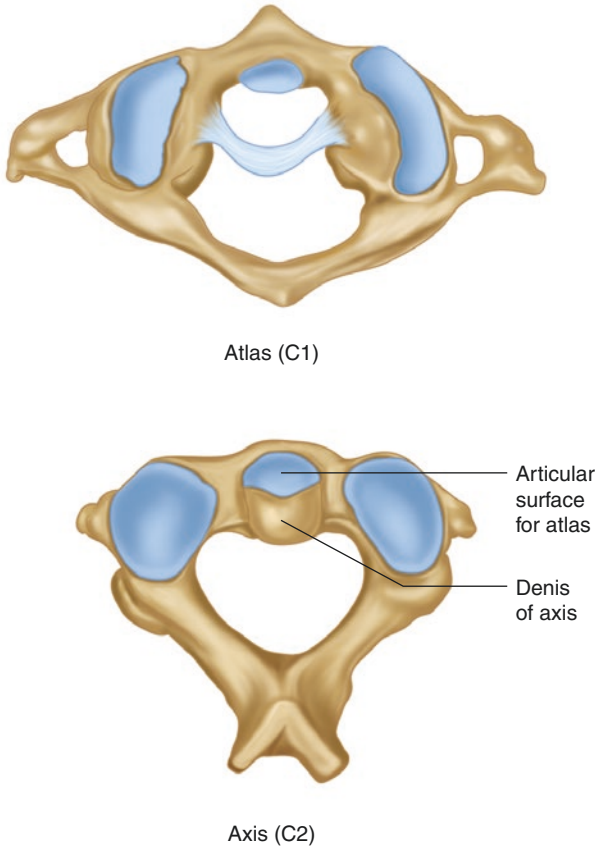

Fig. 13.1 Atlas (C1) and axis (C2): superior views. The denis of the axis projects upward into the atlas, forming a bony articulation

With the exception of C1 and C2, the remainder of the cervical, thoracic, and lumbar segments consist of vertebral bodies separated by intervertebral discs. Each vertebra consists of a vertebral body, the primary weight-bearing structure, and a bony arch, which projects dorsally from the vertebral body, forming the spinal canal where the spinal cord and spinal nerves travel [1]. Two short, thick, flanking processes known as pedicles originate from the vertebral body on either side, projecting dorsally and fusing with two broad bony plates known as lamina. The two laminae extend further posteromedially to the midline where they fuse and give off the spinous process (Fig. 13.2, top). The sliver of bone intervening between the ipsilateral pedicle and lamina is known as the pars interarticularis (Fig. 13.2, bottom). The pars interarticularis serves as the origin for the superior articular process, the inferior articular process, and the transverse process, thus producing four articular processes and two transverse processes for each segment. The three spinal processes, two transverse and one spinous, serve origins and insertions for muscles and ligaments, thereby anchoring and guiding spinal movement. The articular processes, which project superiorly and inferiorly, articulating with one another to form the zygapophysial or facet joints, confer sites to mechanically guide coordinated spinal movement, to bear roughly one-third of the axial load, and to resist anterior shear stress.

Joints of the Spine

Specific types of synovial joints exist from the skull base to the lumbo-pelvic junction, including atlanto-occipital, atlantoaxial, uncovertebral, and zygapophysial (facet) joints.

The atlanto-occipital joint is formed by the articulation between the occipital condyles of the cranium and the superior articular processes of the C1. The atlantoaxial joint is formed by the articulation between the posterior surface of the anterior arch of the atlas with the dens and the articulation of the lateral masses of C1 with the superior articular surface of C2 (Fig. 13.3). Together movement at these joints accounts for roughly 50% of total cervical rotation in addition to slight flexion, extension, and lateral flexion.

Uncovertebral joints, also known as joints of Luschka, are formed by the articulation between the uncinate processes, which arise from the posterior and lateral margins of the superior end plates of C3–C7, with the unci of the superior vertebrae. The joints of Luschka guide and permit flexion and extension of the cervical spine while simultaneously restricting lateral flexion.

The zygapophysial or facet joints are formed by the synovial articulation between the inferior articular and superior articular processes of the adjacent vertebrae [2] (see Fig. 13.2). Biomechanically, facet joints work in pairs to constrain the motion of the vertebrae while aiding the transmission of spinal loads [3]. In the cervical spine, the planes of the facet joints slope downward from an antero-superior to a postero-inferior position, thereby creating a plane of movement that facilitates rotation and extension while restricting lateral flexion and resisting shear stress in a coronal plane and bearing a minority of axial load [4]. Clinically this configuration guides one's ability to turn the neck and look up. In the thoracic spine, the facets are similarly oriented but at a more acute angle [5]. Taken together with the attachment of ribs along the lateral aspects of the vertebrae, this configuration confers significant rotational freedom of motion while limiting movement in all other planes. Finally, in the lumbar spine the planes of the facets are oriented to limit rotational range of motion but to allow greater range of motion in forward flexion, lateral flexion, and extension.

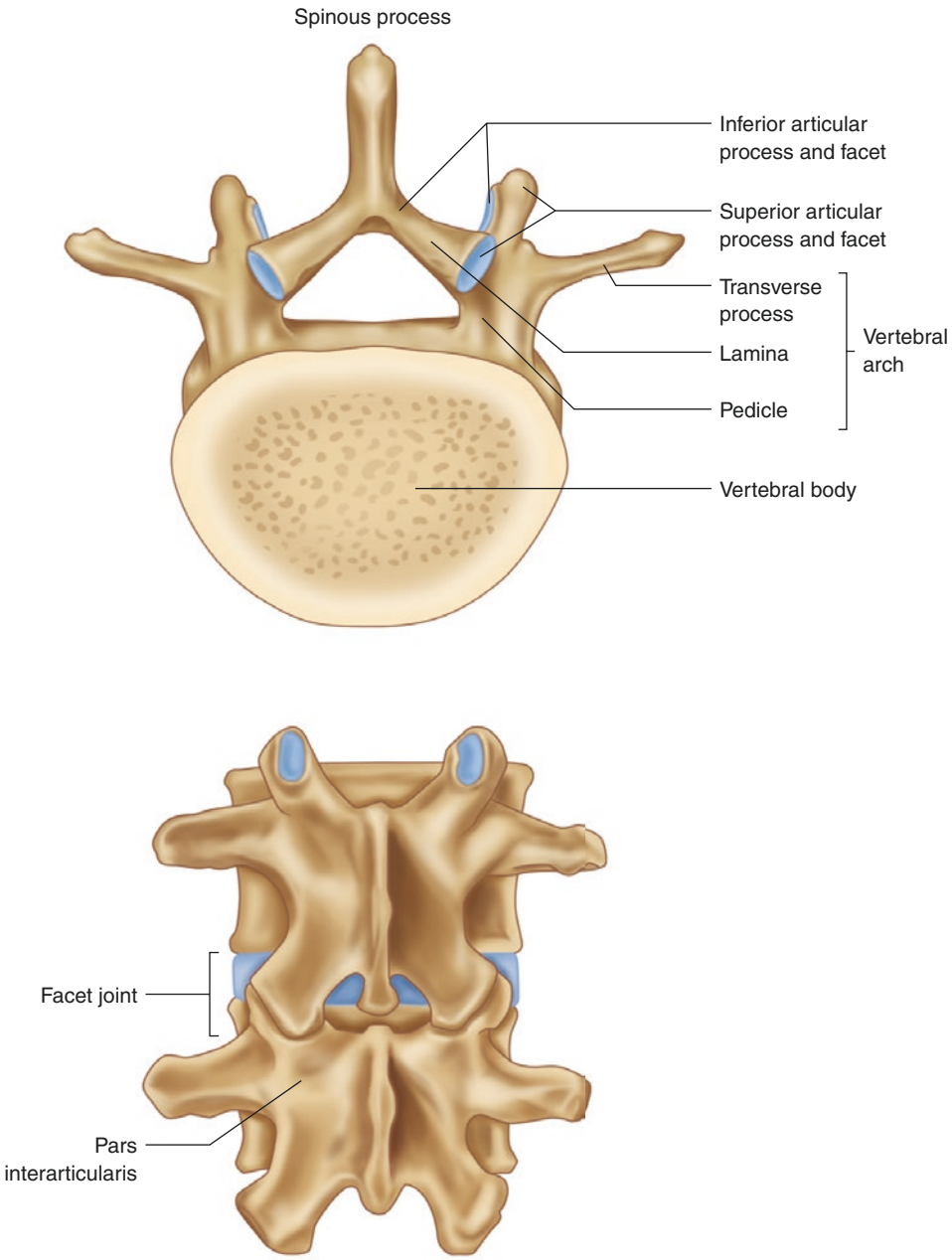

Fig. 13.2 Superior view of lumbar vertebral body (top). Labels include vertebral body, pedicle, lamina, transverse process, vertebral arch, superior articular process and facet, and inferior articular process and facet. Posterior view of two vertebrae (bottom) to better illustrate the pars interarticularis and the facet joint

Associated Joints: Sacroiliac Joints and Hip Joints

The bony pelvis is a large, relatively immobile ring-like basin designed primarily to bear weight of the body and transfer the load of the vertebral column laterally and inferiorly through the hip joints and into the lower limbs (Fig. 13.4). The pelvis is comprised of two innominate bones, joined anteriorly at the pubic symphysis and posteriorly to the sacrum at the sacroiliac joints [1]. Each innominate bone is comprised of three distinct bones which typically fuse by the end of puberty, the ilium, the ischium, and the pubis.

On the lateral aspect of the innominate, these three bones converge and fuse to form a cup-shaped concavity known as the acetabulum, which receives and articulates

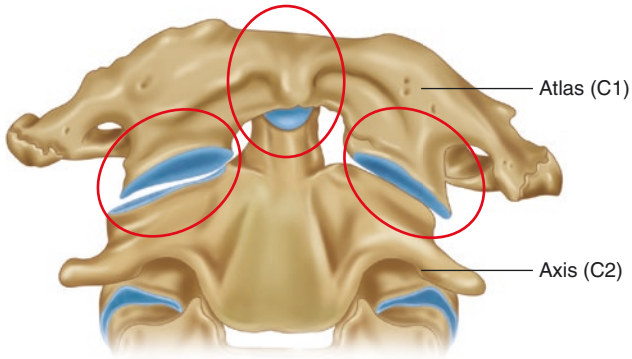

Fig. 13.3 Anterior view of atlas and axis. Circled components illustrate the atlantoaxial joint. The midline articulation is the dens of the axis projecting onto the atlas. The lateral articulations are that of the superior articular surface of the axis with the lateral masses of the atlas

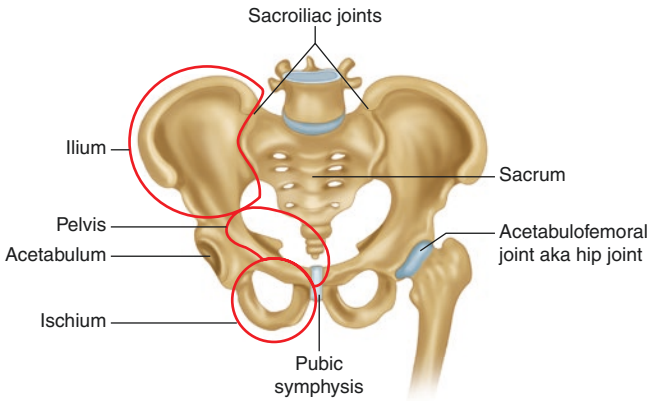

Fig. 13.4 Inferior view of a (male) bony pelvis to illustrate the sacroiliac joints, which is an articulation of the sacrum with the ilium, and the acetabulofemoral joint, which is an articulation of the acetabulum of the pelvis with the femur. Also illustrated are the three regions of the pelvis – ilium, pubis, and ischium – which are distinct regions that fuse by the end of puberty

with the head of the femur to form the acetabulofemoral joint, colloquially known as the hip joint. Each of the two sacroiliac joints (SI) is formed from the broad sinusoidal articulation occurring between the lateral border of the sacrum and the medial border of the ilium [6, 7]. Due to their role in bearing and dispersing axial spinal load, a sound understanding of both the sacroiliac and hip joints, biomechanically, in health, and in disease, is essential to a complete understanding of spinal degenerative disease and biomechanics.

Cascade of Degeneration and Osteophyte Formation

Intervertebral motion can be isolated to the two vertebral bodies and the three-joint complex, consisting of the disc anteriorly and the two facet joints posteriorly [8]. Degenerative change in any segment of the three-joint complex can influence degenerative changes in the other two [9–11]. Degeneration of the disc typically progresses to a subsequent loss of disc height. Lack of sufficient disc height can overwhelm the facet joints during axial loading and leads to inward bowing of the annulus and ligament's flavor, which will subsequently lead to neural foramina stenosis. The degenerated disc also allows for increased micro-axial rotation during axial loading and, consequently, exacerbating mechanical stress upon the longitudinal ligaments outermost annulus fibrosis [12–14]. Osteoblasts at the attachment sites on the margins of the vertebral bodies and annulus fibrosis are stimulated to form osteophytes. Disc-osteophyte formation further reduces spinal range of motion; posterior osteophytes can also contribute to central spinal stenosis.

Facet Arthropathy

Overview

Facet arthropathy refers to any acquired, degenerative, or traumatic process that affects the facet joints, often resulting in axial neck, mid-back, and low back pain as well as referred pain into the head as well as into the lower extremity [15–17]. Facet arthropathy can be a primary source of pain after whiplash injury or secondary to degenerative disease of the disc, vertebral compression fracture, or ligamentous injury. Facet arthropathy may result in pain due to the intrinsic nociception of the facet joints or its extrinsic compression of the lateral recess or neural foramen.

Normal Anatomy and Function

Facet joints, also known as zygapophysial joint, are formed from the articulation of the inferior articular process of one vertebra with the superior articular process of the adjacent caudal vertebra (see Fig. 13.2). The articular surface of the facet joints is covered by a layer of hyaline cartilage; the external joint is surrounded by a thin fibrous capsule and lined with a synovial membrane. Facet joints are crucial in stabilizing the spine and guiding flexion, extension, and rotation; when the spine is in extension, the facet joints bear a

significant portion of the weight of the spine [18, 19]. The facet joint ensures that the spinal column resists joint distraction, shear forces, and lateral or anterior-posterior translation and imparts sufficient torsional stiffness [8].

Nociceptive nerve endings are located in both the capsule and synovial membrane of the facet joints [20, 21]. Nociceptive signals from the facet joints are transmitted through the medial branch nerves, which also supply the motor innervation of the multifidus muscle as well as interspinous and supraspinous ligaments. Medial branch nerves originate from the posterior ramus which also divides into the lateral and intermediate branches, and in turn, the medial branch divides into two branches that supply the facet joint at the same level and the joint at the level below [21, 22].

The medial branch nerve courses over the medial posterior surface of the transverse process one level inferior to where it originates. Each lumbar facet joint is innervated by the medial branch of the nerve exiting at the same level as well as by the medial branch of the nerve one level above [23]. For example, at L4–L5 facet, which is the most common level for lumbar facet arthropathy, innervation of the inferior articular process of L4 is supplied by the medial branch nerve of L3, while the innervation of the superior articular process of L5 is supplied by the medial branch of L4. L5–S1 facet joint is unique in that it is innervated by the medial branch of L4 as well as the dorsal ramus of L5, which course along the junction of the S1 superior articular process and the sacral ala.

Pathology

Facet joints are weight-bearing structures and normally can carry up to one-third of the axial load. As described in the disc degeneration section, a cascade of degeneration can result when a degenerated disc can no longer contribute an adequate disc height. While it is challenging to determine the true sequence in the cascade, many researchers theorize that the disc degeneration usually precedes facet arthropathy since the degeneration in the disc is frequently accompanied by arthropathy of the associated facet joints, while arthropathy is minimal when the discs are relatively normal and disc degeneration also frequently occurs without facet arthropathy. With disc degeneration, studies suggest that it is the increased micro-axial rotation that results that places additional mechanical stress on facet joint [8]. The increased biomechanics load can lead to a molecular response, involving osteoarthrosis, osteophyte formation, and production of inflammatory cytokines within the cartilage and synovial membrane of the facet joints—the end result of which is hypertrophic and fibrocartilaginous changes of the facet joints [24, 25]. MRI findings may include hyperintensities of the bone marrow and periarticular soft tissue edema on T2 weighted imaging as well as widened facet joints with effusions [26]. The relationship between facet degeneration and back pain remains unclear. Establishing a clear relationship between joint degeneration and pain has been challenging, though in the past two decades, the trend is toward the conclusion that facet joints can be and often are a primary source for back pain [27]. Studies show that chemical or mechanical stimulation of the facet joints or the medial branches elicit concordant back pain [28–31], while local anesthetic blocks of the facet joints or the medial branches have been shown to relieve pain significantly in patients with chronic pain [32].

Spondylosis

Spondylosis is the term that describes age- and stress-related degenerative changes that occur within the articular components of the spine [24, 33, 34]. The degenerative changes affect all aspects and components of the spine, including the ligaments, discs, end plates, and bones. These degenerative changes result in spinal canal and nerve root narrowing. The general term for spondylosis is osteoarthritis of the spine. As with osteoarthritis that affects other areas of the body, it is a nonreversible, natural occurrence that is age and use related. Other degenerative changes that occur as a result of spondylosis are bony osteophytes and spurs [35]. These further contribute to degeneration and pathology by narrowing the spinal canal space, and the nerve roots exit. Thus, spondylosis is considered a mechanical hypertrophic response of adjacent vertebral bone to disc degeneration and includes facet joint osteoarthritis, degenerative disc disease from dehydrated discs, spinal canal stenosis, ligament and bony hypertrophy, or any other age-related degeneration of the spine [24].

Spondylolisthesis

Spondylolisthesis is the general term given to a slipped vertebra. Most often occurring in the lumbosacral region, it is broadly defined as anterior or posterior slipping of one vertebra over another [36]. Neugebauer was one of the first to describe the pathology of spondylolisthesis in 1888 as the separation of the posterior neural arch from the vertebral body. The bony defect, he noticed, was commonly encountered at the pars interarticularis which allowed for anterior displacement of the vertebral body, while the spinous process and inferior articulating surfaces remained aligned with

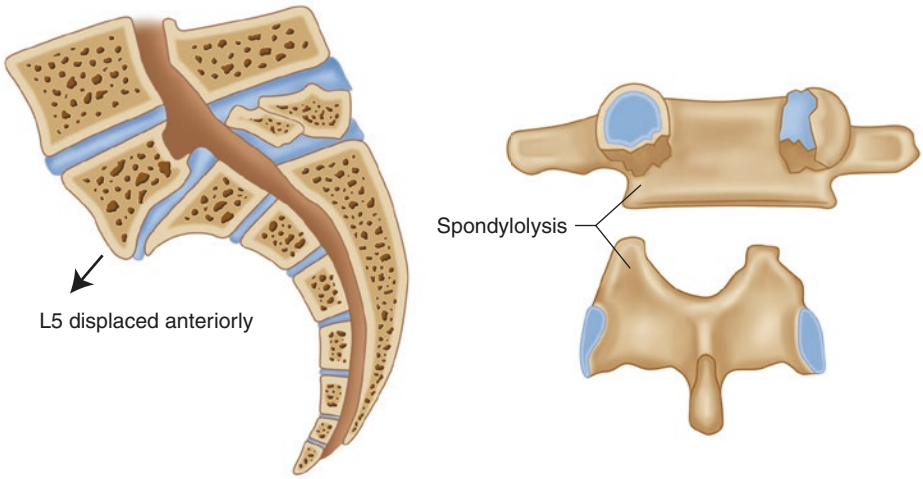

Fig. 13.5 Sagittal view illustrating spondylolisthesis, more specifically L5 anterolisthesis, in addition to posterior section illustrating spondylolysis, which is fracture of the pars interarticularis

the posterior sacrum [37]. The bony defect at the pars interarticularis would later be termed *spondylolysis* (Fig. 13.5). In the majority of cases, spondylolisthesis is an incidental finding on x-ray and is asymptomatic. The pars interarticularis appears to be a particularly vulnerable area in the spinal architecture that predisposes to the development of spondylolisthesis [38, 39].

Numerous studies have pointed to both a genetic predisposition as well as repetitive stress-related trauma to the pars as the leading cause of the development of spondylolisthesis [38, 39]. In 1957, Wiltse et al. described the presence of congenital bone abnormalities and defects of the pars interarticularis as a cause of spondylolysis which eventually progresses to spondylolisthesis [40].

Because of the pars interarticularis' vulnerable position, stress forces make the area prone to fracture. The structure thus weakened, and the vertebral body is then more inclined to forward slippage eventually leading to spondylolisthesis. The current classification of spondylolisthesis, made popular by Wiltse, accepts that the cause of the primary lesion is multifactorial [41, 42]. Type 1 spondylolisthesis is due to congenital dysplastic defects in the bony architecture of the vertebrae and occurs in approximately 20% of cases. A congenital deficiency of the superior sacral facet or the posterior neural arch of the fifth lumbar vertebra can allow for forward slippage of L5 over S1. Some argue that defects in the pars interarticularis are absent in this classification. Type 2 spondylolisthesis, also called isthmic spondylolisthesis, is the most common presentation of the defect occurring in approximately 50% of cases; traumatic or stress-related fracture in the pars interarticularis, both acute and chronic, results in the slippage. Type 3 spondylolisthesis occurs secondary to degenerative processes and is commonly found at L4/L5. The slippage occurs due to intersegmental instability and subsequent remodeling of the articular process. Type 4 often involves trauma in areas other than the pars resulting in slippage, and Type 5 involving pathologic causes like malignancy or other inherent bone abnormality is a very rare cause of spondylolisthesis.

Age-Related Hyperkyphosis

Overview

Hyperkyphosis is a fixed and exaggerated convex anterior-posterior curvature of the thoracic spine, also known as "postural roundback" or "dowager's hump." The presence of this deformity has been known to impair balance and increase risks of falls and injury. The condition develops from age-related muscle weakening, degenerative disc disease, vertebral fractures, genetic predisposition, or any combination of these. The prevalence of hyperkyphosis is 20–40% in both men and women over the age of 60 [43].

Normal Curvature

Developmentally, the lateral curvature of the spine is C-shaped and concave anteriorly. The thoracic and sacrococcygeal spine are referred to as primary curves as they remain kyphotic or concave anteriorly, whereas the cervical and lumbar curves are secondary curves as they change after birth [1]. Developmentally, lordosis of the cervical spine evolves from biomechanical changes that occur when a child begins to maintain an upright head posture. In contrast, lordosis of the lumbar spine evolves from the biomechanical changes elicited when a child begins to walk upright. The gold standard

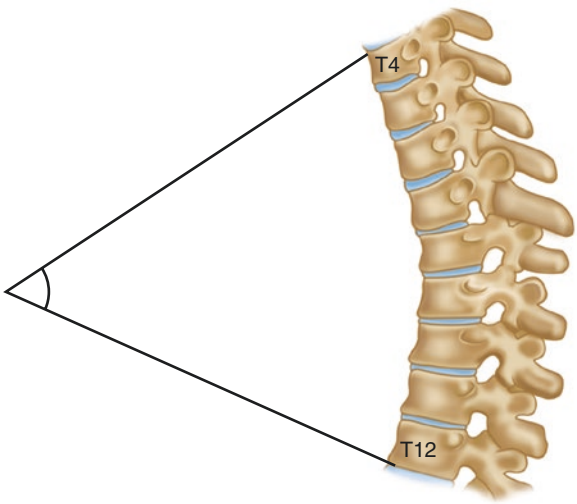

Fig. 13.6 Cobb angle can be calculated from the extension of the line from the superior end plate of T4 and the inferior end plate of T12. Cobb angle is one measure of the severity of the hyperkyphosis

for measuring kyphosis is with standing lateral radiographs from which the Cobb angle can be calculated from the interval of the thoracic curve (usually T4–T12) [44] (Fig. 13.6).

Pathology

A small amount of anterior curvature of the thoracic spine is normal. However, a kyphosis angle of greater than 40°, which is greater than the 95th percentile of normal, is considered hyperkyphosis. An increasing kyphotic angle is inversely correlated to quality of life and physical activity. Multiple musculoskeletal, neuromuscular, and sensory impairments are significant predictors of age-related hyperkyphosis [45, 46]. Stress loading on the aged, osteoporotic spine during daily activities can cause vertebral wedging and compression fractures. The severity of wedging and vertebral fractures correlates with decreased bone density and aging. A history of anterior wedge thoracic vertebral fractures is strongly correlated with hyperkyphosis [47].

Degenerative disc disease is another common finding seen on radiographs with patients with severe hyperkyphosis. There is significant correlation between anterior disc height and kyphotic angle. Some studies have shown hyperkyphosis in individuals without vertebral compression fractures, which supports the stronger correlation between degenerative disc disease [47]. With age-related extensor muscle weakness and the loss of inability to stand erect, the normal postural alignment is lost. Thus, others have postulated that hyperkyphosis is associated with spinal extensor muscle weakness [46, 48–50]. Additionally, the age-related calcification and ossification of anterior longitudinal ligament may also contribute to worsening hyperkyphosis. Finally, the aging population has loss of cerebellar function, vestibular, and proprioceptive feedback mechanisms. This may worsen already impaired erect vertebral alignment and serve to worsen hyperkyphosis [45, 50].

Sacroiliac Joint Dysfunction

Overview

The sacroiliac joint is the connection of the spine to the pelvis and therefore a significant region for transmission of weight from the trunk to the lower extremities. Sacroiliac joint dysfunction is estimated to be a generator of low back pain approximately 15–30% of the time [51, 52]. Predisposing factors for sacroiliac joint pain include leg length discrepancy, age, and previous spine surgery. With aging, the capsular surface of the ilium becomes coated with more fibrous plaques, and motion at the sacroiliac joint becomes noticeably restricted by the sixth decade. Erosions of the sacroiliac joint may be present by the eighth decade [53].

Normal Anatomy and Function

The sacroiliac joint is an ear-shaped articulation of the sacral segments S1–S3 with the ilium with only the inferior one-half to two-thirds of the joint to be considered truly synovial, while the superior aspect is more ligamentous (Fig. 13.7).

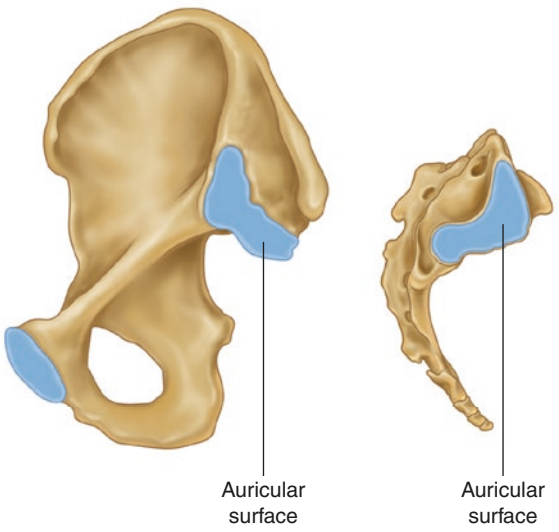

Fig. 13.7 The sacroiliac joint illustrated from the medial ilium view (on the left) and the lateral sacral view (on the right). The joint surface is often called the auricular surface as it is ear shaped

The sacral surface of the joint is made of hyaline cartilage, whereas the iliac surface of the joint is made of fibrocartilage—these surfaces are made of convoluted, interlocking grooves and ridges, which add to the stability of the joint against vertical and anterior shearing [54–56]. The intricate ligamentous system surrounding the sacroiliac joint further enhances the strength of the joint and functions to limit the amount of motion available to the sacrum and coccyx with respect to the ilium [57]. Due to the stability of the joint and surrounding ligaments, the sacroiliac joint is only capable of slight movement, such as flexion and extension of the sacrum, which are referred to as nutation and counternutation, respectively [58].

Innervation of the sacroiliac joint and adjacent ligaments is variable and may explain the different patterns of referred pain between individuals [59–61]. The anterior portion of the sacroiliac joint receives innervation from the lateral branches of dorsal rami of L2–S2, while the posterior portion of the joint receives innervation from L4 to S3. Effective reduction of sacroiliac joint pain has been achieved in multiple studies with lesioning of the L5 dorsal ramus in addition to the lateral branches of the dorsal sacral rami from S1 to S3 [62].

Pathology

Biomechanically, because there are intimate connections between the surrounding ligaments of sacroiliac joint with the biceps femoris, piriformis, and gluteus maximus, any imbalance of the muscle dynamics could lead to abnormal sacroiliac joint mobility, leading to mechanical stress and accelerated degeneration [63]. While arthropathy of the sacroiliac joint can occur in isolation, sacroiliac joint dysfunction occurs more commonly in association with other degenerative syndromes, such as degenerative disc disease, spinal stenosis, and facet syndrome [64]. Spinal fusion and laminectomy may be a significant predisposing factor as the altered spinal mechanics can subject the sacroiliac joints to increased mechanical load [65]. Pathologic changes, more commonly found in individuals over 50 years of age, include cartilage erosion, denudation of the joint surface, and osteophytic formation, in addition to para-articular and intra-articular fibrosis ankylosis—these can all lead to the gradual obliteration of the joint space until the sacrum and ilium are completely apposed [66].

Hip Joint Disorders

Overview

The hip is a ball and socket synovial joint. It consists of articulation between the head of the femur and acetabulum of the pelvis. It serves as a connection between the spine and the lower extremities, providing stability and dynamic support of the body by distributing axial load evenly to the lower extremities. The hip joint is subject to extreme forces, facilitating movement in three axes, all perpendicular to each other and centered around the femoral head [2].

Normal Anatomy and Function

The stability of the hip is maintained by the activity of the ligaments, muscles, and tendons working in tandem [67, 68] (Fig. 13.8). The "socket" of the hip joint consists of tight articulation of three bones: the pubis medially, the ischium inferiorly, and the ilium superiorly. At the junction of these three bones is the triradiate cartilage which fuses by the age of 16. The acetabular notch is the only part of the acetabulum that does not cover the femoral head. The transverse acetabular ligament runs inferiorly to the acetabular notch, creating a portion of the acetabular labrum, completing the ring of the joint, and helping to stabilize the hip joint by preventing inferior displacement of the femoral head [67, 68].

The femoral head is the most proximal part of the femur and forms the "ball" of the joint (see Fig. 13.8). Its articulating surface is lined with a durable layer of hyaline cartilage. A small depression in the head of the femur, called the fovea capitis femoris, houses the attachment of the round ligament. The femoral neck lies at an angle of approximately 130° to the axis of the femoral shaft. The greater and lesser trochanter of the femur serves as attachments for the hip joint's muscular stabilizers.

The acetabular labrum is a fibrocartilage inserted on the base of the acetabular edge. It blends in with the transverse acetabular ligament and helps increase the overall depth and stability of the hip joint. Additionally, the labrum helps to keep the synovial fluid within the joint capsule. As mentioned above, the femoral head, as well as the entire acetabular articulating surface, is covered by durable hyaline cartilage. Its main function is to serve as a shock absorber to help dissipate weight during weight-bearing activities, decrease friction, and allow free motion of the joint.

The articular capsule is a fibrous sheath which encases the hip joint from the acetabulum to the femoral neck. There are three peripheral thickenings of the capsule, named for their pelvic attachments, which form three important extracapsular ligaments. The *iliofemoral ligament* is the strongest ligament in the body and originates below the anterior inferior iliac spine and inserts on to the femur at the greater trochanter and onto the intertrochanteric line. It reinforces the anterior aspect of the joint capsule and serves to restrict overextension and external rotation of the hip joint. The *pubofemoral ligament* originates from the pubic portion of the acetabular edge and from the ilio-pectineal eminence and

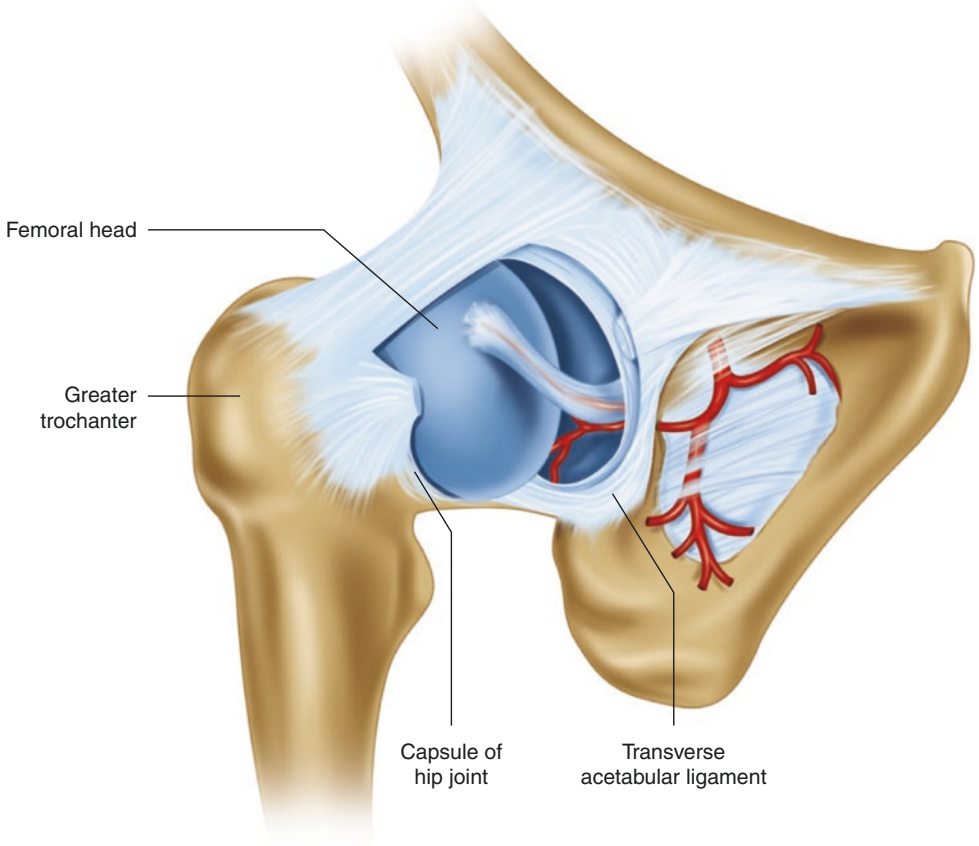

Fig. 13.8 Anterior view of the acetabular fossa and ligament of the femoral head

blends with the joint capsule. It serves to restrict movement in abduction. The *ischiofemoral* ligament spans from the ischium below and behind the acetabular edge and attach to the intertrochanteric line. It serves to restrict movement in internal rotation.

The *ligamentum teres femoris*, also known as ligament of the head of the femur, round ligament, or foveal ligament, is located intracapsular and attaches the apex of the notch to the fovea of the femoral head. The base of the ligament is attached by two bands that each attach to the acetabular notch and blend with the transverse ligament. The ligamentum teres was initially thought to be an embryological remnant. However, it is now accepted that the ligamentum teres is integral to the hip joint as it serves as a carrier for the foveal artery (posterior division of the obturator artery) which supplies the femoral head. Injuries to the ligamentum teres can occur in dislocations, which can cause injury to the foveal artery, resulting in osteonecrosis of the femoral head. Congenital absence of the ligamentum teres is a classic feature in patients with hip dysplasia.

The hip houses attachments of many muscles and muscle groups. They are arranged anteriorly, medially, laterally, and posteriorly around the hip joint. Anteriorly, the rectus femoris, sartorius, iliopsoas, and pectineus are the primary flexors of the hip. The adductors longus, brevis, and magnus form the medial group responsible for adduction of the hip. The gracilis muscle is often included in this group as well. Posteriorly are the semimembranosus, semitendinosus, and the biceps femoris. Laterally, the muscles are gluteus minimus, medius, and maximus, as well as the tensor fascia lata which serve to abduct the hip.

The bursae involved in hip articulation, the iliopsoas bursa and the peritrochanteric bursae, have a particularly important role from a clinical point of view. The iliopsoas bursa, the largest bursa in the human body, is bounded by the iliopsoas muscle and tendon anteriorly, the capsule of the hip posteriorly, and femoral vascular structures medially. The peritrochanteric bursae located in the subgluteus maximus region of the lateral thigh include multiple distinct bursal components. Inflammation of these bursae presents as lateral hip pain, often confused with lumbar radiculopathy.

Adhesive Hip Capsulitis

Primary or idiopathic adhesive hip capsulitis, "capsular constriction" or "frozen hip," is characterized by a painful limitation in active and passive hip motion, usually external

rotation and abduction, without known trauma or pathology. The disease usually affects middle-aged individuals without sexual predominance. Radiographic imaging usually discerns only mild degenerative changes. Adhesive hip capsulitis is thought to be the result of synovial inflammation that progresses to capsular fibrosis [69].

The incidence of the disease is rare and is usually diagnosed after careful consideration of other more common etiologies such as osteoarthritis and hip impingement syndromes. The most convincing physical evidence of adhesive hip capsulitis is capsular fibrosis on arthroscopy. Rodeo et al. biopsied surgical samples of 19 patients with adhesive capsulitis of the shoulder and concluded that while synovial hyperplasia and capsular fibrosis played a pivotal role in the pathology of adhesive capsulitis, cytokines were also involved in the inflammatory and fibrotic process of the disease as well. These cytokines provide a persistent stimulus that results in fibrosis of the capsule. Many believe that the same mechanism applies to capsulitis of the hip joint.

Hip Osteoarthritis

Osteoarthritis is the prevailing joint disorder in the United States, and over 200,000 hip arthroplasties are performed annually in an effort to combat this disease. Both primary and secondary causes of hip osteoarthritis have been described. Primary osteoarthritis of the hip occurs due to normal wear and tear of the cartilaginous structures of the weight-bearing joint, typically becoming symptomatic in adults over the age of 40. Secondary hip osteoarthritis is caused by congenital or developmental etiologies.

Hip osteoarthritis is the term used to describe degenerative and degradative changes of the cartilaginous structures that occur in the hip joint in a nonuniform manner [70–73]. As the lubricating surfaces of the joint capsule begin to deteriorate and the bony structures closely appose each other, the body compensates by forming bone spurs and osteophytes which further impedes motion and further causes painful degeneration. Mild to moderate synovial fluid inflammatory changes also occur at this time as well as thickening of the synovium and ligaments.

Risk factors of primary osteoarthritis of the hip include age, genetic disposition, high BMI, participation in weight-bearing activities, and occupations that require prolonged standing, lifting, or moving heavy objections. Risk factors for secondary osteoarthritis include hemochromatosis, hyperthyroidism, hypothyroidism, acromegaly, connective tissue disorders, Paget's disease, and gout, among others [70–73]. Some studies suggest that hip osteoarthritis is more prevalent in females because a reduction in hormones, particularly a decrease in estrogen levels, worsens the progression of the disease.

Spine-Hip Syndrome and Hip-Spine Syndrome

The spine and the hip joints are intimately related due to kinematics; pathologies in the spine can lead to compensatory changes in the hip joint, leading to hip pathology and vice versa. In spine-hip syndrome, the aging of the spine due to degenerative disc disease and osteoporotic vertebral collapse can lead to progressive loss of lumbar lordosis and increased pelvic retroversion; with time, the patient will become sagittally imbalanced with under-coverage of the femoral head anteriorly therefore developing increased risk for hip osteoarthritis. In the hip-spine syndrome, the osteoarthritic hip joint becomes stiffened and immobile due to osteophytosis; in reaction, the spine will compensate by increasing the lumbar lordosis so that the individual can stand upright – overtime, this compensation can lead to pathologic degeneration of the spine [74].

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Degenerative Disc Disease

14

Aneesh P. Goel, Eric J. Wang, and Mark C. Bicket

Key Points

- Degenerative disc disease represents a broad category of back pain resulting from the degeneration of intervertebral discs.
- Disc degeneration may result from a variety of causes, including age, trauma, or excessive or repeated stress.
- In addition to damage to intervertebral discs, surrounding axial structures may also be affected and serve as pain generators. These nearby structures may include the vertebral bodies, facet joints, spinal ligaments, and exiting nerve roots.
- First-line treatment for degenerative disc disease consists of physical therapy, which works to reduce stress on the degenerated discs. When analgesic medications are needed, start with nonsteroidal anti-inflammatory oral medications.
- Epidural steroid injections may relieve pain and enhance rehabilitation from degenerative disc disease by facilitating improved participation in physical therapy and core-strengthening exercises.
- If function remains impaired despite conservative therapy, surgical options may be considered, though disc herniation and spinal stenosis are the two patient groups with the best evidence for improvement following spine surgery.

Introduction

Degenerative disc disease is a pathologic process that can result in acute or chronic low back pain from the loss of structure or integrity of intervertebral discs. When discs become dehydrated, they can narrow in height and collapse, resulting in aberrant changes in anatomical alignment that may result in nerve compression and pain symptoms. Radiographic findings of degenerative disc disease include disc space narrowing, osteophyte formation, degeneration of vertebral bodies, end plate changes, and vacuum disc [1–3]. However, advanced imaging demonstrating degenerative pathology has a poor predictive value in identifying pain in older adults between the ages of 53 and 70 [3]. Many patients in this age group have degenerative changes on imaging studies yet do not report significant low back pain. Degenerative disc disease may result in pain from multiple specific pathologies including discogenic pain, facet arthropathy, vertebral degeneration, disc herniation, and spinal stenosis.

Epidemiology and Natural Course

Low back pain as a result of degenerative disc disease has a significant socioeconomic impact in the United States. Factoring in lost wages and medical treatment, the financial cost of low back pain in the United States is estimated to exceed $100 billion annually [4]. The economic impacts stem from decreased quality of life from pain and associated neurological deficits. However, most degenerative disc disease is asymptomatic, making a true understanding of its prevalence difficult to discern. While exact estimates may vary widely, degenerative discs remain increasingly prevalent as patients age, with rates of 71% in men and 77% in women aged <50 years increasing to >90% in both men and women aged >50 years [5]. However, the incidence of low back pain in the entire cohort was 43%, suggesting that imaging findings do not always correlate

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with clinical symptoms. Thus, a practitioner must consider patients' presenting symptoms in conjunction with imaging findings when investigating the cause of low back pain.

Relevant Anatomy

Intervertebral discs are located between each vertebral body of the spine. The fibrocartilage-based pad of these discs provides flexibility, support, and minor load-sharing for the spine. Often considered as "shock absorbers" for the spine, discs balance the weight-bearing function of the spine with mobility needed to permit movement including rotation and bending [6]. They are primarily composed of two layers: an inner, soft, pulpy nucleus pulposus and an outer firm structure known as the annulus fibrosus. The annulus fibrosus is made up of fibrocartilage from type I and II collagen. Type I collagen provides greater strength and support to the disc and can withstand significant compressive force. The annulus fibrosus helps to distribute stress and pressure evenly across the disc and prevents damage to the underlying vertebrae. It also encircles the nucleus pulposus. The nucleus pulposus is made of a mucoprotein gel containing loose fibers and keeps the vertebrae separated in addition to absorbing impact from the body's movements. Disruptions in the normal architecture of the intervertebral discs, such as from herniation or degeneration, may result in significant pain and morbidity [6].

Mechanisms

In degenerative disc disease, pathologic changes occur in the intervertebral discs and, very frequently, in the vertebral bodies as well. Within the discs, the nucleus pulposus may suffer a reduced concentration of proteoglycans in its matrix, resulting in disc dehydration, loss of disc height, and narrowing of the intervertebral disc space. This usually occurs as a result of abnormal, repetitive microtrauma to the disc or from normal aging. The loss of disc height is also responsible for the normal age-related decline in height in the elderly [7]. In addition, with age, the annulus fibrosus becomes weaker and has a higher risk of tearing. If the fibrosus tears, the nucleus pulposus can extrude out of the disc, introducing a cascade of inflammatory cytokines and other chemicals that cause low back pain with or without radiating symptoms. The resultant disc herniation can additionally impinge on exiting nerve roots on the left or right side, leading to unilateral radiculopathy. Central canal narrowing may also result, leading to bilateral radiculopathy.

When disc height is lost, there is additional stress on the vertebral bodies themselves. This can result in degradation of vertebral end plates with compensatory sclerotic changes of the subchondral bone of the end plate [8]. These sclerotic changes can lead to the formation of osteophytes, which can protrude out from the vertebral bodies and impinge on exiting nerve roots. This impingement applies pressure to the spinal cord or nerve roots, resulting in radiating pain and sometimes focal areas of weakness. The specific symptoms reported by the patient will depend on which nerve roots are impinged upon by the protruding osteophytes and can vary greatly from patient to patient.

Recent studies have revealed that a number of genetic alterations are linked with structural changes in the intervertebral discs, predisposing patients to degenerative disc disease [9]. Mice studies with specific knockouts for genes suspected to play a role in disc degeneration, along with twin studies, reinforce this association between genetic factors and degenerative disc disease. Specific genes that may be involved in degenerative disc disease include those that code for scaffolding responsible for the integrity of the discs, such as collagens I, IX, and XI, as well as other genes for interleukin 1 (IL-1), the vitamin D receptor, aggrecan, and matrix metalloproteinase 3 (MMP-3) [9]. Patients with defects in any of these genes may have an increased risk for developing degenerative disc disease. Although each individual gene likely plays a small role, the complex interaction among these genes and the environment leads to the development of degenerative disc disease. Repetitive micro-stress from various physical activities and the aging process itself are likely the primary environmental contributors to degenerative disc disease.

Pathophysiology

In addition to intervertebral disc dehydration predisposing to disc tears, osteophyte formation, and nerve compression, the discs themselves can also be a source of pain. When discs serve as the primary pain generator, this clinical entity is termed discogenic pain [8]. Nociceptors in the annulus fibrosis can be stimulated by disc degeneration and cause nociceptive pain. Reactive nerve fibers in the outer layer of the annulus fibrosus can release inflammatory mediators including substance P, vasoactive intestinal polypeptide (VIP), calcitonin gene-related peptide, and other cytokines in response to repeated mechanical loads [8]. Degeneration of discs can also lead to abnormal mechanical stimulation of disc nociceptors. When this occurs, disc nociceptors generate an amplified response known as peripheral sensitization, leading to significant pain and morbidity. Low pH with rising lactic acid levels can also stimulate peripheral sensitization, worsening discogenic pain as well.

In addition, mast cell infiltration into torn fissures of the annulus fibrosis can lead to significant disc tissue inflam-

mation and degradation, fibrosis formation, neovascularization, and release of signaling factors, which can contribute to back pain. For example, phospholipase A2 (PLA2) has been detected at high concentrations in degenerative discs, stimulating the nociceptors of the outer third of the annulus fibrosus. This results in the further release of inflammatory materials that trigger pain [8]. In summary, discogenic pain originates from a structural failure of the disc that, through a variety of methods, leads to nociceptive stimulation and pathologic neurovascular proliferation into the annulus fibrosus.

Clinical Findings

Signs and symptoms of degenerative disc disease can vary significantly depending on the specific pathology occurring in the presenting patient, such as discogenic dysfunction, spinal stenosis, or facet arthropathy. Symptoms can include low back pain with or without radiculopathy, lower extremity weakness, and paraspinal tenderness.

Discogenic pain is a result of disc degeneration and is usually worsened with spine flexion owing to additional compressive stress on the discs. The patient may report pain with the act of sitting down or while walking uphill, as both of these activities typically result in some degree of spinal flexion [6]. In addition, any increase in intra-abdominal pressure from coughing, sneezing, or other Valsalva-like maneuvers can worsen pain due to this pressure being transmitted to the disc. Discogenic pain can often be difficult to differentiate from other sources of low back pain as it can present in a variety of ways.

If the degenerative disc disease results in spinal canal stenosis, the patient may report low back pain that is worse with spinal extension, with or without radiculopathy [7]. If radiculopathy is present, it is usually bilateral, since circumferential narrowing of the spinal canal will often affect the exiting nerve roots of both sides. Pain may radiate to the buttocks, hips, knees, or down to the feet. Pain is usually worse when standing from a sitting position or walking downhill, since both activities usually require significant spinal extension. Pain is often relieved when moving from a standing to sitting position due to lumbar flexion. If cord compression is significant enough, the patient may report weakness down one or both legs. This should alert the provider that further imaging and surgical consultation may be needed.

Sclerotic changes in the vertebral end plates can result in osteophyte formation, which may cause radicular pain as well [8]. Osteophytes can compress nerve roots as they exit the neural foramina, causing radiculopathy with or without lower extremity weakness. The specific type of activities that cause pain will vary significantly among patients, as this depends on which nerves are being compressed. Patients may endorse worsened pain after sitting or standing or after walking short distances. Osteophyte protrusion leading to radicular pain may be difficult to differentiate clinically from a herniated disc, as symptoms are similar.

Disc degeneration can also result in increased stress on the facet joints, causing facet pain [10]. This pain is often non-radiating and is usually relieved with lying down. Pain may be increased by extension of the lower back but not necessarily by flexion. It can be difficult to clinically distinguish between facet arthropathy and other pathologic sequelae of degenerative disc disease.

When evaluating a patient with possible degenerative disc disease, it is important for the practitioner to rule out other important causes of back pain, including abdominal pathologies such as abdominal aortic aneurysm, renal calculi, and pancreatic pathology [6–8]. In addition, identification of "alarm symptoms" is imperative. These include night sweats, significant weight loss, loss of bowel or bladder function, lower extremity weakness, recent history of trauma or assault, and saddle anesthesia. These signs or symptoms could suggest significant pathology other than degenerative disc disease, such as cauda equina syndrome, infection, tumors, or previously unrecognized trauma. Efficient workup and potentially urgent or emergent surgical consultation are especially important in these circumstances.

Imaging Findings

Initial imaging workup for patients with suspected degenerative disc disease without alarm symptoms should include cervical, thoracic, or lumbar radiographs depending on the region of reported pain symptoms. Radiographic images should include posteroanterior (PA) and lateral films. Radiographic findings of late degenerative disc disease include loss of disc space height, osteophyte formation, bony endplate sclerosis, and vacuum phenomenon [1, 2, 11]. The graphic in Fig. 14.1 shows degeneration of L5–S1 intervertebral discs with loss of disc height and osteophyte formation, while Fig. 14.2 shows multilevel degeneration. Figure 14.3 shows a lateral radiograph with loss of disc height and posterior articulation arthrosis. Vacuum phenomenon refers to the accumulation of nitrogen within the crevices of intervertebral discs or vertebrae. Figure 14.4 shows vacuum phenomena on a sagittal non-enhanced CT scan. Although not routinely utilized in degenerative disc disease, a non-contrast CT of the back may also be useful in the assessment of bulges, focal disc herniations, osteophyte formation, facet arthropathy, and central stenosis.

If a patient's degenerative disc disease does not respond to conservative therapy (see section "Treatment"), further imaging with MRI of the affected spinal region is warranted. The MRI sequence chosen will determine which

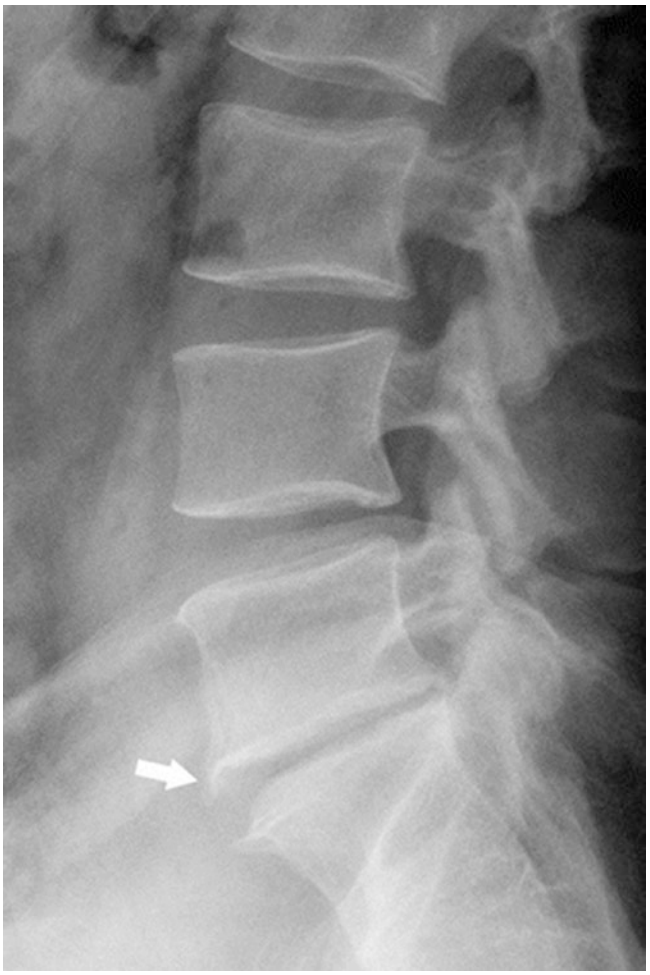

Fig. 14.1 Lateral radiograph of the lumbar spine shows reduction of disc height at L5–S1. Also pictured at L5–S1 are anterior osteophytes (arrow). (Reprinted by permission from Springer Nature: Imaging of Degenerative Disk Disease by Guillaume Bierry, Jean Louis Dietemann. Copyright 2016)

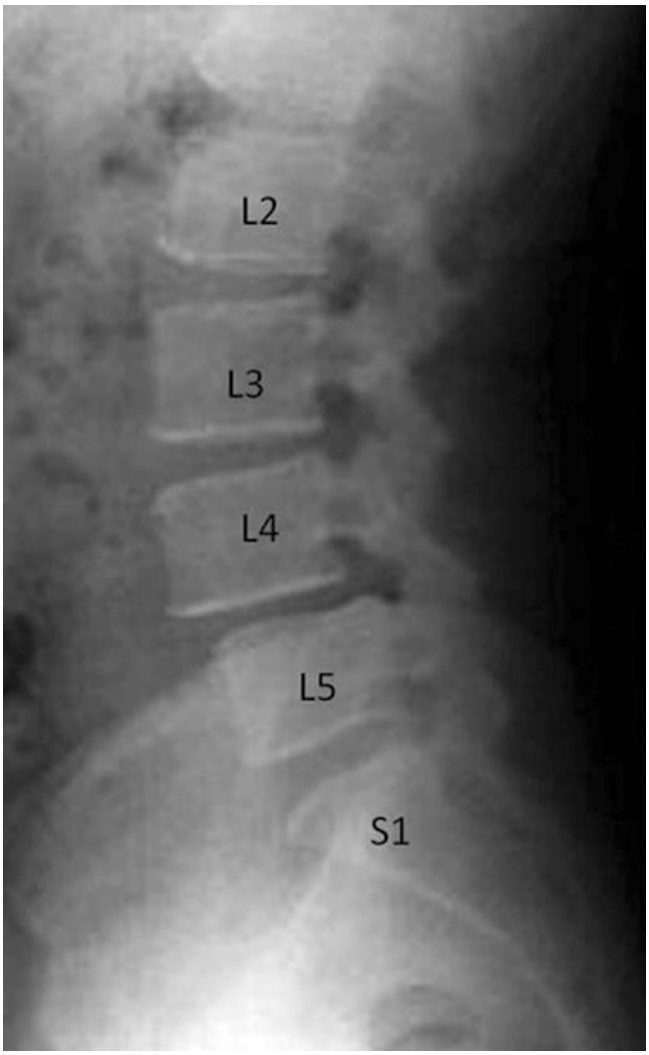

Fig. 14.2 Lateral radiograph of the lumbar spine shows reduction of disc height at multiple levels, most prominently at L4–L5. Also pictured at L4–L5 is spondylolisthesis, where the L5 vertebral body is located posteriorly to the L4 vertebral body. (Reprinted by permission from Springer Nature: Surgical Indications for Lumbar Degenerative Disease by Ravi R. Patel, Jeffrey A. Rihn, Ravi K. Ponnoppan et al. Copyright 2014)

findings of degenerative disc disease can be seen. In T1-weighted images, loss of disc space height, vacuum phenomenon (low signal within the disc), and degenerative end plate changes (graded I to III) can be identified. MRI with contrast and T1-weighted images can reveal discs with linear enhancement or enhancement within Schmorl's nodes. Schmorl's nodes are an upward or downward protrusion of a spinal disc's soft tissue into the bone of an adjacent vertebra and may also suggest the presence of degenerative disc disease on radiologic imaging [12]. In T2-weighted images, loss of signal from the nucleus pulposus can be seen, along with a loss of horizontal nuclear cleft. In addition, degenerative end plate changes can be found (graded I to III) [11, 12]. Figure 14.5 shows a sagittal MRI T2-weighted images with degenerated disc as low signal at L5–S1 compared to normal disc signal intensity at L3–L4 and L4–L5. MRI T2-weighted images may also reveal a hyperintense zone (HIZ) on the posterior annulus fibrosus of the disc, as seen in Fig. 14.6.

Although radiographs and MRI can identify disc pathology, they cannot reliably correlate pathology to clinical symptoms. Discography has historically been utilized as a means of localizing back pain to specific degenerated discs, though it has fallen out of favor due to concerns regarding the possibility of long-term damage that otherwise healthy discs incur during the procedure. This procedure involves the injection of contrast dye into the nucleus pulposus while simultaneously scanning the patient with CT (or fluoroscopic) imaging to identify extravasation of dye [13]. Positive extravasation suggests an annular tear. As the dye is injected, the patient's intra-

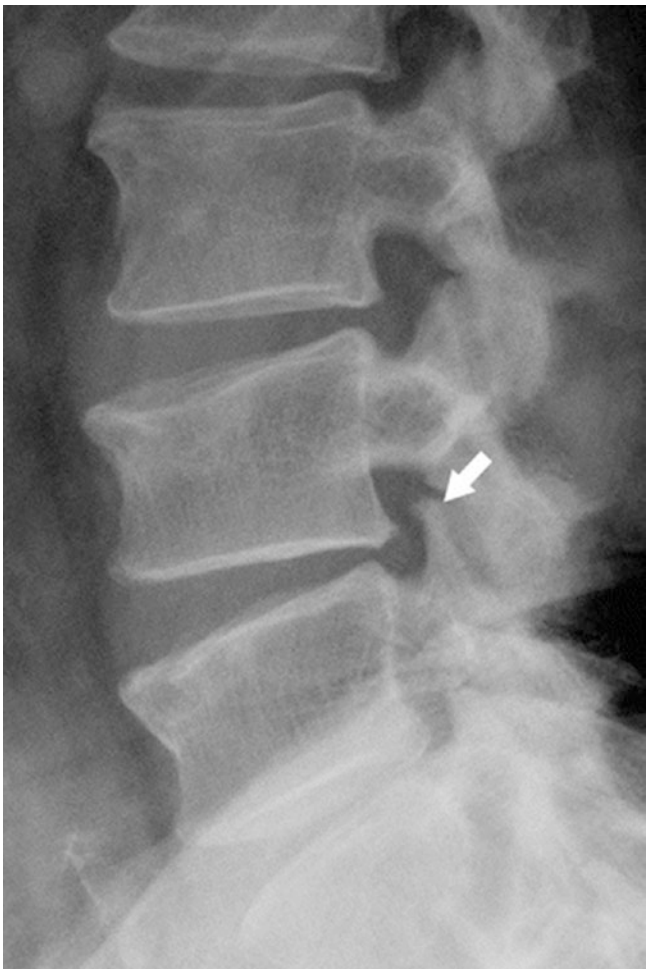

Fig. 14.3 Lateral radiograph of the lumbar spine shows narrowing of the intervertebral foramen in the setting of disc height loss and posterior articulation arthrosis (arrow). (Reprinted by permission from Springer Nature: Imaging of Degenerative Disk Disease by Guillaume Bierry, Jean Louis Dietemann. Copyright 2016)

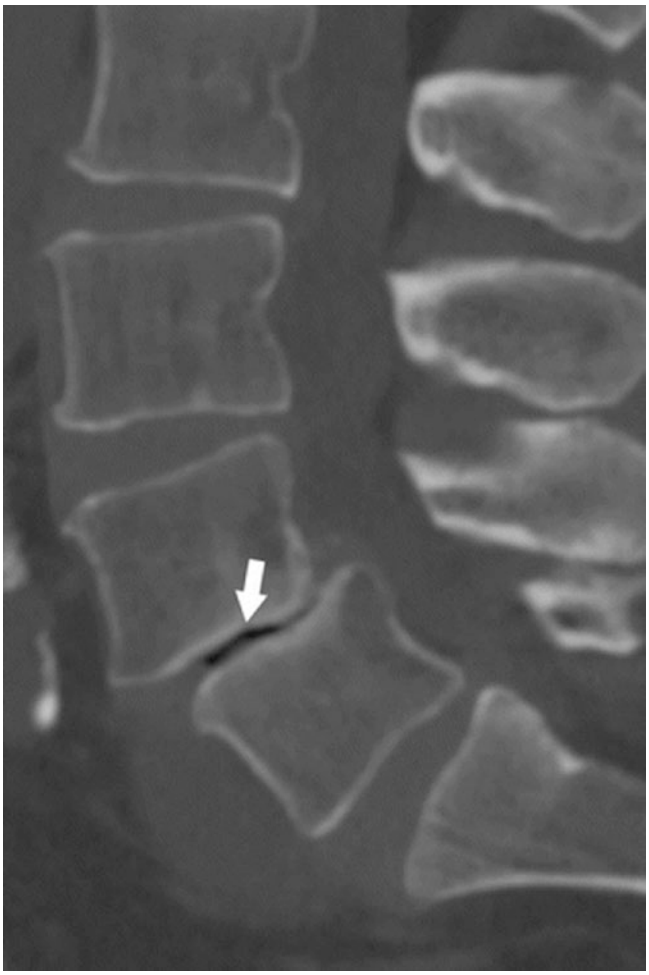

Fig. 14.4 Sagittal computed tomography (CT) of the lumbar spine showing degenerative changes with disc height loss at L4–L5. Also note intradiscal gas (arrow). (Reprinted by permission from Springer Nature: Imaging of Degenerative Disk Disease by Guillaume Bierry, Jean Louis Dietemann. Copyright 2016)

discal pressure is measured, and if pain occurs that is similar to the patient's usual back pain at a low injection pressure, the discogram is concordant [13]. If pain is produced with a high injection pressure or the pain on injection is different from the patient's usual back pain, then this is a discordant study and that particular disc is not likely the source of pain. However, discography has been found to have false-positive rates of up to 25% in asymptomatic individuals.

Treatment

Non-pharmacologic Therapy

Conservative management is the initial treatment strategy for a patient with suspected degenerative disc disease in the absence of alarm symptoms. Depending on the patient's functional status, a 6-week course of supervised physical therapy emphasizing strengthening of core muscles and stretching should be initiated [6, 7]. This would include physical therapy sessions one to two times a week, along with home exercises on all other days. Goals of therapy include improvement in core muscle strength, reduction in load-bearing on the intervertebral discs, and allowance for disc resorption/healing.

Pharmacologic Treatment

In addition, pharmacologic therapy can be initiated during the physical therapy course with nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen. One of the most common over-the-counter or prescribed NSAIDs, ibuprofen, has usual doses ranging from 400 to 800 mg every 6–8 h and a maximum total dose of 3200 mg within 24 h [6]. Caution

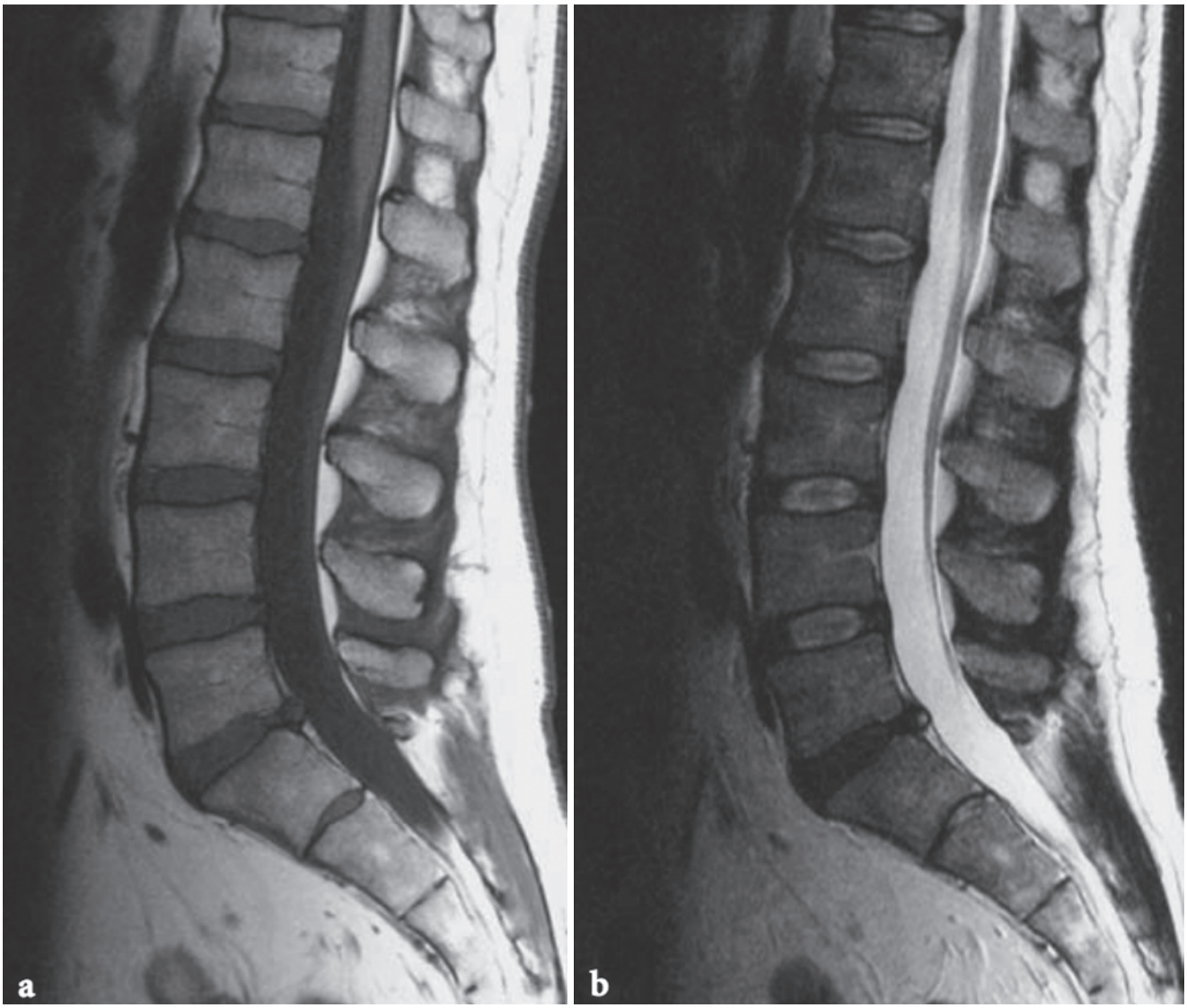

Fig. 14.5 Sagittal MRI images of lumbosacral spine of a 38-year-old man. T1-weighted images (**a**) show disc protrusion at L5–S1 disc. T2-weighted images (**b**) show decrease in signal intensity, suggestive of desiccation, and loss of disc height, which predispose to disc protrusion. Note retention of signal intensity in discs at higher levels such as L3–L4 and L4–L5 levels. (Reprinted by permission from Springer Nature: Degenerative Disc Disease by Paul M. Parizel, Johan W. M. Van Goethem, Luc Van den Hauwe . Copyright 2007)

should be taken when prescribing NSAIDs for patients with a history of renal insufficiency, GI ulcers, or bleeding disorders. Acetaminophen can also be prescribed during the conservative treatment period with a dose of 500–1000 mg every 4–6 h, with a recommended total dose of 3000 mg within 24 h [6]. Patients with mild liver disease should have their dose reduced, while those with moderate to severe liver disease should likely avoid acetaminophen.

Fortunately, many patients respond to conservative therapy, and their symptoms improve significantly. If this occurs, patients should continue home physical therapy exercises and try to reduce usage of NSAIDs and acetaminophen as tolerated, as long-term use can lead to kidney and liver dysfunction, respectively.

Injection Therapy

A conservative therapy modality that may be offered to patients with radicular pain as a result of their degenerative disc disease is an epidural steroid injection. The physician injects steroid medication directly into the epidural space to reduce inflammation of the exiting nerve roots. The steroid medication can be administered directly to the affected side with a transforaminal approach or bilaterally with an interlaminar approach [14, 15]. Literature suggests that epidural steroid injections may provide moderate, short-term pain relief from radicular pain resulting from disc herniation [14]. However, the benefit of epidural steroid injections for chronic non-radiating back pain is less clear.

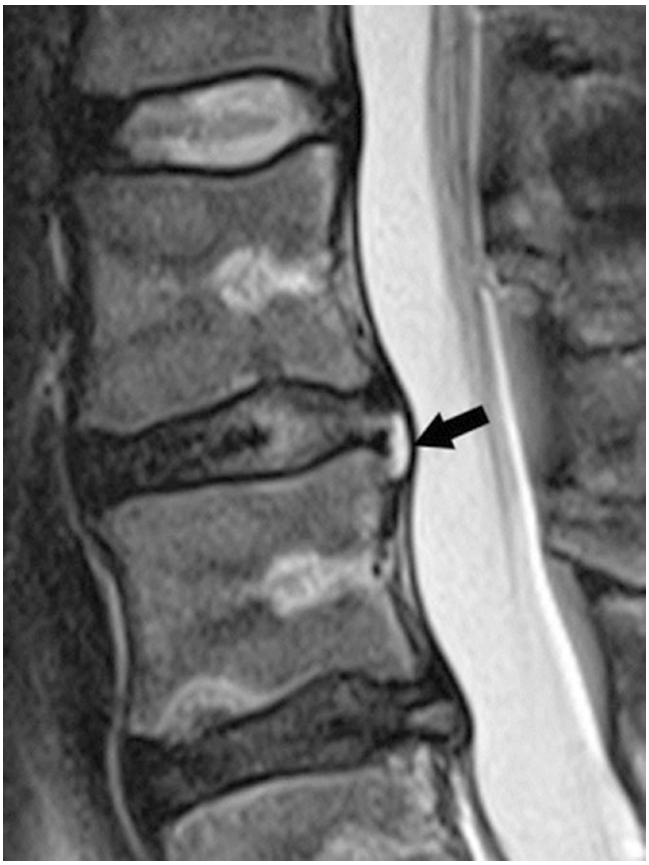

Fig. 14.6 Sagittal MRI images of lumbar spine shows disc degeneration with decrease in signal intensity at L2–L3 and L3–L4 when compared to L1–L2. Also pictured at L2–L3 is a posterior hyperintense zone (HIZ) (arrow). (Reprinted by permission from Springer Nature: Imaging of Degenerative Disk Disease by Guillaume Bierry, Jean Louis Dietemann. Copyright 2016)

Epidural steroid injections, when mixed with local anesthetic, begin to work immediately due to the local anesthetic component in the injectate, but this phase of pain relief usually wears off after a few hours. The onset of pain relief for steroid medication may take up to 2–5 days after the injection, but when effective, treatment with steroid offers sustained relief ranging from a few days to a few months [14, 15]. The goal of an epidural steroid injection is to reduce the patient's pain long enough so that the patient can fully participate in physical therapy and strengthening exercises to ultimately reduce load-bearing stress and improve pain for the long term.

Surgical Intervention

Despite an adequate trial of conservative therapy, some patients will continue to experience an unacceptable level of pain. Patients can choose to avoid activities that elicit pain or opt for surgical intervention. Patients with degenerative disc disease who may benefit from surgical intervention are those specifically with disc herniation or degenerative spinal stenosis [6, 7]. Surgery should likely be reserved for patients with severe pain limiting daily activity, neurologic deficits including lower extremity weakness, or spondylolisthesis. The Spine Patient Outcomes Research Trial (SPORT) compared conservative versus surgical management of lumbar disc herniation and spinal canal stenosis. For patients with lumbar disc herniation who underwent discectomy versus medical management, improvements after 3 months in measures of bodily pain, physical function, and Oswestry Disability Index (ODI) were greater with discectomy [16]. However, after 2 years, these differences narrowed and were not statistically significant.

For patients with lumbar spinal stenosis who underwent decompressive laminectomy, greater improvements were seen in bodily pain, physical function, and the ODI after surgery compared to medical management when assessed at 6 weeks, 3 months, 6 months, and yearly for up to 4 years [17]. However, these benefits diminished in years 4 through 8, with the surgical patients faring no better than those in the medical management group [18]. Thus, patients must be informed that surgical intervention for disc herniation or lumbar stenosis may have favorable outcomes for a number of years, but their pain will likely return. Results for surgery for non-radiating lower back pain are even less predictable.

Summary

Degenerative disc disease represents a broad category of back pain resulting from the degeneration of intervertebral discs. When discs degenerate, whether from aging or excessive or repeated stress, the surrounding axial structures can also be affected, causing pain. These may include the vertebral bodies, facet joints, spinal ligaments, and exiting nerve roots. Thus, symptoms from degenerative disk disease can mirror primary pathology from any of these other structures. It is important for the clinician to elicit a detailed history and physical exam and use appropriate imaging modalities in order to determine the cause of a patient's low back pain. Treatment for degenerative disc disease begins with conservative therapy, including physical therapy and anti-inflammatory oral medications. Epidural steroid injections can also relieve pain, with the purpose of facilitating improved participation in physical therapy and core-strengthening exercises so that stress on the degenerated discs may be reduced. If these conservative therapies fail, surgical options are available for patients with radiculopathy or lower extremity weakness, including discectomy or decompressive laminectomy. Pain relief from these surgeries may be superior compared to medical management in the short term, but the benefits are likely not sustained after

a few years. Thus, degenerative disc disease can pose significant challenges to the physician and patient when multiple strategies for treatment have been attempted.

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Cervicogenic Headache

15

Adam Nassery and Nathaniel M. Schuster

Key Points

- The initial assessment of the headache patient should be focused on ruling out a secondary cause.
- The diagnosis of cervicogenic headache is made based on specific criteria that rely on evidence of causation as well as diagnostic blockade.
- The pathophysiology of cervicogenic headache likely involves cervical nociceptive stimulation relayed via the trigeminocervical complex.
- Noninterventional treatments for cervicogenic headache, including pharmacotherapy and exercise techniques, are supported by limited substantive evidence.
- Interventional treatments for cervicogenic headache include trigger point injections, occipital nerve blockade, medial branch blockade, and radiofrequency ablation.

Introduction

Spine specialists will encounter patients with headache and must be prepared to deliver an adequate evaluation. Cervicogenic headache, while less common than migraine and tension-type headache, is not uncommon with a 1-year prevalence of about 4.1%. It is especially common following whiplash injury. Patients should be examined for underlying myofascial pain, facetogenic pain, and occipital neuralgia. Pharmacotherapy is generally extrapolated from treatments for tension-type headache and myofascial pain. Common interventional treatments for cervicogenic headache include trigger point injections, occipital nerve blocks, and medial branch radiofrequency ablation. One particularly common pain generator in cervicogenic headache is the C2/C3 facet joint, which can be treated with third occipital nerve radiofrequency ablation. In this chapter we explore these forms of treatment and additionally discuss evidence about botulinum toxin and neuromodulation.

Approach to the Patient with Headache

Headache is ubiquitous and has a broad range of etiologies, from benign to life-threatening. The first step in approaching a headache patient is determining whether the headache is secondary to an underlying disease or whether it is a primary headache such as migraine, tension-type headache, or cluster headache. This is ascertained by taking a thorough history and performing a neurologic exam while being aware of potential alarming "red flag" signs and symptoms warranting further diagnostic workup [1].

An adequate headache history focuses on headache onset, characteristics [location, quality, and intensity], duration, frequency, and associated features [1]. Associated features can include migrainous features [photophobia, phonophobia, nausea, vomiting, and visual aura] and autonomic features. Patients may describe both headache triggers and relieving factors such as emotional stress and relaxation techniques, respectively [2].

A detailed physical and neurologic examination is important to detect any alarming signs although the majority of headache patients will present with a normal exam. Abnormalities in vital signs raise concern for a secondary headache such as fever in meningitis or elevated blood pressure in hypertensive encephalopathy. With that being said, a patient may present with hypertension and tachycardia as a result of pain. Body habitus may be a clue toward diagnosis; obesity is a known risk factor for migraine and idiopathic

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intracranial hypertension, while tall and thin features may point toward a connective tissue disorder such as Marfan syndrome which may be a risk factor for spontaneous intracranial hypotension. The presence of a bruit on auscultation of the carotid or vertebral artery can signify the presence of a dissection. Palpable superficial temporal artery tenderness is likely to be present in temporal arteritis, wherein cervical tenderness and decreased range of motion are described in cervicogenic headache. Papilledema on funduscopic exam and cranial nerve palsies may reflect increased intracranial pressure [2]. The remainder of the neurologic assessment consists of mental status, cranial nerves, motor (bulk, tone, strength,), reflexes, coordination, sensation (pain and temperature, vibration and position), and gait exams; derangements in any of these capacities may indicate a lesion somewhere along either the central or peripheral nervous system.

There are four categories of primary headache as per the International Classification of Headache Disorders (ICHD), version 3: migraine, tension-type headache, trigeminal autonomic cephalalgias (TAC), and other uncommon primary headache disorders [3].

Secondary headache is initially considered or excluded in the differential diagnosis based on alarming symptoms in the history or signs on neurologic exam. The following mnemonic, *SNOOP4*, is a useful tool for making this distinction:

Systemic symptoms, signs, and secondary causes
- Fever, chills, myalgias, and night sweats
- Nuchal rigidity, rash, and weight loss
- Immunocompromised state/infection (i.e., HIV), inflammatory disease (i.e., giant cell arteritis), and malignancy

Neurologic symptoms and signs
- Altered mental state, diplopia, loss of consciousness, tinnitus, and visual loss (i.e., IIH)

Onset sudden
- Arterial dissection, cerebral venous sinus thrombosis, reversible cerebral vasoconstriction syndrome, and subarachnoid hemorrhage

Onset older than 50 years
- Infection, inflammatory disease (i.e., giant cell arteritis), and malignancy

Pattern change
- Progressive headache
- Precipitated by Valsalva maneuver (i.e., Chiari malformation)
- Position (i.e., intracranial hypo-/hypertension, neck movements associated with cervicogenic headache)
- Papilledema [4]

Cervicogenic headache has been defined based on two separate, but similar, sets of criteria. In 1998 the Cervicogenic Headache International Study Group put forth the following major criteria:

I. Symptoms and signs of neck involvement:
   (a) Precipitation of head pain, similar to the usually occurring one:
      1. By neck movement and/or sustained awkward head positioning
      2. By external pressure over the upper cervical or occipital region on the symptomatic side
   (b) Restriction of the range of motion (ROM) in the neck
   (c) Ipsilateral neck, shoulder, or arm pain of a rather vague nonradicular nature or, occasionally, arm pain of a radicular nature.

II. Confirmatory evidence by diagnostic anesthetic blockades

III. Unilaterality of the head pain, without sideshift [5]

As per the International Classification of Headache Disorders, 3rd edition, the diagnosis of cervicogenic headache can be made according to the following:

A. Any headache fulfilling criterion C
B. Clinical, laboratory, and/or imaging evidence of a disorder or lesion within the cervical spine or soft tissues of the neck, known to be able to cause headache.
C. Evidence of causation demonstrated by at least two of the following:
   1. Headache has developed in temporal relation to the onset of the cervical disorder or appearance of the lesion.
   2. Headache has significantly improved or resolved in parallel with improvement in or resolution of the cervical disorder or lesion.
   3. Cervical range of motion is reduced, and headache is made significantly worse by provocative maneuvers.
   4. Headache is abolished following diagnostic blockade of a cervical structure or its nerve supply.
D. Not better accounted for by another ICHD-3 diagnosis [3]

Epidemiology of Cervicogenic Headache

The best epidemiological evidence with regard to the prevalence of cervicogenic headache comes from the Vågå study. In this cross-sectional study performed by Sjaastad in 2007, 1838 Norwegian inhabitants of the commune of Vågå were interviewed to establish prevalence data for cervicogenic headache. Of this group, 75 individuals (4.1%)

met the Cervicogenic Headache International Study Group criteria. Forty-one of these participants (2.2%) had exclusively met cervicogenic headache criteria without meeting criteria for another headache disorder as well (termed "core cases"). The remaining 34 (1.8%) composed the "extra" headache group; 23 had migraine without aura, 16 had migraine with aura, and 9 had tension-type headache. Migrainous features in this cohort included nausea and vomiting, photophobia and phonophobia, pulsatile quality, and exacerbation with exercise. Autonomic features were rare and consisted of lacrimation; conjunctival injection and nasal secretion were not reported. While duration and frequency varied greatly, 61% of cervicogenic headache events exceeded 72 hours, and attacks occurred at a mode of 1 per 2–4 weeks. The headache was continuous in 54% of these patients [6].

There was a male predominance (female/male ratio of 0.71) among the 41 subjects with pure cervicogenic headache and a slight female predominance (female/male ratio 1.06) among the entire cohort. In comparison, migraine has a 1-year prevalence of about 12% with a female-to-male ratio of 3:1. In this study the mean age of onset of cervicogenic headache was 32.7 years; migraine age of onset is usually during the teenage years or twenties [6, 7].

In another study, 21.4% of those with cervical spine disease necessitating surgery were found to suffer from cervicogenic headache [8]. Over 50% of patients with whiplash injuries may experience cervicogenic headache [9].

Pathophysiology of Cervicogenic Headache

The anatomy involved in other headache disorders including migraine is likely also involved in the pathogenesis of cervicogenic headache. The trigeminocervical complex contains second-order neurons that receive afferent stimulation from both the meninges and upper cervical roots. Central sensitization of this complex can result from excessive dural stimulation, in the case of migraine, and in turn render hypersensitivity to cervical afferents. Both dural-based and cervical nociceptive sensitization may yield a self-perpetuating circuit wherein neck pain and headache can trigger one another [10]. It is postulated that this pathway is complicit in cervical hyperesthesia that is frequently comorbid with migraine headache [11]. Possible pain-generating structures that can contribute to cervicogenic headache include soft tissues, bones, facets, nucleus pulposus, adjacent neural structures such as the greater occipital nerves (GON) and lesser occipital nerves (LON), cervical nerve roots, and more. Episodic neck pain and cutaneous allodynia can also be symptoms of migraine, potentially mimicking cervicogenic headache [11, 12].

Noninterventional Treatments for Cervicogenic Headache

There is a large and diverse pharmacologic armamentarium for headache treatment, which varies based on headache type. Tables 15.1, 15.2, 15.3, and 15.4 present a series of examples delineated by diagnosis and drug class of both acute management and preventative therapy.

While NSAIDs, antidepressants, antiepileptics, and muscle relaxants are commonly prescribed, there is no substantial

Table 15.1 Acute therapy for migraine [13]

Drug	Class
Acetaminophen	NSAID (nonsteroidal anti-inflammatory drug)
Almotriptan	$5HT_{1B/D}$-agonist
Aspirin	NSAID
Chlorpromazine	Antiemetic
Diclofenac	NSAID
Dihydroergotamine	Ergot alkaloid
Domperidone	Antiemetic
Eletriptan	$5HT_{1B/D}$-agonist
Ergotamine	Ergot alkaloid
Frovatriptan	$5HT_{1B/D}$-agonist
Ibuprofen	NSAID
Metoclopramide	Antiemetic
Metamizol	NSAID
Naproxen	NSAID
Naratriptan	$5HT_{1B/D}$-agonist
Prochlorperazine	Antiemetic
Rizatriptan	$5HT_{1B/D}$-agonist
Sumatriptan	$5HT_{1B/D}$-agonist
Zolmitriptan	$5HT_{1B/D}$-agonist

Table 15.2 Preventative therapy for migraine [14]

Drug	Class
Amitriptyline	Antidepressant
Atenolol	Beta blocker
Candesartan	Angiotensin receptor blocker (ARB)
Coenzyme Q10	Other
Divalproex sodium	Anticonvulsant
Feverfew	Other
Fluoxetine	Antidepressant
Frovatriptan	Triptan
Gabapentin	Anticonvulsant
Lisinopril	Angiotensin-converting enzyme (ACE) inhibitor
Methysergide	Serotonin antagonist
Metoprolol	Beta blocker
Nortriptyline	Antidepressant
Nadolol	Beta blocker
Onabotulinumtoxin A	Neurotoxin
Petasites	Other
Riboflavin	Other
Timolol	Beta blocker
Topiramate	Anticonvulsant
Venlafaxine	Antidepressant

Table 15.3 Acute therapy for tension-type headache [15]

Drug	Class
Acetaminophen	NSAID
Aspirin	NSAID
Caffeine	Other
Ibuprofen	NSAID
Ketoprofen	NSAID
Naproxen sodium	NSAID

Table 15.4 Preventative therapy for tension-type headache [15]

Drug	Class
Amitriptyline	Antidepressant
Mirtazapine	Antidepressant
Tizanidine	Muscle relaxant
Venlafaxine	Antidepressant

evidence supporting the use of oral pharmacotherapy for cervicogenic headache [16, 17].

Trials on exercise techniques for neck pain, including cervicogenic headache, were appraised in a Cochrane Review published in 2015. This review classified the evidence supporting the use of craniovertebral stretch and range of motion exercises as low quality. Additionally, evidence of static and dynamic cervical strengthening and endurance exercises including pressure biofeedback was considered moderate quality [18].

Interventional Treatments for Cervicogenic Headache

Myofascial Pain

Myofascial pain affects millions of Americans and results from excessively shortened or contracted muscle whose focus is localizable to a trigger point. Trigger points are small firm nodules that elicit radiating soft tissue pain on palpation. While this syndrome may result from trauma, strain, deconditioning, or posture, the exact pathogenesis of trigger points is uncertain [19, 20].

Trigger point injections (TPIs) are commonly used therapies which involve needling and may include injecting a medication into the trigger point (Figs. 15.1, 15.2 and 15.3). The most common TPI injectate is composed of local anesthetics, but some practitioners also include corticosteroids [21]. To date there is no clear evidence demonstrating the efficacy of standardized TPIs as a form of monotherapy for myofascial pain [21]. Likewise for the treatment of headache, there is heterogeneity of both pharmacotherapy and technique with a paucity of randomized controlled trials (RCT) [22].

The most commonly chosen TPI location for headache is the trapezius, whose pain is typically referred in an ipsilateral and hemicranial distribution [22, 23]. The trapezius, splenius, and semispinalis capitis as well as cervicum all compose the

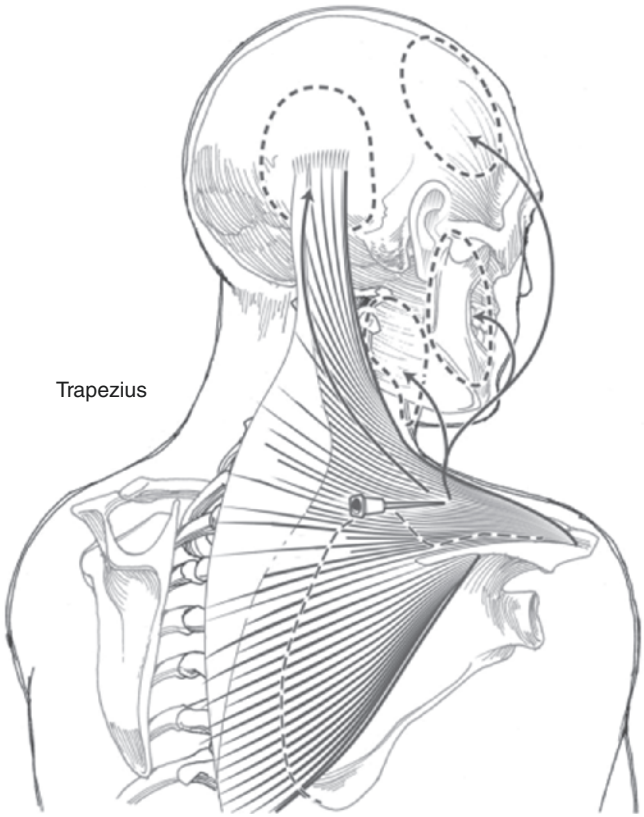

Fig. 15.1 Common trigger point injection location in the trapezius, as indicated by the needle. Pain referral trajectories and destinations are represented by the arrows and dotted lines, respectively. (Reproduced from Robbins et al. [22]; with permission from John Wiley and Sons)

cervical paraspinal muscles. Cervical paraspinals can potentially refer pain in a holocephalic pattern as well as to the shoulders and neck. Frequent tension in the neck, however, may be explained by myofascial pain derived from the levator scapulae. The sternocleidomastoid is another common injection site which potentially refers pain in a circumferentially cranial distribution including the anterior and lateral regions of the neck [22, 23]. Other muscle groups in which trigger point injections can be performed for cervicogenic headache include the temporalis and masseter muscles [22]. In a systematic literature review of the efficacy of dry needling, used interchangeably with acupuncture, for cervicogenic headache, the available evidence was classified as level D (poor) given limited studies on this treatment modality [24].

Botulinum toxin A injection was shown to decrease headache when applied to myofascial pain in cervical and shoulder girdle muscle groups in a randomized, double-blind, placebo-controlled trial in a population enriched for treatment responders. Baseline data on headache prevalence, frequency of headache, and headache diagnosis was not included. In this study, 54 participants responsive to an initial injection of botulinum toxin A in anterior neck flexor and posterior neck extensor muscles were randomized to either a second dose or saline placebo. Subjects

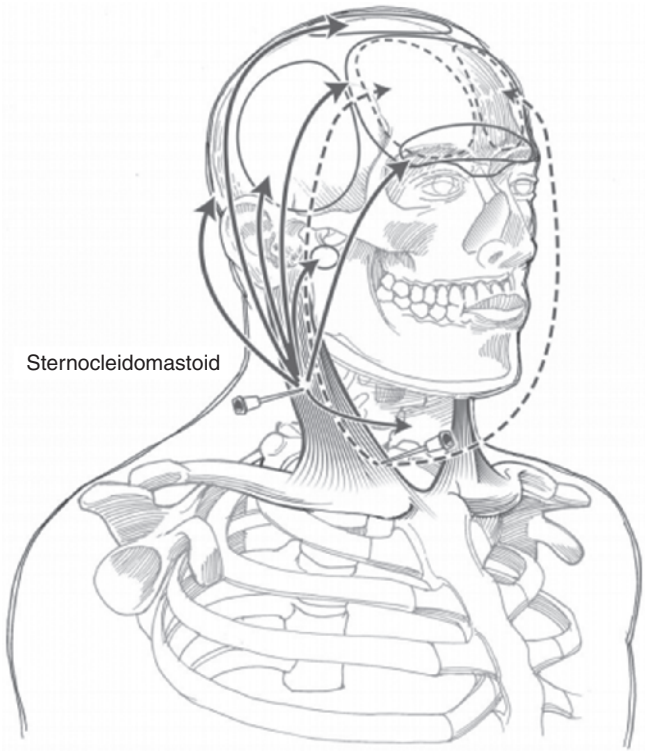

Fig. 15.2 Common trigger point injection locations in the sternocleidomastoid, as indicated by the needles. Pain referral trajectories and destinations are represented by the arrows and dotted lines, respectively. (Reproduced from Robbins et al. [22]; with permission from John Wiley and Sons)

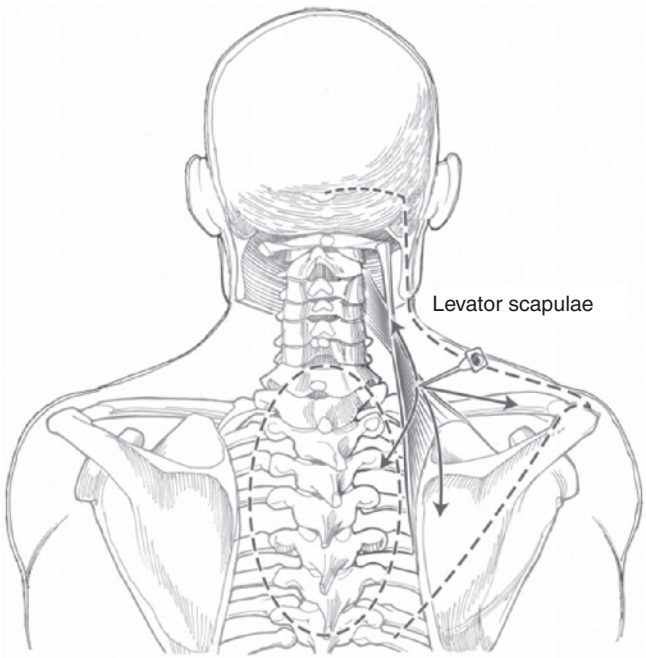

Fig. 15.3 Common trigger point injection location in the levator scapulae, as indicated by the needle. Pain referral trajectories and destinations are represented by the arrows and dotted lines, respectively. (Reproduced from Robbins et al. [22]; with permission from John Wiley and Sons)

received up to 300 units of botulinum toxin A. Headache frequency, duration, and Numerical Scale (NS) pain scores at baseline and 26 weeks were compared as secondary outcome measures. A significant reduction in headaches experienced per week was found in the treatment group in addition to a trend in reduction of worst NS pain scores (p = 0.07); there was no difference in headache duration between the two groups [25]. While only from a single RCT not specifically studying cervicogenic headache, the results of this study suggest that off-label use of botulinum toxin A may be beneficial for cervicogenic headache with concomitant myofascial pain of the neck and shoulder girdle. Unfortunately, access to this treatment is often limited, as botulinum toxin A does not have a US Food and Drug Administration (FDA) indication for myofascial pain or cervicogenic headache.

Occipital Neuralgia, Occipital Nerve Blocks, and Occipital Nerve Stimulation

Occipital pain is present in many headache disorders including migraine and cervicogenic headache. In a retrospective study of 64 patients treated with peripheral nerve blocks for headache management, nearly half of the cohort endorsed GON tenderness [26]. Occipital pain can be referred from other locations via the trigeminocervical complex or may be intrinsic to the distribution of the greater or lesser occipital nerves in the case of occipital neuralgia [27]. Occipital neuralgia (ON) can be unilateral or bilateral and is described by the International Headache Society as paroxysmal shooting or stabbing pain with subsequent dysesthesia [27]. The ICHD-3 diagnostic criteria are as follows:

A. Unilateral or bilateral pain in the distribution(s) of the greater, lesser, and/or third occipital nerves and fulfilling criteria B–D.
B. Pain has at least two of the following three characteristics:
   1. Recurring in paroxysmal attacks lasting from a few seconds to minutes
   2. Severe intensity
   3. Shooting, stabbing, or sharp in quality
C. Pain is associated with both of the following:
   1. Dysesthesia and/or allodynia apparent during innocuous stimulation of the scalp and/or hair
   2. Either or both of the following:
      (a) Tenderness over the affected nerve branches
      (b) Trigger points at the emergence of the greater occipital nerve or in the area of distribution of C2
D. Pain is eased temporarily by local anesthetic block of the affected nerve(s).
E. Not better accounted for by another ICHD-3 diagnosis [3].

There is significant overlap in the symptomatology of occipital neuralgia with other headache disorders. Because of this, the diagnosis may be challenging, rendering the importance of both criteria D and E [27].

Occipital nerve blocks are a nonspecific treatment; they have been found to attenuate migraines [28–31], cluster headaches [32–36], chronic daily headaches [32, 37, 38], and cervicogenic headaches [30, 39–43] along many studies of varying designs, utilizing medications spanning many drug classes. GON blockade has been found to provide immediate, intermediate, and long-term relief for cervicogenic headache [30, 39, 41]. In a single-arm unblinded study of 180 patients with non-whiplash-induced cervicogenic headache, 169 patients experienced full remission of pain lasting a mean 23.5 days when injected depot methylprednisolone in the GON and LON [43]. Occipital nerve blockade was found to yield a 50% improvement from baseline pain intensity in a double-blind RCT using a mixture of lidocaine, bupivacaine, epinephrine, fentanyl, and clonidine for GON, LON, and facial nerve blocks. Cervicogenic headache frequency and duration in addition to accompanying symptoms such as nausea, vomiting, photophobia, phonophobia, appetite, and normal daily activity were all significantly improved as compared to saline placebo [42]. This cohort of 47 patients then underwent a prospective noncomparative stimulator-guided nerve block trial using the same formula at the same anatomic locations. Ninety-six percent of patients achieved continuous pain relief for 6 months; 87% of these patients required repeated injections ranging from 2 to 13 total [41]. Both GON and C2/C3 nerve blockade were found equally effective in decreasing pain frequency and duration in a prospective study of 28 patients with cervicogenic headache. The minimum duration of pain relief was 2 months when using lidocaine 1% followed by bupivacaine 0.25% 1 week after [40].

The above studies were comprehensively reviewed by Ashkenazi et al. in 2010 [44]. In the interim there have been two RCTs displaying significant benefit of GON blockade in chronic migraine, both comparing bupivacaine to saline [45, 46], and two RCTs demonstrating a reduction in cluster headache frequency after suboccipital steroid injections [36, 47].

Another method for treating occipital pain is pulsed radiofrequency (PRF). In a double-blind RCT comparing PRF versus depomethylprednisolone for the treatment of ON and/or migraine with occipital nerve tenderness, average occipital pain among 42 patients had significantly diminished for 6 weeks as compared to 39 patients in the steroid group [48].

Facetogenic (Zygapophysial Joint) Pain

Facet arthropathy is most common in the cervical spine, with estimated point prevalence ranging from 45% to 55% [49, 50]. These patients may complain of axial neck discomfort accompanied by pain radiating in a facet referral pattern with an exam notable for paraspinal tenderness [49]. In a prevalence study utilizing pain maps in 194 patients with cervical facet pain, 36% of symptomatic joints were C2/C3 joints, followed by C5/C6 (35% of symptomatic joints) and C6/7 (17% of symptomatic joints). Fewer than 5% of symptomatic joints were at C1/C2, C3/C4, or C4/C5 [51]. Similarly, those with post-whiplash cervical facet pain were found to predominantly have symptoms emanating from C2/C3 and C5/C6 [52].

The atlanto-occipital joint is a potential pain generator for cervicogenic headache; however it is a rare focus of intervention given its proximity to vital structures. For example, the third segment of the vertebral artery passes posterior to the atlas and at this level has an anatomically variable course. This poses significant risk of unintended needle penetration and catastrophic consequences [53]. Caudally, the lateral atlantoaxial joint is also a potential pain generator for cervicogenic headache and also carries similar opportunities for iatrogenic injuries. Intervention at both locations can result in unintended dural puncture, breach of periforaminal arteries, direct nerve root damage, and spinal cord injury [54, 55].

The C2/C3 facet joint is innervated by the third occipital nerve (TON), which is the superficial medial branch of the C3 dorsal ramus [56]. Whiplash is a common cause of C2/C3 facet arthropathy. In a study in which subjects with whiplash received double-blind, comparative diagnostic TON blocks, the prevalence of TON headache among 100 subjects was 27%; 53% of subjects with headache as their predominant symptom were diagnosed with TON headache [9]. When this research group performed double-blind comparative diagnostic cervical medial branch blocks (MBB) at lower cervical levels in a post-whiplash cervical zygapophysial joint pain prevalence study, 31 of 52 patients (60%) suffered pain localizable to C2/C3 and below. Pain emanating from C2/C3 was found in 50% of patients with headache as the predominant symptom [52].

TON blocks and cervical MBBs serve to localize the origin of a patient's pain and prognosticate response to radiofrequency ablation (RFA). MBBs may be a final treatment step in those with long-standing analgesia, whereas RFA is offered to those whose relief from MBBs is transient [9, 57]. In a cadaveric study exploring a series of commonly recommended injectate volumes for ultrasound-guided TON blocks, vertical injectate spread was greater than the distance between the TON and GON using both 0.3 and 0.5 mL of methylene blue. A volume less than 0.3 mL was recommended for use given the likelihood of concomitant blockade at a greater quantity and thus lower specificity when evaluating patients for RFA [57].

The evidence supporting RFA for chronic C2/C3 facet pain is limited. While C2/3 RFA was at one time considered to be a technically difficult intervention, these difficulties

were overcome by increasing electrode diameter, fluoroscopically monitoring electrode placement, and allowing for no uncoagulated tissue between consecutive lesions. In a prospective observational study, 49 patients underwent RFA of TON after meeting the inclusion criterion of positive comparative diagnostic C2/C3 MBBs. Forty-three of forty-nine patients reported complete analgesia for at least 90 days, an initial success rate of 88% [58].

There have been two negative RCTs evaluating medial branch RFA for cervicogenic headache; however neither used MBB response to determine RFA candidacy. Stovner and colleagues randomized 12 subjects with cervicogenic headache to either C2–C6 medial branch RFA versus sham [59]. Haspeslagh et al. randomized 15 subjects to a protocol of C3–C6 facet joint denervation followed by dorsal root ganglion denervation based on physical exam and diagnostic blockade when necessary [60]. The remaining 15 subjects received GON blocks with local anesthetics and steroids followed by transcutaneous electrical nerve stimulation if needed.

Neuromodulation

Occipital nerve stimulation (ONS) and high cervical spinal cord stimulation may be considered for refractory cervicogenic headache. ONS has not been studied in cervicogenic headache, rather primarily in chronic migraine and to a lesser degree in cluster headache, short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT), and short-lasting unilateral neuralgiform headache attacks with cranial autonomic features (SUNA). There have been three RCTs studying ONS for refractory chronic migraine; all of these studies have shown promise in a minority of patients; however none have met their prespecified primary endpoints. Furthermore, lead migration rates were high [61–67].

High cervical spinal cord stimulation has also shown promise in small, single-arm studies for intractable migraine and cluster headache [68]. Neither of these neuromodulatory approaches have been studied to date in cervicogenic headache.

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Infectious and Autoimmune Disease and Spine Pain

16

Shane J. Volney

Key Points

- Inflammatory autoimmune disorders of the spine are a broad group of conditions with variable associated peripheral and extra-articular involvement.
- Inflammatory autoimmune conditions involving the spine are often initially misdiagnosed as mechanical back pain, especially during earlier stages of disease onset.
- Clinical history of prolonged morning stiffness, nocturnal pain, peripheral or extra-articular-associated features, elevated inflammatory markers, or family history of autoimmune disorders should prompt suspicion for autoimmune inflammatory sources of spine pain.
- Early diagnosis and treatment of inflammatory autoimmune spine conditions can significantly improve functional outcomes, quality of life, and deleterious complications of disease progression.
- Although spinal infections are relatively rare, delayed diagnosis can result in significant morbidity and mortality if left untreated.
- Initial clinical manifestations of spinal infections are often vague and nonspecific. Given the deleterious consequences of delayed treatment, the critical initial step for clinicians is to consider infection early in the differential diagnosis of patients with back pain and risk factors for spinal infection development.

Autoimmune Disease and Spine Pain

Autoimmune disorders of the spine are a diverse group of chronic inflammatory immune-mediated conditions with variable associated peripheral, axial, and extra-articular involvement. Autoimmune conditions associated with the spine, particularly in the early stages of disease, often present with nonspecific clinical features that are not uncommonly misdiagnosed as mechanical back pain. Delay in diagnosis is therefore common, resulting in exacerbated disease sequelae, unnecessary diagnostic procedures, and delay in efficacious therapies. Early identification of autoimmune inflammatory conditions can significantly improve functional outcomes and quality of life and minimize deleterious disease-related complications [1]. This chapter will review common inflammatory immune-mediated diseases affecting the spine including relevant pathogenesis, epidemiology, clinical features, diagnosis, and treatment.

Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disorder affecting the synovium of joints leading to joint deformity, destruction, and instability [2]. RA is the most common inflammatory arthritis, with an incidence of 0.5–1%, affecting women two to three times more often than men. Although RA can present at any age, onset typically begins between 30 and 50 years of age with peak incidence between the fourth and sixth decades [2]. The cause of RA is not well understood, but it is suspected to involve an inflammatory autoimmune response against the synovium triggered by a complex interplay between environmental and genetic factors in genetically susceptible individuals [3]. Affected joints histologically show inflammation of the synovium with infiltrate consisting of lymphocytes, polymorphs, and macrophages with release of numerous inflammatory cytokines including IL-1, IL-6, and tumor necrosis factor, among other mediators. Osteoclast activation and

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production of proteases result in destruction of ligaments, bone, tendon, and cartilage over time.

After the joints of the hands and feet, the cervical spine is the most common region involved in RA and is the most common inflammatory arthritis affecting the cervical spine [4, 5]. Although any region of the cervical spine can be involved in RA, the occipitoatlantoaxial junction is most often affected due to the predominantly synovial characteristics of the joint [6]. Atlantoaxial subluxation may occur in up to 49% of patients with RA and is the most common cervical lesion in patients with RA [5]. Pannus, inflammatory granulation tissue that forms over synovial cells in RA, may form in the odontoid region of the atlantoaxial joint, in some instances resulting in spinal cord compression over time [5]. Subaxial cervical involvement can occur late in the disease course, characterized by destruction and erosion of cervical zygapophyseal joints, interspinous ligament, and the discovertebral junction at multiple levels leading to anterior subluxation. Severe subaxial cervical subluxation can cause cervical spine instability and neurologic impairment from compression of the spinal cord, nerve roots, or vertebral arteries [5].

Clinical Features

RA classically presents with morning stiffness, symmetric inflammatory polyarthritis, and constitutional symptoms such as fatigue, anorexia, and low-grade fever [2, 7]. Clinical features vary from one patient to another; however, the most common mode of onset is the insidious development of symptoms over weeks to months commonly accompanied by prodromal symptoms such as fatigue, low-grade fever, or anorexia [2, 7]. Joints commonly involved include joints of the hands [proximal interphalangeal and metacarpophalangeal joints], elbows, knees, ankles, and metatarsophalangeal joints [8]. The chronic inflammatory process can eventually lead to irreversible destruction of cartilage and bone resulting in debilitating joint deformities and contractures, most often involving the hands.

Neck pain is a common clinical manifestation of RA involving the cervical spine, occurring in 40–80% of patients, although cervical changes may be asymptomatic. Cervical pain is characteristically described as deep, aching cervical pain and stiffness that may radiate to the occipital, retro-orbital, or temporal regions [5]. Patients with subluxation may report difficulty with maintaining an upright head posture or the sensation of the head falling forward during neck flexion [5]. Neurologic deficits on exam are less frequent than pain, reported in 7–34% of patients [5]. Neurologic signs and symptoms are highly variable and may include radicular pain, focal motor weakness, sensory loss, spasticity, changes in reflexes, gait disturbances, or evidence of myelopathy. The thoracolumbar spine or sacroiliac joints are rarely involved in RA, unlike most other forms of chronic inflammatory diseases affecting the spine.

Diagnosis

Diagnostic criteria, such as those published by the American College of Rheumatology (ACR) and European League Against Rheumatism (ELAR), can be useful as a frame of reference in the diagnosis of RA (Table 16.1). The characteristic symmetric inflammatory polyarthritis and typical serologic findings may not be evident in earlier stages of disease onset; therefore, the diagnosis of RA may be presumptive early in the disease course. Despite the variability in clinical presentation, findings of inflammatory synovitis (synovial fluid leukocytosis, histologic evidence of synovitis, or radiographic evidence characteristic of erosions) and exclusion of other causes of synovitis should be considered when establishing diagnosis of RA [3].

There are no laboratory tests, histologic findings, or radiographic features pathognomonic for RA; rather a constellation of findings may serve to support diagnosis and clinical findings. Routine laboratory data may demonstrate anemia of chronic disease, occurring in 33–60% of patients with RA [3]. Inflammatory markers including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are often elevated in active RA, although these markers are nonspecific for RA. Rheumatoid factor (RF) is present in about 80% of patients with RA but also may be present in other diseases and a minority of the healthy population. Anticitrullinated peptide protein antibodies (ACPA) have a sensitivity of 50–75% and specificity of over 90% in RA.

Routine screening of patients with RA should include cervical plain film series, including anteroposterior, lateral, open mouth, and flexion-extension views to identify odon-

Table 16.1 2010 ACR/EULAR classification criteria for rheumatoid arthritis[a]

Joint distribution (0–5)	Score
1 large joint	0
2–10 large joints	1
1–3 small joints	2
4–10 small joints	3
>10 joints	5
Serology (0–3)	
Negative RF and negative ACPA	0
Low-positive RF and low-positive ACPA	2
High-positive RF or high-positive ACPA	3
Symptom duration (0–1)	
<6 weeks	0
≥6 weeks	1
Acute phase reactants (0–1)	
Normal CRP and normal ESR	0
Abnormal CRP or abnormal ESR	1

Patients with score of ≥6 (of a possible 10) are classified as having rheumatoid arthritis

ACPA anticitrullinated protein antibody, *ACR/EULAR* American College of Rheumatology/European League Against Rheumatism, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *RF* rheumatoid factor

[a]Adapted from Aletaha et al. [73]

toid erosions, subluxation, apophyseal joint erosions, and disc narrowing [5]. Plain cervical radiographs should also be considered for patients undergoing general anesthesia to evaluate for instability. For patients with neurologic deficits, cervical spine MRI is the imaging modality of choice, allowing for thorough visualization of pannus, ligaments, erosive changes, and changes affecting the spinal cord, nerves, and bone. Radiographs of the hands and feet should be performed to evaluate for erosive periarticular erosive changes [3].

Treatment

Goals of treatment include relieving pain and swelling, minimizing joint damage, and preventing disability and disease-related morbidity [3]. Disease-modifying antirheumatic drugs (DMARDs) such as methotrexate should be initiated early in the disease course (often at time of diagnosis) given the benefits with treatment, including reduced morbidity and mortality, slowing of disease progression, and preserved joint function. Treatment may also involve nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroids for controlling pain and inflammation, but they do not prevent tissue injury or joint damage. Operative management is reserved for patients with cervical subluxation with signs of serious or progressive neurologic deficits, cervical spine instability, intractable pain, or disease resulting in vertebral artery compromise. The most common surgical procedure performed for RA is C1-C2 fusion followed by occipitocervical fusion [5].

Spondyloarthritis

Axial spondyloarthritis (axial SpA) is a group of chronic inflammatory diseases involving the sacroiliac joints (sacroiliitis) and spine (spondylitis) that share common clinical and genetic features [9]. Axial SpA falls under the broader spectrum of SpA, a phenotypically diverse group of inflammatory disorders that are further categorized into axial and peripheral spondyloarthritis, depending on the joint distribution pattern and predominance of clinical manifestations. Some SpA phenotypes, such as psoriatic arthritis, reactive arthritis, and enteropathic arthritis, may fall under either peripheral or axial SpA depending on the predominance of clinical manifestations.

Axial SpA characteristically presents with morning pain and stiffness involving the axial skeleton (sacroiliac joints and spine), asymmetric peripheral arthritis, enthesitis, and variable extra-articular clinical manifestations such as uveitis, psoriasis, or inflammatory bowel disease [9]. In ankylosing spondylitis, a form of axial spondyloarthritis, the progressive course of disease can lead to irreversible spinal immobility, joint damage, and functional impairment that can have profound impact on quality of life. Historically, an average of 10 years delay from time of clinical onset to diagnosis of axial SpA has resulted in exacerbated disease sequelae, unnecessary diagnostic procedures, inappropriate management, and delay in efficacious therapies [10, 11]. Prompt diagnosis of axial SpA and referral for targeted treatment are associated with improved quality of life and functional outcomes [12].

Axial SpA is comprised of two subtypes: ankylosing spondylitis (AS) and nonradiographic axial SpA (nr-Axial SpA) [13]. AS is defined by the presence of sacroiliac joint structural changes on plain radiographs, whereas nonradiographic axial SpA shows no radiographic evidence of sacroiliac disease, but diagnosis is supported by evidence of sacroiliac joint inflammation detected on MRI or the presence of human leukocyte antigen HLA-B27 in combination with other clinical features typical of spondyloarthritis (Table 16.2) [9]. These radiographically defined variants, however, are similar in regard to pain burden, disease activity, extra-articular manifestations, and impairment in quality of life [14, 15]. In upwards of over two-thirds of patients with nonradiographic axial SpA may go on to develop radiographic evidence of sacroiliitis within 20 years of disease duration [16]. It is unclear if AS and nonradiographic spondyloarthritis represent distinct overlapping disorders or a single entity along a continuum with varying chronicity and severity [13]. In clinical practice, distinction between the

Table 16.2 ASAS classification criteria for axial spondyloarthritis (SpA)

Patients with ≥3 months back pain and age at onset <45 years with: sacroiliitis on imaging[A] plus ≥1 SpA feature[B] or HLA-B27 plus ≥2 other features[B]	
A. Sacroiliitis on imaging:	B. SpA features:
Active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA	Inflammatory back pain
	Arthritis
	Enthesitis (heel)
Definite radiographic sacroiliitis according to Modified New York criteria	Uveitis
	Dactylitis
	Psoriasis
Classification as AS requires clinical criteria for SpA and radiographic sacroiliitis ≥ grade 2 bilaterally *or* grade 3 or 4 unilaterally[a]	Crohn's/ ulcerative colitis
	Good response to NSAIDS
	Family history of SpA
	HLA-B27 positivity
	Elevated CRP

Adapted from Sieper et al. [74]

AS ankylosing spondylitis, *ASAS* Assessment of Spondyloarthritis International Society, *CRP* C-reactive protein, *HLA-B27* human leukocyte antigen B27, *MRI* magnetic resonance imaging, *NSAIDS* nonsteroidal anti-inflammatory drugs, *SpA* spondyloarthritis

aModified New York radiographic sacroiliitis grading: 0, normal; 1, suspicious changes; 2, sclerosis and minor erosions; 3, severe erosions, joint space widening, some ankylosis; and 4, complete ankylosis

subtypes of axial spondyloarthritis has little impact on management and may not be relevant outside of clinical research interests [13]. Clinical suspicion for SpA, regardless of phenotype, should trigger prompt, early referral to a rheumatology specialist to facilitate early diagnosis and initiate appropriate therapies [9].

Axial SpA typically presents with insidious, progressive spine stiffness beginning in adolescence or young adulthood, most commonly occurring in the third decade of life, with a male to female ratio of 2–3:1 for radiographic evident disease (AS) and 1:1 for nonradiographic evident forms (nr-Axial SpA) [17]. The prevalence of axial spondyloarthritis is estimated to be about 0.09–1.4% in the United States [18]. The underlying pathogenesis of axial SpA is not completely understood, but strong evidence supports a genetic factor to play a role in disease susceptibility together with environmental triggering factors, thought to trigger release of pro-inflammatory cytokines in genetically predisposed individuals [19]. Nearly 90% of patients with AS and 70% of patients with axial SpA are positive for HLA-B27, although only about 10% of patients positive for HLA-B27 in the general population develop axial SpA [9].

Clinical Features

Axial SpA typically presents in early adulthood with low back and buttock pain for greater than 3 months, accompanied by morning stiffness (due to sacroiliitis) for at least 1 hour, that improves with exercise [19]. Since back pain is a rather ubiquitous presenting symptom in the general population, it is important for clinicians to identify and distinguish inflammatory back pain symptoms from non-inflammatory back pain typically exhibiting at least four of the five clinical features (Table 16.3). Spinal stiffness and loss of spinal mobility begin in the lumbar spine and characteristically ascend to the spine over the course of years, sometimes involving the thoracic and cervical regions of the spine late in the disease course.

Table 16.3 Inflammatory versus mechanical back pain clinical features (>3 months)

Features	Inflammatory back pain[a]	Mechanical back pain
Age at onset	<40 years	Any age
Onset type	Insidious	Variable
Improvement with exercise or activity	Yes	No
Improvement with rest	No	Yes
Pain at night (with improvement upon getting up)	Yes	No

Adapted from Sieper et al. [74]

aFour out of five clinical features commonly present in patients with inflammatory back pain. Inflammatory back pain may also include morning stiffness lasting ≥60 min, in contrast with mechanical back pain, typically lasting ≤30 min

Inflammatory changes in axial SpA characteristically affect ligament and tendon insertion sites into bone (enthesitis) producing focal pain, stiffness, and tenderness at bony insertion sites. The most commonly occurring peripheral sites of enthesitis in axial SpA include the calcaneal attachments of the Achilles tendon, plantar fascia of the foot, costochondral junctions of the chest wall, and supraspinatus tendon insertion into the greater tuberosity of the humerus over the shoulder [6, 19]. Up to one-third of patients have peripheral joint arthritis, frequently involving the hips, shoulders, elbows, knees, and ankles. Dactylitis (sausage digits), or swelling of the toes and/or fingers, may be present in either AS or nr-axial SpA presentations [20]. Extra-articular manifestations associated with axial SpA include acute anterior uveitis, inflammatory bowel disease, and psoriasis [21]. Less common extra-articular features may include cardiovascular disease [conduction abnormalities, acute coronary syndrome, and aortic root disease] and pulmonary fibrosis [22, 23].

Axial SpA, particularly AS, progressively alters the strength and biomechanical properties of the spine, causing an increased risk for spinal cord injury and neurologic manifestations, even with minor low-energy trauma [24]. AS is associated with vertebral bone loss and vertebral fractures due to trauma, occurring at least twice as frequently as the general population [25]. Spinal cord or nerve compression can occur due to spinal fracture and spontaneous subluxation of spinal joints. Patients with AS are at risk for delayed diagnosis of spinal cord injury and neurologic compromise, especially after minor trauma; therefore a high index of suspicion and thorough neurologic examination is warranted when evaluating patients with any form of spondyloarthritis involved in trauma [24, 26].

Physical exam findings are nonspecific for axial SpA and are often more helpful in monitoring disease progression than diagnosis [6]. Examination may reveal decreased range of motion of the lumbar, thoracic, or cervical spine, although considerable variability is common. Postural abnormalities such as increased cervical flexion, increased thoracic kyphosis, loss of lumbar lordosis, and hyperkyphotic lumbar deformities causing a stooped posture can occur in later stages of patients with AS. Other findings may include tenderness over the sacroiliac joints, flexion deformities of the hips, peripheral joint synovitis, dactylitis, evidence of psoriasis on the skin, eye redness or pain, or entheseal site tenderness, most commonly in the heel.

Laboratory findings are of limited benefit in the diagnosis of AS. Inflammatory markers including ESR and CRP may be elevated indicating active inflammatory disease, but neither is sensitive nor specific. The presence of HLA-B27 is not specific for axial SpA and may be positive in patients in a minority of patients in the general population.

For further classification of axial SpA as ankylosing spondylitis (AS), sacroiliac joint changes on plain radiographs

are a key component of diagnosis in combination with other suggestive clinical features of axial spondyloarthritis (see Table 16.2) [6]. While the low cost and wide availability of plain films of the pelvis make them a useful first-line imaging modality when sacroiliitis is detected, radiographic changes may not be seen early on in the disease course. Even after 10 years, only about 40% of patients with AS have objective radiographic signs of sacroiliitis on plain films [6]. If clinical suspicion of AS is high and there are no signs of sacroiliac joint pathology on plain radiographs, then MRI of the pelvis is a significantly more sensitive imaging modality that may aid in earlier diagnosis of spondyloarthritis.

Diagnosis

The progressive, irreversible loss of spinal mobility, functional impairment, and deleterious impacts on quality of life with axial SpA conditions can be profound, especially when diagnosis and appropriate management is significantly delayed. There is wide variability between the time of clinical onset of symptoms and diagnosis of AS, some studies reporting 5–10 year delays or longer, especially in females [6]. Axial SpA, particularly in early stages of the disease, often presents with nonspecific clinical features that are not uncommonly misdiagnosed as mechanical back pain (see Table 16.3). Therefore, clinical features suggestive of inflammatory back pain or chronic back pain in patients positive for HLA-B27 should be considered for rheumatologic referral for further diagnostic evaluation [6].

Clinical diagnosis is based on a combination of history, physical examination, laboratory data, and diagnostic imaging [27]. Based on the Assessment of Spondyloarthritis International Society (ASAS) classification criteria for axial spondyloarthritis, diagnosis is established in patients with back pain for at least 3 months with onset before the age of 45 years, who have sacroiliitis confirmed on MRI or plain radiographic imaging and who have at least one clinical or laboratory finding characteristic for spondyloarthritis. These features include inflammatory back pain, heel pain (enthesitis), dactylitis, uveitis, positive family history of axial spondyloarthritis, positive response to nonsteroidal anti-inflammatory drugs (NSAIDs), and elevated ESR or CRP (see Table 16.2) [27]. Alternatively, patients who are positive for HLA-B27 plus two features characteristic for spondyloarthritis would also suggest diagnosis.

Management

Early multidisciplinary care coordinated by a rheumatologist is recommended for optimal management of patients with axial SpA or AS. First-line treatment for pain usually involves NSAIDs with physical therapy for posture, extension exercises, and symptomatic relief. Biologic tumor necrosis factor inhibitors (anti-TNF) have been shown to be effective in improving symptoms and daily function. Corrective spine surgery is rarely necessary and reserved for severe debilitating spinal deformities. Extra-spinal manifestations such as uveitis, severe joint arthritis, and myocardial conduction abnormalities require prompt evaluation and management by appropriate specialists.

Reactive Arthritis

Reactive arthritis (ReA) is an inflammatory arthritis characterized by aseptic peripheral arthritis triggered by infections of the genitourinary or gastrointestinal tracts [28]. It is categorized as a form of SpA and can be associated with inflammatory back and/or sacroiliac joint pain. Historically, Reiter's syndrome has been used synonymously with ReA; however, it was later recognized that Reiter's syndrome is a subset of the broader category of ReA [29].

Reactive arthritis is thought to occur due to an immune response to infection resulting in cross-reactivity with endogenous antigens causing inflammation in joints and the eyes. Reactive arthritis affects men three times more than women, a majority of which are young adults within the ages of 20 and 40. Like other forms of SpA, ReA is believed to have a genetic component that predisposes individuals to infectious triggers, with HLA-B27 positive in 50–80% of patients with ReA [29, 30]. Common triggering organisms of the genitourinary and gastrointestinal tract include [but are not limited to] *Chlamydia*, *Shigella*, *Salmonella*, *Yersinia*, and *Campylobacter* species [28].

Clinical Features

Clinical features typically present with asymmetric arthritis 1–4 weeks after venereal infections or gastroenteritis, with new joints often sequentially involved over subsequent days. Affected joints are preferentially more involved in the lower extremities and often present as swollen, warm, tender, and painful with active and passive range of motion. Peripheral and systemic features common among SpA conditions may be associated, such as enthesitis, dactylitis, fatigue, malaise, fever, and weight loss. Skin manifestations are reported in 5–10% of patients with ReA including keratoderma blennorrhagica, a scaly rash on the palms and soles, later appearing as scaly patches that can resemble psoriasis [30]. Conjunctivitis is also reported in 30% of patients [30].

Diagnosis

Reactive arthritis is a clinical diagnosis, based on disease manifestations and laboratory findings. ReA should be considered, especially in young adults who present with acute asymmetric oligoarthritis, involving joints of the lower extremities with sequential progression from one joint to another after recent genitourinary or gastrointestinal illness. Synovial fluid analysis of affected joints can help rule out

infectious sources of arthritis or crystals. Testing for HLA-B27 may help support the diagnosis, but it is not present in all patients with ReA. Serologic testing for rheumatoid arthritis including rheumatoid factor and anti-cyclic citrullinated peptide antibody testing for patients with possible rheumatoid arthritis are both usually absent in reactive arthritis. There are no specific imaging findings characteristics of ReA. Radiographic abnormalities are usually limited to non-specific findings associated with joint inflammation, and in some instances, radiographic evidence of sacroiliitis [31].

Treatment

The clinical course of ReA is usually self-limited, lasting 3–12 months. However, nearly half of patients have recurrent episodes, and 15–30% develop chronic sacroiliitis [28]. NSAIDs are considered first-line therapy for symptomatic relief of joint pain and inflammation. Inadequate response of articular symptoms with NSAIDs may lead to consideration of intra-articular steroid injections for symptomatic relief. In more chronic refractory conditions, sulfasalazine and immunosuppressive agents such as azathioprine may be effective. Antibiotic therapy may provide benefit in the setting of chlamydial infection; however, the long-term antibiotic use in most cases of ReA is controversial and has not been shown to be effective in most clinical trials [28, 32].

Psoriatic Arthritis

Psoriatic arthritis (PsA) is a chronic inflammatory arthritis that may occur in 10–30% of patients with psoriasis [33–35]. PsA is classified as a form of SpA sharing similar clinical and genetic features. The prevalence of psoriatic arthritis ranges from 6 to 25 cases per 10,000 people in the United States, occurring equally among men and women [35]. PsA can begin during childhood, but onset most often occurs in patients between the ages of 30–50 years [35, 36]. Like other forms of SpA, PsA is thought to be an aberrant immune response triggered by environmental factors in genetically susceptible individuals. In PsA, the immune response appears to have parallel mechanisms occurring in the joints and skin. Inflammatory infiltrates containing CD4+ and CD8+ T-cells support that T-cells play a role in PsA and psoriasis pathogenesis. Destructive joint features involve various inflammatory cytokines and chemokines including TNF, interleukin (IL)-23, IL-17, and IL-13, leading to joint disruption and osteoclast formation [35, 36].

Clinical Features

There are five clinical subtypes of PsA: polyarticular (five or more joints affected); oligoarticular (four or fewer joints affected), distal interphalangeal (DIP); arthritis mutilans; and axial or spondyloarthritis primarily involving the spine and sacroiliac joints [28, 35]. The oligoarticular pattern subtype is the most common accounting for more than 70% of cases [28].

Skin manifestations of psoriasis, characterized by erythematous plaques covered by thick silvery scaling on extensor surfaces, often develop over months to years before the onset of arthritis in a majority of patients. PsA is usually asymmetric, affecting predominantly distal joints (PIP and DIP joints) especially in the upper extremities, helping to distinguish PsA from rheumatoid arthritis. Nail changes such as pitting and onycholysis are present in 80–90% of patients with PsA [37, 38]. Axial spine involvement presenting with features of morning stiffness and inflammatory back pain occurs in more than 40% of patients with SpA [35, 39]. Other presenting features may include clinical manifestations found among other forms of spondyloarthritis such as dactylitis and enthesitis.

Diagnosis

Diagnosis of PsA is made clinically in patients with typical psoriatic skin and nail lesions, absence of rheumatoid factor, and clinical evidence of joint inflammation. There are no diagnostic laboratory findings, imaging abnormalities, or clinical features that are pathognomonic for PsA. Laboratory findings commonly positive in RA, such as rheumatoid factor and anti-cyclic citrullinated peptide antibodies, are negative in 95% of patients with PsA, but may be present in a minority of cases [35]. Plain films of peripheral joints may show evidence of bone loss with eccentric erosions and joint space narrowing and new bone formation characterized by periostitis. Radiographs of the spine may reveal unilateral sacroiliitis [in contrast to bilateral sacroiliitis in AS] and paramarginal syndesmophytes [thin spicules bridging vertebral bodies, also seen in patients with AS] [35]. For patients with unclear skin manifestations, a skin biopsy may help differentiate psoriasis from other types of skin lesions [40].

Treatment

Treatment of PsA includes managing both skin and arthritis manifestations. The general principles of treating joint-related inflammation and pain is similar to other SpA conditions. For mild inflammatory pain, NSAIDs therapy occasionally combined with intra-articular injections when needed is effective in most patients for initial treatment. Intra-articular injections into psoriatic lesions should be avoided because the skin may be colonized with staphylococci or streptococci. In patients with more persistent or severe symptoms that do not respond adequately to NSAIDs, disease-modifying antirheumatic drugs (DMARDs) should be considered early [35]. In refractory cases not responsive to DMARDs or patients with severe erosive disease at the time of initial presentation, antitumor necrosis factor (anti-TNF) should be considered [39, 41].

Enteropathic Arthritis

Enteropathic arthritis (EA) is an inflammatory spondyloarthritis which occurs with inflammatory bowel diseases (IBD) and other gastrointestinal (GI) diseases [42]. Rheumatologic manifestations in IBD are common, occurring in about 17–39% cases [42]. Enteropathic arthritis is equally common among adults and children with IBD and can affect both the axial skeleton and the peripheral joints. Arthritic symptoms usually occur during or after onset of IBD clinical manifestations, although in some cases axial spine involvement and peripheral arthritis have preceded bowel disease [28, 43]. EA shares common clinical features of other SpA conditions such as peripheral synovitis, inflammatory back pain, peripheral enthesopathy, and dactylitis. EA may occur in patients with other GI-related conditions, such as Whipple disease, celiac disease, or after intestinal bypass surgery.

The pathogenesis of enteropathic arthritis remains unclear; however, joint inflammation occurs in genetically predisposed patients with bacterial gut infections, suggesting a possible relationship between inflammation of the gut mucosa and associated arthritis [42]. Spondylitis in IBD is associated with the presence of HLA-B27, but in lower frequencies when compared to ankylosing spondylitis and other forms of spondyloarthritis [44].

Clinical Features

Peripheral arthritic manifestations in IBD occur more frequently than axial spine involvement. Peripheral arthritis is often acute with peak symptoms occurring within 48 h of onset. Arthritis in EA is often asymmetric, mono- or oligoarthritis that preferentially affects the large joints of the lower extremities (although upper extremity involvement can occur). Episodes of peripheral arthritis are episodic and recurrent, with spontaneous improvement of symptoms within 6 months [42]. In a minority of patients with EA, peripheral joint pain can persist chronically.

Axial spine involvement is more common in patients with Crohn's disease than in those with ulcerative colitis [45]. Clinical features of spine involvement are typical of SpA-associated inflammatory back pain, characterized by insidious onset, associated with morning stiffness, and relieved with movement [43]. Axial spine symptoms are independent of IBD activity, whereas peripheral arthritis tends to coincide with IBD exacerbations [28, 43]. Both progressive ankylosing spondylitis and sacroiliitis can occur in patients with EA with similar debilitating spine immobility possible at later stages of the disease. Extra-articular manifestations of EA can occur, including acute anterior uveitis, aortic insufficiency, and skin lesions, such as erythema nodosum and pyoderma gangrenosum [43].

Diagnosis

There are no specific diagnostic criteria for EA; therefore, diagnosis is based on clinical history and exam findings. Clinical suspicion should be raised in patients with IBD presenting with symptoms suggestive of inflammatory back pain and/or development of asymmetric peripheral arthritis, especially in the lower extremities [43]. There are no pathognomonic diagnostic tests or imaging abnormalities associated with EA. Acute phase reactants including ESR and CRP usually reflect the activity of the intestinal disease [43]. RF is negative in a majority of cases, but a positive RA does not rule out EA. Radiographs or MRI of the spine and pelvis may show evidence of sacroiliitis or spondylitis, as common among spondyloarthritis inflammatory conditions. If joint involvement is limited to monoarthritis or oligoarthritis, it is important to consider joint aspiration to rule out septic arthritis, especially in patients receiving immunosuppressants [43].

Treatment

Enteropathic arthritis is ideally co-managed through collaboration with both gastroenterology and rheumatology specialists, in addition to other multidisciplinary consultants such as physical and occupational therapists based on the patient's individual care needs. Treatment of musculoskeletal manifestations of EA aims to reduce inflammation and prevent disability. NSAIDs may exacerbate bowel disease and should be used with caution. Corticosteroids, DMARDs, and Anti-TNF have been effectively used to treat intestinal inflammation and arthritis manifestations, with therapy choice depending on clinical presentation and associated comorbidities [43]. Physical therapy and exercise can help preserve range of motion and reduce pain when there is prominent axial inflammatory spine involvement.

Polymyalgia Rheumatica

Polymyalgia rheumatica (PMR) is a chronic inflammatory immune-mediated disease characterized by aching and morning stiffness in the muscles of the neck, shoulders, upper arms, and pelvic girdle [46]. PMR is associated with giant cell arteritis (GCA), a common interrelated inflammatory vasculitis among older adults that may lead to blindness if not promptly identified and treated [47]. The incidence of PMR increases after the age of 50 years and peaks between 70 and 80 years of age, generally affecting women twice as often as men [47]. PMR occurs at a frequency of about 3–10 times that of GCA. The pathogenesis of PMR is unclear, but genetic and environmental factors are thought to contribute to susceptibility and severity [46, 48].

Clinical Features

Clinical presentation includes pain and morning stiffness in the neck muscles, shoulders, and hip girdle in patients over the age of 50 [48]. Duration of symptoms is typically over 2 weeks and may be associated with systemic features, such as fatigue, malaise, anorexia, low-grade fever, and weight loss in about one-third of patients [46, 47]. Physical exam findings may include limited range of motion of the neck, shoulders, and hips secondary to pain, inflammation of the bursae in the shoulder and hips, synovitis, evidence of weight loss, or low-grade temperature elevations [47]. Patients with PMR must be evaluated carefully for possible clinical manifestations of GCA including new onset occipital or temporal headaches, scalp tenderness, jaw claudication, temporal tenderness, or acute visual disturbances (blurred vision, visual loss or field deficits, diplopia) [47].

Diagnosis

Diagnosis of PMR is made clinically based on medical history, examination, and supportive laboratory findings. Diagnosis should be considered in patients older than 50 years of age with bilateral neck, shoulder, or pelvic girdle for a duration of over 2 weeks and laboratory findings suggestive of a systemic inflammatory syndrome (elevated ESR or CRP) and normocytic anemia. There are no pathognomonic tests for PMR, and it is critical to rule out other diseases with similar clinical presentations, such as cancer, active infection, systemic lupus erythematous, and seronegative rheumatoid arthritis [47]. Imaging is not routinely needed for the diagnosis of PMR.

The diagnosis of GCA is made from a combination of clinical evaluation, history, and laboratory data and confirmed by histopathology [6]. Patients over the age of 50 with clinical features suspicious for GCA as previously described, with laboratory findings indicative of an acute phase response such as elevated ESR or CRP, and normocytic anemia should warrant further investigation. Prompt histologic assessment with temporal artery biopsy should be performed when clinical and laboratory findings suggest evidence of GCA [47].

Treatment

Corticosteroid therapy is the mainstay of treatment for both PMR and GCA. The aim of treatment is to both restore function and symptomatic relief. For patients with clinical features suggestive of GCA, corticosteroid therapy should not be delayed while awaiting temporal artery biopsy to minimize the risk of irreversible vision loss, as histologic pathologic findings persist even after more than 2 weeks after steroid initiation [6, 49].

Infectious Disease and the Spine

Spinal infections include diseases affecting the vertebral body, intervertebral disc, and adjacent paraspinal tissue, representing 2–7% of all musculoskeletal infections [50]. Patients commonly present with vague clinical symptoms of back pain that may be difficult to distinguish from other common causes of back pain. Although spinal infections are relatively rare, delayed diagnosis can result in significant morbidity and mortality if left untreated.

Spinal Epidural Abscess

Spinal epidural abscess (SEA) is a rare but serious purulent infection of the central nervous system. Although SEA remains uncommon, the incidence has risen over the past several decades, attributed to improved diagnostic accuracy by magnetic resonance imaging (MRI), increasing rates of spinal interventions, an aging population, rising prevalence of IV drug use, and iatrogenic immunosuppression [51–53]. When left unrecognized and untreated, SEA is associated with high morbidity and mortality. Prognosis is dependent on timeliness of treatment before neurologic deficits develop. Unfortunately, delay in diagnosis is common, owing to its rare occurrence and often nonspecific clinical presentation which is frequently misdiagnosed on initial healthcare encounter [54].

A number of risk factors have been associated with SEA, including chronic disease with impaired immunity (diabetes mellitus, HIV, alcoholism, end stage renal disease), local or systemic infection, factors that may lead to hematogenous spread of microorganisms (indwelling catheters, trauma, IV drug use, tattooing, acupuncture), and history of spinal procedures [50, 51]. In surgical-associated SEA, additional risk factors include prolonged surgical time, high blood loss, type of instrumentation (posterior and lumbar higher risk than anterior and cervical), and number of spine interventions (spine procedures or revisions) [50, 55].

SEA forms when microorganisms gain access to the epidural space either through hematogenous spread from a distant infectious source; from a contiguous source such as a psoas muscle abscess or vertebral body infection; or via direct inoculation (spinal injections or spinal surgery). Hematogenous spread is the most common portal of entry, accounting for about one half of all cases, followed by contiguous spread (about one-third of cases), and in the remaining cases, no source of infection can be identified [51, 53, 54]. Common distant sources of bacteria include the urinary tract, skin, respiratory tract, or heart valve vegetations.

Anatomically, SEAs most commonly form in the thoracic and lumbar regions of the spine, where the epidural space is larger and contains more infection-prone fat [51]. Most SEAs form in the posterior epidural space, although when anterior formation occurs, it is usually below L1. The mechanism of SEA-associated neurologic deficits has been attributed to a number of mechanisms, including direct mechanical spinal cord compression resulting in ischemia and injury, impaired local circulation due to venous stasis, and thrombosis of spinal arteries [54].

Pathogens responsible for a vast majority of SEA infections are of bacterial origin. *Staphylococcus aureus* (*S. aureus*) accounts for a majority of cases (about two-thirds of identifiable cases), with methicillin-resistant *S. aureus* (MRSA) accounting for an increasing proportion of these cases over the past two decades [54]. Less common causative bacteria include Gram-negative bacilli, streptococci, and coagulase-negative staphylococci [56, 57]. *Mycobacterium tuberculosis* is a rare cause of SEA but more frequently occurs in immunosuppressed patients or in regions of the developing world [58]. Fungi, such as *Candida* species, are less common and are often associated with spinal instrumentation. Parasites causing SEA are very rare, but cases have been reported in certain geographic regions [59].

Clinical Features

Initial clinical manifestations of SEA are often nonspecific, lending to the difficulty of accurate and timely diagnosis. Focal, often severe back pain is the most common presenting symptom, occurring in 70–90% of patients [59]. The classic clinical triad of back pain, fever (documented in about one half of patients), and neurologic deficit (reported in about 20–30% of patients) is present in only a minority of patients [51, 59]. If left untreated, the natural course of neurologic symptoms often progresses sequentially from focal back pain to nerve root irritation at the level of the affected spine ("shooting" or "electric" sensations), followed by motor weakness, sensory deficits, bladder or bowel dysfunction, and eventually paralysis [51, 60]. The duration from initial presenting symptoms to hospital admission varies widely, ranging from 1 day to 2 months [51]. Although the sequence of neurologic deficits remains relatively constant, the rate at which these neurologic changes take place is also highly variable; neurologic deficits may evolve over the course of hours, days, or gradually over weeks [51]. Once paralysis develops, neurologic deficits may quickly become irreversible.

Diagnosis

Diagnosis of SEA is made on the basis of clinical suspicion and presenting symptoms and supported by laboratory findings and imaging studies. Definitive diagnosis can only be confirmed by abscess drainage with biopsy. Since delayed diagnosis can have significant deleterious consequences on patient outcome, the critical initial step for clinicians is to first consider SEA in the differential diagnosis of patients with back pain and risk factors for SEA development. Clinical suspicion should be high in patients presenting with back pain and fevers or who carry risk factors associated with SEA. Additionally, patients who have undergone spinal procedures such as postoperative epidurals may not show signs or symptoms of infection for weeks after the procedure; initial clinical features of SEA have been documented as late as 2 months after epidural catheter placement in some cases [61].

Laboratory studies may help support clinical suspicion but may be unremarkable. Leukocytosis is detected in about two-thirds of cases. Inflammatory markers including ESR and CRP have higher sensitivities and are nearly uniformly elevated in patients with SEA [51, 54]. Blood cultures reveal an organism in about half of patients diagnosed with epidural abscess and should always be collected when clinical suspicion is high, as culture data can help guide antibiotic therapy [54]. When possible, CT-guided needle aspiration of the abscess is the best specimen for culture and antibiotic guidance. Lumbar puncture with CSF analysis is not routinely obtained, as it rarely adds additional diagnostic information and may potentially add risk of meningeal or subdural spread of infection [51].

MRI with intravenous gadolinium remains the diagnostic imaging method of choice with greater than 90% sensitivity and specificity for detecting SEA [62]. Gadolinium results in a hyperintense signal from the abscess, helping to facilitate infection location and extent of involvement and identify other potential areas of infectious involvement such as vertebral osteomyelitis or discitis [62]. Consideration should be given to image the entire spine even when pain is defined in a focal region, as multiple skip lesions can occur even in regions unaffected by pain.

Treatment

In most cases of SEA, treatment of choice is prompt surgical decompression and drainage with systemic antibiotic therapy [51, 62]. Empiric antibiotic therapy should be initiated immediately after blood cultures are drawn, typically with broad-spectrum antibiotics with antimicrobial coverage against staphylococcal, streptococci, and Gram-negative bacilli until a causative pathogen is identified, whereby treatment can then be streamlined [62]. Although surgical decompression remains the treatment of choice in a majority of cases, there are select instances where less invasive management with CT-guided needle aspiration or medical therapy alone may be considered, such as in cases of clinical

instability. Regardless of the treatment method pursued, multidisciplinary management involving spine surgeons, radiologists, and infectious disease specialists is recommended, when available, to establish an appropriate treatment plan.

Prognosis and neurologic outcome correlate strongly with the severity and duration of neurologic deficits prior to surgery [51, 62]. Once neurologic deficits such as motor weakness occur, there is a higher incidence of permanent neurologic impairment. Furthermore neurologic recovery is unlikely to improve if paralysis is present for over 24 h prior to surgical decompression [62, 63]. About 5% of patients with SEA die due to severe uncontrolled sepsis or other infectious-associated complications [51]. These prognostic features again highlight the importance of prompt diagnosis and treatment in patients suspected of having SEA.

Vertebral Osteomyelitis and Discitis

Vertebral osteomyelitis (VO) is an infectious process affecting one or more vertebrae of the spine. Vertebral osteomyelitis (also termed spinal osteomyelitis, or spondylodiscitis) may involve adjacent intervertebral disc spaces, and therefore the terms VO and discitis are commonly used interchangeably. Clinical presentation, diagnosis, and treatment of the two entities are similar in most cases. The incidence of VO increases with age, most commonly occurring in adults over the age of 50 years [64]. Vertebral osteomyelitis is the most common hematogenous form of osteomyelitis in patients over the age of 50 years old, representing 3–5% of all cases of osteomyelitis [65, 66]. There is a slight male predominance, with about 60% cases occurring in males [67]. Vertebral osteomyelitis carries significant morbidity and mortality, with median length of hospitalization of approximately 1 month [67]. Risk factors associated with VO include patients who have undergone spinal procedures or surgery, intravenous drug use, endocarditis, diabetes, corticosteroid therapy, degenerative spine disease, use of hemodialysis, and immunocompromised hosts.

Vertebral osteomyelitis can be further classified by infectious etiology, either pyogenic or granulomatous. A significant majority of cases are caused by a bacterial infection, also referred to as pyogenic vertebral osteomyelitis (PVO). Bacterial infection in PVO occurs through two main pathways: hematogenous spread from a distant site of infection and direct inoculation [67]. Hematogenous spread is the most common portal of entry in PVO, accounting for approximately 50% of cases [67]. A primary focal source of infection can be identified in about a half of cases; among the most commonly identified are infections of the urinary tract, skin, and soft tissue, site of vascular access, endocarditis, bursitis, and septic arthritis [68]. Hematogenous spread often results in spread to involve the two adjacent vertebral bodies and their intervertebral disc due to the common bifurcation of the vertebral artery blood supply to adjacent vertebral bodies. Direct inoculation accounts for between 15% and 40% of cases, commonly occurring after spinal procedures, such as discography, lumbar puncture, or spinal surgery [67].

A third less common portal of entry is through contiguous spread from adjacent areas of infection, such as retropharyngeal abscesses or infected surgical grafts, accounting for about 3% of cases [67, 68].

The most common causative pathogen of PVO is *Staphylococcus aureus*, accounting for over 50% of cases [68, 69]. Other common microorganisms vary based on the primary site of infection and patient comorbidities and include Gram-negative bacteria, *Candida* species, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Haemophilus influenzae* [67, 68]. *Mycobacterium tuberculosis* is a rare but serious cause of morbidity and mortality and is the most common cause of granulomatous vertebral osteomyelitis [67].

Clinical Features

Back pain is the most common clinical manifestation of VO; in a systematic review of 1008 patients diagnosed with VO, back pain was reported in 86% of cases [70]. Neurologic changes, such as focal weakness, numbness, or radiculopathy, are only present in about one-third of cases and tend to present later in the disease course. Fever is relatively variable, present in only 35–60% of patients [68]. Tenderness to percussion of the spine was less common, reported in fewer than a fifth of patients [68]. Since a majority of cases of PVO are secondary to a distant infection through hematogenous spread, the initial clinical presentation may be predominantly the clinical manifestations of the primary infection. Less commonly, patients may experience associated systemic symptoms of infection, including weight loss, malaise, and night sweats.

Diagnosis

A diagnosis of VO is suspected on the basis of clinical findings and supported by laboratory data and imaging studies. Although leukocytosis is detected in about two-thirds of cases, increases in inflammatory markers including ESR and CRP are highly sensitive, reported in 98% and 100% of cases, respectively [68]. Blood cultures should be collected with suspected cases of PVO; an identifiable pathogen has been established in anywhere from 30% to 78% of cases [70]. If PVO is suspected and blood cultures do not yield a causative microorganism, image-guided aspiration biopsy is generally recommended [68].

Imaging can help identify findings suggestive of spinal infection, aid in ruling out other causes of symptoms, and detect complications of vertebral osteomyelitis such as epidural spread or paravertebral infection [68]. Plain radiography is not a sensitive imaging modality for PVO and is often

nondiagnostic in the earlier stages of infection. MRI is considered the imaging modality of choice for detecting spinal osteomyelitis due to a high degree of accuracy (over 90%) in detecting signs suggestive of infection [71]. The addition of gadolinium contrast improves diagnostic accuracy, especially in the earlier stages of disease onset. Computed tomography is less sensitive than MRI for early detection of PVO and therefore is only indicated if MRI is contraindicated or unavailable. Three-phase technetium bone scan is typically positive within days of onset of symptoms, although findings are nonspecific for vertebral osteomyelitis [68].

Treatment

Most patients diagnosed with VO and discitis can be successfully managed nonoperatively with antimicrobial therapy and supportive care. In contrast to the management of epidural abscess, in VO cases every effort should be made to identify the causative pathogen by blood cultures or biopsy before starting antimicrobial therapy with the exception of cases associated with hemodynamically instability, sepsis, epidural abscess formation, or spinal cord compression. Choice of antimicrobial therapy should be guided based on culture results. Decision regarding antibiotic selection, route (oral versus intravenous), and duration is best made under the guidance of an infectious disease specialist when available. Antimicrobial therapy is routinely required for 6–8 weeks or longer. Inflammatory markers such as CRP may be used to follow the progress of treatment. Surgical management is only necessary in a small minority of patients with vertebral osteomyelitis. Indications for surgical management include failure of nonoperative management, focal neurologic deficits, paravertebral or epidural abscess formation, mechanical instability, or cord compression.

Long-term complications of vertebral osteomyelitis include abscess development (epidural, paravertebral, disc space), neurologic deficits, and sepsis. Mortality is estimated at less than 5%, and rate of residual neurologic deficits is less than 7%, although delay in diagnosis and treatment can have serious deleterious consequences on outcomes [66]. Prompt diagnosis and early antimicrobial therapy are important to improved patient outcomes.

Granulomatous Vertebral Osteomyelitis

A majority of cases of VO are pyogenic in origin. In a small minority of patients, vertebral osteomyelitis is secondary to granulomatous infection. A granulomatous infection of the spine is characterized by an infectious process with vertebral or peridiscal involvement that results in the formation of a granuloma. A granuloma is an organized focal aggregation of macrophages and other inflammatory cells, formed through a chronic inflammatory response initiated by various infectious and noninfectious agents. Although causative organisms may include a variety of bacteria, fungi, and parasites, the majority of granulomatous vertebral osteomyelitis (GVO) is due to *Mycobacterium tuberculosis* (Pott's disease) [72]. Overall skeletal tuberculosis accounts for slightly over 2% of tuberculosis cases in the United States. Infection commonly affects the lower thoracic and upper lumbar regions of the spine, typically beginning with inflammation of the intervertebral joints, followed by spread to involve the adjacent vertebral body [72]. Infection can eventually progress to vertebral collapse, spinal deformity, and cord compression if left unrecognized.

One of the greatest challenges in diagnosing tuberculosis-associated vertebral osteomyelitis is initially considering granulomatous disease among the differential diagnosis in at-risk patients. Clinicians must maintain an awareness of the possibility of a granulomatous infection in patients with acquired immune deficiency syndrome (AIDS), history of organ transplant, the homeless population, history of travel to Asia, Africa, or South America, or known exposure to a patient with tuberculosis infection [72].

Clinical Features

The most common presenting symptom of GVO is back pain, most frequently in the thoracic spine that is progressive over weeks to months. Patients may experience constitutional symptoms such as malaise, night sweats, weight loss, and fevers. Neurologic deficits including focal weakness, numbness, and radiculopathy vary among cases documented ranging from 10% to 61% [72]. Serum testing for leukocytosis and inflammatory markers such as ESR and CRP is nonspecific for tuberculous spine infections. MRI is the imaging modality of choice for granulomatous vertebral osteomyelitis [72]. Intravenous gadolinium is frequently added to assist in differentiating other sources of infectious processes, although distinguishing bacterial and tuberculous infection is challenging by MRI findings alone. MRI findings that have been shown to correlate more consistently with tuberculous infection include well-defined abnormal paraspinal signal, smooth abscess walls, and the presence of paraspinal or intraspinal abscesses on T2-weighted and fat-suppressed T1-weighted axial and sagittal images [72]. Chest radiographs are recommended in patients with active tuberculosis, which may demonstrate pleural involvement, often seen as segmental infiltrates and hilar or mediastinal lymphadenopathy. Diagnosis is established by microscopy and image-guided biopsy or culture of infected material.

Treatment

Treatment of *Mycobacterium tuberculosis*-associated GVO requires timely diagnosis, prompt medical management, and in a minority of cases, surgical intervention. First-line therapy is anti-tuberculous therapy, including

rifampin, isoniazid, ethambutol, and pyrazinamide for 6–18 months, based on culture results. Treatment choice and duration should be guided by an infectious disease specialist. Although pharmacotherapy is first-line treatment in patients with tuberculosis-associated osteomyelitis, surgical intervention may be indicated in a minority of cases involving spinal cord compression, progressive neurologic deficits despite appropriate pharmacologic therapy, or spinal instability.

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Oncology and Spine Pain

17

Daniel K. Partain and Mihir M. Kamdar

Key Points

- Spine pain due to bony metastases is a common clinical scenario that can result in a significantly impact patient morbidity and mortality.
- The ability to effectively manage spine pain is imperative, as is the ability to rapidly recognize symptoms of impending neurologic compromise.
- A multimodal, multidisciplinary approach is key to managing oncologic spine pain effectively.

Introduction

Cancer-associated pain is highly prevalent, with over 50% of patients with cancer reporting pain at some point in their illness and 64% of patients reporting pain with advanced or metastatic disease. Over one third of patients with cancer-associated pain report their pain as moderate or severe despite advances in pain management techniques and pharmacotherapies [1]. Bone pain is the most common cancer pain syndrome, with as many as 40% of patients with cancer pain reporting a bone pain syndrome and 70% of patients found to have osseous metastases at the time of death [2–4]. The most common sites of bone metastases are in the axial skeleton, with the vertebrae, pelvis, and ribs being the most common sites. Common cancers that metastasize to the bone include prostate, breast, lung, and multiple myeloma.

Spinal metastases are common and can cause significant morbidity and mortality in cancer patients. The common site of tumor involvement is the thoracic spine (70%), followed by the lumbar spine (20%) and cervical spine (10%) [5]. Cancer-associated spinal pain syndromes are often mediated by a complex interplay of local nociceptive, neuropathic, and inflammatory factors, in addition to tumor-specific processes through chemokines and cytokines [6]. Patients with vertebral metastases are at risk of pathologic vertebral fractures, radicular pain from nerve root compression, or acute spinal cord compression [7].

Given the high prevalence of cancer-associated spinal bone pain syndromes and the potential for significant neurologic catastrophe, it is essential to have a standard diagnostic and therapeutic approach for patients with cancer and back pain. In this chapter, we will cover the diagnostic approach to cancer-associated spine pain with a special focus on epidural spinal cord compression, as this can be a life-threatening diagnosis that can cause permanent neurologic sequelae. We will then review pharmacologic management approaches in the context of the underlying mechanisms that mediate and sustain cancer-related spine pain. Finally, we will discuss non-pharmacologic management options for oncologic spine pain including radiation, radionuclide therapy, interventional pain techniques, and surgery.

Diagnostic Approach

The nature of a patient's pain syndrome often depends on the location of the bone metastasis and the associated spinal and neural structures. Many bone metastases are non-painful, and it can sometimes be a diagnostic challenge to identify which lesion is responsible for a patient's pain. A cervical lesion may cause localized neck pain with upper extremity radicular pain and motor effects that correspond to the level of the nerve root affected. For example, a superior C5 vertebral body lesion that is impinging on the C5 nerve root might cause pain along the shoulder and lateral arm with an associated decreased biceps deep tendon reflex on physical examination. If the C5 lesion is more inferior and impinging on the C6 nerve root, it might cause forearm pain and a decreased

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brachioradialis deep tendon reflex. Thoracic lesions tend to cause mid-back pain with radiating pain around the thorax. Lumbosacral lesions generally cause low-back pain with radicular pain down the lower extremities and can cause gait impairment. It is also important to note that tumors of the spine that are confined to bone and do not involve the spinal cord or roots may manifest as focal pain without a radicular element. Pain from vertebral compression fractures is often positional and worsens when the patient is upright.

The first step in identifying a patient's spinal pain syndrome is a detailed history and physical examination. Cancer-associated spine pain may be high on the differential diagnosis in a patient with known metastatic prostate cancer with a history of bone lesions, but it may not always be immediately apparent in patients without a history of cancer. Concerning features in the history that should raise suspicion for cancer-associated spine pain include associated constitutional symptoms (fevers, night sweats, weight loss), progressive pain for greater than 1 month, new neuropathic or myelopathic symptoms, or any new focal complaints that could be consistent with a primary cancer (e.g., new breast lump). Patients with advanced age (>65 years old) are also more likely to have a malignant cause of back pain, particularly when there is no history of pre-existing musculoskeletal conditions such as degenerative joint disease. The physical examination may help with identifying a potential location for the pain generator. A detailed strength, sensation, reflex, and gait exam can help narrow down a potential location, as well as palpation along the full length of the spine. Central pain over bony prominences is more concerning for malignant bone pain than lateral soft tissue pain, and any new radicular symptoms such as pain or objective deficits on the physical exam should warrant additional evaluation.

One of the most important parts of the diagnostic workup for a patient with a suspected metastatic spinal lesion is selecting an appropriate imaging modality. In many patients with acute nonmalignant pain, imaging is often not even indicated [8], but in patients with a history of cancer, MRI with intravenous contrast is the preferred imaging technique to evaluate back pain. This modality carries a sensitivity of 95% and specificity of 90% for identifying metastatic bone lesions [9]. Other imaging modalities are not sufficient for evaluating patients with a history of cancer when there is reasonable clinical suspicion that their back pain is from a bone metastasis. MRI is the only imaging modality with high enough resolution to identify critical diagnostic findings such as impending fractures, epidural extension of tumor, epidural spinal cord compression, or cauda equina compression.

Compromise of the spinal cord can lead to lifelong morbidity and can even be fatal if it goes undiagnosed. Epidural spinal cord compression is considered a medical emergency, and prompt evaluation by both radiation oncology and spine surgery is indicated. Patients have a much greater chance of long-term mobility, neurologic recovery, and pain relief when cord compression is rapidly identified and treated [10, 11].

Management Approach

Pharmacologic Management

The World Health Organization(WHO) developed their seminal approach to pain management, the three-step pain ladder, in 1986, and it has been used by thousands of physicians over the last 30 years to successfully treat patients with cancer pain (Fig. 17.1) [12]. In this model, the choice of analgesic agents is made based on pain severity. For patients with mild pain (step 1), non-opioid medications are used. For patients with moderate pain (step 2), "weak" opioids such as codeine or tramadol are suggested. Lastly for severe pain (step 3), "strong" opioids such as morphine and oxycodone are recommended. When employed across all cancer pain syndromes, the WHO stepladder has demonstrated efficacy. However, this requires that clinicians actively screen and treat pain in accordance to these guidelines. In one study, only 50–60% of patient with known cancer-associated bone pain were prescribed appropriate opioids, and another study found that about 10% of patients with known cancer-associated bone pain received adequate analgesia from strong opioids alone [13, 14]. Hence, the management of bony pain remains a challenge.

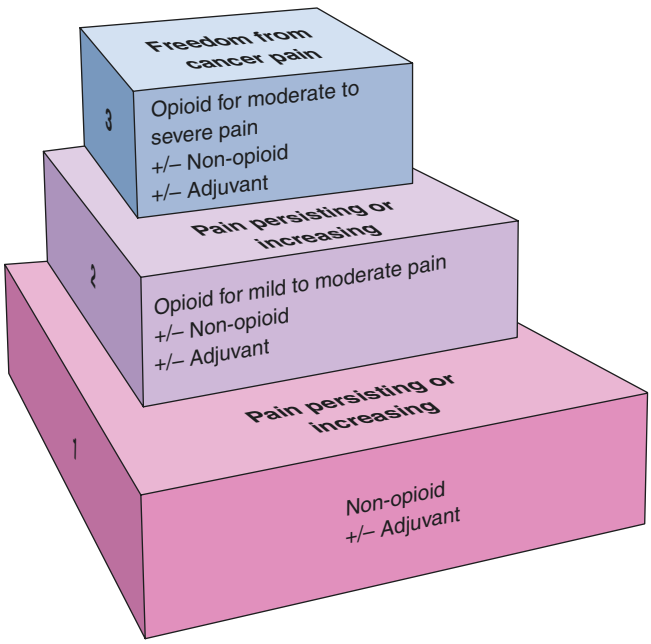

Fig. 17.1 WHO stepladder for cancer pain. (Adapted with permission from WHO stepladder for cancer pain http://www.who.int/cancer/palliative/painladder/en/)

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

Painful bone metastases are thought to create a surrounding microenvironment of inflammatory cytokines and chemokines that mediate pain. NSAIDs and corticosteroids have long been used in the management of this pain syndrome and have been found to be quite effective in clinical practice. One large meta-analysis found enough positive data for NSAIDs that the authors questioned whether the WHO step 2 ("weak" opioids) was indicated in the management of cancer pain [15]. Clinical use of NSAIDs is often directed by patient-specific factors such as renal impairment, history of gastrointestinal (GI) bleeding, stroke risk, and cardiovascular disease [16, 17]. Use of anticoagulants and the existence of thrombocytopenia are common in cancer patients, which may complicate the use of nonselective NSAIDs. In these settings, cyclooxygenase-2 (COX-2)-selective NSAIDs may be an option as they do not increase bleeding risk.

Corticosteroids

As with NSAIDs, corticosteroids are thought to alleviate pain by targeting the inflammatory component of cancer-associated spine pain. Steroids are indicated in the urgent management of a suspected epidural cord compression and can decrease radicular pain syndromes by decreasing perineural edema [18]. Steroids have also been demonstrated to prevent radiation-associated pain flares [19]. In a patient with concern for cord compression, a single dose of intravenous dexamethasone followed by 16 mg daily, often divided into four doses of 4 mg each, should be implemented as soon as possible while MRI imaging is being obtained [20]. For patients without concern for cord compression, lower doses of dexamethasone such as 2–8 mg per day in single or divided doses may provide significant analgesia of bony or radicular spine pain. Systemic corticosteroids have several potential side effects, including immunosuppression, hyperglycemia, neuropsychiatric symptoms, and insomnia. Steroids may also impact the efficacy of newer immunotherapeutic anticancer therapies. Hence non-emergent use of steroids should be discussed with the patient's oncologist.

Bisphosphonates

Bisphosphonates have been shown to decrease metastatic bone pain and prevent adverse effects such as pathologic compression fractures. Bisphosphonates inhibit osteoclast activity, which is thought to result in decreased bone pain. There is no data specifically in spinal metastases, but there is convincing data for bisphosphonates for bony cancer pain as a whole. A review of multiple trials of bisphosphonates for bone pain found evidence for improved pain, decreased analgesic use, and decreased adverse skeletal events with the use of bisphosphonates [21]. The most common bisphosphonates utilized for cancer-related bone pain are zoledronic acid and pamidronate, and intravenous dosing of these agents generally occurs every 3–4 weeks [21, 22]. Bisphosphonates must be used with caution in renal impairment and are contraindicated when a patient's creatinine clearance is below 30 mL/min. It is important to note that the analgesic effects of bisphosphonates are not immediate, but they do provide longitudinal benefits over time.

RANK-Ligand Inhibitors

Much like bisphosphonates, RANK-ligand inhibitors have been shown to improve metastatic bone pain and prevent adverse skeletal events. As with bisphosphonates, there is no data specifically focusing on spinal metastases, but there is good data for using RANK-ligand inhibitors for metastatic bone pain in general. Denosumab, a monoclonal antibody that binds to the receptor activator of NF-kB ligand (RANK-ligand), inhibits osteoclast formation and improves pain. One large review found that denosumab was superior to zoledronic acid in relieving bone pain and preventing adverse skeletal events [23]. One factor that may limit the use of denosumab is its high cost. Denosumab is also relatively contraindicated in patients with a creatinine clearance below 30 mL/min.

Opioids

Opioids remain the standard of care for patients with moderate to severe cancer-associated bone pain of the spine. A comprehensive review of opioid management is beyond the scope of this chapter, but several key principles will be reviewed here. First, despite the WHO stepladder guidelines, many clinicians avoid using the so-called weak opioids in real-world clinical practice of managing patients with oncologic bone pain. Both tramadol and codeine undergo complex metabolism to active metabolites, which can lead to significant inadequacies in analgesia or opioid toxicity [24]. Opioids such as morphine, oxycodone, hydromorphone, fentanyl, and methadone form the backbone of the approach to managing patients with moderate to severe cancer-associated spine pain.

Fundamental principles of opioid management are no different with cancer-associated bone pain syndromes. Opioid selection is often guided by patient-specific factors such previous experience or side effects, hepatic/renal impairment, and available routes of delivery. Patients should initially be started on short-acting opioids to determine analgesic needs and manage breakthrough pain. Given the persistent nature of vertebral bone pain syndromes, most patients will also need sustained-release long-acting opioid formulations to treat continuous pain. All patients on opioid therapy should receive guideline-based care, which currently includes a standard bowel regimen to mitigate the effects of opioid-induced constipation. Of note, cancer-associated spinal pain syndromes can fluctuate rapidly and require frequent re-evaluation and titration of opioids. For

example, acute skeletal adverse events can dramatically increase the pain stimulus and require higher doses of opioids, but opioid requirements can rapidly decrease again after radiation, surgery, or an interventional therapy such as vertebroplasty.

Calcitonin

Calcitonin has been used for many years in real-world clinical practice as an adjuvant pain medication for bone metastases. It became quite popular after some earlier studies from the literature on osteoporosis vertebral compression fractures found calcitonin to be helpful in the acute treatment of this pain syndrome [25]. However, several comprehensive systematic reviews and meta-analyses over the last 15 years have consistently found no evidence of clinically significant benefit for calcitonin in the treatment of malignant bone pain [26, 27]. Hence, calcitonin is not currently indicated in the treatment of cancer-associated spine pain.

Non-pharmacologic Management

Radiation

Radiation therapy is a first-line treatment for treatment of painful bony metastases involving the spine. Radiation can significantly improve pain and nearly half of radiation therapy is palliative in intent [28]. It is important to note that some types of cancers are more radiosensitive than others to the palliative effects of radiation. Consultation with a radiation oncologist can be significantly helpful in determining the benefit of radiation for patients with pain due to metastatic disease in the spine.

For patients with a limited prognosis, shortened course of palliative radiation, known as hypofractionated radiation, may be considered. In patients who have already received maximal doses of traditional external beam radiation (EBRT) to the spine, stereotactic body radiotherapy (SBRT) may be a consideration. Stereotactic body radiotherapy allows targeted doses of radiation to a localized tumor while minimizing radiation to adjacent normal tissue. SBRT may also be helpful for spine tumors that are less likely to be initially radiosensitive to EBRT.

In patients for whom epidural cord compression is a worry, emergent radiation oncology consultation should be obtained. Data suggests that a combination of surgical decompression and radiation therapy yields the most optimal neurologic outcomes in patients <65 years old with epidural cord compression and an unstable spine [29, 30]. However, if a patient is not a surgical candidate due to poor functional status or a limited prognosis, palliative radiation monotherapy of epidural cord compression should be considered.

Radionuclide Therapies

Radionuclide therapy can be helpful for pain from widespread bony metastases that are too diffuse to be targeted by a single radiation field. Commonly referred to as "targeted bone-seeking agents," radionuclides are radioactive isotopes that are absorbed by areas of high bone turnover such as bony metastases. Once absorbed, these agents cause cell death of painful cancer cells. Samarium, strontium, and radium are the best studied and most commonly used radionuclides. Data suggests these agents can be significantly helpful in reducing pain from widespread osteoblastic metastases [31]. Indications for radionuclide therapy include diffuse pain refractory to analgesics and radiation, positive bone scan, and a life expectancy greater than 3 months,

Vertebral Augmentation

Malignant vertebral compression fractures are common in patients with metastases to the spine. Vertebral augmentation can be an effective intervention for patients with painful pathologic vertebral compression fractures [32]. Vertebral augmentation involves the injection of bone cement, typically polymethyl methacrylate (PMMA), into a fractured vertebral body. The goal of the procedure is to restore mechanical stability and improve pain. Vertebroplasty and kyphoplasty are two common vertebral augmentation techniques. Kyphoplasty utilizes an inflatable balloon that is expanded within the vertebral body cavity to reduce kyphosis prior to injection of cement. Vertebroplasty involves direct injection of bone cement into the fractured vertebral body without the balloon component of kyphoplasty. Both procedures can rapidly reduce pain from malignant compression fractures and are relatively safe when performed by experienced operators. Post-augmentation radiotherapy is often utilized once the fracture is stabilized.

Neuraxial Drug Delivery: Epidural and Intrathecal Analgesia

Neuraxial drug delivery involves direct administration of analgesic medications in close proximity to pain receptors in the spine. Intrathecal and epidural analgesia are two common modes of neuraxial drug delivery. Through direct effects on spinal pathways, neuraxial drug delivery can yield greater analgesia at significantly lower doses than with systemic administration. For example, 1 mg of intrathecal morphine is equianalgesic to 10 mg of epidural morphine, which is equianalgesic to 300 mg of oral morphine. The increased potency at lower doses can also reduce opioid side effects seen with higher-dose systemic administration [33].

In patients with a prognosis greater than 3 months who have poorly controlled pain or side effects with systemic analgesics, an implantable intrathecal drug delivery system (also known as an "intrathecal pump") is a consideration. Before implanting a permanent intrathecal pump,

candidates often undergo an inpatient percutaneous trial of neuraxial analgesia with a temporary intrathecal or epidural catheter. Morphine and ziconitide are the only FDA-approved intrathecal analgesics. However, other agents such as hydromorphone, sufentanil, clonidine, and bupivacaine are often used intrathecally [34]. If the patient does well during the trial period, the next step is surgical implantation of a permanent subcutaneous intrathecal pump. Transcutaneous electronic programming of the pump allows for adjustments in dosing. The device is refilled periodically by percutaneously accessing a drug reservoir within the pump.

For patients with a prognosis of less than 3 months, a tunneled percutaneous intrathecal or epidural catheter connected to an external drug pump may provide a less invasive option than a surgically implanted pump. Risk of infection and catheter dislodgement is greater with this approach.

Specific contraindications to neuraxial drug delivery for patients with spine metastases include presence of tumor in the posterior spinal elements along the specific needle path to the neuraxial space. In this situation, alternative levels to access the intrathecal or epidural space may be considered. Catheter placement should be avoided in patients with impending cord compression, and intrathecal access should be avoided in patients with significant brain metastases due to the risk of herniation.

Spine Surgery

Indications for surgery in patients with pain from spinal metastases include pain refractory to conservative measures, neurologic dysfunction, and cord compression in an unstable spine. Patients younger than age 65, those who were ambulatory prior to surgery, and those with a shorter time from onset of neurologic symptoms to surgery have a greater likelihood of posttreatment ambulatory status [35, 36]. In patients with limited prognoses (less than 3 months), poor functional status, and advanced age, a less invasive palliative approach may be a better option [37].

Special Clinical Scenario: Epidural Spinal Cord Compression

A 71-year-old lady with a history of stage IIB ductal carcinoma of the right breast presents to the emergency department for acute 10/10 lumbosacral back pain with radiation down both legs into the feet. She had breast cancer at age 54 and is status post lumpectomy, radiation, and completion of both chemotherapy and hormonal therapy over 10 years ago and has had no evidence of recurrent disease in that time. The remainder of her previous medical history is relatively unremarkable. Her daily medications include aspirin, a statin, and hydrochlorothiazide for hypertension. She has not taken any opioids since her surgery. She is up to date on age-appropriate health maintenance exams. Prior to onset of her back pain, she had been very active and functional. Her physical exam reveals bilateral lower extremity weakness and numbness with focal weakness of the ankle dorsiflexors.

Questions

1. What is the most appropriate immediate medical management?
2. What is the most appropriate diagnostic test to order?
3. What consults must be obtained urgently to evaluate this patient?

Answers

1. This patient has a history of breast cancer, which is well-known to recur with axial bone metastases, even after decades of cancer remission. This patient not only has concerning findings for bone metastases including severe acute onset lumbosacral pain but is also exhibiting features concerning for acute epidural spinal cord compression with objective neurologic deficits. She should be treated with dexamethasone 10 mg IV immediately and then started on dexamethasone 4 mg IV Q6H. She should be given IV opioids to rapidly treat her cancer pain crisis and bring her pain under control. A reasonable option in this opioid-naïve patient would be to administer morphine 5 mg IV and reassess in 15 minutes to determine the need for repeat dosing.
2. The patient needs an emergency MRI of the spine with intravenous contrast to confirm the suspected diagnosis and provide high-resolution imaging to spine surgery and radiation oncology.
3. Radiation oncology and spine surgery specialists should be consulted emergently to evaluate the patient for immediate treatment. Assuming she is an acceptable candidate for surgery, immediate surgical decompression followed by postoperative radiation is the best approach.

Summary

Cancer involving the spine can cause significant patient morbidity and even mortality. Clinicians should utilize a diagnostic approach to cancer patients with spine pain and employ a low threshold to obtain urgent imaging to assess for impending cord compression or neurologic compromise. Clinicians should familiarize themselves with the wide array of pharmacologic options to treat oncologic spine pain, including opioid and non-opioid agents. Non-pharmacologic interventions such as radiation, vertebral augmentation, radionuclide therapy, and neuraxial drug delivery should be considered and utilized in the context of a patient's prognosis, functionality, and goals of care.

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Pediatric Spine Pain

18

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Key Points

- Determining the etiology of pediatric spine pain requires a detailed history and physical examination, and occasionally specific laboratory evaluation and imaging modalities.
- Management plans for pediatric spine pain can require the integration of pediatrics, orthopedics, and many other specialties.
- Treatment plans are constantly evolving for the pediatric spine patient.

Case Presentation

Patient is an otherwise healthy 14-year-old female with a history of progressive scoliosis and back pain. Her pediatrician had monitored her condition since she was 8years of age, but the patient began noting a progression of the curvature in the 6 months prior to surgical evaluation. Her symptoms were notable for severe medial scapular pain. She was placed on acetaminophen, diazepam, and oxycodone for pain control. She had no complaints of weakness, paresthesias, or bowel/bladder complaints.

Physical Exam

- Notable for 5/5 strength in all upper extremity muscles.
- Sensation intact to light touch in upper and lower extremities.
- Deep tendon reflexes 2+ in upper and lower extremities.
- Coordination and balance within normal limits.
- Scoliometry noted curvature of 15° in the thoracic spine and 12° in the thoracolumbar region.

Initial Imaging (Fig. 18.1)

Management

The patient was treated with 6 months of bracing. Her scoliosis continued to progress, and a T4-L2 instrumented spinal fusion was performed. Her pain resolved, and she progressed well with improved spinal straightening.

Post-procedure Imaging (Fig. 18.2)

Introduction

Pediatric spine pain is a diverse entity. While some conditions and their treatments may be familiar to an adult pain specialist, many etiologies of pain (Table 18.1) as well as medication choices and dosing (Table 18.2) require review for this population. Mechanical causes of pediatric back pain include disorders characterized by abnormal curvature of the spine, namely, scoliosis and Scheuermann's disease. In these disease states, the degree of deformity accelerates during childhood but correlates variably with pain. Other mechanical causes include lumbar disk herniation and sacroiliac joint inflammation – disorders common in adults but whose optimal diagnosis and treatment have yet to be fully elucidated in the pediatric population. In addition, trauma – resulting chiefly from motor vehicle accidents and sports injuries – continues to be a major cause of morbidity in children and commonly results in spinal injury with associated neurologi-

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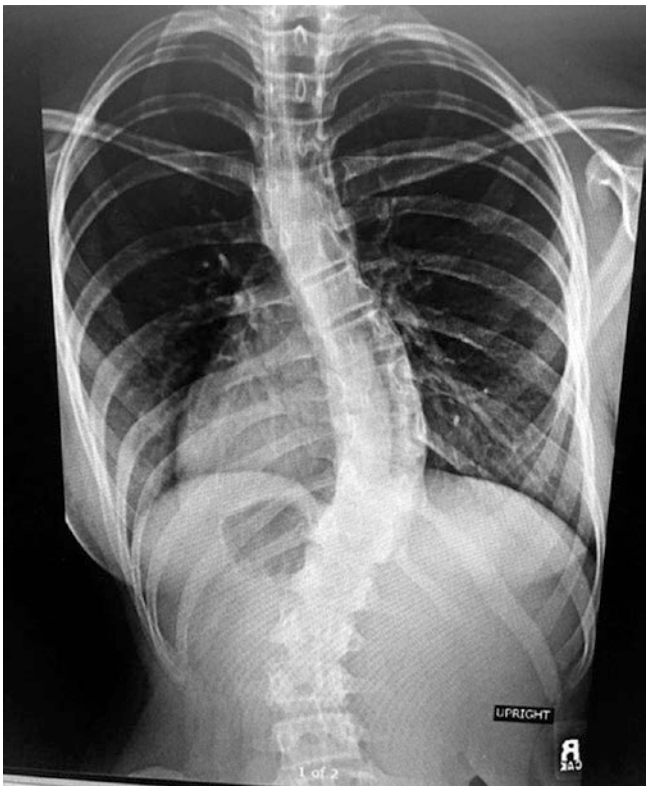

Fig. 18.1 Progressive thoracolumbar scoliosis, with no change after 6 months of bracing

cal deficits and pain. Finally, there are numerous infectious, neoplastic, and autoimmune etiologies of pediatric spine pain whose presentation frequently overlaps with more common causes, making them difficult to diagnose.

Scoliosis

Scoliosis is defined as a lateral curvature of the spine greater than 10° and is associated with vertebral rotation and distortion and a lack of normal spinal flexibility [1–3]. Severity is graded by measuring the Cobb angle (Fig. 18.3), which is identified by drawing lines perpendicular to the upper end plate of the highest involved vertebral body and the lower end plate of the most inferior involved vertebral body and noting the angle produced by their intersection. Scoliosis can be divided into three broad categories: congenital, idiopathic, and secondary.

Congenital scoliosis arises from abnormal in utero development of the spine, most commonly manifesting as incomplete formation of the vertebrae or failure of the vertebrae to segment, leading to congenital fusion.

Secondary scoliosis (of known etiology) is most commonly due to neuromuscular disorders, connective tissue disorders, rheumatoid disease, or Scheuermann's disease.

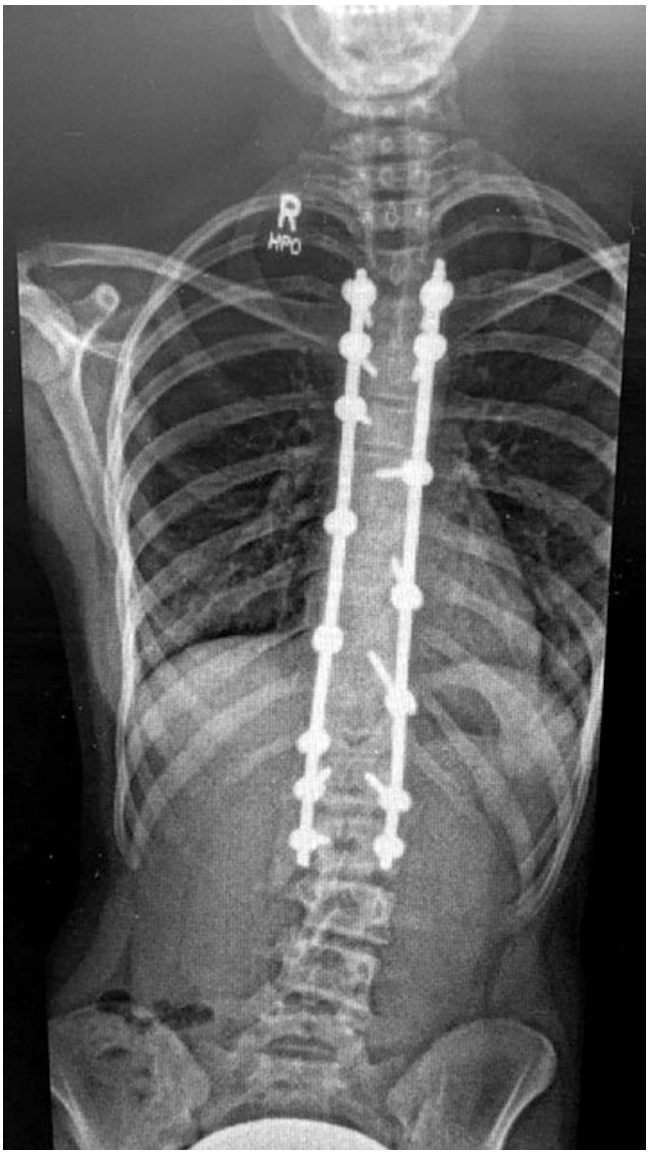

Fig. 18.2 Marked decrease in scoliosis after T4–L2 spinal fusion

Examples of conditions associated with scoliosis include spinal muscular atrophy, cerebral palsy, muscular dystrophy, fragile X syndrome, syringomyelia, Friedreich's ataxia, neurofibromatosis, and Prader-Willi syndrome.

Idiopathic scoliosis (of unknown etiology) is the most common form of scoliosis, accounting for 80–90% of all cases and affecting 1–3% of children by adolescence [1, 2]. Age of onset is typically 10 years or older, but curve progression can start any time from birth until skeletal maturity is reached. The incidence is the same in males and females, but females have up to a tenfold greater risk of curve progression to severe disease that necessitates treatment [4, 5].

Management is complex, often combining careful observation (generally for curvature <20–30%), bracing (generally for curvature >20–30%), and various surgical techniques includ-

Table 18.1 Common causes of back pain in children

Mechanical	Scoliosis Scheuermann's disease Lumbar spondylosis Intervertebral disk herniation Sacroiliac joint pain
Trauma	Neonatal (cervical) Motor vehicle accidents Falls Trauma-associated cord infarction
Infectious	Pott's disease Spinal epidural abscess Discitis
Inflammatory	Chronic recurrent multifocal osteomyelitis Juvenile idiopathic arthritis
Benign neoplasm	Osteoid osteoma Osteoblastoma Bone cyst
Malignancy	Lymphoma Neuroblastoma Ewing's sarcoma Osteosarcoma Langerhans cell histiocytosis Metastatic disease
Vasculitis	Takayasu arteritis

Table 18.2 Commonly used pain medications in the pediatric population

Drug	Route	Dose	Comments
Oxycodone	PO/SL	0.1–0.2 mg/kg q4–6h	
Morphine	IV/SC	0.05–0.1 mg/kg q2–4h	
	PO/SL/PR	0.15–0.3 mg/kg q4h	
Hydromorphone	IV	15 mcg/kg q4h	
	PO/SL	0.05 mg/kg q4h	
Fentanyl	IV	1–2 mcg/kg q1–2h	
	Transdermal	12–25 mcg/h q72h	
Methadone	IV	Variable	
	PO	PO dose = 2× IV dose	
Ibuprofen	PO	5–10 mg/kg	Max 40 mg/kg/day
Acetaminophen	PO/IV	10–15 mg/kg q4–6h	Max 60–90 mg/kg/day
Ketorolac	IV	0.25–0.5 mg/kg q6h	Max 2 mg/kg/day Use not to exceed 3–5 days
Celecoxib	PO	1–2 mg/kg	

ing fusion, resection, and insertion of growing rods (generally for curvature >40%). Adjunct treatment modalities including physical therapy and chiropractic care have not shown any benefit in reducing the progression of scoliosis [2, 6].

Among children with known back pain, a number of studies have shown scoliosis to be the most common coexisting pathologic entity, followed variably by Scheuermann's kyphosis or spondylolisthesis [7–9]. However, to date, the available literature does not suggest a strong causal relationship between idiopathic scoliosis and back pain in children [10], and existing studies have not been sufficiently powered to detect a smaller effect size or association. Furthermore, when back pain and scoliosis coexist, there does not appear to be a correlation between Cobb angle and severity of pain [11–14], and existing studies do not suggest that corrective surgery resulting in reduction of Cobb angle leads to a clinically significant decrease in pain [15–18]. There have been several small studies showing some benefit to Pilates [19] and spinal stabilization exercises [20] in providing relief for these patients.

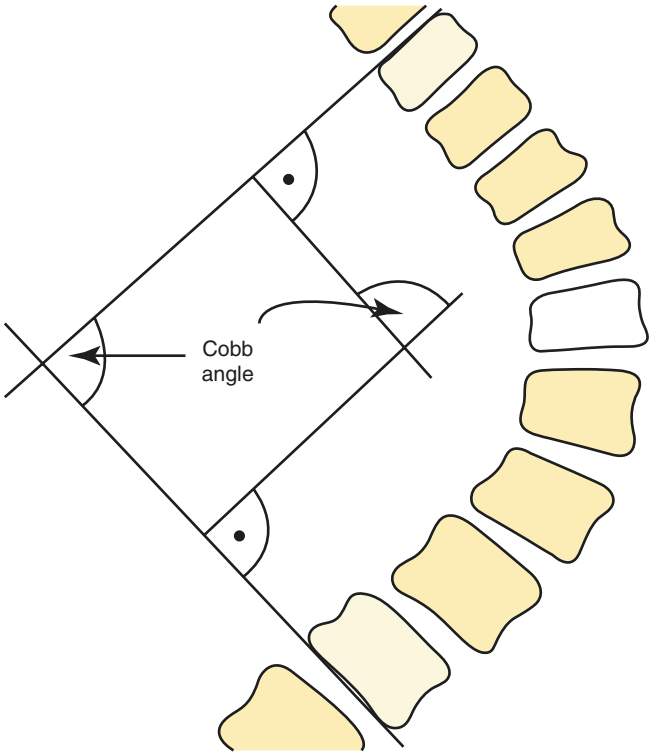

Fig. 18.3 Method for measuring the Cobb angle in scoliosis

Scheuermann's Disease

Scheuermann's disease, also known as juvenile disk disease, is the most common cause of thoracic back pain in adolescents. The reported incidence ranges from 0.4% to 10% during adolescence with no gender predominance but a strong genetic contribution [21–23]. Scheuermann's disease manifests as an increasing, fixed thoracic or thoracolumbar kyphosis, which is defined by an angle greater than 45° with thoracic vertebral wedging and disk space narrowing [24].

Pain is present in 20–60% of patients with Scheuermann's kyphosis [25] and is most commonly a dull, aching thoracic back pain aggravated by palpation, physical activity, pro-

longed sitting, standing, and forward flexion. The severity of pain is not correlated with the degree or progression of kyphosis [26], and pain tends to abate as the patient reaches skeletal maturity. Patients often have a compensatory lumbar hyperlordosis, tight hamstrings, and stiffness of the anterior shoulder girdle [24]. The resulting cosmetic appearance can be distressing to patients. In addition, patients with large curves >85° had a lower inspiratory capacity. However, despite some mild functional limitation, patients with untreated Scheuermann's disease report no major interference with their lives [27].

Treatment is guided by the severity of the deformity and degree of skeletal maturity. Orthopedic consultation should be obtained in all cases for further evaluation. Kyphosis less than 50° can be managed with a therapeutic exercise program and interval radiographic monitoring, while kyphosis greater than 50° may require bracing. A program consisting of manual therapy, exercise, and osteopathy demonstrated up to a 30% reduction in pain and decreased frequency of pain [28]. Indications for surgical treatment include kyphosis greater than 70°, severe pain, and neurologic deficits. These deficits are uncommon and are typically secondary to disk herniation, tenting of the spinal cord, or compression fractures [26]. Existing studies show that 52–71% of patients undergoing corrective surgery reported some degree of pain relief, although pain was not reported on in many of these studies [29].

Lumbar Spondylolysis

Lumbar spondylolysis is defined as a unilateral or bilateral defect of the pars interarticularis. It can occur any time after a child begins to walk, suggesting that an upright posture plays a role in creating or widening the defect. In roughly 90% of patients, spondylolysis occurs at the level of the lumbosacral joint [30]. The incidence steadily increases over childhood, from 4.4% in children 6 years of age to 6% of 18 year olds [31]. The condition does not typically develop after skeletal maturity [32].

Amplification of lumbar lordosis during sports that involve repetitive hyperextension – such as weight lifting, gymnastics, and diving – causes increased stress in the pars interarticularis, resulting in a significantly higher incidence of spondylolysis [33]. Untreated spondylolysis can lead to anterior slippage of a vertebra over the one immediately below it, a phenomenon referred to as spondylolisthesis.

Patients typically present with axial lumbar pain worsened by activity and prolonged standing. Depending on the degree of associated spondylolisthesis, patient may also experience pain in the buttock radiating into the posterior thighs during standing as well as neurological deficits, which most commonly manifest as L5 or S1 nerve palsies. With high-grade spondylolisthesis, the deficits can progress to bowel or bladder dysfunction [34].

The approach to treatment of spondylolysis varies depending on the severity of pain, presence of neurologic deficits, age of the patient, and degree of associated spondylolisthesis. In children and adolescents, most cases are treated conservatively with rest, nonsteroidal anti-inflammatory drugs, physiotherapy focused on flexion exercises and improved flexibility, and bracing, with the application of a thoracolumbar orthosis for a 3- to 6-month period. Bracing alone has been shown to alleviate low back pain in up to 80% of patients with spondylolysis and grade 0 or 1 spondylolisthesis [35] and can also result in full healing of spondylolytic lesions [36]. However, a more recent meta-analysis of conservative treatment measures to treat spondylolysis – which showed a similar pooled success rate of 84% among all studies – did not show a significant difference in groups treated with or without a brace, suggesting bracing is not responsible for the clinical improvement [37]. Transforaminal epidural steroid injections have been performed in the adult population and were effective at decreasing pain [38]. There are no available studies in the pediatric population evaluating the effectiveness of injections, chiropractic manipulations, or acupuncture in spondylolysis.

Surgical fusion should be considered in growing children with >50% spondylolisthesis, patients with radiological evidence of progression of displacement, and in those with persistent back pain not relieved by conservative measures. In one case series of 56 patients undergoing fusion with iliac crest bone grafting, over 80% reported that their symptoms markedly improved or completely resolved after surgery [39]. Surgical management of high-grade spondylolisthesis remains a challenge with significant risk of complications [40, 41].

Intervertebral Disk Herniation

Disk herniation is defined as the protrusion of the disk beyond the vertebral borders or the extrusion of nuclear contents outside of the disk's annular border. This entity results from acute movements and/or chronic structural changes of the spine that lead to increased intradiscal pressure. Initially, pain is axial and results from annular stress but may progress to radicular symptoms as the herniated disk causes irritation of surrounding nerve roots.

Symptomatic disk herniation in the pediatric population is rare and accounts for 0.4–15.4% of all disk herniations treated. MRI studies reveal that many disk herniations are asymptomatic; indeed, one study of adolescent tennis players with herniations showed that up to one-third were symptom-free [42]. More than 99% of pediatric operative disk herniations occur in the lumbar spine [43], with approximately

90% of these occurring at L4–L5 and L5–S1 levels [44]. Most herniations in the pediatric population are contained (no extrusion of nucleus pulposus) and paracentral [45].

Risk factors for herniation include heavy lifting and athletic activities involving body contact or high risk of falls [43], with 30–60% of patients reporting a recent history of trauma or sports-related injury [44]. The most common initial complaints are low back pain and radicular sciatic pain [46]. Neoplastic and infectious causes of pediatric low back pain are rare but must be excluded. Red flag symptoms included fever, chills, and weight loss. Further imaging and workup should be pursued in the correct clinical context.

On physical exam, the clinician should assess mobility of the lumbar spine, as well as lower extremity strength, sensation, and reflexes. In a case series of 87 children requiring microdiscectomy for lumbar disk herniation, Cahill et al. reported motor deficits in 26% of patients, sensory changes in 41% of patients, and loss of deep tendon reflexes in 22% of patients [47]. Straight leg raise testing should also be performed. However, case series have reported variable sensitivity of straight leg testing in children, with anywhere from 41% to 95% of surgically managed patients with confirmed lumbar disk herniation testing positive [46, 47].

Conservative management should be attempted in most patients prior to surgery and includes rest, initial restriction from sports, physical therapy, and pharmacotherapy with anti-inflammatory agents. Although infrequently used in the pediatric population, a number of centers have had success using epidural steroid injections (ESI) for symptomatic relief as an adjunct to conservative treatments [47–49], but there is limited evidence to suggest which pediatric patients are more likely to respond to these injections and if patients treated with ESIs can avoid surgical intervention at a higher rate.

There is fairly broad agreement that conservative therapy is not as effective in pediatric lumbar disk herniation as it is for adults. Available studies in children suggest recovery rates in the range of 25–50% with conservative therapy [50–52], wherein the adult population, randomized controlled trials have shown >50% recovery rates after 6 months of conservative therapy [53]. There are several postulated reasons for inferior results with conservative treatment. These include a more hydrated, viscous, nucleus pulposus in children that is less amenable to resorption as well as an injury-based mechanism of herniation with concomitant severe rupture of the annulus fibrosus, which is not as amenable to spontaneous healing.

Indications for surgical management include extreme or debilitating pain, progressive neurological deficit, or failure of conservative management. Open discectomy remains the standard of care [43]. The short-term results of lumbar discectomy are excellent, with >90% of pediatric patients reporting minimal or no pain 1 year after surgery [54, 55]. In the years that follow, recurrent pain requiring surgery is not uncommon, with reported reoperation rates ranging from 0% to 24% [45, 47, 56–58]. A retrospective review of 72 lumbar discectomy patients by Papagelopoulos et al. [44] predicted a 20% probability of additional surgery at 10 years and 26% at 20 years following initial intervention.

Sacroiliac Joint (SIJ) Pain

It is not known how often sacroiliac joint acts as the primary pain generator in the pediatric population, though one case series reported that roughly one-third of 150 pediatric patients with low back pain presenting to their clinic had symptoms due to their SIJ [59].

It is difficult to reliably diagnose SIJ pain in any patient, and there is even less literature to support the sensitivity of applying historical or physical examination signs used in adult patients to the pediatric population. The most reliable physical exam findings studied to date are maximal pain localized below L5 and tenderness at the sacral sulcus [60, 61]. There is no pathognomonic pain radiation pattern. SIJ block remains the only definitive diagnostic tool and is considered positive when there is greater than 75% pain relief [62]. Radiologic findings correlate poorly with results of diagnostic blocks and can often reveal confounding disc bulges, leading to unnecessary surgery.

The approach to treatment includes physical therapy, steroid injections of the SIJ, and radiofrequency ablation to achieve denervation of the joint. Of note, Stoev et al. [59] reported a series of 48 pediatric patients that underwent SIJ realignment via isometric hip contraction and extension. Of these patients, 53% showed complete resolution, and 80% showed dramatic improvement.

Trauma

Injury is the leading cause of death for children and adolescents in the United States [63]. Trauma-related spine injuries in the pediatric population are rare but can result in significant pain and in some cases, neurological deficits. Traumatic pediatric spine injury should be suspected when a child shows symptoms of torticollis, neck pain, or neurologic deficits (both fixed and variable) [64].

Motor vehicle accidents are the most common cause of injury across all age groups [64], but the mechanism of injury in the pediatric population can vary with age. In neonates, obstetrical complications commonly lead to cervical spine injury. In children less than 9 years of age, spine injury primarily results from falls and automobile versus pedestrian accidents (>75%). Between ages 10 and 14, motor vehicle accidents are the leading cause of lumbar fractures (40%). In children ages 15–17, motorcycle accidents contribute to

overall incidence and when combined with other motor vehicle accidents lead to more than 70% of spine trauma [65]. Sports-related spine injuries are also common in the pediatric population, with approximately one quarter of pediatric cervical spine injuries presenting to the emergency department being sports-related [66].

In a patient presenting with possible spine trauma, radiographic evaluation of the type and extent of injury can be complex. The National Emergency X-Radiography Utilization Study (NEXUS) group was an observational, prospective multicenter study involving 21 centers that evaluated over 30,000 stable patients at risk for blunt cervical trauma. Per their findings, any patient found to have one of the clinical criteria (Table 18.3) requires radiographic evaluation with cervical spine X-ray. This study was also validated in children.

However, most pediatric spinal injuries are ligamentous in nature. Thus, though the NEXUS study provides guidance for plain film utilization, and computed tomography (CT) scans are superior to X-ray for evaluation of fracture, neither must be used exclusively for cervical spine clearance [68]. Magnetic resonance imaging (MRI) is an invaluable tool to evaluate spinal cord and ligamentous injury. It is also useful for cervical spine clearance in the intubated, obtunded, or uncooperative child [69].

Most injuries can be treated conservatively, as even ligamentous injuries will generally heal with time. Accordingly, rest and external immobilization are the mainstays of treatment. Surgical management is indicated for grossly unstable injuries, decompression of neurologic structures, and nonreducible dislocations [64].

Rare causes of spine injury after trauma must also be considered. Spinal cord infarction has been reported in the pediatric population even after minor trauma. Fibrocartilaginous embolism – which can lead to infarction – is a rare and feared complication of minor trauma, mainly due to falls. In autopsy studies, disk material has been found within the spinal cord vasculature, suggesting this etiology. Other studies looking at patients who have undergone antemortem laminectomies have also shown disk materials within the spinal cord microvasculature.

These patients present with abrupt changes in physical exam that precede radiographic findings. The classic MRI findings are increased T2 signal changes and spinal cord enlargement. Treatment goals focus on spinal immobilization and maintenance of hemodynamics. Therapies such as dexamethasone, mannitol, and hyperbaric oxygen therapy have also been suggested. In spite of this, in most reported cases, there is no substantial recovery [70].

Table 18.3 NEXUS clinical criteria

1	Tenderness at the posterior aspect of the cervical spine
2	Focal neurologic deficit
3	Decreased level of alertness
4	Evidence of intoxication
5	Clinically apparent pain that may distract from the pain of a cervical spine injury

Hoffman et al. [67]

Infection

Infectious etiologies must also be considered when evaluating a child with spine pain. The history and physical exam are of utmost importance in obtaining an accurate diagnosis. There are many structures in the pediatric spine that are vulnerable to infection, including the vertebrae, cord structures, and intervertebral discs.

Pott's disease is an infection of the vertebrae caused by *Mycobacterium tuberculosis*. The bacteria are thought to spread hematogenously and can seed the discs, spinal cord, and surrounding tissues. In addition to back pain, there may be fevers, leukocytosis, and neurologic symptoms. A high index of suspicion must be maintained, as it can be difficult to diagnose. Recent travel to an area with a high prevalence of TB or a family member with tuberculosis can be suggestive of this diagnosis. Imaging of the spine may demonstrate abscesses and/or destruction of the vertebrae [71]. Treatment includes standard quadruple therapy for TB (rifampicin, isoniazid, pyrazinamide, ethambutol) and occasionally surgical debridement and decompression if the spine is rendered unstable [71].

Spinal epidural abscesses (SEA) are rare in the pediatric population but can have devastating neurologic consequences. These abscesses represent 7% of overall vertebral infections and usually occur in patients with a history of immunodeficiency, cancer, diabetes, spinal anesthesia, or intravenous drug abuse [72]. Bacteria can gain access to the epidural space through contiguous spread (known as primary SEA) or hematogenously. The most common causative organism is *Staphylococcus aureus*, both methicillin-sensitive and methicillin-resistant types. Symptoms can include an insidious onset of back pain and point tenderness, along with fever, neck pain, and neurologic deficits. Heusner has divided the clinical features of SEA into four stages (Table 18.4) [73]. Laboratory studies are notable for elevated erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and a leukocytosis. Diagnosis is confirmed with contrast-enhanced MRI of the spine, which has a sen-

Table 18.4 Stages of spinal epidural abscesses

Phase I	Spinal ache, back pain
Phase II	Nerve root pain
Phase III	Voluntary muscle weakness, sensory deficit, bowel, bladder dysfunction
Phase IV	Paralysis

sitivity and specificity of about 90% for detecting SEA [74]. Management includes intravenous antibiotics with neurosurgical consultation for possible abscess drainage.

While uncommon in children, discitis is an infection of inflammation involving the intervertebral discs or the vertebral end plate. The average age at diagnosis is 2–8 years old. Discitis has a gradual onset, with the presenting symptoms being back pain and persistent pain at nighttime [75]. Diagnosis is confirmed with narrowing of the intervertebral disk space seen on radiographic imaging and increased uptake of Technetium Tc 99 in the discs on bone scan [76]. *Stapholococcus aureus* and *K. kingae* are the pathogens most commonly seen on disk aspiration. Laboratory studies are notable for increased inflammatory markers, including ESR and CRP levels [77]. Varying degrees of neurologic impairment were seen across studies, from no impairment [78] to decreased muscle tone, muscle weakness, and deep tendon reflexes [76]. Treatment with antibiotics, however, remains controversial. Long-term follow-up with these patients shows that the outcomes are favorable, but this condition requires rigorous conservative treatment and inpatient therapy within a specialized pediatric orthopedic care ward.

Inflammation and Autoimmune Disease

Chronic recurrent multifocal osteomyelitis (CRMO) is a childhood autoimmune disease that is often mistaken for bacterial osteomyelitis. However, the lesions of CRMO are sterile, and no antibiotic therapy is indicated [79]. The pathophysiology of the disease is currently unknown. It is often accompanied by other autoimmune conditions, such as psoriasis and inflammatory bowel disease. It presents as bone pain with or without associated fever and is marked by exacerbations and remissions. While more common at the metaphyses of long bones, it can also occur at the sternum and vertebrae. It is primarily diagnosed in adolescence and is more common in females than males. Plain radiographic findings are notable for lytic bone lesions surrounded by sclerosis [79]. Whole body MRI is useful for diagnosis and follow-up of children with CRMO [80]. Laboratory findings demonstrate normal cell counts with normal to high makers of inflammation (ESP, CRP). Antibiotics have no effect on disease course. Treatment consists of nonsteroidal anti-inflammatory drugs, methotrexate, sulfasalazine, and TNF-alpha inhibitors [79].

Juvenile idiopathic arthritis (JIA) is a diagnosis that includes all forms of chronic arthritis (lasting at least 6 weeks) of unknown etiology with an onset before 16 years of age. It is the most common rheumatologic disease of childhood. Diagnosis focuses on the history – determining the nature and severity of the pain – along with careful examination of all joints. A careful rheumatologic history and physical also must be obtained, with special attention to rashes, respiratory and cardiac findings, and hepatosplenomegaly [81]. No laboratory findings are confirmatory for JIA. Patients should be assessed by a pediatric rheumatologist and managed by a multidisciplinary team. Unfortunately, most children still experience a chronic course with periods of active disease, despite the availability of disease-modifying therapy. Treatment consists of NSAIDs, intra-articular joint injections (triamcinolone hexacetonide), and methotrexate. Those with polyarticular involvement at symptom onset may require systemic steroid therapy.

Neoplasm

Pediatric spinal neoplasms are rare, but they must be considered when evaluating a child with back pain. Causes of benign neoplasms include osteoid osteoma, osteoblastoma, and bone cysts. Malignant causes include lymphoma, neuroblastoma, Ewing's sarcoma, osteosarcoma, Langerhans cell histiocytosis, and metastatic disease.

Red flag symptoms that should prompt consideration of a malignancy include fever, chills, night sweats, and weight loss. Pain stemming from a neoplasm is generally not alleviated by rest and occasionally results in nighttime crying in this population [75]. Physical exam may be notable for local tenderness, sciatica, nonstructural scoliosis, and a palpable mass. MRI is the best imaging modality when a neoplasm is suspected, as it can reveal soft tissue masses in and around the vertebral column [75].

Osteoid osteomas and osteoblastomas are rare bone tumors involving the spine and long bones. Osteoid osteomas are less than 2 cm at maximum dimension, while osteoblatomas are larger. These patients usually present with spine pain. Whereas osteoid osteomas can be safely managed solely with pain control or radiofrequency ablation [82], osteoblastomas have the potential for malignant transformation. As a result, the primary treatment for osteoblastomas is local resection [83].

Langerhans cell histiocytosis (LCH), also known as histiocytosis X, is an eosinophilic granuloma (EG) that affects the bone. These lesions originate from the reticuloendothelial system and can affect the skeletal system in a unifocal and multifocal manner. Common sites for lesions include the femur, mandible, pelvis, and spine. The thoracic spine is most commonly affected, followed by lumbar and cervical areas. The vertebral body is the most common component of the spine that is affected. Patients with LCH commonly present with dull, focal back pain that increases over time. Back stiffness, radiculopathy, and restricted spine motion are also common. Lytic lesions can be seen on radiographic images. These lesions put patients at high risk for vertebral collapse; typically, vertebral collapse is characterized by

flattening of the vertebral body on imaging. Since the advent of MRI and CT, the role of plain radiographs in diagnosis has diminished. CT scans can show lytic bone destruction of the involved vertebrae, and MRI has a high diagnostic accuracy in spinal secluded lesions [84]. Treatment includes methotrexate, prednisone, or radiation for severe disease burden [85].

Primary spinal tumors in children most commonly occur in late childhood and early adolescence. The most common tumors are glial tumors, including ependymomas and astrocytomas [71]. Unfortunately, the presenting symptoms can be nonspecific, including motor weakness, gait disturbance, and back pain. 25–30% of children with spinal tumors suffer from recurrent episodes of back pain, which can be characterized as spinal pain, root pain, or tract pain. Spinal pain localizes to the bone segments adjacent to the tumor and is described as dull and aching. Root pain may mimic pain from disk herniation. Tract pain results from direct infiltration of the spinothalamic tract in the spinal cord by tumor. Diagnosis of spinal tumors is confirmed by MRI imaging. CT is contraindicated due to the high radiation dose required to image the entire spine [86]. Treatment for spinal tumors is surgical intervention [87].

Vasculitis

Another rare but significant cause of low back pain in pediatric population is vasculitis – the systemic inflammation of blood vessels [71]. Takayasu Arteritis (TA) is a chronic, autoimmune inflammation of the large blood vessels, predominantly the aorta and its major branches. This results in dilation, occlusion, and stenosis of the arteries. When the mid-aorta is involved, TA can lead to referred low back pain [88]. The average age at diagnosis is 13 years, with most children being diagnosed in adolescence. Worldwide, TA has an incidence of 1.2–2.6 million per year in Caucasians and a 100-fold higher incidence in East Asians [89]. It is the third most common cause of vasculitis in the pediatric age group.

During the acute inflammatory phase, systemic symptoms – including anorexia, fever, night sweats, and rash – predominate, and as these symptoms are nonspecific, TA commonly goes undiagnosed during this stage. This diagnostic delay can result in significant vascular sequelae in up to one-third of children with hypertension, headache, and weight loss commonly to develop over time. Once vascular occlusion leads to ischemia, organ-specific dysfunction occurs; renal injury, absence of extremity pulses, and cardiac involvement are the most common manifestations in childhood TA.

Laboratory evaluation can reveal elevated ESR, CRP, and matrix metalloproteinases (MMP). MMP level has been shown to correlate with disease activity [88]. Angiography is the gold standard for diagnosis, but MR angiogram and CT imaging are useful in diagnosis as well. Treatment includes glucocorticoids, immune-suppressants, antihypertensives, and anticoagulants.

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Part V

Treatment of Spine Pain

Opioid and Non-opioid Therapy

19

Dermot P. Maher, Bunty J. Shah, and Yakov Vorobeychik

Key Points

- Opioids provide analgesia by binding to the opioid receptors and altering cell membrane potential.
- The defining feature of opioid analgesia is the presence of significant interpatient and intrapatient variability. Different opioids work better in some people but not others, and prediction of response has not been optimized.
- Opioids for chronic non-cancer pain have a role in chronic pain management. However, caution must be exercised when working with these patients in the form of random urine toxicology, monitoring multistate prescription monitoring programs, etc. Physicians should be mindful of the risks posed by individual medications.
- NSAIDs work via the COX (cyclooxygenase) pathway inhibition, resulting in decreased levels of prostaglandins and thromboxanes.
- Although NSAIDs are probably effective in treating back pain in acute settings, there is a dearth of evidence supporting their long-term use.
- NSAIDs can be associated with gastrointestinal, hematological, cardiac, and renal side effects. As with all drugs, risks and benefits, including patient-specific factors, should be considered prior to initiation of therapy.
- Antidepressants have largely been studied for the treatment of neuropathic pain states, but few studies have examined the effectiveness of antidepressants in spine pain.
- Antidepressants act mainly by enhancing monoaminergic inhibition via the descending inhibitory nociceptive pathways. The antinociceptive effect of antidepressants could be independent of their antidepressant effects. Balance of both serotonin and norepinephrine reuptake inhibition is required for antidepressants' antinociceptive effect. SSRIs (selective serotonin reuptake inhibitors) are less effective than TCAs and SNRIs in treating pain.
- Adverse drug-related side effects must be weighed against the potential benefits when deciding to prescribe antidepressants for low back pain, as the effect on pain may be modest.
- Anticonvulsants may be helpful to treat neuropathic spine pain. There is limited and inconsistent evidence to support the use of anticonvulsants for the treatment of axial low back pain.
- Gabapentin and pregabalin, being a scheduled substance, may have addictive potential and warrant caution prior to prescription in patients at risk for substance abuse.
- Skeletal muscle relaxants are useful for the treatment of spasms causing acute back pain, but there is no long-term or chronic indication for the treatment of back pain with these medications.
- The side effect profile and patient comorbidities must be considered prior to initiation of muscle relaxant therapy.
- Carisoprodol and benzodiazepines are scheduled substances with proven addictive potential that should not be routinely prescribed for chronic spine pain treatment.

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- Topical analgesics exhibit properties of local penetration with decreased systemic absorption, theoretically leading to less adverse effects. They are available in gels, patches, lotions, creams, and ointments.
- Evidence is lacking for the use of topical herbal medications for the treatment of back pain
- Clinical trials demonstrate that some chronic pain conditions, particularly the ones presenting with neuropathic pain, may be treated by cannabinoids (CB) with the different degree of success. However, due to the lack of studies evaluating the potential therapeutic effects of CB in patients with chronic axial or radicular spinal pain, their potential benefits in treating these conditions cannot be determined at the present time.

Introduction

Spine pain conditions, such as low back pain (LBP), are the leading cause of disability worldwide [1]. Although a source of spine pain is often identifiable, the interventional treatment is not always effective or even possible. For example, procedures or surgeries usually fail to provide any significant relief in many patients suffering from lumbar discogenic pain, arguably the most common cause of axial LBP [2, 3]. When interventional treatment is unavailable or not fully successful, the medication therapy plays a pivotal role in comprehensive pain management. As the nature of spine pain may be nociceptive or/and neuropathic, different classes of medications can be prescribed to treat spine pain conditions.

Part 1. Opioids for the Treatment of Spine Pain Including Chronic Back Pain

Opioid Pharmacology and Basic Science

Opioid Receptors

Opioids act on serval receptors and receptor subtypes. Opioid receptors are a four-member group of the larger type A or rhodopsin-like G-coupled protein receptors (GCPRs) family that mediate the effects of endogenous and exogenous opioids [4]. The four receptors are designated: the mu opioid receptor (MOR, gene *OPRM1)*, kappa opioid receptor (KOR, gene *OPRK1*), delta opioid receptor (DOR, gene *OPRD1*), and the orphanin receptor (ORL, gene *OPRL1*). Functional opioid receptors have been identified by genomic studies and radioligand binding assays in almost all vertebrates with an impressive degree of cross-species genetic homology [4]. Opioids are required to exist in an ionized state in order to efficiently interact with an opioid receptor. Additionally, only the levorotary enantiomer of an opioid is capable of binding to a receptor.

Natural Ligands and Physiologic Functions

The primary endogenous ligands of the opioid signaling system are beta-endorphin, met-enkephalin, leu-enkephalin, and dynorphin [5]. These neuropeptides all have a conserved YGGFL/M N-terminus which also has structural similarity to morphine. The endogenous opioids are converted to active peptides by enzymatic cleavage from inactive precursors including proopiomelanocorticotropin, preproenkephalin, and preprodynorphin. Beta-endorphin and enkephalins appear to be the natural ligand for the MOR, dynorphin for the KOR, and the encephalin for the DOR.

Downstream Signaling Processes

Opioid receptors are G_o/G_i inhibitory GCPRs. Opioids activate inwardly rectifying potassium channels and inhibit voltage-dependent calcium channels resulting in both presynaptic and postsynaptic neuronal hyperpolarization. Presynaptic hyperpolarization inhibits the release of excitatory neurotransmitters, such as substance P and glutamate. In the central nervous system (CNS), approximately 70% of opioid receptors are located presynaptically. Opioids may also modulate cAMP signaling and mitogen-activated protein (MAP) kinase signaling cascades. Opioid receptors also undergo rapid phosphorylation of intracellular C-terminus domains. β-arrestin then binds to these phosphorylated domains with subsequent endocytosis and receptor recycling possibly contributing to rapid clinical desensitization.

Opioid receptors are localized to CNS regions involved in nociceptive transmission and processing including the periaqueductal gray, amygdala, corpus striatum, and hypothalamus. In the spinal cord, opioid receptors are most abundant in Rexed lamina 2, also known as the substantia gelatinosa.

Clinical Use of Opioids

Several classification schemes have been used for opioid grouping them by natural occurrence, chemical structure, receptor agonism profile, or physiologic effect.

Naturally occurring opiates, such as morphine and codeine, are chemically described as phenathrenes. Benzylisoquinolones, such as papaverine and noscapine, occur in opium but require chemical modification to achieve the analgesic activity. Semisynthetic opioids are chemical modifications of these naturally occurring substances to

analgesics such as heroin, hydromorphone, oxycodone, and buprenorphine. Synthetic opioids are not found in nature and belong to the chemical class of phenylpiperidines including meperidine, fentanyl, alfentanil, sufentanil, and remifentanil.

Opioids have also been broadly classified as "strong" and "weak." However, this may be a functionally inaccurate division because, with the exception of the partial agonists, opioids do not have an upper dosing limit (in pharmacological terms) beyond which additional medication will fail to provide additional analgesia. In practice, many opioid medications are limited due to lack of meaningful added analgesia with dose escalation, side effects such as severe constipation, or side effects due to interaction with other receptors, such as serotonergic effects of tramadol. Another reason for practical dose limitation is the fixed-dose combinations of opioids and other dose-limited medications, such as acetaminophen. The "strong" and "weak" designation continues to be advanced as an easy conceptualization tool and by organizational guidelines such as World Health Organization (WHO) cancer analgesic guidelines. The WHO guidelines were not developed or ever intended to serve as a model for the treatment of musculoskeletal or neuropathic pain, including low back pain. One of the opioids' most challenging characteristics is the wide range of doses required for effective analgesia. Key dates in the development of opioid analgesics are provided in Fig. 19.1.

Evidence for Treatment

The use of opioids to treat low back pain may be thought of as a swinging pendulum. Until the late twentieth century, opioids were not recommended for the treatment of chronic pain outside the setting of cancer as they were felt to be relatively ineffective and recognized to have serious side effects including addiction and loss of potency [6, 7]. However, in the mid-1980s, opioids started to be used for the treatment of chronic pain driven largely by evidence from retrospective analyses and industry-sponsored studies [8–11]. The rational for this paradigm shift was the perception that pain was undertreated and the potential benefits of long-term opioid treatment outweighed the known risks. In 2000, the Joint Commission for Accreditation of Hospitals Organizations published their first standards on the management of pain causing a reactionary increase in prescription of pain medications, including opioids, for chronic pain. Early studies examining the effectiveness of opioid therapy for the treatment of chronic non-cancer pain fueled enthusiasm for treatment but failed to provide data on long-term use or adverse side effects in broad populations and only focused on highly selected cohorts for relatively brief periods of time [12].

When rigorously studied in randomized, controlled trials, opioids have been demonstrated to produce modest short-term benefits for the treatment of chronic low back pain [13–15]. However, the solid evidence for the long-term reduction of chronic back pain or increased in function with opioid treatment are lacking [16, 17]. Opioid use for chronic back pain ranges from 3% to 66%, with the increased utilization in subspecialty centers [18]. Studies regarding the efficacy of opioids for chronic LBP have not demonstrated superior outcomes compared to placebos or other non-opioid medications,

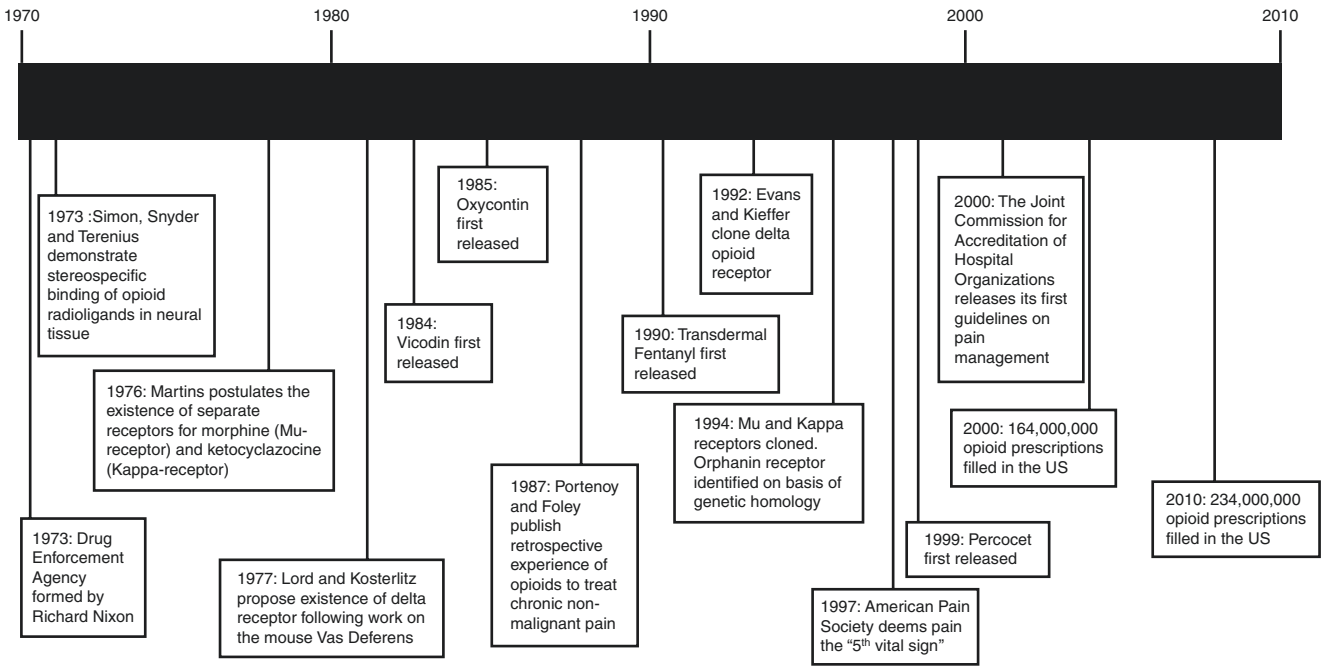

Fig. 19.1 Important dates in the discovery and development of opioids

such as nonsteroidal anti-inflammatories (NSAIDS) or acetaminophen [13, 15, 17–19]. Studies also have not been able to demonstrate improvements in function or return to work with opioid use in the setting of chronic LBP [18, 20]. A high rate of placebo response is noted in many studies in response to sham opioid treatment [21]. It should also be noted that the longest prospective comparative study, which failed to demonstrate superiority to a control, only had a 1-year study period and the longest prospective comparative study which did demonstrate superiority to a control had only a 12-week study period [15, 17]. This could indicate a usefulness of opioids for short-term, but not long-term pain management.

The systematic evaluation of opioids for the treatment of chronic pain has proven difficult due to challenges associated with even maintaining study subjects on trial medications. In one meta-analysis, it was noted that 31.4–61.9% withdrew due to adverse events and additional 3.3–29.6% withdrew due to a lack of efficacy [15].

There are no consensus guidelines for initiation, titration, or long-term maintenance of opioids therapy for the treatment of back pain. However, many guidelines suggest that pain should initially be managed with non-opioid analgesics. Initiation of opioid therapy for the treatment of spine pain must take into account the patients' entire medical condition, including the pathology of the pain and the expected clinical course. The choice of which agent to use should be determined through a discussion with the patient regarding past experiences with opioid therapy, severity of pain, and coexisting medical conditions. In general opioids should be administered in the most convenient format available for the patient. For the treatment of acute pain, more frequent titration of an agent is required compared to less frequent titration that is indicated in the treatment of more chronic pain. In the treatment of chronic non-cancer pain, unlimited dose escalation may not be appropriate. Increased doses may have diminished return with each log dose increase only decreasing pain by 12.0/100 points [15]. Frequent monitoring and evaluation for analgesic efficacy and side effects should be done. Physicians and patients should be prepared to explore alternative treatments in the event that opioid therapy results in suboptimal outcomes. Additionally, strong consideration should be given to simultaneous use of alternative treatments which may reduce the amount of opioid needed for adequate analgesia, such as non-opioid medications, physical therapy, and interventional pain procedures, which may either reduce opioid use or provide similar benefit [15, 22, 23].

Side Effects Associated with Opioid Therapy

The side effect profiles of individual opioid analgesics will vary in both intensity and prevalence. However, many side effects are common to all analgesic agents.

Central Nervous System Effects

Opioids alleviate the distress and anxiety caused by pain without causing complete resolution of pain. Anxiolysis may be accompanied by euphoric or dysphoric reactions. Chronic pain patients with coexisting depression initially report improvement in their mood symptoms followed by an inevitable worsening of depression. Opioids also cause a powerful, reinforcing, positive reward pathway that appears to be separate from their analgesic effects and may explain their addictive properties [24]. Consequentially, a high rate of behavioral side effects has been noted including addiction and tolerance [15].

Decreased secretion of sex-hormone-releasing hormones from the pituitary is frequently seen with chronic use of opioids and can lead to clinical evidence of hypogonadism.

Miosis is due to an excitatory action of opioids on the Edinger-Westphal nucleus resulting in increased oculomotor nerve outflow. Tolerance to opioid-induced miosis is rarely observed.

Other Side Effects

In general, morphine and other opioids do not cause hypotension or cardiac depression. However, it can decrease sympathetic nervous system output. Morphine can also stimulate the nucleus tract solitarius in the brain resulting in increased vagal tone and bradycardia. The sinoatrial node can also be directly inhibited by morphine furthering bradycardia. There is some evidence that prescription opioid use is associated with the increased risk of death from cardiovascular disease in females [25]. Morphine is unique in that it also can cause release of histamine and subsequent hypotension, decreased venous return, and increased venous capacitance.

All opioids produce a dose-dependent and gender-specific change in ventilation due to direct stimulation of opioid receptors in the ventral and dorsal medullary respiratory nucleus. Opioids decrease the rate of ventilation and often produce apneic spells. This is accompanied by an incomplete compensatory increase in tidal volume with the development of hypercapnia. Opioids will also decrease the sensitivity of CNS chemoreceptors to hypercapnia causing an increase in resting carbon dioxide (CO_2) and a shift in the CO_2 ventilatory response curve to the right in women but not men. Conversely, opioids increase the apneic threshold in men but not women. In clinical settings, chronic opioid use may induce a variety of abnormal breathing [26].

Opioids produce a dose-dependent decrease in ciliary activity. Opioids can also cause an increase in airway resistance due to stimulation of bronchial smooth muscle and chest wall rigidity rather than direct effects of histamine release. Cough suppression is due to effects on medullary cough centers by dextrorotary enantiomer of opioids, in contrast to analgesia which is caused by levorotary enantiomers.

Opioids cause dose-independent increases in intrabiliary pressure, including contracture of the sphincter of Oddi and the pancreatic duct smooth muscles. This can complicate the management of pancreatitis with opioid therapy.

Delayed gastric emptying in the setting of opioid use is due to increased tone at the gastroduodenal junction. Peristaltic motion is decreased in both the small and large intestine. Prolonged passage of stool results in increased water resorption and worsening of resultant constipation. Tolerance to opioid-induced constipation is rarely observed. Opioid-induced constipation can be reversed by naloxone or specific peripherally acting agents such as methyl-naltrexone or naloxegol.

Nausea and vomiting are among the common dose-limiting side effects of opioids and are caused by stimulation of the chemoreceptor trigger zone at the base of the forth ventricle. Fenestrations in the blood-brain barrier at this point allow for detection of high levels of many toxins, including opioids [27].

Contrary to the effects of opioids on the gastrointestinal system, opioids can cause an increase in peristaltic activity of the ureters and a higher detrusor muscle tone, leading to urinary urgency. However, opioids will also increase the tone of the vesicular sphincter which can make voiding difficult causing urinary retention.

Treatment of chronic pain with long-term opioid therapy may result in a wide spectrum of changes in sensory perception. Opioid-induced hyperalgesia (OIH) is an acquired neuropathic pain state characterized by sensitivity and paradoxically increased pain associated with escalating dose of opioid agonists [28]. The development and maintenance of OIH share common intracellular pathways with neuropathic pain [29–31].

Accumulating evidence suggests that opioids induce suppression of both innate and adaptive immunity through direct interaction with opioid receptors on the cell surface of many leukocytes [32].

Survey of Individual Opioid Pharmacology

If a patient is a candidate for opioid therapy, the choice of opioid analgesic is determined by a conversation with the patient to determine the most convenient route and frequency. Different medications will afford unique dosing schedules and, in some cases, present unique benefits and side effects. Individual differences can be attributed to opioids chemical and pharmacokinetic differences which are presented in Table 19.1.

Morphine

Morphine is among the most frequently utilized opioids and is the medication to which all other opioids are compared. It is available for administration in a number of different routes and preparations including immediate- and controlled-release tablets, elixirs, suspensions, gels, intravenous (IV), epidural, and intrathecal. Oral morphine is almost fully absorbed but undergoes rapid but variable, first-pass metabolism such that the effective bioavailability is reported as between 10% and 45%. It is approximately 30% bound to plasma proteins and is mostly ionized at a physiologic pH of 7.4. Peak plasma morphine concentrations occur about 15 minutes before peak cerebrospinal fluid (CSF) concentrations and peak physiologic manifestations. Acidosis causes an increase in the ionized fraction but also causes an increase in cerebral blood flow with a net increase of morphine in the CNS compared to normocarbia. This indicates the importance of tissue perfusion over solubility in morphine's penetration to the CNS. The expected duration of analgesia is usually between 2 and 4 hours with immediate-release (IR) morphine and 8–12 hours with controlled-release (CR) preparations. Several CR preparations are available including MS Contin, Kadian, and Oramorph. Abuse-deterrent formulations of morphine are also available including Embeda and Arymo ER. Currently morphine is the only opioid approved for use in intrathecal drug delivery systems (IDDS).

A study of 103 subjects with non-radicular low back pain randomized to receive either extended-release morphine titrated to effect or placebo demonstrated a 44% decrease in pain and a 31% increased self-reported functionality. Interestingly, at the end of a 30-day treatment period, a 42% reduction in analgesic potency of opioids were noted which indicated rapid development of tolerance [33].

Approximately 75–85% of a morphine dose is metabolized by UGT-2B7 to morphine-6-glucuronide (M6G) and 5–10% metabolized to morphine-3-glucuronide (M3G) as measured by recovered urinary metabolites, respectively. M6G has a longer duration and greater potency than morphine. M3G is devoid of significant opioid receptor activity. Genetic variation in UGT-2B7 does not appear to have any clinically relevance on analgesia or risk of overdose [34]. Additionally, isolated hepatic impairment has been reported to not significantly influence morphine pharmacokinetics, likely owing to a large hepatic reserve for glucuronidation [35]. Decreased renal function will result in accumulation of morphine metabolites. Morphine can be removed by hemodialysis.

Codeine

Codeine is a naturally occurring prodrug with limited intrinsic analgesic efficacy. Approximately 10% of ingested codeine undergoes o-demethylation by hepatic CPY-2D6 and is converted to morphine, which provides analgesia. Approximately 10% of US Caucasian population are "poor metabolizers" in that they do not achieve a significant conversion of the prodrug to morphine and, subsequently, achieve poor analgesia

Table 19.1 Pharmacologic properties of clinically used opioids

Medication	Bioavailability	Prodrug	pKa	vd_{ss} (L/Kg)	% Protein bound	Time to analgesic onset (minutes)	$t1/2_{ss}$ (hours)	Metabolism	Active metabolites	Renal adjustment	Hepatic adjustment
Morphine	IV = 100% Oral 10–45%	No	8.2	1–4.7	30%	60	2–4	UGT-2B7 10% unchanged	Yes	Yes	No
Codeine	Variable	Yes	8.2	2.6	Minimal	30–60	4–6	CYP2D6 to morphine	Yes	Yes	Yes
Tramadol	80–90%	Yes	9.41	2.6–2.9	20%	30–60		CYP2D6 and CYP3A4	Yes	Yes	Yes
Methadone	41–99%	No	8.94	1–8	90%	60	8–80	CYP3A4, CYP2B6, and CYP2C19	No	No	No
Hydromorphone	24%	No	8.6	1.22	20%	15–30	2.3–2.5	UGT 2B7	Yes	Yes	No
Tapentadol	32%	No	9.34–10.45	7.7	20%	3–60	4	UGT2B7, UGT1A, CYP2C9, and CD2C19	No	No	No
Oxycodone	50–87%	No	8.3	2.6	45%	10–30	3–5.7	CYP3A4, CYP3A5, and CYP2D6	Minor	Yes	Yes
Meperidine	50%	No	8.7	3.84	65–75%	45	3–5 h	CYP2B6, CYP3A4, and CYP2C19	Yes	Yes	Yes
Fentanyl	92% for patch	No	7.3	3–8	84.4%	5–15, 24 hours for patch	3.1–6.6	CYP3A4	No	No	No
Hydrocodone	70%	No	8.23	3.3–4.7	Minimal	10–20	3–4	CYP2D6 and CYP3A4	Minor	Yes	No
Buprenorphine	10–15%	No	8.31	2.7–5.1	96%	30	6–9	CYP3A4 and CYP2C8	No	Yes	Yes

[36]. Conversely, there are also a small percentage of patients who are "ultra-rapid metabolizers" in whom CYP-2D6 is overly active and dangerously high serum concentrations of morphine are frequently achieved, often with adverse clinical outcomes [37]. Elimination as non-metabolized codeine is approximately 80% by UGT-2B7-glucoronidation and CYP-2D6 N-demethylation to norcodeine. Constipation is the primary dose-limiting side effect of codeine. At low doses (15 mg), codeine is an effective antitussive.

Hydromorphone

Hydromorphone is a semisynthetic opioid with a short onset of action of 30 minutes and approximately 4-hour duration of action. Hydromorphone is well absorbed from the upper gastrointestinal tract but undergoes extensive and variable first-pass metabolism leading to low bioavailability. Hydromorphone is metabolized by UGT-2B7 and UGt-1A3 to hydromorphone-3-glucuronide (H3G) and hydromorphone-6-glucuronide (H6G). Similar to morphine, accumulation of active metabolites is observed in the setting of renal failure. Liver dysfunction or isolated dysfunction of either the CYP or UGT systems does not appear to significantly influence the clinical pharmacokinetics of hydromorphone. CR formulations are available such as Exalgo. Preservative-free hydromorphone is also occasionally used off-label in IDDS.

In a study, 266 patients with low back pain were randomized to receive between 12 and 64 mg of hydromorphone daily (n = 133) or placebo (n = 133) and were followed for 12 weeks. A total of 60% subjects in the hydromorphone arm achieved at least 30% reduction in pain, while only 42% subjects of the placebo group did [38].

Hydrocodone

Hydrocodone is frequently marketed as a fixed combination formulation combined with acetaminophen (Vicodin). Combination with acetaminophen limits the maximal daily dose that can be administered. Hydrocodone is metabolized by CYP-2D6 to form hydromorphone and by CYP-3A4 to form norhydrocodone. In a study, 252 subjects with low back pain were randomized to either extended-release hydrocodone (20–100 mg daily, n = 151) or placebo. A total of 68% subjects randomized to hydrocodone had at least 30% reduction in pain compared to 31% subjects in the placebo group [39]. An abuse-deterrent formulation of hydrocodone is available marketed as Hysingla ER. Additionally, Zohydro is an extended-release formulation of hydrocodone.

Heroin

Heroin, diacetylmorphine, is a prodrug with no intrinsic mu opioid receptor activity. It is metabolized to 6-monoacteylmoprhine (6-MAM) and then to morphine. 6-MAM allows for toxicologists to differentiate morphine and heroin use. It is considered a high-risk schedule 1 medication in the USA, but it has found uses mostly in palliative care in Canada, England, and several other countries. Heroin has not been formally evaluated for use in spine pain such as low back pain.

Oxycodone

Oxycodone is a semisynthetic derivative of thebaine. It is currently the most widely utilized opioid in the USA and across the world. It is available as both a short-acting IR and long-acting CR preparation. Abuse-deterrent formulations are also available. It has a bioavailability of 50–87% with peak plasma concentrations seen after 2 hours. The duration of analgesia is approximately 3–5.7 hours for IR oxycodone and 4.5 hours for CR oxycodone. Given the short half-life, steady-state kinetics are reached with oxycodone CR after 24–26 hours. Abuse-deterrent formulations of oxycodone are available including reformulated OxyContin and Xtampza.

A study randomized 83 subjects with chronic low back pain to either oxycodone combined with naloxone (10/5, 20/10, and 40/20 mg BID, n = 39) or placebo (n = 44) for 8 weeks. An intention to treat analysis of 54 patients who completed the 8-week follow-up demonstrated a 20% reduction in pain with oxycodone and an 8.3% reduction in pain with the placebo [40]. Another study compared oxycodone QID (n = 206) to placebo (n = 101) to fixed-dose combinations of oxycodone and naloxone (Oxytrex, n = 412). At 12 weeks, the placebo group demonstrated a 32.2% reduction in pain and compared to 46.2% in the oxycodone group. Oxytrex produced similar analgesia but less pruritus than oxycodone [41].

Approximately 80% oxycodone is metabolized by N-demethylation mediated by CYP-3A4 and CYP-3A5 to noroxycodone, and 20% is metabolized by o-demethylation mediated by CYP2D6 to oxymorphone. Metabolites of oxycodone contribute minimally to its activity, and inhibition of either metabolic pathway is usually compensated by increased activity of an alternative pathway. Inhibition of both CYP-2D6 and 3A4 can result in accumulation of unmetabolized oxycodone [42]. Accumulation of clinically relevant concentrations of oxycodone metabolites is rare. Oxycodone is frequently combined in fixed combination formulations with acetaminophen (Percocet, Norco). CR formulations are also available. The potential for euphoric effects of oxycodone and its prevalence make abuse potential a major concern of prescribing this medication.

Tramadol

Tramadol produces analgesia through action as an opioid agonist prodrug and has additional analgesic effects through central serotonin and norepinephrine reuptake inhibition. The additional mechanisms of action caused some to support the use of tramadol in the treatment of neuropathic pain over other opioids. It undergoes O-desmethylation mediated by

both CYP-2D6 and CYP-3A4 to O-desmethyltramadol, also referred to as M1. While M1 is a significantly more potent agonist at the MOR, it lacks significant monoamine reuptake inhibition activity, unlike its parent compound. Genetic variation in CYP-2D6 and CYP-3A4 may alter production of M1, while variation in catechol-o-methyltransferase (COMT) may influence the clinical activity of the parent drug. The maximum daily dose of tramadol is usually listed as 600 mg daily, but this is also poorly supported by clinical studies. Side effects with tramadol, especially nausea and vomiting, are reported to occur at approximately the same, or possibly a slight reduced, frequency compared to other opioids. A review of seven prospective studies of tramadol, either alone or in combination with acetaminophen, for the treatment of low back pain ($n = 2641$), demonstrated modest benefits of chronic tramadol use [15].

Tapentadol

Tapentadol has activity as a MOR agonist and an inhibitor of central norepinephrine reuptake. Tapentadol is metabolized by UGT-2B7 and UGT-1A to inactive compounds and does not interact with the cytochrome system. A study of 965 subjects with low back pain randomized to tapentadol extended release (100–250 mg BID $n = 313$), oxycodone (20–50 mg BID $n = 322$), or a placebo ($n = 313$) demonstrated similar analgesia between tapentadol and oxycodone at 15 weeks. Tapentadol demonstrated less constipation, nausea, and vomiting compared to oxycodone but more when compared to placebo [43].

Meperidine

Meperidine is a synthetic opioid medication that acts as a MOR agonist, a cholinergic receptor antagonist, and also voltage-gated sodium channel antagonism. Meperidine's anticholinergic properties cause mild atropine-like effects with tachycardia. The sodium channel inhibition confers local anesthetic-like properties. Meperidine is metabolized by CYP2B6, CYP3A4, and CYP2C19 to normeperidine, which is excreted in urine. Accumulation of this metabolite in patients with renal failure is associated with CNS excitation and clinically resulting in agitation, myoclonus, and generalized seizures.

Buprenorphine

Buprenorphine is a semisynthetic analog of thebaine. Clinically, it is a long-acting, highly lipophilic partial MOR agonist and KOR antagonist with a minimal DOR activity. Partial agonism and high bioavailability have expanded buprenorphine's utility to opioid replacement and maintenance treatment programs. Onset of action is usually within 30 minutes, and analgesia duration of action is reported to be 6–9 hours, requiring TID dosing. Two randomized studies compared ($n = 620$) buprenorphine patches to placebo, and one study compared buprenorphine to oxycodone ($n = 660$), and these studies found that, while oxycodone was slightly more effective than buprenorphine at 12 weeks for pain reduction, buprenorphine was more effective than placebo [15]. Transdermal preparations of buprenorphine are available for continuous delivery of medication for 72 hours. Unlike methadone, buprenorphine does not cause QTc prolongation. Buprenorphine is metabolized by CYP-3A4 and CYP-2C8 to mostly inactive metabolites. Renal failure may cause accumulation of norbuprenorphine, which is thought to be clinically insignificant.

Fentanyl

Fentanyl is a synthetic opioid with a rapid onset and cessation of action. Fentanyl's potency and rapid onset and short duration of action are attributed to a low molecular weight and high lipophilicity. Several formulations take advantage of these properties and are clinically available including sublingual dissolving strips, 72-hour transdermal preparations, and oral transmucosal (lozenge) formulation, which has proven very useful in the pediatric population. The use of sublingual transdermal fentanyl has an onset of 5–15 minutes and greater than 50% bioavailability due to avoidance of first-pass metabolism. The pulmonary vasculature serves as a pharmacologically inert depot for an estimated 75% of administered fentanyl.

A study of 680 subjects with low back pain randomized to receive either 25 mcg/72 ($n = 338$) or oral morphine 30 mg BID ($n = 342$) demonstrated similar analgesia at 13 months follow-up. The fentanyl group experienced less constipation [44].

Transdermal fentanyl patches are frequently used for continuous analgesia in patients who no longer require dose titration. Most (92%) of transdermal fentanyl enters the systemic circulation. Peak fentanyl plasma concentrations are observed 12–24 hours after patch application, and a subcutaneous depot effect causes fentanyl to still enter the circulation for approximately 24 hours after patch discontinuation. Acute toxic delirium has been reported in cancer pain patients treated with transdermal fentanyl. Unfortunately, fentanyl has also been increasingly identified as a drug of abuse [45]. Fentanyl is primarily metabolized by CYP-3A4 to inactive metabolites. Similarly, fentanyl-derived opioids such as sufentanil, alfentanil, and remifentanil are also metabolized by different routes to inactive products. Fentanyl exhibits a high degree of protein binding such that disease-related changes in circulating alpha-1-glycoprotein will cause significant changes in fentanyl's pharmacokinetics.

Methadone

Methadone is a synthetic opioid with several unique properties that make it advantageous for the treatment of pain. It is chemically unique among opioids as the sole clinically used member of the diphenylpropylamine class. It has high bioavailability, long duration of action, low cost, and a lack

of major active metabolites even in the setting of hepatic and renal failure. Methadone exerts analgesic activity by the mu opioid receptor agonism, NMDA receptor antagonism, and inhibition of serotonin reuptake. Its pharmacologic action at multiple sites has made it a preferable medication to treat neuropathic pain compared to other opioids.

The pharmacokinetics of methadone make its use in the treatment of spine pain conditions challenging. A high degree of vigilance and individualization is warranted. Methadone has excellent bioavailability generally reported as greater than 85% with a range from 41% to 99%. It is highly bound to alpha-1-glycoprotein and to acute phase reactant proteins that can cause plasma levels to fluctuate with disease state. The starting parenteral dose of methadone is recommended to be 50–80% of the oral dose. An impressively wide range of half-lives have been reported for methadone from 8 hours to 80 hours. The half-life of methadone is initially a function of its slow redistribution from plasma to tissues, and later, as tissues become saturated, it correlates primarily with metabolism of the drug itself. The clinical consequences of this prolonged half-life are that steady-state kinetics may only be achieved after 10 days. Additionally, methadone has a large volume of distribution due to even more tissue binding than plasma binding such that the effects of methadone persist for several hours after medication discontinuation. Dose titration outside a highly monitored setting should not be attempted more rapidly than every 10 days in the outpatient setting.

The potency of methadone relative to morphine has also been reported as a range from 4.4 to 16.4 that also appears to be related to the dose of methadone. For the treatment of chronic low back pain, methadone is either dosed twice a day or three times a day. Methadone maintenance uses once daily dosing.

Methadone is known to prolong QTc intervals, which can cause potentially fatal arrhythmias such as torsade de pointes (TdP). However, this is usually observed at doses greater than 80 mg per day [46]. It is recommended to check a baseline, 1 week and then annual EKG when initiating methadone. In males and females, a prolonged QTc is greater than 450 milliseconds (ms) or 470 ms, respectively. QTc greater than 500 ms or a 40 ms increased over baseline is considered high risk for TdP. Baseline and follow-up EKG studies are recommended when managing methadone. Methadone undergoes complex metabolism to pharmacologically inert products.

Methadone is metabolized primarily by N-methylation via CYP-3A4 with lesser contributions from CYP-2D6 and CYP-1A2. Several other cytochrome enzymes are potentially involved including CYP-2B6, 2C8, 2C9, and 2C19 [47]. Methadone has also been observed to be a CYP-3A4 autoinducer, leading to plasma concentration stabilization even with impaired clearance. Final clearance of its metabolites is usually through hepatobiliary and, to a lesser extent, renal clearance.

The Opioid Epidemic

The opioid epidemic represents a series of medical and societal events that are ongoing related to the abundant use of opioids in modern culture. The quantity of opioids that are prescribed in the USA alone for the treatment of chronic pain has increased 104% from 2000 to 2010, from 43.8 million prescriptions to 89.2 million prescriptions [4]. Further increases were observed between 2010 and 2015 [5]. Approximately 4% of the US population is now prescribed an opioid for pain on a regular basis [5, 6]. The rise in the prescription of opioids to treat nonmalignant pain can be attributed to many factors, such as government mandates to measure and treat pain, encouraging but short-term clinical trial evidence to support their use, aggressive marketing from pharmaceutical companies, a public demand for immediate pain relief, and inadequate education of side effects and adverse consequence of long-term opioid use. Concurrent with the increase in prescription opioids, the USA observed a dramatic rise in the incidence of opioid overdoses and opioid-related deaths [48–50]. Several strategies have been implemented to address the situation of which a practicing physician should be aware. In October 2017, the executive branch of the US government declared the US opioid crisis a "public health emergency" with several states declaring localized states of emergency.

The US Federal Government has adopted policies to address the rise in opioid deaths. The US Drug Enforcement Agency (DEA) was created by Richard Nixon in 1973 to enforce the Controlled Substances Act of 1970. The DEA's role in the opioid crisis is far reaching and includes monitoring pain clinics with abundant and reckless opioid prescribing practices, also known as "pill mills," and to block the import of opioids, including heroin, fentanyl, and carfentanil, from foreign countries [51]. The Food and Drug Administration (FDA) has not made naloxone preparations available as over-the-counter medications. However, as of 2017, 35 states have allowed both patients and third parties to obtain naloxone without a prescription. Many states have also implemented "Good Samaritan" laws which protect medical professionals from naloxone-related liability and bystanders from prosecution. Finally, many states have Prescription Drug Monitoring Programs (PDMPs) which can track filled prescriptions in a state to monitor for "doctor shopping." The PDMPs of many states are now being linked, but there is not a National PDMP at this point.

In 2016, Centers for Disease Control and Prevention (CDC) developed and published the CDC Guideline for Prescribing Opioids for Chronic Pain, which provides recommendations for prescribing opioid pain medications for patients in primary care settings [52]. It should be noted that over a dozen guidelines have been previously published emphasizing various aspects of the management of chronic pain with opioid therapy [53].

There is also a simultaneous effort to educate physicians and trainees, including medical students, on proper pain management practices and appropriate opioid prescribing practices. Surveys have shown that in most US and Canadian medical schools, formal instruction on pain management is rarely offered and is brief when offered [54]. In addition to providing education on pain management options, trainees are also instructed on recognition of opioid use disorders, appropriate initial treatment, and methods of referral to specialists for more definitive treatment [55]. The public is also the recipient of educational efforts. Public perceptions regarding pain pathology, treatments, and expected outcomes remain underdeveloped. The goal of public education is to maintain patient's functional recovery by offering more appropriate and alternative non-opioid therapies [55].

In conclusion, opioids are a potentially useful treatment for spinal pain conditions including low back pain. However, safe and effective use of this therapy requires an understanding of opioid pharmacology, anticipated benefits, potential risks, as well as the knowledge of how to address opioid-related side effects and adverse consequences such as addiction, abuse, and overdose.

Non-opioid Treatment of Chronic Low Back Pain

NSAIDs

Nonsteroidal anti-inflammatories (NSAIDs) are among the most common analgesics prescribed for the treatment of acute and chronic spine pain [56, 57]. They are the most widely prescribed medications worldwide and are commonly used in the treatment of low back pain based on their analgesic properties and anti-inflammatory activity [58]. NSAIDs also possess antipyretic properties.

NSAID Pharmacology

NSAIDs are a chemically heterogeneous group of medications consisting of one or more aromatic rings connected to an acidic group. The traditional and most widely accepted mechanism of action of NSAIDs is via inhibition of the cyclooxygenase (COX) pathways. COX was isolated from the vesicular glands of sheep in 1976 by Hemler who noted that the isolated COX was responsible for the catalysis of the reaction leading to the insertion of two oxygen molecules required for the formation of prostaglandins and thromboxanes from polyunsaturated fatty acids [59, 60] (Fig. 19.2).

NSAIDs inhibit the COX activity of prostaglandin H and G synthase, which is the catalyst for the conversion of arachidonic acid to prostaglandin [61]. In turn, prostaglandin H is a precursor of thromboxanes, prostaglandin G, and a number of other pain and inflammatory modulators. It has been demonstrated that prostaglandins may cause hyperalgesia via sensitization of nociceptors to mechanical or chemical stimulation [62]. COX-1 is commonly referred to as a "constitutive isoform," whereas COX-2 is commonly referred to as an "inducible isoform" [59, 63]. COX-1 is implicated in important physiologic functions including anti-thrombogenesis and gastric mucosal protection. This is accomplished through the production of prostacyclin through COX-1 induction. When released by the endothelium, prostacyclin has antithrombogenic and cytoprotective properties [59, 64]. COX-2, on the other hand, induces inflammation and related cytokines. Therefore, the anti-inflammatory properties of NSAIDs have been linked to COX-2 inhibition, whereas most adverse effects (gastric lining irritation) have been attributed largely to COX-1 inhibition. Older-generation NSAIDs (diclofenac, ibuprofen, indomethacin, naproxen, and piroxicam) prevent the production of prostaglandins through the inhibition of both COX-1 and COX-2. Newer-generation medications (celecoxib, etodolac, meloxicam, and nabumetone) block COX-2 more selectively and theoretically cause less adverse effects compared to the traditional nonselective NSAIDs [56, 62]. Meloxicam is more selective for COX-2 than nabumetone, while celecoxib is more selective for COX-2 than meloxicam, etodolac, and nabumetone [65, 66].

Evidence of Efficacy

In 2016, a Cochrane review on NSAIDs was published [67]. The study included 13 trials, of which 10 studies were deemed to be at "low" risk of bias. Six of the included studies compared NSAIDs with placebo, numbering 1354 participants in total [68–73]. The authors of the review concluded that there was low-quality evidence that NSAIDs are more effective in low back pain treatment than placebo. The mean difference in pain intensity was −6.97 (VAS scale 0 to 100; median follow-up of 56 days). Disability was considered as an outcome measure in 4 of the included studies as assessed by the Roland Morris Disability Questionnaire. As with pain intensity, the authors of the review concluded that there was low-quality evidence that NSAIDs are more effective than placebo in decreasing disability. The mean difference from a baseline was −0.85 (scale of 0 to 24; median follow-up of 84 days). When considering adverse effect profiles of NSAIDs versus placebo, all six placebo-controlled studies suggested that there was no statistically significant increased frequency in adverse effects in study participants treated with NSAIDs versus their placebo-treated counterparts (RR 1.04, 95% CI 0.92 to 1.17). However, the authors do caution that this may be an underrepresentation of the true frequency of adverse events given the small sample size and duration of follow-up in most of the trials included.

Two studies compared effectiveness of various nonselective NSAIDs (ibuprofen versus diclofenac and piroxicam versus indomethacin) [74]. No differences were found between

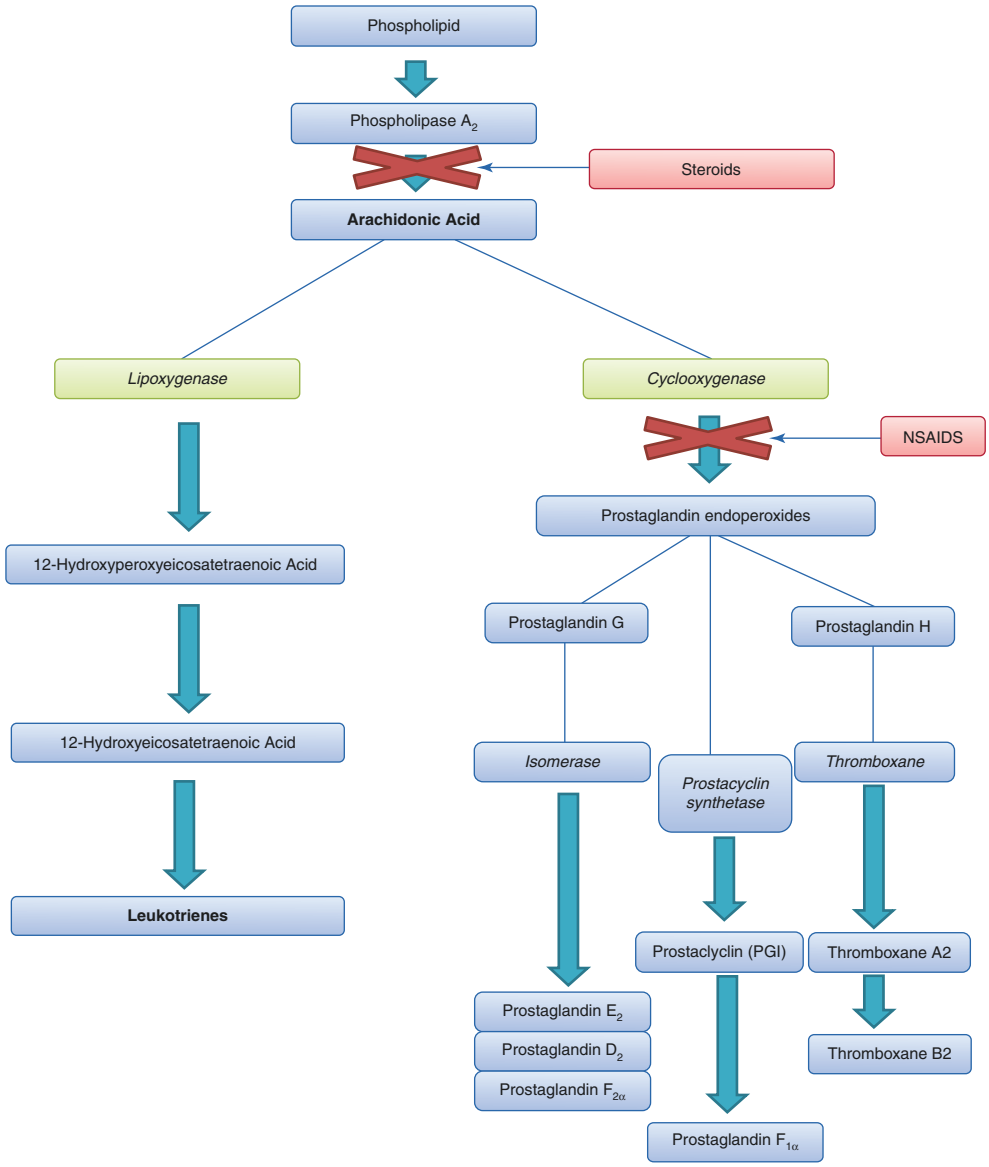

Fig. 19.2 The arachidonic acid metabolic pathway. NSAIDs inhibit COX, resulting in decreased production of prostaglandins and thromboxanes

different NSAIDs in these studies of relatively small size. Another trial in the review reported no difference in pain intensity between groups treated with selective versus nonselective NSAIDs [75]. Another trial comparing diflunisal with paracetamol (acetaminophen) showed no statistically significant difference in reduction of pain scores between the two treatment groups [76]. One study found better outcome in global improvement with celecoxib versus tramadol [77]. One trial compared outcomes in patients treated with NSAIDs vs. home exercise [78]. The exercise treatment group showed greater improvement in the disability domain without a significant difference in pain scores [78]. Six of the 13 randomized controlled trials (RCTs) included in this systematic review indicated that NSAIDs are more effective than placebo in low back pain treatment [68–71, 73, 79]. However, when considering the effect of NSAIDs on disability, they are only slightly more effective than placebo. The magnitude of these effects is judged to be small by the authors with a low level of evidence. When considering only the studies at low risk of bias, the differences in effect between NSAIDs and placebo were less apparent. Further, no difference in efficacy between NSAID types, including between COX-2 inhibitors and nonselective NSAIDs, was identified. The authors could not offer a firm statement on the long-term safety of NSAID therapy or the incidence of adverse events in light of the fact that the review included only RCTs with small sample sizes with relatively short durations of follow-up.

Adverse Effects of NSAIDs

Based on the concept that COX-2 selectivity can decrease the risk of GI side effects compared to nonselective COX

inhibitors, much attention has been given to the development of selective NSAIDs. However, with time, concerns have arisen over the potential increased risk of cardiovascular side effects associated with the use of selective COX-2 inhibitors. A placebo-controlled trial demonstrated evidence for adverse cardiovascular outcomes associated with the COX-2 selective NSAID, rofecoxib, which resulted in its withdrawal from the market in 2004 [80]. The Prospective Randomized Evaluation of Celecoxib Integrated Safety versus Ibuprofen or Naproxen (PRECISION) trial was conducted to compare the risk of cardiovascular, gastrointestinal, renal, and other outcomes with celecoxib compared to two other nonselective NSAIDs (naproxen and ibuprofen) [81]. The study showed that, at moderate doses, celecoxib was non-inferior when compared to naproxen or ibuprofen, as far as the primary cardiovascular outcome was concerned. A lower frequency of gastrointestinal side effects was observed with celecoxib compared to either naproxen or ibuprofen, and a lower frequency of adverse renal effects was observed with celecoxib compared to ibuprofen.

With respect to the gastrointestinal system, NSAIDs have been implicated in gastrointestinal damage of the stomach as well as the small intestine, including ulcers, bleeding, strictures, and perforations. In part, these adverse events have been traditionally explained by COX-1 (and to some degree COX-2) inhibition with decreased prostaglandin secretion, which can lead to decreases in microcirculation resulting in gastrointestinal ischemia. Recently, COX-independent mechanisms for GI-related side effects have garnered attention [82]. This includes the direct effect of the contact of NSAIDs with the lumen and mucosa. When combined with the aforementioned COX inhibition and uncoupling of mitochondrial oxidative phosphorylation, this can result in gastrointestinal damage via a cascade which leads to increased GI mucosal permeability [82]. Other mechanisms for GI damage include increased NSAID-induced endothelial expression of neutrophil adhesion molecules, which could further compromise microvascular circulation. COX-2 selective NSAIDs, however, do not cause a significant degree of uncoupling of mitochondrial oxidative phosphorylation and are not associated with increased gastrointestinal damage. Gastric acid has also been implicated in gastroduodenal damage associated with NSAIDs use, and this is buttressed by the decrease in observed frequency of lesions with co-administration of proton pump inhibitors or H2 receptor blockers. Macroscopic damage is thought to be a result of gastric acid diffusion through an impaired barrier, which results from NSAIDs-related topical effects [82].

A recent systematic review and meta-analysis of five cohort studies were performed to compare the risk of acute kidney injury (AKI) in NSAID users versus nonusers with respect to various individual NSAIDs [83]. Pooled risk ratios were similar across seven traditional NSAIDs, including indomethacin, piroxicam, ibuprofen, naproxen, sulindac, diclofenac, and meloxicam and two COX-2 inhibitors rofecoxib and celecoxib. The pooled risk ratios for AKI of COX-2 selective inhibitors and the two traditional NSAIDs with the most COX-2 selectivity (diclofenac and meloxicam) were also comparable with other traditional NSAIDs. The mechanistic explanation for renal injury in the setting of chronic NSAIDs use goes back to the COX-mediated decrease in prostaglandin production. Under normal circumstances, renal hemodynamics are not significantly dependent on prostaglandins. In the setting of chronic kidney disease or volume depletion, however, prostaglandins are important for their ability to decrease glomerular vascular resistance to maintain renal blood flow and glomerular filtration rate [83]. In light of these risks, the authors provide the practical advice of treating patients with NSAIDs for the shortest possible duration, with the lowest possible dose.

Antidepressants for the Treatment of Chronic Spine Pain

The main pain modulatory mechanism of action of antidepressants is serotonin and norepinephrine reuptake inhibition and thereby augmentation of the descending monoaminergic inhibitory pathways. Antidepressants have been used in the treatment of neuropathic pain states with varying degrees of success [84]. The use of antidepressants in the treatment of chronic axial spine pain, however, is more controversial [85]. One reason that antidepressants have been employed for the treatment of patients with spine pain is the frequent coexistence of pain with depressed mood; however it has been demonstrated that the effect of antidepressants on reduction of pain intensity can be independent of their function on depression [86, 87]. Pain inhibitory pathways are modulated by both serotonergic and noradrenergic neurons; thus, medications that modulate levels of both norepinephrine and serotonin, versus serotonin alone (i.e., SSRIs), may confer added benefits in the treatment of painful conditions [88–90]. In fact, the descending serotonergic pathways have been shown to have some pro-nociceptive effects through their activity on 5-hydroxytryptamine (5-HT) type 2 and 5-HT type 3 [91–93]. A comparison of the ratio of norepinephrine to serotonin reuptake inhibition can help to explain the increased efficacy of SNRIs and TCAs compared to SSRIs. This ratio is reported 0.002:1 in citalopram, 0.09:1 in desvenlafaxine, 0.1:1 in venlafaxine, 0.2:1 in duloxetine, 1.1:1 in amitriptyline, 3:1 in milnacipran, and 38.2:1 in nortriptyline [94, 95].

Other possible antinociceptive mechanisms of antidepressants include alpha-1 receptor and N-methyl-D-aspartate (NMDA) receptor antagonism, blockade or activation of some ion channels (sodium and calcium channel blockade, potassium channel activation), increased availability

of adenosine, increased type B gamma-aminobutyric acid ($GABA_B$) receptor function, mu and delta opioid receptor agonism, and an anti-inflammatory effect secondary to decreased prostaglandin E2 (PGE_2) and tumor necrosis factor-alpha (TNF-α) production [96].

As antidepressants have traditionally been used to treat neuropathic pain states, the question may be asked how its use can be justified in conditions in which a neural lesion is not apparent, such as in axial spine pain. It is suggested that nociceptive inputs can lead to a prolonged augmentation in the excitability of neurons in the central nociceptive pathways, resulting in changes in pain sensitivity [97]. As such, central sensitization may be considered to be an important contributor to pain in patients with such conditions as fibromyalgia, osteoarthritis, and some musculoskeletal disorders. Interestingly, Cohen and Hooten found that nearly one half of all patients presenting with chronic neck pain actually exhibit mixed neuropathic and nociceptive symptoms or neuropathic symptoms predominantly [98].

When considering the effect of antidepressants on radiculopathy, there is some evidence to support the use of duloxetine. A randomized, double-blind, placebo-controlled crossover study aimed to compare the efficacy of duloxetine in the treatment of low back pain with associated neuropathic leg pain (radiculopathy) [99]. Though the number of participants was low (21 patients completed both phases of the study), the intention to treat analysis ($n = 25$) showed that the visual analog scale (VAS) scores at week 4 were significantly lower in the duloxetine phase compared with placebo (4.1 ± 2.9 vs. 6.0 ± 2.7; $P = 0.001$), translating to an average pain reduction of 32%. PainDETECT scores were also noted to be significantly lower (17.7 ± 5.7 vs. 21.3 ± 3.6 points; $P = 0.0023$). There was no significant difference noted in adverse events between the two phases (65% for duloxetine vs. 62% for placebo).

Selective Serotonin Receptor Inhibitors

Selective serotonin receptor inhibitors (SSRIs), such as escitalopram, fluvoxamine, sertraline, citalopram, paroxetine, fluoxetine, and zimelidine, are antidepressants that, as indicated by the antidepressant class' name, block the reuptake of serotonin. They tend to have less secondary side effects compared to other antidepressants such as tricyclic antidepressants (TCAs) [96, 100]. Selective serotonin receptor inhibitors function by acting upon 5-HTT, a serotonin transporter, thereby preventing the presynaptic reuptake of serotonin and increasing its availability in the synaptic cleft [100, 101]. While SSRIs have been utilized in the treatment of chronic pain, their effects have been predominantly ascribed to the modulation of mood symptoms, rather than via the inhibitory nociceptive pathways, leading to an increased focus on more balanced norepinephrine- and serotonin-modulating medications such as tricyclic antidepressants and serotonin-norepinephrine reuptake inhibitors (SNRIs) [100]. A double-blind, controlled-concentration study by Atkinson found that low-concentration and high-concentration desipramine resulted in greater reductions in pain intensity compared to placebo and all concentrations of fluoxetine, an SSRI [102]. A 2016 topical review of SSRIs for the treatment of chronic pain led the authors to conclude that, although SSRIs have some effect on many pain conditions, more studies with low risk of bias and good methodology are required to make more solid conclusions about their efficacy in chronic pain [100]. Of the studies that investigated SSRI effects on chronic low back pain, one trial found that paroxetine didn't provide pain relief greater than placebo, though the patients who were treated with paroxetine were more likely to decrease analgesic usage. Another study included patients with low back pain and compared the effects of maprotiline to placebo and paroxetine in which paroxetine was not found to provide a significant decrease in mean pain intensity compared to placebo [103]. One study did seem to find the SSRI escitalopram to be effective in the treatment of chronic non-radicular low back pain, with no significant differences when compared with duloxetine [104]. This study, however, was of relatively short duration (13 weeks) and included a small number of patients (39 in the escitalopram group; 41 in the duloxetine group).

Overall, the body of literature does not support the use of SSRIs for the treatment of chronic low back pain, and more studies at low risk for bias, with longer durations of therapy and larger numbers of patients, may be necessary to make a conclusive statement about their efficacy or lack thereof in this patient population [96].

Tricyclic Antidepressants

The core structure of tricyclic antidepressants is composed of three rings, and the variation of the terminal amine determines their specific categorization as a tertiary, secondary, or even quaternary amines [105]. Examples of tertiary amines are amitriptyline, doxepin, clomipramine, trimipramine, and imipramine. They may be further metabolized to secondary amines, including desipramine, nortriptyline, and protriptyline. Nortriptyline is a by-product of amitriptyline, and desipramine is a metabolic by-product of imipramine. Due to their metabolism involving demethylation, the secondary amines are not associated with as high an incidence of sedative properties as their tertiary amine counterparts. This is mostly related to the greater reuptake inhibition of norepinephrine compared to 5-hydroxytryptophan, an intermediate in the synthesis of serotonin [105].

Proposed mechanisms for the effectiveness of tricyclic depressants as analgesics include augmentation of the inhibitory pathways via the descending tracts (corticospinal, spinal, and supraspinal) in which norepinephrine and serotonin are important neurotransmitters. As such, nociceptive input from the peripheral nervous system may be diminished in their path to the central nervous system [105]. Furthermore, serotonin may be involved in the modulation of endorphin-related activities [106].

With respect to low back pain, a randomized, placebo-controlled trial was performed to compare nortriptyline to an inert placebo in 57 male subjects [107]. Decrease in pain scores was significantly greater for the nortriptyline group (22% vs. 9% pain reduction accordingly). Patients with radicular pain also demonstrated a larger magnitude of pain reduction compared with the placebo group. Interestingly, none of these patients had concomitant depression. Four patients in this trial withdrew due to adverse effects. The authors conclude that prescribers should balance the risk of adverse effects with potential benefits given the modest benefit observed with nortriptyline in this patient population.

A systematic review appraised seven studies that included randomized, placebo-controlled trials of patients with chronic low back pain treated with oral antidepressants [86]. Of these seven studies, five included antidepressants that inhibit norepinephrine reuptake, including tetracyclic and tricyclic antidepressants [103, 107–109]. One study reported reduction in pain intensity in patients taking nortriptyline vs. placebo but with no significant differences in health-related quality of life, mood, or physician rating of outcomes [107]. Another study compared maprotiline vs. placebo and paroxetine, as reported above [103].

Serotonin Norepinephrine Reuptake Inhibitors

While TCAs are among the most well-known and historically utilized antidepressants for the treatment of painful conditions, recent research has focused on SNRIs, given the recognition of their combined effects of noradrenaline and serotonin on pain pathways. Examples of these medications include milnacipran, venlafaxine, and duloxetine. This class of antidepressants is presumed to have a more balanced effect on serotonin and norepinephrine reuptake with fewer adverse effects, owing to less receptor interactions [110].

At low doses, venlafaxine exhibits more serotonergic activity, with noradrenergic activity increasing in a dose-dependent manner [111]. Because of the rather moderate effect these drugs have on pain and the frequency of medication-related side effects that limit dosing, it is important for the clinician to understand the mechanism of action of these medications when faced with prescribing decisions [110]. While venlafaxine blocks the reuptake of norepinephrine and serotonin, anticholinergic, histaminergic, and alpha adrenergic effects are typically absent, potentially explaining its more favorable side effect profile [110]. Duloxetine is a potent SNRI which received FDA approval for the treatment of chronic low back pain in November 2010 [111]. It is an SNRI that has a side effect profile similar to that of venlafaxine, including nausea, elevated blood pressure, somnolence, dizziness, and dry mouth [110].

A 12-week, randomized, placebo-controlled trial in patients suffering from chronic low back pain compared the effects of duloxetine at a fixed dose of 60 mg daily with placebo [111]. Of note, patients with radiating pain were only included if their pain radiation was restricted to the proximal lower limb. Patients with findings consistent with radiculopathy were excluded from the study. This study was funded by the pharmaceutical company Eli Lilly. The primary outcome measure was average pain intensity, which improved in the duloxetine group to a significantly greater extent than in the placebo group. Acknowledged limitations of this study included a short duration of the trial, exclusion of patients taking commonly prescribed analgesics, which may not represent the typical pain patient population who are normally taking more than one analgesic simultaneously, and the lack of an active comparator to potentially allow for the comparison of duloxetine to a commonly prescribed analgesic.

Anticonvulsants for the Treatment of Chronic Back Pain

The effectiveness of anticonvulsants in treatment of neuropathic pain conditions has been evaluated in the past. Examples include the use of carbamazepine for the treatment of trigeminal neuralgia and pregabalin for the treatment of post-herpetic neuralgia (PHN) and fibromyalgia. However, the utility of these medications in spine pain treatment was studied less extensively. The side effects associated with these medications warrant careful weighing of risks vs. benefits prior to initiation of the therapy. The following is an overview of the various anticonvulsants and a discussion of their utility in the treatment of chronic spine pain conditions.

Gabapentinoids

Gabapentinoids are anticonvulsants that exert their anticonvulsant and analgesic effects by binding to the alpha-2/delta subunit of the voltage-sensitive calcium channel [112]. Gabapentin is approved by the FDA as an adjunct in the treatment of partial seizures and postherpetic neuralgia [113]. Pregabalin is FDA approved as an adjunct in the treatment of partial seizures, fibromyalgia, diabetic peripheral neuropathy associated pain, post-herpetic neuralgia, and spinal cord injury-related neuropathic pain [114]. While gabapentin and pregabalin are similar structurally and exert their effects on

the same calcium channel subunit, there are some pharmacokinetic and pharmacodynamic differences between the two medications. Gabapentin absorption is slow and exhibits nonlinear, zero-order kinetics. As such, plasma concentrations of gabapentin do not increase proportionally with the dose. This is not true of pregabalin, which exhibits first-order kinetics, has a relatively fast absorption, and achieves maximum plasma concentrations within 1 hour vs. 3–4 hours for gabapentin [115].

The more frequent side effects associated with the use of gabapentinoids for the treatment of low back pain include dizziness, fatigue or lethargy, visual disturbances, and difficulties with mentation [116]. Recent attention has been focused on the potential for misuse of gabapentinoids related to indirect/direct effects on the dopaminergic "reward system" [117]. An observational, retrospective study examined electronic poison center data from January 1, 2002, to December 31, 2011, and identified 116 gabapentin and 23 pregabalin overdose cases [118].

A systematic review of pharmacologic therapies for low back pain in 2017 identified only six fair quality trials employing anticonvulsants for the treatment of low back and radicular pain, which are summarized below [119]:

An RCT comparing outcomes of pregabalin vs. placebo treatment used time to loss of response during the double-blind phase as a primary endpoint in patients with chronic lumbosacral radiculopathy [120]. There was no significant difference found in the time to loss of response between the two groups, despite most patients on pregabalin responding to the medication. The authors were unable to draw any definitive conclusions based on the study and emphasized the need for further study of pregabalin for the treatment of pain related to chronic lumbosacral radiculopathy.

A pragmatic double-blind RCT (randomized controlled trial) was conducted to evaluate the effectiveness and tolerability of tapentadol prolonged-release (PR) monotherapy (500 mg/d) vs. a combination of tapentadol PR at a lower dose (300 mg/d) with pregabalin in patients with chronic low back pain with a neuropathic component [121]. The difference in pain intensity and quality of life between the groups was not statistically significant at the end of the study, but participants in tapentadol monotherapy group had fewer side effects, leading the authors to suggest that tapentadol PR monotherapy may be a favorable treatment option for such patients.

A recent explanatory double-blind, crossover RCT randomized 29 patients with neurogenic claudication to receive either pregabalin followed by active placebo (diphenhydramine) or active placebo followed by pregabalin [120]. The primary outcome variable was time to first moderate pain symptom (development of neuroclaudicant pain), which was defined as a numeric rating scale (NRS) score ≥ 4, during a 15-minute treadmill test. There was no observed difference in time to first moderate pain symptom between the two groups. Various secondary outcome measures, such as pain intensity at rest or distance walked, were similarly comparable between the two groups.

A single-blind RCT was performed comparing two groups of subjects suffering with chronic low back pain treated for 3 weeks initially with transdermal buprenorphine [122]. After a 3-week period, the patients were randomized either to a group with buprenorphine and pregabalin or buprenorphine and placebo for an additional period of 3 weeks. Forty-four patients were included in the final analysis. During the first week of treatment, all patients on buprenorphine had significant reductions in pain. After randomization, only the index treatment group showed further reduction in pain and a lower incidence of rescue medication use. The authors concluded that the addition of pregabalin to transdermal buprenorphine at the doses used in the study led to significant improvement in pain and sleep quality. However, both the tapentadol/pregabalin study and buprenorphine/pregabalin study have been criticized for methodological shortcomings, rendering "insufficient evidence" to determine the effects of pregabalin combined with another medication versus monotherapy with another medication [119, 121, 122].

A prospective, randomized trial evaluated 36 patients with mixed chronic low back pain receiving 3 consecutive 4-week treatment regimens, which were randomly assigned, and included celecoxib and placebo, pregabalin and placebo, and celecoxib and pregabalin [117]. Assessment was performed by a blinded investigator using a visual analog scale (VAS) and Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) score. LANSS scores were pooled, and the authors reported greater effectiveness of a combination of celecoxib and pregabalin as opposed to monotherapy with either agent, which was statistically significant. VAS scores in patients treated with a combination of celecoxib and pregabalin experienced the largest percent reduction (51.8% in patients with a LANSS score > 12), which was also statistically significant. Similarities were observed between the combined celecoxib and pregabalin and monotherapy groups concerning adverse effects.

Another RCT of 55 patients with lumbar spinal stenosis and significant intermittent neurogenic claudication, a hallmark symptom of lumbar spinal stenosis, was randomized into two groups [112]. Both groups were treated with exercises, lumbosacral corset with bracing, and NSAIDs while the index group patients also received gabapentin. At the 4-month follow-up, the gabapentin group had an increase in walking distance compared to the standard treatment group ($P = 0.006$) as well as recovery in sensory deficit ($P = 0.04$). Limitations of the study included no patients older than age 65, lack of long-term duration of treatment, and inability to eliminate placebo effect through placebo-controlled, double-blinded studies.

Topiramate

Topiramate is an anticonvulsant which has multiple different mechanisms of action including voltage-gated sodium channel blockade, GABA agonist-like effects, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA)/kainate glutamate receptor blockade, and voltage-gated calcium channel modulation [123]. A systematic review identified two studies that evaluated topiramate for chronic low back pain [119]. Both trials reported inconsistent effects of this medication [123].

Skeletal Muscle Relaxants

Another class of medications available for the treatment of spine pain conditions is skeletal muscle relaxants. Despite the variety of skeletal muscle relaxants available, there is scarce literature to support their regular use in patients outside of the acute setting. In fact, the majority of muscle relaxants are used to treat acute low back pain. Their side effects can be limiting in some cases. Multiple studies show that the incidence of significant sedation related to the administration of skeletal muscle relaxants reaches up to 50% of patients [119, 124–126]. With regard to neck pain, there is weak evidence supporting the use of muscle relaxants for subacute neck pain related to muscle spasm [98]. The following is a discussion of commonly used muscle relaxants for the treatment of back pain.

Benzodiazepines

Benzodiazepines are thought to exert their effect via an indirect action of relieving muscle spasm by binding to the GABA receptor [124]. It is important to bear in mind that benzodiazepines are in and of themselves CNS depressants with activity also exerted on the limbic system, brainstem reticular formation, and cortex [124]. A systematic review of muscle relaxants for the treatment of nonspecific low back pain included two high-quality trials that showed "strong evidence" that tetrazepam 50 mg orally three times daily is more effective than placebo for short-term pain relief and overall improvement [127]. Another high-quality study showed that tetrazepam is more effective than placebo for the short-term decrease of muscle spasm. As is evident from the above, long-term efficacy is not demonstrated for this category of skeletal muscle relaxants in chronic pain. Coupled with the potential for central nervous system effects and the known addictive potential of benzodiazepines, there is no evidence-based justification for the long-term prescription of benzodiazepines for the treatment of chronic back pain.

Cyclobenzaprine

Cyclobenzaprine is a centrally acting skeletal muscle relaxant that is closely structurally related to the tricyclic antidepressants. The mechanistic explanation for its utility in back pain is its action in the central nervous system. Namely, it has been shown in animal studies to decrease gamma and alpha motor neuron discharge activity [128, 129]. As such, the medication should be used cautiously owing to the side effect profile that is potentially similar to that of anticholinergic medications including drowsiness, dry mouth, dizziness, and nausea [130]. A review of cyclobenzaprine in the treatment of low back pain performed in 2016 considered multiple studies on this medication, but mainly focused on a systematic review performed by an independent group [125, 130]. This review concluded that, based on the number needed to treat (NNT) of three to experience global improvement in symptoms at 10 days, and the number needed to harm of four, the benefits of using cyclobenzaprine as therapy for this condition are unclear. Consideration of the closeness of these numbers warrants caution and careful weighing of the risks and benefits of utilizing this medication.

Tizanidine

Tizanidine is a skeletal muscle relaxant that exerts its effect via agonism of the adrenergic alpha-2 receptor, producing presynaptic inhibition of motor neurons, thereby reducing spasticity. While the imidazoline structure of tizanidine resembles that of other alpha adrenergic agonist medications such as clonidine, which is used commonly as an antihypertensive medication, in animal studies tizanidine was found to be 1/10th to 1/50th as potent as clonidine in its ability to decrease blood pressure. Chronic tizanidine use has been associated with hepatotoxicity, necessitating monitoring of liver function tests in patients treated with this medication on a chronic basis [131]. In a recent systematic review and meta-analysis assessing the efficacy and tolerability of muscle relaxants for low back pain, pooled estimates from the three trials that included tizanidine failed to show a clinically significant benefit [131–134].

Baclofen

Baclofen is an antispastic medication primarily used in the treatment of upper motor neuron-related spasticity, including multiple sclerosis. Its effectiveness is related to its activation of the $GABA_B$ receptor. While its mechanism is not completely known, it is capable of inhibition of mono- and polysynaptic reflexes at the spinal level and possibly supraspinally as well. The most common side effect associated with baclofen is drowsiness, and it is present in 10–63% of patients. Abrupt discontinuation of baclofen should be avoided, as a withdrawal reaction to baclofen may be lethal. There is sparse evidence for the use of antispastic medications such as baclofen in musculoskeletal conditions [135].

Carisoprodol

Carisoprodol is indicated in the treatment of acute pain related to musculoskeletal conditions, but there is no evidence supporting its use beyond a 2- to 3-week period. Its activity, based on animal studies, is thought to be mediated by altered interneuronal activity at the level of the spinal cord and in the descending reticular formation in the brain. A metabolite of carisoprodol, meprobamate is addictive and has itself been classified federally in the USA as a controlled substance. Carisoprodol has also been classified in many states as a schedule IV controlled substance [136]. Despite some trials showing carisoprodol's effectiveness [96], the abuse potential of this medication should prompt consideration of an alternative drug, especially in patients at risk of substance abuse.

Topical Analgesics

Topical medications have been used for centuries in the treatment of painful disorders. There is spare literature, however, to support their common use for spine pain conditions. Topical analgesics are used for their ability to penetrate local tissues with decreased systemic absorption, theoretically leading to less adverse effects. Some topically available medications include NSAIDs, capsaicin, salicylates, and local anesthetics.

Topical NSAIDs

NSAIDs, through their inhibition of COX-1 and COX-2 isoenzymes as discussed earlier in this chapter, may have a perceived benefit in low back pain as well. Examples of topically available NSAIDs included diclofenac (available in gel, solution or patch form) and ketoprofen. A systematic review was carried out to determine the safety and efficacy of topical NSAIDs for chronic musculoskeletal pain in adults [137]. Most of the RCTs included in this review considered patients with knee osteoarthritis, with some studies including patients with more poorly defined pain diagnoses. Data was sufficient to pool only for diclofenac and ketoprofen in the systematic review. The authors conclude that topical diclofenac and ketoprofen can provide good levels of pain relief beyond that imparted by the carrier in osteoarthritis for only a minority of patients. Evidence for its efficacy in other chronic painful conditions is absent. There is some evidence to suggest that there is long-term benefit from the placebo effect derived from the carrier itself and that NSAIDs may augment this [137]. One study by Hohmeister, however, specifically included patients with cervical and lumbar back pain [138]. Flufenamate 3% plus salicylate 2% gel (Mobilisin) was administered three times daily to patients for 3 weeks and compared with placebo gel. The number of patients with patient global evaluations that were either very good or good in the topical NSAID group was higher (44/49) compared to the placebo group (4/51).

Capsaicin

Capsaicin, widely used previously for the treatment of pain related to post-herpetic neuralgia, has also been studied for treatment in other neuropathic pain states. Capsaicin is the active compound in chili peppers, and its analgesic utility is believed to be derived from agonism of the transient receptor potential vanilloid 1 (TRPV 1) channels, which play an important role in nociception [139]. Desensitization of the sensory nerve endings involved in nociception is the mechanism by which capsaicin is considered to be therapeutic in neuropathic pain [140]. Though the mechanisms by which this desensitization occurs are poorly understood, some evidence exists for the role of substance P depletion in TRPV1-expressing nerve fibers, as well as calcium influx of extracellular calcium [141–146]. A 2013 retrospective analysis considered use of the 8% capsaicin patch for patients with a variety of neuropathic pain conditions, including failed back surgery syndrome (FBSS) [147]. Using an 11-point Numeric Pain Rating Scale, patients receiving the capsaicin patch reported a decrease from baseline pain score of up to 43.4% up to 12 weeks posttreatment. While patients with FBSS only comprised a portion of the patients in this analysis, the authors acknowledged that the study was not powered to demonstrate equivalence. Capsaicin is associated with a severe burning sensation in some patients when applied topically and may lead to intolerance to the treatment.

Lidocaine

Lidocaine is a local anesthetic that exerts its effect via blockade of sodium channels. It can be administered via many routes, but its main use in the treatment of back pain is in the form of topical gels, creams, or patches. These formulations are available in over the counter (OTC) or via prescription in various different concentrations. Creams and gels unfortunately do not generally provide long durations of action and may require frequent dosing, making them impractical for patients suffering from chronic back pain. While the local anesthetic lidocaine is available in prescription patch form, the only indication for which most insurers cover them is post-herpetic neuralgia, and financial barriers in obtaining these patches are often present. Recent developments in over-the-counter lidocaine patches have combined lidocaine with menthol in an effort to increase permeability and to provide the patient with an immediate soothing sensation, as lidocaine does not act immediately [148]. A recent randomized control trial was carried out comparing OTC lidocaine and menthol combined patches with prescription 5% lidocaine patches and placebo in a double-blind fashion

[149]. Fifty-eight patients with back pain were included in the final calculations. A requirement for inclusion was at least 3 months of pain. The results showed that lidocaine 3.6% combined with 1.25% menthol was non-inferior to the prescription 5% lidocaine patches at day 10 of treatment in the domains of efficacy, safety, and quality of life.

Rubefacients/Counterirritants

Another class of topical medications includes the category of topical salicylate containing rubefacients. These medications, when applied topically, act as skin irritants resulting in increased blood flow [150]. They are present in both over-the-counter and prescription formulations. A recent review examined the effectiveness of salicylates containing rubefacients in the treatment of acute and chronic painful musculoskeletal conditions [150]. Of the chronic conditions studied, four papers included the treatment of chronic back pain with this category of medications. While limited data seemed to show that this category of medications could be helpful in the short-term, there was no evidence found by the authors to support the use of topical salicylate containing rubefacients in the treatment of either acute injuries or chronic conditions, including back pain.

Herbal Medications

Of the reviews that were included that specifically looked at chronic pain conditions that included neck and/or back pain, at least two specifically compared herbal remedies to placebo or active placebo [115, 116, 151, 152]. Herbal topical preparations have also been used to some degree to treat low back pain, but without a significant amount of large, well-designed randomized controlled trials to assess their efficacy. At this point, a determination about their role in treating spine related pain is not possible. A systematic review from 2010 considered Chinese herbal medications for the treatment of chronic neck pain due to cervical degenerative disc disease, including cervical radiculopathy [151]. Adequate information was not available from this review, which included 200 participants, to judge the efficacy of the herbal remedies (including topical). Likewise, another review including 200 participants showed no herbal remedy to have adequate information on efficacy in low back pain with quality of evidence being very low via GRADE assessment [152].

Cannabinoids for Treatment of Chronic Low Back Pain

The cannabis plant, also known as marijuana or hemp, has been cultivated and used for medicinal purpose in ancient China, India, and Egypt for thousands of years. The references of marijuana in treatment of back pain and headache date back to the sixth and seventh century [153]. The drug was later introduced into the Western civilization where it became used for its analgesics and other properties [154, 155]. By the mid-nineteenth century, cannabis was medically prepared and available at American pharmacies. Increasing scrutinization of marijuana due to its psychoactive effects and recreational use in the early twentieth century led to its removal from pharmacopeia in 1942 [156]. In 1976, cannabis was classified as a schedule I drug in the USA, which implies a high potential for abuse and no accepted medical use [157]. However, novel pharmacological developments of the past half a century rekindled interest in medical use of marijuana. The use of medicinal cannabis has become more accepted globally and in the USA. As of November 2017, 29 states, the District of Columbia, Guam, and Puerto Rico passed laws allowing the medicinal use of cannabis [158].

Endocannabinoid System (ES)

The ES consists of cannabinoid receptors (CB1 and CB2), endocannabinoids receptor ligands, exemplified by anandamide (AEA) and 2-arachidonoylglycerol (2-AG), and their degrading enzymes. There are three enzymes that hydrolyze AEA, namely, fatty acid amide hydrolase (FAAH), FAAH-2, and *N*-acylethanolamine acid amidase (NAAA). 2-AG is mainly hydrolyzed by monoacylglycerol lipase and to a lesser extent by the enzymes ABHD6 and ABHD12 [159].

Both CB1 and CB2 receptors are located presynaptically and inhibit adenylate cyclase via interactions at the G-protein complex. Activation of these receptors by cannabinoids leads to opening of potassium channels and blocking of N-/P-/Q--type calcium channels. The former action causes hyperpolarization of the presynaptic terminal, while the latter results in inhibition of release of stored excitatory and inhibitory neurotransmitters, which may explain analgesic and many other effects of cannabinoids [160]. CB1 receptors are widely distributed in the central and peripheral nervous system, not only including the anatomical pain pathways such as periaqueductal gray (PAG), rostral ventrolateral medulla (RVM), spinal cord dorsal primary afferent and substantia gelatinosa, spinal interneurons, and peripheral nerves, but also in many brain regions. CB2 receptors are expressed mainly by immune cells and implicated in immune regulation resulting in some anti-inflammatory and antihyperalgesic effects [161]. The endocannabinoids are “made on demand” in the postsynaptic terminals and enhanced by neural activity. AEA has higher affinity for CB1 and is reported to produce antinociception, hypomotility, and reduced memory effects. The role of CB2 receptors in antinociception has been demonstrated in inflammatory and neuropathic models. Some of the

pain-relieving effects of endocannabinoids may be explained by their interaction with other neurotransmitters and by cannabinoid-opioid interaction [162, 163].

Phytocannabinoids

Marijuana contains more than 500 compounds, of which approximately 107 are called cannabinoids [164]. To date, the two best studied cannabinoids implicated in antinociception are Δ-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), although there are many others (Fig. 19.3). THC is a partial CB1 and CB2 agonist, but it is at least ten times more potent in binding to CB1 receptors. THC's CB1 agonistic activity accounts for its psychoactive actions believed to be mediated by inhibition of both glutamate and GABA release. This cannabinoid also has been shown to have antinociceptive effects in the periaqueductal gray [165, 166]. Other potentially medicinal effects of THC include antispasmodic and anti-inflammatory actions.

In contradistinction to THC, CBD has virtually no phsychoactivity. It has low affinity for both CB1 and CB2 but may behave as an inhibitor of AEA deactivation system, enhancing the analgesic effects of this endocannabinoid [167]. CBD also interacts with 5-HT1a, TRPV1, and μ- and δ-opioid receptors as well as with a multitude of various ion channels and enzymes accounting for its potential analgesic, antiepileptic, antiemetic, anti-inflammatory, anxiolytic, antipsychotic, and anti-ischemic properties [168–171]. Both THC and CBD have strong antioxidant activity and reduce NMDA and kainate receptor-mediated neurotoxicity [172].

The other studied phytocannabinoids (cannabinol, cannabigerol, tetrahydrocannabivarin, and many others) also have different degrees of analgesic, anti-inflammatory, and anticonvulsant properties [173–175]. Among various compounds of marijuana, terpenes contribute to the distinctive qualities among cannabises but also may have many other properties including anti-inflammatory, antianxiety, antioxidant, antineoplastic, antibacterial, and antimalarial abilities [176].

Synthetic Cannabinoids

Synthetic cannabinoids (SC), also called cannabimimetics, have been developed in the hope of enhancing medicinal properties of cannabis by achieving higher selectivity toward the particular cannabinoid receptors. The goal was to synthesize formulations with the high therapeutic activity and minimal side effects. Animal studies show that pharmacological effects of SC are 2–100 times more potent than THC. SC has a broad spectrum of potential therapeutic properties including analgesic, anti-seizure, anti-inflammatory, anticancer growth, and weight loss effects. Several SC are available for medical use in the USA, but none of them are FDA approved for pain management; therefore, any application of these substances for analgesic purpose is off-label. Dronabinol is synthetic THC marketed under the name Marinol® or Syndros® (liquefied dronabinol). It is most commonly used for chemotherapy-induced nausea and vomiting and for AIDS-related anorexia [161]. Nabilone is a semisynthetic analog of THC that is tenfold more potent and longer lasting. It is marketed under the name Cesamet® and indicated only for nausea and vomiting associated with cancer therapy in patients who failed conventional antiemetics [177]. Nabiximol (Sativex®) is an oral spray that contains approximately equal amounts of THC and CBD. It is undergoing phase III clinical trial in the USA in patients whose cancer pain is inadequately controlled by opioids. In Canada, the UK, and Israel, nabiximol is used for neuropathic pain resulting from multiple sclerosis [178].

Unfortunately, SC also produce undesirable physiological effects that are much stronger than the ones caused by THC. The long list of such adverse reactions that limit SC clinical use includes nausea and vomiting, respiratory depression, hypertension, tachycardia, chest pain, muscle twitches, acute renal failure, anxiety, agitation, psychosis, suicidal ideation, and cognitive impairment. Both physiologic and psychoactive actions of SC may result in medical and psychiatric emergencies.

Multitude of SC produced in the clandestine laboratories has appeared in the US market for the past 10 years. They were mixed with herbal products and sold on the Internet under different brand names. Because of their high potency resulting in

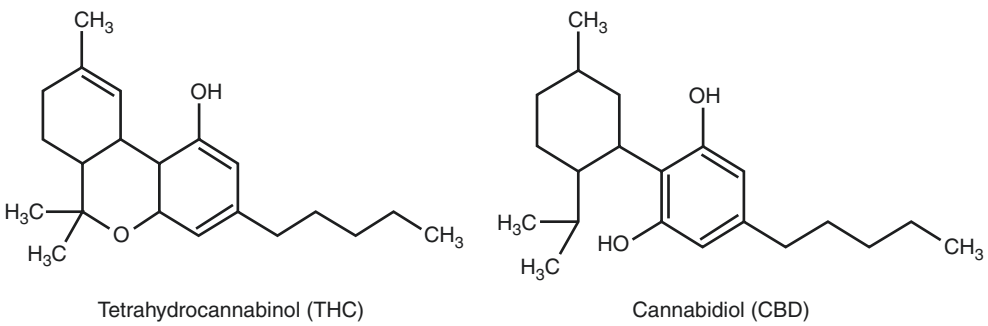

Fig. 19.3 Chemical formulas of THC and CBD

intense psychoactive effects and lack of detectability in routine urine drug screen, the consumption of such SC has become a popular alternative to marijuana [179]. The number of patients brought to emergency department with symptoms caused by the consumption of SC that are not approved by the FDA has dramatically increased. Because of the limited human pharmacological data and documented serious side effects, SC intake may present a public health and safety concern. Many of these SC are designated as Schedule I drugs under the US Controlled Substance Act [180].

Cannabinoid's Antinociceptive Mechanisms

CB1 receptors are expressed in many parts of the CNS including the areas involved in pain modulation and transmission. Injection of CB1 agonists into PAG, ventroposterolateral thalamic nucleus, and the spinal cord or intrathecally in animal studies elicits an antinociceptive response [159]. The effectiveness of CB in reducing hyperalgesia and allodynia in experimental models of neuropathic pain via both CB1 and CB2 mechanisms has been demonstrated in many studies [181–184]. CB2 agonists may also suppress pain through its anti-inflammatory effects, including their ability to reduce the activation of microglia in the CNS [185, 186]. THC has been shown to stimulate lipoxygenase and inhibit prostaglandin E-2 synthesis [178].

Some of the CB antinociceptive effects implicate non-cannabinoid receptors. Non-CB active phytocannabinoids have been shown to target transient receptor potential channels [187]. CBD acts as a full 5-HT1A agonist, 5-HT2A partial agonist, and noncompetitive 5-HT3A antagonist [168, 188]. In experimental studies this phytocannabinoid also enhanced adenosine receptor A2A signaling through inhibition of its transporter [189]. AEA, TCH, and SC have been demonstrated to be able to suppress glutamatergic neurotransmission and inhibit NMDA receptors that are believed to play a key role in the development of chronic pain conditions [172].

Another important interaction takes place between CB and endogenous opioid system. Administration of CB induces endogenous opioid peptide release, and chronic THC use increases endogenous opioid precursor gene expression in structures involved in pain expression [190]. CB may exert additive or even synergistic analgesic effects if combined with opioids [191]. There is also some evidence that they may have an opioid-sparing effect, prevent opioid tolerance and withdrawal, and regain opioid analgesia after loss of effect [163, 177, 192, 193].

Cannabinoids in Chronic Pain Treatment

The number of RCTs evaluating the efficacy and effectiveness of CB in chronic pain management has been exponentially increasing during the past two decades. At least 11 systematic reviews that appraised these studies and even 1 overview of systematic reviews have been published since 2001 [194]. There are no studies to date that assess the effectiveness of CB in chronic axial low back or radicular pain treatment. The studies on cancer pain are scarce and mostly not from recent years. Overall, they provide insufficient evidence due to methodological flaws, including high dropout rate, use of non-validated outcome measures, and lack of randomization and blinding [195]. The most recent and the largest of these studies that enrolled 360 patients with advanced cancer reported that the 30% responder rate from primary analysis was not significant for different doses of nabiximols versus placebo, although the secondary outcome measures (continuous responder analysis and the analysis of change from baseline in mean average pain and worst pain scores) showed more improvement in the index group [196].

Several studies examined the outcomes of CB treatment of chronic non-cancer non-neuropathic pain. Two studies enrolled patients with rheumatoid arthritis and osteoarthritis, two studies evaluated the patients with fibromyalgia, and one trial included patients with abdominal pain and one study with mixed pain. Limitations of these studies include lack of follow-up, inadequate allocation concealment, selection bias, and high attrition rate [197]. A detailed analysis of the outcomes of these studies concluded that there were no consistent results proving CB superiority over placebo [198]. Based on the available body of evidence, the German guideline on fibromyalgia and the European League Against Rheumatism gave a negative recommendation for the use of CB in fibromyalgia treatment [199, 200]. Israeli guideline also mentioned lack of evidence supporting the efficacy and safety of CB in fibromyalgia treatment [201]. However, the Canadian guideline recommended a CB trial consideration in patients with fibromyalgia who have significant sleep disturbance [202].

CB treatment was probably most investigated in neuropathic pain. A total of 25 RCTs evaluated the effects of CB in patients with a broad spectrum of central and peripheral neuropathic pain, including diabetic, HIV-associated, and chemotherapy-induced polyneuropathy as well as central pain associated with multiple sclerosis and spinal cord injury. Andreae et al. performed a systematic review and a meta-analysis of individual patients' data from five high-quality double-blind, placebo-controlled RCTs that assessed the outcomes in the patients with peripheral neuropathic pain treated with inhaled cannabis [203–208]. One of these studies used a parallel design [204] and the other four used a crossover design. The authors pooled data from 178 participants and concluded that for the success defined as at least 30% reduction in pain scores, the inhaled cannabis provided short-term relief with an NNT

of 5.6. Another systematic review and meta-analysis of eleven RCTs showed more benefit for CB over placebo and suggested that this treatment may be effective for different neuropathic pain conditions [209]. Although the Special Interest Group on Neuropathic Pain (NeuPSIG) of the International Association for the Study of Pain gave a weak recommendation against CB use in neuropathic pain treatment, the Canadian Pain Society recommended these medications as a potential third-line treatment [210, 211]. The American Academy of Neurology stated that THC/CBD oromucosal spray or oral THC are probably effective and can be trialed to reduce pain and spasticity associated with multiple sclerosis [212].

Adverse Effects (AE) of CB

The information concerning CB side effects often comes from the studies evaluating recreational drug users rather than from therapeutic RCTs. CB may affect almost all physiological systems of a human body, but most commonly reported AE implicate CNS and gastrointestinal (GI) systems as well as developing psychiatric disorders. The most prevalent CNS-related AE are dizziness and drowsiness, while some of the frequently reported GI-related AE are nausea and vomiting (cannabinoid hyperemesis syndrome) [213–215]. CB are associated with causing depression and suicide, impairment in memory and cognition, and even developing psychosis and schizophrenia [216–218]. Some serious cardiovascular complications from CB include myocardial infarction, cardiomyopathy, arrhythmias, stroke, and cardiac arrest [219]. Smoking of marijuana may cause respiratory symptoms, such as asthma, or induce other allergic reactions, especially with manifestation in the respiratory system [220]. Severe infections, such as tuberculosis and aspergillosis, have also been associated with smoking cannabis. It was estimated that among those who use marijuana daily, 10–20% develop dependence [221–223]. Long-term marijuana use may lead to addiction in vulnerable individuals. The adjusted odds ratio of developing cannabis use disorder was reported as 9.5 in a large prospective cohort study [224].

Despite the plethora of AE reported in marijuana users, most trials indicate that in therapeutic settings, it rarely produces serious medical problems. The estimated human lethal dose of intravenous THC is 30 mg/kg, although there has been no documented evidence of death exclusively attributable to cannabis overdose to date [225]. A comparative risk assessment to quantify the risk of death associated with commonly used recreational substances suggested that cannabis was approximately 114 times less lethal than alcohol [226].

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Surgical Interventions for Spine Pain Management

20

Andrew B. Pham and Louis G. Jenis

Key Points

- Surgical intervention in the spine is a useful treatment option in select patient populations.
- An intimate knowledge of the spinal anatomy is essential to optimize surgical outcomes.
- Interventions in the spine include bony and soft tissue decompression, fusions, and reconstructive procedures.
- Future advances in spine surgery focus on minimally invasive approaches and motion sparing technologies.

Introduction

Surgery is an effective option in the treatment of spine-related pathology, though appropriateness, timing, and patient selection are key factors leading to predictable and satisfactory clinical outcome. Apart from cases of myelopathy, neurologic compromise, or worsening deformity, all patients looking to undergo elective spine surgery should complete a course of nonoperative treatment. This may include a combination of anti-inflammatory agents (NSAIDs, steroids), physical therapy, and injections (epidural, transforaminal, selective nerve root). Once conservative management has been exhausted, patients who have been medically optimized should be counseled at length regarding the risks and benefits of surgery as a form of shared decision-making. The most common risks to surgery are pain, complications from bleeding, infection, nerve injury, dural tears, pseudoarthrosis, and adjacent segment disease.

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The topic of spine surgery is a broad subject that can be covered in multiple volumes. For the sake of this chapter, we will divide the topic of surgical intervention of the spine into three separate categories: decompression, fusion, and reconstruction.

Decompression

Compression of the neural elements in the spine results in a variety of clinical symptoms depending on the location and severity. Central compression of the spinal cord in the cervical and thoracic spine results in myelopathy with more chronic conditions or incomplete/complete cord with acute injuries. In the lumbar spine, compression of the thecal sac from spinal stenosis can result in symptoms of neurogenic claudication of the lower extremities. Radiculopathy pain in the extremities results from compression of the nerve roots throughout the entire spine. Sources of compression include the vertebral discs, bone, ligamentum flavum, as well as instrumentation and foreign bodies.

When addressing these symptoms surgically, one must have an intimate understanding of the anatomy as well as the underlying pathology in order to effectively and successfully decompress the spine and relieve the patient's pain (Figs. 20.1 and 20.2).

Bony Decompression

Distortions in the normal bony anatomy can cause compression of the neural elements. This can be caused by degenerative changes resulting in osteophyte formation and progressive spondylolisthesis, congenital issues causing stenosis of the foramen and canal, and traumatic and pathologic causes such as tumors. The literature reveals that in properly indicated patients, outcomes can be more favorable and may occur more rapidly with surgical decompression [1, 2].

The posterior bony structures that can potentially serve as a source for compression include the lamina and facet

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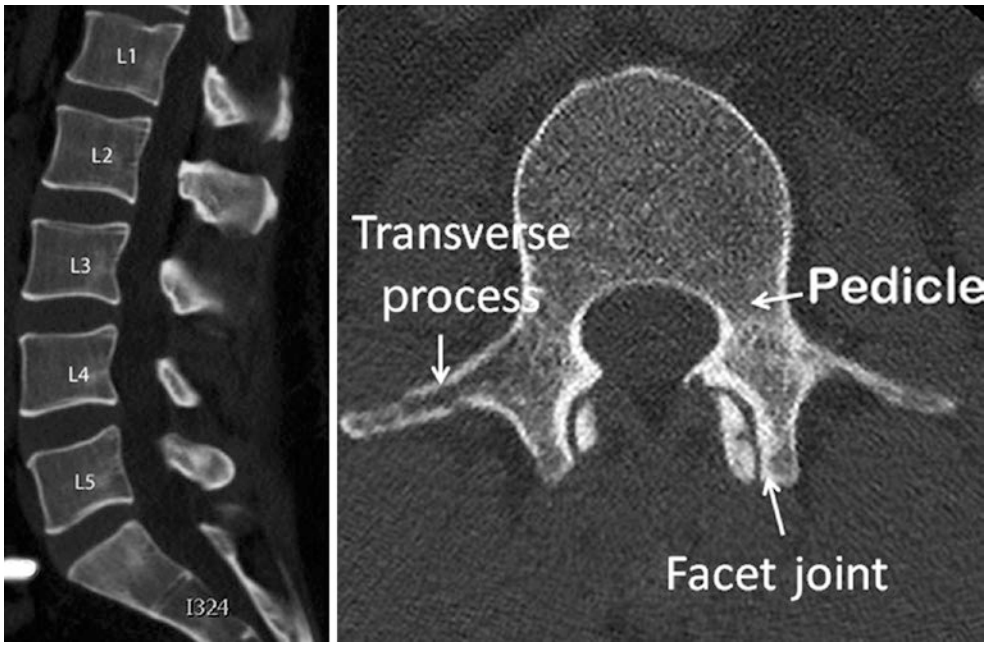

Fig. 20.1 Sagittal and axial imaging of the lumbar spine

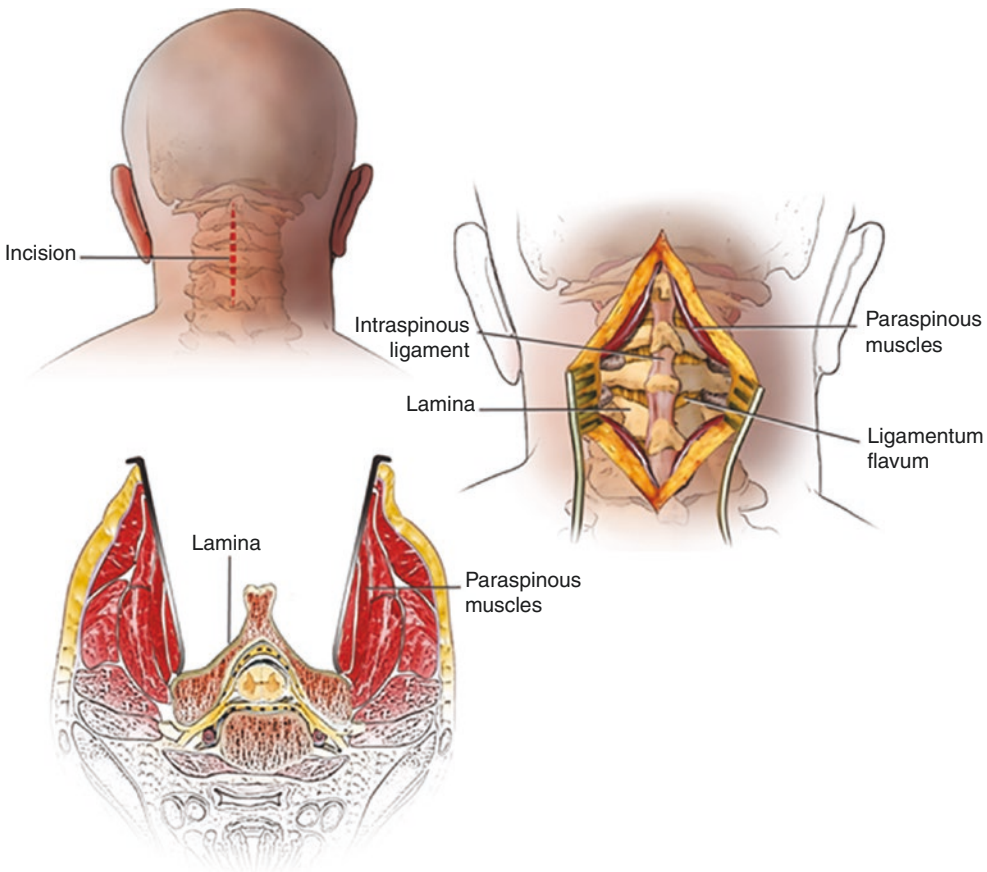

Fig. 20.2 Posterior cervical anatomy

joints. The facet joints serve as the articulation between the inferior articulating process of the cephalad vertebra and the superior articulating process of the caudal vertebra. When central compression must be addressed, partial or complete resection of the bony lamina is needed. This allows decompression of the central structures such as the spinal cord and thecal sac. To achieve full central decompression, the ligamentum flavum is often times excised as well. To achieve this, the laminectomy must be carried out to the proximal and distal attachments of the ligamentum at the level of the pars cephalad and the top edge of the inferior lamina caudally. As the laminectomy/laminotomy

is carried out more laterally, the surgeon will be able to palpate for the borders of the pedicles and the foramen in order that a foraminotomy can be performed to decompress the nerve roots. The facet joints can also be accessed to decompress the lateral recesses (facetectomy) (Fig. 20.3).

While addressing posterior bony decompression, care must be taken not to destabilize the spine. As a general rule, removing more than half of each facet joint in a segment or all of one facet joint on one-side results in instability. Also, when decompressing in the lumbar spine, care should be taken to keep the decompression at least 1 cm medial to the lateral edge of the pars in order to maintain spinal stability [3, 4]. These parameters are often unable to be maintained when performing laminectomies in the cervical and thoracic spine so that often times a fusion will be needed in these areas. In cases of pure myelopathy in the cervical and thoracic spine, a laminoplasty procedure can be carried out where one side of the lamina is burred completely through, while the other side is burred down just enough for the lamina to be hinged up and propped with special plate and screws that lift the lamina off the back of the spinal cord and allow for more space. This is an effective motion preserving posterior decompression procedure that is useful in patient with minimal spondylosis. It is also considered a less invasive procedure, and some data indicate that the rate of complications is lower with laminoplasty versus laminectomy and fusion [5] (Fig. 20.4).

Bony anterior compression of the neural elements typically results from pathology involving the vertebral body. This can be seen in instances of trauma and tumors. A corpectomy, or partial or complete removal of the pathologic vertebral body, can be undertaken to decompress the spine. In the cervical spine, a corpectomy can be approached through the standard anterior Smith Peterson approach to the cervical spine [6]. Additionally, the determination of performing an anterior or posterior approach in the cervical spine also involves an evaluation of the amount of kyphosis or lordosis is seen. With kyphosis greater than 10–13°, it is generally recommended to perform anterior-based surgeries as the lack of lordosis does not permit "float back" of the decompressed spinal cord [7]. In the thoracic spine, an anterior approach is complicated by the presence of the ribs, lungs, and cardiac structures, while the posterior approach is impeded by the spinal cord. The approach undertaken by the surgeon is dependent on the location of compression and the amount of the vertebral body needed to be removed. In the lumbar spine, an anterior approach often requires the assistance of an approach surgeon to carefully dissect down to the spine through the abdominal muscles and vessels, while a posterior approach necessitates careful retraction of the thecal sac and nerve roots (Fig. 20.5).

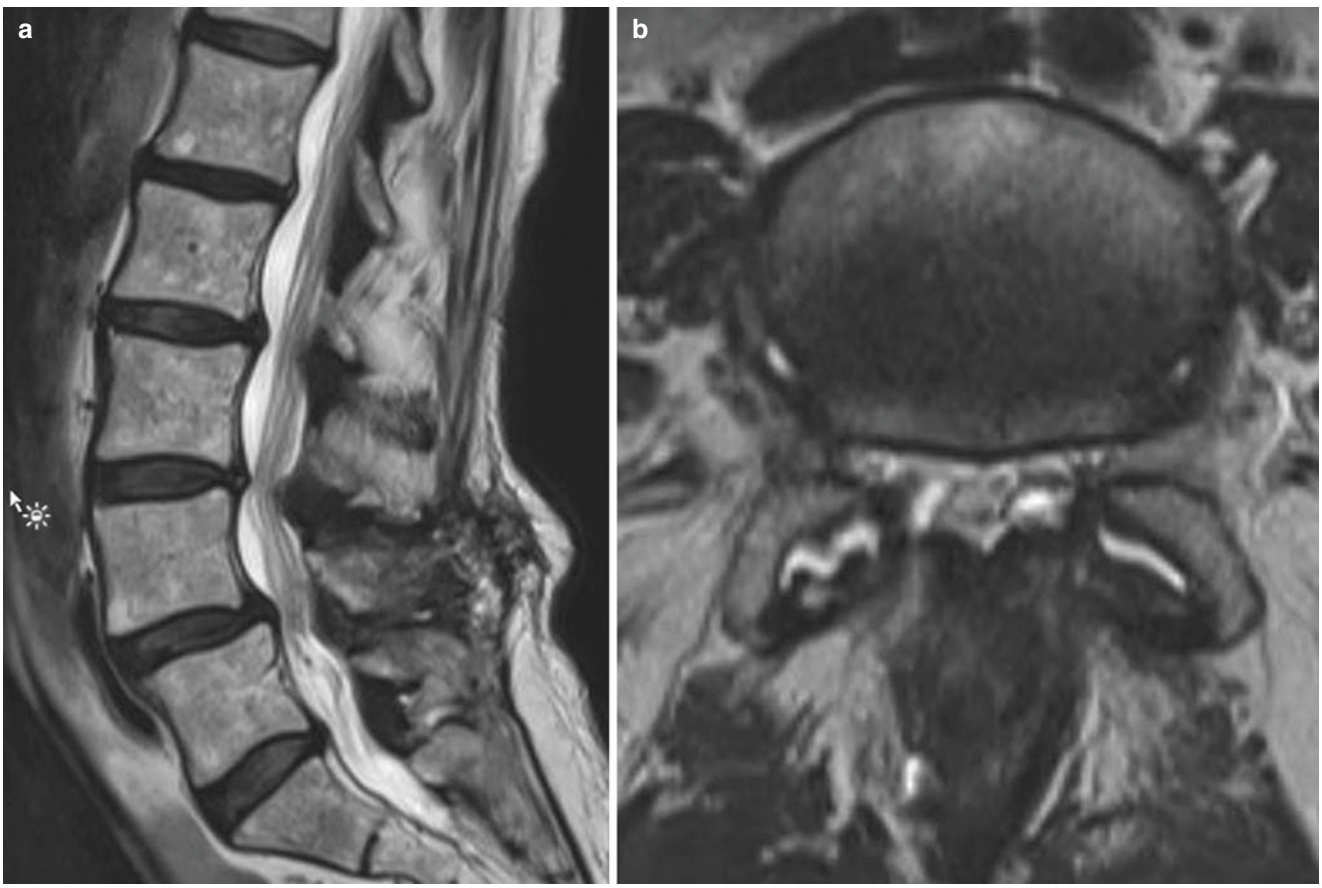

Fig. 20.3 Sagittal (**a**) and axial (**b**) MRI of the lumbar spine showing severe spinal stenosis at L2/3, L3/4, and L4/5

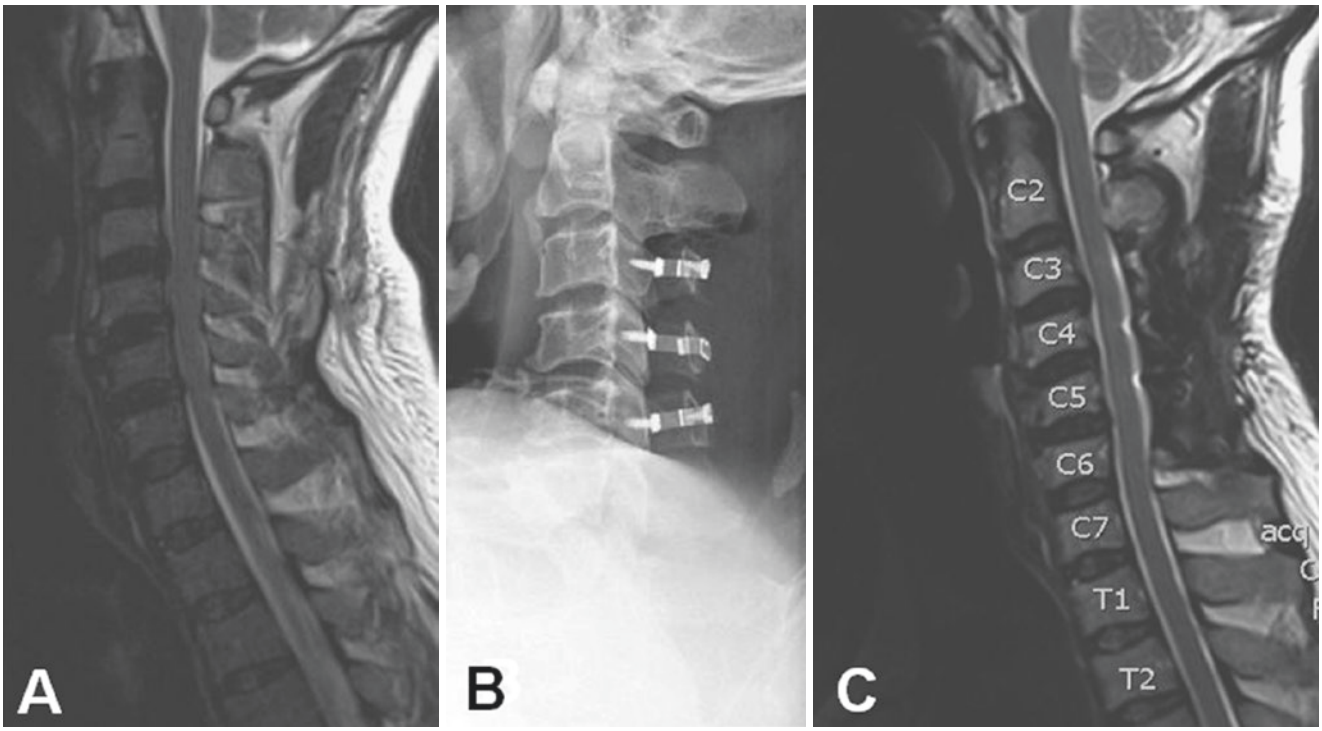

Fig. 20.4 (**a**) Preoperative cervical spine MRI demonstrating congenital cervical stenosis with spinal cord compression worse at C3/C4–C5/C6. (**b**) Postoperative lateral radiograph following laminoplasty C3–C5. (**c**) Postoperative cervical spine MRI demonstrating significant increase in canal diameter and relief of spinal cord compression

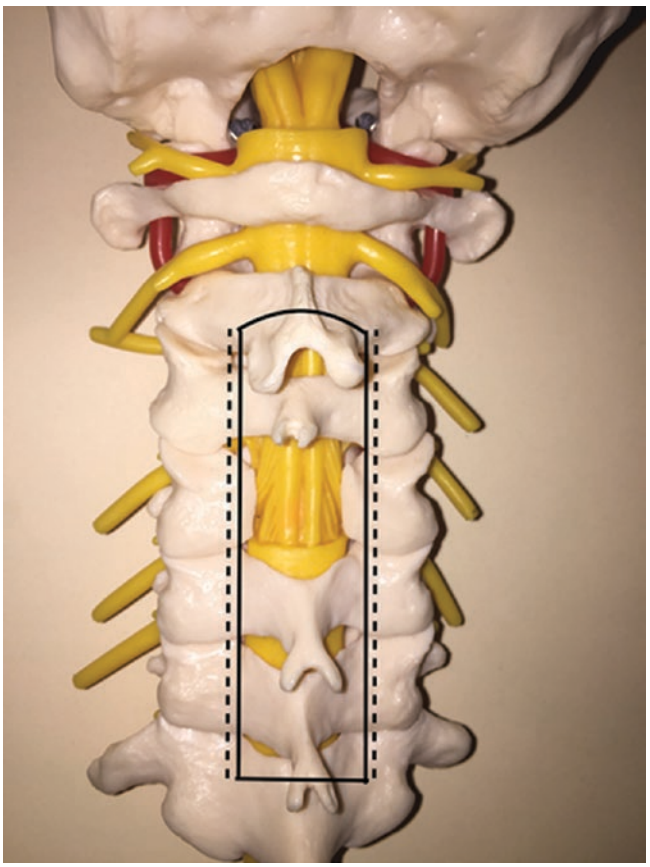

Fig. 20.5 Resection area for posterior cervical laminectomy (C2–C7)

Discectomy/Microdiscectomy

Pathology of the intervertebral disc can lead to neural compression in the setting of disc herniations and discogenic back pain with degenerative disc disease. Although the vast majority of disc herniations improve clinically with observation, those with persistent symptoms stand to benefit from surgical removal of the disc material [8]. To understand the surgical approach to a diseased disc, one must understand the anatomy of a disc along with the bony and neural elements that surround it.

The disc is composed of two layers: an outer fibrous layer called the annulus and a gelatinous filling known as the nucleus pulposus. A disc herniation occurs when elements of the nucleus pulposus protrudes or extrudes out of the disc through a defect in the annulus. This can lead to compression of the nerve roots, spinal cord, thecal sac, and cauda equina. The surgical approach to a symptomatic disc herniation is dependent on what is being compressed and where the herniation is along the spinal column.

While disc herniations in the lumbar spine can be approached both posteriorly and anteriorly, herniations in the cervical and thoracic spine are approached anteriorly or laterally secondary to the position of the spinal cord. In the posterolateral and lateral approach to the disc in the thoracic spine, a unilateral resection of the rib head is typically needed to approach the disc. In the lumbar

spine, posterior exposure of the disc is done through either a laminectomy or a unilateral laminotomy in order that enough of the dural sac and nerve root is seen to safely mobilize the neural elements. Once the disc is exposed, an annulotomy is typically made with a surgical blade, and then the nucleus is carefully removed with a combination of curettes, pituitaries, and Kerrison rongeurs. In order to avoid injury to the spinal cord and major vessels, care must be taken at this step to not plunge instruments through the opposite-sided annulus that may or may not be intact. If an interbody implant is to be utilized, the discectomy must be done thoroughly and meticulously with removal of as much disc material as possible in order to expose the bony end plates. If no interbody fusion is to be performed, enough disc material is removed in order to adequately decompress the neural elements. Adequacy of decompression is assessed both visually and by feel with surgical instruments.

Fusion

Abnormal movement across the spine through an unstable segment or in the setting of degenerative changes can cause significant pain, neurologic deficits, and/or progressive deformity. In these settings, patients may benefit from fusion of the spine to stop the atypical motion.

The evolution of fusion in the spine has seen constant advancements in techniques and instrumentation. Surgery can be undertaken from the front or the back of the spine and can involve an array of hardware. In addition to stabilizing the spine and preventing motion, certain techniques and implants allow for alignment correction and indirect decompression of the neural elements. Ultimately, the procedure choice depends on the location and features of the underlying pathology and patient characteristics.

The basics of obtaining a fusion, regardless of approach and instrumentation, first involve the removal of any soft tissue or cartilaginous material between the two bony surfaces to be fused. Next the exposed bony surfaces are decorticated to a bleeding surface, and then the two surfaces are placed in contact with one another. Bone autograft, allograft, or other bone growth-stimulating materials are then placed on these bleeding surfaces spanning the levels to be fused. Instrumentation may or may not be used to keep the spine immobilized as a fusion mass develops over the next 6–12 weeks.

Posterior Fusion

When fusing the spine from a posterior approach, the lamina, pars, facet joints, and transverse processes can all be decorticated to place bone graft and allow for fusion from a midline approach. If not doing a laminectomy, the lamina provides the largest surface area for fusion; however, in the setting of a patient undergoing laminectomy or having an open canal, further dissection out laterally is needed to expose the other bony elements. In this circumstance, a posterolateral fusion is performed between the transverse processes as bone graft is laid along the sides of the vertebral body against the decorticated pars and transverse processes. Some practitioners advocate fusion across the facet joints as they sit in a state of constant contact and compression with one another. If this is done, the soft tissue and cartilage within the joint must be meticulously taken down prior to decortication.

Posterolateral fusion can also be performed through a paraspinal approach lateral to the midline (Wiltse approach). This approach spares the midline structures (spinous process, lamina) and typically results in a smaller incision, less dissection, and subsequently less blood loss [9] (Fig. 20.6).

Instrumentation of the spine can be utilized to stabilize the spine as the fusion mass develops. The history of spine instrumentation shows surgeons using wires, hooks, and rods. Most modern-day surgeons utilize pedicle screws in the thoracic and lumbar spine. These have the advantage of providing capture of all three spinal columns. Studies have shown that with modern-day pedicle screw and rods constructs, the fusion rate in the thoracic and lumbar spine is substantially improved compared to fusion without instrumentation [10]. In the cervical spine where the pedicles are smaller and the risk of injury to the vertebral artery and spinal cord is elevated, screws can be placed in the lateral masses from C3–C7, the lamina of C2 and C7, the pars at C2, and across the joint (transarticular screws) at C1/C2 [11]. If needed in a trauma setting, fusion is also sometimes carried up to the occiput in which case, an occipital plate is utilized that allows placement of screws into the thick occipital bone (Fig. 20.7).

Interbody Fusion

Interbody fusion involves performing a discectomy between two vertebral bodies, removing the soft tissue and cartilage off either end plate and then placing graft material between the two prepared vertebral bodies. To assist with minimizing the pseudoarthrosis rate, the interbody fusion is supplemented with instrumentation via plating or a screw and rod construct.

By fusing between the vertebral bodies, interbody fusion confers a few advantages over posterior based fusion: The vertebral bodies provide a larger and more reliable surface area for fusion that naturally sits under compressive loads

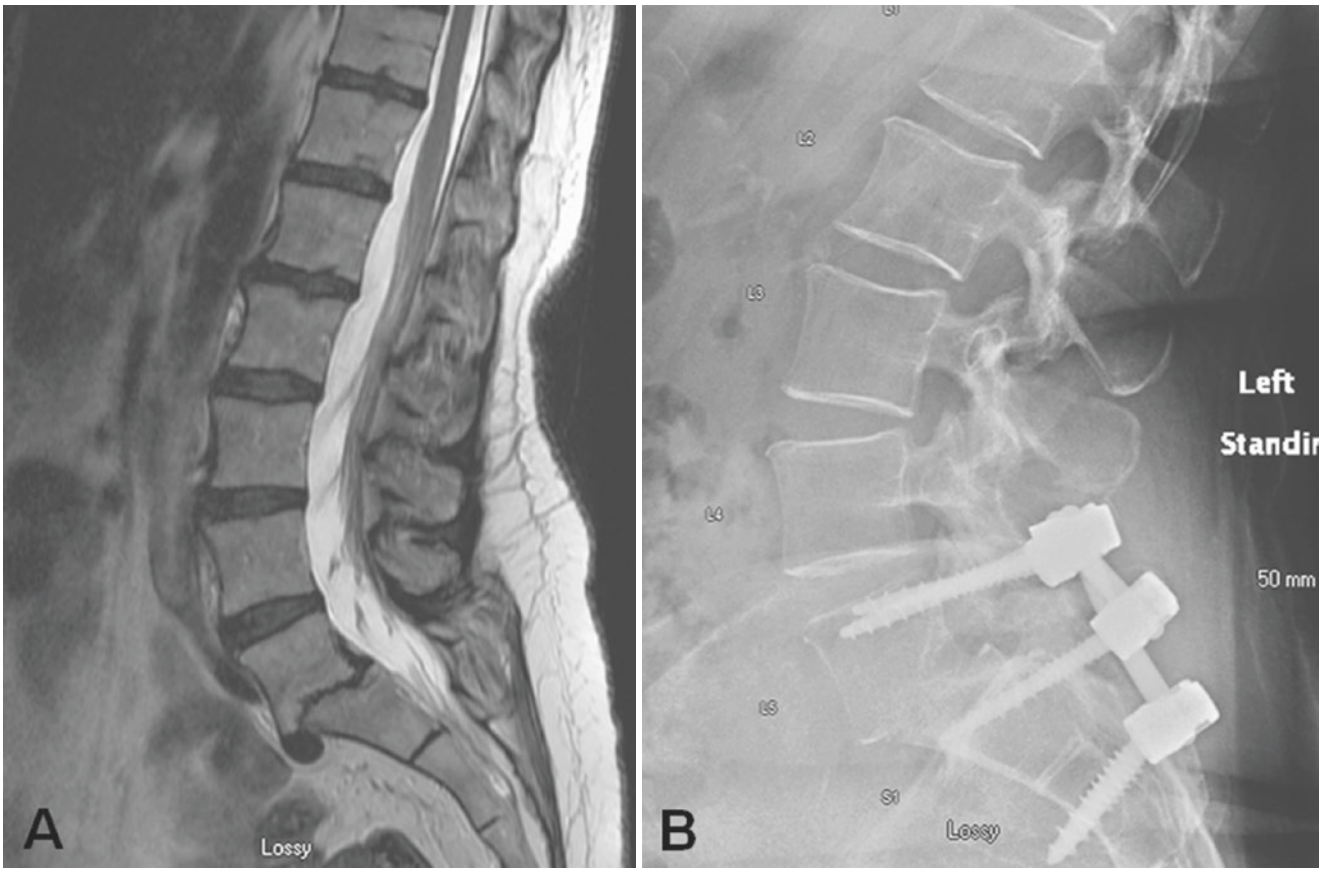

Fig. 20.6 (**a**) Sagittal MRI of a lumbar spine demonstrating L5/S1 spondylolisthesis with disc space collapse. (**b**) Postoperative sagittal radiographs demonstrating L5-S2 posterior spinal fusion and pedicle screw instrumentation

with upright weight bearing. Additionally, the height and shape of the graft/cage can be shaped to allow for restoration of disc height and altering the coronal and sagittal alignment of the spine. Most commonly, this is applied with lordotic cages in the cervical and lumbar spine.

In the cervical spine, the spinal cord prevents safe take down of the disc and preparation of the end plates from a posterior approach; therefore, an anterior discectomy and cervical fusion (ACDF) is performed. The graft, as with other interbody fusions, can consist of autograft, allograft, or synthetic cages. Data has shown that the addition of a plate helps with fusion rates also prevents anterior displacement of the graft [12]. The literature demonstrates that performing up to three single-level ACDFs can be performed before issues with pseudoarthrosis come into play [13]. In the thoracic spine, the disc and vertebral body are addressed posterolaterally or laterally, and either plates or a screw and rod construct can be utilized to stabilize the spine while the fusion mass develops (Fig. 20.8).

In the lumbar spine, interbody fusion can be addressed in several different ways and approaches owing to the mobility of the thecal sac and the anatomy laterally and anteriorly to the vertebral column (image of the different techniques?). An anterior lumbar interbody fusion (ALIF) is often performed concurrently with a general or vascular surgeon who performs the approach with the spine surgeon then performing the discectomy and the insertion of the interbody graft. The direct lateral lumbar interbody fusion/extreme lateral interbody fusion (DLIF/XLIF) and oblique lumbar interbody fusion (OLIF) are lateral-based procedures. The DLIF/XLIF is limited by the ribs cephalad and the iliac crest caudally, whereas the OLIF can avoid these structures owing to the oblique approach to the interbody space. Posteriorly, a posterior lumbar interbody fusion (PLIF) and a transforaminal lumbar interbody fusion (TLIF) can be performed. The window that a PLIF graft is placed into is directly posterior to the vertebral body and requires a central laminectomy and manipulation of the thecal sac. One or two PLIF grafts can be placed. Meanwhile, the TLIF involves performing a laminectomy and partial facetectomy and placing a single interbody graft through the foramen into the prepared disc space and across the midline. In this approach, the nerve root is at risk. The lumbar interbody grafts are typically supplemented with pedicle screws and rods posteriorly [14, 15] (Fig. 20.9).

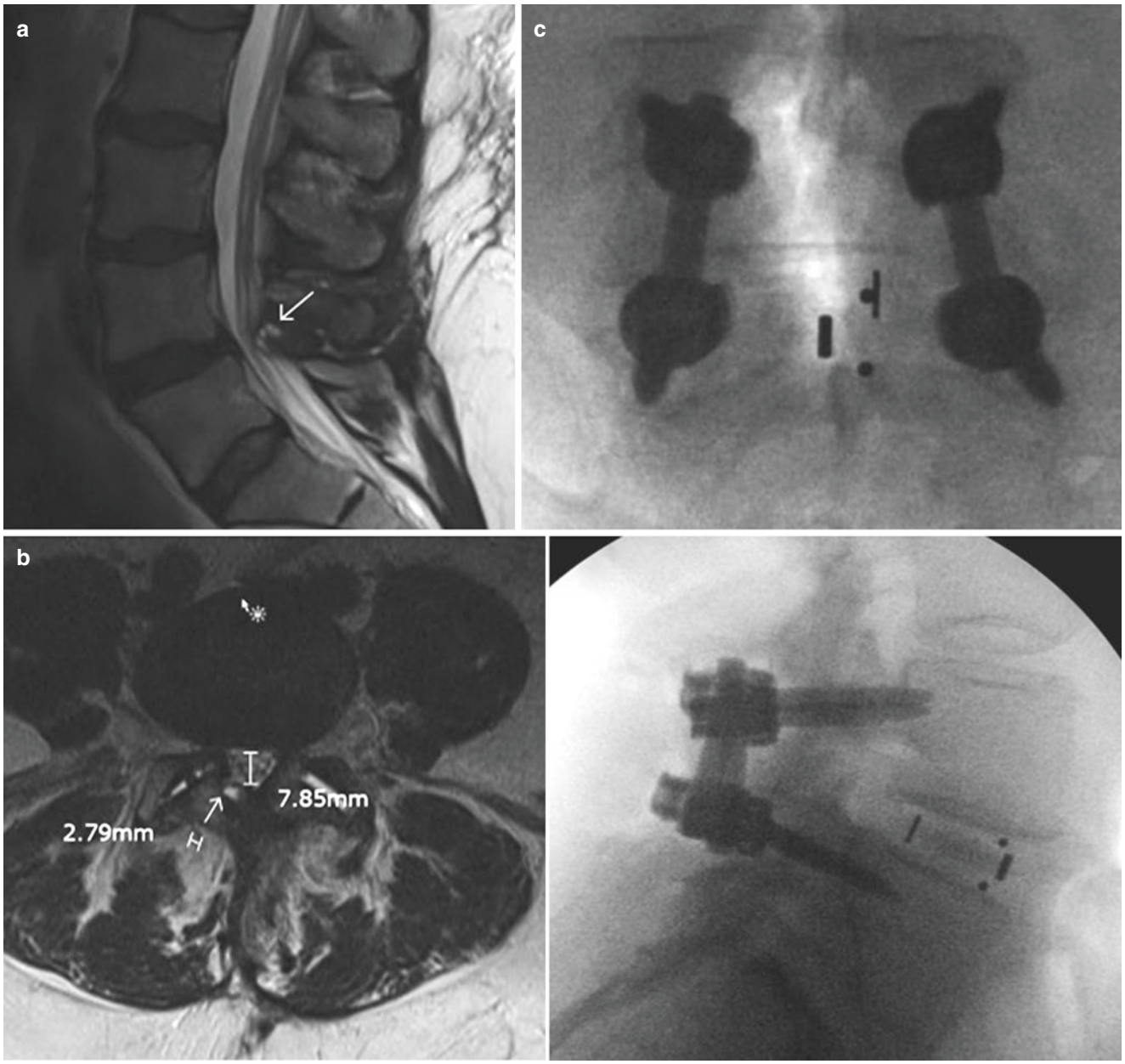

Fig. 20.7 (**a**) Sagittal lumbar spine MRI demonstrating degenerative disc at L4/5 with mild spinal stenosis. (**b**) Axial imaging of the lumbar spine demonstrating a facet joint cyst (arrow). Postoperative lateral radiograph of lumbar spine following L4L5 decompression and positioning of pedicle screw fixation and interbody cage. (**c**) Postoperative anterior-posterior radiograph of lumbar spine following L4L5 decompression and positioning of pedicle screw fixation and interbody cage

Reconstruction

The clinical significance of coronal and sagittal plane alignment in the spine remains debated among the community of spine practitioners. While the negative cosmetic aspect of having an abnormal curvature of the spine provides enough of a reason for many to undergo surgery, the literature also demonstrates that coronal and sagittal imbalance significantly contributes to pain and poor long-term outcomes.

Realignment of the spine is performed in conjunction with many of the fusion techniques already discussed. This section will discuss the methods that the spine surgeons employ to correct spinal alignment. It will also describe disc replacements and their role in restoring motion.

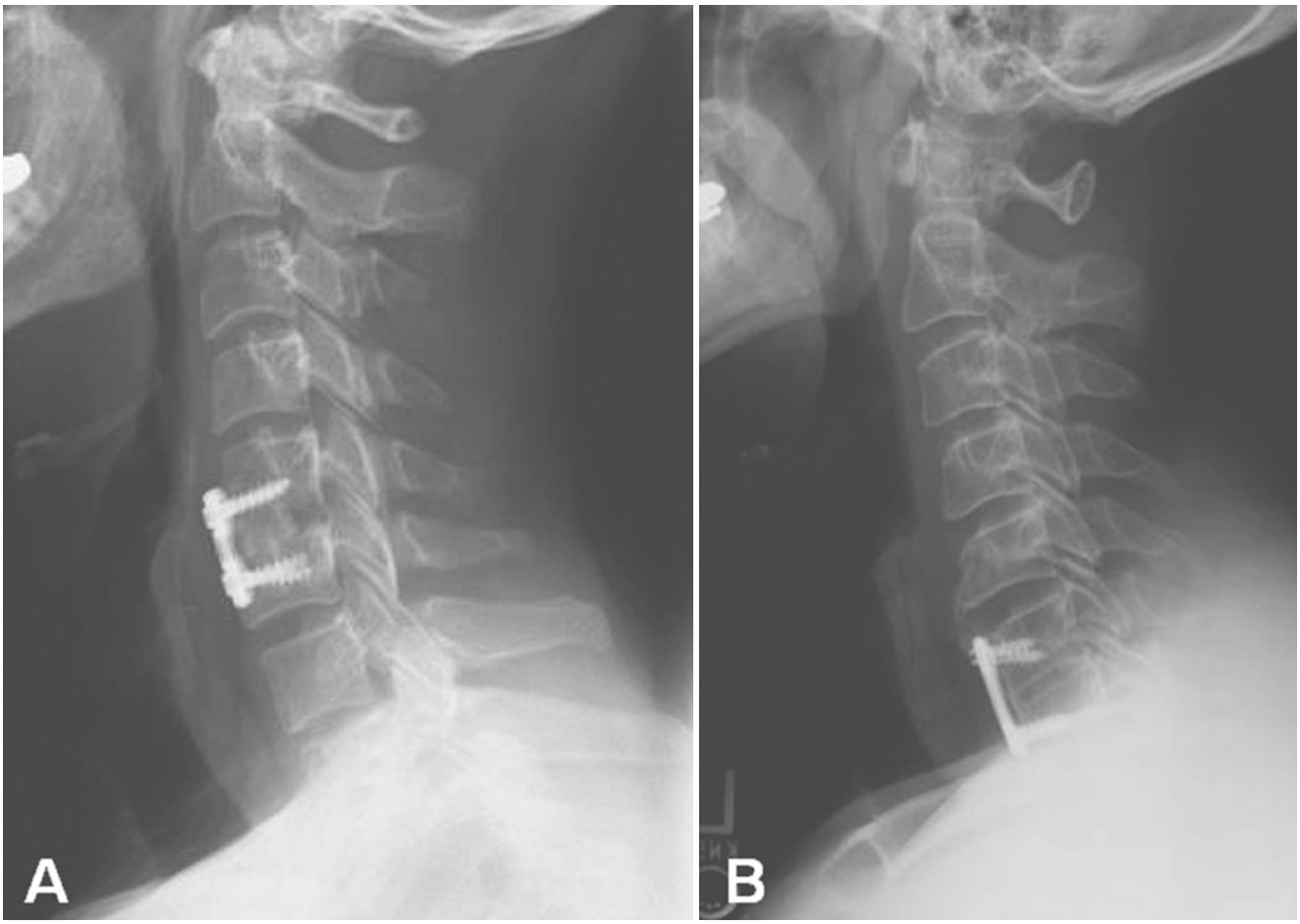

Fig. 20.8 (**a**) Postoperative imaging of C5/6 anterior cervical discectomy and fusion (ACDF)F. (**b**) Postoperative imaging of C6/7 ACDF

Osteotomies

The purpose of corrective osteotomies in the spine is to primarily provide additional lordosis in a fixed or flexible deformity. These osteotomies typically involve removing, at the least, the posterior stabilizing elements and then locking the position of the spine with a fusion. At the mildest end of the spectrum is the Smith-Peterson osteotomy (SPO), which involves removal of the ligamentous structures and facet joints in the posterior column of the spine. This allows more space for the spine to bend back into and helps reduce a kyphotic deformity. This can be done at multiple levels and typically provides 10–20° of correction per level. It is more effective in the lumbar spine owing to the increased disc space height and flexibility of the lumbar spine.

Next, a pedicle subtraction osteotomy (PSO) involves making a wedge osteotomy through all three columns of the spine, removing the facet joints similar to the SPO as well the pedicles from the vertebral body. This allows for approximately 30° of correction in the lumbar spine. A vertebral column resection (VCR) involves the complete removal of one or multiple vertebral bodies, and essentially, the surgeon can achieve as much post-op lordosis as he or she wants with this procedure. A structural autograft/allograft of synthetic cage is then utilized to fill the previous interbody space. This can be done both anteriorly or posteriorly [16] (Figs. 20.10 and 20.11).

Disc Replacement

Although typically not indicated in the thoracic spine due to the relative rigidity conferred by the ribs and sternum, a disc arthroplasty or replacement can be utilized in the cervical and lumbar spine to address disc-related pain while allowing preserved motion at the operated spinal segment. There is typically more success with the procedure in the cervical spine. The procedure involves performing a discectomy as if performing an interbody fusion, and instead of placing a structural graft, an articulated implant is placed into the space, thus allowing continued motion and flexibility. In the cervical spine, there are currently implants indicated for up to two level procedures, and the literature demonstrates similar efficacy to ACDF in terms of treatment of symptomatic disc herniations [5].

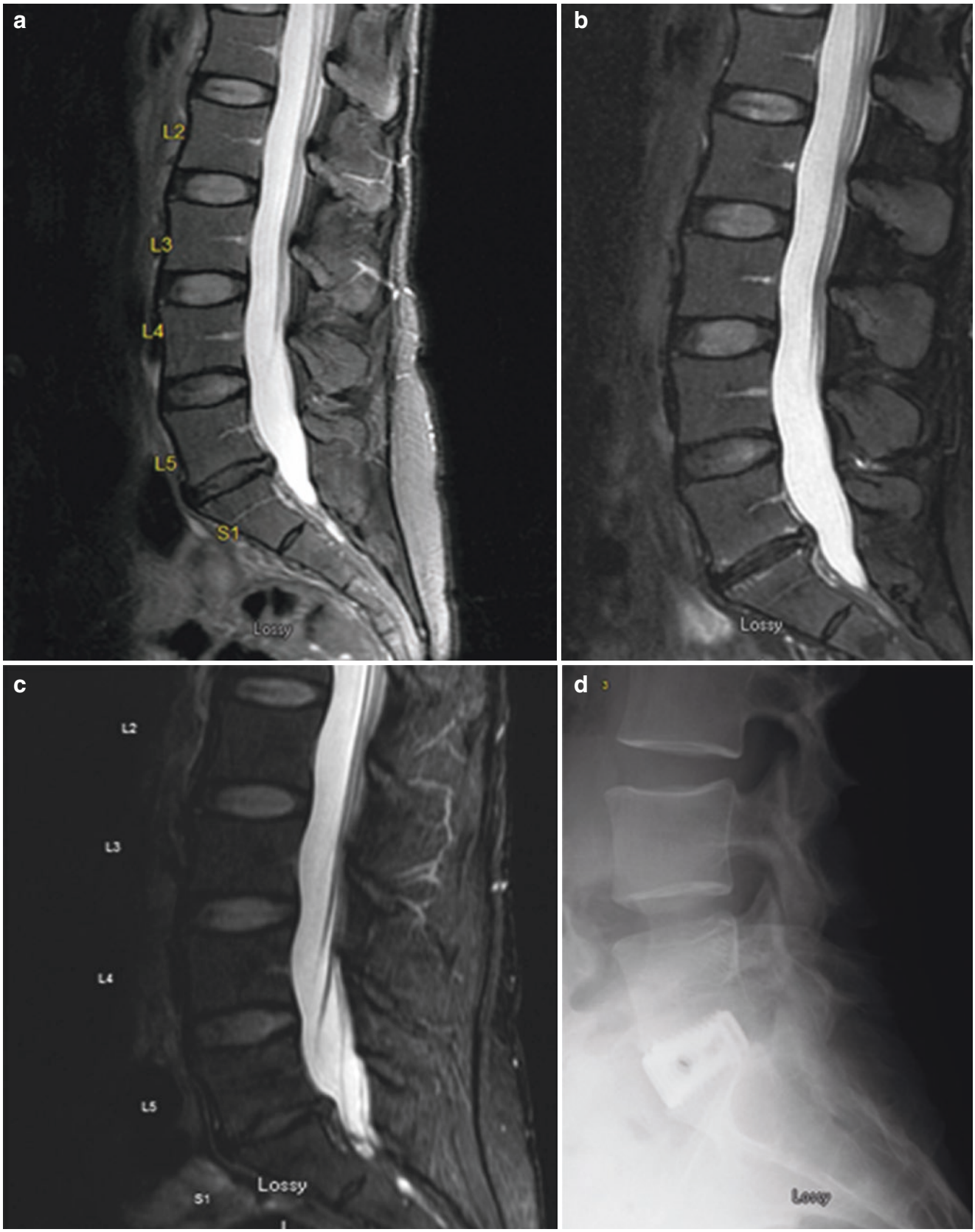

Fig. 20.9 (**a**–**c**) Sagittal MRI of the lumbar spine demonstrating progression of L5/S1 disc degeneration ultimately leading to significant disc height collapse. (**d**) Postoperative lateral radiograph following L5/S1 anterior lumbar interbody fusion (ALIF)

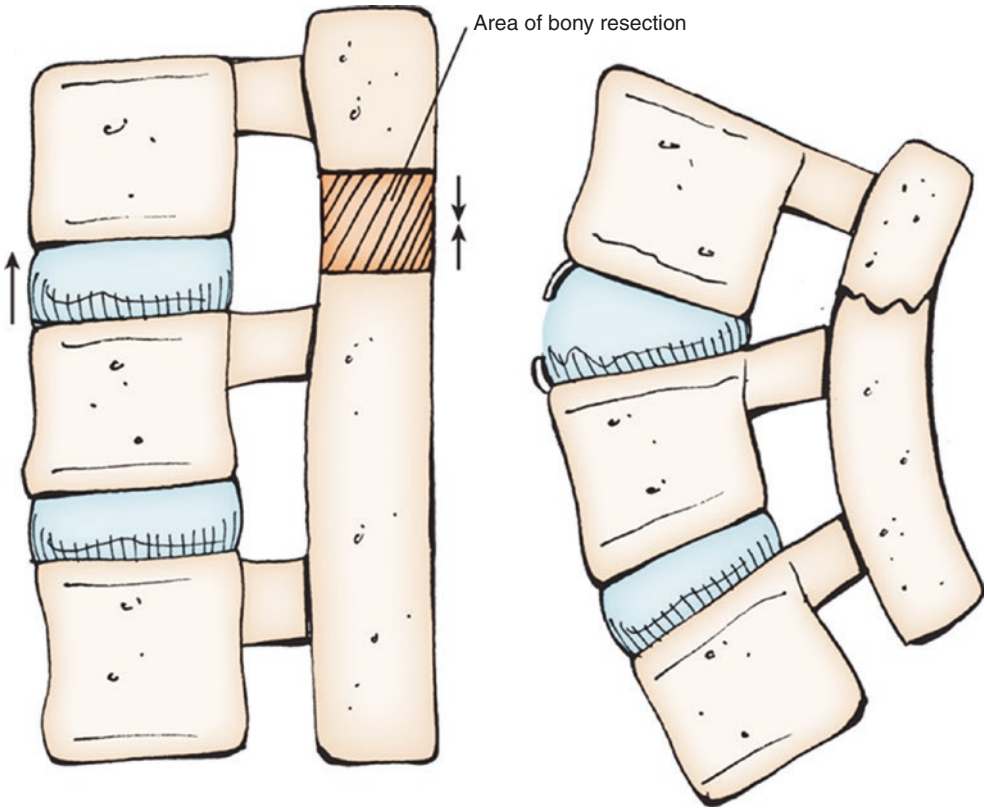

Fig. 20.10 Posterior column osteotomy

Minimally Invasive Surgery

Minimally invasive surgery (MIS) is a broad category of spine surgery that describes any surgical procedure that is performed through a minimal incision. These procedures are typically performed with the assistance of such tools as radiographic fluoroscopy and tubes that allow the surgeon to utilize surgical instruments and place instrumentation if needed into an area that is not completely open and visible. The definition of what characterizes an MIS procedure can defer among surgeons, but regardless, this has a positive connotation for most patients. The assumption is that an MIS procedure will be approached in a less aggressive manner, theoretically allowing the patient to recover quicker in less pain. In practice, however, not all pathologies of the spine can be visualized through minimally invasive approaches and attempting MIS when not indicated can lead to iatrogenic injury and poor outcomes [17, 18] (Figs. 20.12 and 20.13).

Summary

The field of spine surgery is vast with a long history. Over time, spine surgeons have developed techniques to treat a large range of ailments originating from the spine. These techniques can be grouped broadly into three categories: decompression of the neural elements, fusion of diseased and pathologic segments, and reconstruction of fixed and flexible deformities. As we move into the future, the hope is to develop additional tools and methods that will allow the surgeon to address these pathologies through less invasive procedures while preserving motion segments; however, the greatest tool for the surgeon remains his or her own clinical judgment in choosing the appropriate surgery and approach for the right patient and pathology.

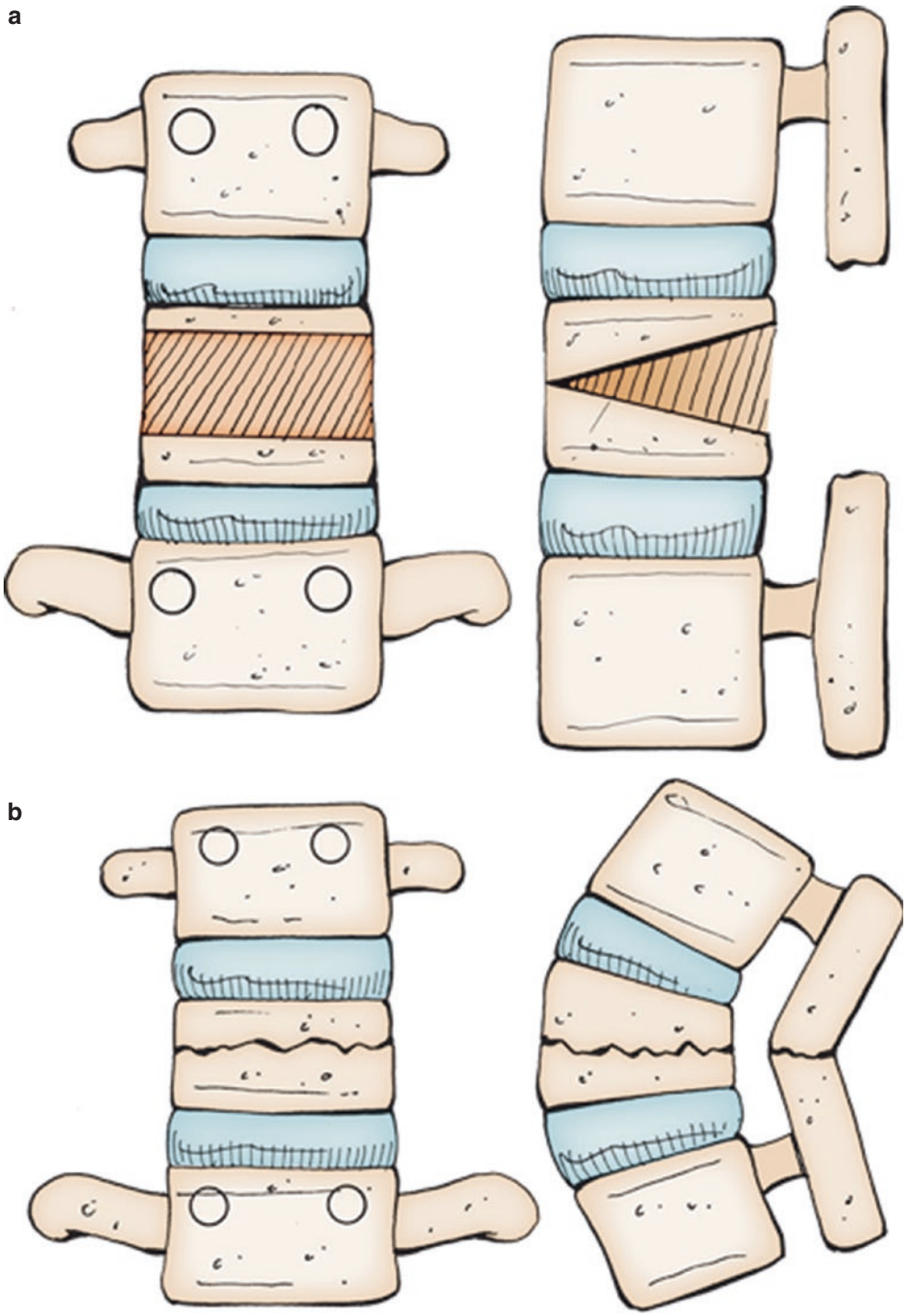

Fig. 20.11 Posterior column osteotomy, before (**a**) and after (**b**) compression

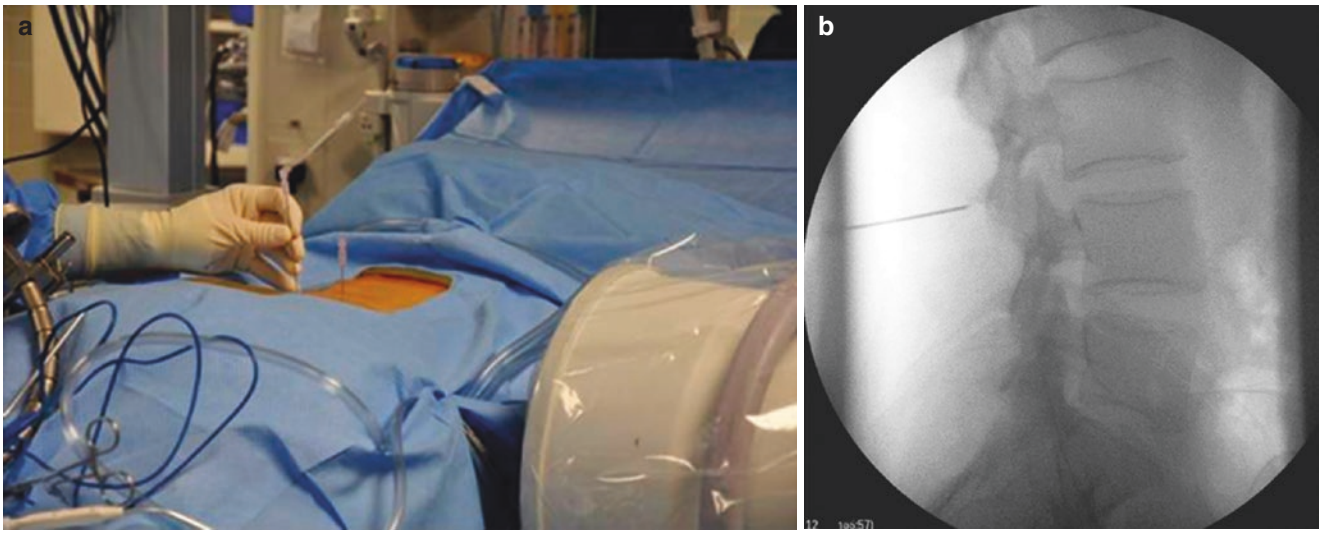

Fig. 20.12 (**a**, **b**) Intraoperative percutaneous needle localization of the L3/4 disc space with fluoroscopic confirmation for a minimally invasive procedure

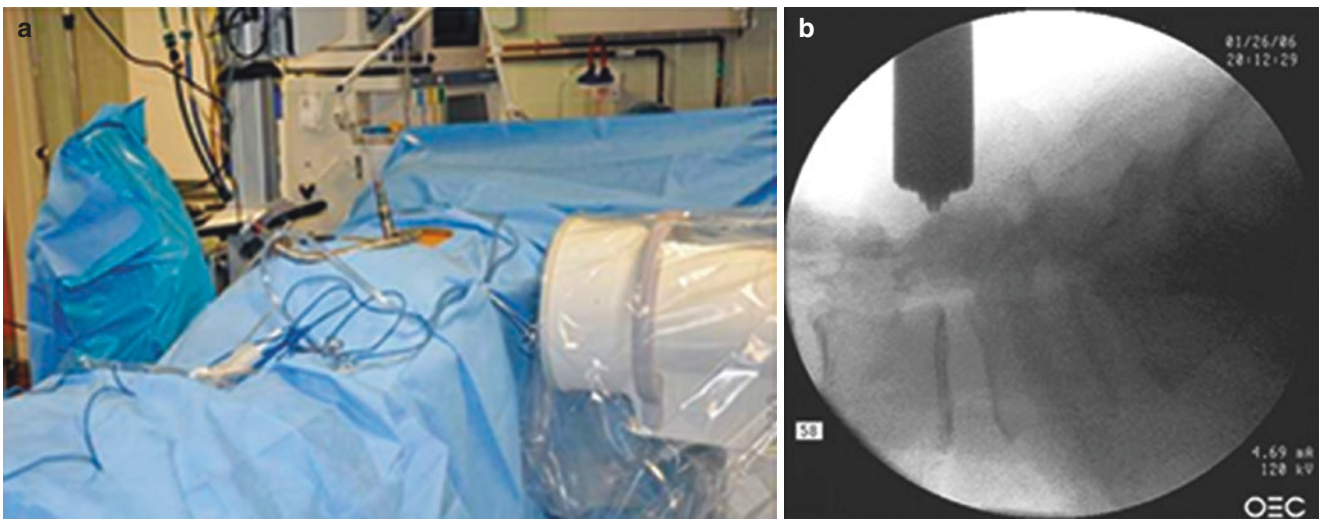

Fig. 20.13 (**a**, **b**) Placement of surgical tube at L3/4 utilizing minimally invasive surgical technique with intraoperative fluoroscopic confirmation. Tools and instruments are passed through the tube

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Minimally Invasive Surgical Procedures for Spine Pain Management

21

Hamid M. Shah and David A. Edwards

Key Points

- Patients undergoing minimally invasive spine (MIS) surgery have earlier postoperative mobilization, lower blood loss, and less narcotic usage.
- MIS surgery is a tissue-sparing technique applied to standard surgeries.
- The spine can be approached from the back or the side using these techniques.
- MIS techniques are continuing to evolve, and smaller portals are being employed.
- Robotics will add to the sophistication of MIS techniques.

Introduction

Currently, minimally invasive lumbar spine surgery has quite a robust representation. Broadly, it can be divided into decompressive procedures and stabilizing procedures with decompression. Minimally invasive lumbar spine surgery, or the concept of minimal access to the lumbar spine, has had a long history of attempts. An anatomic study performed by Burman et al. in 11 fresh cadaveric specimens first described the techniques and findings [1]. The earliest recorded attempt was myeloscopy performed by Pool et al. in 1938 with the intent to aid in the diagnosis of spinal nerve pathology [2]. This is an interspinous approach in the lateral decubitus position using local anesthesia. A cystoscope had been adapted and attached to her battery-operated light source from an otoscope [2]. Separately, the Japanese group decades later reported on a similar technique [3]. While these demonstrated observational studies could be completed, there is still a significant gap in using this to provide therapy. Subsequent attempts at performing minimally invasive spine procedures included chemical treatments such as chymopapain, arthroscopic discectomies, foraminoscopies, as well as laser-assisted techniques. Chymopapain was isolated in the 1940s and subsequently noted to digest disc tissue in the rabbit [4]. It was subsequently tested in humans and originally found to be quite beneficial in early European studies, but this did not bear out in American studies [4]. This prompted the withdrawal from the US market, with a brief reintroduction in 1982 as a different formulation until it was finally removed from the market as surrounded by a significant amount of controversy. The underlying premise of this technique was minimally invasively address disc herniations. This was accomplished by delivering chymopapain directly into the intradiscal space. This would then digest portions of the nucleus pulposus within the disc and decrease the intradiscal pressure thereby allowing the prolapsed disc to reduce into the disc space or be digested. Ultimately this technique was abandoned for several reasons despite several clinical trials due to concerns of greater than expected chemically induced radiculitis with and without motor deficits, chronic back pain, insufficient reduction of radicular symptoms, as well as a lack of durability in symptom resolution [4]. A similar concept, intradiscal laser therapy, aimed to decrease the intradiscal volume and pressure by vaporizing a volume of nucleus pulposus. This did not consistently occur, but frequently did lead to contraction of the disc material. Both techniques had unreliable efficacy and were limited by the fact they could not address free fragments, disc herniations isolated from the disc space. Additionally, both techniques are not effective at addressing bony pathology which often exists concomitantly with the disc herniations. Both techniques rely on an indirect approach to addressing compressive pathologies. The earliest attempts at mechanically addressing disc herniations in a minimally invasive technique included microendoscopic discectomy. Essentially this was

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very similar to open microsurgical techniques. It used a paramedian muscle-splitting technique to introduce an endoscope through which micro-graspers could deliver the disc herniation [5, 6]. Several studies have reviewed microendoscopic discectomy, some have compared it to open discectomies and have demonstrated that while there is similar efficacy in symptom resolution the cost and complication profile were significantly higher in the microendoscopic cohorts [5, 6]. Unlike in the open and microdiscectomy techniques which views surgical loupes and a microscope, respectively, microendoscopic technique relies on a two-dimensional camera to provide visualization. It was thought to be stereoscopic vision is what distinguishes the techniques and what contributed for more nerve root injuries as well as durotomies and persisted despite additional experience [5, 6].

Kevin Foley published in 1997 his techniques in performing a minimally invasive discectomy through a tubular retractor using a microscope for direct visualization [7–9]. This provided access to the lumbar spine through a 16–18 mm tubular retractor and preserved stereoscopic vision in order to perform a hemilaminectomy with or without a microdiscectomy. This has the benefit of directly decompressing the nerve root in the lateral recess along with addressing the disc herniation. Several studies subsequently have evaluated the clinical efficacy, risk profile, as well as cost-effectiveness of this newly introduced technique. A recent review and analysis of literature indicated there was no difference in risk or an outcome between open and minimally invasive techniques as level I evidence with regard to spinal fluid leak, recurrent disc herniations, nerve root injury, as well as suggesting level II evidence that operative times were actually shorter in the minimally invasive groups and blood loss being similar to the open group [7]. Another study reviewed the cost-effectiveness of tubular microdiscectomy and reported no difference and operating room time and charges, but the tubular group had total hospital charges which were US$5453 less than the open group [8]. Of note, there was a demonstrable decrease in level of analgesic use in the tubular group [7].

With added facility of using the tubular retractor systems, surgeons began to use the tubular retractor systems for much more complex interventions. The tubular retractor system is now used fairly routinely for unilateral approaches for bilateral lumbar laminectomies with and without fusion, as well as transforaminal lumbar interbody fusions (TLIF). Unilateral approach for bilateral decompression of lumbar spine has benefit of providing direct decompression of the neural elements by removal of the ipsilateral hemilamina and undermining the contralateral hemilamina along with removal of ligamentum flavum to reconstitute the spinal canal. This essentially accomplishes the same as an open procedure with much less tissue disruption. A European study reviewed the midterm outcomes on this technique in a retrospective review of similarly matched patients. Patients who had undergone 1 and 2 level laminectomies with similar VAS leg and back scores were followed for 26 months [13]. Over this period of time, it was noted a durable clinically significant as well as statistically significant change in their ODI's, back pain, and leg VAS scores [13]. More broadly, the outcomes of this technique have been extensively reviewed, as have the outcomes of open laminectomy procedures. Several meta-analyses as well as primary investigations have recapitulated these outcomes [14]. In addition, reviews have compared the efficacy of minimally invasive laminectomies to open laminectomies. A recent meta-analysis which included randomized clinical trials as well as some non-randomized clinical trials comparing minimally invasive laminectomies for lumbar stenosis indicated that a minimally invasive approach is associated with less blood loss, shorter hospital stays, and similar complication rates to open [10, 11]. Figures 21.1 and 21.2 are cartoons depicting the expected view from a unilateral approach for a laminectomy and bilateral mesial facetectomies. The ipsilateral and contralateral traversing roots and central thecal sac should be easily visualized after bony decompression and resection of the ligamentum flavum. This meta-analysis also evaluated the studies for operational as well as publication bias by evaluating the study characteristics and reported a low risk of bias [10]. Overall this meta-analysis reported minimally invasive laminectomies are associated with higher patient's satisfaction scores and lower visual analog pain scores compared to the open and lower blood loss with a similar complication rate for dural tears and wound infections and are marginally longer than open cases but are associated with significantly shorter hospitalizations [10, 12]. Figures 21.3 and 21.4 are pre- and postoperative axial T2 images of the same patient. Figure 21.3 exemplifies severe central and bilateral lateral

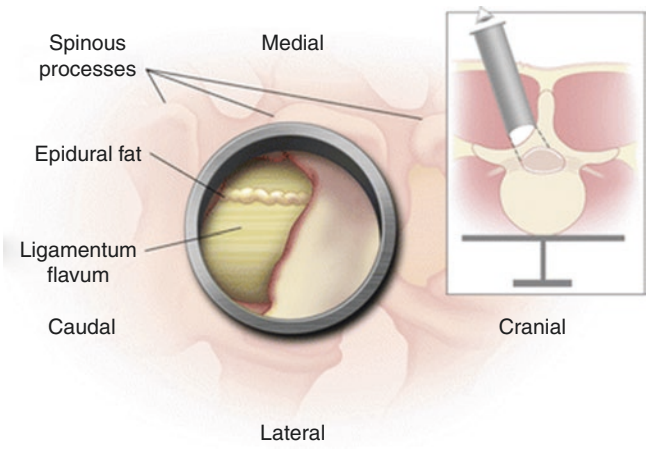

Fig. 21.1 An 18 or 19 mm tubular retractor was placed over a series of tubular dilators for retraction, and under the microscope, the inferior edge of the lamina and the inferior edge and base of the spinous process were exposed. (Reprinted with permission from Alimi et al. [13])

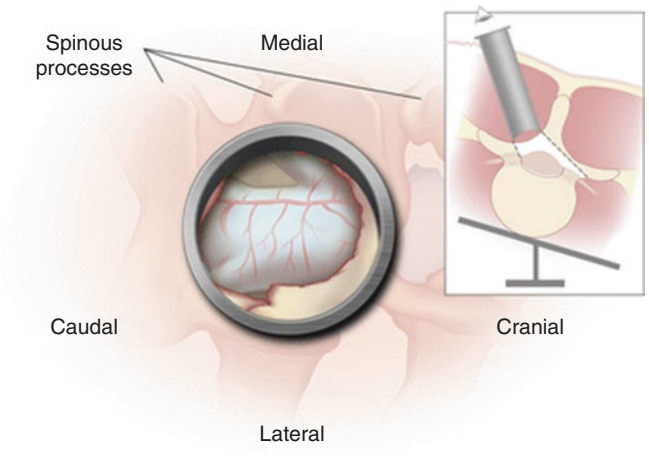

Fig. 21.2 Dural exposure and decompression after complete removal of the ligamentum flavum. The contralateral approach allows visualization and decompression, if needed, of the contralateral exiting and traversing nerve root. It is clear from this drawing that the decompression achieved on the contralateral side appears to be much more generous than the ipsilateral decompression. (Reprinted with permission from Alimi et al. [13])

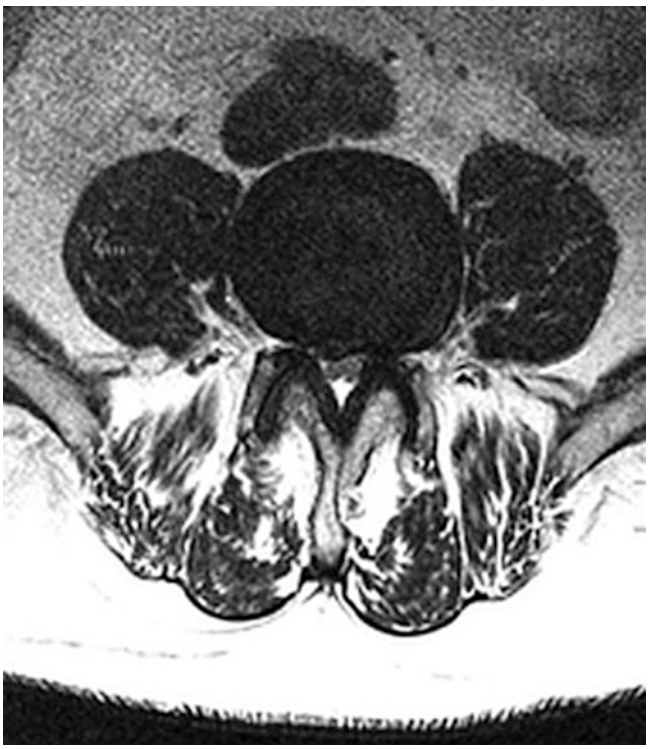

Fig. 21.3 Preoperative T2 MRI

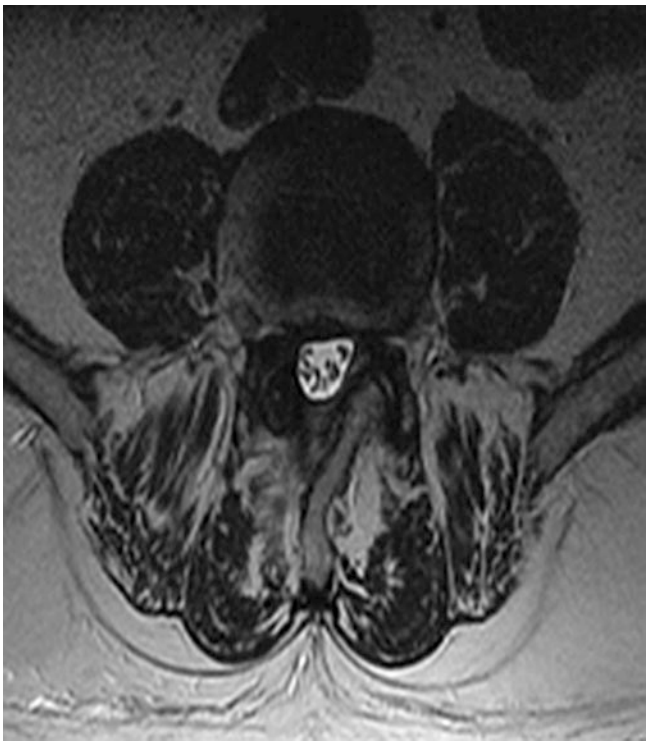

Fig. 21.4 Postoperative T2 MRI

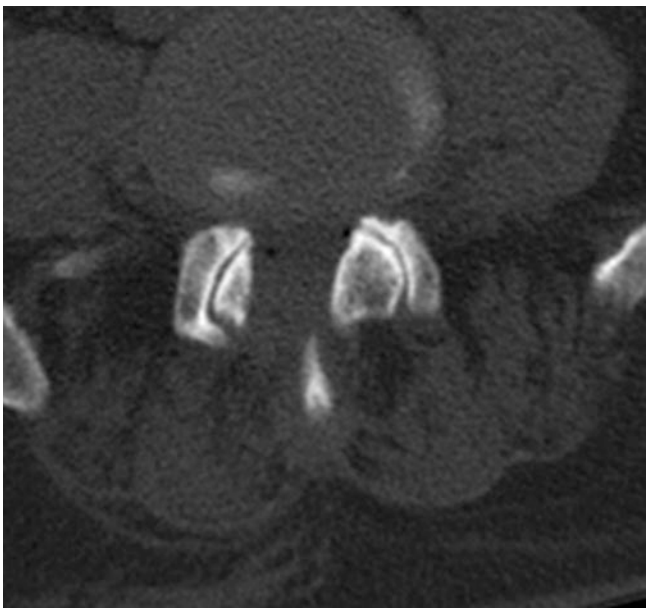

Fig. 21.5 Postoperative CT

recess stenosis. Figure 21.4 demonstrates reconstitution of the central canal and both lateral recesses after a unilateral approach for a tubular laminectomy. This was completed through an 18 mm portal. Figure 21.5 demonstrated the bony decompression achieved and demonstrates the ability to perform bony removal on the contralateral portion of the lamina. Figures 21.6 and 21.7 are T2 sagittal images pre- and postoperatively, respectively, and denote the reconstitution of the canal at L4/5. Also of note is the limited amount of soft tissue disruption.

Along with the evolution of minimally invasive decompression techniques, there has been avid interest as well in

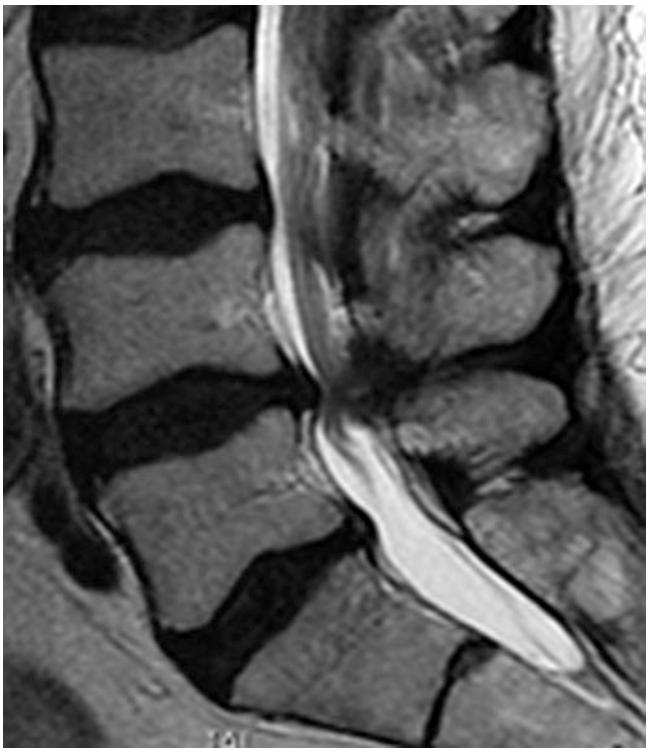

Fig. 21.6 Preoperative T2 MRI

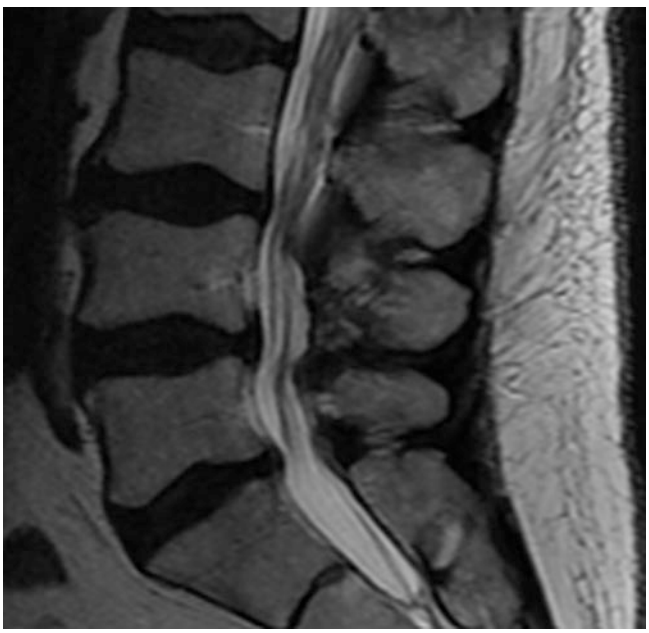

Fig. 21.7 Postoperative T2 MRI

minimally invasive screw fixation. This was pursued in order to decrease approach-related morbidities associated with open pedicle screw fixation. This included significant blood loss, significant local tissue trauma, and protracted hospital stays to use. A paramedian approach to pedicle screw fixation, the Wiltse approach, rather than midline approach could potentially answer this through an open technique but was still limited in the amount of tissue damage reduction it could provide. This approach corridor could be exploited as well through percutaneous techniques. The earliest attempts at percutaneous screw fixation began in 1982 and continued on until 2001 when a usable percutaneous fixation system was finally developed [15]. The initial attempts at percutaneous screw placement were associated with external fixation and were limited by the morbidities unique to this, such as high infection rates and poor fixation due to long-moment arms. Foley et al. in 2001 described a total percutaneous screw and rod delivery system. The clinical and radiographic outcomes of 12 patients, the majority of whom had excellent to good outcomes using modified McNab criteria, with 12-month follow-up were reported and demonstrated the fact screws could safely and effectively be placed percutaneously to promote fusion without the approach-related morbidities of the traditional open route [16, 17]. Building on the advances in percutaneous pedicle screw fixation as well as minimally invasive decompression by way of tubular access, the next step was delivering an interbody into the disc space for circumferential fusion as well as tackling more complex degenerative disc disease such as Meyerding grade 1 and grade 2 spondylolistheses. The combination of these techniques together culminated into what's known as a minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF). This technique is the workhorse for most minimally invasive spinal fusions. Schwender et al. and Park et al. reported on the initial outcomes of tubular MIS-TLIF in degenerative disc disease as well as degenerative disc disease associated with spondylolisthesis in 2005 and 2008, respectively. Both studies followed the surgical cohort for minimum of 2 years and demonstrated clinically significant and durable decreases in ODI as well as VAS scores [18–21]. This distinguishes itself from other minimal access techniques (MAST-TLIF) that are currently also employed by the use of a tubular retractor to perform both a decompression and delivery of the interbody. Currently, there are other techniques which provided as small a surgical corridor as possible through a midline approach. This does not approximate the significantly smaller access provided by the tubular MIS-TLIF. MAST-TLIF also suffers from similar approach-related morbidities associated with open TLIF from muscle stripping and denuding of the spinous process and lamina. Figures 21.8, 21.9, and 21.10 are preop, intraop, and post-op images of the same patient who underwent a MIS L5/S1 TLIF for bilateral L5 radiculopathies with back pain. The preoperative radiograph demonstrates bilateral pars defects at L5/S1 and a grade 2 spondylolisthesis which was mobile on flexion/extension images. Figure 21.9 is an intraoperative fluoroscopic image denoting the reduction of the spondylolisthesis and placement of the percutaneous instrumentation and interbody cage. Figure 21.10 is 4 weeks post-op and exemplifies the small paramedian incisions

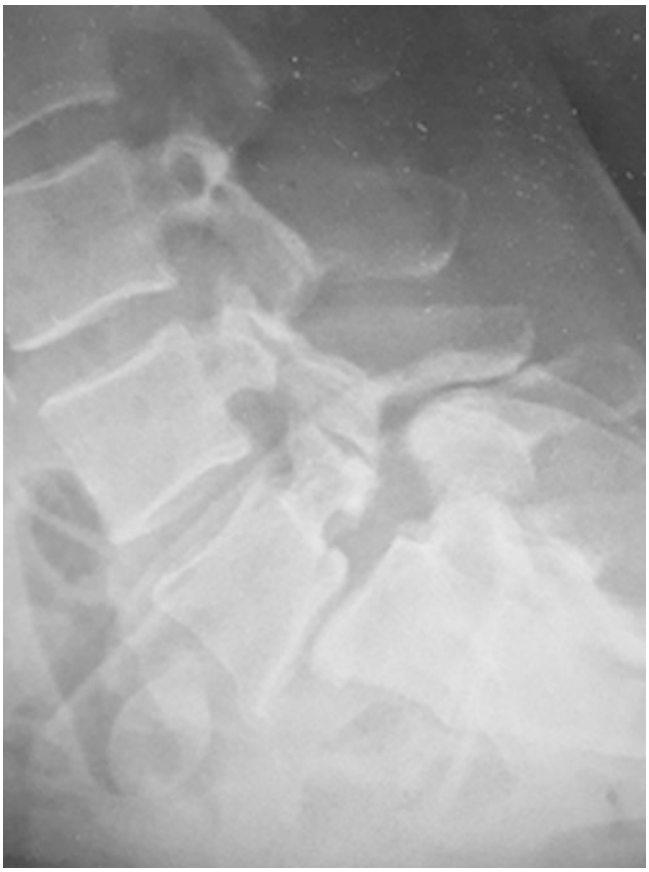

Fig. 21.8 Preoperative X-ray of L5/S1 Meyerding grade 2 spondylolisthesis

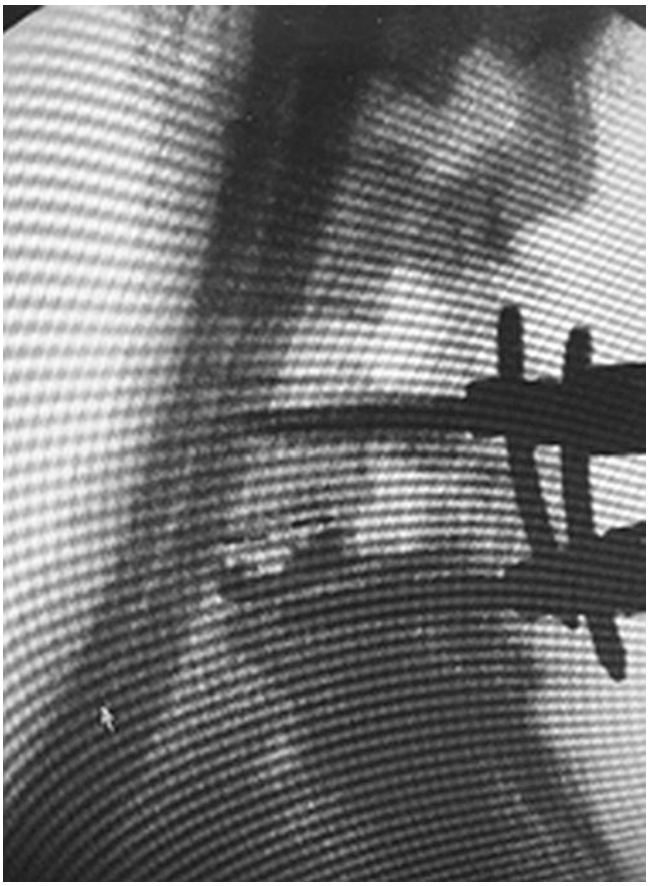

Fig. 21.9 Intraoperative fluoroscopy image

employed for this technique and the small stab incisions for delivery of the rod.

Frequently, tubular MIS-TLIF is criticized for not being able to provide the same degree of decompression, excessive operative room time, increased cost, and increased rate of complications. It is accepted there is a steep learning curve with minimally invasive techniques, but they are not prohibitive of employing them. This may have been an accurate concern when the technology was nascent. With the current instrumentation, this does not bear out to be true. A 2014 systematic review comparing minimally invasive to posterior lumbar fusion reviewed 26 studies with 1600 patients, and it was noted there were similar operative times, faster discharge from hospital, less blood loss, low rates of surgical or medical adverse events, and similar patient reported outcomes regarding VAS and ODI scores [24, 25]. Criticisms notwithstanding, there are noted benefits to minimally invasive spine surgery beyond lower blood loss. It has been reported in a 2011 review of literature a 0.6% incidence of surgical site infection representing a 3.4% difference between open and minimally invasive and a direct cost savings of $98,974 per 100 minimally invasive TLIFs performed [26]. This followed in line with a previous analysis of 108,000 spine surgery procedures reviewed by the scoliosis research society, in which it was noted that there is a similarly low incidence of surgical site infection in minimally invasive procedures [27]. Not only do patients undergoing MIS-TLIFs discharge from hospital faster, but there is a trend toward decreased narcotic use as well as faster return to work compared to the open TLIF cohorts [23]. The comparative effectiveness of invasive TLIFs was also compared to the open counterpart. It was noted there was a reduction of cost with minimally invasive TLIFs over 2 years of $9295 with similar QALYs gained [22]. Overall, the adoption and evolution of tubular MIS-TLIFs have greatly increased in safety and efficacy profile.

In keeping with the sentiment of achieving most robust surgery through the smallest portal possible, surgeons have sought alternative corridors to the lumbar spine. The traditional anterior lumbar interbody fusion (ALIF) uses an anterior access to arrive at the front of the spine while remaining retroperitoneal. This involves a rather extensive dissection through either the linea alba or paramedian through the rectus abdominis and other muscles. This is associated with significant postoperative pain and in the long-term contributes to persistent back pain. While there are challenges with this approach, a very large and robust graft can deployed

thereby more likely promoting a fusion. The lateral transpsoas approach takes advantage of the capacity to deliver a large interbody device, much like an ALIF, through the retroperitoneal space. Ozgur and Pimenta first described this in 2006 [28]. Since then, there have been subsequent expansion upon this to deliver interbody devices. This surgical path involves positioning the patient in a lateral decubitus position and planning a flank incision at the level of interest. As in the ALIF, it is important to remain retroperitoneal. The dominant advantages of this approach are the small portal of entry, limited muscle dissection, and ability to deliver a large graft [28]. Multiple levels can be accessed in a smaller incision ventrally in the abdomen as well as thorax. Upon entry into the extraperitoneal space, a blunt finger dissection can be performed to arrive at the lateral spine while remaining retroperitoneal. As the technique has evolved, so has understanding of the anatomic considerations. In particular, the lumbar plexus is particularly vulnerable as it courses through and around the psoas muscles. There is a fairly consistent posterior to anterior migration of the lumbar plexus as it progress rostral to caudal [29]. There is particular vulnerability at L4/5 with injury to the femoral nerve. As a routine, free-running EMG intraoperative monitoring is performed to identify the plexus. It has been noted, despite this, that the nerve can be injured at this level and has been associated with prolonged retractor time. Lateral lumbar fusion can be used to address degenerative lumbar disease in conjunction with pedicle screw instrumentation with or without direct decompression. Currently, studies are aimed at identifying the limitations of the technique and long-term outcomes on function, quality of life, and radiographic improvement in alignment and balance. Figure 21.11a–c shows examples of a patient with neurogenic claudication from mobile spondylolistheses at L3/4 and L4/5 treated with a lateral approach delivery of interbody cages and percutaneous instrumentation.

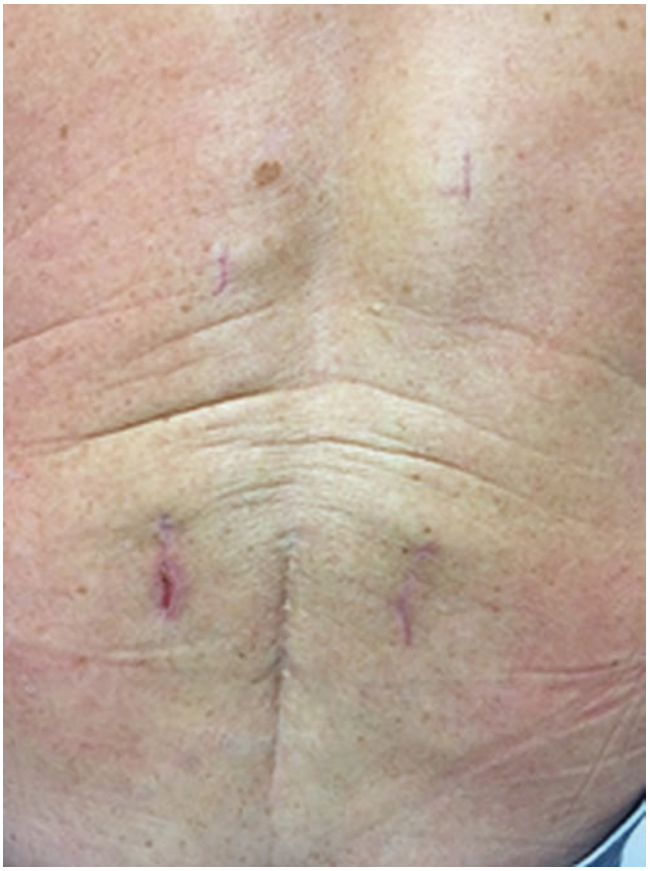

Fig. 21.10 Same patient 4 weeks postoperatively

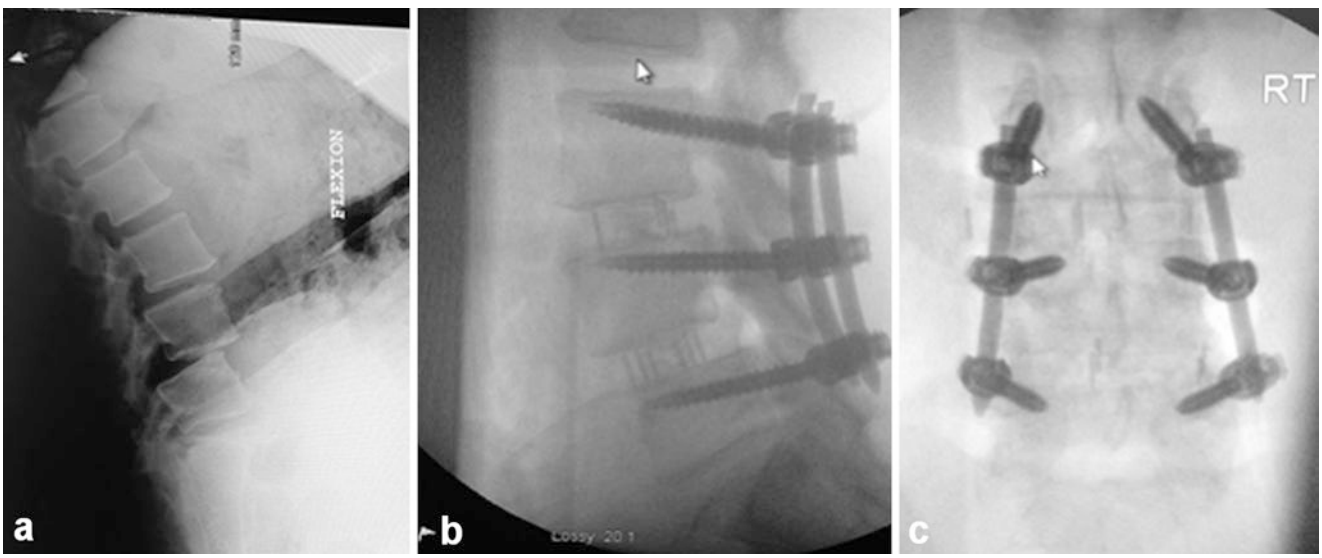

Fig. 21.11 (**a**–**c**) Examples of XLIF for isthmic spondylolisthesis

Surgeons have been striving to provide interventions through progressively smaller portals while intending to maintain comparable efficacy to open counterparts. Currently the tubular retractor approach is the most frequently employed method and can be used to access the spine posteriorly in order to achieve a decompression as well as deliver an interbody cage along with percutaneous instrumentation to construct a fusion. A similar combination can be utilized from a lateral approach to provide an indirect decompression as well as instrumentation. As the tools for minimally invasive surgery continue to evolve, so to the breadth of procedures capable evolve. Experienced surgeons have demonstrated removal of spinal tumors through these portals as well performing long-segment instrumentations for deformity corrections. In parallel with expanding the numbers of procedures able to be performed, advances in instrumentation has allowed for even smaller portals to be used. More recently, endoscopic approaches for discectomies and fusions have been explored. This was made possible from improvements in the endoscopic cameras which can provide high-resolution and near three-dimensional imaging of the surgical field. As the field continues to mature, outcomes research will be a strong driver in the longevity of some procedures while demonstrating lack of efficacy in others.

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Epidural Steroid Injections

22

Thomas Suchy, Jack Diep, and Jianguo Cheng

Key Points

- The incidence of radicular pain associate with spine disorders has become increasingly common throughout the industrialized and developing world.
- Epidural injections are the most commonly utilized intervention for managing chronic and acute radicular pain associated with spine and other pathologies. Multiple systematic reviews of the efficacy, safety, and cost-effectiveness for specific indications of epidural injections have been published.
- The outcomes of epidural injections are determined by a number of factors including judicious selection of patients with appropriate indications, clinicians' knowledge, technical skills and experience, appropriate use of imaging and other techniques, and clinician's ability to identify and manage risk factors and complications.
- The decision on the need for repeat injections and the interval between injections have to be individualized and supported by monitoring patients' outcomes in terms of the duration of pain relief and functional improvement.
- There are multiple techniques for performing epidural injections at cervical, thoracic, lumbar, and sacral levels. The selection of transforaminal, interlaminar, paramedian, and caudal approaches to epidural injection is dependent on the location and nature of the pathology, patients' anatomical variations, clinician's training and skill set, and risk/benefit assessment.
- Appropriate use of imaging guidance and early detection of deviation of needle position for the intended target are critical to minimizing the risk of inadvertent intravascular and/or intraneural injections and their consequent complications. The use of particulate steroids has also been associated with devastating complications.

Introduction

Experiencing lower back or neck pain has become increasingly common throughout the industrialized and developing world [1, 2]. While the majority of those affected recover within a reasonable timeframe [3], many of them progress to develop chronic or recurrent pain. These disorders can result in a significant burden for both the individual and the community they inhabit. According to the Global Burden of Disease Study 2015, lower back and neck pain causes more disability than any other condition [4]. Sick leave and early retirement are most frequently associated with chronic lower back and neck musculoskeletal disorders [5]. These issues place a tremendous financial cost to both the domestic and global economies [6, 7]. In addition, the incidence of both new cases of neck and back pain, as well as the diagnosis of ongoing cases, is rapidly increasing [8].

Epidural injections for management of back pain have been performed for decades. In 1901, the first described epidural injection was performed for a patient with lower back pain and sciatica [9]. During the next 50 years, physicians continued to develop treatments utilizing this route of drug delivery. The introduction of hydrocortisone [10] and its eventual use for treatment of radicular pain [11] laid the groundwork for today's practice. Epidural steroid injections have become an integral part of the pain practice for both axial and radicular spine pain. In fact, in the United States, epidural steroid injections have become the most commonly

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utilized intervention for managing radicular pain related to chronic and acute lower back pain [12].

Improvement in anatomic knowledge, coupled with major advances in medical equipment and imaging devices, has led to rapid growth in the use of epidural steroid injections beyond the lower back origin. Cervical, thoracic, and sacral anatomic sites are becoming more utilized to target spine pain by interventional clinicians. According to the Medicare fee-for-service data, from 2000 to 2011, cervical and thoracic epidural injections increased over 100% [13]. This growth is a product of the expanding role epidural steroid injections are having in managing patients with pain emanating from the cervical and thoracic spine [14, 15]. The route of medication delivery is also having an impact on the increasing prevalence of epidural steroid injections. Pain localization and anatomic site identification, for diagnostic purpose, have become a major indication. This has likely led to the rapid rise in the use of transforaminal epidural steroid injections. Over the same time period, cervical/thoracic and lumbar/sacral transforaminal epidural steroid injections increased 142% and 665%, respectively [13]. Transforaminal injections have shown utility in helping identify spinal nerve roots responsible for symptoms and potentially have a role in determining surgical outcomes [16, 17].

The purpose of this chapter is to discuss the indications/contraindications for these therapies, the technique and anatomic considerations in performing the procedures, the data behind their use, and the potential complications.

Indications/Contraindications

There are a variety of indications for epidural steroid injections. These injections may benefit patients with radiculopathy, degenerative disc disease, disc herniation, refractory discogenic pain, spinal nerve compression, spinal nerve root irritation or inflammation, foraminal or central canal stenosis, vertebral compression fractures, herpes zoster/postherpetic neuralgia, post laminectomy syndrome, complex regional pain syndrome, peripheral neuropathy, phantom limb, or cancer-related pain. Additionally, thoracic epidural steroid injections may benefit patients with angina, pancreatic disease, and incisional neuralgia after thoracotomy or breast surgery. Caudal epidurals may benefit patients with sacral or coccygeal neuralgia, interstitial neuritis, as well as pelvic, rectal, perineal, penile, or testicular pain.

Absolute contraindications include hemodynamic instability, patient refusal, local malignancy, local infection, uncorrected coagulopathy due to current use of anticoagulation or bleeding disorders, acute spinal cord compression, increased intracranial pressure, anaphylaxis to any of the injected materials, and the inability for a patient to remain still during the procedure. A clinician should refer to the antiplatelet and anticoagulation guidelines for interventional pain procedures published by the American Society of Regional Anesthesia and Pain Medicine (ASRA) [1].

Relative contraindications include systemic infection, allergy to medications or contrast, immunosuppression, pregnancy, or difficult anatomy precluding a safe procedure.

Patient Selection Considerations

The approach for an epidural steroid injection should be individualized to ensure patient safety and minimize complications. A clinician must obtain a detailed history, perform a physical examination, as well as review allergies and medications for every patient. A history of bleeding disorders and use of anticoagulation can affect approaches and choice of needles. A higher gauge (smaller) needle and a transforaminal approach may be preferred in a patient with slightly elevated bleeding risks, provided that the ASRA Guidelines for anticoagulation and pain procedures are followed [18]. Careful review of imaging should be performed to assess the anatomy, evaluate for anatomical variations, and determine the most suitable and safest approach for the patient. New or worsening motor or sensory deficits would require imaging and/or surgical consultation. Existing hardware can make it difficult to perform a transforaminal injection and may necessitate a more oblique trajectory. Scar tissue from previous spinal surgery can make it difficult to safely perform a midline interlaminar epidural injection. An oblique transforaminal approach may be employed in this circumstance. A clinician may need to enter at a level above or below the target interspace due to anatomic changes (e.g., scarring secondary to previous spinal surgery, absence of posterior epidural fat, or calcification) precluding a safe procedure. A Racz catheter may be considered to deliver medication at the target level. For example, in patients with severe lumbar spinal stenosis and radiculopathy, a sacral transforaminal approach or the caudal approach can be used, and a Racz catheter may be considered to deliver the medications to the L5–S1 level.

Selection of Techniques

Cervical Epidural Steroid Injections

Cervical epidural steroid injections are generally utilized in neck pain with a radicular component secondary to irritation or impingement of cervical spinal nerves caused by lateral disc herniation or foraminal and spinal stenosis. The procedure was first reported in the literature in 1986 [19–

21]. Initial techniques were performed blindly using loss of resistance and without fluoroscopic guidance in patients with chronic neck pain with or without a radicular component. However, this technique has fallen out of favor, and such injections are now commonly performed with the use of fluoroscopy and epidurography to ensure correct needle placement and delivery of medication [22]. In addition, digital subtraction technology may be used in conjunction with live fluoroscopy during the cervical transforaminal approach to help avoid catastrophic complications secondary to intravascular injection. The cervical transforaminal approach is typically employed for single-level foraminal disc herniation or when symptoms are limited to a very specific nerve root. It can be used diagnostically to determine the level of symptom origin and to aid with surgical planning. However, due to the lack of strong evidence supporting the efficacy of cervical transforaminal epidural steroid injections along with catastrophic complications [23, 24] reported in the literature, most physicians have removed such approach from their practice. There is, however, limited evidence that patients have received long-term pain relief obviating the need for cervical spine surgery in 20–80% of patients [25–30]. The largest study to date is a multicenter, randomized, controlled study conducted to compare the effectiveness of cervical interlaminar epidural steroid injections, conservative treatment consisting of pharmacotherapy (gabapentin and/or nortriptyline) and physical therapy, or a combination treatment for cervical radicular pain [12]. The study involved 169 patients, and the primary outcome measure was average arm pain score over the past week at 1-month follow-up. They found no statistically significant differences between groups; however, the combination treatment provided improved and more sustained relief in some patients. Although there is accumulating evidence that CESIs provide effective pain relief and improve functional capacity in both short and long term, larger controlled studies are still needed.

Lumbar Epidural Steroid Injections

Lumbar epidural steroid injections are perhaps the most commonly performed procedures. They are generally utilized in low back pain with a radicular component secondary to irritation or impingement of lumbar spinal nerves caused by lateral disc herniation or foraminal and spinal stenosis. There are extensive studies and systematic reviews on the efficacy of these injections with an overall consensus that they reliably provide short-term benefit in patients who have low back pain with a radicular component [22, 31–34]. Strong evidence is lacking for use in axial back pain or spinal stenosis [35]. Lumbar transforaminal epidural steroid injections (TFESI) have been demonstrated to be superior to the caudal and interlaminar approach for radicular pain [36, 37]. They have been shown to provide moderate benefit at 3 months in patients with lumbosacral radicular pain secondary to lumbar disc herniation [38, 39]. Another systematic review demonstrated moderate evidence that TFESI provided long-term (more than 3 months) pain relief due to spinal stenosis or lumbar disc herniation. They did not decrease physical disability at 1–3 months after the procedure or incidence of surgery at 12 months after the procedure compared with local anesthetic or saline. Long-term (more than 6 months) pain management using TFESI for radicular pain secondary to lumbar disc herniation was further supported by another systematic review [40].

Technical and Anatomic Considerations

Lumbar Transforaminal Approach

The patient is positioned prone, and an AP view of radiograph is used to identify and confirm the level to be injected. The C-arm is rotated 20–30° ipsilaterally to achieve oblique view until the sagittal plane of the pedicle of the superior level is in line with the SAP of the inferior level. The SAP (superior articular process) should be midway between the anterior and posterior borders of the superior end plate while ensuring that the superior end plates are superimposed. It is preferential to line up the superior end plate, so that the needle tip trajectory is directed cephalad to end up supraneural. This is accomplished by tilting the fluoroscope cephalad or caudad. Once the optimal view is obtained, a 22- or 25-gauge 3.5–5 inch spinal needle is placed coaxially and advanced incrementally just inferior (6 o'clock) to the pedicle of the superior level and inferolateral to the pars interarticularis (Fig. 22.1). Some authors advocate first contacting the base of the pedicle and then slipping off into the neural foramen, but this is not essential if multiplanar images (anterior-posterior, oblique, and lateral) are employed.

The next steps will be to confirm the needle location in AP and lateral views. The spinous process should be midline with the pedicles equidistant from the midline in the AP view. The target in the AP view should be the safe zone or "safe triangle area." The boundaries are the pedicle, lateral border of the vertebral body, and exiting spinal nerve which are the superior, lateral, and medial (hypotenuse) borders, respectively. Placing the needle in the safe triangle ensures avoidance of neural structures. The needle tip should not go beyond the midsagittal plane of the pedicle to avoid dural puncture. The needle tip should be in the superior portion and midsagittal plane of the neural foramen in the lateral view. Confirm placement with real-time contrast enhancement and multiplanar imaging.

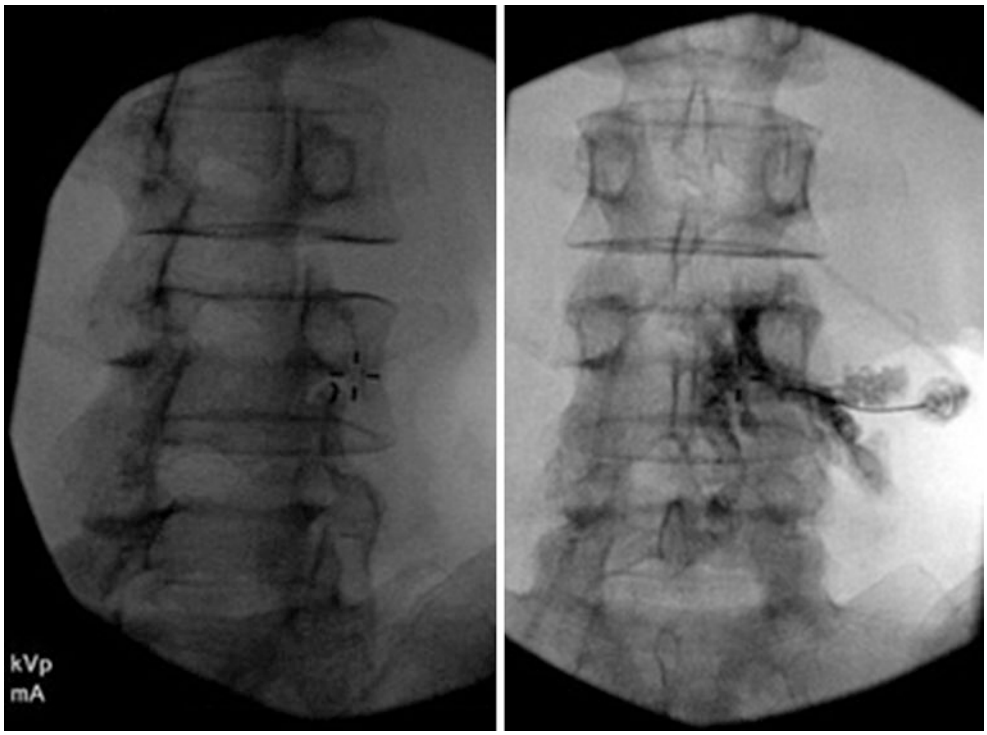

Fig. 22.1 Transforaminal lumbar epidural injections. Oblique view (left) showing needle placement in a coaxial view and AP view showing epidural spread of contrast

Following negative aspiration, 0.5–1 mL of nonionized contrast is infused through an extension tubing under live fluoroscopy, not only to visualize spread but to assess for vascular uptake. The contrast should outline the proximal lumbar nerve root and spread medially through the neural foramen into the lateral epidural space (see Fig. 22.1). Once confirmed, the local anesthetic and steroid admixture may be injected. This is important due to the location of the artery of Adamkiewicz, which supplies the anterior spinal artery of the spinal cord. This artery is most commonly located on the left side between levels L3 through T12. There is a high degree of anatomic variation, which is why clinicians should inject contrast under live fluoroscopy and even consider the digital subtraction technique. One must ensure that the needle and tract is cleared of steroid with either saline or local anesthetic flush before removing the needle.

Thoracic Transforaminal Approach

The thoracic transforaminal approach is almost identical to the lumbar transforaminal approach; however, the C-arm is rotated to approximately 20° ipsilaterally to achieve optimal oblique view due to anatomic differences. The pedicles of the thoracic vertebrae are located posterosuperiorly from the transverse process. Additionally, there is a superior costal facet located inferolateral to each pedicle at the thoracic level. A transverse costal facet is located at the lateral border of the transverse process at each level.

Cervical Transforaminal Approach

The more common approach is to have the patient positioned supine with the head facing directly forward. The C-arm is rotated 45–65° ipsilateral oblique until the optimal, maximal transverse view of the neural foramina is obtained. Identify the correct level by counting caudally from the C2–C3 neural foramen. Ensure that the superior end plates are superimposed by tilting the fluoroscope cephalad or caudad. Patients can be asked to turn their head to the contralateral side (oblique position) and have their ipsilateral shoulder elevated with a pillow or wedge to facilitate access; however, this change can distort the anatomy and alignment of the neural foramina and bony elements of the cervical spine.

Once the optimal cervical neural foramen view is obtained, a 22- or 25-gauge spinal needle is placed coaxially and advanced to the anterior surface of the SAP. Once contacted, the needle is gently walked (anteriorly) ventromedially into the posterior aspect of the foramen. The needle should only be advanced a few millimeters. The target is the mid-posterior element of the neural foramen to avoid vertebral artery penetration. The position is then checked in the posterior-anterior view, and the needle is advanced halfway to the facet column. The needle tip should not extend beyond the midsagittal plane of the cervical articular pillar to avoid inadvertent subarachnoid injection, cervical spinal cord trauma, or vertebral artery injection. The patient should be warned about pain or paresthesia into the scapula or upper extremity due to contact with the nerve root. If contact is

made, the needle should be slightly withdrawn off the nerve and the procedure halted until the sensation disappears.

Confirm placement with real-time contrast enhancement and multiplanar imaging. The digital subtraction technique is necessary if concerned about vascular uptake. Following negative aspiration, 0.5–1 mL of nonionized contrast is infused through an extension tubing under live fluoroscopy. The contrast should outline the proximal cervical nerve root and spread medially through the neural foramen into the lateral epidural space. The procedure should be aborted if there is vascular or subarachnoid spread. Once confirmed, the local anesthetic and steroid admixture may be injected. Dexamethasone sodium phosphate 4–15 mg can be administered. Ensure that the needle and tract are cleared of steroid with either saline or local anesthetic flush before removing the needle.

Sacral Transforaminal Approach

The patient is positioned prone, and an AP view of radiograph is obtained to identify the level to be injected. The C-arm should be tilted cephalad to line up the sacral end plate. The C-arm may need to be ipsilaterally rotated slightly oblique to optimize visualization of the dorsal sacral foramen. The oblique approach reduces the procedure length, radiation exposure, and intravascular injection rate [41, 42]. The dorsal S1 foramen is located just inferior to the S1 pedicle and to the medial side of the lateral sacral line. Once the optimal foramina view is obtained, a 22- or 25-gauge 1.5–3.5 inch spinal needle is placed coaxially and advanced to the medial side of the foramen to avoid the nerve running inferolaterally, as well as to allow for a more effective spread of the contrast and reduced incidence of intravascular uptake [43]. The position is then checked in the lateral view, and the needle is advanced just beyond the ventral epidural space. Following negative aspiration, 0.5–1.0 mL of nonionized contrast is infused through an extension tubing under live fluoroscopy. The contrast should outline the sacral nerve root and spread medially through the neural foramen into the lateral epidural space (Fig. 22.2). Once confirmed, the local anesthetic and steroid admixture may be injected. Ensure that the needle and tract are cleared of steroid with either saline or local anesthetic flush before removing the needle.

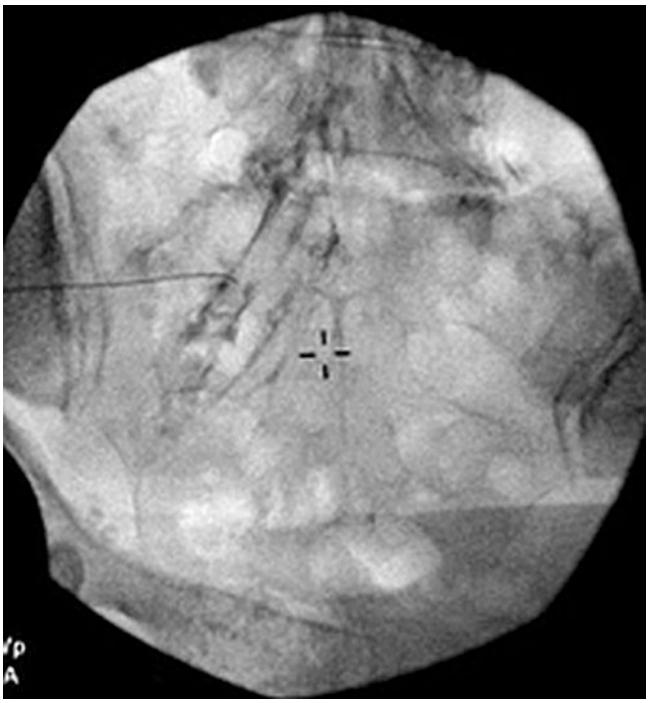

Fig. 22.2 Transforaminal sacral epidural injection. AP view showing needle entry through the S1 foramen and IV contrast spread in the epidural space and along the S1 nerve root

Cervical Interlaminar Approach

The patient is positioned prone with a folded pillow or foam cushion located under the chest at the level of the shoulder. Elevation of the thorax allows the interventionalist to obtain proper flexion of the cervical spine increasing the success of a timely and safe injection. The patient must have their arms positioned at their side with shoulders retracted from baseline posture. An AP radiograph is used to find the desired level for entry into the epidural space, which is most commonly C7–T1 or T1–T2. The C-arm can be swung in a cephalad or caudal direction to maximize the radiolucent interlaminar space. The C-arm is then directed 5–10° off midline (typically toward the affected side) to avoid the spinous process. Once a target is identified and optimized, a local anesthetic can be used to create a skin wheal and infiltrate the surrounding subcutaneous tissue. Most commonly, a Tuohy needle is selected and entered into the subcutaneous tissues directed toward the interlaminar space or the superior aspect of the inferior lamina in a coaxial view. The needle is typically followed with intermittent fluoroscopy to maintain a midline approach toward the epidural space until the needle begins to engage ligament or touches the inferior lamina. At this time, obtaining a lateral or contralateral oblique (approximately 60° oblique) allows for depth assessment as the needle is advanced or "walked off" lamina. During this time, a glass/plastic syringe containing 2 ml of saline is attached, or the Tuohy needle is filled with saline until a "hanging drop" is created. As the needle is advanced, the operator continues to monitor the syringe for "loss-of-resistance" or notable respiratory variations in the fluid level exposed at the end of the Tuohy needle. Once the needle has entered the epidural space, 0.5–1 ml of nonionic contrast dye is injected to confirm an epidural spread. Both the AP and lateral/contralateral

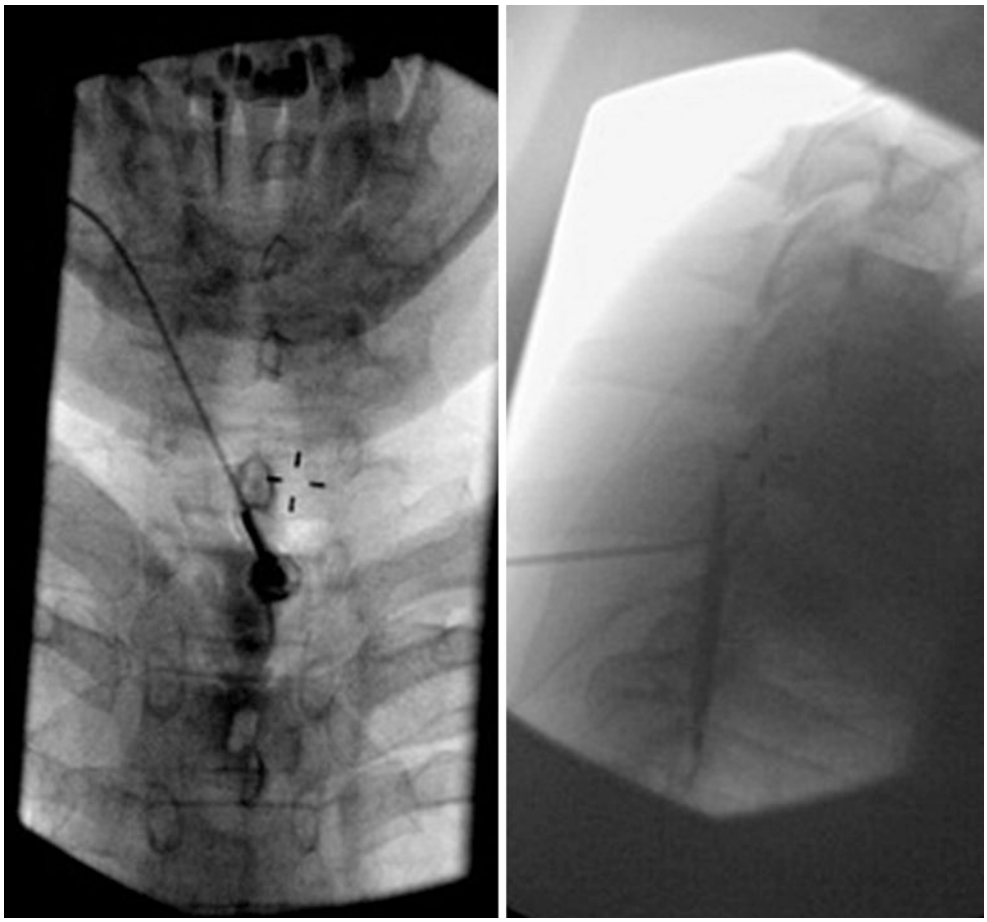

Fig. 22.3 Interlaminar cervical epidural injection. AP view (left) showing needle placement in a coaxial view and oblique view (right) showing the depth of the needle and spread of contrast in the posterior epidural space

oblique view (Fig. 22.3) should be used to confirm epidural spread of the contrast prior to medication administration. Live fluoroscopy can be used to confirm no vascular or subarachnoid uptake of contrast. Once confirmed, the medication can be administered. The needle is then removed from the patient and a bandage may be applied.

Lumbar Interlaminar Approach

The patient is placed in the prone position. A pillow or folded blanket may be located under the abdomen to diminish the natural lordosis of the lumbar spine. An AP radiograph is then used to identify the desired level of entry. The C-arm can be directed in a caudal or cephalad direction to maximize the radiolucent interlaminar space. A 5–10° oblique tilt toward the affected side may be applied. Once a target is identified and optimized, a local anesthetic can be used to create a skin wheal and infiltrate the surrounding subcutaneous tissue. A Tuohy needle is then directed toward the interlaminar space in a coaxial view. Intermittent fluoroscopy is typically used to assure that the needle maintains a midline approach. As the needle approaches the epidural space, it will encounter more dense tissue likely ligamentum flavum. At this time, lateral radiograph can be used to assess needle depth and proximity to the epidural space. A glass or plastic syringe with 2 ml of saline or air can be placed on the Tuohy needle prior to further advancing. Once attached, further advancement can begin with assessment of loss-of-resistance. After entry into the epidural space, 1 ml of nonionic contrast dye can be injected in the lateral and AP views (Fig. 22.4) to confirm epidural spread of contrast. Live fluoroscopy can be used to confirm no vascular or subarachnoid uptake of contrast. Once confirmed, the medication can be administered. The needle is then removed from the patient and a bandage may be applied.

Thoracic Interlaminar Approach

The thoracic interlaminar technique is very similar to that of the cervical interlaminar injection; however, a paramedian approach is more commonly used due to the overlapping spinous processes. The spinous process of the superior vertebral segment has an increased likelihood of overlaying the exposed interlaminar space. The patient is positioned prone typically without any augmentation of the spinal curvature, as the thoracic kyphosis should allow for access to

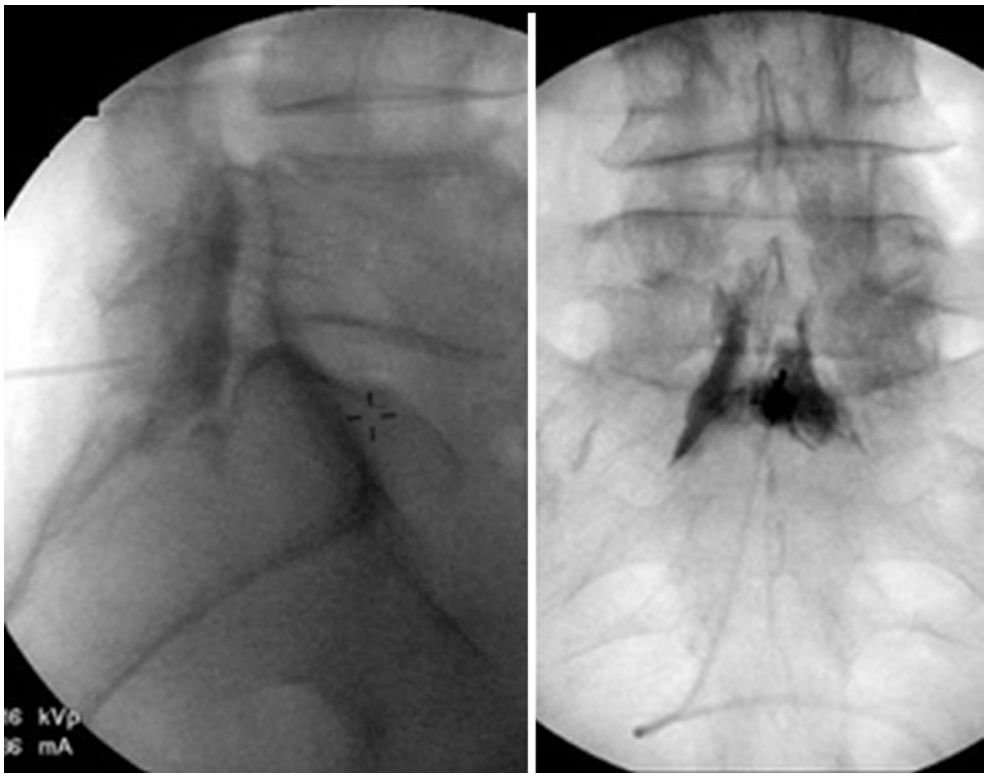

Fig. 22.4 Interlaminar lumbar epidural injection. Lateral view (left) showing the depth of the needle and spread of contrast in the posterior epidural space and AP view (right) showing needle placement in coaxial view and spread of contrast in the epidural space

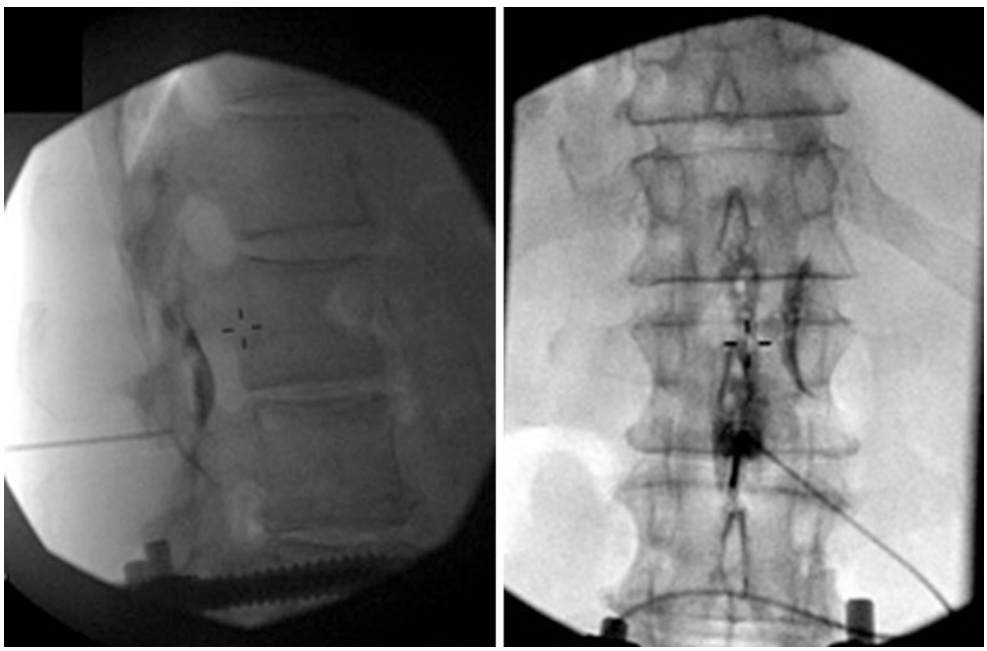

Fig. 22.5 Interlaminar lumbar epidural injection. Lateral view (left) showing the depth of the needle and contrast spread in the posterior epidural space and AP view (right) showing needle placement in a coaxial view and contrast spread filling the epidural sleeves and epidural fat (bubble look filling defects)

the interlaminar space. The C-arm will have a more significant caudal angulation to accommodate this native curvature. All other aspects of this injection including needle selection, epidural access technique, and confirmation with contrast and live fluoroscopy are similar to injections in the cervical spine. Again, lateral and AP views (Fig. 22.5) should be used to confirm epidural spread of contrast.

Caudal Epidural Approach

The patient is positioned prone on the fluoroscopy table. The interventionist may palpate to identify the sacral hiatus. To assure a midline needle trajectory, AP fluoroscopy should be used to identify midline of the sacrum. A radiopaque marker can be placed on the patient and traced to create a visual

reference. Lateral fluoroscopy can be used to confirm the position of the sacral hiatus and identify a needle trajectory. It is critical that the needle enter the sacral hiatus at an angle of a minimum of 45° in order to correctly access the epidural space. Using both the tactile reference along with this fluoroscopic technique, the entry site for the injection can be identified. A local anesthetic can be used to create a skin wheal and infiltrate the subcutaneous tissue surrounding the sacral hiatus to assure for more patient comfort. Needle selection for this procedure depends on the desired effect. A 25-gauge needle is sufficient for most cases. Injecting a volume of 10 ml typically can achieve spread to the sacral and lumbar epidural space. If the target is above this area, a Tuohy needle may be used, and a catheter can be thread in the epidural space and directed toward the desired target (Fig. 22.6). Once the needle has been inserted, lateral fluoroscopy can be utilized to guide the trajectory toward the sacral hiatus (see Fig. 22.6). After entering the epidural space, 1–2 ml of nonionic contrast dye is injected to confirm an epidural spread in both the lateral and AP views. The medication can be administered and the needle removed from the patient. The site should be inspected for bleeding; if stasis has been achieved, a bandage can be applied.

Complications

As with any intervention, complications can occur while performing epidural steroid injections. The severity and frequency of these events depend on several factors including the type of injection (transforaminal vs interlaminar), location (cervical vs lumbar, etc.), and selected injectate (contrast, particulate vs non-particulate steroid, concentration and amount of local anesthetic, etc.). These complications include issues with steroid use, infection, tissue injury, and consequences resulting from incorrectly placed injectate.

Use of corticosteroids has been associated with multiple complications including obesity, insulin resistance, diabetes, and osteoporosis [44]. While the effects from systemic use are known to most physicians, the degree of these effects following epidural injections has been somewhat controversial. The relative low dose and infrequent occurrence of injections have been anecdotally cited as a reason for less concern. Improved awareness and increased surveillance have led to a conclusion that the systemic effects of injections have been under recognized [45]. One study followed glucose and cortisol levels after epidural or shoulder intra-articular injections over a 3-week period and concluded that at 21 days following injection, diabetic patients continued to have a significant drop in cortisol levels following an epidural steroid injection [46]. Another study has found transient increases in systolic blood pressure following epidural steroid injections [47]. A relationship between decreased bone mineral density and frequent epidural steroid injections in postmenopausal women has been described following a retrospective analysis [48]. Ultimately, a therapy and its frequency should be tailored to patient based on clinical necessity and underlying comorbidities.

Several case reports describe infections following epidural steroid injections. The frequency of these infections is roughly 1–2% with more severe cases approaching 1 in 1000 to 1 in 10,000 [49]. The severity ranges from simple cellulitis to more severe cases of meningitis [50], epidural abscess [51], and osteomyelitis [52]. Patients typically present with severe back or neck pain, fever, and chills. Risk factors include diabetes, history of active smoking, and other immunocompromising conditions. *Staphylococcus aureus*,

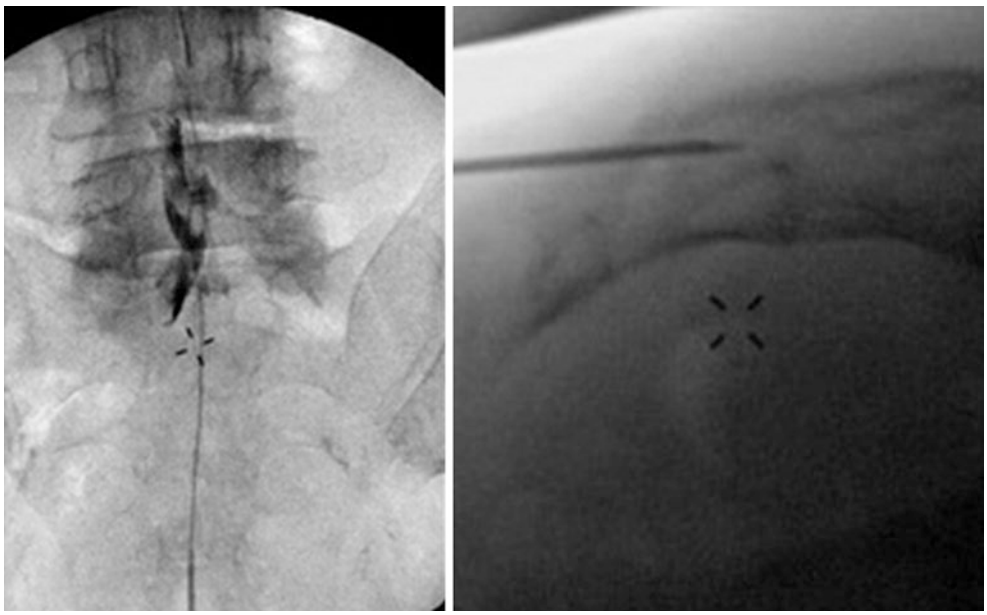

Fig. 22.6 Caudal epidural injection with or with a catheter. AP view (left) showing a Racz catheter used to reach epidural space in the lumbar region; lateral view (right) showing a Tuohy needle used to access the caudal epidural space and through which a Racz catheter was introduced

although only making 1–2% of the skin flora, is the most common pathogen associated with epidural abscess [53, 54]. In general, a high degree of clinical suspicion must be part of a pain medicine physician's decision-making process when presented with these symptoms following an epidural steroid injection.

Incorrect needle placement and subsequent injection can lead to a variety of complications. These range from paresthesia, pain exacerbation [55], unintentional dural puncture, and subsequent headache [56] to infrequent but devastating complications such as intra-arterial injection and direct cord damage resulting in stroke, seizure, or spinal cord injury. The incidence of complications has some variance in the literature, but common complications occur in approximately 2.4% of transforaminal and interlaminar epidural injections [55]. Rare complications have proven much more difficult to study as there is inconsistent reporting and data collection [57]. Direct spinal injury in both cervical and thoracic interlaminar epidural steroid injections is infrequent but has been reported [58, 59]. Complications from injection of particulate corticosteroids into important vasculatures including vertebral artery or radiculomedullary artery include infarctions of the spinal cord and brainstem resulting in devastating ischemia and significant loss of function [60–63]. Despite the reported and unreported complications, these procedures continue to be frequently performed.

Many of the complications may be avoided by adhering to strict sterile techniques, careful patient selection, adequate technical training, and appropriate use of imaging guidance. It is also important for clinicians to be able to identify risk factors during the procedure and recognize complications early after the procedure when they occur and manage them timely and appropriately. Precautions and all available means to prevent complications must be incorporated in clinical practice. Several retrospective studies have reviewed years of data from several practices and concluded that fluoroscopically guided epidural steroid injections are a safe and well-tolerated procedure [55, 64, 65].

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Nerve Block and Radiofrequency Ablation

23

Joel Castellanos and Krishnan Chakravarthy

Key Points

- Nerve ablation can occur via chemical and physical means.
- An understanding of principles of nerve ablation, nerve degeneration, and nerve regeneration is integral to the proper use of any nerve ablation procedure.
- Knowledge of the different types of radiofrequency ablation, the proper technique, and their evidence-based uses is integral for the optimization of patient safety and outcomes.
- Patients with chronic pain are a complex and non-ubiquitous group, making it challenging to research the efficacy of any interventional pain treatment modality, including radiofrequency ablation.
- Appropriate patient selection is a key component to the success of radiofrequency ablation.
- The complexity of chronic pain prevents any single treatment method from being 100% efficacious, despite even the most rigorous patient selection criteria.
- When a patient suffering from chronic pain has failed conservative measures and understands the potential risks and benefits of radiofrequency ablation, RFA remains a viable option to potentially provide relief to many patients suffering from subacute and chronic pain.
- Radiofrequency ablation, in its various forms, can be used in many different areas of the body to help patients improve their quality of life.

Types of Neurolysis

Neural ablation can be achieved both chemically and physically through disruption of the neuronal structures by alcohol or modalities such as heat or electricity, respectively. The local neuronal damage leads to nerve fiber and myelin sheath degeneration distal to the damage site, a process known as Wallerian degeneration (Fig. 23.1). The nerve cell is not completely destroyed. The basal lamina of the Schwann cells is preserved and allows for axonal regeneration [2, 3].

Alcohol Neurolysis

Neurolysis by way of alcohol, glycerol, or phenol disrupts the transmission of pain signals for 3–6 months. The mechanism by which these compounds initiate nerve damage is through protein denaturation and extraction of fat-soluble substances from the neural cells. This focal neuronal damage leads to Wallerian degeneration distal to the lesion [2]. The use of caustic chemicals provides adequate neural ablation, but if not concentrated to the desired area, can also cause damage to other structures [4]. Because of this, in 2010, the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine recommended that chemical denervation should not be routinely used in non-cancer patients [5].

Nerve Regeneration

Nerve repair can occur via re-myelination, collateral sprouting from axons, or proximal to distal axonal regeneration based on the level of injury. When less than a third of the axons are damaged, collateral sprouting occurs from the remaining healthy axons. When the majority of the axons are damaged, axonal regeneration occurs beginning at the site of the lesion, with the axons growing at approximately 1 mm/day in a proximal to distal fashion [6]. On a cellular level,

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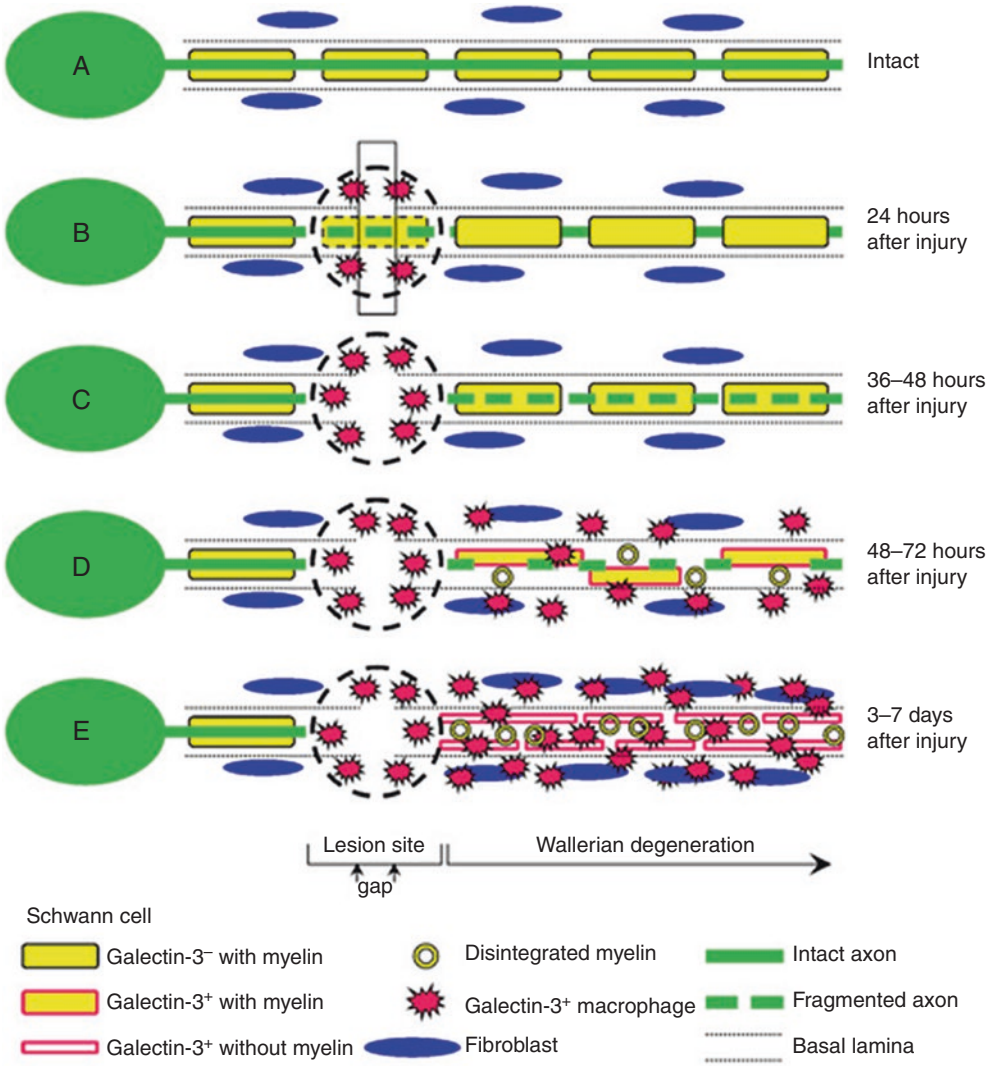

Fig. 23.1 Wallerian degeneration. (Reproduced with permission from Rotshenker [1])

after nerve injury, macrophages travel to the injury site, degrade the axon distal to the injury site, and initiate Schwann cell proliferation. The Schwann cells then produce laminin and fibronectin; both are proteins that help form the basement membrane of new axonal cells. Nerve growth factor is a key factor for axonal regeneration [7]. Nerve regeneration can become aberrant through reinnervating nontarget tissues or through neuroma formation when the regenerating axon fails to follow the tract of the previous axons [2]. A summary of this process is outlined in Fig. 23.2.

Radiofrequency Ablation (RFA)

Conventional radiofrequency ablation applies a constant electrical field via alternating current to induce ionic molecules in tissue to oscillate to the point that they generate heat. Heat production above approximately 60 °C causes a thermal lesion to the target area via irreversible protein denaturation [2]. Nerve regeneration after radiofrequency ablation occurs more quickly compared to alcohol neurolysis but also provides more focused lesioning resulting in less collateral tissue damage compared to alcohol neurolysis [4]. This thermal lesion, when targeted at the wrong area, can lead to unwanted nerve damage, motor dysfunction, and deafferentation pain [9]. When radiofrequency is applied in a nonconstant or pulsed method with high-voltage bursts, it prevents target and surrounding tissues from heating to the point of protein denaturation and instead creates an electromagnetic field that causes ultrastructural damage at the organelle level, specifically mitochondria, microfilaments, and microtubules in axons [2].

Basic Principles of Radiofrequency

Electromagnetic waves in the radiofrequency range lie between 20 kHz and 300 GHz (Fig. 23.3). In clinical practice, the use of radiofrequency waves in the range of

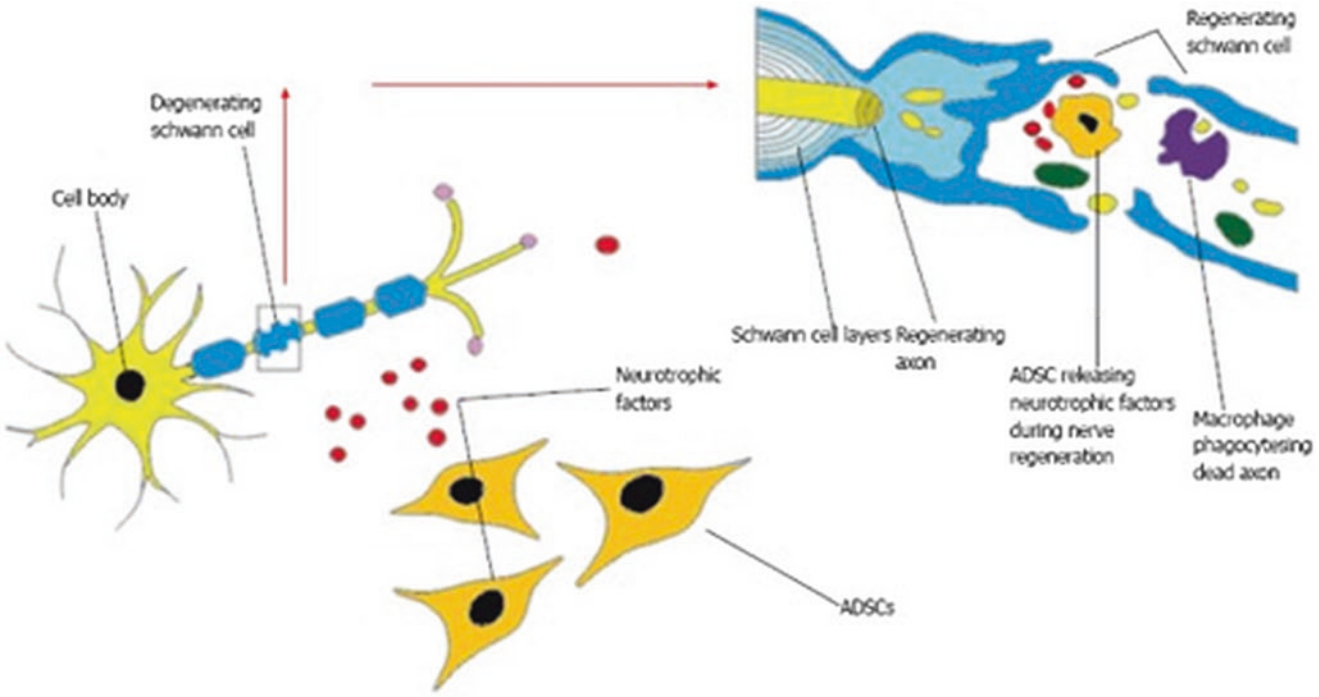

Fig. 23.2 Nerve regeneration. (Reproduced with permission from Zack-Williams et al. [8])

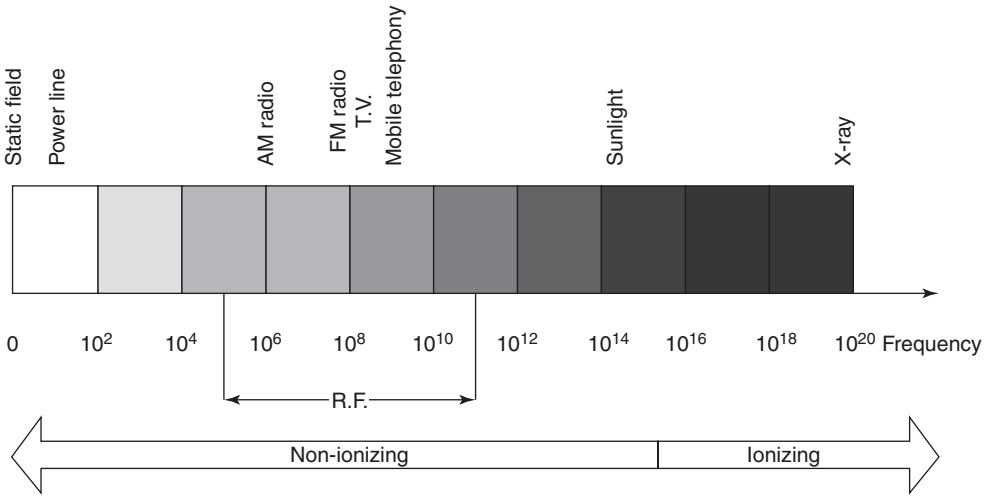

Fig. 23.3 Electromagnetic spectrum. (Reprinted with permission from Acharya et al. [10])

250 kHz–1 MHz to cause thermal lesions has become a technique used to treat arrhythmias, neoplasms, and chronic pain [11]. In pain therapy, the thermal damage is targeted at sensory nerves to disrupt afferent nociceptive signals traveling to the central nervous system. The radiofrequency ablation system includes the alternating current radiowave generator, radiofrequency electrode, and the ground electrode.

The radiofrequency electrode is essentially a metal cylinder containing the radiofrequency probe with a distal thermocouple to measure the temperature at the target tissue site as seen in Fig. 23.4. The electrode is insulated proximally with Teflon to limit the heating to the area surrounding the distal aspect of the electrode. In water-cooled radiofrequency electrodes, the metal cylinder also contains a water inlet and outlet at the distal aspect of the electrode with a sealed tip to allow water to circulate within the electrode at the lesion site.

During radiofrequency ablation, heat (joules) is produced through capacitive current where the applied radiofrequency electromagnetic field causes ionic movement in the electrons of the radiofrequency probe which are then transmitted into the charged molecules in surrounding tissues. This energy transmitted to the charged particles in the tissue in contact with the radiofrequency probe causes the charged particles to oscillate and in turn to produce heat. The greatest amount of

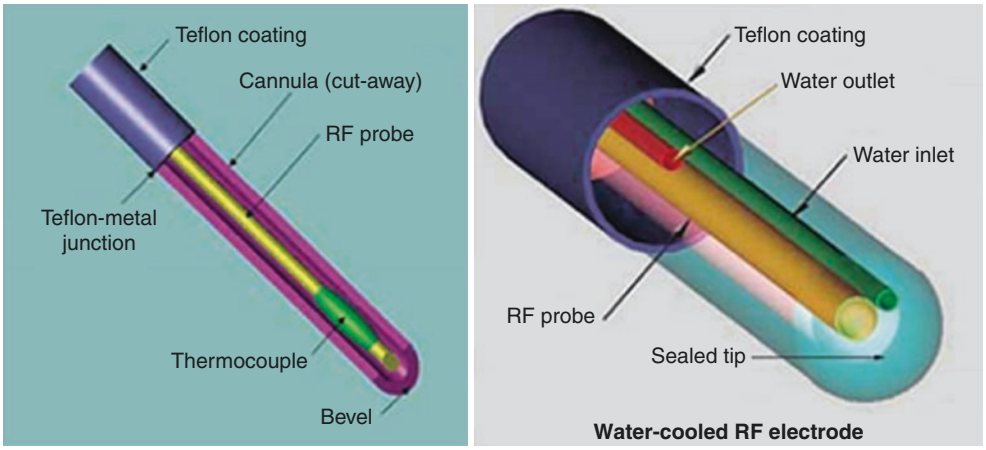

Fig. 23.4 Radiofrequency catheter. (Reproduced with permission from Ball [11])

heat is generated in the tissues in closest proximity to the radiofrequency electrode. The heat produced is then redistributed to local cooler tissues through conduction and convection.

Tissue with higher conductivities allows for higher current transmission, which usually allows for a higher temperature increase when the tissue also has a higher level of resistance (compared to the electrode) to absorb the transmitted energy and create heat. Skeletal muscle has the highest conductivity, followed by adipose and connective tissue and then bone having the lowest conductivity. Table 23.1 is a list of the relative tissue conductivities of many tissues in the body compared to increasing levels of NaCl solution. Practically, if the tissue surrounding the distal electrode is an insulator due to its poor thermal conductivity (i.e., bone or connective tissue), the current is unable to flow to distal tissues and causes the energy to be focused to a smaller area [11].

Human cells are irreversibly damaged at temperatures around 50 °C, known as the critical lesioning temperature. The lesion zone is the volume of tissue that is able to achieve this critical lesioning temperature. When tissue at the electrode-tissue interface becomes charred, typically at around 100 °C, it becomes a high-impedance insulator and prevents large lesion zone from being obtained. This is called the electrode interface disruption temperature [11]. This can be beneficial when the target tissue is in an area with sensitive surrounding tissues (i.e., medial branch ablation) but can prevent clinical efficacy when larger lesion zones are indicated (i.e., lateral branch ablation for sacroiliac denervation). In water-cooled radiofrequency ablation, water is circulated in the interior of the distal end of the electrode with the goal of keeping the electrode-tissue interface below the electrode interface disruption temperature while increasing the radiofrequency signal intensity to allow for energy to be distributed to a larger area through conduction and convection [12].

In pulsed radiofrequency ablation, the radiofrequency is applied in a nonconstant or pulsed method with high-voltage bursts. This method has gained clinical popularity in the recent years as it prevents target and surrounding tissues from heating to the point of protein denaturation and thus prevents the target tissue and surrounding tissue from reaching the electrode interface disruption temperature and critical lesioning temperature. Instead, it acts as a neuromodulator by creating an electromagnetic field that causes ultrastructural damage at the organelle level, specifically mitochondria, microfilaments, and microtubules in axons of target tissue. This limits the harmful side effects of reaching critical lesioning temperature of unwanted nerve damage, motor dysfunction, and deafferentation pain [2, 9].

Table 23.1 Relative tissue conductivities

Tissue type	Electrical conductivity (S/m)
Normal liver	0.36
Liver tumor	0.45
Myocardium	0.54
Fat	0.10
Bone	0.03
Blood	0.70
Vaporized tissue	~ 1e–15
NaCl 0.1%	0.30
NaCl 0.2%	1.00
NaCl 0.5%	2.70
NaCl 1.0%	4.50
NaCl 5.0%	25.00
NaCl 36%	45.00

Reproduced with permission from Ball [11]

Clinical Applications

Introduction

Radiofrequency ablation in its various forms has been used as a minimally invasive treatment option for pain that is resistant to conservative measures. Historically it has been used to peripherally disrupt and prevent afferent pain signals from distal noxious stimuli from reaching the central nervous system and in turn preventing the pain experience.

Some patients who have persistent pain in the order of months to years may strengthen the neuronal pain pathways via maladaptive neuroplasticity rendering any level of afferent pain signal blockade less effective, especially without a multidisciplinary approach.

Below are descriptions of the most common uses for radiofrequency ablation for pain along with the rationale and evidence behind its use. Patients with chronic pain are a complex and non-ubiquitous group. This inherent characteristic, along with the anatomical variance of structural innervations, makes it challenging to research the efficacy of any interventional pain treatment modality, including radiofrequency ablation. Although appropriate patient selection is a key component to the success of radiofrequency ablation, the complexity of chronic pain prevents any single treatment method from being 100% efficacious, despite even the most rigorous patient selection criteria. When a patient suffering from chronic pain has failed conservative measures and understands the potential risks and benefits of radiofrequency ablation, RFA remains a viable option to potentially provide relief to many patients suffering from subacute and chronic pain.

Head and Facial Pain

Headaches affect close to 50% of the population worldwide, and facial pain affects 26% of the population at some point in their lifetime [13, 14]. This pain can be debilitating and affect function, limiting the ability to work and live a normal life. The etiology of headaches and facial pain is typically complex and multifactorial. When medications and conservative therapy fail to give adequate improvement in symptoms alone and if medications are contraindicated, or if medications are not tolerated secondary to adverse side effects, there are several interventional targets that have demonstrated efficacy in improving head and facial pain. Recent systematic reviews have demonstrated a paucity of high-quality randomized placebo-controlled double-blinded studies investigating the efficacy of interventions at the occipital nerves, sphenopalatine ganglion, and trigeminal ganglion. These reviews concluded that targeting the sphenopalatine ganglion using blocks, radiofrequency ablation, and neurostimulation is promising for treating cluster headaches, trigeminal neuralgia, chronic migraine, as well as other facial and head pain. However, secondary to no high-quality randomized controlled trials evaluating radiofrequency ablation for cervicogenic headaches, there is limited evidence to support its use in cervicogenic headaches. Both of these studies called for increased research in the form of high-quality randomized controlled trials [15, 16].

Cervicogenic headache is described as a unilateral pain (although bilateral can occur) with restricted range of motion of the neck. Pain is typically exacerbated with neck movement and palpation of the upper cervical or occipital regions on the symptomatic side [13]. Cervicogenic headaches typically have only a marginal response to classic migraine headache medications [17]. C2–C3 facet joint is the most common cause of cervicogenic headache and is innervated by the third occipital nerve (Fig. 23.5) [19, 20]. The medial branch of the third occipital nerve is the target area for both blocks and radiofrequency ablation for cervicogenic headaches. There is limited evidence to support the use of conventional and pulsed radiofrequency ablation for cervicogenic headaches, and there is a need for high-quality RCTs to evaluate the efficacy of these procedures [21, 22].

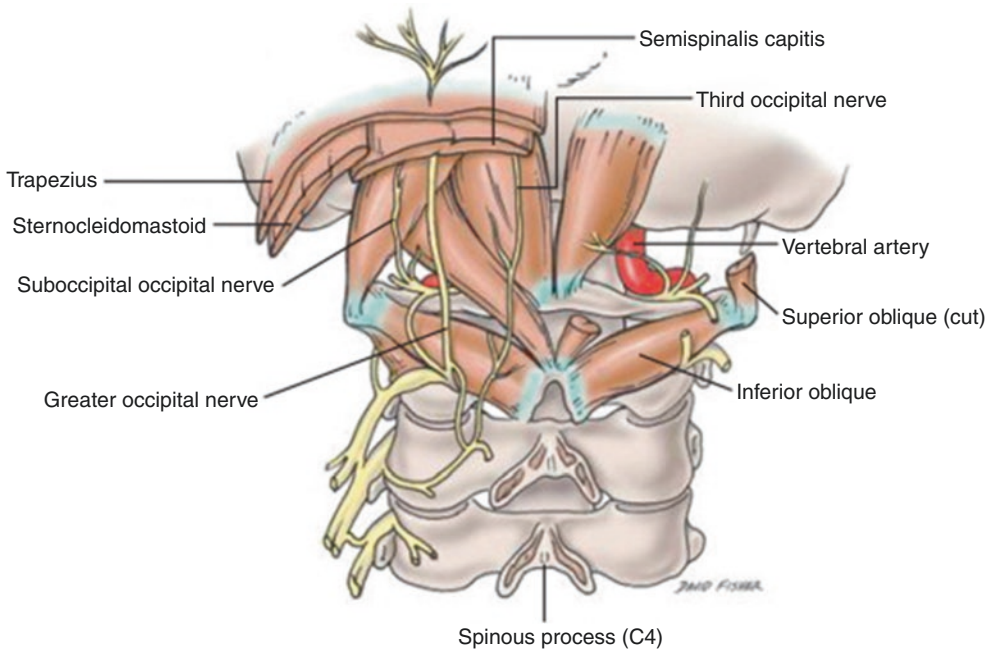

Fig. 23.5 The course of the third occipital nerve as it traverses over the C2–C3 facet joint. (Reproduced with permission from Sodde and Tunstall [18])

The sphenopalatine ganglion is the largest collection of neurons in the calvarium outside the brain and has sensory, sympathetic, and parasympathetic fibers. It is unique in that it is accessible to the outside environment through the nasal mucosa [15]. The sensory input is derived from maxillary nerve. The parasympathetic and sympathetic inputs are from the greater petrosal nerve, a branch of the facial nerve, and the deep petrosal nerve, respectively [15]. The pterygopalatine ganglion supplies the lacrimal glands, paranasal sinuses, nasal cavity, pharynx, and the hard palate. The anatomy of the sphenopalatine ganglion and its branches can be seen in Fig. 23.6. Sphenopalatine ganglion blocks and radiofrequency ablation have been reported to be used successfully for a myriad of conditions including cluster headaches, trigeminal neuralgia, migraine, postherpetic neuralgia, atypical facial pain, and intractable cancer pain, but most of the evidence for the use of sphenopalatine ganglion blocks is at the case report and case series level. The transnasal approach for sphenopalatine ganglion block can be seen in Fig. 23.7. The evidence for treating cluster headache, trigeminal neuralgia, and migraine with sphenopalatine nerve block is based on a few studies. There has only been one double-blinded placebo-controlled study evaluating sphenopalatine nerve block for migraine. It found benefit in the short-term but not the long-term [15, 25]. Compared with nerve blocks, radiofrequency ablation or modulation of the sphenopalatine ganglion has shown increased duration of relief for cluster headaches [26]. Although nerve blocks and radiofrequency ablation of the trigeminal ganglion have been investigated at the case report and case series level, microvascular decompression remains the gold standard with a success rate approaching 90% in patients with headache or facial pain secondary to trigeminal neuralgia.

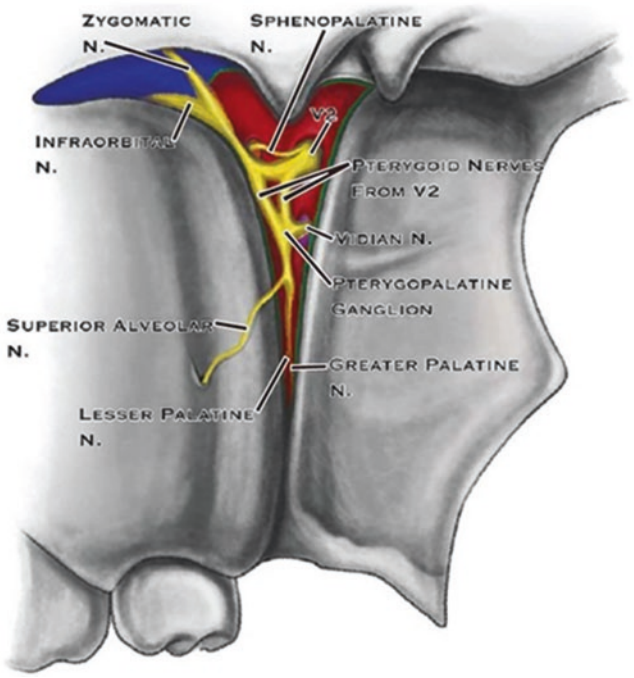

Fig. 23.6 Sphenopalatine ganglion and its branches as seen in pterygopalatine fossa through pterygomaxillary fissure. (Reproduced from Khonsary et al. [23]. Copyright: © 2013 Khonsary SA). This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited

Facet Joint

The facet joint, or zygapophyseal joint, is a diarthrodial joint between the posterior elements of neighboring vertebrae and is comprised of the bone from inferior articular process from the cephalad vertebrae and the superior articular process from the caudal vertebrae, along with the fibrous capsule, synovial membrane, and hyaline articular cartilage [27]. They are true synovial joints with fluid capacity between 0.5 and 1.5 ccs [28]. The facet complex is innervated by the terminal branch of the dorsal ramus and the median branch. The median branch of the dorsal ramus also innervates the multifidus muscle and the interspinous ligament. The atlantoaxial joint is innervated by the ventral ramus of C2 nerve root [29]. The C2–C3 facet joint is supplied by the larger branch of the dorsal ramus of C3 and the third occipital nerve [30]. The remaining cervical facets to C7-T1 are supplied by the dorsal ramus medial branches that arise one level cephalad and caudad to the joint. Each facet joint from T1–T2 to L5-S1 is innervated by the medial branch of the same level and the medial branch just cephalad.

In patients with localized spine pain, the prevalence of facet-mediated pain is 36–67%, 34–48%, and 16–41% in the cervical, thoracic, and lumbar regions, respectively [31]. Facet joint nociception is typically initiated by mechanical injury and facet capsular stretching beyond the normal range resulting from facet arthropathy through chronic strain and surrounding degeneration at the intervertebral disks [32–34]. With chronic pain, central sensitization and decreased pain thresholds occur [35]. The pain itself is described as a deep, poorly localized, aching pain with consistent referral patterns (Fig. 23.8). Pain is typically exacerbated by extension, side-bending, and rotation toward the painful side, with flexion relieving symptoms [37]. Unlike radiculopathy, cervical facet joint pain is not associated with changes in reflexes, strength, or sensation of the corresponding myotome and dermatome [32, 38, 39]. Unfortunately, there are no pathognomonic signs or symptoms for facet-mediated pain.

Facet joint pain is initially managed with physical therapy and other conservative modalities, despite the lack of studies evaluating the efficacy of these conservative treatments [40]. If a patient's pain persists after conservative measures have

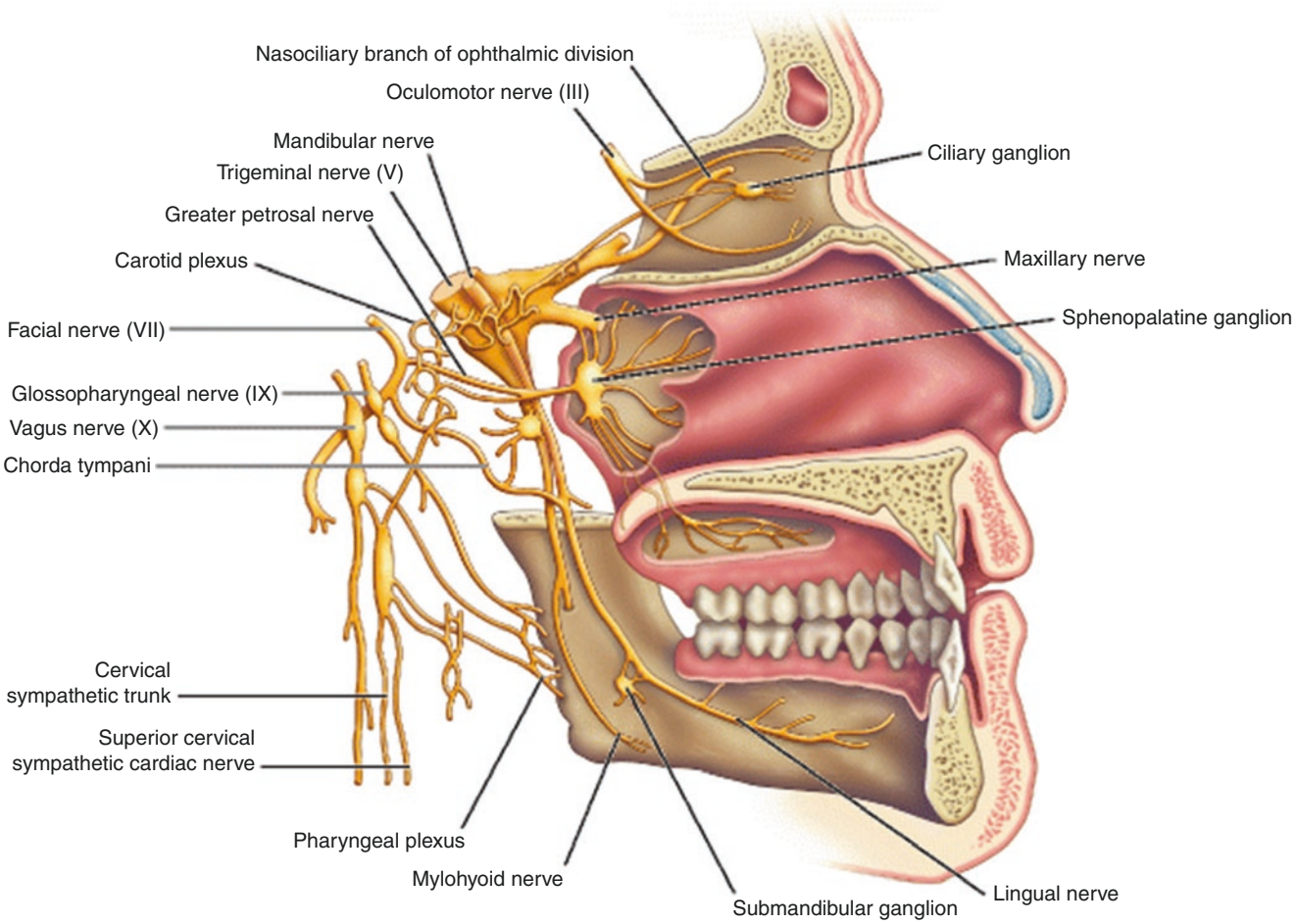

Fig. 23.7 Schematic diagram showing location of the sphenopalatine ganglion. (Reproduced with permission from Narouze [24])

been exhausted, interventional procedures may be pursued. Blocking the medial branches with local anesthetic or injecting local anesthetic directly into the facet joint can confirm the diagnosis if pain relief follows [41]. These injections are performed under fluoroscopic guidance. It has been reported that with two separate instances of pain relief after blocking of the medial branch with local anesthetic, the success rate of radiofrequency ablation of the medial branch is very high; with the number needed to treat being 1.1, nearly every patient improves with treatment [42]. A recent systematic review found the effectiveness of cervical medial branch blocks and radiofrequency ablation to vary greatly in the literature [40]. Lorde et al. [43] demonstrated at least 50% pain relief lasting for 263 days in the cervical medial branch radiofrequency ablation compared to 8 days of relief in the placebo group in a placebo-controlled double-blinded randomized controlled trial. In a non-randomized study by Macvicar et al. [44], patients with pain with suspected cervical facet joint etiology demonstrated a median relief duration of 20–26 months with radiofrequency ablation. In these studies, 80–100% relief with diagnostic local anesthetic blocks was used as a successful diagnostic block.

A systematic review on thoracic facet joint interventions done by Manchikanti et al. [45] demonstrated an extreme lack of high-quality evidence regarding both thoracic medial branch blocks as well as radiofrequency ablation to the thoracic medial branches. There were no randomized double-blind placebo-controlled trials evaluating either medial branch blocks or radiofrequency ablation of the thoracic medial branches. There were one observational report [46] and one double-blinded randomized controlled trial [47] comparing thoracic medial branch blocks with and without non-particulate steroid that both demonstrated positive short-term and long-term relief. There were no randomized controlled trials evaluating radiofrequency ablation of thoracic medial branches. There were two prospective outcome studies. Stolker et al. [48] demonstrated that 84% of the patients reported greater than 50% pain reduction, with over 60% having excellent long-term results. Speldewinde [49] demonstrated a successful outcome (defined by at least 50% reduction of pain for at least 2 months in the region relevant to the joints treated) that was found in 68% of the patients and that 65% of the patients had 85% pain relief for 9 months. These findings demonstrate the need for future randomized

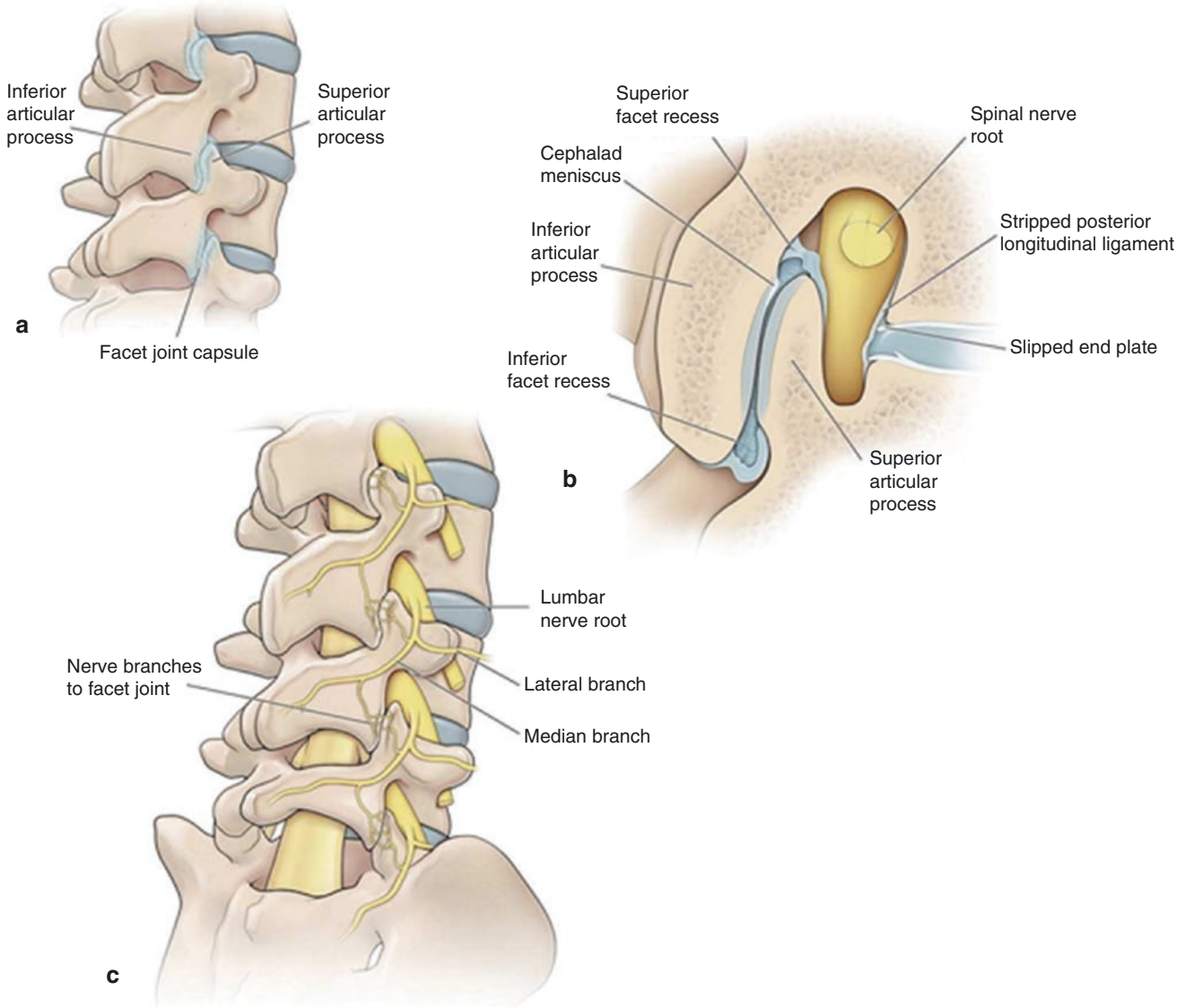

Fig. 23.8 Cervical and lumbar facet referred pain patterns. (Reproduced from Gellhorn et al. [36])

double-blind placebo-controlled trials and that in the properly selected patient with thoracic spine pain consistent with facet-mediated pain that has failed conservative measures, medial branch blocks and radiofrequency ablation may improve symptoms in both short-term and long-term.

A recently published multidisciplinary guideline on lumbosacral pain found that although the relevant RCTs [50–53] had low power and low evidence for improved functionality, conventional lumbar medial branch radiofrequency ablation has a favorable effect on pain anywhere from 3 to 12 months and has a beneficial effect on functionality for 3–6 months [37]. They concluded that because the benefits clearly outweigh the risks, conventional radiofrequency ablation for lumbar medial branch can be performed when conservative measures fail. This group also evaluated the use of pulsed radiofrequency ablation. Based on the paucity of evidence along with the results of two randomized controlled trials [53, 54] that patients undergoing conventional radiofrequency experienced more relief compared to pulsed radiofrequency ablation of the lumbar medial branches, they recommended that pulsed radiofrequency not be used for lumbar facet pain.

A recent paper by Juch et al. [55] on the findings of the MINT study concluded that in patients with chronic low back pain resulting from facet joints, sacroiliac joints, intervertebral disks, or a combination of these pain generators, radiofrequency ablation with a standardized exercise program did not clinically improve chronic low back pain when compared to a standardized exercise program without radiofrequency ablation. Provenzano et al. [56] later published an interpretation paper concluding that the study was flawed in a number of areas. The first was in the use of a pragmatic

study design that instead of having strict selection criteria, evaluates an intervention with more liberal selection criteria to maximize the study's ability to be generalized. The use of pragmatic study design becomes a problem when its selection criteria for the intervention being studied are more lenient than the recommended criteria for the intervention itself (i.e., dual medial branch blocks). The interpretation paper also noted the 90-second current application time with a perpendicular probe placement using a small 22-gage needle as a glaring weakness to the study. The use of a parallel probe placement with a larger gage needle is required to increase the lesion area to a point to overcome small anatomic variations and ablate the medial branches. The interpretation paper concluded by calling for increased education on appropriate patient selection, radiofrequency dynamics, and proper technique for performing radiofrequency ablation.

Sacroiliac Joint Pain

The sacroiliac joint connects the lateral sacrum with the medial ilium and is the largest axial joint in the body. It is considered part synovial and part syndesmosis joint. The sacroiliac joint helps transfer weight from the spine to the lower limbs [57, 58]. The stability of the sacroiliac joint is provided by the long posterior sacroiliac ligament, the short posterior sacroiliac ligament, the anterior sacroiliac ligament, the sacrotuberous ligament, the sacrospinous ligament, and the iliolumbar ligaments (Fig. 23.9). The sacroiliac joint does not have any muscles that control its movement directly, but indirectly the sacroiliac joint has limited rotational and gliding mobility through muscles that act around the lumbar spine, pelvis, and hips. The posterior aspect of the sacroiliac joint is innervated by the L4–L5 dorsal rami via the medial branches and the dorsal rami of the S1–S3 via the lateral branches. The anterior sacroiliac joint is innervated predominantly by the L5 ventral ramus with 10% of people having innervation from the L4 ventral ramus and another 10% having both the L4 and L5 ventral rami [60, 61].

There is no single physical exam or radiological pathognomonic finding for pain originating from the sacroiliac joint. Patients can describe unilateral or bilateral lower back pain with variable radiation into the buttock, groin, or leg (Fig. 23.10). On physical exam, FABER (Flexion, Abduction, and External Rotation), Gaenslen's test, Yeoman's test, distraction test, compression test, sacral pressure test, and sacral thrust are physical exam maneuvers suggestive of pain of the sacroiliac etiology. Studies have demonstrated a sensitivity of 94% and specificity of 78% when any three of these physical exam maneuvers are positive [63]. Imaging studies can identify arthritis, sacroiliitis, or fracture, but in the absence of these, there is poor correlation between radiographic findings and sacroiliac pain [64].

Nerve blocks of both the L4 and L5 medial branches and the S1–S3 lateral branches with local anesthetic have been used to diagnose pain originating from the sacroiliac joint and have guided further treatment with radiofrequency ablation. For traditional lateral branch radiofrequency ablation (Fig. 23.11), there have been several different techniques published including strip lesion, single multi-electrode, three puncture techniques, guide-block technique, as well as water-cooled and pulsed radiofrequency ablation [66–70]. Because of the variation in techniques as well as variation in innervation of the sacroiliac joint, the research has demonstrated mixed results as to the true efficiency of radiofrequency ablation. A meta-analysis in 2010 concluded that radiofrequency is an effective treatment of sacroiliac pain at both 3 and 6 months [71]. Another systematic review that looked at the effectiveness of all sacroiliac joint interventions reported the

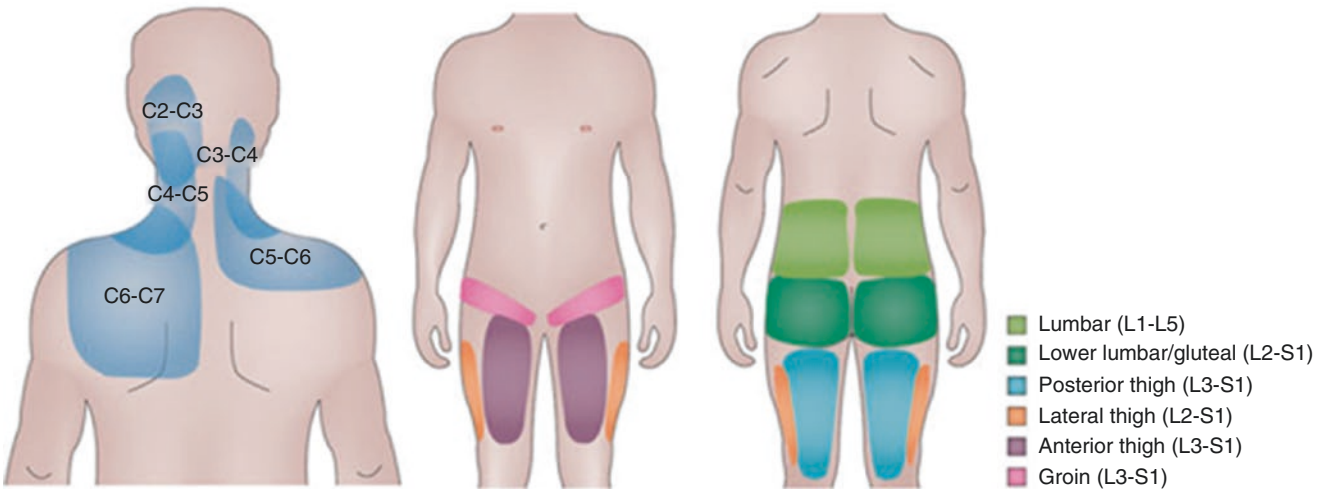

Fig. 23.9 Ligaments of the sacroiliac joint. (Reproduced with permission from Hammoud et al. [59])

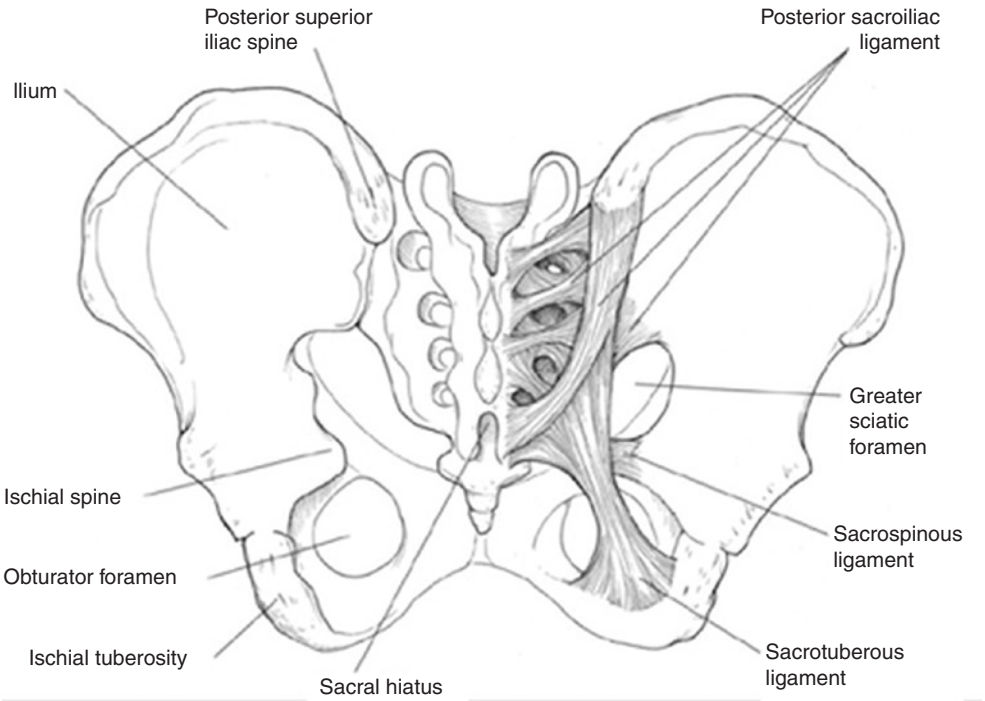

Fig. 23.10 Sacroiliac joint referred pain. (Reproduced with permission from van der Wurff et al. [62])

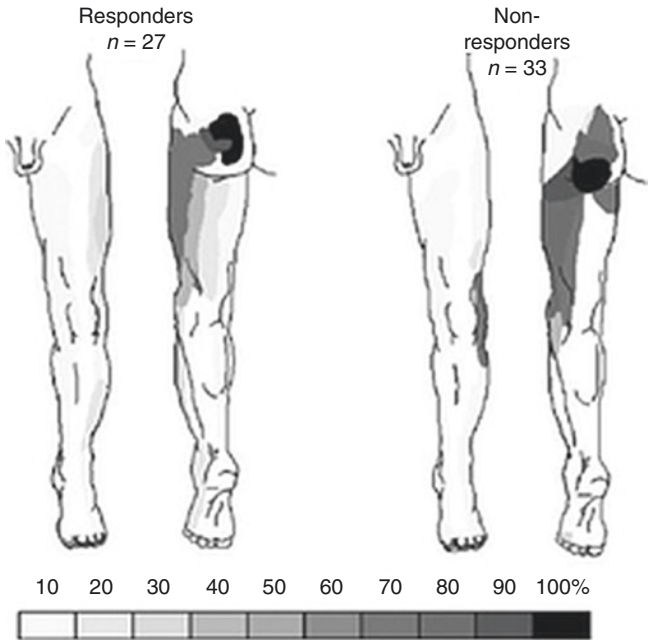

Fig. 23.11 Location of lateral branch radiofrequency ablation for sacroiliac joint. (Reproduced with permission from Cohen et al. [65])

best evidence was for water-cooled radiofrequency ablation of the sacral lateral branches [72]. This conclusion was based on two randomized controlled trials and two observational studies. Both of these reviews noted the scarcity of evidence and need for more high-quality studies. In regard to the evidence behind intraarticular radiofrequency ablation of the sacroiliac joint, there have been mixed results in the literature in the form of case reports, case series, and retrospective studies using both conventional and pulsed radiofrequency, and this requires more investigation in the form of randomized double-blinded placebo-controlled trials to elucidate the efficacy of these interventions [73–75].

Radicular Pain

The term radiculopathy comes from the Latin word radix, meaning root. Pathology of the nerve root can come from structural compression, commonly seen with herniated disks and facet arthropathy, as well as inflammation, infection, or infarction. A radiculopathy results in the loss of the corresponding nerve root function with resulting sensory loss or paresthesias in the nerve root dermatome, along with decreased reflex and weakness to the muscles supplied by that spinal nerve root. On physical exam, a positive straight leg raise, the area of pain radiation and sensory loss, along with diminished reflexes and focal muscle weakness can lead a clinician to the pathologic nerve root. This can further be confirmed with MRI as well as EMG if patient fails conservative measures such as physical therapy and more invasive interventions are being pursued.

In younger patients, a herniated disk is frequently the cause of radiculopathy, leading to local inflammation which can be treated with an epidural steroid injection to decrease the swelling and inflammation around the nerve root [76]. In more chronic conditions, where the nerve impingement is related to facet arthropathy and resulting foraminal stenosis or in patients

where epidural steroid is contraindicated, radiofrequency at the dorsal root ganglia is a viable treatment option. The dorsal root ganglia are the collection of somatic and visceral nerve cell bodies located at the distal end of the dorsal root in the lateral epidural space bilaterally and function to relay afferent information from the periphery to the central nervous system, thus playing an important role in nociception.

A 2013 systematic review by Pope et al. [77] looked at the evidence for various interventions at the dorsal root ganglion. When looking at conventional radiofrequency ablation at the dorsal root ganglion, the investigators based their conclusion on four randomized, prospective, controlled trials, two of which were sham controlled [78–81], and concluded that due to the differentiated pain potential as well as the study done by Geurts et al. that demonstrated traditional radiofrequency to be no better than local anesthetic injection alone, conventional radiofrequency of the dorsal root ganglion should not be performed in the lumbar and cervical regions. Thoracic segmental pain, however, as demonstrated by both Niv and Chayen and Stolker et al. [82] may be amenable to conventional radiofrequency ablation with both studies demonstrating short-term and long-term pain relief.

Compared to conventional radiofrequency and the risk of deafferentation pain at radiofrequency temperatures above 42 °C, the lower heating temperature with pulsed radiofrequency ablation has a relatively favorable safety profile and is gaining popularity as a modality [83, 84]. Both the previously mentioned 2013 study by Pope et al. [76] and a more recent review of the dorsal root ganglion treatment options by Liem et al. [85] had a more positive outlook on pulsed radiofrequency ablation despite the paucity of randomized controlled trials. Van Kleef et al. performed pulsed radiofrequency at the dorsal root ganglion in the cervical region in a double-blinded randomized placebo-controlled trial and found that pulsed radiofrequency demonstrated significantly more pain relief than sham treatment at both 3 and 6 months posttreatment [78, 81, 83, 84]. Additionally, Choi et al. [86] performed pulsed radiofrequency ablation in 21 patients with cervical radicular pain that did not respond to transforaminal epidural steroid injection that resulted in two-thirds of the patients experiencing at least 50% pain reduction after 12 months.

Lumbosacral radicular pain has also been treated via pulsed radiofrequency of lumbar DRGs, although there have been no double-blinded randomized placebo-controlled trials to date [77, 85]. Sluijter et al. [87] treated 60 patients with a variety of causes of lumbar radicular pain with pulsed radiofrequency and compared it with conventional radiofrequency and found that 86% of the pulsed radio group had 50% improvement at 6 weeks, as compared with 12% in the conventional group. Additionally, of the 15 patients with failed back surgery syndrome (FBSS) who underwent RFA of dorsal root ganglia, 53% and 40% of patients had at least a 2-point VAS reduction at 6 months and at 1 year, respectively. Tsou et al. [88] performed pulsed radiofrequency at the L2 dorsal root ganglion in patients with lumbar herniated disks or failed back surgery syndrome and found that approximately half of the patients had back pain relief and leg pain relief at 1 year.

Intervertebral Disk Pain

Any pain thought to originate from the nucleus pulposus, the annulus fibrosus, the vertebral end plate, or its accompanying innervation is considered discogenic pain. Discogenic pain is the cause of pain in over a third of the population with lower back pain and is related to a certain amount of degeneration of the disk [89, 90]. Both genetic and history of smoking are well-established factors that predispose patients to discogenic pain [91–93]. Different body positions exert different pressures on the intervertebral disk.

The intervertebral disk is made up of a central nucleus pulposus, which is surrounded by the annulus fibrosus. The intervertebral disk is innervated anteriorly from the sympathetic chain via the rami communicantes and posteriorly from the ventral ramus via the sinuvertebral nerve (Fig. 23.12). These nerves innervate the outer third of the annulus fibrosus in healthy disks [95]. With mechanical trauma, the annulus fibrosus can develop fissures which lead to both neovascularization and in-growth of the nerve supply to greater than just the outer third of the disk as well as an inflammatory response from exposure of the nucleus pulposus. The neovascularization and inflammatory response are thought to be the main mechanism through which discogenic pain occurs [96].

Patients with discogenic pain complain of medial pain that is worse in positions with increased axial strain, i.e., standing or sitting, especially when flexed at the waist and relieved by lying down. Imaging can reveal disk degeneration, but disk degeneration can be found incidentally on asymptomatic patients. Provocative discography, although controversial, is considered to be the most specific diagnostic test for discogenic pain [97]. Using radiofrequency ablation to alleviate discogenic pain once the disk is identified has demonstrated mixed reviews. A recent systematic review [98] found no benefit from intradiscal radiofrequency ablation but concluded that radiofrequency lesion of ramus communicants had stronger evidence for positive effect on pain reduction and restorative function compared to other treatment modalities including intradiscal injections (methylene blue, corticosteroid, restorative solution), intradiscal electrothermal therapy, and even surgery. These conclusions on radiofrequency ablation were based on two studies, and more studies are indicated, but in patients with debilitating discogenic pain, ramus communicant radiofrequency ablation may provide some benefit [99, 100].

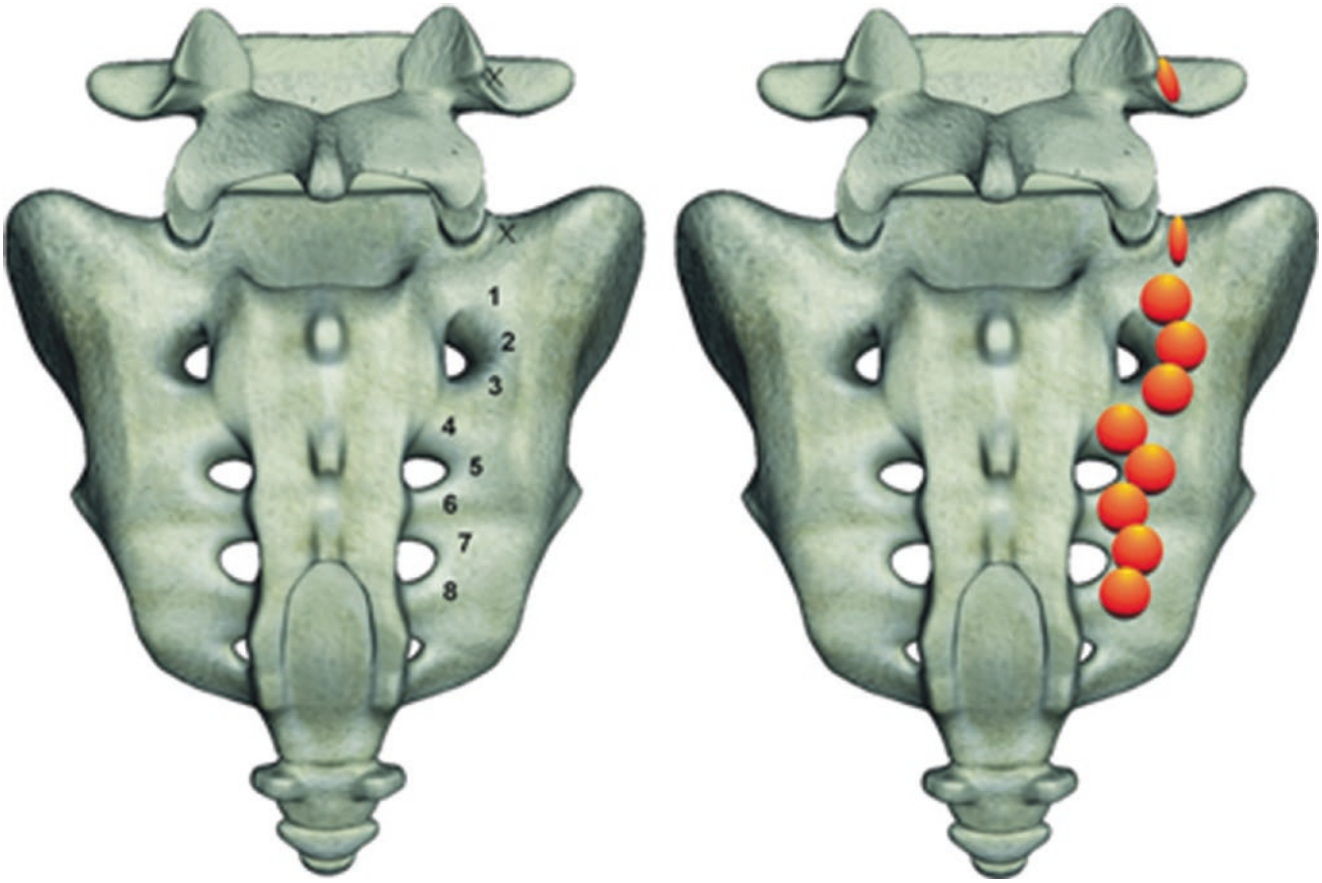

Fig. 23.12 Dorsal root ganglion in the afferent pain pathway. (Reproduced from Yang [94])

Palliative Care

Cancer pain resistant to analgesic medication occurs in 10–15% of cancer patients [101]. The pathophysiology of cancer pain is variable and consists of nociceptive, visceral, and neuropathic pain mechanisms. Neuropathic pain and pain related to boney metastasis are typically resistant to traditional analgesic medications [102]. Interventional therapies can be used when analgesic medications are ineffective or when side effects from the medications themselves limit use. Below are several common uses of both nerve blocks and radiofrequency techniques to help alleviate pain resistant to pharmacological management in cancer patients.

Head and Neck Cancer Pain

The prevalence of cancer pain in patients diagnosed with head and neck cancer is as high at 85% of patients at the time of their cancer diagnosis [103] with 93% of patients experiencing pain of mixed nociceptive and neuropathic qualities [104]. This pain varies in location from the head, face, mucous membranes, ears, neck, and shoulders [105]. Head and neck cancer pain can be difficult to treat because of the density of neural structures and the reliance of speech and swallowing on these neural structures. Diagnostic and therapeutic nerve blocks with local anesthetic are useful to confirm correct targets prior to neuroablative or neuromodulating procedures. Commonly blocked nerves in head and neck cancer include the glossopharyngeal, occipital, trigeminal, and vagal nerves along with the sphenopalatine ganglion and the cervical plexus. The greater and lesser occipital nerves are typically targeted for neuroablative procedures when a patient is suffering from metastatic invasion of the skull base [106]. The glossopharyngeal nerve, which contains both motor and sensory fibers, is a target for non-ablative neuromodulation via pulsed radiofrequency ablation for pain of the tongue, pharynx, or tonsils after diagnostic blocks have provided relief [107]. Likewise, pulsed radiofrequency is used at the maxillary

and mandibular branches of the trigeminal nerve when the pain is located in these respective anatomical distributions, as these are mixed nerves as well [107].

Chest Wall Cancer Pain

Pain from metastatic bony invasion of the chest wall is often resistant to pharmacologic management and requires intercostal block and radiofrequency ablation. Diagnostic intercostal nerve blocks at three consecutive levels are necessary to identify the involved nerve due to overlapping innervation. Diagnostic intercostal nerve blocks alone may provide prolonged relief in some patients [108]. Neurolysis of intercostal nerves via radiofrequency ablation or 6–10% phenol can be used, and patients typically have immediate pain relief [109]. Development of neuritis, deafferentation pain, and pneumothorax are risk factors of performing blocks and neurolysis of the intercostal nerves [110].

Upper Abdominal Cancer Pain

Pancreatic ductal adenocarcinoma invades local nerves in over 80% of cases with severe abdominal pain as a major symptom in the majority of patients diagnosed with pancreatic cancer [110–112]. The pain is typically located in the epigastric region although it can be diffuse and poorly localized with a deep-boring radiation to the back. It often has a cramping character and is exacerbated by lying supine and relieved with bending forward [113].

Visceral nociception is transmitted from the pancreas as well as the gallbladder and GI tract from the distal portion of the stomach to the transverse colon through the celiac plexus, a collection of several ganglia located anterior and inferior to the posterior diaphragm via visceral afferent sensory fibers [102]. From the celiac plexus, these visceral pain signals are then relayed by the greater (T5–T10), lesser (T10–T11), and lesser (T12) splanchnic nerves posteriorly and superiorly through the diaphragm to the sympathetic chain to the central nervous system [114].

Neurolytic celiac plexus block can be performed with a variety of approaches. It can be performed with the patient prone or supine using an anterior or posterior approach with image guidance options of fluoroscopy or ultrasonography. Alcohol (50–100%) is the chemoneurolytic agent of choice secondary to phenol's affinity to vascular structures and the proximity to the aorta [115]. Neurolytic celiac plexus blocks are a highly effective intervention for upper abdominal visceral pain, and its efficacy has been demonstrated in three separate randomized controlled trials which demonstrated a statistically significant difference in both the visual analog pain scale and opioid consumption at 4 weeks after undergoing celiac plexus block along. A Cochrane review gave the recommendation that it should be considered at the same time as initiating opioids for pain [113, 116–119]. Effects of these blocks can last up to 6 months and have a success rate of close to 85% in pancreatic cancer patients [115]. The most common complications are transient diarrhea and orthostatic hypotension which can occur in up to 25% and 42% cases, respectively, with more serious complications such as weakness, duoenitis, pneumothorax, and shoulder pain being rare [120].

Pelvic Cancer Pain

The nerves innervating the pelvic organs travel predominately through the superior hypogastric plexus as well as the inferior hypogastric plexus, which carries nerves innervating the lower pelvic organs. The external genitalia as well as the perineum and perianal afferent fibers travel through the ganglion impar. The locations of these structures can be seen in Figs. 23.13, 23.14, 23.15, 23.16, and 23.17.

Pelvic visceral and cancer pain as well as chronic noncancer pelvic pain and refractory penile pain can all be treated with a neurolytic superior hypogastric plexus block with 70–90% of patients achieving adequate pain relief [125]. Neurolytic inferior hypogastric plexus blocks are a relatively new procedure that has the potential to reduce pain and opioid consumption related to lower pelvic organs, but large prospective RCTs are still needed [126]. Ganglion impar blocks can help manage patient with visceral sympathetically mediated perineal pain. These patients often have complaints of dysuria and bowel and bladder urgency [127]. Ganglion impar blocks can also be employed for rectal pain, coccydynia, tenesmus, and excessive perineal sweating [128]. Complications include vascular injury, nerve root damage (specifically L5 nerve root for superior hypogastric plexus block), bowel and rectal perforation, and discitis when using a transdiscal approach. These complications are reduced with proper technique and use of imaging guidance. Radiofrequency ablation of nerve structures that mediate pelvic pain has been published in case reports and may help decrease the complications that come with the use of phenol and alcohol but has not been studied extensively [129, 130].

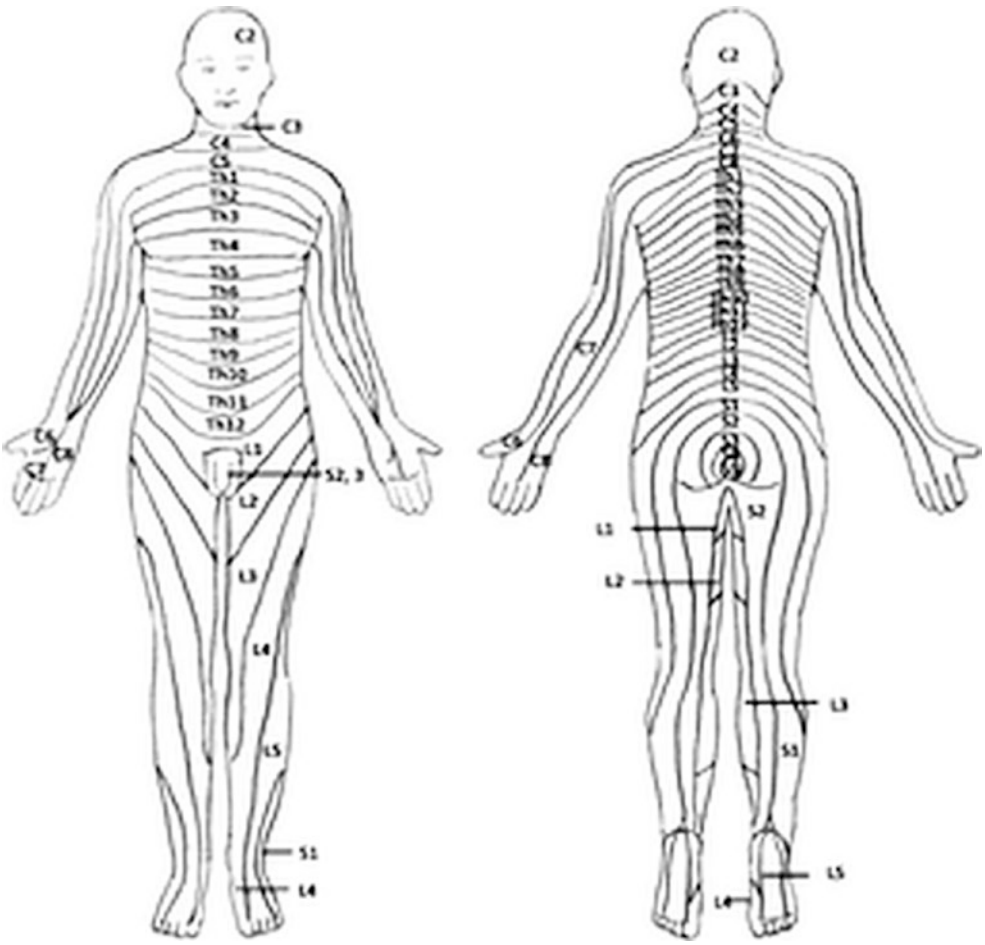

Fig. 23.13 The load on lumbar disks in different positions of the body. (Reproduced with permission from Nachemson [121])

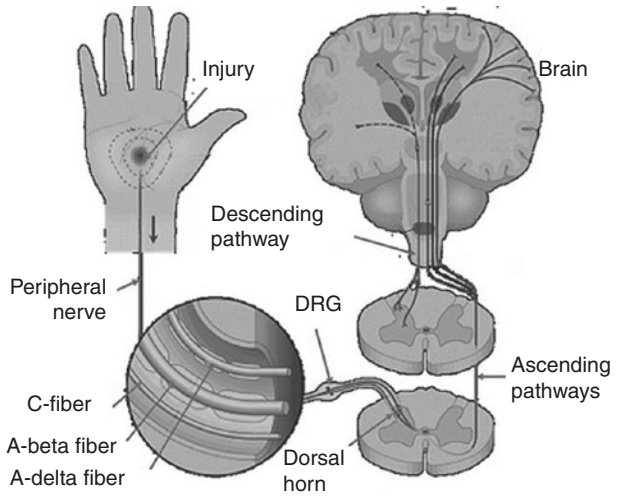

Fig. 23.14 Innervation of the intervertebral disk. Reprinted with permission of Douglas M. Gillard, DC

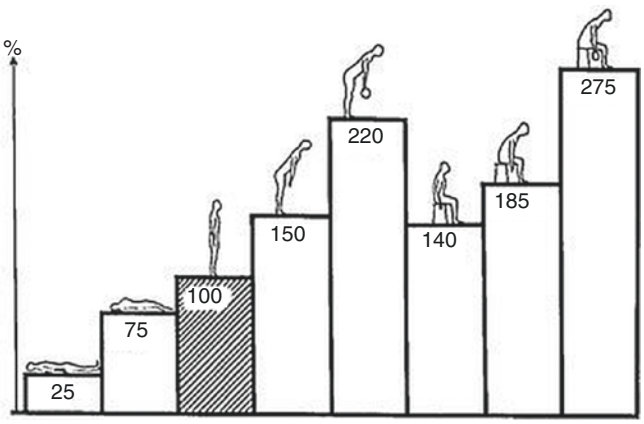

Fig. 23.15 Splanchnic nerve block. (Reproduced with permission from Waldman [122])

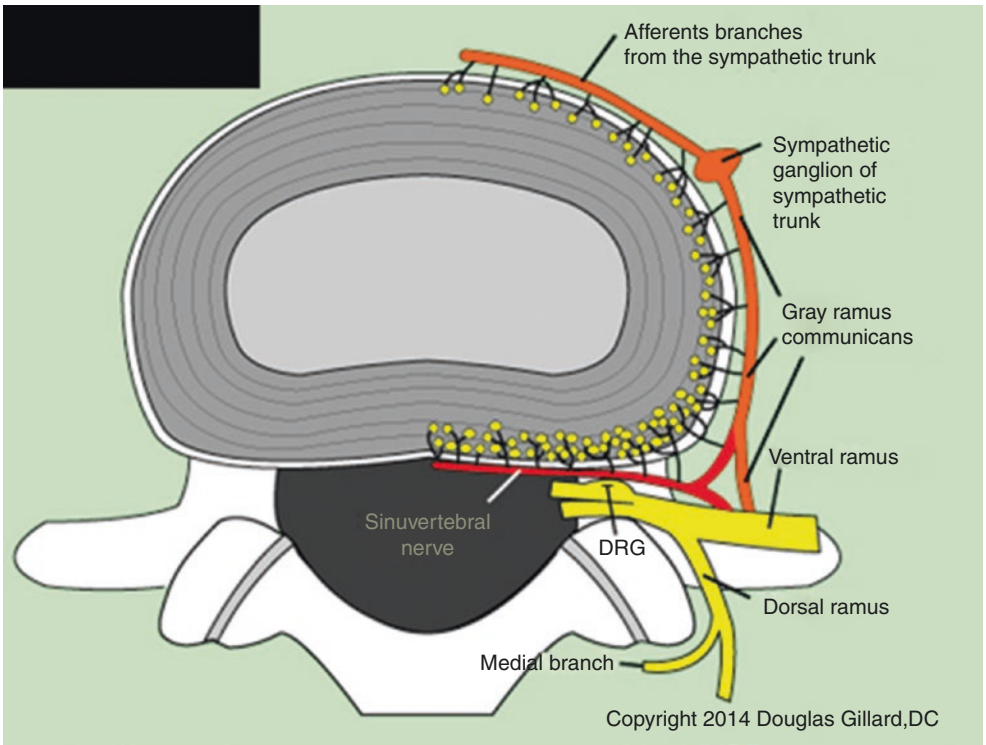

Fig. 23.16 Illustration of lumbar sympathetic chain [123])

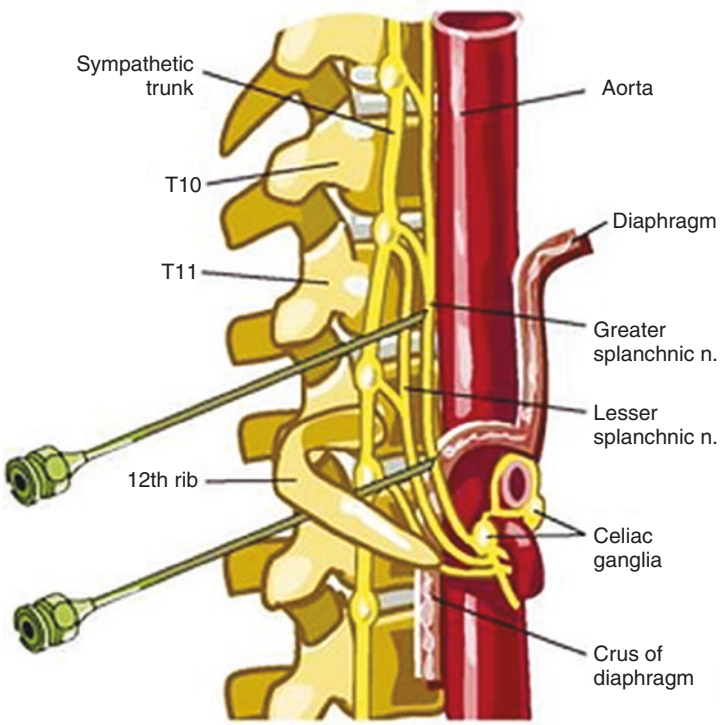

Fig. 23.17 Illustration of thoracic sympathetic chain. (Reproduced with permission from Schultz [124])

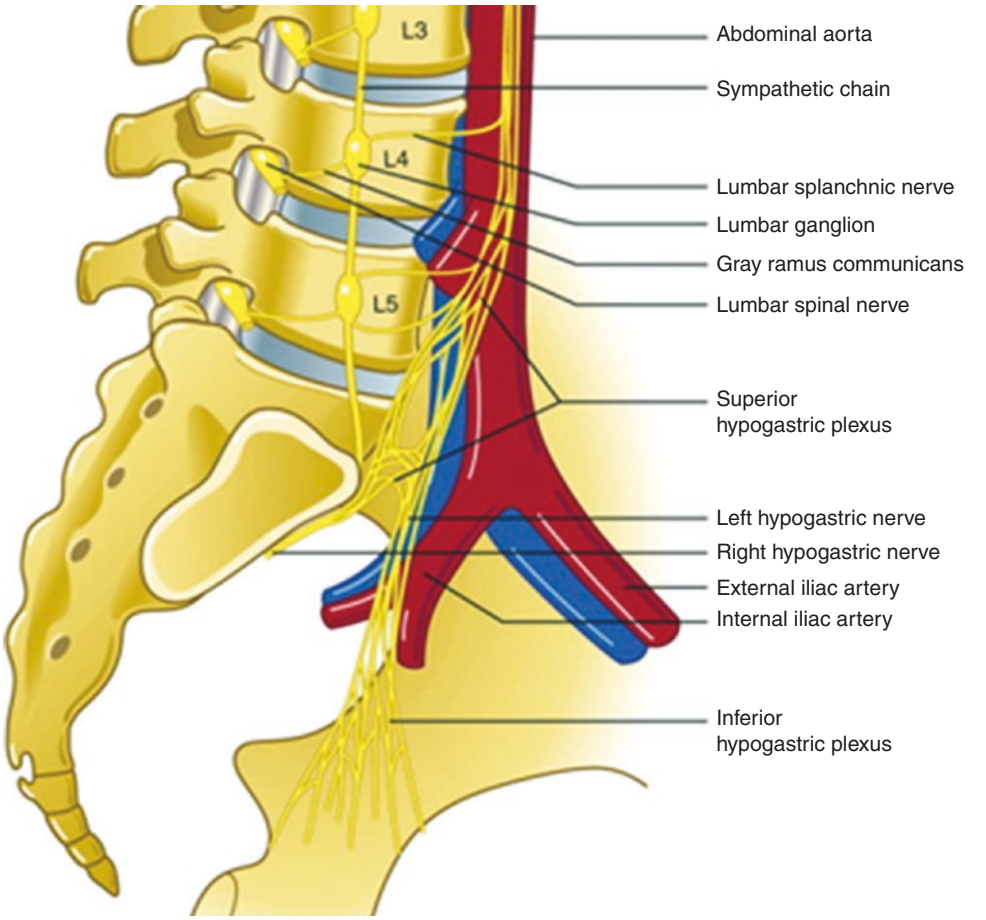

Fig. 23.18 Illustration of lumbar sympathetic chain

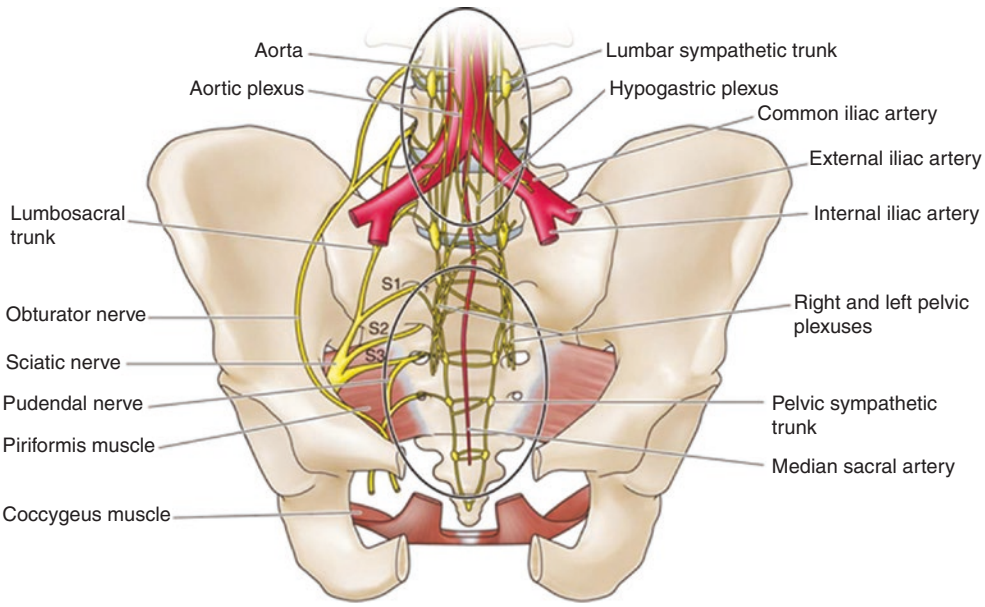

Fig. 23.19 Illustration of sacral/pelvic sympathetic chain

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Neuromodulation for Spine Pain Care

24

Alexandra R. Adler, Mark C. Bicket, and Shihab U. Ahmed

Key Points

- Spinal cord stimulation (SCS) therapy for chronic pain relief was first introduced over 50 years ago. In the past 10 years, there has been a renewed interest in the use of neuromodulation for the treatment of chronic pain, especially spine-related pain.
- Research has demonstrated that SCS may modulate pain at both the segmental spinal and supraspinal levels, but there is still much work to be done to understand the underlying mechanisms of neuromodulation.
- Spinal cord stimulation therapy can be divided into two major categories: one type produces a paresthesia (tingling sensation over the painful area), and the other uses higher frequencies without the production of any sensation (paresthesia-free).
- The main indication for SCS is persistent spine pain (e.g., lower back and leg pain) after spine surgery, formerly referred to as failed back surgery syndrome (FBSS). Newer SCS technologies have shown promise to address axial back pain as well as more focal pains such as groin or distal limb pain.
- Prior to receiving an implanted SCS device, a patient must undergo a comprehensive psychological evaluation and successful temporary trial.
- There is a great need for blinded and randomized controlled trials as well as long-term follow-up to better understand the true efficacy and durability of SCS therapy.

A Brief History

The application of electricity to treat pain has a long and storied past. Historians attribute the first use of electricity as a medical treatment to the era of the Roman Empire. In 46 AD, a physician named Scribonius Largus treated conditions such as headaches and gouty joints by applying a live black torpedo fish to various parts of the body. This fish discharges an electrical shock when it contacts skin and thus could be laid on the forehead of a headache sufferer or under the feet of a gout sufferer. Many years later, in his book *The Desideratum*, the reverend John Wesley described experiments in which he used electric shocks for the relief of pain. Among many others, he described a man named William Tyler, who, seized with rheumatic pains, began to "shriek out, like a Woman in Labor … After the second Shock, he felt some Change: After the third he was able to raise himself … After two more he rose and walked about the Room…" [2].

Many centuries later, Melzack and Wall proposed their seminal theory of pain transmission, which held that the communication of nociceptive signals from the periphery to the brain could be regulated at the level of the dorsal horn of the spinal cord [1, 3]. This theory, while incomplete at the time, made use of the fact that two types of afferent fibers carrying sensation from the periphery – large-diameter Aβ fibers that carry tactile information and smaller-diameter Aδ and C fibers that carry nociceptive information – both project to the same type of neuron, the inhibitory interneuron

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in the spinal cord dorsal horn. The inhibitory interneurons receive these signals and relay them through projections to transmission cells, known as wide dynamic range (WDR) neurons, in the dorsal horn. Melzack and Wall compared the action of inhibitory interneurons to that of a gate, which can either permit or prevent the WDR neurons from transmitting nociceptive signals along the pathways to eventually reach the brain. Taken another way, if the gate can be closed, one could theoretically prevent nociceptive signals from traveling to the brain.

While pain processing proved to be more complex, this "gate control theory" kick-started decades of investigation and led to novel treatments [1, 3]. Soon after, in 1967, C. Norman Shealy and colleagues reported that electrical stimulation of Aβ fibers in the dorsal columns could activate the inhibitory neurons and thus reduce the transmission of pain signals via WDR neurons. They presented the first case of SCS therapy by placing a plate over the dorsal column of the spinal cord at T3 via a laminectomy to relieve right-sided chest wall pain in a man with metastatic lung cancer [4, 5]. In 1968, Medtronic® released the first implantable SCS device for pain management, the "Myelostat" [6]. In 1981 Cordis® introduced the first implantable internal pulse generator (IPG) [6]. In 2004, Boston Scientific® pioneered the first rechargeable IPG [7].

Over the last decade, there have been significant advancements in technology such as MRI compatible systems, wireless programming capability, rechargeable batteries, accelerometer technology, and the arrival of different waveforms and frequencies of SCS, which deliver on the promise of personalizing therapy to the needs of individual patients.

Basic Mechanisms of Pain Relief with Spinal Cord Stimulation

The underlying mechanism of pain relief from SCS remains incompletely understood. Melzack and Wall's "gate theory" provided an initial biological basis for how conventional, low-frequency tonic SCS may work – that activation of Aβ fibers by an electrical field in the dorsal column closes a "gate" and prevents ascending transmission of nociceptive signals via WDR neurons [8, 9]. However, clinicians and researchers have observed that SCS ineffectively addresses nociceptive pain and more effectively treats neuropathic pain, suggesting that the current understanding of pain transmission is incomplete [10].

In neuropathic pain states, WDR neurons become hyperexcitable, which leads to increased basal release of excitatory substances such as glutamate and dysfunction of local GABA signaling [10, 11]. Preclinical studies have demonstrated that SCS reduces the excitability of WDR neurons, thereby the ascending transmission of pain, in animal models of neuropathic pain [12, 13]. In animals, SCS may attenuate neuropathic pain behavior by modulating signaling pathways in the spinal cord including those involving GABA [14], glutamate [11], adenosine [15], and acetylcholine [16]. It may also activate supraspinal pathways, thereby releasing substances involved in the descending inhibition of pain, such as serotonin and noradrenaline (Fig. 24.1) [3, 17, 18].

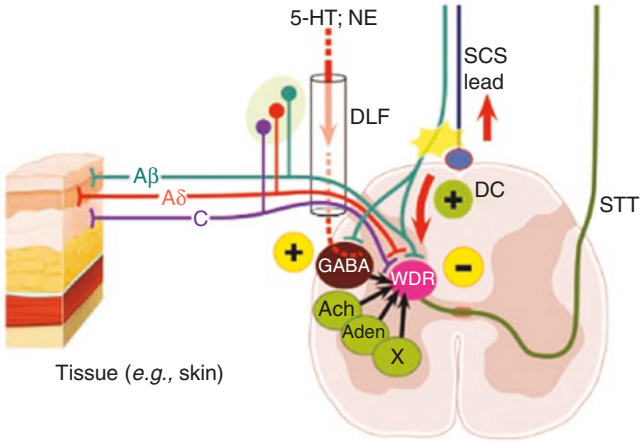

Fig. 24.1 SCS-mediated pain relief via segmental spinal and supraspinal modulation. Preclinical studies have found several neurotransmitters to be involved in the effects of SCS on neuropathic pain. SCS increases the availability of GABA, which may decrease the release of the excitatory neurotransmitters like glutamate. There is also increased release of acetylcholine (Ach) and adenosine (Aden) for pain modulation. An important supraspinal mechanism may involve the activation of descending inhibitory pathways, serotonergic (5-HT) and noradrenergic (NE) via dorsolateral funiculus (DLF), originating from brainstem centers. Many mechanisms remain unknown at the current time (X). *WDR* wide dynamic neuron, *DC* dorsal column, *STT* spinothalamic tract. (Reproduced with permission from Linderoth and Myerson [18])

Two other systems that may be important in the SCS-induced attenuation of pain are the descending opioid pathway [19], which leads to release of endogenous opioids and modulation of the immune system. The latter is an emerging area of research, but there does appear to be a connection between the immune system, certain pain disorders (such as CRPS), and SCS [20].

Functional MRI (fMRI) studies have provided evidence of how SCS may affect pain processing in the brain. For example, Rasche et al. demonstrated that SCS affects multiple areas involved in pain processing and inhibition in patients with FBSS [21, 22]. Other studies have suggested that patients treated with spinal cord stimulation show reduced connections between their somatosensory cortex and limbic system. This suggests that SCS may reduce the formation and persistence of negative emotions associated with pain [23].

In summary, we now know that pain modulation may occur at both spinal and supraspinal levels and that SCS may

also inhibit cortical pain processing and lead to remodeling of supraspinal structures in a way that affects not only pain but also psychological, emotional, and cognitive responses to pain [24, 25].

When used in patients with peripheral vascular disease, SCS may reduce or eliminate tissue ischemia and thus ischemic pain via modulation of the peripheral nervous system. Mechanisms include the release of vasodilatory molecules, which lead to smooth muscle cell relaxation and decreased vascular resistance, as well as reduced sympathetic vasoconstriction and pain transmission [26, 27]. A similar mechanism may also explain how SCS can be used to relieve anginal pain [28].

Modes of Spinal Cord Stimulation

A basic distinction between the modes of SCS is whether or not SCS elicits a paresthesia (tingling sensation). Conventional SCS produces a paresthesia over the painful area (Fig. 24.2). Recently, there have been advances in paresthesia-based stimulation algorithms that account for the individual's spinal anatomy in relation to the SCS electrodes, known as three-dimensional neural targeting. Another paresthesia-based method – dorsal root ganglion (DRG) stimulation – can provide more targeted pain relief for difficult-to-treat areas. The recent introduction of paresthesia-free or subparesthetic SCS therapy (i.e., systems that produce no or less paresthesia) has provided an important advance in this field. With these systems, namely, high-frequency SCS (HFSCS) and burst stimulation, the patient should experience little or no additional sensation [29].

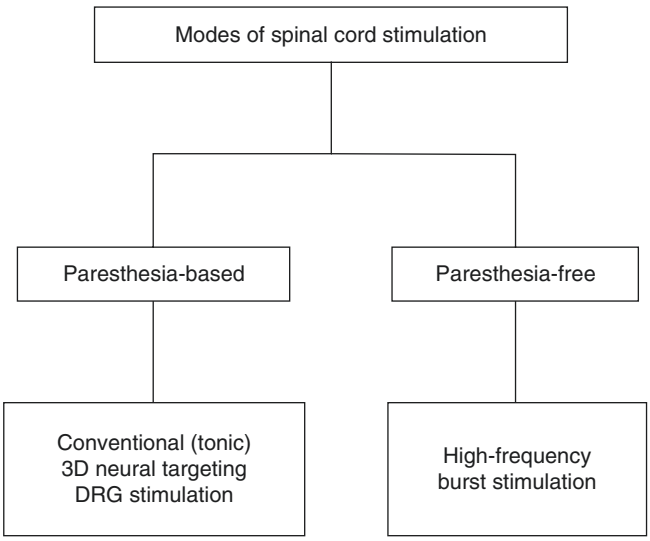

Fig. 24.2 Spinal cord stimulators can be divided into two categories depending on whether they produce a paresthesia (tingling sensation) or not. The paresthesia category includes lower frequency, tonic, conventional stimulation, as well as DRG stimulation and new programming algorithms such as 3D neural targeting. The paresthesia-free category includes high-frequency and burst stimulation

Spinal cord stimulators are programmed based on three basic parameters: amplitude, frequency, and pulse width (Table 24.1). Amplitude affects the intensity and breadth of a paresthesia, and the threshold for the amplitude is based on patient discomfort from the paresthesia. The frequency or number of pulses per second affects the quality of the paresthesia. The pulse width is the duration of a single stimulation. As it is increased, more nerve fibers are recruited. With conventional paresthesia-based stimulation, physicians can adjust all three parameters. However, with the paresthesia-free systems, the amplitude is the only variable that can be adjusted.

Conventional

Conventional SCS, also referred to as tonic SCS, was designed to produce a constant paresthesia that overlaps with an anatomical area affected by pain (Fig. 24.3a). Using implanted leads, an SCS device can produce a frequency between 2 Hz and 1200 Hz, although a frequency between 40 Hz and 60 Hz is most commonly used.

Three-Dimensional Neural Targeting

Three-dimensional (3D) neural targeting is a paresthesia-based SCS device that aims to tailor the delivery of an electrical current to an individual's anatomy. Unlike the programming of a conventional device, which involves turning on and off electrodes in a trial-and-error fashion to map a paresthesia to a painful area, 3D neural targeting uses additional calculations that account for anatomical variations between the leads and the dorsal column. For example, the depth of CSF varies by the location in the spinal cord, which in turn affects impedance [30]. This mode allows the programmer to calculate how much current is needed at each contact (electrode) [31].

Dorsal Root Ganglion Stimulation

Dorsal root ganglion stimulation, another paresthesia-based modality, addresses another limitation of conventional SCS – the difficulty in providing adequate pain relief in certain anatomical locations, especially the groin, hands, and feet [32, 33]. The DRG is somatotopically organized and is located in the lateral epidural space within the spinal foramen. It contains the cell bodies of primary sensory neurons, which send

Table 24.1 Spinal cord stimulator devices. Devices are grouped by the manufacturer and then further by the specific implantable pulse generator (IPG)

Manufacturer	IPG	Mode	Rechargeable	Pulse width (us)	Frequency (Hz)	Amplitude (mA)	Volume (cc)	MRI
Nevro	Senza	HF	Yes	20–1000	2–10,000	0–15	40	Head and extremity, 1.5 T and 3 T, for percutaneous leads[a]
Nuvectra	Algovita	T	Yes	20–1500	2–2000	0–30	20–21	In submission
St. Jude Medical	Proclaim	T, B	No	20–1000	2–1200	0–25.5	30.4–38.6	Full body[a]
	Prodigy	T, B	Yes	50–500	2–1200	0–25.5	<18	Full body[a]
	Proclaim DRG	DRG	No	40–1000	4–80	0–6.0	32	Head and extremity[a]
Bos Sci	Montage	T, B, 3D	Yes	20–1000	2–1200	0–25.5	19.8	Full body[a]
	Spectra WaveWriter	T, B, 3D	Yes	20–1000	2–1200	0–25.5	21.2	Head[a]
	Precision spectra	T, B, 3D	Yes	20–1000	2–1200	0–25.5	22	Head[a]
Medtronic	Intellis	T	Yes	60–1000	2–1200	0–25.5	13.9	Full body, 1.5 T up to 2.0 W/kg[a]
	PrimeAdvanced	T	No	60–450	2–260	0–10.5 V	39	1.5 T up to 2.0 W/kg for percutaneous and paddle leads[a]
	RestoreSensor	T	Yes	60–1000	2–1200	0–10.5 V	22	Full body, 1.5 T up to 2.0 W/kg[a]

The mode of stimulation is generally categorized as conventional or tonic (T), burst (B), three-dimensional neural targeting algorithm (3D), dorsal root ganglion (DRG), or high-frequency (HF) stimulation. However, algorithms, modes, and specific stimulation patterns differ between devices. In this case, HF refers to stimulation at 10,000 kHz

[a]When MRI safety conditions are met. This table includes commonly encountered devices but is not exhaustive. Please see individual device manuals for further instructions

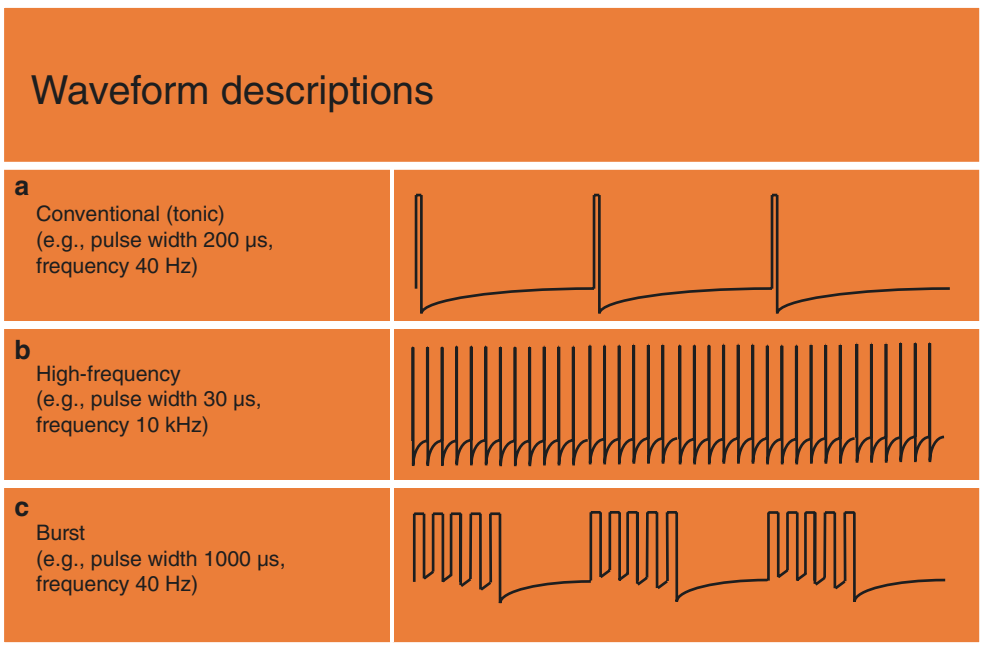

Fig. 24.3 Waveforms of electrical stimulation vary in characteristics such as frequency, amplitude, and distribution of pulses. Conventional or tonic stimulation consists of low-frequency pulses of similar amplitude with a pulse wave consisting of one pulse width (**a**). In contrast, high-frequency stimulation often has an abbreviated pulse width to accommodate a much higher frequency, typically at or above 1000 Hz (**b**). Unlike these two waveforms, burst stimulation consists of clusters of pulses, also called burst trains, which are separated by periods without stimulation (**b**)

nociceptive signals to the brain. Like conventional SCS, it consists of epidural leads and an IPG. The leads are threaded into the intervertebral foramen, and the IPG is implanted similarly to conventional SCS. Placement of this device may require additional training.

High Frequency

Paresthesia can be uncomfortable for some patients, especially when there is a variation in intensity with positional changes. One study demonstrated that up to 71%

of patients experienced uncomfortable paresthesia when changing position to the point that they turned off the device [34]. In addition, while conventional SCS showed efficacy for treatment of radicular pain, it did not have the same effect for axial back pain [35]. High-frequency SCS (HFSCS) delivers energy at a supraphysiological tonic frequency (frequently 10 kHz), which relieves pain but does not produce a paresthesia [36] (Fig. 24.3b). It has shown increased efficacy for the treatment of axial back pain and was approved by the FDA in 2015 with the indication for chronic refractory trunk and/or limb pain. High-frequency devices are limited by the need for frequent recharging of the battery. It is unclear how HFSCS relieves pain without the production of a paresthesia. Studies in animals have shown that there is a positive correlation between increasing frequency and greater inhibition of mechanical hypersensitivity [37].

Burst Stimulation

While conventional tonic stimulation is constant, burst stimulation delivers intermittent groups of closely-spaced, high-frequency stimuli (Fig. 24.3c). Burst stimulation is frequently paresthesia-free, but some patients do still experience a paresthesia [29]. A common setting is a 40 Hz burst mode with five spikes each at 500 Hz, with a pulse width of 1 ms. The bursts are separated by a quiescent period (an "interburst" period), which is usually 1 ms. Passive repolarization occurs during this period. The terms (burst and tonic) were historically used to characterize the response of neuronal cells to stimulation, particularly in the thalamus, and are being investigated as an additional way to provide pain relief through neuromodulation [38]. Some studies have shown that SCS applied in a burst instead of tonic pattern may provide superior pain relief, as has been demonstrated in rats with neuropathic pain [39] as well as in humans [38].

Clinical Indications and Efficacy

The most common indication for spinal cord stimulation is extremity pain, especially lower extremity pain that persists after back surgery (formerly referred to as FBSS). Treatment of axial back pain has now gained interest with the introduction of newer technologies particularly HFSCS. The use of SCS for several other pain conditions has been studied, and there is some data available on efficacy. However, in the US, SCS is only approved by FDA for the management of chronic intractable pain of the trunk and/or limbs.

Limb Pain

Lower extremity radicular pain is the most common indication for SCS in the USA, and there is significant (level I–II) evidence for it as a treatment in patients who have failed conventional medical management (CMM). Studies have reported that conventional SCS is superior to CMM or repeat back surgery, an effect that is sustained up to 24 months [40–43]. In 2005, a prospective randomized control trial (RCT) of 50 patients with FBSS assigned to SCS or reoperation showed 47% of the patients who received SCS had >50% pain relief versus only 12% in the reoperation group [40]. The largest trial assessing the efficacy of conventional SCS is the ProCESS trial, which was a prospective multicenter RCT of 100 patients with FBSS comparing SCS plus CMM versus CMM alone. It demonstrated that the SCS plus CMM group had significantly better pain relief than the CMM group and that this effect persisted for up to 2 years [44, 45].

With the advent of paresthesia-free SCS, studies have demonstrated moderate (level II) evidence for HFSCS for the treatment of chronic back and leg pain and limited evidence for burst stimulation [41, 46]. For HFSCS, studies found improved pain relief compared with conventional SCS such that approximately 70% of patients experienced a greater than 50% decrease in limb pain compared to 49% who received conventional SCS [47–51]. However, the only current truly "blinded" trial did not show a difference in pain relief between high-frequency stimulation at 5 kHz and sham in 33 patients using indwelling conventional SCS [52]. In this randomized, double-blind, two-period crossover study, a significant period effect was seen (patients tended to benefit from the first exposure they had regardless of what it was). Critics of this trial have pointed out that 5 kHz and 10 kHz stimulation may not be equivalent and that patients who have previously had paresthesia-based therapy may be biased. A newly published small study also showed no difference between conventional and HFSCS at 1 year, although the patients were not blinded in this study and the extent of pain relief in both groups (about 25%) was less than seen in most other studies [53].

The SUNBURST trial is the largest RCT comparing burst versus tonic SCS for the treatment of neuropathic pain in the back and legs. The trial demonstrated that, in 96 patients who had all previously received conventional SCS, burst stimulation was both non-inferior and superior to conventional SCS at 1 year for the treatment of trunk and limb pain and preferred by 68.2% of subjects at 1 year [38, 46].

Finally, DRG stimulation has been successful for pain relief in traditionally difficult-to-treat areas of the limbs, especially the feet. In a study of patients with back and limb pain, 60% of patients reported a >50% reduction in pain; pain in the feet was reduced by 80% [32].

Axial Low Back Pain

Conventional SCS has not been effective for patients with isolated or axial low back pain (LBP) [54], and indeed patients with LBP as their predominant symptom have been excluded from many studies of conventional SCS [44, 45]. Newer technologies, including HFSCS, burst stimulation, and 3D neural targeting, have better addressed this condition. Initial proof-of-concept studies demonstrated the efficacy of HFSCS in reducing pain, opioid use, and sleep disturbances in patients with axial LBP [48, 49]. The largest trial (198 patients) to compare conventional versus HFSCS, the SENZA trial, demonstrated that approximately 75% of patients experienced a >50% pain reduction in LBP at 12 months and approximately 80% reported this outcome at 24 months with use of HFSCS [47]. This was superior to the conventional SCS group, in which approximately 50% of patients reported this level of relief at these time points. A recent update by Al-Kaisy (21 patients) demonstrated efficacy of HFSCS for the relief of LBP at 36 months [49]. While this data provides hope for clinicians and patients, the results will need to be reproduced. The evidence for burst stimulation for axial LBP comes from the SUNBURST trial, which demonstrated that burst stimulation yielded significantly better pain reduction for LBP than tonic stimulation (approximately 20–40% better) [38].

The LUMINA study included 213 patients who received treatment with either conventional SCS or a new anatomically based algorithm known as 3D neural targeting. Nearly 80% of the patients in this study had axial LBP (with or without limb pain). At 2 years, 71% of the patients in the 3D neural targeting group had greater than 50% relief of their LBP compared to only 41% in the conventional group. The results were similar regardless of whether patients had isolated axial LBP or a combination of back and limb pain [31].

Complex Regional Pain Syndrome

Complex regional pain syndrome (CRPS) is characterized by pain, swelling, and skin changes in the affected extremity. The exact cause for CRPS is unknown, but implicated factors include sympathetic dysregulation, small fiber damage, inflammation, and tissue hypoxia of the affected limb. This may lead to cortical reorganization and centralization of the pain [55]. Spinal cord stimulation has been shown to be superior for pain relief in patients with CRPS compared to physical therapy, but has not been shown to improve functional status [56]. Unfortunately, this relief waned with time, and 3 years after implantation, the two groups had similar results [57]. Additional work has shown that while SCS may improve constant pain in CRPS, it does not improve allodynia (pain in response to a non-painful stimulus) [58].

The ACCURATE study, a prospective, multicenter RCT comparing DRG stimulation and conventional SCS in 152 patients with CRPS, demonstrated superiority in the DRG group with 81% of patients achieving >50% pain reduction (as compared to approximately 50% of patients in the conventional group) at 3 months. This effect persisted at 12 months [59].

Only case reports exist of HFSCS in patients with CRPS. One example showed that HFSCS provided superior pain relief for a patient with CRPS of the right leg [60].

Peripheral Vascular Disease

Patients who have pain caused by ischemia, such as those with circulatory disorders, may benefit from SCS. In particular, those patients who have failed limb salvage surgeries or have medical contraindications to major surgery may be SCS candidates [27]. The use of SCS has been shown to improve pain, promote the healing of ischemic wounds, improve exercise tolerance, and possibly salvage the limb [26, 27]. Outcomes may be better when candidates for SCS are selected based on measures of skin microcirculation, such as transcutaneous oxygen (tcpO2), as well as an improvement in these measurements during a SCS trial. Therefore, the authors have suggested using tcpO2 screening prior to implantation of SCS.

Other Neuropathic Pain Conditions

Apart from neuropathic and ischemic pain, small studies and case reports have suggested efficacy of SCS for the treatment of chronic groin, pelvic, and abdominal pain and for some peripheral neuropathies [61]. Chronic groin, pelvic, and abdominal pain can occur postoperatively, for example, after hernia surgery [62], or as a part of visceral pelvic pain syndromes (such as pudendal neuralgia, interstitial cystitis, and chronic prostatitis). Interestingly, in one case report, the leads were placed in a retrograde fashion to treat resistant pelvic pain [63]. Peripheral neuropathies that have been treated using SCS include those secondary to diabetes, HIV, and chemotherapy [64].

The Implantation Process

Contraindications

The Neuromodulation Appropriateness Consensus Committee (NACC) lists the following as contraindications to SCS implantation: active infection, continued use of anticoagulant or antiplatelet therapy, inability to comply with

SCS therapy, and unstable psychiatric conditions [35, 65, 66]. There are no definitive guidelines on SCS implantation in patients on chronic anticoagulation therapy [67]. Other contraindications include pregnancy, immunosuppression, and gross spinal instability.

Preoperative Psychological Evaluation

Psychological evaluation prior to implantation of a SCS, which is an implanted object that creates a foreign body sensation, is critical, especially given the prevalence of depression and other mental health conditions among patients with chronic pain. Factors associated with poor outcomes include somatization, major psychiatric disorders, poor coping ability, drug addiction or drug-seeking behaviors, cognitive impairment, and inadequate social supports [65, 66, 68]. Therefore, patients must undergo a psychological evaluation prior to implantation, although there are no standardized criteria for evaluation. Please see Chap. 35 for further information on this topic.

Trial

Prior to permanent implantation, all SCS candidates must undergo a trial to establish the efficacy of pain relief. Although there are no standard guidelines, the objective is to document the impact of the therapy on daily function and sleep along with percent pain relief. One recently published pain and functional assessment tool by Stojanovic and his colleagues provides a quick assessment and can be used at both the beginning and end of a trial [69]. Frequently, a patient must report a 50% or greater improvement in pain to be considered for a permanent implant.

Typically, trials are done percutaneously in the outpatient clinical setting. A thin epidural lead is implanted using a Tuohy needle under fluoroscopic guidance. The lead is connected to an external generator and programmer. The patient then uses the device for 3–8 days at home and returns to the office for a follow-up and removal of the temporary lead. A trial can predict a positive long-term outcome with SCS in 50–70% of cases [70]. If there is anticipated difficulty with the percutaneous trial, a spine surgeon can instead place a surgical lead via laminectomy or laminotomy. The trial occurs in the inpatient setting, and if the patient reports a benefit, a permanent implant can be placed during the stay.

Permanent Implant

A permanent indwelling SCS system is comprised of a lead or leads placed in the epidural space and an internal pulse generator (IPG) placed subcutaneously within a pocket. The lead is tunneled subcutaneously and connected to the IPG either directly or using an extension. There are two primary types of leads – a percutaneous lead is cylindrical catheter with sequentially spaced electrodes at its distal end and a surgical or paddle lead is paddle-shaped and contains multiple columns of electrodes. As above, the placement of a paddle lead requires either laminectomy or laminotomy and thus surgical assistance. A third type of lead – the hybrid percutaneous lead – is shaped like a paddle lead but is much narrower and can be placed percutaneously with the assistance of an introducer. The IPG is implanted in a subcutaneous pocket, the area of which should be marked prior to the implantation procedure. Most pockets are near the upper buttock area, but an IPG can also be placed near the abdominal wall, subclavicular area, or the upper lumbar or lower thoracic areas of the back. Typically, the IPG is placed on the patient's dominant side.

At our institution, we follow the antibiotic recommendations of the 2013 ASHP/IDSA/SIS/SHEA guidelines for patients undergoing clean neurosurgical procedures [71] (Table 24.2).

Complications

The complications related to SCS can be divided into mechanical, biological, and technique-related complications (Table 24.3). Mechanical complications include lead migration, lead fracture, unwanted stimulation, lead connection failure, hardware malfunction, and IPG failure. The most common,

Table 24.2 Our institution uses weight-based dosing for cefazolin as antimicrobial prophylaxis administered within 30–60 minutes prior to surgical incision for implantation of a spinal cord stimulator

Recommended agent <80 kg	Recommended agent ≥80 kg	Alternative if β-lactam allergy <80 kg	Alternative if β-lactam allergy ≥80 kg	Recommended re-dosing intervals (hrs)
Cefazolin 2 g	Cefazolin 3 g	Clindamycin 900 mg (as a single preoperative dose; if multiple doses, use 600 mg)		Cefazolin, 4 Clindamycin, 6
		Or		
		Vancomycin 1 g	Vancomycin 2 g	

For patients colonized with MRSA, we add vancomycin to this regimen. Alternative medications for patients with beta-lactam allergies include clindamycin and vancomycin

Table 24.3 Complications associated with spinal cord stimulators divided into mechanical, biological, and technique-related complications and expressed as the percent of implants

Spinal cord stimulator complications					
Mechanical (%)		Biological (%)		Technique-related (%)	
Lead migration (requiring repair)	2.1–27	Infection	3.0–8.0	Inadvertent dural puncture	0.3–7.0
Lead migration (requiring repair)	5.0	Subcutaneous hematoma	3.1–9.0		
Lead fracture or disconnection	0.0–10.2	Pain at IPG site	0.9–12.0		
Unwanted stimulation	2.4–6.8	Implant site pain	0.9–12.0		
Lead connection failure	9.5	Epidural hematoma	0.2–0.3		
Hardware malfunction	1.7–10.2	Paralysis	0.03		

Data is compiled from multiple studies and is expressed as a range when studies differ. See text for further references

lead migration, has been reported in up to 27% of patients [33, 44, 45, 72–74], although more recent studies have shown that significant migration (requiring intervention) occurs less than 5% of the time [47]. Percutaneous electrodes are more likely to migrate than paddle electrodes [75]. Many of these complications can be reduced with modification of techniques and reducing patient movement in the first 3 months after implant, which allows for scarring around the leads [33, 76].

Biological complications include infection, subcutaneous hematoma or seroma, implant site pain, epidural hematoma, and very rarely, neurological injury or allergic reaction [72–74, 77]. The most common complication is infection. Infection rates following SCS implantation have been reported as 3–8% [33, 42, 78], most of which are superficial [35, 73, 79]. A recently published retrospective study found an infection rate of 2.45% among nearly 3000 devices [80]. The use of a presurgical bath with an antiseptic agent, preoperative antibiotics, application of occlusive dressings in the operating room, and the use of postoperative antibiotics appear to lower infection rates, whereas longer trials appear to increase them [72, 80].

Technique-related complications (most importantly dura puncture leading to CSF leakage) are reported as between 0.3% and 7% [33, 72, 74].

Summary

Spinal cord stimulation is an ever-evolving field. This chapter aims to review the history, mechanisms, efficacy data, implantation process, and complications associated with this technology. Over the past 10 years, research on mechanisms has highlighted the complex interaction of spinal and supraspinal signaling that may explain pain relief with spinal cord stimulation. SCS has shown to be a safe and effective therapy for multiple pain indications, including lower back pain, limb pain, and CRPS. With the advent of high-frequency SCS and other paresthesia-free systems, it will finally be possible to conduct a large, double-blinded randomized controlled trial to determine the true efficacy of SCS, an invasive and expensive therapy but potentially life-changing therapy for pain relief.

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Intrathecal Drug Delivery

25

Saiyun Hou and Salahadin Abdi

Key Points

- Intrathecal drug delivery has been shown to be very beneficial for patients who are intolerant or refractory to other analgesic routes of administration; intrathecal drug delivery is associated with high patient compliance but also high costs and high maintenance.
- Intrathecal drug delivery to the cerebrospinal fluid (CSF) modulates nociceptive signal transmission by targeting pain receptors, thereby providing pain relief with a minimal analgesic dose to patients.
- Careful patient selection is a key to successful intrathecal therapy.
- Indications for intrathecal therapy include nociceptive pain, neuropathic pain, or mixed pain.
- A trial of intrathecal therapy prior to permanent implantation provides the patient and physician with the opportunity to assess the immediate side effects and efficacy of intrathecal analgesia. However, a trial is not necessary for patients with advanced disease and limited lifetime.
- Catheter malfunction is the most common complication associated with intrathecal devices.
- The Polyanalgesic Consensus Conference (PACC) 2017 has provided recommendations for the use of intrathecal therapy.

Introduction

Chronic pain is very common and difficult to treat. It was previously found that 19% of US adults are affected by chronic pain, including pain related to cancer and noncancer conditions [1]. Pain also causes economic costs through lost productivity, patient disability, and increased healthcare utilization. It also results in poor quality of life [2].

The mainstay of severe chronic pain primarily requires opioid therapy, which is typically delivered via the oral or transdermal route. Although this approach can be effective, some patients will develop intolerable side effects (e.g., nausea, vomiting, constipation, sedation, respiratory depression), and the addictive and euphoric effects of these agents have led to widespread abuse, misuse, and diversion, thereby contributing to an epidemic of opioid-related adverse outcomes and negative societal effects. Furthermore, some patients with severe chronic pain do not experience sufficient analgesia following systemic opioids use. These patients are considered to have refractory severe chronic pain and require different approaches for effective analgesia.

The intrathecal delivery of drugs utilizes the neuromodulation concept by targeting the neural transmission of pain impulses to treat patients with nociceptive, neuropathic, or mixed-etiology pain syndromes, such as those associated with nerve injury, cancer, or other neurological diseases. Intrathecal therapy presents several advantages, including greater efficacy and reduced medication doses (with a reduction in side effects), compared to systemic administration. Notably, only ziconotide, which is a nonopioid and selective N-type calcium channel blocker, and morphine, which is a mu-opioid receptor agonist, have been approved for intrathecal analgesia by the US Food and Drug Administration (FDA). However, a wide variety of agents is currently used intrathecally for both nociceptive or neuropathic pain conditions [3].

Historical Perspective

German surgeon August Bier first performed intrathecal anesthesia on himself and his assistant with cocaine in 1898. Bier and his assistant were the first to describe a postdural puncture headache after these experiments. Bier is

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thus recognized as the father of intrathecal anesthesia. Rudolph Matas was the first in the USA to utilize intrathecal anesthesia in 1899. He may have also been the first to perform lumbar puncture with morphine. Some years later, Thomas Jonnesco of Romania promoted intrathecal anesthesia for a variety of surgical procedures in 1908. Jonnesco published the first textbook on intrathecal anesthesia, called *La rachianesthesie generale*, in Paris in 1919 [4].

Opioid receptors were discovered in 1971 and isolated in 1973. Following these advances, the identification of specific opioid receptors in the spinal cord has led to new pain treatment concepts. Animal studies demonstrated that intrathecal opioids could be used to induce selective analgesia with few sensory, motor, or autonomic side effects [5–8]. Wang reported the first human study in 1979. Wang successfully confirmed pain relief with an intrathecal administration of morphine [9].

In 1940, William T. Lemmon was the first to perform a clinical continuous spinal anesthesia. Lemmon employed an indwelling malleable needle at the Mayo Clinic [10]. In 1944, Edward Tuohy from the Mayo Clinic passed a nylon ureteric catheter into the subarachnoid space utilizing a 15-gauge directional spinal needle. Tuohy developed the concept of continuous spinal anesthesia and recorded its relative safety [11].

The use of intrathecal drug delivery systems (IDDS) started with the development of permanent intrathecal catheter implantation in combination with internal or external ports, reservoirs, and programmable pumps. The first clinical application of IDDS was at the University of Minnesota in 1969. In 1982, the first human clinical implant of an intrathecal programmable pump was introduced [12]. In 1988, Medtronic, Inc. received approval from the FDA for the first programmable, battery-powered pump for cancer-related pain. In 1991, they received approval for its use in chronic pain [13].

Indication

Intrathecal therapy is indicated by the FDA for moderate to severe pain of the trunk and limb, as well as intractable pain when more conservative therapies have failed. Patients with severe chronic pain demonstrating significant side effects from oral, transdermal, or intravenous opioids with dose titration can be considered for intrathecal therapy. Those who do not achieve adequate analgesia despite increased doses of opioids should also be considered. The 2017 Polyanalgesic Consensus Conference (PACC) guidelines include a variety of disorders (see Tables 25.1 and 25.2).

Logistical issues, including insurance coverage for intrathecal therapy, need to be addressed when considering therapy. For patients with poor performance status or risk factors for poor outcomes (e.g., psychiatric conditions or obstructive sleep apnea), having a responsible family member or caregiver is especially important for adequate patient monitoring.

Table 25.1 Disease indications for intrathecal drug delivery

Axial neck or back pain; not a surgical candidate
Multiple compression fractures
Discogenic pain
Spinal stenosis
Diffuse multiple-level spondylosis
Failed back surgery syndrome
Abdominal/pelvic pain
Visceral
Somatic
Extremity pain
Radicular pain
Joint pain
Complex regional pain syndrome (CRPS)
Trunk pain
Postherpetic neuralgia
Post-thoracotomy syndromes
Cancer pain, direct invasion, and chemotherapy-related
Analgesic efficacy with systemic opioid delivery complicated by intolerable side effects

Adapted from Deer et al. [15]; with permission from John Wiley and Sons

Table 25.2 Recommendations for evidence assessment of intrathecal therapy by the PACC using USPSTF criteria

Statement	Evidence level	Recommendation grade	Consensus level
Intrathecal therapy should be utilized for active cancer-related pain with opioids	I	A	Strong
Intrathecal therapy should be utilized for active cancer-related pain with ziconotide	I	A	Strong
Intrathecal therapy should be utilized for noncancer-related pain with opioids	III	B	Strong
Intrathecal therapy should be utilized for noncancer-related pain with ziconotide	I	A	Strong

Adapted from Deer et al. [15]; with permission from John Wiley and Sons

Contraindications

Contraindications include:

- Local or systemic infection
- Poorly controlled or untreated coagulopathies

- Spinal instrumentation or anatomical structural abnormalities that do not allow for intrathecal access of the catheter
- Intracranial processes that may lead to cerebellar herniation in the setting of cerebral spinal fluid (CSF) leak
- Patients with active psychosis, suicidality, homicidality, somatization, alcohol/drug dependency, severe depression, or neurobehavioral or cognitive deficits
- Patients with poor cardiopulmonary status or significant cardiopulmonary comorbidities, including obstructive sleep apnea or central sleep apnea
- Patients with orally prescribed centrally acting medications that may interact with intrathecally delivered medications and may cause an increased risk of opioid-induced sedation, confusion, or respiratory depression

Guidelines

The PACC was formed in 2000 to promote the safe and appropriate use of intrathecal therapy by providing guidance and recommendations to clinicians who manage patients with refractory severe chronic pain [14]. Since 2012, use of intrathecal therapy has grown with the development of new devices, emergence of new evidence, and expansion of clinical experience, resulting in the need for updated guidelines to reduce healthcare provider variability and to improve patient outcomes. The recently updated guidelines provide consensus points based on evidence ranking rather than subjective analysis [15]. These new consensus points address topics such as considerations for patient and medication selection, intrathecal therapy in neuropathic and nociceptive pain states, recommended starting doses, and psychological considerations. Intrathecal therapy was previously reserved for salvage therapy after the failure of oral high-dose opioids or positioned at the end of the pain care algorithm. However, the updated guidelines indicate that the intrathecal drug delivery approach should be considered at an earlier point in time if other therapies have failed [15].

Technique

Preimplantation Trial

Patient success following an intrathecal therapy trial plays a critical role when making the decision to implant an intrathecal pump. The trial can be used to determine pain score change, improvement in function, decrease in reliance on oral analgesics, or opioid-related side effects [16]. Trials may be performed using a single bolus intrathecal injection, a multiple bolus injection, or a continuous infusion through a percutaneous intrathecal or epidural catheter. Unfortunately, there are currently no commonly accepted guidelines establishing procedures to perform a trial. The PACC concluded that, in a scenario of noncancer pain, no study has shown that a continuous intrathecal trial is superior to other intrathecal trial methods. Equal levels of evidence support single-shot trialing, bolus trialing, and continuous infusion [17]. Whether to eliminate systemic opioid therapy prior to the trial also remains controversial; however, the PACC recommended that the elimination of systemic opioid therapy can be accomplished before or during the trial or after implanting an IDDS. Unless otherwise indicated, intrathecal ziconotide should be considered as an alternative to opioids and should be considered as a first-line therapy for neuropathic pain. The PACC further recommended that acceptable pain relief should be achieved during a trial. The amount of pain relief that is considered acceptable varies between 30% and 70%. No long-term prospective studies have determined the best practice percentage or reduction extent for systemic opioids. Before the trial, the expected goal of pain relief should be discussed with the patient/caregivers. A trial is not needed in patients with advanced disease who present with limited survival time, a high risk of procedures, or a risk of bleeding/infection that makes the trial at a high risk; however, cancer pain patients experiencing full remission may be considered for a trial [17].

Preoperative Preparation

Permanent implantation of an intrathecal drug delivery system is most commonly performed under monitored sedation but can also be performed under general anesthesia, spinal blockage, or local anesthesia. Common preoperative tests include CBC with differentials, PT/PTT, electrolytes, urinalysis, ECG, and chest x-ray. During the preoperative preparation, the patient should be counseled on his or her treatment, personal responsibilities, expected pain relief, and possible side effects and complications. The primary issues to be covered during the preoperative education and informed consent process include, but not are limited to, implant procedures, preoperative procedures, postoperative procedures, postoperative precautions and self-care responsibilities, postoperative pain or discomfort, follow-up care, and refill schedules and procedures.

Before surgery, the patient should be consulted to determine the most appropriate site for the intrathecal pump pocket. Patient comfort is of great importance. The pump must be situated away from bony prominences, such as the iliac crest and ribs, to avoid discomfort and rubbing. Restrictive clothing, braces, orthotics, and/or the sides of a wheelchair may irritate the area of the pump, and placement should avoid these areas. Subcutaneous fat is also an important factor. In average-sized patients, there may be insuffi-

cient space and tissue in the flank. However, in morbidly obese patients, there may be too much subcutaneous fat in the abdomen. Having the patient sit up to identify the pocket site helps ensure comfort with the planned pump site because skin tissue can substantially shift intraoperatively. Discuss sleeping habits with the patient to assess if they sleep on the side of planned pump site. If this is true, place the pump in the contralateral abdomen. In most cases, the most appropriate pump placement location is either the abdominal lower left or lower right quadrant. If reimplantation of a pump is required after a previous pump site infection, a new pump location, such as in the contralateral abdomen, is preferred to minimize reinfection risk. Pump placement into scar tissue is not recommended because this can impair blood supply, which limits the ability of antibiotics to flow to the area during implantation.

Intraoperative Preparation

The two most important factors in preventing wound infections are good sterile technique and the use of antibiotic prophylaxis [18, 19]. The most common complication has been noted as infection with an incidence of 7% from a multicenter prospective study assessing intrathecal pump implantations for both spasticity and pain [20]. Most surgical site infections following clean surgeries occur due to microorganisms on the skin. Carefully cleaning the surgeon's hands as well as the patient's operative site skin with either a povidone-iodine scrub or chlorhexidine-alcohol can reduce skin bacteria levels. Chlorhexidine-alcohol scrubs have been suggested as superior to povidone-iodine scrubs in several studies [21, 22]. However, this issue remains controversial. Few studies and meta-analysis reviews demonstrated that the choice of chlorhexidine-alcohol or povidone-iodine for preoperative skin antisepsis impacted the postoperative infection incidence [23, 24]. Other antibiotic selections to reduce the infection risk include (1) soaking the pump in saline mixed with povidone-iodine solution, (2) packing the wounds with sponges soaked in povidone-iodine for a few minutes, (3) tracing the perimeter of the wound with povidone-iodine as well as redraping the edge of the wound before pump placement, and (4) performing a re-gloving after completion of surgical dissection but before handling the pump [25, 26].

Surgical Technique

The patient is positioned in the lateral decubitus position with the side of the reservoir site up. The procedure starts with the catheter placement. Typically, the entry site ranges from the L2 to L4 interlaminar space unless anatomic considerations or previous surgery dictates otherwise. The needle advances toward the thecal sac in a paramedian plane until the dura is punctured. The shallow angle of the paramedian approach reduces the potential for shearing or excess stress on the catheter, minimizes catheter kinking, and facilitates advancing the catheter to the desired level. Good CSF flow should be seen through the needle, and the catheter should be placed under fluoroscopic guidance. Keeping the patient awake and communicating provides a greater margin of safety. If there is any sign of paresthesia or motor change, the procedure should be aborted.

The level of catheter placement should be on the level of the "pain generator." When the catheter tip passes the distal portion of the needle, extra care should be taken, should the catheter require withdrawal, because sheering or damage to the catheter may occur. The slightest resistance when withdrawing the catheter through the needle indicates that the needle and catheter should be removed together. The process should then be restarted with needle placement.

Once the catheter tip is at the desired level, the catheter is anchored to the supraspinous ligament caudally using a nonabsorbable suture, 0 silk suture. The reservoir pump pocket is then created. This is achieved by incising along the previously marked site on the anterior abdominal wall and down through the scarpas fascia to the subcutaneous fat. A deep subcutaneous pocket is then expanded using blunt dissection caudal to the incision. The pocket should be proportional to the size of the pump. If the pocket is too large, the pump may have an increased risk of seroma, shifting and flipping of the pump; if the pocket is too small, it may lead to tissue tension, reduced blood supply, and increased risk of wound dehiscence and breakdown. Once the pocket is created, the pump should be anchored to the fascia with a nonabsorbable suture.

The intrathecal catheter and pump are finally connected by tunneling the dorsally secured catheter to the ventrally placed pump reservoir. Excess catheter length is coiled beneath the pump to prevent catheter tension and kicking when the patient bends or rotates. The incisions are closed in sequential fashion using a 2-0 or 4-0 monofilament absorbable suture. The device is programmed to begin drug delivery.

Complications/Troubleshooting

Complications of the intrathecal therapy may arise anytime from the day the device is implanted until it is removed or the patient's life ends. The complications are procedure/technique-related, device-related, and medication-related. The following paragraphs will focus on several specific complications.

CSF leakage is the most common technique-related complication. Postdural puncture headache is the main com-

plaint indicative of a CSF leak. Generally speaking, CSF leakage may occur due to enlarged dura puncture site during the procedure. This is often self-limiting and may be conservatively treated. Notably, if the symptoms and leak persist, an epidural blood patch can be used with fluoroscopic guidance to avoid damaging the catheter. CSF leaks of severe nature may lead to the collection of fluid in the posterior area of the catheter site pocket. If the leakage is not resolved by an epidural blood patch, 1 ml of fibrin glue can be injected at the dural entry site. In rare cases, CSF leaks may occur due to catheter disconnect from the pump, which is accompanied by a CSF leak into the pump pocket. This manifests as recurrent or persistent pump pocket fluid collection after percutaneous drainage. Percutaneous side port access with the injection of contrast under fluoroscopy can be used to diagnose this complication. If a catheter disconnect is demonstrated, replacement of a new catheter is warranted.

Granuloma at the tip of the intrathecal catheter may occur commonly with increased follow-up intervals. Granuloma is an inflammatory mass composed of monocytes, neutrophils, and macrophages with granulation tissue. It is a noninfectious buildup of inflammatory tissue that can cause problems ranging from no symptoms or a loss of analgesic efficacy to frank flaccid paralysis. Granuloma formation risk factors include a high dose as well as high concentration of opioids infusion. Morphine has been the most commonly implicated drug, although other opioids have also, rarely, been implicated. An animal study showed that clonidine combined with opioids has been anecdotally reported to prevent granuloma formation [27]. Imaging via MRI with a contrast or CT myelogram can help evaluate a suspected granuloma. The treatment depends on the presence and severity of any neurologic symptoms. Options include replacing the infusion with saline, removing the catheter, or surgical exploration with mass resection.

Catheter malfunction is the most common complication associated with intrathecal devices. This includes puncture, fracture, migration, disconnection, or dislodgement from within the intrathecal space. Catheter migration is the most common of these and often results from improper catheter anchoring to the fascia. Catheter malformation can manifest with CSF leaks, inadequate pain control, or opioid withdrawal symptoms. A first assessment of the side port may aid in evaluating catheter malfunction. If the CSF can be aspirated freely, a fluoroscopic evaluation with a contrast injection may help identify catheter leak locations. If the CSF cannot be aspirated, the pump must be filled with saline, and the drug within the catheter must be cleared before injecting contrast to avoid a large bolus drug injection intrathecally. If contrast studies cannot detect the catheter fracture, leaks, and kinks, the injection of contrast through the side port followed by a CT myelogram may be considered.

Summary

Intrathecal drug delivery is an invasive interventional surgical procedure that is useful for the treatment of intractable chronic nonmalignant pain and cancer-related pain. Since the 1960s, intrathecal therapy has become a promising therapeutic option due to advances in technology. There has been an increased use of implanted intrathecal pump systems for managing cancer and chronic noncancer pain. With appropriate patient selection and careful attention to technical issues, the outcomes are extremely positive. The main risk associated with the implantation of an intrathecal system is catheter malfunction. Good catheter anchoring during surgical implantation can minimize the risk. Further development in analgesic pharmacology, new catheter material, and new pump technology can further improve intrathecal therapy. Recommendations for the development of new pump technology, as well as materials and drugs, would address issues related to formulation, chemical/material stability and compatibility, pharmacokinetics, and toxicology [28–31]. The development of newer technology and agents for intrathecal therapy, as well as utilization of active agents at a number of receptor systems involved in pain transmission and modulation pathways, may help reduce the suffering of many patients with intractable pain.

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Vertebroplasty and Kyphoplasty

26

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Key Points

- Vertebral compression fractures are common complications of osteoporosis and spinal malignancies. They may often be satisfactorily treated with conservative therapies, but in a subset of patients, pain and restricted mobility will persist despite conservative treatment. In this population, vertebral augmentation is an effective treatment option.
- Vertebral augmentation procedures, comprising vertebroplasty and kyphoplasty, involve the percutaneous injection of bone cement into a vertebral compression fracture. In vertebroplasty, cement is injected directly into the vertebral body, while balloon kyphoplasty involves an additional step in which a tamp creates a cavity within the bone for cement infiltration.
- The evidence for vertebral augmentation has evolved over time. Positive early results were followed by two high-profile trials of vertebroplasty that found it conferred no benefits over active control placebo. A more recent randomized trial of vertebroplasty in acute fractures demonstrated improvements in pain and quality of life. Trials comparing vertebroplasty and kyphoplasty to real-world conservative management demonstrate a strong advantage to the procedures.
- Vertebral augmentation procedures are safe, with a low risk of complications. Cement leakage outside the vertebral body is the most common 'complication', although the vast majority of leaks are asymptomatic. Serious complications that may result from unrecognized cement leakage include nerve or spinal cord injury or pulmonary embolism. Mortality from vertebroplasty or kyphoplasty is exceptionally rare.

Case Presentation

A 76-year-old man presented with 4 weeks of worsening lower back pain which was described as deep pain, localizing to the midline of his lower back and exacerbated by standing and relieved by lying down. He rated his pain severity as 10/10 and required narcotic analgesia. His Roland-Morris Low Back Pain and Disability Questionnaire (RMDQ) score was 22/24 indicating severe back pain-related

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disability. He required assistance from his wife to put on his socks and had markedly reduced walking distance. Clinical examination revealed midline tenderness at the lumbar spine but no lower limb neurological deficit.

Magnetic resonance imaging of the spine revealed an acute compression fracture of the L3 vertebra. There was T2-weighted hyperintense signal consistent with bone marrow oedema, a T1-hypointense fracture line and 50% loss of vertebral body height. Additional ^{99m}Tc scintigraphic bone scan with single-photon emission computed tomography (SPECT CT) correlation confirmed intense increased osteoblastic activity across the L3 vertebral body with a linear morphology of radiotracer uptake corresponding to the fracture plane. Following discussion with the patient and family regarding the potential conservative management options with opioid analgesics, bed rest or orthotic bracing, the decision was made to perform vertebroplasty of the L3 vertebral body, 6 weeks after initial fracture diagnosis.

The L3 vertebral body was accessed using an 11-gauge needle via a unilateral transpedicular approach. The trocar was advanced further under image guidance, and midline position was achieved.

Under continuous fluoroscopic guidance, polymethylmethacrylate (PMMA) cement was instilled via the unipedicular trocar. There was good filling within the L3 vertebral body. There was no posterior cement leakage nor venous extravasation evident; no procedural complications occurred.

Follow-up at 7 days after the vertebroplasty revealed significant reduction of his back pain, rated as 1/10 with reduced narcotic analgesic requirement. At 30-day follow-up, he rated his back pain as 1/10, and his RMDQ score was 4/24, indicating marked improvement in pain control with associated reduction in back pain-related disability. His mobility had improved, with restoration of his normal walking distance. Continuing management included anti-osteoporosis treatment, managed by his primary care physician.

Introduction

Vertebral compression fractures (VCFs) are the most common complication of osteoporosis, comprising around 700,000 of the 1.5 million osteoporotic fractures that occur annually in the United States [1]. In most symptomatic patients, satisfactory pain relief can be achieved with conservative medical therapies, including analgesics and a period of bed rest. However, a small percentage of patients will experience severe pain and limitation of function that persists despite an adequate trial of conservative management or have pain severe enough to require high doses of narcotic analgesia or hospitalization. These patients may benefit from vertebral augmentation.

Vertebral augmentation procedures (vertebroplasty and kyphoplasty) involve the image-guided injection of bone cement into a fractured vertebral body. Vertebroplasty uses a percutaneous approach to inject cement directly into the fractured vertebra, while kyphoplasty involves the additional step of creating a cavity. The most common way to create that cavity involves inflating a balloon tamp within the vertebral body into which the cement is introduced (Fig. 26.1). The central goals of these procedures are the relief of back pain, enhancement of functional status and mobility and biomechanical stabilization of the vertebral body. Vertebral aug-

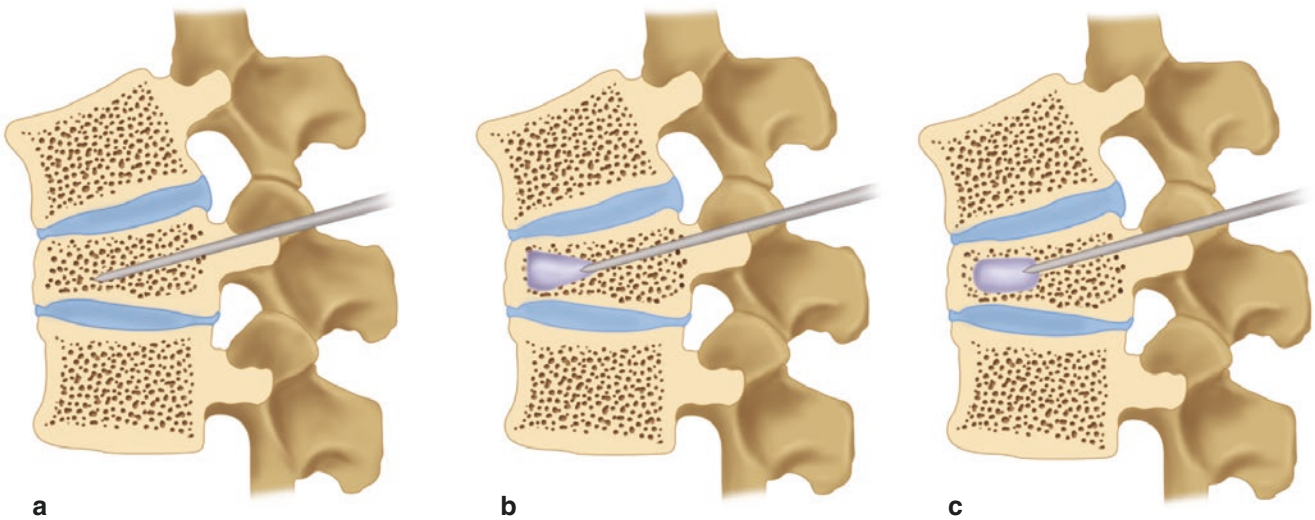

Fig. 26.1 (**a**) Vertebral augmentation procedures involve the percutaneous injection of cement into a fractured vertebral body. (**b**) Vertebroplasty involves cement infiltration directly into the vertebral body. (**c**) Kyphoplasty involves the additional step of utilizing a balloon tamp to create a cavity within the bone, into which cement is injected

mentation may also be performed for symptomatic neoplastic VCFs. Osteolytic or osteopenic bone disease occurs in up to 70% of patients with multiple myeloma, and up to 30% will sustain a VCF during the course of disease [2, 3]. Bony metastasis in the spine may also weaken the structural strength of the vertebral body, leading to elevated fracture risk. VCFs may also be caused by osteonecrosis from radiotherapy or osteopenia due to androgen deprivation or aromatase inhibitors.

This chapter will outline the background, indications and procedural technique for vertebroplasty and kyphoplasty and examine the current literature on the efficacy and safety of these procedures.

Background

Conservative Management of VCFs

For most patients with symptomatic VCFs, conservative medical therapies form the mainstay of treatment. The goals of conservative management are pain relief (with analgesics and a period of reduced physical activity, often involving bed rest), improved mobility and functional status (with orthotic bracing and physical therapy) and the prevention of future VCFs (with bisphosphonates and supplementation of calcium and vitamin D). In patients with milder symptoms, satisfactory results can typically be achieved using this approach. However, in those with more severe pain or limitation of function, conservative management may be insufficient, and extended use of these therapies can be harmful. Prolonged immobilization can lead to bone loss (at an estimated rate of 1–2% per week) [4] and loss of lower extremity strength (10–15% per week) [5]. Immobilization also increases the risk of pressure ulcers and thromboembolic disease. The adverse effects of opioid analgesia, including sedation and confusion, present additional risk. Together, the complications of bed rest and narcotic agents can lead to a cycle of physical deconditioning and subsequent increased risk of future fractures.

Historical Background

Vertebroplasty was first performed in 1984 by Galibert et al. who injected polymethylmethacrylate (PMMA) cement into a vertebral body partially destroyed by vertebral haemangioma [6]. Following successful results, the procedure was applied to treat pain associated with both osteoporotic and neoplastic VCFs [7]. In 1997, Jensen et al. published results from 29 patients with 47 painful osteoporotic VCFs [8]. Ninety percent of patients reported improved pain and mobility within 24 hours of the procedures. These promising findings led to increased uptake of the procedure, and in 2006, a pooled analysis of vertebroplasty studies encompassing 2086 patients reported significant post-procedure pain reduction in the 19 students that evaluated pain outcomes [9].

Kyphoplasty was initially described in 2001 by Lieberman et al., who hypothesized that inflation of a balloon tamp within the vertebral body had the potential to restore vertebral height and result in lower rates of cement leakage than vertebroplasty [10]. In a pooled analysis of 26 kyphoplasty studies that included 1710 patients, there were significant post-procedure improvements in pain relief, functional capacity, vertebral height and kyphosis reduction [11].

Indications and Contraindications

The decision to proceed with vertebral augmentation should be based on thorough evaluation of the patient involving history, examination, imaging and assessment for potential contraindications.

Indications

(a) Acute (≤6 weeks) symptomatic osteoporotic VCF, refractory to medical management
(b) Symptomatic VCF due to spinal neoplasia, refractory to medical management

Failure of medical management can be defined as:

- Pain persisting to a level that compromises mobility and quality of life, despite medical therapies
- Unacceptable side effects (e.g. sedation, confusion or constipation) occurring due to the analgesic doses required to relieve pain

A reasonable trial of medical management is 2–4 weeks, but earlier treatment may be considered for those requiring narcotic analgesia, analgesic infusions or hospitalization due to pain.

(c) Subacute (6–12 weeks) and chronic (>12 weeks) fractures are also considered with advanced imaging selection and with stringent clinical-imaging correlation.

Absolute or Near-Absolute Contraindications

- Sepsis or spinal infection
- Known significant allergy to bone cement
- Uncorrectable coagulopathy
- Progressive myelopathy resulting from fracture retropulsion or epidural tumour extension
- Inability to tolerate procedural sedation or anaesthesia due to cardiac or pulmonary risk

Relative Contraindications

The following conditions are best treated only by experienced operators:

- Procedure above the level of T5
- Loss of ≥75% vertebral height
- Substantial tumour destruction of vertebral body walls
- Disruption to posterior cortex of vertebral body
- Epidural tumour extension into central spinal canal or neural foramina

History and Examination

The characteristic symptom of VCF is deep midline pain, which may occur with minimal or no trauma. Typically, pain is aggravated by weight-bearing and motion, particularly by flexion. It affects the patient's ability to stand or sit for extended periods of time and is relieved by recumbency. Physical examination typically reveals midline tenderness over the spinous process of the vertebral body. A neurologic examination of the lower limbs should be performed to screen for myelopathy.

Pre-procedural Imaging

Imaging of the spine is performed in all cases to confirm the fracture level, assess fracture acuity and evaluate for potential contraindications or technical difficulties. Initial imaging often involves conventional frontal or lateral radiographs or computed tomography (CT), yet the capacity of these modalities to assess fracture acuity is limited. Magnetic resonance imaging (MRI) is the investigation of choice. Unhealed acute fractures are optimally shown on a combination of fluid-sensitive short-tau inversion recovery (STIR) or T2-weighted fat-saturated fast spin echo sequences, with T2 hyperintense signal representing bone marrow oedema and a T1 hypointense fracture line occasionally visible (Fig. 26.2). MRI allows for the assessment of the vertebral body posterior cortex, spinal canal and neural foramina and can evaluate for fracture retropulsion and epidural tumour extension. It may also identify fractures at other vertebral levels that may not be demonstrated on conventional radiographs. CT is a useful adjunct for pre-procedural imaging, particularly to assess the integrity of the posterior cortex.

In patients who cannot tolerate MRI or have technical contraindications (e.g. incompatible cardiac pacemaker or aneurysm clip), ^{99m}Tc nuclear scintigraphic bone scan may be performed. Unhealed fractures may be identified through higher uptake of the injected radiotracer. A combination of bone scan and single-photon emission computed tomography (SPECT) is particularly useful, allowing three-dimensional imaging as well as anatomic evaluation afforded by the CT component of the scan (Fig. 26.3).

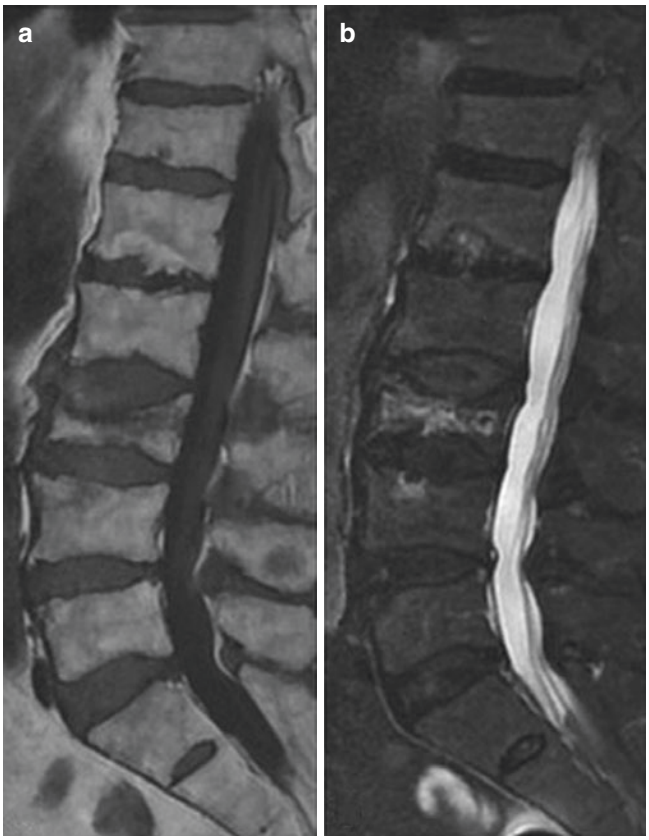

Fig. 26.2 Magnetic resonance imaging (MRI) of the lumbar spine for the clinical case described at the beginning of this chapter. (**a**) Sagittal T1-weighted image shows reduced T1 signal intensity with a lower-intensity central linear component at the L3 vertebral body from marrow oedema and the fracture plane. (**b**) T2-weighted fat-suppressed image displays corresponding increased signal intensity at L3 due to marrow oedema

Laboratory Investigations

Routine pre-procedural laboratory investigations should screen for infection, coagulopathy and metabolic abnormality. The use of additional investigations is dictated by patient history and practitioner discretion and may include electrocardiography or chest radiographs.

The Procedure

Procedure Materials

Vertebral augmentation needles are typically hollow and straight and are available in diamond-shaped, single-bevelled

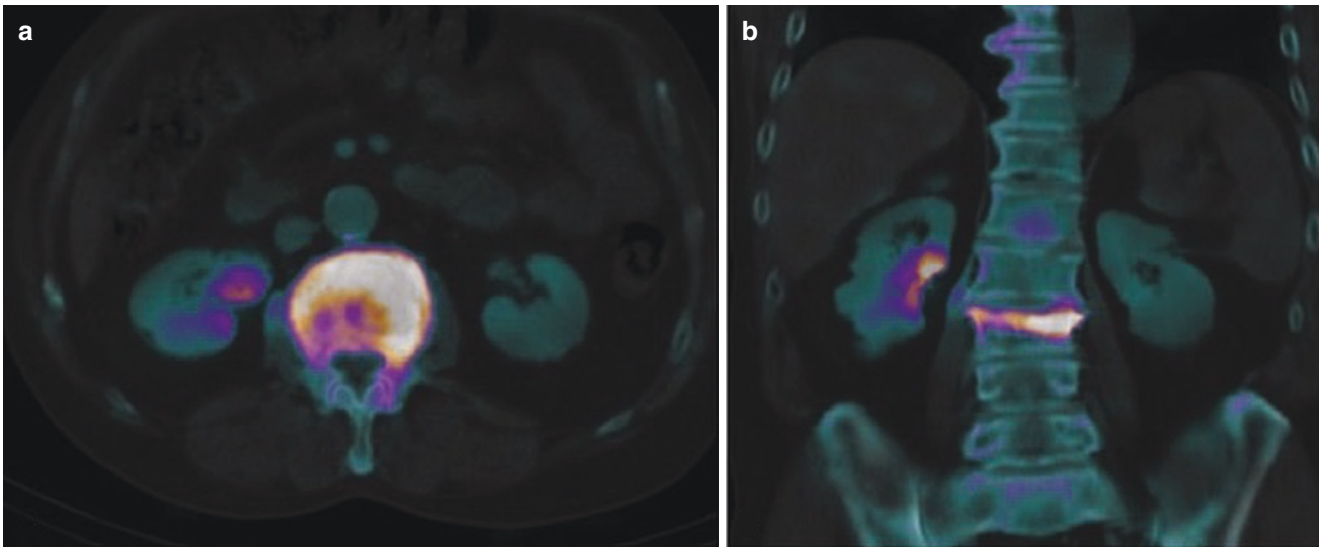

Fig. 26.3 Nuclear scintigraphic bone scan with single-photon emission computed tomography correlation for the clinical case described utilized to assess the L3 vertebral compression fracture, axial (**a**) and coronal (**b**) views. There is increased uptake of radioactive tracer at the L3 vertebral body with a linear configuration seen best on the coronal image, consistent with increased osteoblastic activity at the fracture site

or multi-bevelled stylets. Diamond-tip needles offer optimal ease of penetration into cortical bone, while bevelled needles have superior manoeuvrability. Curved needle systems are also available and possess the ability to navigate up to 90°, allowing access to sites that are difficult to reach using straight needles. Balloon kyphoplasty utilizes an inflatable tamp that may be inserted through the needle cannula. While multiple types of bone cement are available, polymethylmethacrylate (PMMA) remains the most common cement utilized.

The procedure room should include equipment for patient monitoring, including electrocardiography and blood pressure monitoring, as well as equipment for cardiopulmonary resuscitation. Pre-procedural imaging should be available in the procedural room. It is important to ensure prompt access to MRI and CT facilities in the uncommon event of complications during the procedure.

Fill Materials

PMMA is the most widely used bone cement for the treatment of osteoporotic and neoplastic VCFs, although numerous types of cement are commercially available [12]. PMMA preparation involves combining a powdered polymer with a liquid monomer, which results in thickening of the cement [13]. The polymerization of PMMA is an exothermic reaction, resulting in increased cement temperatures of up to 80–120 °C. These temperatures may exert a cytotoxic effect on tumour cells. However, in the event of cement extravasation, it may damage healthy tissue [12].

Alternative cements include composite and calcium phosphate cements; both of these types have high biocompatibility. However, composite cements have low viscosity that can lead to increased leakage risk, and calcium phosphate cements are limited by higher cost and lower radio-opacity [12, 14].

Preparation of the PMMA should take place after final placement of the needle(s), though experienced operators may prefer to have a second person prepare in parallel. The appropriate consistency for injection should be similar to toothpaste. The appearance should be matte; any 'glossy' shine indicates that the cement is too dilute for use. A 'drip' test is recommended, whereby the cement should ball up at the end of the needle and not drip downwards [15]. Working time for the cement is typically 10–20 minutes, but this varies depending on temperature and specific preparation. Delivery systems vary from 1 mL syringes with a spatula to specialized delivery systems. For optimal control of delivery combined with minimal exposure to radiation, the authors recommend a screw-syringe injector with long and flexible delivery tubing [16].

Image Guidance

Vertebral augmentation is typically performed with fluoroscopic guidance. High-quality fluoroscopy allows real-time, continuous monitoring of needle positioning and cement injection. Fixed fluoroscopic equipment is recommended over mobile C-arms due to higher image quality and lower risk of radiation exposure to the patient and practitioner. Biplane fluoroscopy (two perpendicular

image detectors utilized simultaneously) is recommended, as it allows swift oscillation between imaging places without needing to move equipment or realign the projection. Image guidance strategies may be anteroposterior (AP) or 'down-the-barrel' (end-on). For the latter strategy, ipsilateral oblique rotation of the image intensifier places the needle tract and fluoroscopy beam parallel to each other. CT is a potential adjunctive tool for image guidance, particularly for the detection of small cement leaks due to its superior contrast resolution. However, it does not allow real-time monitoring of needle placement or cement injection [17, 18].

Sedation and Anaesthesia

Most vertebral augmentation procedures are performed under a combination of moderate conscious sedation and local anaesthesia although some operators continue to prefer the use of general anaesthesia. Moderate sedation allows the patient to give feedback (such as worsening pain or neurologic symptoms) that may alert the practitioner to complications. Local anaesthetic, typically lidocaine or bupivacaine, is infiltrated to the skin, subcutaneous tissues and periosteum along the needle tract and bone entry point. The patient may experience additional discomfort during injection of the PMMA cement; intravenous analgesia may be required in these cases. General anaesthesia is used in rare cases where conscious sedation is contraindicated, such as in those with severe pain, high requirements for narcotic analgesia or the inability to tolerate prone positioning for prolonged periods. All cases require continuous cardiopulmonary monitoring with blood pressure measurements, electrocardiography and pulse oximetry. Patients with significant cardiac or pulmonary disease may require evaluation by an anaesthesiologist to determine if additional monitored anaesthetic care is necessary. In all patients, fasting from food and drink is required for at least 6 hours prior to vertebral augmentation.

Positioning

Vertebroplasty and kyphoplasty of the thoracic and lumbar spine are typically performed in the prone position. It is acceptable to allow the patient to place themselves in a prone oblique position should it improve comfort during the procedure. Analgesia should be considered prior to positioning, as transfer onto the procedural table may be painful. Care should be taken when positioning the elderly or those with advanced osteoporosis to avoid new fractures. Cushion support is applied under the lower abdomen and upper chest. This allows clear access to the spine, reduces kyphosis and extends the fractured vertebral segments to widen fracture clefts and permit cement penetration. The patient's arms should be placed towards the head, remaining out of the path of the fluoroscope beam.

Antibiotic Prophylaxis

Antibiotic prophylaxis is typically used for vertebral augmentation procedures, although there is little data to support or oppose its routine use [19]. Infection is a rare complication of vertebral augmentation, with only a few sporadic cases reported in the literature. However, given the potential risks of serious spinal infection [20], most practitioners elect to use prophylactic antibiotics. Standard regimens include cefazolin (1–2 g) or clindamycin (600–900 mg) in the case of penicillin allergy.

Needle Placement

The vertebral augmentation procedure involves making a small incision in the back and advancing the needle through the subcutaneous tissues and into the target vertebra. To prevent the needle passing into the spinal canal or neural foramen, it is crucial to maintain the needle trajectory lateral to the medial cortex and superior to the inferior cortex of the pedicle. This lowers the risk of spinal cord or nerve root injury. Particularly in the case of a unipedicular approach, the final needle position should ideally be as close to midline as possible, with the final aim being a midline spread of cement across the vertebral body.

For augmentation of the lumbar and thoracic spine, the needle may be placed via a transpedicular or parapedicular approach (Fig. 26.4). The transpedicular approach involves directing the needle from the posterior surface of the pedicle, through the length of the pedicle, then into the vertebral body. Taking this long intraosseous pathway lowers the risk of injury to surrounding tissues. However, due to the pedicle shape, it may be difficult to obtain a midline position of the needle. The parapedicular approach may allow a more medial needle placement and is useful when treating small pedicles, such as in the thoracic spine. In this approach, the needle is advanced along the lateral surface of the pedicle. It penetrates the pedicle along its path or penetrates the vertebral body at its junction with the pedicle.

Procedures may be performed with a single unilateral needle (unipedicular) or bilateral needles (bipedicular). Typically, a unilateral approach is sufficient to achieve midline placement. However, if midline positioning of the needle is difficult, a second system on the contralateral side may be placed. No significant difference in clinical outcome between unipedicular and bipedicular approaches has

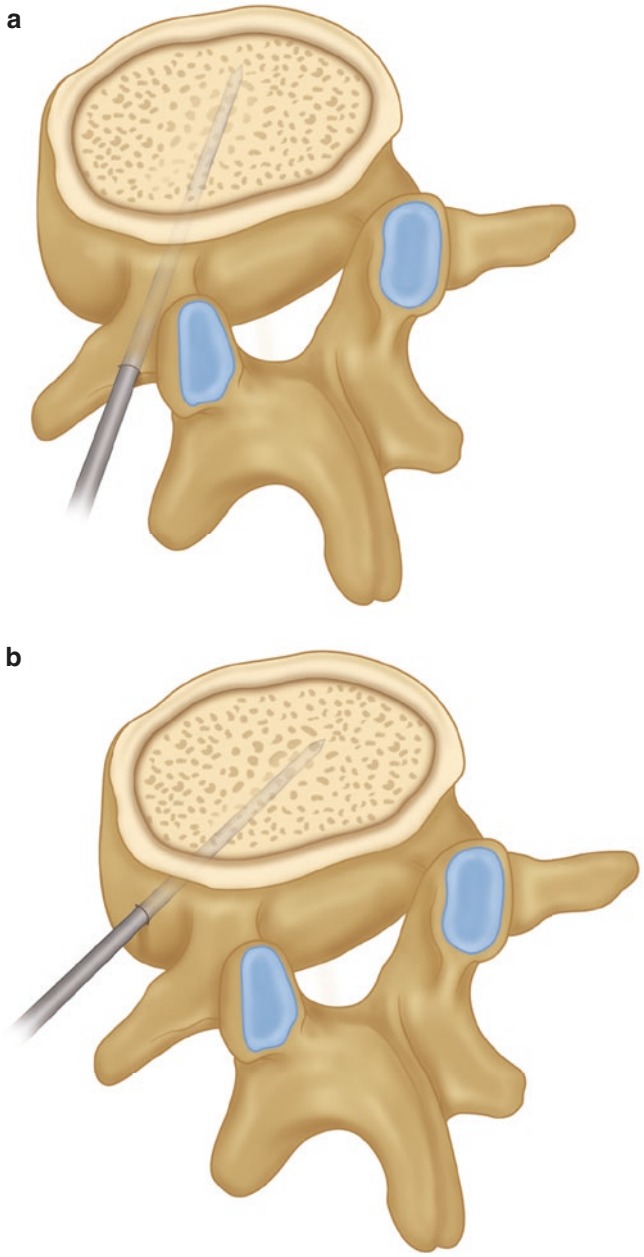

Fig. 26.4 Transpedicular and parapedicular approaches to the vertebral body for the clinical case described. (**a**) The transpedicular approach takes the needle from the posterior surface of the pedicle, through the pedicle's length, and into the vertebral body. (**b**) The parapedicular advances the needle along the lateral surface of the pedicle and penetrates the vertebral body at its junction with the pedicle. This approach may achieve a more medial position of the needle when treating smaller pedicles

been reported. Each approach has advantages [21]. A unipedicular method typically involves a reduced procedure time and lower rates of cement leakage [22]. The main benefit of a bipedicular method is the ability to inject greater cement volumes [23, 24] and potential biomechanical advantages.

Needle Insertion

- Firstly, the fluoroscopy image detector should be rotated to a true AP position by aligning the spinous processes at midline between the pedicles (Fig. 26.5). In this position, the vertebral body is visualized with a superior and inferior end plate, and the pedicles appear ovoid in shape. The pedicles are centred within the margins of the vertebral body by making adjustments in the craniocaudal angulation. The lateral fluoroscopic view is useful in determining the necessary craniocaudal adjustment.
- If using the 'end-on' view, the image detected is rotated 20° ipsilateral to the pedicle, which places the medial pedicle cortex in the middle third of the vertebral body. The needle is centred in the circle formed by the pedicle cortex and should appear as a dot.
- Planning the needle trajectory and predicting the ultimate route allows for alterations to be made as the needle is injected. For transpedicular needle placement, target the lateral margin of the pedicle. The entry position of the needle is the 3 o'clock position of the right pedicle or the 9 o'clock position of the left pedicle. The optimal entry position for a parapedicular approach is just lateral to the 3 or 9 o'clock position.
- The skin is thoroughly anaesthetized along the expected needle pathway, using subcutaneous local anaesthetics via a 22-gauge needle. A small vertical incision is made, with its location decided based on vertebral level and procedural approach.
- The needle (typically an 11- or 13-gauge diamond-tip stylet, sheathed in a cannula) is advanced to the bone surface. Location of the needle should be confirmed when bone is contacted. The needle is then advanced into the vertebral body. The entire needle trajectory is extrapolated during initial access to achieve optimal final needle position (Fig. 26.6). In soft osteoporotic bone, the needle may pass through with ease and can usually be advanced with a drilling motion and controlled forward pressure. In non-osteoporotic bone, an orthopaedic mallet may be utilized.
- If using the 'end-on' view, the needle should be kept as a dot during placement of the needle through the pedicle. It should stay lateral to the medial pedicle cortex until it has advanced through the entire pedicle on the lateral view.
- The diamond-tip needle stylet is optimal for initial needle placement into the pedicle. Once in the vertebral body, the needle may be replaced with a bevel-tipped stylet for improved manoeuvrability. Using the lateral projection, the needle is advanced to the anterior third of the vertebral body. Prior to cement injection, the final needle position should be confirmed on lateral and AP views. If the needle is anterior to the posterior margin of the vertebral body, the spinal canal has been safely cleared.

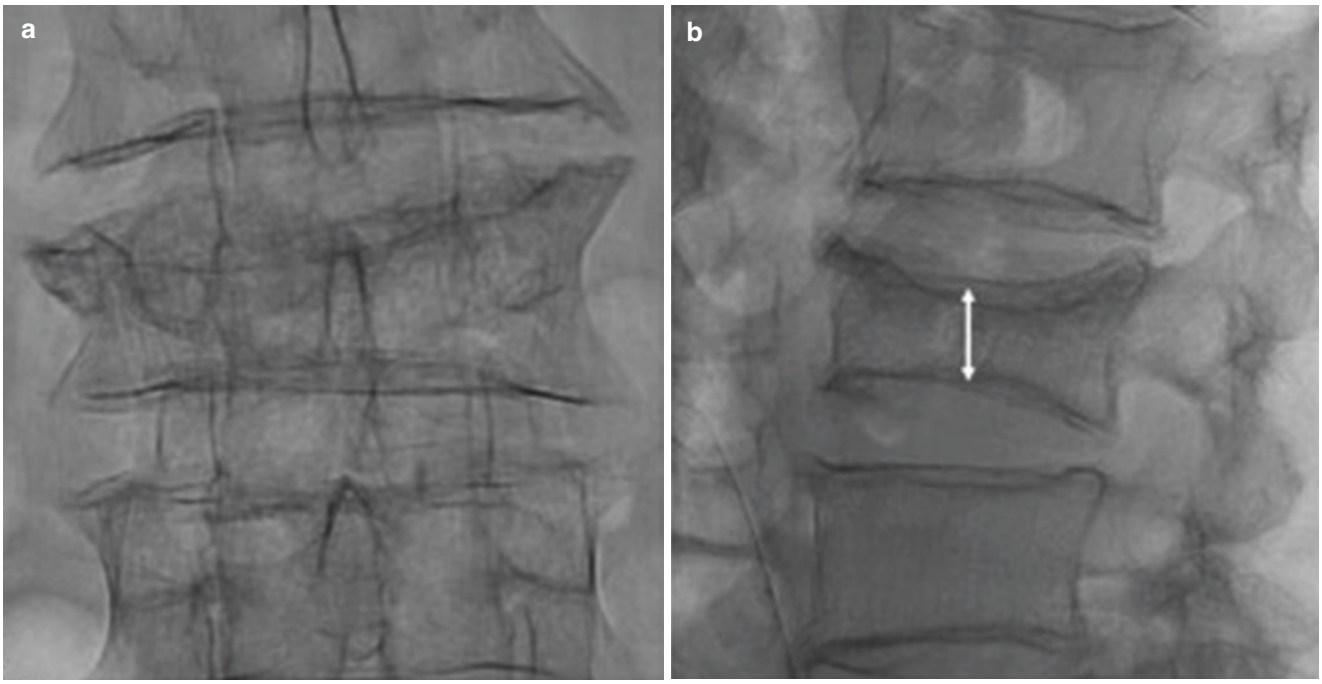

Fig. 26.5 (**a**) Anteroposterior (AP) and (**b**) lateral fluoroscopic images prior to L3 vertebroplasty for the clinical case described. Note the central loss of height demonstrated in the L3 vertebral body (white arrow)

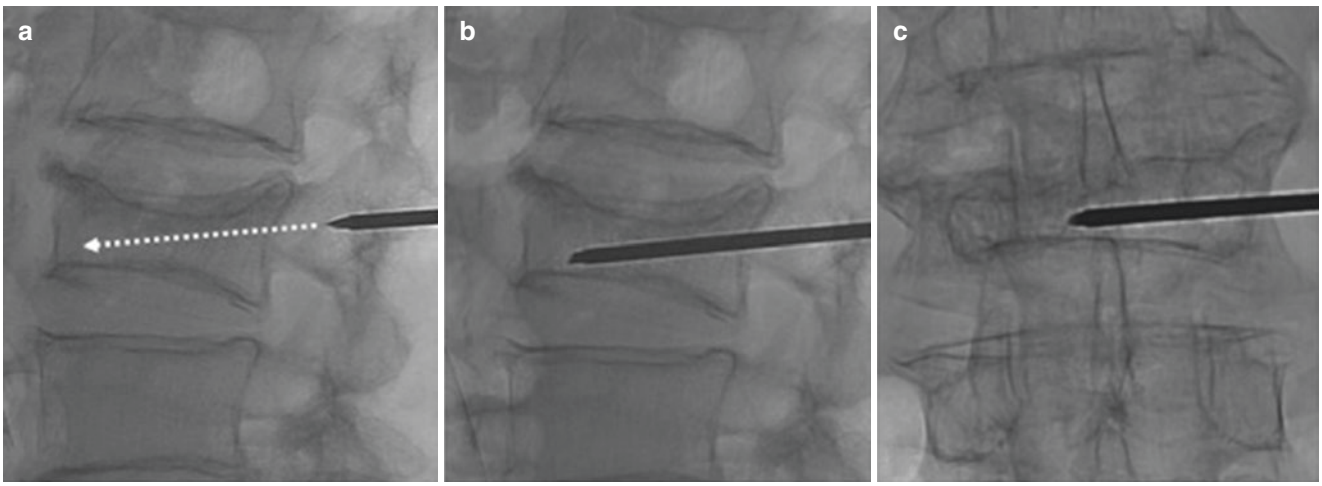

Fig. 26.6 Needle trajectory for a unilateral transpedicular approach in the lumbar spine for the clinical case described. (**a**) Lateral fluoroscopic image of the vertebral body prior to vertebroplasty. The entire needle trajectory is extrapolated during initial transpedicular access to achieve optimal final needle position (dotted arrow). (**b**) The needle is advanced into the vertebral body. (**c**) Anteroposterior fluoroscopic showing final needle position at midline

Vertebroplasty

Following needle placement, the needle stylet is removed from the needle track. The cannula is filled with saline to prevent injecting air and causing air embolism. The delivery system is connected to the needle. Once cement is at optimal consistency for use, it is injected. A slow pace of injection with continuous fluoroscopic monitoring is vital to avoid causing extravasation of cement into the central canal. The risk of extravasation may be higher at the beginning of injection, when the cement is least viscous. If cement leakage into a vein is detected, the procedure should be paused to allow the cement to solidify, and then injection may be recommenced to see if cement passes safely within the vertebral body. If new pain is reported by the patient, the procedure should be ceased while additional imaging views are obtained.

Volume of Injected Cement

The optimal volume of cement to inject is a matter of debate. In theory, more complete filling restores biomechanical strength and height of the vertebral body. However, lower-volume injections have inherently lower risk of cement leakage [22, 25]. Smaller volumes of cement have been reported to produce similar clinical outcomes to larger-volume injections in the principal goal of pain relief. Conversely, positive results from the recent VAPOUR trial achieved by injecting larger volumes (average 7.5 mL) have supported more complete filling [26]. In the absence of any clear consensus on this topic, the goal should be maximum cement filling with careful monitoring to ensure the injection is ceased prior to complications occurring. We recommend ceasing injection when cement reaches the posterior quarter of the vertebral body on the lateral view or when cement passes beyond the marrow space. The end goal of injection is a column of cement extending across midline from one pedicle to another on the AP projection (Fig. 26.7). It is important to avoid leaving a 'tail' of cement at the conclusion of injection. This can be achieved by reinserting the needle stylet to dispense any cement that remains in the cannula.

Kyphoplasty

Kyphoplasty involves additional steps of creating a cavity. Typically, this occurs following placement of the needle when a balloon tamp is inserted and inflated to create a cavity for cement injection. After final needle position is reached (by either a unipedicular or bipedicular approach), the cannula should be pulled back to the posterior aspect of the vertebral body. The needle stylet is removed, and the balloon tamp is inserted through the cannula. The tamp is then slowly inflated with contrast medium. An inflation syringe with a manometer is attached to the balloon, and the inflation is carefully monitored by the pressure transducer and by fluoroscopy. Inflation of the balloon continues until the system reaches maximal pressure or balloon volume, or until further inflation causes patient discomfort. The balloon is deflated and removed, leaving a cavity within the bone.

The cavity allows for injection of cement that is theoretically more viscous than with vertebroplasty. Sufficient time must be allowed for the cement to lose its 'shiny' appearance and reach a doughy consistency. Cement injection in kyphoplasty can occur via injector systems or manual bone filler devices. Following connection of the delivery system to the cannula, the cement is infiltrated slowly under continuous fluoroscopic monitoring. The cavity is filled with cement, and the cement then fills beyond the volume of the inflated balloon tamp and into the surrounding bone trabeculae (Fig. 26.8).

Post-procedural Care

Following removal of the needles, manual pressure should be applied to the entry sites for 5–10 minutes to promote haemostasis. Transfer to the stretcher using logroll manoeuvres can typically occur immediately, except in the case of vertebral cleft within the fracture, whereby the patient should remain prone for 15–20 minutes before transfer. Once in recovery, the patient should remain

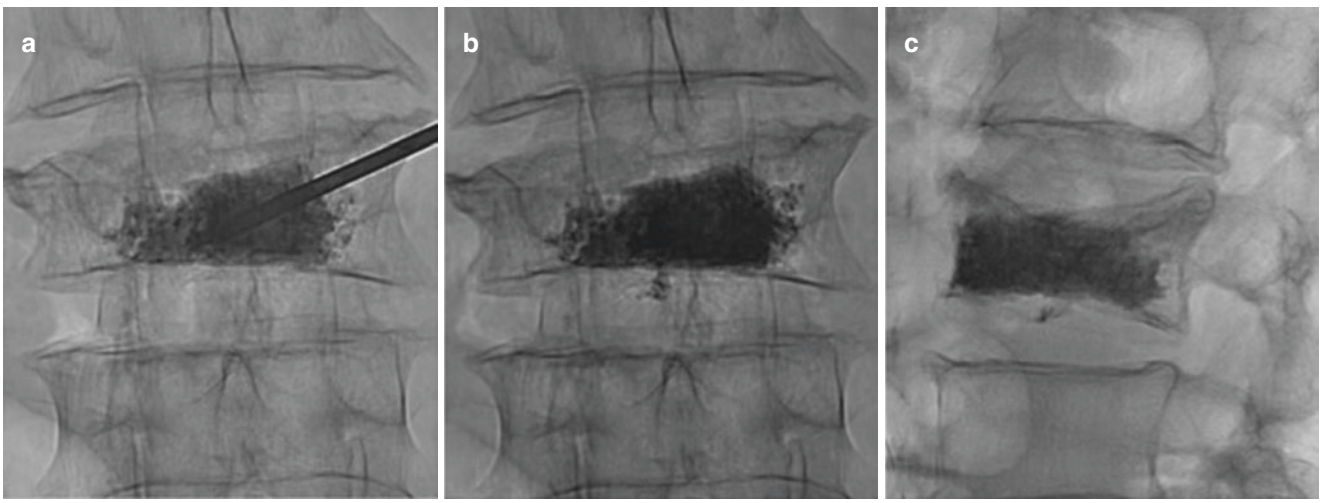

Fig. 26.7 Fluoroscopic images showing cement injection in vertebroplasty for the clinical case described. (**a**) Polymethylmethacrylate cement is slowly infiltrated into the vertebral body. (**b**) Cement forms a column extending across the midline of the vertebral body. (**c**) On the lateral view, cement fills the anterior three-quarters of the vertebral body. No posterior cement leakage has occurred

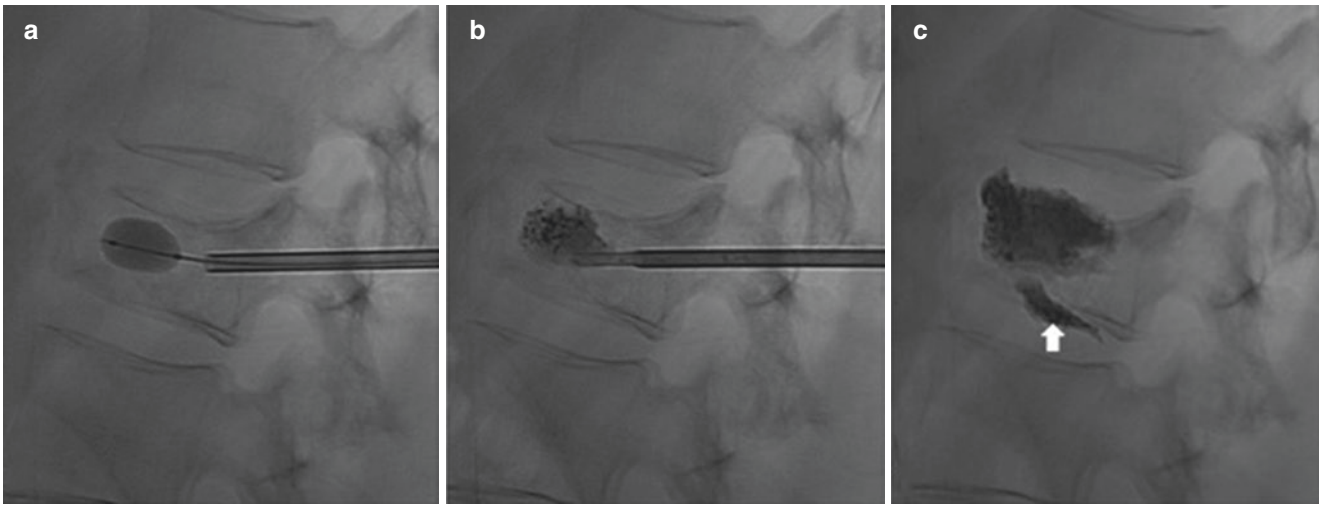

Fig. 26.8 Lateral fluoroscopic images demonstrating cavity creation with kyphoplasty at L1. (**a**) The inner stylet of the unipedicular needle has been removed from the needle track. The balloon tamp has been introduced into the needle track and inflated to create a cavity within the vertebral body. (**b**) Cement is injected into the cavity. (**c**) The final result of cement injection. Note that cement fills the cavity and extends beyond it to fill adjacent trabecular bone. Minor disc leakage of cement is noted (white arrow), but no posterior or venous leakage has occurred

supine; during the first 2 hours, the patient should remain flat, and then the head of the bed is inclined 30° for 1 hour. Pain over the first few hours to days is usually procedure-related and manifests as moderate discomfort over the procedural site. This pain can be relieved by acetaminophen and will typically resolve over 24–72 hours. Persistent severe pain, new pain of a different character, signs of spinal canal stenosis or altered bowel or bladder function should prompt immediate imaging with CT to evaluate for cement leakage into the spinal canal or neural foramina. Delayed pain may indicate repeat vertebral fracture, and MRI should be performed. However, caution should be taken in interpreting any demonstrated bone marrow oedema, as this may be a normal MRI finding for up to 6 months after vertebral augmentation [27].

Follow-up in outpatient clinics should occur after 3–4 weeks, at which time the practitioner should review the durability of pain relief and the presence of any concerning features that might indicate complications. Management of the underlying cause of fracture should be emphasized, including treatment of osteoporosis with calcium and vitamin D supplementation, as well as medical treatment with bisphosphonates or other targeted therapies [28].

Special Considerations

Vertebra Plana

Vertebra plana involves the near-complete loss of vertebral body height. Safe placement of the vertebral augmentation needle becomes challenging in these cases. In vertebra plana, a 'bow-tie' configuration is typically seen, in which the centre is maximally compressed. This usually necessitates a more lateral needle position with the placement of bilateral needles [29], and only a small amount of cement is typically necessary to achieve pain relief [30].

Multilevel Treatment

Frequently, a patient with osteoporosis or spinal neoplasm may have multiple VCFs that would benefit from vertebral augmentation that in theory could be treated in a single session. However, multilevel treatment has limitations and risks, including an extended operative time (and the associated risks of lying prone), potential PMMA toxicity or increased post-procedural pain due to placement of multiple needles. While no clear guidelines exist for a maximal number of levels to treat, there have been two deaths reported in patients undergoing augmentation at more than eight levels [31]. We recommend a maximum of three levels at a single session [32, 33].

Clinical Outcomes of Vertebral Augmentation

Evidence for Efficacy

The precise mechanism of vertebral augmentation pain relief is unknown but is thought to involve biomechanical stabilization of fracture segments or the direct cytotoxic or thermal effects of PMMA [34]. Debate persists regarding the efficacy

of vertebral augmentation and its utility in clinical practice. Several large randomized controlled trials (RCTs) have compared vertebral augmentation procedures to conservative therapy or sham procedures. All currently published trials have limitations, yet the most recent high-quality evidence suggests that vertebroplasty and kyphoplasty are safe and effective pain relief options for osteoporotic and neoplastic VCFs.

The first RCT on vertebral augmentation, the 2007 VERTOS trial, compared vertebroplasty to medical management for osteoporotic VCFs [35]. In total, 34 patients were enrolled, with the following inclusion criteria: severe back pain despite at least 6 weeks of medical management, fracture aged <6 months, focal tenderness on examination and bone marrow oedema on magnetic resonance imaging (MRI). Patients were randomized to receive vertebroplasty ($n = 18$) or medical management ($n = 16$). The primary outcomes were back pain (as measured with visual analogue scale (VAS) and analgesic requirements at 1 day and 2 weeks post-procedure. Significant pain relief was observed in the vertebroplasty group at 1 day post-procedure, although this outcome was not maintained at the 2-week endpoint. Analgesic use was also reduced in the vertebroplasty arm, as were secondary outcomes of disability and quality of life scores. VERTOS was limited by its small size, lack of blinding, and lack of long-term follow-up.

Two RCTs with a total of approximately 200 patients were published in the New England Journal of Medicine in 2009, comparing vertebroplasty to sham procedure. The findings of these trials contrasted with earlier data, finding no clinical benefit from vertebroplasty. The Investigational Vertebroplasty Safety and Efficacy Trial (INVEST) randomized 131 patients to receive vertebroplasty ($n = 68$) or a sham procedure involving the injection of local anaesthetic onto the periosteum of the pedicle [36]. The inclusion criteria, which were broadened following low initial recruitment, included the following: age >50 years, pain intensity ≥3/10 on numerical rating scale (NRS) and fracture aged <1 year. Advanced imaging was not required for study inclusion, but fractures of indeterminate age were confirmed on MRI or bone scan. The INVEST trial was limited by the inclusion of fractures up to 1 year in age. The sham procedure, which involved the injection of anaesthetic, may have led to the relief of pain arising from adjacent structures such as the pedicles or soft tissues.

The second 2009 sham-controlled RCT was published by Buchbinder et al. Inclusion criteria included back pain of <1 year in duration with fracture confirmed on MRI [37]. In total, 78 patients received either vertebroplasty ($n = 38$) or sham procedure ($n = 40$). The sham procedure involved the insertion of a blunt-stylet needle onto the lamina, with light tapping of the vertebral body. There was no significant difference between groups in pain scores, disability or quality of life, at any time point (1 week, 3 months or 6 months). As with INVEST, the Buchbinder trial was limited by the inclusion of fractures up to 12 months old (only 32% of patients had fractures aged <6 weeks) and the lack of a physical examination component.

Several authors published responses to these trials, raising concerns about the broad inclusion criteria and lack of long-term follow-up [38–40]. The INVEST authors responded by publishing a long-term follow-up of the trial cohort to 12 months [41]. They found modest pain relief in the vertebroplasty group at 12 months, but no difference between groups in disability measures. Concerns were also raised about the potential for the INVEST sham procedure to have confounded results by acting as an 'active control' [42, 43].

In 2010, the VERTOS II RCT compared vertebroplasty with medical management [44]. Inclusion criteria were more stringent than previous trials: fractures aged ≤6 weeks, pain intensity ≥5/10, localized tenderness on physical examination and bone marrow oedema demonstrated on MRI. A total of 202 patients were enrolled and randomized equally into vertebroplasty and conservative arms. Vertebroplasty resulted in significant reductions in back pain at 1 month, and this effect was sustained at 1-year follow-up. Quality of life (as measured by several standardized questionnaires) was also reduced in the vertebroplasty arm. The key limitation of this trial was a lack of blinding. The same authors have designed VERTOS IV, a multicentre RCT that will compare vertebroplasty with a sham procedure while utilizing similar strict inclusion criteria to VERTOS II. Results from this trial are forthcoming.

The 2016 Vertebroplasty for Acute Painful Osteoporotic Fractures (VAPOUR) RCT compared vertebroplasty to a sham procedure, while focusing on more rigorous methodology to address limitations of prior trials [26]. Inclusion criteria included severe pain of ≥7/10 intensity (compared with ≥3 in INVEST and ≥5 in VERTOS II), fractures aged ≤6 weeks and fractures imaged with MRI or single-photon emission CT (SPECT). The 120 enrolled patients were divided into vertebroplasty ($n = 61$) or sham procedure arms ($n = 59$). At 2 weeks post-procedure, significant pain relief was achieved in the vertebroplasty group (pain scores reduced to ≤4/10 in 44% of patients), and this effect was durable at 1 and 6 months. Vertebroplasty also resulted in improved functional capacity, reduced analgesic use and increased vertebral body height.

There is less available data on vertebroplasty for neoplastic VCFs. A 2011 systematic review reported results from 30 studies (987 patients), finding that vertebroplasty resulted in pain reductions ranging from 20.3% to 78.9% by 1 month and 47% to 87% by 6 months [45]. In 2016, a systematic review reported results from 2545 patients in 78 studies evaluating vertebroplasty for multiple myeloma, spinal haemangioma or spinal metastases [46]. Overall, vertebroplasty

resulted in rapid pain relief (within 48 hours), reduced disability and decreased narcotic analgesic requirements.

The 2009 Fracture Reduction Evaluation (FREE) trial was a large multicentre RCT that compared kyphoplasty to medical management for VCFs [47]. While osteoporotic and neoplastic VCFs were included, 96% of fractures were related to osteoporosis. In total, 300 patients (149 receiving kyphoplasty; 151 receiving conservative therapy) were enrolled based on the following inclusion criteria: back pain intensity of ≥4/10 for ≤3 months, localized tenderness on physical examination and fractures confirmed on MRI with minimum 15% height loss. At 1 month, kyphoplasty resulted in significantly improved quality of life, as measured by the short-form (SF)-36 physical component summary scale. This effect was sustained at 3 and 6 months, but not at 12 months. Kyphoplasty also resulted in reduced back pain intensity at 1 week and 12 months and reduced analgesic use at 1 and 6 months. At 2-year follow-up, there remained a significant reduction in back pain in the kyphoplasty group, although no difference was seen between groups in SF-36 scores or disability outcomes.

The Cancer Patient Fracture Evaluation (CAFE) trial aimed to compare kyphoplasty with medical management for malignant VCFs [48]. The inclusion criteria were back pain intensity ≥4/10, Roland-Morris Disability Questionnaire (RMDQ) scores of ≥10 and fracture demonstrated on plain spinal radiograph or MRI. The 134 enrolled patients were randomized to receive kyphoplasty (n = 70) or conservative management (n = 64). At 1 month, RMDQ scores were significantly reduced in the kyphoplasty group (difference between groups –8.4 favouring kyphoplasty). Kyphoplasty also resulted in reduced back pain intensity, decreased narcotic analgesic requirement and improved SF-36 scores. The CAFE trial is potentially limited by a lack of histological confirmation of fracture aetiology. Despite including only patients with spinal neoplasm, it was unknown whether the VCF was caused by the neoplasm or by another concurrent cause such as osteoporosis or radionecrosis. The trial was also limited by lack of blinding.

In 2014, the KAVIAR trial aimed to directly compare vertebroplasty and kyphoplasty in the management of osteoporotic VCFs [49]. Patients with acute (≤6 months) painful VCFs were included, with all fractures confirmed by bone marrow oedema on MRI, increased uptake on bone scan or vertebral height loss on CT or plain radiograph. In total, 381 patients received vertebroplasty (n = 190) or kyphoplasty (n = 191). Despite early termination of the trial due to low enrolment, the trial found that the two procedures were similar in long-term pain relief and disability improvements. The safety profile was also similar, although vertebroplasty led to shorter procedural time and kyphoplasty caused lower rates of cement leakage.

Evidence for Safety

Vertebroplasty and kyphoplasty carry a low risk of serious complications, although major adverse events have been reported in literature [50–53]. Across major RCTs of augmentation for osteoporotic fractures, the rate of major adverse events is approximately 1% with no procedural mortalities reported. Although rare, the potential complications that have been reported in literature include nerve or spinal cord damage, pulmonary embolism resulting from cement embolization, allergic reactions to PMMA (including one case of death from anaphylaxis), infection, haematoma or new fracture to vertebrae or ribs [31, 54–59].

The only complications associated with vertebroplasty that occurred in the VERTOS II trial were one case of asymptomatic PMMA leakage into a segmentation pulmonary artery, and one urinary tract infection. In INVEST, one case of osteomyelitis was reported in a patient who did not receive antibiotic prophylaxis, while Buchbinder et al. reported one thecal sac injury. In the VAPOUR trial, the only major complications in the vertebroplasty group were one case of pre-procedural respiratory arrest following sedation and one humeral fracture sustained during transfer onto the procedural table. Two cases of vertebral collapse occurred in the VAPOUR conservative arm; both cases resulted in spinal cord compression, and one patient remained paraplegic. The FREE trial reported only one case of urinary tract infection and one soft tissue haematoma.

The primary source of ‘complications’ from vertebral augmentation is the leakage of cement outside the vertebral body. While this is a relatively common occurrence, the vast majority of leaks are asymptomatic and result in no significant issues [28, 31]. In the VERTOS II trial, 72% of treated vertebrae displayed leakage on post-procedural CT. All leaks were asymptomatic, and the majority occurred into discs or into small segmental veins, with no leakage into the spinal canal. VAPOUR reported a cement extravasation rate of 34% when assessed with plain radiographs.

The risk of cement extravasation is theoretically lower in kyphoplasty, since cement is injected into the cavity created by balloon inflation. Only 27% of treated vertebrae in the FREE study demonstrated leakage on fluoroscopy and plain radiography; all were symptomatic. Of the 70 patients in the CAFE trial, only two cases of leakage were reported. One patient remained asymptomatic, while the other case was associated with fracture in an adjacent vertebral level on the first day post-procedure.

It is unlikely that the risk of adjacent level VCF is higher following vertebral augmentation than medical management. Zhang et al. compared the incidence of new VCFs following augmentation and conservative management in a 2017 meta-

analysis of 12 studies (1328 patients) [60]. There was no significant difference between the two arms in total new or adjacent VCFs. Similar meta-analyses were performed by Anderson et al. and Shi et al., which both found no differences between vertebral augmentation and conservative cohorts with regard to new fractures [61, 62].

Summary

Vertebroplasty and kyphoplasty are safe and effective treatment options for osteoporotic or malignant VCFs that persist despite conservative therapies. With meticulous attention to technique, successful outcomes in pain relief, mobility and functional capacity may be achieved in the correct patient population. While the data for vertebral augmentation has evolved over time, there is recent high-quality evidence that supports its use. The risk of complications from vertebral augmentation is very low, with no increase in the risk of subsequent VCFs.

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Fluoroscopic Images of Spinal Procedures and Radiation Safety

27

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Key Points

- Knowledge of the fluoroanatomy of the spine, both of the visible and non-visible structures, is fundamental to properly and safely performing spine interventions.
- Axial back pain is treated by interventions targeting the elements of the spinal axis, vertebra, intervertebral discs, joints, and/or myofascia.
- Radicular pain caused by neural irritation or compression close to the neuraxis is treated by epidural injection or neuromodulation.
- The pain maintained by the sympathetic nervous system can be treated by targeting ganglia or nerve tracks that exist near the spinal axis.

Introduction

The treatment of spine-related pain disorders is facilitated by fluoroscopy. Application of this technology for interventional treatment of pain requires understanding of both the observable radiopaque fluoroanatomy and the relevant non-radiopaque anatomy. Fluoroanatomical representations of the most common interventional pain procedures near the spine are presented here.

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Fluoroscopy

Fluoroscopy is the use of X-radiation (X-ray) in a continuous manner to image structures in motion. It is useful for interventional procedures to enable visualization of a proceduralist's needle, the placement of a device such as a spinal cord stimulator lead, and contrast medium spread to confirm proper needle placement, for example. Absorbed X-rays ionize atoms in tissue. Any dose absorbed can have a detrimental effect on tissue. The degree of radiation absorbed determines the level of detriment. Absorbed dose is measured in joules/kg of tissue which is equivalent to gray (Gy), 0.01 rad equals 1 Gy. Tissue dose accumulation must therefore be monitored during fluoroscopic procedures, and providers should know when the dose to the patient or clinicians in the room approaches substantial, potentially unsafe levels.

Basic understanding of fluoroscopy and the principles of radiation safety can help the provider use fluoroscopy to obtain the needed images efficiently while minimizing the risks. Modern fluoroscopes have the ability to run in several modes. Conventional continuous mode takes 30 images per second. Pulsed mode uses a lower frame rate to obtain images. These can be taken at 1/2 the speed (15 frames per second), 1/4 the speed, 1/8 the speed, and so on. As long as the real-time image quality is acceptable, the fractional modes are preferred as they significantly reduce the overall X-ray dose.

Fluoroscopes, such as the C-arm commonly used by interventional pain proceduralists, obtain their images by sending X-radiation from an X-ray tube (source) toward the image receptor. Between the source and receptor is the patient's body part. High beam energy, measured as peak kilovoltage, passes through the patient and is received by the receptor and processed into a digital image. Lower-energy beams are also created by the tube, and if not filtered out, these would be absorbed by the patient entirely and not contribute to the image. So, low-dose beams are commonly filtered before they leave the source in order to lower the patient dose. It is

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recommended to use the highest beam energy (peak kilovoltage) that creates an acceptable image contrast to perform the procedure.

Limiting Radiation Dose to Patients

It is the operator's responsibility to use all available methods to limit patient radiation dose during each procedure and limit or adjust future exposure if a patient is likely to approach a *substantial radiation dose level* (SRDL). Dose to the patient can be limited in several ways (Table 27.1). The beam energy and low-dose beam filtration should be controlled to ensure an acceptable image quality. Pulsed mode and low frame rate (2–7.5) should be set as the preferred default. The procedure imaging should be planned so that the fewest images necessary are taken. Prior images and image sequences should be used as references rather than repeat imaging. Long digital subtraction angiography (DSA) sequences and spot imaging should be limited [1]. Magnification and detail modes should be used sparingly. The image should be collimated to narrow the beam to only the region of interest. The highest radiation intensity is close to the image source, and it drops off at a rate inversely proportional to the square of the distance ($1/d^2$) according to *the inverse square law*. Therefore, the X-ray tube source should be as far away from the patient as possible, and the image receptor should be as close to the patient as possible while still allowing for procedure performance. Sensitive areas of the patient's body should be covered by a lead drape (gonadal shield) if it doesn't interfere with the procedure. The operator and clinician should monitor the fluoroscopy on time and measures of absorbed dose to the patient.

Individual procedures result in small incremental absorbed dose to patients, however, adverse effects of radiation result from cumulative dose over time. Patients may be exposed to other imaging studies or treatments such as computed tomography (CT) or standard diagnostic X-rays or radiation therapy over shorter periods of time that can result in adverse effects. It is prudent to continue to limit X-rays during fluoroscopic interventions. Annual background radiation for an individual in the United States is around 3 mSv per year, with a cumulative lifetime average of about 250 mSv [2]. The effect of cumulative radiation dose below 100 mSv above the background on a patient's health is not significant [2]. See Table 27.2 for units of radiation and their definitions.

Table 27.1 Methods to limit radiation dose during fluoroscopy

For clinicians	For patients
Wear personal protective equipment (PPE) Lead gloves Thyroid shield Vest and apron Eye wear Use barriers Install table curtains Lead lined glasses Monitor exposure Wear dosimetry badges Review cumulative dose reports Adjust body position to minimize exposure dose Stand by the image receptor Do not stand near the fluoroscope tube Fluoroscope (C-arm) Use *pulsed mode* if available Use reference images to reduce need for repeat imaging	Provide personal protective equipment when possible Gonadal shield if it won't interfere with imaging procedure Monitor dose Track dose times for patients Record dose time in the medical record Limit procedures for patients exposed to high cumulative doses, requiring several procedures Fluoroscope (C-arm) Avoid long fluoroscopy runs Use *pulsed mode* if available Use reference images to reduce need for repeat imaging

Limiting Radiation Dose to Providers

Clinicians monitor their cumulative dose by wearing dosimetry badges. These are typically worn on the thyroid shield (neck) or vest pocket (chest) to measure external bodily exposure, and another can be worn under personal protective equipment (PPE). Methods to limit exposure to providers and patients are listed in Table 27.1. The maximal permissible dose (MPD) is the maximum radiation dose a tissue can be exposed to before experiencing side effects (Table 27.3). Annually, the MPD for physicians is 50 mSv. The principle

Table 27.2 Units of radiation exposure

Unit; SI equivalent	Definition
Radiation absorbed dose (rad); gray (Gy)[a] 1 Gy = 100 rad	The amount of energy into the tissue; radiation quantity that results in 1 J/kg deposition
Radiation equivalent man (rem); sievert (Sv)[a] 1 rad = 1 rem = 100 Sv	Occupational exposure

[a]*SI* International System of units

Table 27.3 Maximum permissible dose (MPD) for tissue type

Tissue type	rem	mSv
Whole body	5	50
Eye lens	15	150
Thyroid	50	500
Gonads	50	500
Extremities	50	500

that should be applied when working with fluoroscopy is to employ all methods to keep exposure *as low as reasonably possible* (ALARA).

Flouroanatomy of the Spine

There are 7 cervical vertebrae, 12 thoracic vertebrae, 5 lumbar vertebrae, 5 fused sacral segments that make up the sacrum, and the coccyx. Each vertebral region has distinct morphology observable on X-ray.

Cervical Spine

The first cervical vertebra (C1) is known as the atlas, and C2 is called the axis. These can be seen on fluoroscopy of the cervical spine in the posterior-anterior (PA) view of the face at the level of the jaw (Fig. 27.1). The C2 dens are more easily visualized with the mouth open. In the lateral fluoroscopic view, C2–C5 are easily seen, but C6 and C7 are often partially obstructed by the shoulder. Pulling the arms downward may help improve the image of these lower cervical vertebrae in the lateral view. Notably the vertebral artery passes through the transverse foramen of the transverse processes of C2–C6. The transverse processes and the location of the vertebral artery must be recognized by the proceduralist who is using needles in this vicinity to avoid complications (Fig. 27.1). The lateral cervical spine images demonstrate the long cervical spinous processes, the articular pillar that when aligned with the X-ray forms the shape of a parallelogram, and the vertebral body anterior to this. Ligamentous tissue, intervertebral discs, and muscle are radiolucent. The neuroforamina can be seen in the lateral view.

Thoracic Spine

The C7–T1 juncture between the cervical and thoracic vertebrae can be identified by the articulation of the first rib on T1 (Fig. 27.2). Also in this view are the clavicles attached to the sternum. Thoracic vertebrae are easily identified because at each level they articulate with a rib. The nerve root corresponding to the vertebral body level travels along the caudal aspect of the rib as the intercostal nerve. In the anterior-posterior (AP) fluoroscopic view, it is helpful to identify and adjust the fluoroscope (C-arm) so that the spinous processes are midline. From this perspective the symmetry of the spine can be assessed.

Lumbar Spine

The 5 lumbar vertebrae are large and broad (Fig. 27.3). This region takes much of the body's weight and enables large movements of the spinal axis. As a result, the lumbar spinal

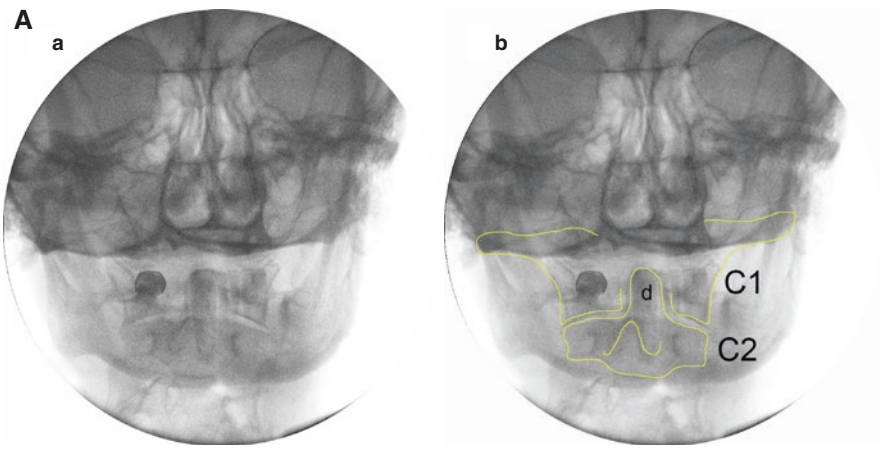


Fig. 27.1 (**A**) Fluoroanatomy of the cervical spine. (**a**) With the patient lying supine, a posterior-anterior (PA) view of the face and superior cervical spine is shown. (**b**) Outlines identify the first cervical vertebra (C1, atlas), second cervical vertebra (C2, axis), and the C2 dens process (d). Notable landmarks in this view are the orbital cavities, the nasal sinuses, the teeth, and the mandible. (**B**) (**a**) Lower cervical and upper thoracic AP image series showing fluoroscopic landmarks important for cervical spine procedures. (**b**) The clavicles (cl) connect to the manubrium of the sternum and appear large because of their proximity to the C-arm image tube on AP imaging with the patient in prone position. (**c**) Also seen are the midline spinous processes (sp), the intervertebral foramen (f), and the first rib (r). C7, T1, and T2 are outlined. (**C**) (**a**) Lateral view of the cervical spine. (**b**) Labelled image showing C1–C6 vertebrae with marker (m) pointing out the articular pillar (p) of C3. Outlines demonstrate the shape of the individual cervical vertebrae and the location of the transverse process (tp) through which the vertebral artery (va) passes. (**c**) An example of a cervical spine image with less clearly definable structures; the person's shoulder (s) partially obscures C5–T1

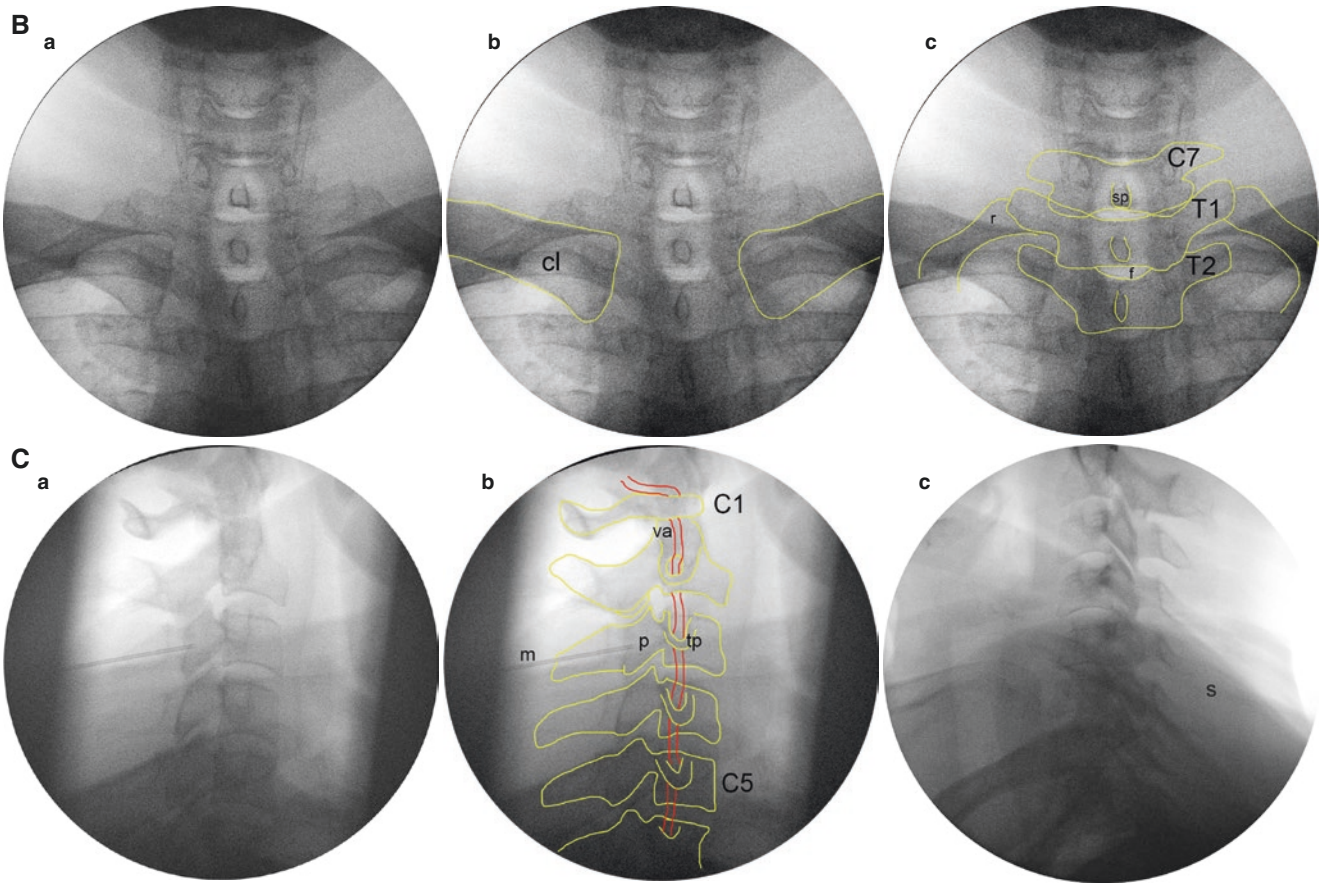


Fig. 27.1 (continued)

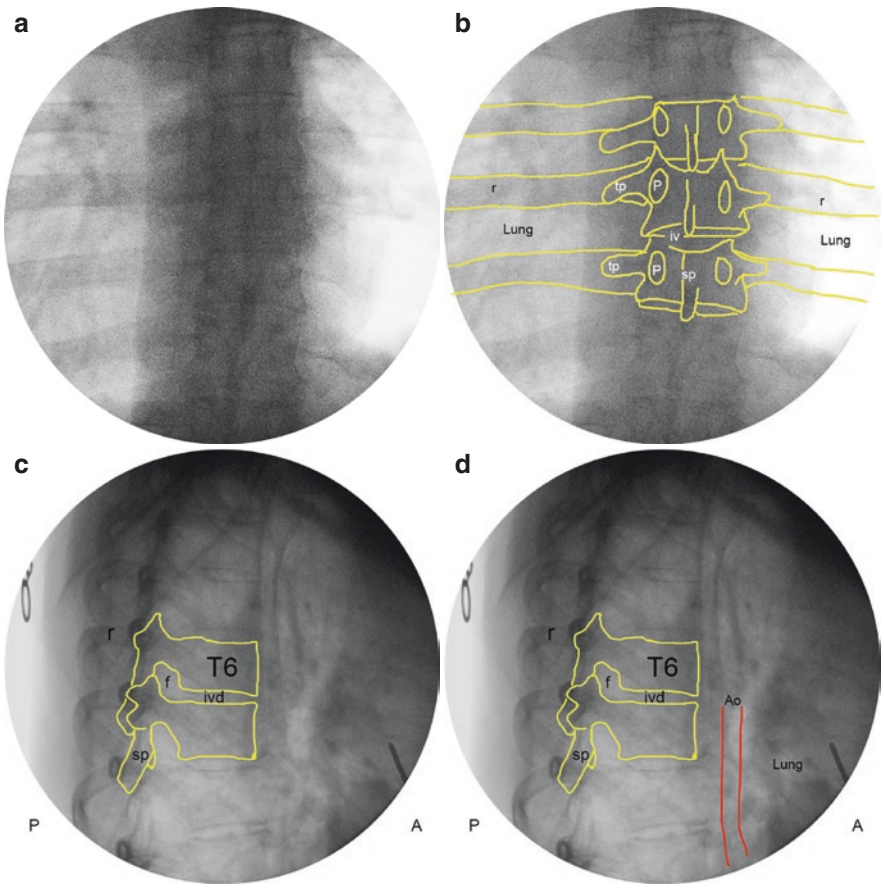


Fig. 27.2 Fluoroanatomy of the thoracic spine. (**a**) PA view of the thoracic spine demonstrating the unique morphology of the thoracic vertebrae. (**b**) Outlined are the relatively long angulated spinous processes (sp), short transverse processes upon which the ribs (r) articulate, and the narrow intervertebral space (iv). Lateral are the lungs. (**c**) Lateral view of the thoracic spine. (**d**) Labelled image showing T3–T9 thoracic vertebrae, the vertebral foramen (f), ribs (r), spinous process (sp), intervertebral disc (ivd), the descending aorta (Ao), and the lung

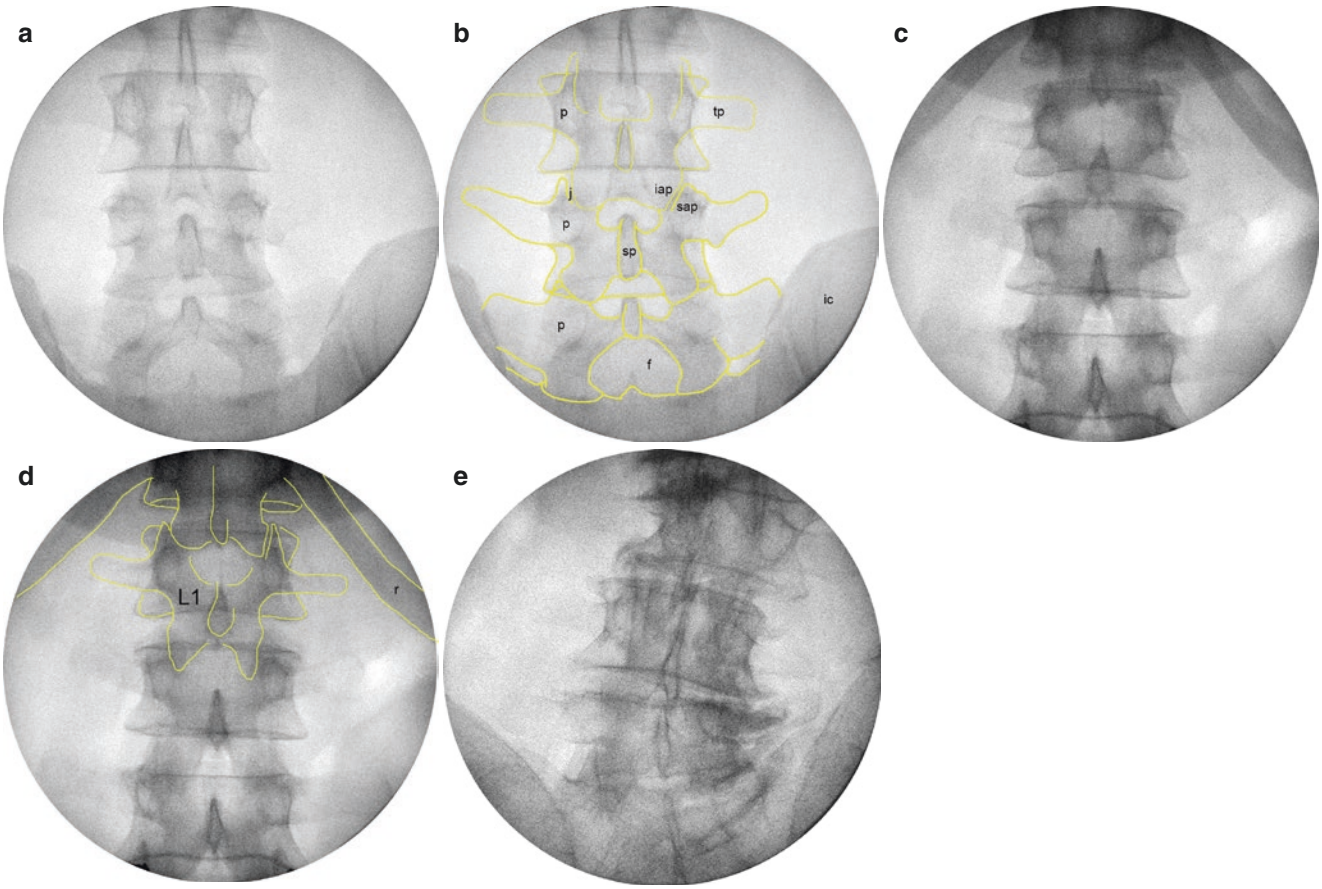


Fig. 27.3 Fluoroanatomy of the lumbar spine. (**a**) The level of the lumbar spine in the AP view can be determined by counting up from the sacrum. (**b**) Here the iliac crests (ic) rise to the level of L4. (**b**) L3, L4, and L5 are outlined to demonstrate the morphology of the lumbar vertebrae. Easily seen at these levels are the long transverse processes (tp), the large spinous processes (sp), the intervertebral foramen (f), the pedicles (p), the superior articular processes (sap), and the inferior articular processes (iap) that make up the facet joints (j). (**c**) L1–L3 shown here can be identified by counting downward from the T12 vertebra (the last vertebral with a rib). (**d**) L1 outlined. Anterior to L1 is the celiac plexus. Lateral to L1–L3 the psoas muscle attaches. (**e**) A lumbar image where the anatomy is less clear in a patient with scoliosis

structures are prone to degeneration. Loss of intervertebral disc height and zygapophyseal (facet) joint arthritis (spondylosis) is commonly observed on fluoroscopic imaging. At the level of L4, the iliac crests are visible in the lateral image field.

Sacral Spine

The sacrum consists of five vertebral segments that ossify and fuse during the first three decades of life (Fig. 27.4).

Axial Back Pain

Axial back pain is pain that originates from the structures that make up the spinal axis and may denote pathology of those structures. These include the vertebral bodies, the zygapophyseal (facet) joints, the intervertebral discs, small nerves that innervate these structures, and the surrounding myofascia. The vertebrae support the body frame and its movements. The facet joints are synovial joints made up of the inferior articular process of the superior vertebra and the superior articular process of the inferior vertebra. The facet joints are innervated by the medial branches of the posterior primary rami of the spinal nerves. Spondylosis (arthritis) or strain on the facet joints can cause pain. Anesthetizing the joints or medial branches, through facet joint injections or medial branch block procedures, can confirm these structures as the source of the pain. Following positive diagnostic tests (the patient feels relief from back pain following the block), radiofrequency ablation (RFA) of the medial branch nerves can extend the duration of pain relief (Figures 27.5A and 27.7A, B).

Case Presentation

A 54-year-old female presents with a prior history of cervical degenerative disc disease with radiculopathy now having progressive cervicogenic headaches worse on the right.

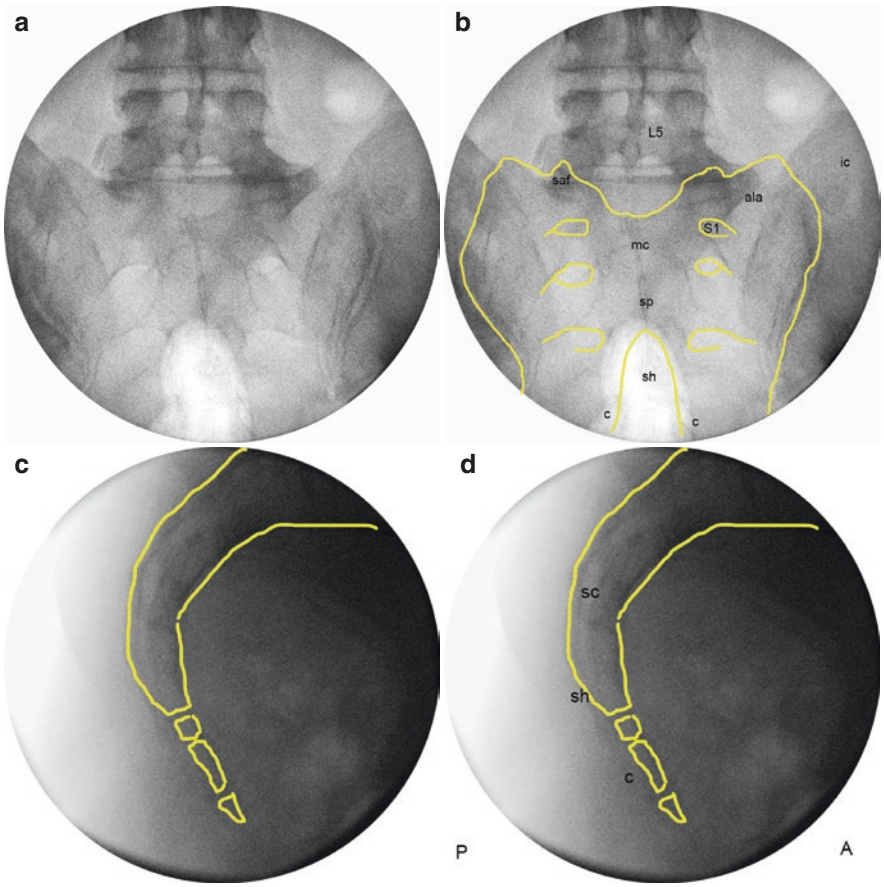


Fig. 27.4 Fluoroanatomy of the sacrum. (**a**) The sacrum and the coccyx are the caudal most aspect of the spine. The sacrum is composed of five fused levels (S1–S5), and at each level a sacral spinal nerve exits through the anterior sacral foramen. There are also posterior sacral foramina at each level (S1–S5). (**b**) The sacrum articulates with the L5 vertebra at the L5/S1 facet joint. The lateral winged aspect of the sacrum, the ala, extends to the sacroiliac joint laterally. The iliac crest (ic), sacral ala, median crest (mc), spinous process (sp), sacral cornu (c), and sacral hiatus (sh) are labelled. (**c**) Lateral view of the sacrum and coccyx. (**d**) Labelled structures are the sacral hiatus (sh), the coccyx (c), and the sacral canal (sc) which is the caudal most aspect of the dural canal and epidural space

Spurling's sign is negative, but there is pain with posterior and rightward movement of the neck (axial loading rightward). It is decided to start with diagnostic block of the C2, C3, and C4 medial branches above the level of the prior anterior fusion (see Fig. 27.5). If this successfully reduces the pain, then radiofrequency ablation of the same nerves at these levels will be pursued.

Radicular Back Pain

Radicular back pain is pain that occurs due to compression, injury, or disease of a spinal nerve. This results frequently from intervertebral disc herniation posteriorly into the neuroforamen. Progressive spondylosis of the facet joints can also narrow the neuroforamen and cause neuroforaminal stenosis and radicular pain. Injection at the level of stenosis can often relieve radicular back pain (Figures 27.5B, C, 27.6A, B, C, 27.7C, D, 27.8A, B).

Case Presentation

A 67-year-old male with metastatic lung cancer and poor prognosis has developed chronic radicular thoracic pain after thoracotomy. The pain is dermatomal and worsening. Diagnostic intercostal blocks relieved 75% of the pain symptoms, and so the next step is to repeat the procedure using radiofrequency ablation.

Myofascial Back Pain

Back pain may not necessarily be the result of structures visible on X-ray. Contributors may be spasm of the psoas muscle or quadratus lumborum muscle. The visible spinal structures are used as landmarks for injection of muscles when fluoroscopy is used for guidance (Fig. 27.7E).

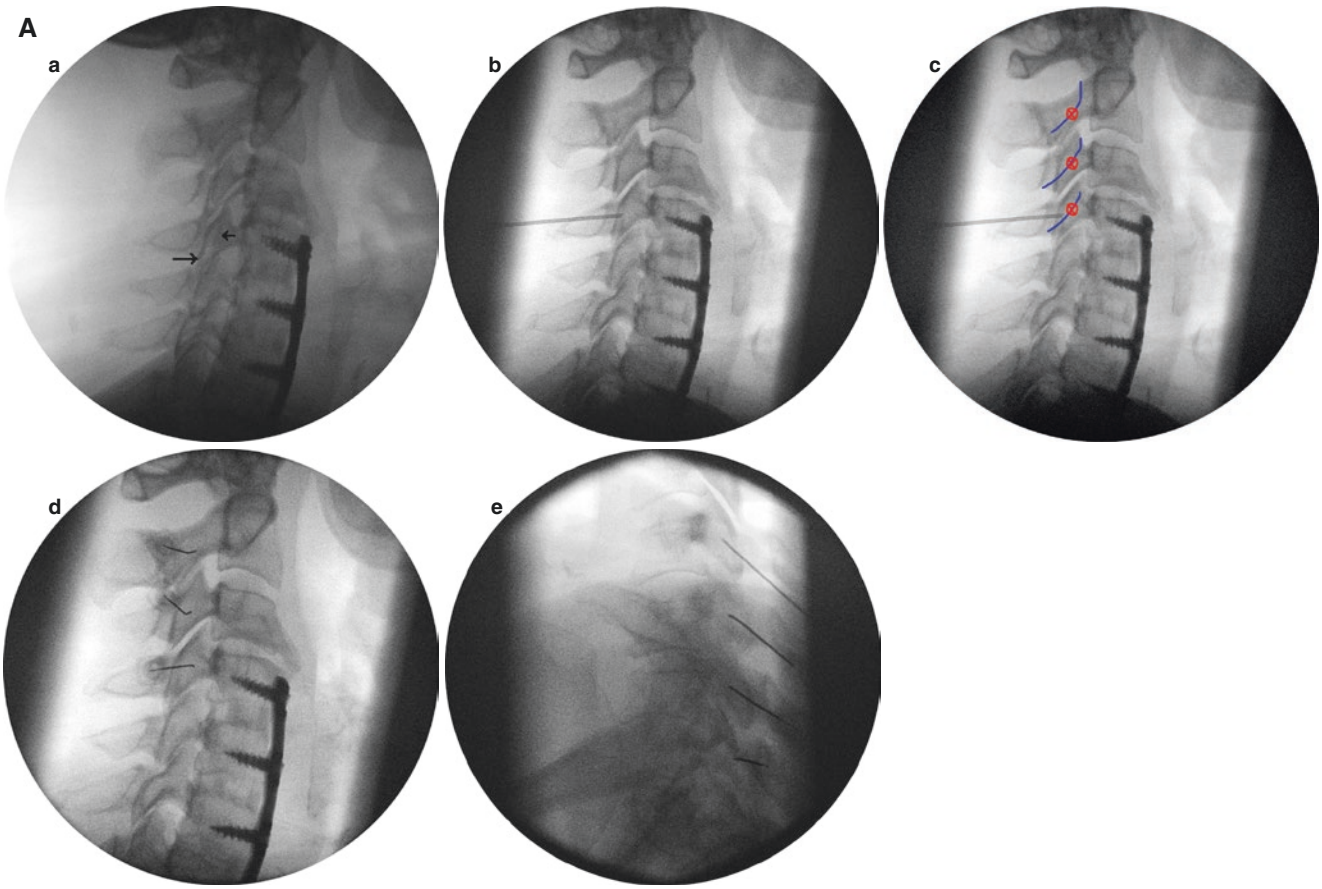


Fig. 27.5 (**A**) Treatment of cervical spine pain. Cervical medial branch block and radiofrequency ablation. Treatment of cervical pain due to spondylosis of the zygapophyseal (facet) joints begins with diagnostic block of the medial branch of the posterior rami of the nerve roots. This is done by placing a needle along the articular pillars of the cervical vertebrae where the medial nerve tracks. Safe needle placement requires that the vertebral body edges are aligned so that the target is clear. (**a**) Lateral fluoroscopic view of the cervical spine shows anterior fusion from C4 to C7. The posterior edges of the articular pillars at C4 are misaligned on this image (arrows), demonstrating the need to further rotate the C-arm to bring them into alignment prior to proceeding with needle placement. (**b**) The marker shows better alignment of the posterior articular pillars at C4. (**c**) Lines show the trajectory of cervical medial branch nerves as they course downward across the articular pillars to innervate the facet joints. Crossed circles show ideal location for placement of needle tips in the center of the pillars. (**d**) Needle tips are in placed on the C2, C3, and C4 articular pillars. (**e**) A less clear image with the patients shoulder partially obscuring the lower cervical vertebrae. The needle tips are in the center of the articular pillar parallelograms. (**B**) Cervical interlaminar epidural steroid injection. (**a**) The patient is positioned prone; an AP image of interlaminar approach to the cervical epidural space at C7–T1 is shown. A 22-gauge Tuohy needle is in place. (**b**) Lateral view contrast injection confirms the needle tip in the posterior epidural space. (**c**) The Tuohy needle is placed slightly rightward in the C7–T1 epidural space. Contrast spread is primarily rightward as well. This patient has previously undergone anterior cervical fusion as evidenced by the hardware. (**d**) Suboptimal lateral fluoroscopic image of needle tip confirmation by contrast injection. The patient's prior fusion hardware is seen across the anterior C6–C7 vertebrae. (**C**) Cervical transforaminal epidural steroid injection. (**a**) For a left-sided intervention. With the patient lying supine, the C-arm is rotated oblique to the patient's left side until the neuroforamen is clear. Needles are placed at the posterior position of the neuroforamen to avoid needle stick of the vertebral artery or the nerve root. This position will put the needle tip in the epidural space. (**b**) Lines demonstrate the location of the cervical nerve roots. (**c**) PA fluoroscopic view confirms the position of the needles. (**d**) Initial digital subtraction imaging (DSA) test shows contrast spread into the tissue lateral to the epidural space. (**e**) After slight adjustment of the needle, the DSA image shows contrast spreading along the epidural space outlining the cervical nerve root

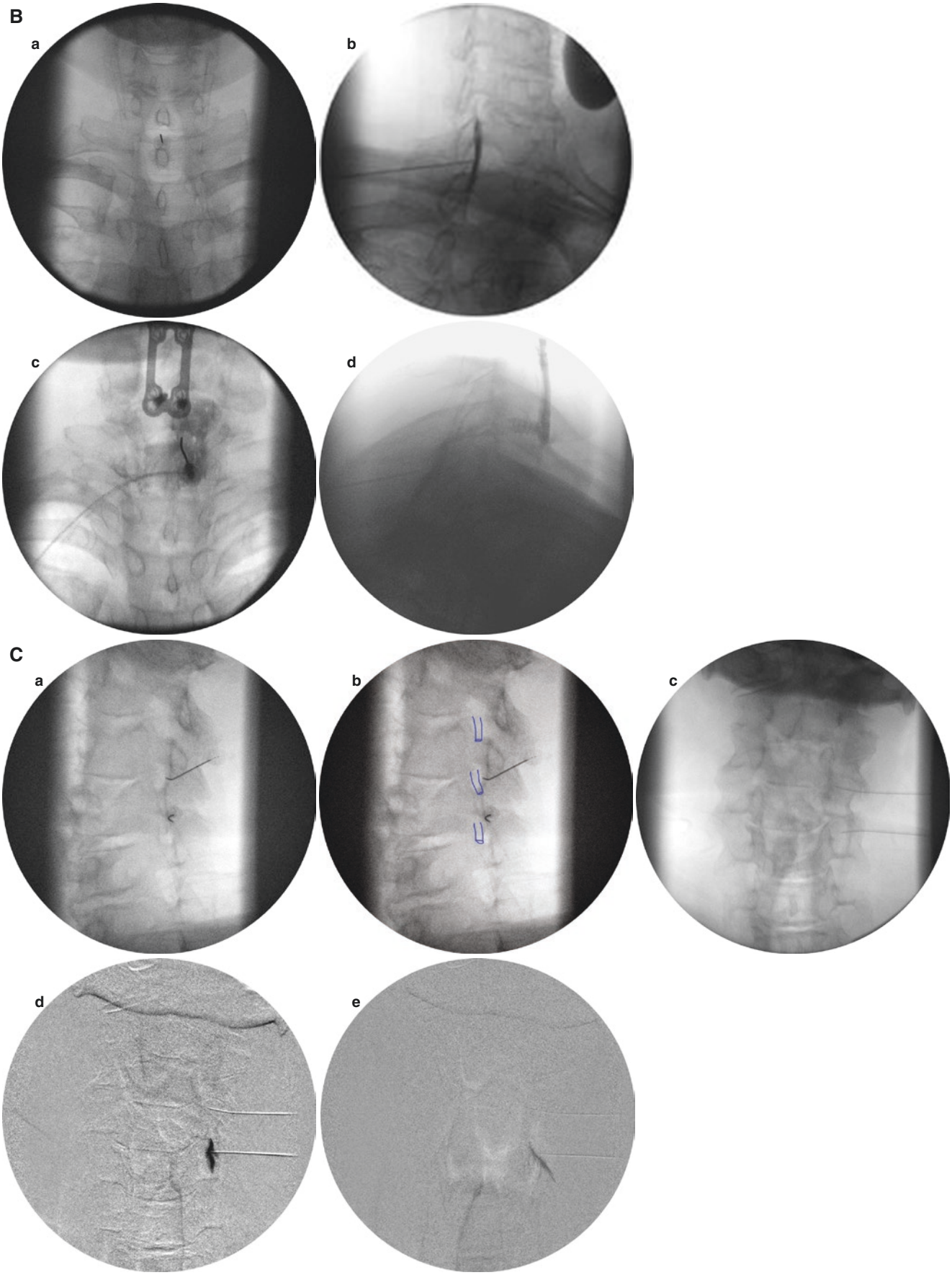


Fig. 27.5 (continued)

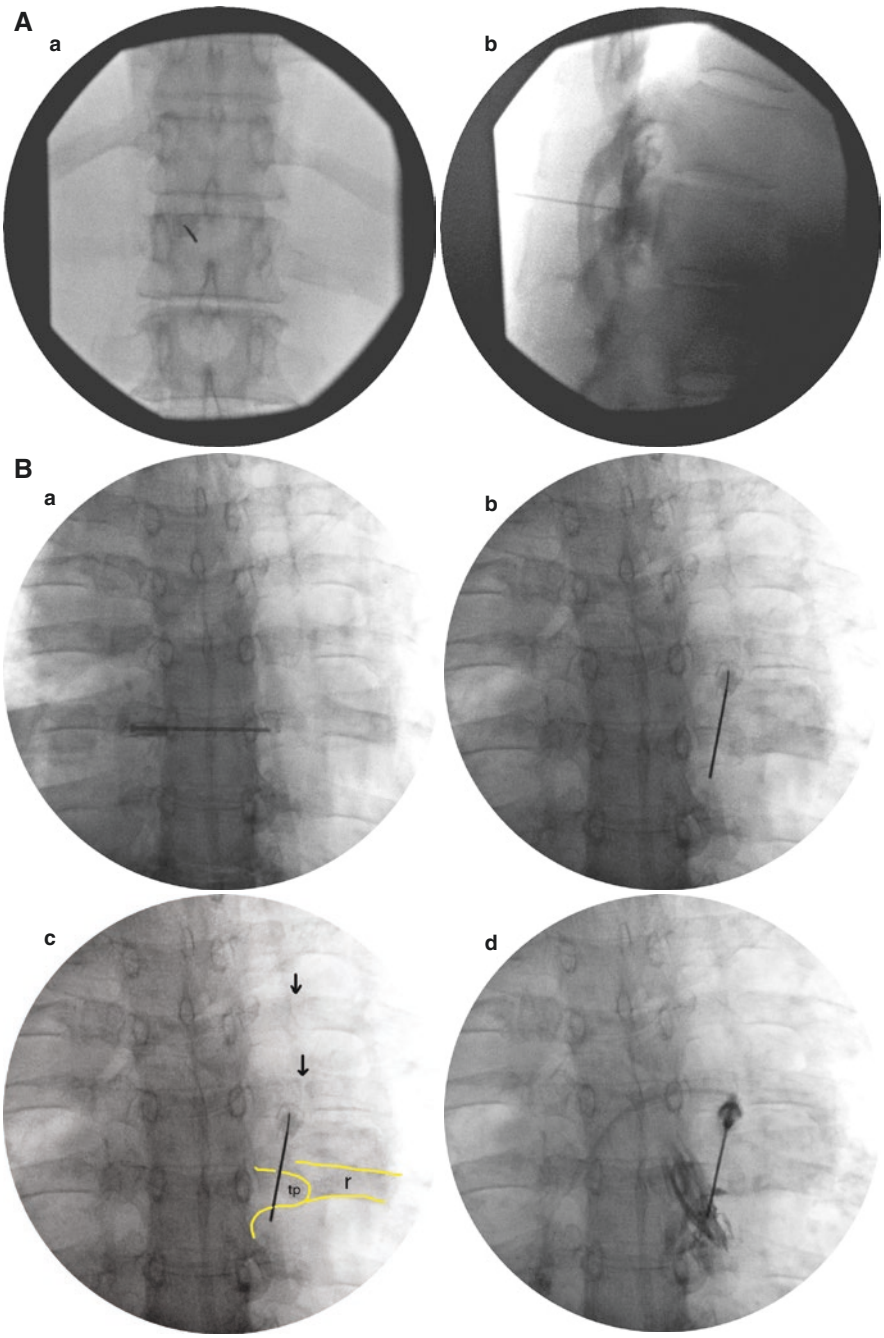


Fig. 27.6 (**A**) Treatment of thoracic spine pain. Thoracic interlaminar epidural steroid injection. (**a**) With the patient lying prone, the C-arm is positioned to obtain an anterior-posterior view of the T11–T12 interspace. The needle is inserted to approach the intervertebral foramen, here just off left in order to avoid contact with the spinous process. (**b**) The needle is advanced using a loss of resistance technique to obtain the epidural space, and the final position confirmed in the lateral fluoroscopic view using contrast. (**B**) Thoracic paravertebral block. (**a**) Paravertebral block at the thoracic level begins with identifying the target level (needle tip is over the transverse process of the fifth thoracic vertebra on the right side). (**b**) The Tuohy needle is advanced approximately 1 cm in depth beyond the depth of the transverse process. In this case, as the Tuohy was advanced, loss of resistance technique was used with saline to detect transit through the costotransverse ligament and entry into the paravertebral space. (**c**) Labelled structures are the transverse process (tp), the rib (r), and arrows showing rib fractures. (**d**) Contrast spread travels distal and proximal within the paravertebral space. (**e**) Another example showing the needle tip placed onto the transverse process of T4, (**f**) the needle advanced in a caudal direction to enter the paravertebral space, and (**g**) confirmation showing contrast spreading proximal and lateral outlining the pleura in PA view and in (**h**) lateral view. (**C**) Intercostal nerve block. With the patient in the prone position, this AP fluoroscopic image shows radiofrequency needles positioned just off the caudal aspect of the T8, T9, and T10 ribs on the right side. After confirming proximity to the intercostal nerves using 2 Hz, 0.3 mV stimulation, the nerves were anesthetized and treated with pulsed radiofrequency ablation

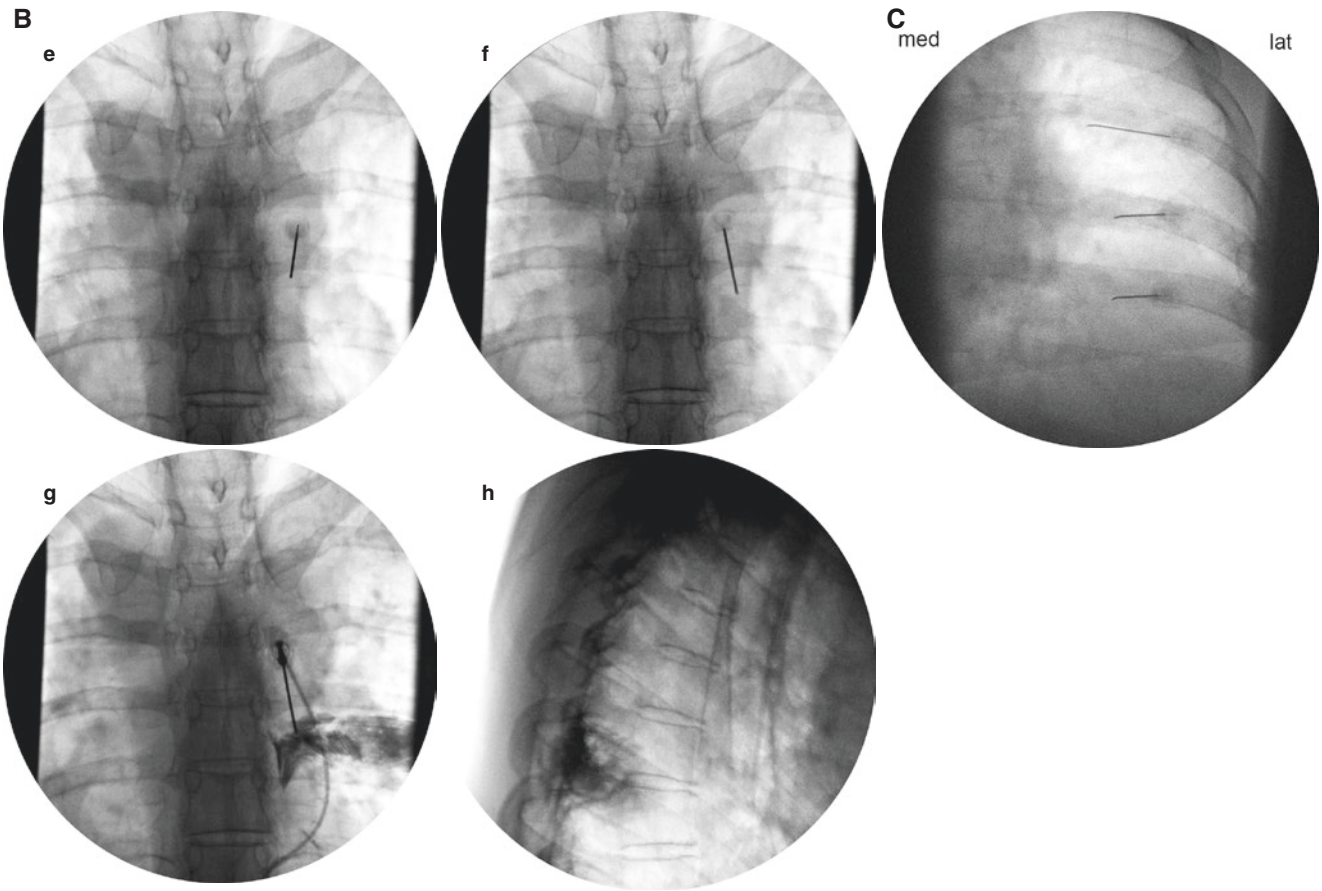


Fig. 27.6 (continued)

Case Presentation

A 48-year-old athletic man had a lumbar fusion operation after a traumatic accident 2 years ago. Still he has severe persistent back pain with hip flexion. On physical exam active and passive stretch of the psoas muscle duplicates the pain. Physical therapy alone has so far been insufficient to relieve the pain. A psoas muscle injection is planned.

Sympathetically Maintained Pain

Chronic severe pain can be exacerbated or maintained by the action of efferent sympathetic nerves. Often treatment of the sympathetic nerves or ganglia results in a sympathectomy and can alleviate the pain and facilitate recovery. The sympathetic nerves are located along the anterior neuraxis, and interventional treatment using fluoroscopy

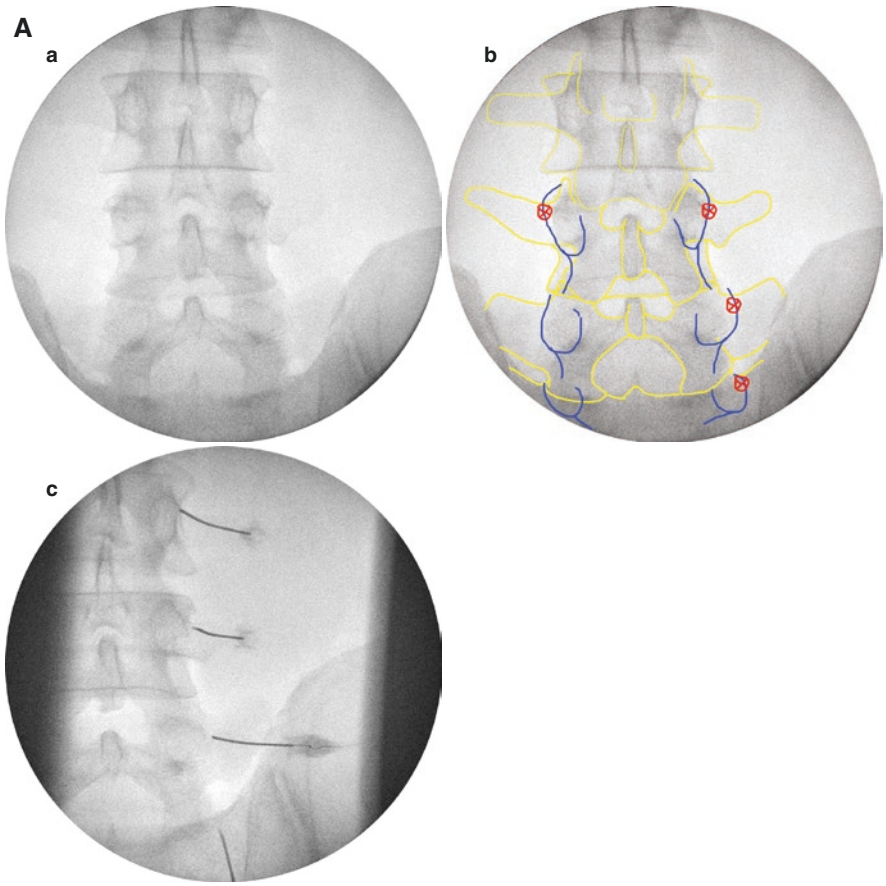
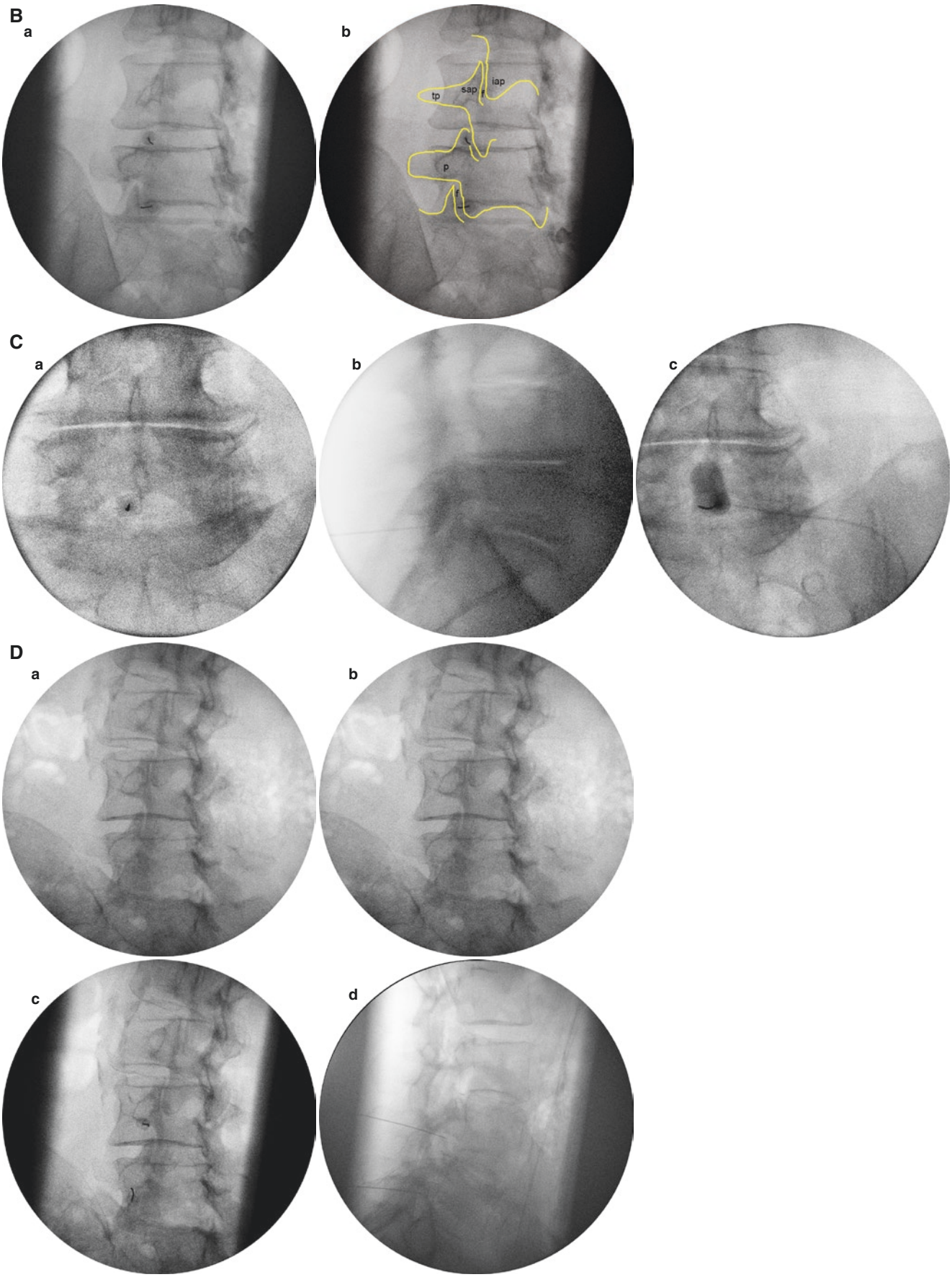


Fig. 27.7 (**A**) Treatment of lumbar spine pain. Lumbar medial branch block and radiofrequency ablation. (**a**) A fluoroscopic image of the lumbar spine. (**b**) The L3, L4, and L5 vertebral bodies are outlined and drawn lines indicate the location and trajectory of the medial branches. The L2 medial branch courses down across posterior aspect of the L3 transverse process and innervates the L2/3 facet joint as well as sends a branch to innervate the L3/4 facet joint. Likewise, the L3 medial branch innervates the L3/4 and the L4/5 facet joints. To completely treat the L4/5 facet joint requires block of the L3 and L4 medial branches. Red circles show the ideal location for needle placement on the superior-medial aspect of the transverse process. (**c**) Radiofrequency needles have been placed with tips at the juncture of the transverse process just lateral to the facet joint, the likely location of the medial branches. (**B**) Lumbar facet joint injection. (**a**) Fluoroscopic image obtained by rotating the C-arm left oblique to visualize the facet joint space between the superior and inferior articular processes. Needles have been inserted into the facet joint to treat the painful joint. (**b**) Outlines of the vertebral bodies with labelled transverse processes (tp), superior articular process (sap), inferior articular process (iap), pedicle (p), and facet joint (f). (**C**) Lumbar interlaminar epidural steroid injection. (**a**) A 22-gauge Tuohy needle is shown coaxial to the fluoroscopic image and overlying the intervertebral foramen between L5 and S1. (**b**) Lateral image shows the needle tip in the epidural space confirmed by the spread of contrast. (**c**) PA fluoroscopic view shops spread of contrast across the posterior epidural space. (**D**) Lumbar transforaminal epidural steroid injection. (**a**) A lumbar fluoroscopic image rotated oblique to the left to reveal the facet joints. This oblique view allows for needle placement under the transverse process proximal to the neuroforamen to attain needle tip position in the epidural space above the nerve root. (**b**) The same image noting the facet joint (f), the outlined view of the so-called Scotty dog, and the ideal target (circled x) for the needle placement under the eye (pedicle) and chin (transverse process) of the Scotty dog. (**c**) Coaxial view of needles in place for transforaminal epidural injection of the L4 and L5 nerve roots. (**d**) Lateral view is used when approaching the foramen to confirm needle position superior to the foramen. (**e**) PA view shows final position of the needle tips in the epidural space at L4 and L5. (**f**) Digital subtraction image with injection of contrast confirms epidural spread without vascular uptake. Note how the contrast outlines the track of the nerve root medial into the epidural space and distally along the nerve sheath. (**g**) PA image showing contrast outlining the L5 nerve root and tracking the epidural space. (**E**) Psoas muscle and quadratus lumborum muscle injection. The psoas muscle is a major hip flexor. It attaches to the transverse processes of T12–L5 and inserts upon the lessor trochanter of the femur. Injection of a spasmed or painful psoas muscle under fluoroscopy is based upon knowledge of fluoroanatomy because muscle is radiolucent. The quadratus lumborum muscle attaches to the 12 rib and the transverse processes of L1–L4 and caudally to the iliac crest. Injection of this muscle requires needle position lateral to the transverse processes. The muscle is relatively thin and advancement under fluoroscopic guidance requires lateral surveillance to ensure shallow depth to avoid peritoneal puncture. (**a**) Needle inserted lateral to the lumbar vertebral column near the distal transverse processes. (**b**) In lateral fluoroscopic view, the needle depth is confirmed lateral to the midline of the vertebra, and injection of contrast confirms intramuscular spread. (**c**) PA view confirms contrast spread in the psoas muscle



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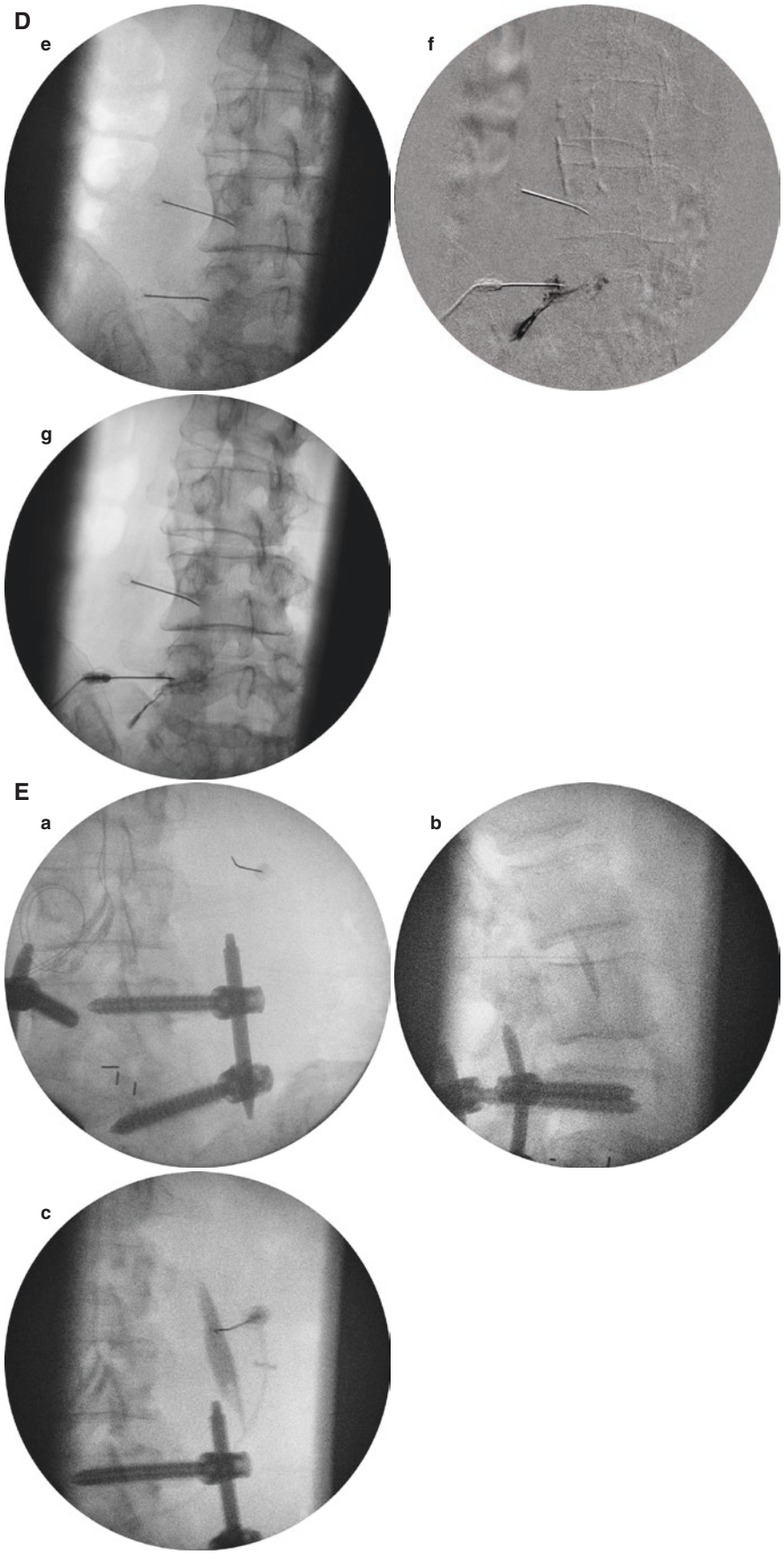

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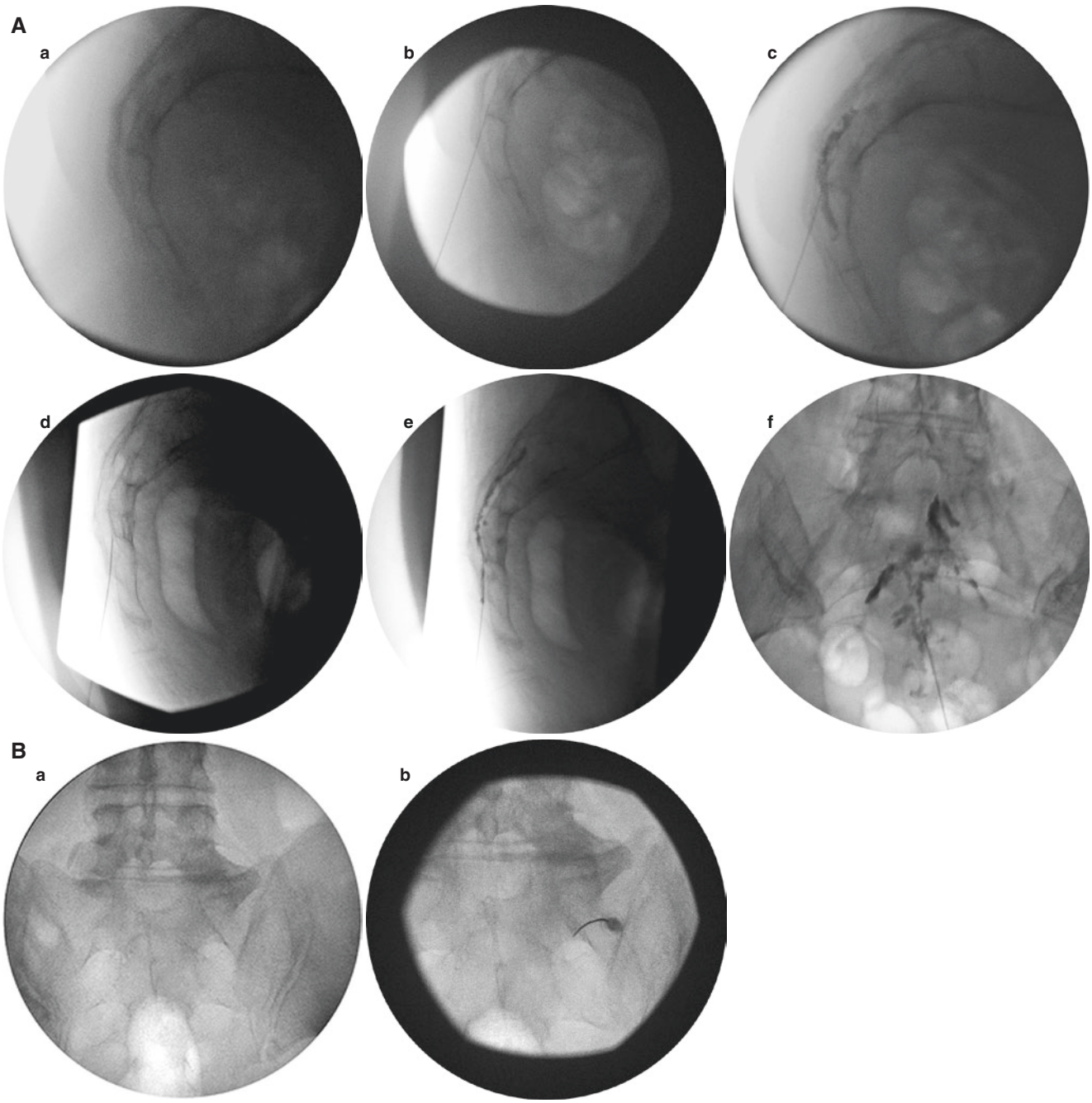

Fig. 27.8 (**A**) Treatment of sacral spine pain. Caudal epidural steroid injection. (**a**) Lateral view of the sacrum and coccyx, (**b**) a 22-guage spinal needle is advanced into the caudal epidural space, (**c**) confirmed by contrast spread. (**d**) A second example showing the needle in the epidural space and (**e**) confirmed by contrast spread in the lateral view and (**f**) PA fluoroscopic view. In this image contrast has spread in the cranial direction and can be seen tracking along S1 nerves bilaterally. (**B**) Sacral transforaminal epidural injection. (**a**) PA fluoroscopic view of the sacrum, (**b**) with needle placement in the superior aspect of the S2 sacral foramen

requires knowledge of the safest location to target either the sympathetic chain or the ganglia. Because the nerves themselves are radiolucent, sympathetic blocks are performed by injection as regional field blocks, so a thorough knowledge of the anatomy of radiolucent and radiopaque structures in the vicinity is crucial for safe performance (Fig. 27.9).

Case Presentation

A 22-year-old patient develops severe sensitivity of the right ankle and foot after fracturing her ankle in a car accident. The pain does not resolve several months after the ankle fracture has healed and seems to be getting more painful over time. Even the skin is sensitive to clothing and is mottled red and

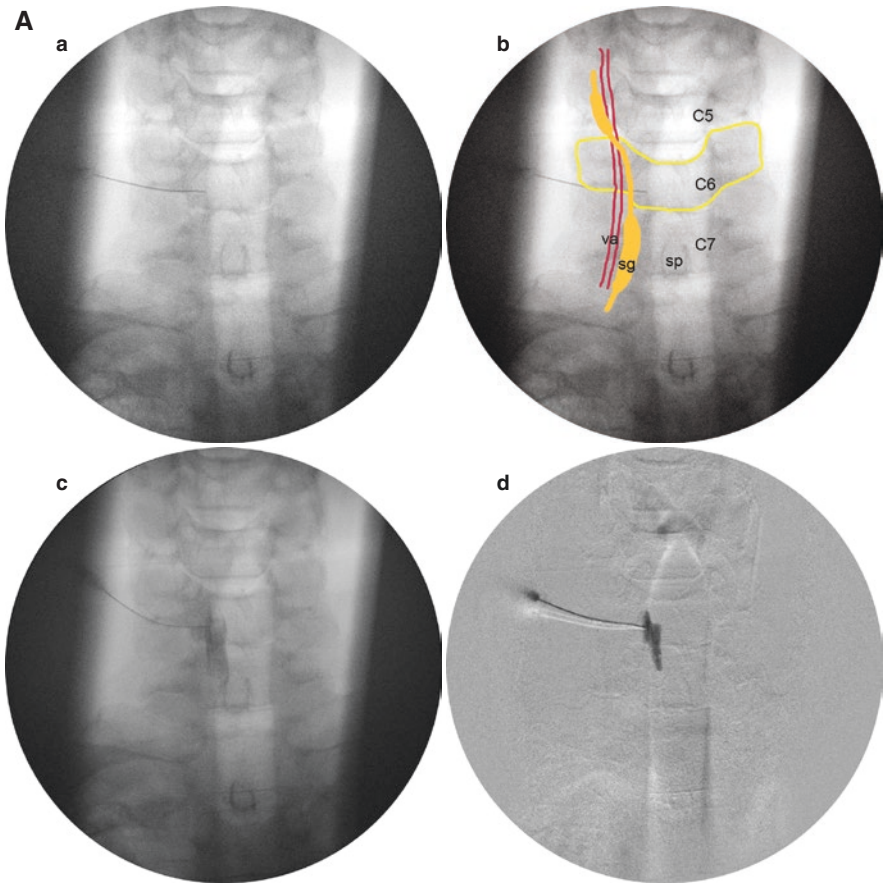

Fig. 27.9 (**A**) Treatment of sympathetically mediated pain. Stellate ganglion block. (**a**) PA fluoroscopic approach to stellate ganglion block showing the needle tip on the periosteum of the C6 vertebral body. (**b**) Lateral to the position of the needle tip is the vertebral artery (va) that is partially protected at this level as it passes through the transverse process. However, the vertebral artery is exposed at the C7 level. The stellate ganglion (sg) is located over the C7 and T1 vertebral bodies anteriorly. (**c**) Contrast spread confirms the position of the needle and the cranial-caudal flow along the sympathetic chain and the stellate ganglion. (**d**) DSA image confirms that the needle is not within vasculature. (**B**) Celiac plexus block. (**a**) The celiac ganglion lies anterolateral to the celiac artery on the anterior surface of the descending aorta at the level of the T12 vertebral body. (**b**) One approach is to rotate the C-arm laterally and align the needle to target the anterior and superior aspect of the L1 vertebral body. (**c**) With two needles in place, aligned to the anterolateral L1 vertebral body, injection here would provide a deep splanchnic block of the greater, lesser, and least splanchnic nerves that make up the preganglionic nerves of the plexus. (**d**) Contrast confirmation of the needle tip demonstrates spread in the region of the splanchnic nerves, and digital subtraction confirms there is no vascular uptake. (**e**) Digital subtraction confirms there is no vascular uptake. (**C**) Lumbar sympathetic chain block. (**a**) PA fluoroscopic view of the lumbar spine in a patient with a prior right side L4–L5 fusion. (**b**) Leftward oblique C-arm rotation with a needle placed so that the tip is aligned to the anterolateral aspect of the L3 vertebral body to target the left sympathetic chain. (**c**) PA view confirms needle depth and the lateral positioning. (**d**) Lateral view confirms needle depth with the tip aligned to the anterior aspect of the vertebral body. (**e**) Contrast spread confirms needle position and demonstrates the expected spread of injectate along the region of sympathetic chain on the left side. (**D**) Superior hypogastric plexus block. (**a**) The superior hypogastric plexus is a located anterior to the L5 vertebral body. As with the lumbar sympathetic block approach, an oblique C-arm angle is used to position each needle tip at the anterolateral aspect of the vertebral body. (**b**) The needle tip is confirmed in place with contrast showing spread along the anterior aspect of the vertebral body around the superior hypogastric plexus. (**E**) Ganglion impar block. (**a**) In the lateral view, a 22-guage spinal needle is advanced through the coccyx cartilage to the location of the ganglion impar and (**b**) confirmed with contrast spread to be just anterior to the coccyx but not within the bowel (b)

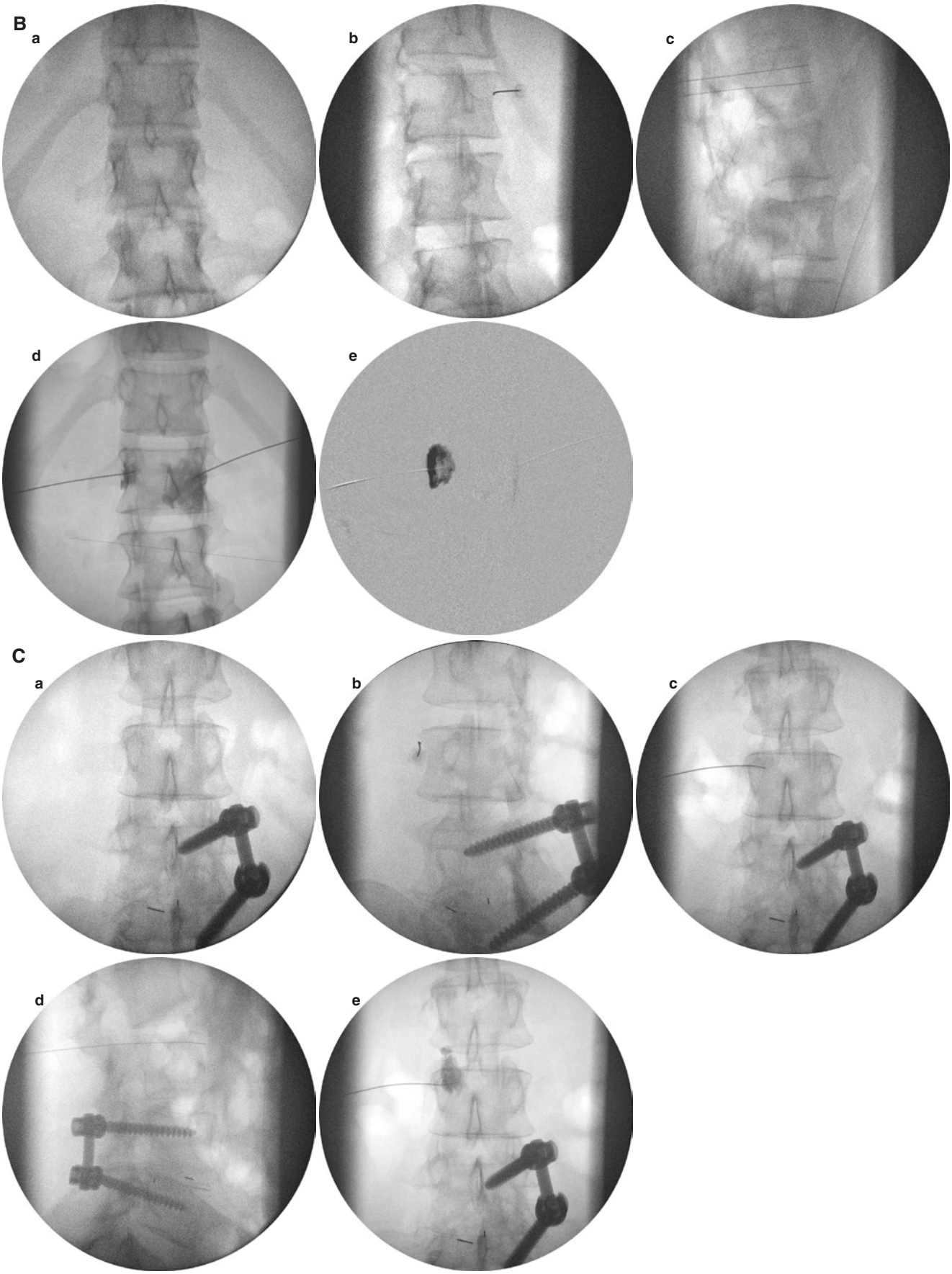

Fig. 27.9 (continued)

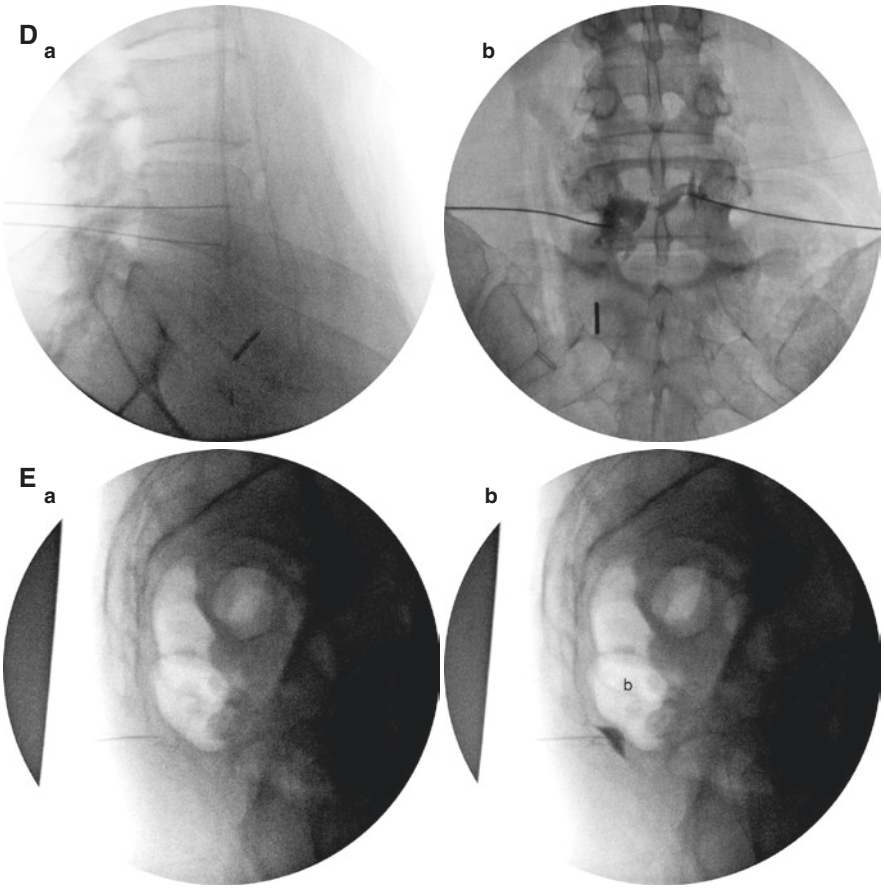

Fig. 27.9 (continued)

purple in color. The interventional pain specialist has given her the diagnosis of chronic regional pain syndrome type I and plans to treat the pain by performing a right side lumbar sympathetic block.

Neuromodulation

Spinal cord stimulator leads are placed using fluoroscopic imaging. The conus of the spinal cord is located at L1 on average. The L1–L2 interspace is an ideal location to access the epidural space safely, although other locations may be preferred given the ultimate level of lead placement. The technique of placing spinal cord stimulator electrodes for trial and implants is the same. Fluoroscopy is used to guide placement of one or two large Tuohy needles to the epidural space. Then electrodes are advanced under live fluoroscopy or intermittent imaging to overlay the dorsal spinal cord at the preferred level. Lateral views are used to confirm the leads end up in the posterior epidural space and do not migrate anteriorly (Fig. 27.10).

Case Presentation

A 45-year-old man with chronic low back pain after spinal fusion has had successful pain relief during the spinal cord stimulator trial period with two leads. He requests to proceed with permanent implant.

Vertebral Augmentation

Augmentation of vertebral body compression fractures can be performed by kyphoplasty. The procedure is done under fluoroscopy viewing multiple image planes to position introducers through the pedicles and gain access to the mid-vertebral

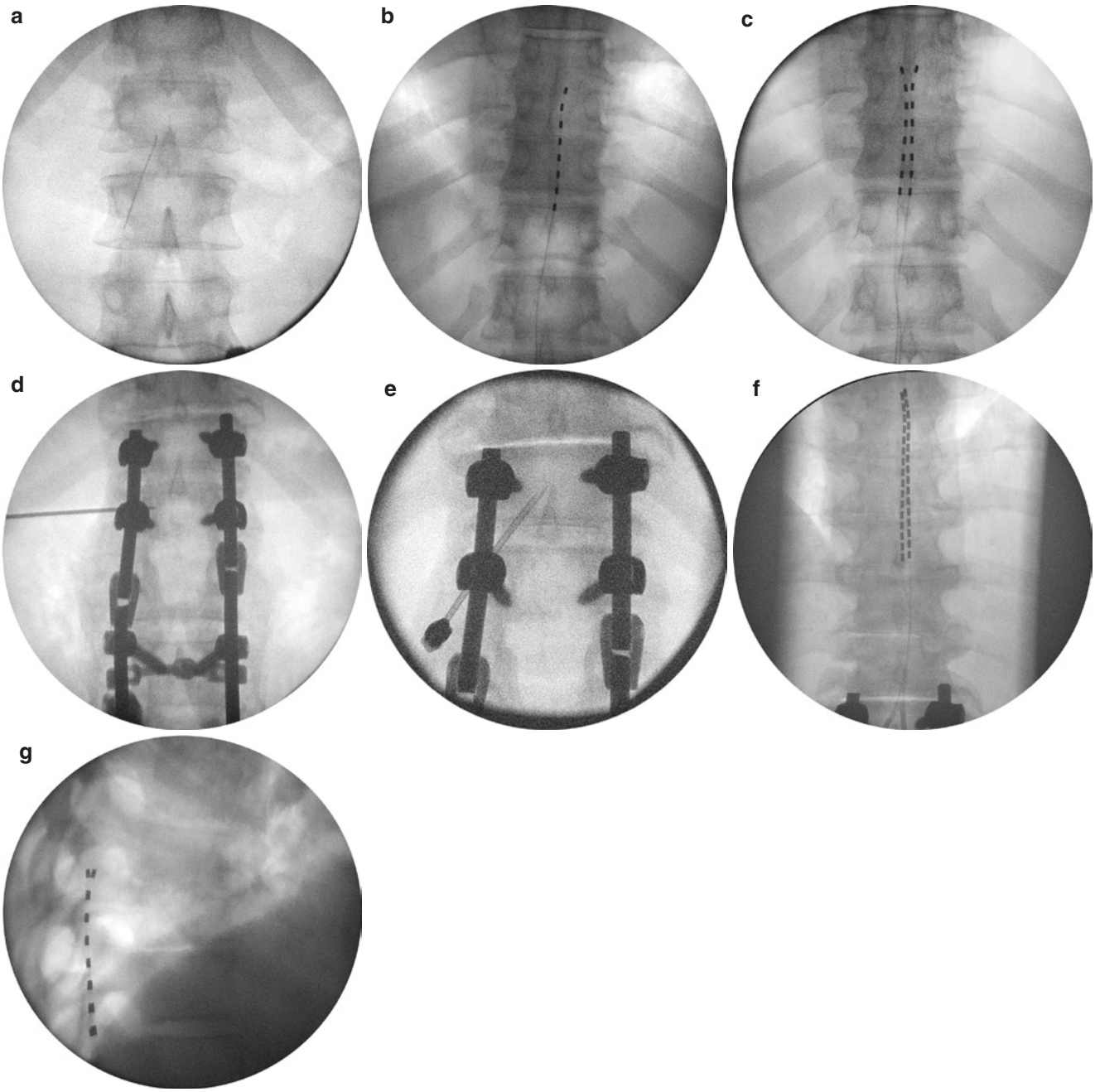

Fig. 27.10 Neuromodulation. Thoracic placement of spinal cord stimulation (SCS) leads. (**a**) The L1–L2 interspace is identified with the marker needle tip placed just caudal to the intervertebral space. (**b**) An AP view of a single lead in place at the top of T9, (**c**) a second octrode lead placed alongside at the same level. (**d**) Another example showing a patient with lumbar fusion hardware. The marker is at the L1–L2 level, and the fusion hardware extends cranial to include T12. (**e**) Laminectomy can be seen below L1, so the Tuohy is placed to access the epidural space between T11 and T12. Two, 16 contact leads are placed alongside, extending from T6 to T9. (**f**) Two, 16 contact leads are placed alongside, extending from T6 to T9. (**g**) The leads are confirmed to be in the posterior epidural space in this lateral fluoroscopic view

body. Radiopaque contrast is injected during the process of balloon expansion, followed by injection of cement.

Case Presentation

A 58-year-old man fell from a ladder and has severe pain in his mid-back. An MRI shows a vertebral body fracture at the T10 level. When he is at rest, his pain is 1/10 on the numeric pain rating scale, but when he stands up to move, the pain is 10/10. On exam the pain is only located at the T10 vertebral body and doesn't radiate anywhere else. He was given pain medication and a brace for 3 months. Pain has worsened, and the fracture is progressing on repeat MRI scan. Kyphoplasty stabilization is planned (Fig. 27.11).

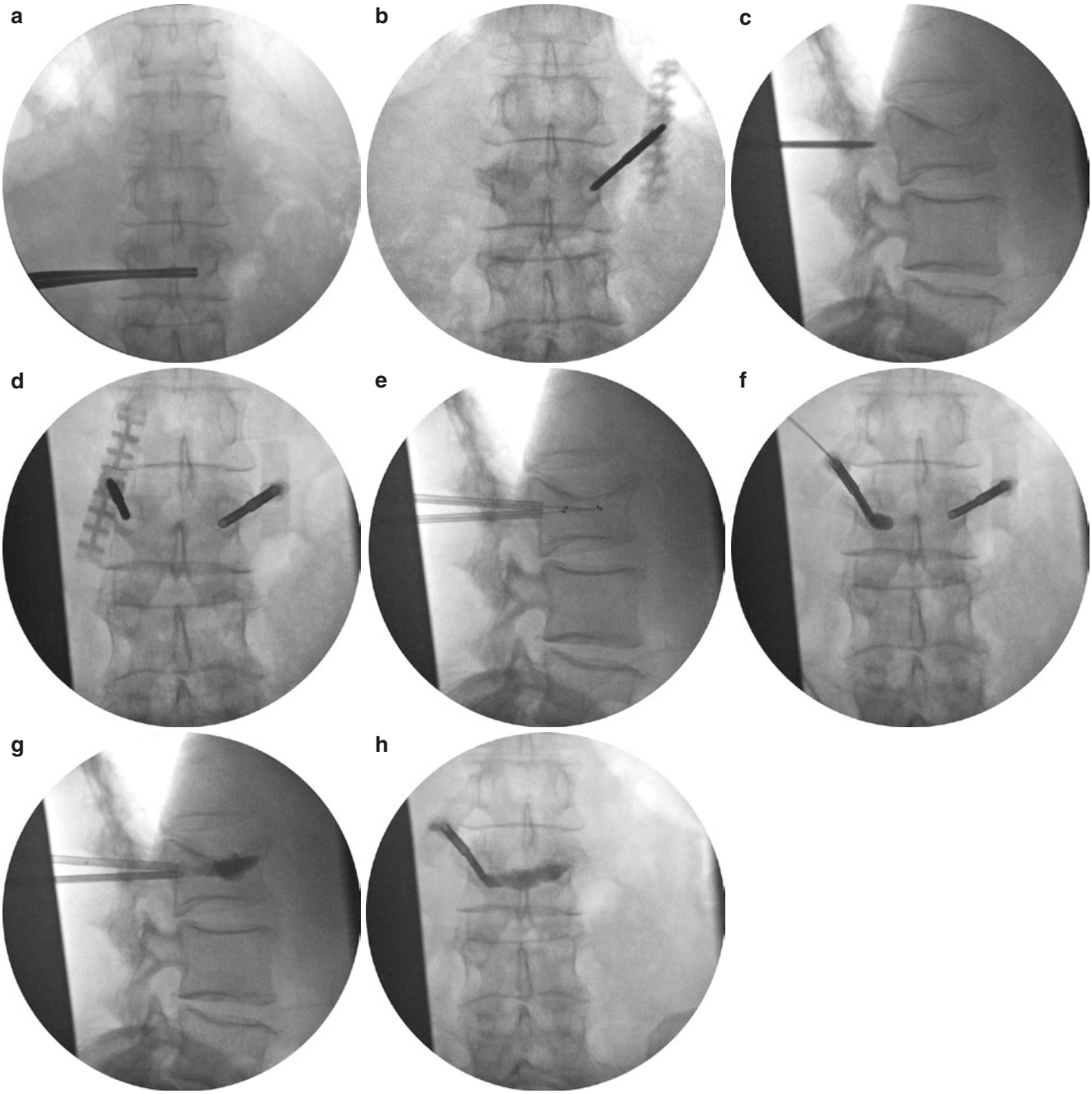

Fig. 27.11 –Vertebral augmentation. Kyphoplasty. (**a**) The L3 vertebral body is identified and the endplates aligned in this PA fluoroscopic image**.** (**b**) The introducer is inserted and engaged in the lateral aspect of the right pedicle of L3. (**c**) In the lateral view, the trajectory of the introducer is confirmed. Compression of the vertebral body is easily observed from this image. (**d**) A second introducer is engaged in the lateral aspect of the left pedicle of L3. The right introducer was advanced and the lateral to medial interpedicular pathway demonstrated. (**e**) Both introducers are aligned with the posterior wall of the vertebral body the balloons advanced. (**f**) The left balloon is expanded, and the direction of expansion observed in multiple fluoroscopic planes to confirm medial directionality. (**g**) Cement polymethylmethacrylate is injected slowly in the lateral view while monitoring for leakage posteriorly into the intervertebral foramen or spinal canal or laterally or anteriorly into vessels. (**h**) The final image shows cement spread across the vertebral body

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Ultrasound-Guided Spinal Procedures

28

Yi Zhang, Baishan Wu, and Ping Jin

Key Points

- While fluoroscopy remains the most frequently used imaging technique employed by interventional spine physicians, the use of ultrasound guidance has been increasingly recognized as both feasible and reliable in performing interventional procedures.
- Cervical transforaminal epidural injection and selective nerve root injection can be performed safely and effectively with ultrasound guidance.
- Ultrasound guidance can be utilized for cervical medial branch nerve blocks and facet joint interventions.
- Ultrasound guidance offers unique advantage in stellate ganglion block.
- Common lumbosacral interventional procedures, including lumbar facet joint interventions, caudal epidural steroid injection, sacroiliac joint injection, etc., can be performed with ultrasound guidance as well.

Introduction

Low back pain and neck pain of spine origin are extremely common health complaints with an enormous social, psychological, and economic burden [1–3]. Interventional spine procedures, though its effectiveness is still being debated, have been utilized for the past several decades, both diagnostically and therapeutically, in the management of spine pain [4, 5]. While fluoroscopy remains the most frequently used imaging technique employed by interventional spine physicians, the use of ultrasound guidance has been increasingly recognized as both feasible and reliable in performing interventional procedures. Several advantages in ultrasound guidance as compared to fluoroscopic guidance have provided the basis for the increasing popularity of such technique among intervention pain physicians. The ability to visualize soft tissue, such as important neural and vascular structures, and the ability to visualize real-time needle advancement make ultrasound guidance appealing to interventional pain physicians. The avoidance of ionizing radiation and the affordability and portability of modern ultrasound machines further add to this appeal. Ultrasonography may be particularly helpful in the cervical area because a multitude of blood vessels and other vital structures are compacted in a small area [6].

Nevertheless, despite progresses in the state-of-art ultrasound scanners, currently the resolution of even the most sophisticated ultrasound units is still not comparable to fluoroscopy; visualization of deep structures with ultrasound as required in performing interventional spine procedures can still be challenging and requires specialized training and considerable experience. In this chapter, we describe the relevant sonoanatomy of the cervical and lumbar spine, as well as technical approaches in performing common interventional spine procedures with ultrasound guidance.

Cervical Transforaminal Epidural Injection (Selective Nerve Root Injection)

Anatomy

The cervical spinal nerve root can be identified as a hypoechoic circle in between the anterior and posterior tubercles of the transverse process at each spinal level. In their early work, Narouze et al. described the technique to identify cervical spinal level with sonography [7]. The cervical spinal level can be identified by the characteristic shape

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of the transverse process of C7, which has a rudimentary or absent anterior tubercle and a prominent posterior tubercle (Fig. 28.1). The transducer is then moved cranially, the C6 transverse process can be visualized with its characteristic sharp anterior tubercle and a smaller posterior tubercle (Fig. 28.2). From C6 and above, both the anterior and posterior tubercles of the transverse process can be visualized; the cervical spinal nerve root exits the foraminal opening between the anterior and posterior tubercles of the transverse process, which can be easily identified as the "2-humped camel" (Fig. 28.2, C6 level; Fig. 28.3, C5 level).

Alternatively, the cervical spinal level can be determined by using the vertebral artery as a landmark. The vertebral artery passes anterior and medial to the transverse process of C7, enters through the transverse foramen of C6, and progresses toward the head through the transverse foramen of each cervical vertebrates before it enters the foramen magnum through the posteromedial side of the atlas. The vertebral artery can be visualized as a pulsating round structure anterior and medial to the C7 transverse process. At this level, the thyrocervical trunk, which arises lateral to the ver-

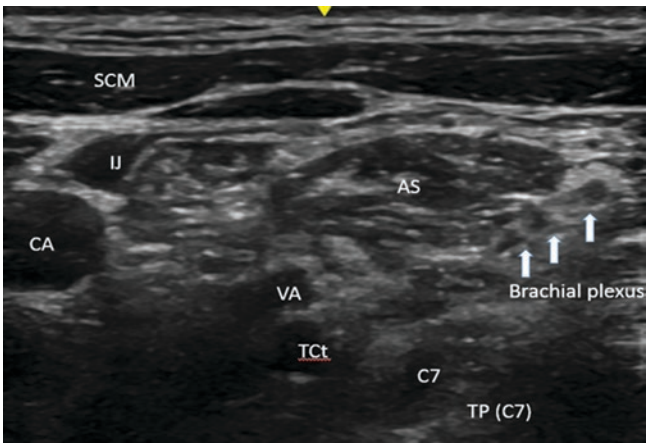

Fig. 28.1 Short-axis view at C7 level. Patient is placed in a supine position with head turned 45 degrees to the left side. Ultrasound transducer is placed in the right side of the neck at C7 level transversely. CA carotid artery, IJ internal jugular vein, SCM sternocleidomastoid muscle, C7 C7 nerve root, AS anterior scalene muscle, TP transverse process, Arrows brachial plexus, VA vertebral artery, TCt thyrocervical trunk

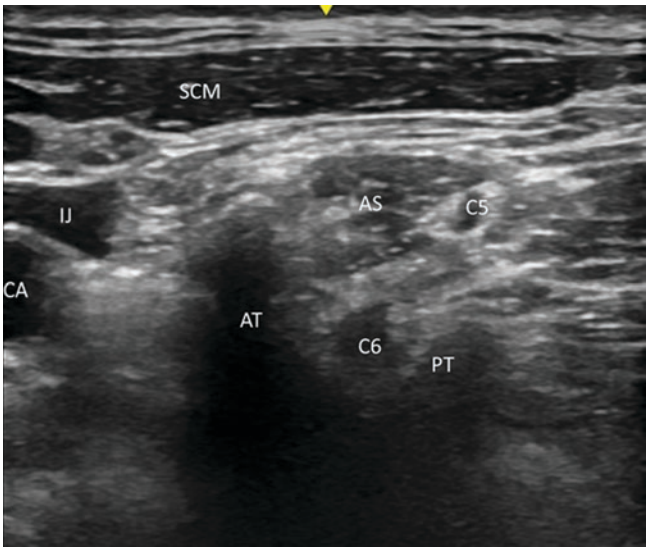

Fig. 28.2 Short-axis view at C6 level. Patient is placed in a supine position with head turned 45 degrees to the left side. Ultrasound transducer is placed in the right side of the neck at C6 level transversely. CA carotid artery, IJ internal jugular vein, SCM sternocleidomastoid muscle, C6 C6 nerve root, C5 C5 nerve root, AS anterior scalene muscle, AT anterior tubercle, PT posterior tubercle

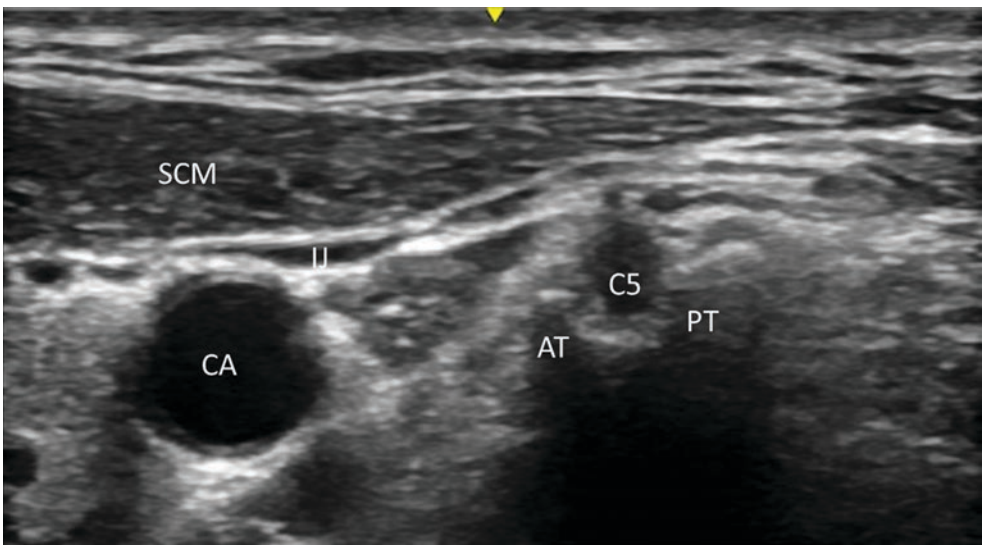

Fig. 28.3 Short-axis view at C5 level. Patient is placed in a supine position with head turned 45 degrees to the left side. Ultrasound transducer is placed in the right side of the neck at C5 level transversely. CA carotid artery, IJ internal jugular vein, SCM sternocleidomastoid muscle, C5 C5 nerve root, AT anterior tubercle, PT posterior tubercle

tebral artery from the subclavian artery, can also be seen immediate medial to the C7 transverse process. Using color Doppler can help identify these important vascular structures and avoid inadvertent vascular injury during procedure (Fig. 28.4). The cervical spinal levels can then be determined by moving the transducer cranially until the transverse process of the next cervical level is seen. Doppler imaging can be very helpful in identifying the vertebral artery at the C7 level [8].

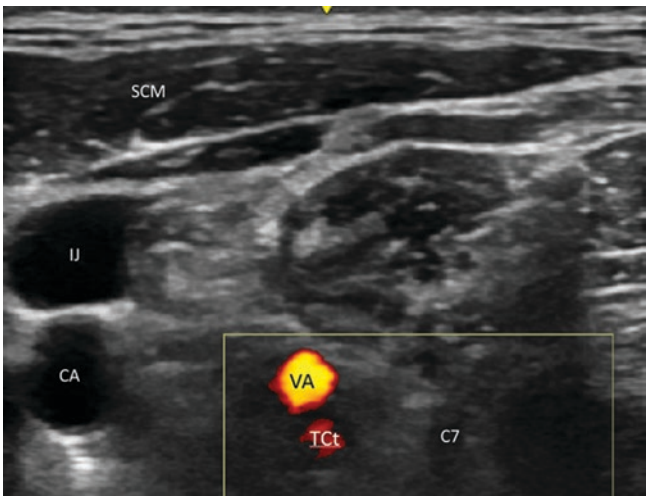

Fig. 28.4 Short-axis view at C7 level with color Doppler. Patient is placed in a supine position with head turned 45 degrees to the left side. Ultrasound transducer is placed in the right side of the neck at C5 level transversely. CA carotid artery, IJ internal jugular vein, SCM sternocleidomastoid muscle, C7 C7 nerve root, VA vertebral artery, TCt thyrocervical trunk

Patient Position

Patient is placed in a lateral decubitus position with the side of intervention up. Alternatively, the patient can be placed in a supine position, with the head rotated 30–45 degrees away from the targeted area. An 8–12 Hz linear array transducer is used. The transducer is placed transversely in the lateral neck.

Approach

Once the appropriate spinal level is identified, the transverse axial view is obtained, a 22-gauge, blunt-tip needle is advanced in the posterior-lateral to anterior-medial direction with an in-plane approach under real-time visualization until the needle tip passes the posterior tubercle (Fig. 28.5). Caution should be exercised not to advance the needle into the hypoechoic cervical spinal nerve root. At this point, 2 ml of injectate (local anesthetics only for diagnostic selective nerve root block, dexamethasone 8 mg for transforaminal epidural steroid injection) is injected under direct visualization.

Outcome Study

In a recent randomized blinded controlled study, ultrasound-guided selective cervical nerve root block was shown to be as effective as the fluoroscopy-guided method in pain relief and functional improvement [9].

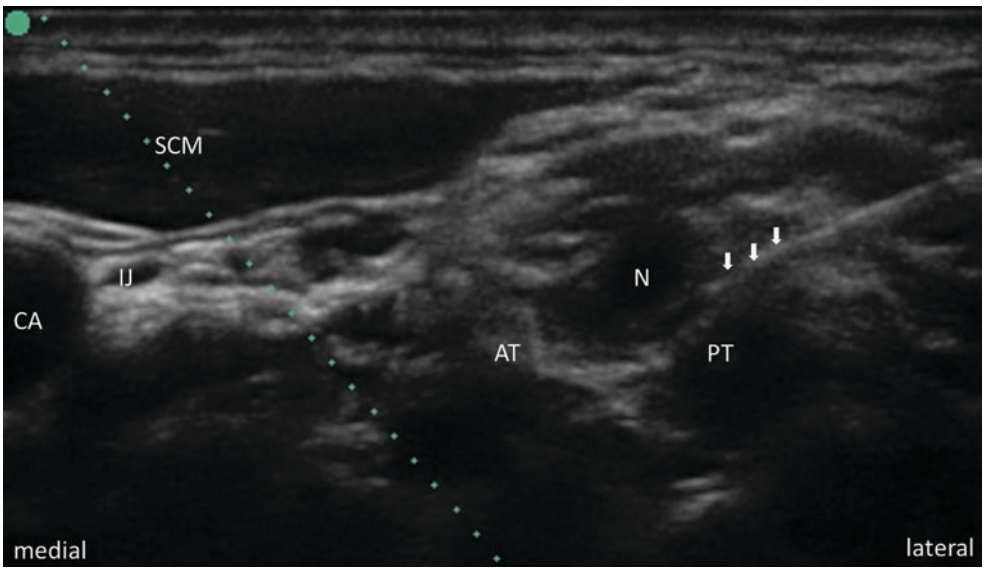

Fig. 28.5 Ultrasound-guided C5 selective nerve root injection. Patient is placed in a supine position with head turned 45 degrees to the left side. Ultrasound transducer is placed in the right side of the neck at C5 level transversely. CA carotid artery, IJ internal jugular vein, SCM sternocleidomastoid muscle, N nerve (C5 nerve root), AT anterior tubercle, PT posterior tubercle, Arrows needle, N C5 nerve root

Cervical Medial-Branch Intervention and Facet Joint Injections

Anatomy

The zygapophyseal or facet joints are important structures in determining the biomechanical properties of the spinal column and are of clinical relevance. The facet joints are diarthrodial joints formed by the superior articular process of one cervical vertebra articulating with the inferior articular process of the vertebra above at the level of the junction of the lamina and the pedicle. The angulation of the facet joint increases caudally, being about 45 degrees superior to the transverse plane at the upper cervical level to assume a more vertical position at the upper thoracic level [10, 11].

The cervical facet joints are innervated by articular branches derived from the medial branches of the cervical dorsal rami. Bogduk described the anatomy of the cervical dorsal rami [12]. The C4–C8 dorsal rami arise from their respective spinal nerves and pass dorsally over the root of their corresponding transverse process. The medial branches of the cervical dorsal rami curve medially, around the corresponding articular pillars, and have a constant relationship to the bone at the dorsolateral aspect of the articular pillar as they are bound to the periosteum by an investing fascia and held in place by the tendon of the semispinalis capitis muscle.

The cervical articular processes and the facet joints can be identified in a longitudinal view parallel to the long axis of the cervical spine. The alternating hyperechoic cervical articular processes and anechoic facet joints forms the characteristic "saw sign" in this view [13, 14] (Fig. 28.6). The cervical medial branch nerve courses at the lowest point (waist) along the hyper echoic line representing the articular pillar (Fig. 28.7).

Patient Position

Patient is placed in a prone position with forehead supported. The advantage of this approach is using the characteristic bifid C2 spinous process (Fig. 28.8) as a landmark in determining spinal levels and the ease of performing bilateral procedures without repositioning the patient [15].

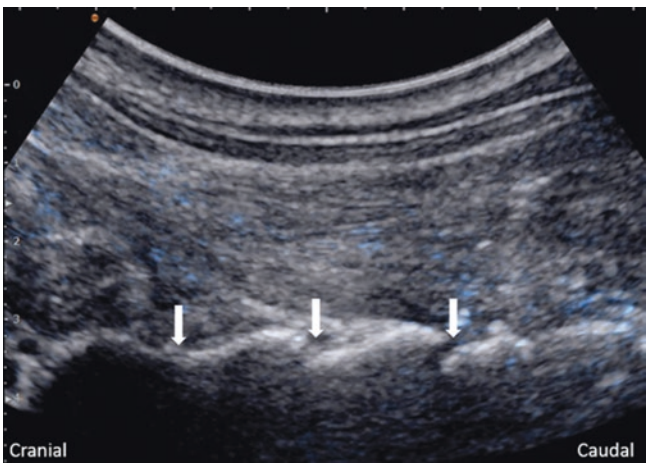

Fig. 28.6 Cervical facet joints. Patient is placed in a prone position with head straight down. Ultrasound transducer is placed in a long-axis plane. The alternating hyper echoic cervical articular processes and anechoic facet joints form the characteristic "saw sign" in this view. Arrows facet joints

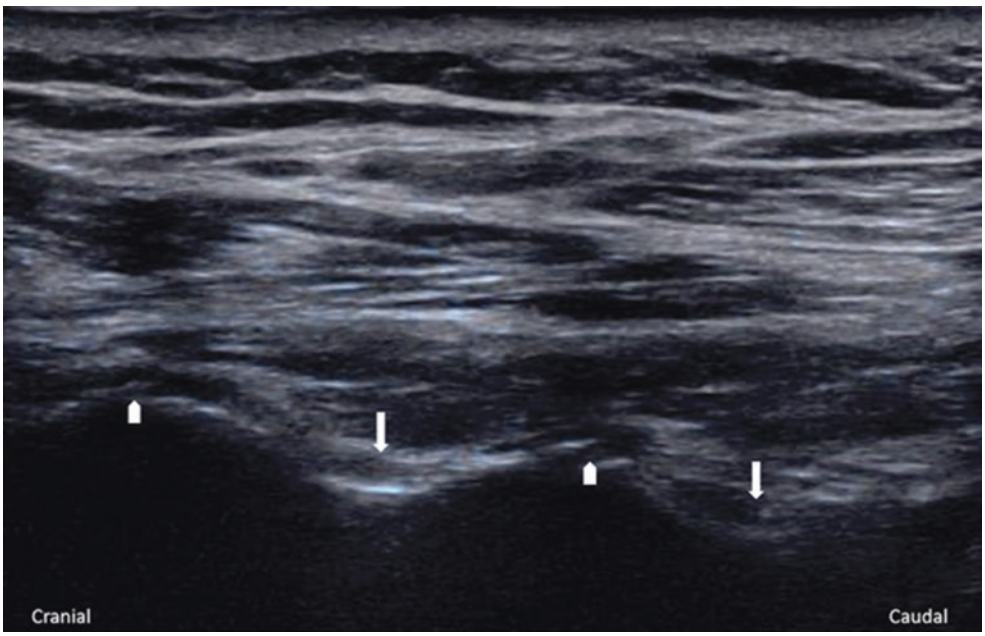

Fig. 28.7 Cervical facet joints and medial branch nerves. Patient is placed in a prone position with head straight down. Ultrasound transducer is placed in a long-axis plane. Arrowheads C3/4 and C4/5 facet joints, Arrows C4 and C5 medial branch nerves

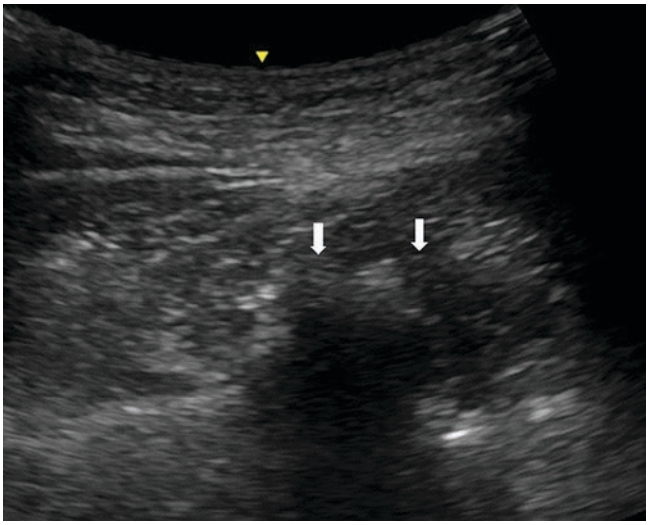

Fig. 28.8 Bifurcate shape of the C2 spinous process. Patient is placed in a prone position with head straight down. Ultrasound transducer is placed in short axis plane at the midline in the posterior neck. The spinous process of C2 has a characteristic bifurcate shape (arrows)

Approach

The cervical spinal levels can be determined by one of two ways: using the characteristic appearance of C7 transverse process (prominent posterior tubercle and absence of anterior tubercle, adjacent pulsating vertebral artery) or using the characteristic bifid shape of C2 spinous process posteriorly (see Fig. 28.8). Once the appropriate spinal level is identified, the probe is turned 90 degrees to obtain the longitudinal view. A 22-gauge, blunt-tip needle is advanced the caudal to cranial direction into anechoic cervical facet joint in between the hyperechoic articular processes under real-time visualization. At this point, 0.5–1 ml of injectate (local anesthetics only for diagnostic block, 2 mg dexamethasone for steroid injection) is injected under direct visualization.

For medial branch nerve block, the needle tip is placed at the midpoint of the articular process at the corresponding level, which corresponds to the deepest point (waist) of the articular pillar (Fig. 28.9). Although the medial branch nerve can be visualized as a hypoechoic oval structure at the deepest point (waist) of the articular pillar, this nerve may not be clearly visible in many cases due to the small size and limitation of scanner resolution. Fluoroscopy may be superior in this application especially in radiofrequency ablation of the medial nerves as this requires precise needle placement along the targeted nerve [15].

Outcome Study

Obernauer et al. reported a randomized controlled trial with 40 patients randomized to CT or ultrasound-guided facet injections. Ultrasound-guided intra-articular injections showed the same therapeutic effect as CT-guided intra-articular injections and the former resulted in a significant reduction of procedure duration without any exposure to radiation [16].

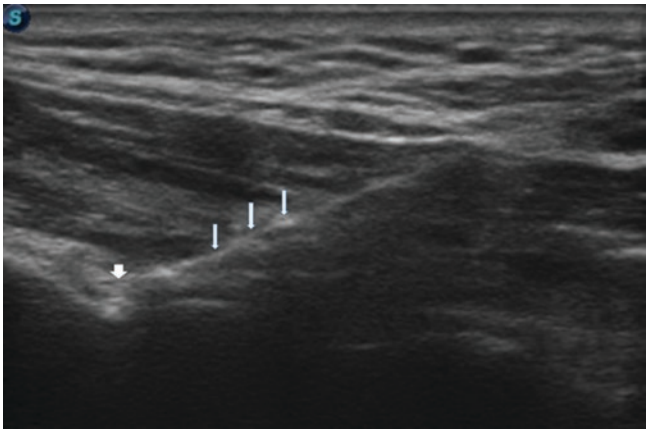

Fig. 28.9 Cervical medial branch block at C5 level. Patient is placed in a prone position with head straight down. Ultrasound transducer is placed in a long-axis plane. Arrowhead C5 medial branch, Arrows needle

Stellate Ganglion Block

Anatomy

The stellate ganglion (cervicothoracic ganglion) is a sympathetic ganglion formed by the fusion of the inferior cervical ganglion and the first thoracic ganglion. Stellate ganglion is located at the level of C7, anterior to the transverse process of C7 and the neck of the first rib and superior to the cervical pleura and just below the subclavian artery. For stellate ganglion block, injection is often given near the Chassaignac's tubercle (anterior tubercle of transverse process of C6) as this is a safer location for intervention. The vertebral artery is projected in the transverse foramen of the cervical vertebrate from the C6 level and up cranially but is exposed at C7 level due to the absence of an anterior tubercle of the transverse process. It is thought that anesthetic spreads along the paravertebral muscles to the stellate ganglion.

Indication

Stellate ganglion block is an established procedure for the diagnosis and treatment of impaired vascular circulation and upper extremity pain including complex regional pain syndrome type I and II and pain from herpes zoster. Left-sided stellate ganglion block has also been used for control of fre-

quent ventricular arrhythmias [17–20]. Right-sided stellate ganglion block has been shown to reduce hot flushes and night awakenings suffered by breast cancer survivors [21, 22] and women experiencing extreme menopause [23]. Recently, stellate ganglion block has also been shown to be effective against post-traumatic stress syndrome (PTSD) [24, 25].

Patient Position

Patient is placed in a lateral decubitus position with the side of intervention up. Alternatively, the patient can be placed in a supine position, with the head rotated 30–45 degrees away from the targeted area. It is often advantageous to place a roll under the shoulder and place the patient in a semi-lateral position to allow more room posterior to the neck to perform the block. An 8–12 Hz linear array transducer is used. For obese patient, a low-frequency curvilinear probe may be needed. The transducer is placed transversely in the lateral neck.

Approach

It is important to identify the correct cervical spinal level before performing this procedure. To minimize the risk of vertebral artery injury, this procedure is best performed at the C6 level where the vertebral artery is protected in the transverse process, as compared to at C7 level where it is exposed. The cervical spinal level can be identified in the short-axis view based on the characteristic view at C6 and C7 levels as described earlier in this chapter (see Fig. 28.1, Fig. 28.2). At the C6 level, in the short-axis view, the C6 transverse process typically appears with a prominent anterior tubercle and a shorter posterior tubercle. The C6 nerve root exits in between the anterior and posterior tubercles. The longus colli muscle can be seen as an oval structure adjacent to the base of the transverse process and vertebral body. The middle cervical ganglion, which is in continuation with the stellate ganglion via the cervical sympathetic chain, is located anteriorly to longus colli muscle (Fig. 28.10).

Gofled et al. presented a posterior lateral approach of stellate ganglion block, which has gain popularity among practitioners due to its superior safety [26]. Once a satisfactory short-axis view at C6 level is identified, a 22-gauge, blunt-tip needle is advanced in posterior lateral to anterior medial direction with an in-plane approach under real-time visualization until the needle tip passes the anterior tubercle of C6 and reaches just beneath the prevertebral fascia on the anterior surface of longus colli muscle (Fig. 28.11). Subfascial injection through this approach, even with a volume as little as 5 ml, has been shown to ensure reliable spread of injectate to the stellate ganglion [26].

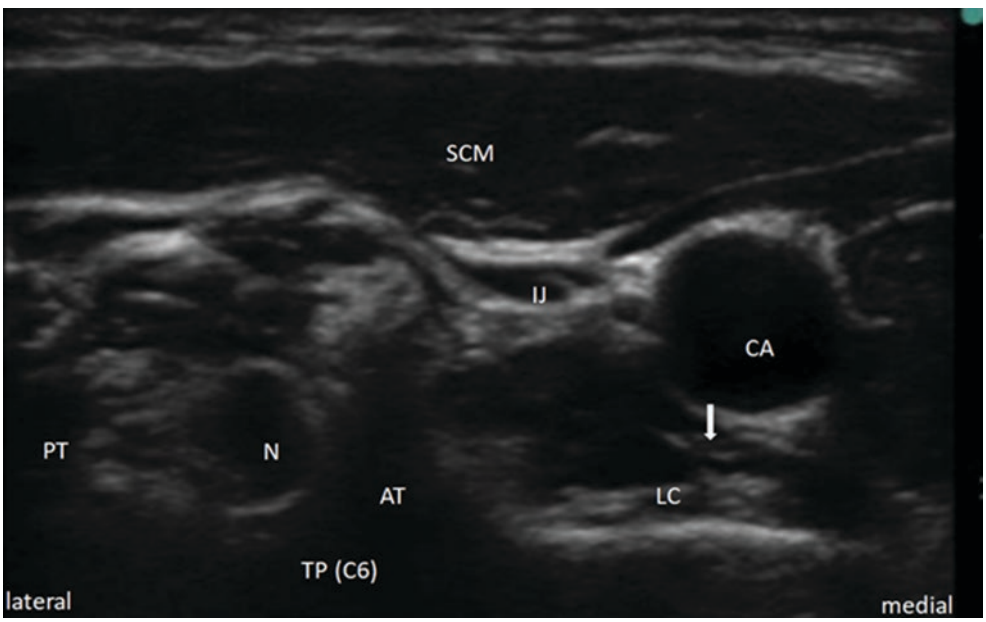

Fig. 28.10 Short-axis view at C6 level. The C6 transverse process typically appears with a prominent anterior tubercle and a shorter posterior tubercle. The C6 nerve root exits in between the anterior and posterior tubercles. The longus colli muscle can be seen as an oval structure adjacent to the base of the transverse process and vertebral body. The middle cervical ganglion, which is in continuation with the stellate ganglion via the cervical sympathetic chain, is located anteriorly to the longus colli muscle. CA carotid artery, IJ internal jugular vein, SCM sternocleidomastoid muscle, N nerve (C6 nerve root), AT anterior tubercle, LC longus colli muscle, PT posterior tubercle, TP transverse process

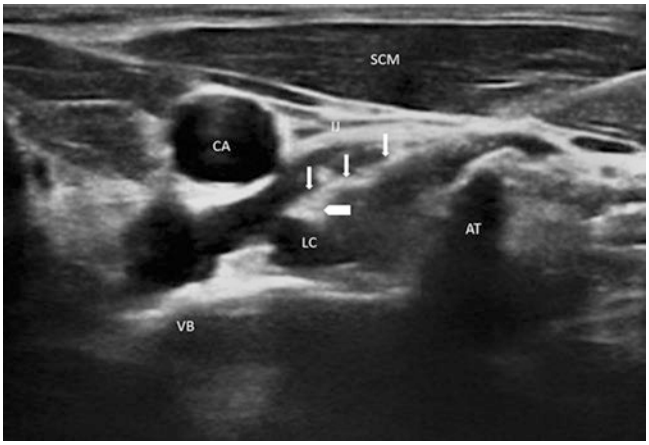

Fig. 28.11 Ultrasound-guided stellate ganglion block at C6 level. The C6 transverse process typically appears with a prominent anterior tubercle and a shorter posterior tubercle. The C6 nerve root exits in between the anterior and posterior tubercles. The longus colli muscle can be seen as an oval structure adjacent to the base of the transverse process and vertebral body. The middle cervical ganglion, which is in continuation with the stellate ganglion via the cervical sympathetic chain, is located anteriorly to the longus colli muscle. CA carotid artery, IJ internal jugular vein, SCM sternocleidomastoid muscle, AT anterior tubercle, arrows block needle, arrowhead middle cervical ganglion, VB vertebral body of C6

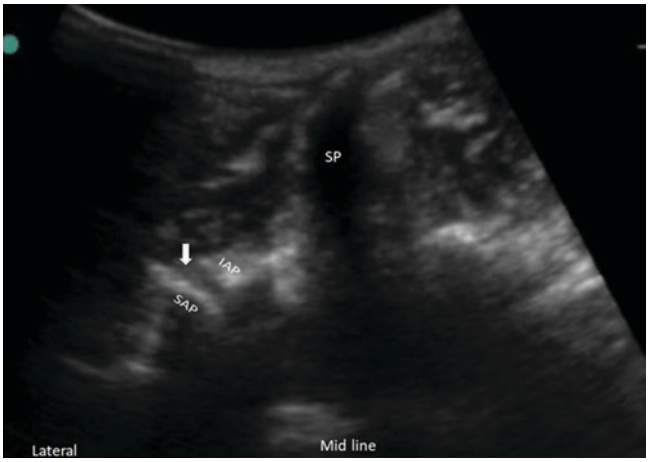

Fig. 28.12 Lumbar facet joint. Patient is placed in a prone position. A curvilinear ultrasound transducer is placed in a transverse plane axis plane. The facet joint space (arrow) is seen between the inferior articular process (IAP) and superior articular process (SAP) of the adjacent vertebrate. SP spinous process, IAP inferior articular process, SAP superior articular process

Lumbar Medial Branch and Facet Joint Injections

Anatomy

Similar to cervical facet joints, lumbar facet joints are also diarthrodial joints involving the cartilaginous surfaces of the articular processes of adjacent vertebra. Each lumbar facet joint is innervated by the medial branches of the dorsal rami from the same vertebral level and from the superior vertebral level. Each medial branch nerve crosses the root of the inferior transverse process and then runs in a groove formed by the junction of the corresponding transverse process and superior articular process where it runs under the medial curve of the mamillo-accessory ligament before it innervates the multifidus muscle [27, 28] and divides into the superior and inferior articular branches to supply the facets above and below at each level. The L5 dorsal ramus differs from the other lumbar dorsal rami. It crosses the sacral ala and gives off the medial branch only as it reaches the caudal aspect of the L5-S1 facet joint [27].

The sonographic anatomy of the lumbar medial branch and facet joints was first described by Greher et al. [29]. A short-axis view through the articular and the transverse process of the lumbar vertebra is obtained. The facet joint space is seen between the inferior articular process and superior articular process (Fig. 28.12). The medial branch nerve may not necessarily be clearly visualized. The junction point between the SAP and the transverse process can be used as the target point for medial branch intervention (Fig. 28.13).

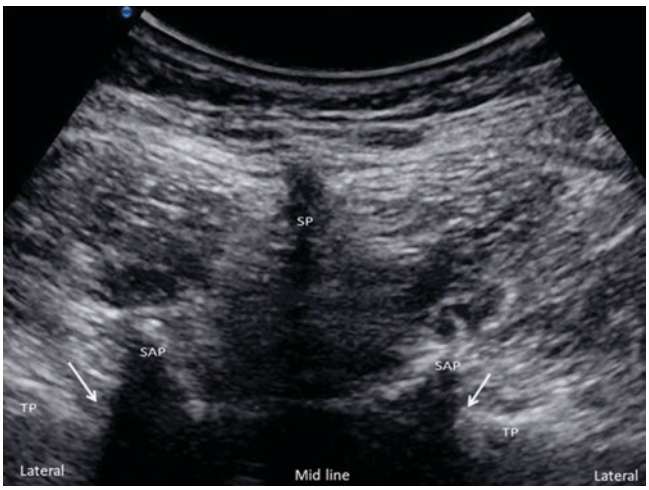

Fig. 28.13 Lumbar medial branch nerve. Patient is placed in a prone position. A curvilinear ultrasound transducer is placed in a transverse plane axis plane. The junction point between the superior articular process and the transverse process can be used as the target point for medial branch intervention. SP spinous process, TP transverse process, SAP superior articular process

Patient Position

Patient is placed in a prone position. Due to the depth of the relevant structures, a low-frequency curvilinear transducer (2–6 Hz) is best suited for this application. The transducer is

first placed in the long axis to identify the sacrum and establishing spinal levels and then rotated to the short-axis view to visualize axial structures.

Approach

First, the correct spinal level needs to be established. The transducer is placed longitudinally in a parasagittal plane over the sacrum. The continuous hyperechoic line represents the dorsal surface of the sacrum. The first interruption to this continuous line cranially represents the L5/S1 interlaminar space (Fig. 28.14). The lamina and interlaminar space alternate as the transducer is moved cranially. Once the correct level is reached, the transducer is rotated by 90 degrees to obtain a transverse view showing the transverse process and the corresponding superior articular process. For medial branch nerve block, a 22-gauge needle is advanced in-plane in a lateral to medial approach under real-time visualization toward the groove at the junction between the base of the superior articular process and the superior border of the transverse process until contacting bone (Fig. 28.15a). The transducer is then rotated to the long-axis view again to confirm the location of the needle tip is at the superior margin of the transverse process (Fig. 28.15b).

For lumbar facet joint injection, similar short-axis view is obtained to show the facet joint space between the inferior and superior articular process. A 22-gauge needle is advanced in-plane in a lateral to medial approach under real-time ultrasound visualization toward facet joint space between the inferior and superior articular process (Fig. 28.16a). The transducer is then rotated to the long-axis view again to confirm the location of the needle tip is in the joint space (Fig. 28.16b).

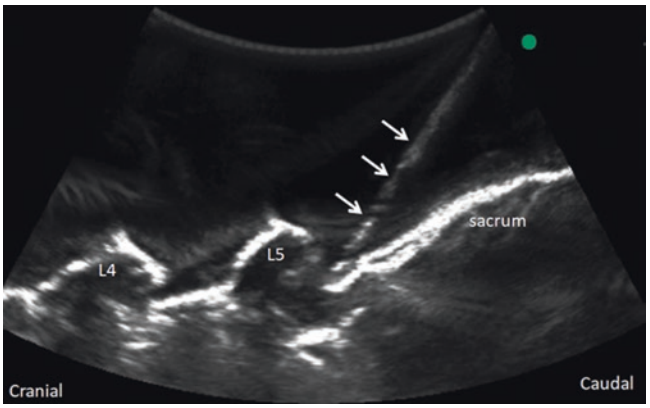

Fig. 28.14 Parasagittal view of the sacrum and lumbar spine. The transducer is placed longitudinally in a parasagittal plane over the sacrum. The continuous hyper echoic line represents the dorsal surface of the sacrum. The first interruption to this continuous line cranially represents the L5/S1 interlaminar space. The lamina and interlaminar space alternate as the transducer is moved cranially. Arrows needle accessing the L5/S1 interlaminar space

Outcome Study

Galiano et al. reported a randomized controlled study comparing ultrasound-guided versus CT-guided lumbar facet joint injection. They were able to visualize the lumbar facet joint in 16 patients out of the 20 patients randomized. There was no difference in benefit detected between the ultrasound-guided versus CT-guided lumbar facet joint injection groups [30]. Due to the depth of the medial branch nerve and facet joints, a low-frequency transducer is often required. As such, the resolution of the sonographic images is relatively low. Visualization of the needle and injectate spread at such depth can be challenging,

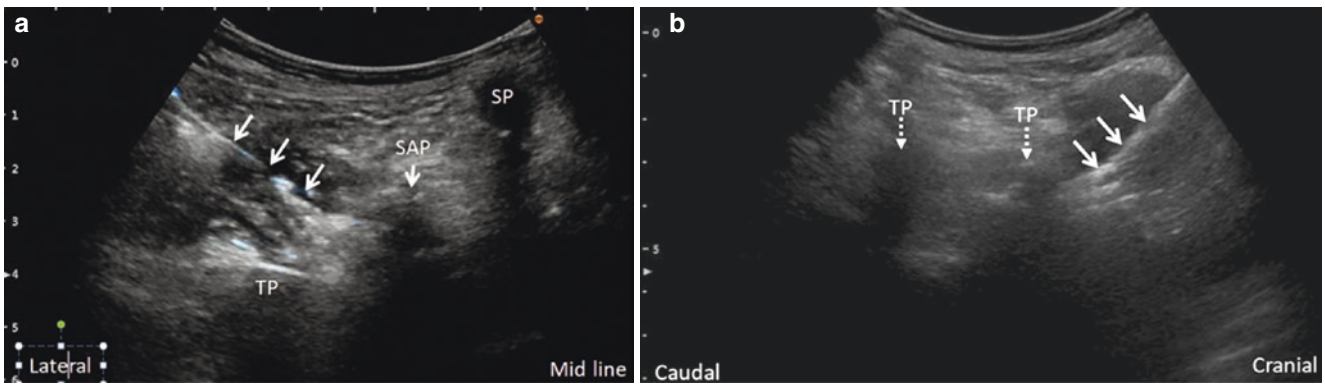

Fig. 28.15 Lumbar medial branch nerve block. Patient is placed in a prone position. A curvilinear ultrasound transducer is placed in a transverse plane axis plane. A 22-gauge needle is advanced toward the groove at the junction between the base of the superior articular process and the superior border of the transverse process until contacting bone (panel **a**). The transducer is then rotated to the long-axis view again to confirm the location of the needle tip is at the superior margin of the transverse process (panel **b**). TP transverse process, SP spinous process, SAP superior articular process, Arrows needle

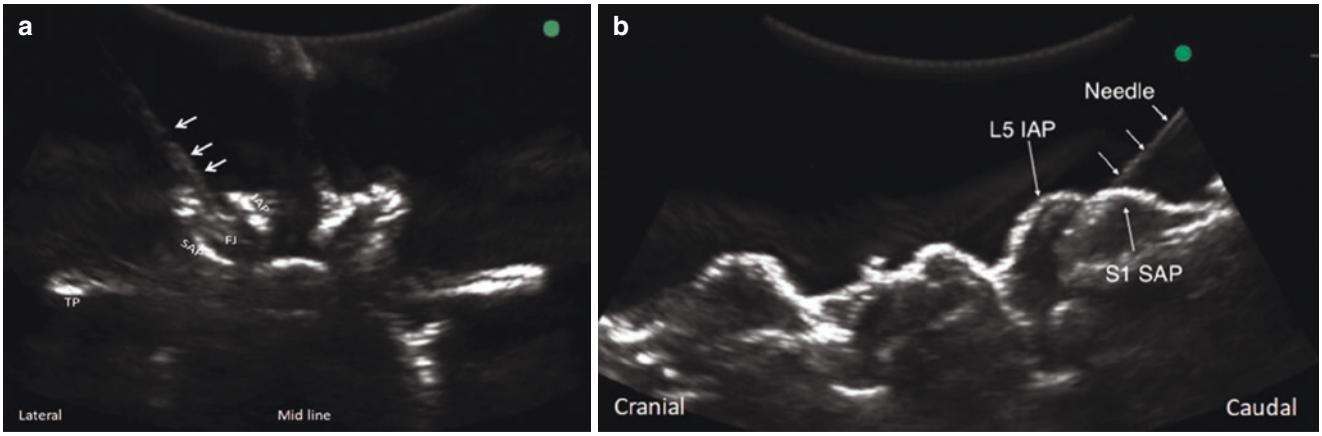

Fig. 28.16 Lumbar facet joint intraarticular injection. Patient is placed in a prone position. A curvilinear ultrasound transducer is placed in a transverse plane axis plane. The facet joint space is seen between the inferior articular process and superior articular process of the adjacent vertebrate. A 22 gauge needle is advanced into the joint space under direct visualization (panel **a**). The transducer is then rotated to the long-axis view again to confirm the location of the needle tip is in the joint space (panel **b**). FJ facet joint, TP transverse process, SAP superior articular process, IAP inferior articular process, Arrows needle

especially in obese patients. At current time, fluoroscopic guidance is still the preferred technique for performing lumbar facet joint interventions.

Lumbar Selective Nerve Root Injection

Although ultrasound-guided cervical selective nerve root injection is feasible and can achieve similar outcome as fluoroscopic-guided injection, such technique is not amendable at the lumbar level. The depth of the lumbar spinal nerve roots renders the visualization challenging. At this depth, it is also difficult to visualize the needle and injectate spread. Few practitioners perform ultrasound-guided lumbar selective nerve root injections. Real-time fluoroscopy and contrast injection with digital subtraction remains the current standard of care [15].

Caudal Epidural Injection

Anatomy

The S1–S5 sacral vertebrae fuse into the sacrum; the three vestige coccygeal vertebrae fuse into the coccyx. The lower portion of sacrum and coccyx is open at the posterior midline. This bony defect is termed the sacral hiatus and is covered by the sacrococcygeal ligament. The hiatus is bounded laterally by the sacral cornua, and the floor is composed of the posterior aspect of the sacrum. The lumbar epidural space continues as the caudal epidural space, which can be accessed via the sacral hiatus [31, 32]. Chen et al. [33] described the first sonography of the caudal structures relevant to caudal epidural needle placement.

Patient Position

Patient is placed in a prone position, similar to fluoroscopic-guided caudal epidural injections. A linear high-frequency transducer can be used for this application. A low-frequency curvilinear transducer may be needed for obese patients.

Approach

The transducer was first placed transversely at the midline to obtain the sonographic transverse view of the sacral hiatus. The two hyperechoic reversed U-shaped structures are the two bony prominences of sacral cornua. Between the two cornua, there are two hyper echoic band-like structures. The band-like structure on top is the sacrococcygeal ligament. The band-like structure at the bottom is the dorsal bony surface of the sacrum (Fig. 28.17). The transducer is then rotated 90 degrees and rested in between the two sacral cornua to obtain the longitudinal view of the sacral hiatus (Fig. 28.18). A 22-gauge caudal epidural needle is inserted and advanced under the sonographic longitudinal view of the sacral hiatus. A "pop" is usually felt as the sacrococcygeal ligament is penetrated. As the caudal epidural needle pierces through the sacrococcygeal ligament, the portion of the needle inside the caudal epidural space is no longer observed [33]. In a sense, this technique is not a "true" direct visualization, although ultrasound is used to guide the needle placement. Due to the inability to visualize the needle after it enters the sacral canal, it is difficult to assess intravascular injection with this technique. Because of the rich vascularity in the caudal epidural space, confirmation with contrast dye spread under fluoroscopy is recommended to rule out intravascular injection.

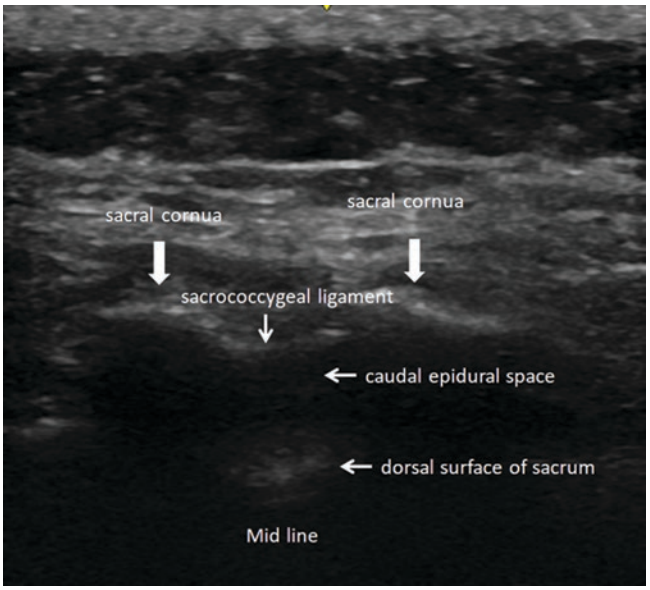

Fig. 28.17 Caudal epidural space. The transducer is placed transversely at the midline to obtain the transverse view of the sacral hiatus. The two hyper echoic reversed U-shaped structures are the two bony prominences of sacral cornua. Between the two cornua, there are two hyper echoic band-like structures. The band-like structure on top is the sacrococcygeal ligament. The band-like structure at the bottom is the dorsal bony surface of the sacrum

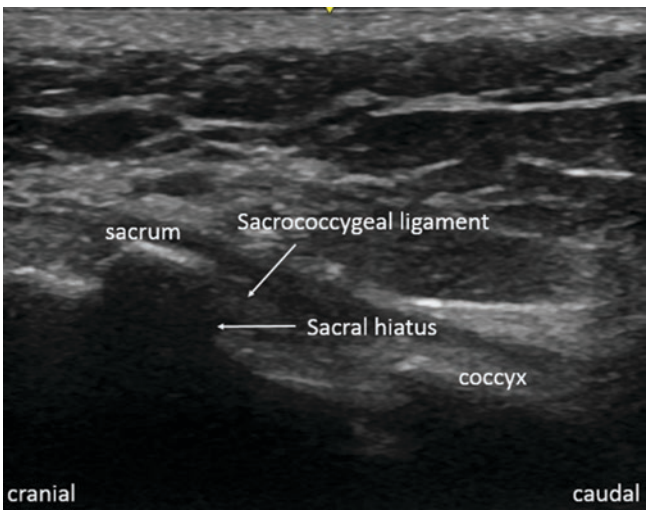

Fig. 28.18 Long-axis view of the sacrococcygeal region. Once a transverse view at the two sacral cornua is obtained, the transducer is then rotated 90 degrees and rested in between the two sacral cornua to obtain the longitudinal view of the sacral hiatus

Sacroiliac Joint Injection

Anatomy

The SI joint is a wedge-shaped diarthrodial joint composed of an inferior cartilaginous joint that contains a joint capsule, synovial lining, and synovial fluid and an upper fibrous articulation [34]. In those cases refractory to conservative treatment, local treatment of the SI joint through intra-articular corticosteroid injection has provided diagnostic value and clinical improvement. Because of its complex anatomical structure, the SI joint injection can be difficult to enter with a needle [35].

Patient Position

Patient is placed in a prone position. A linear transducer (8–12 Hz) is placed transversely at the lower end of the sacrum to obtain a short-axis view. A low-frequency curvilinear transducer may be needed for obese patients.

Approach

The transducer is placed transversely over the lower sacrum at the level of the sacral hiatus. First, identify the lateral edge of the sacrum by slowly moving the transducer laterally. The transducer is then moved cranially following the edge of sacrum until the bony contour of the ileum comes in view. The cleft between the ileum and the lateral sacral edge represents the sacroiliac joint [36, 37]. A 22-gauge needle is then inserted at the medial end of the transducer and advanced from medial to lateral under direct vision in-plane with the US beam until it enters the joint (Fig. 28.19). The major limitation of the

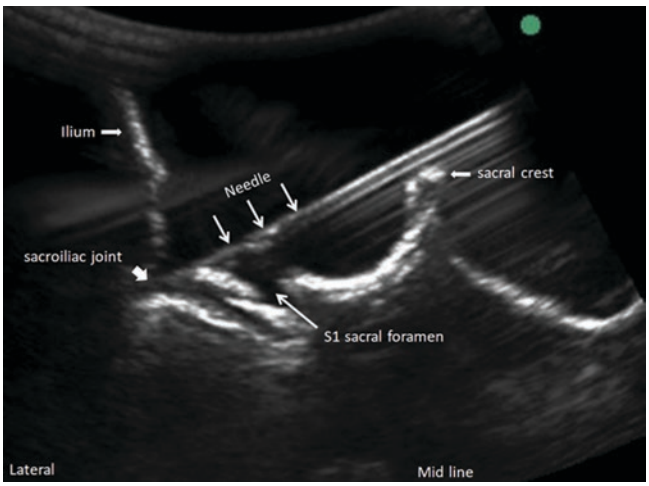

Fig. 28.19 Sacroiliac joint injection. The transducer is placed transversely over the lower sacrum at the level of the sacral hiatus. First, identify the lateral edge of the sacrum by slowly moving the transducer laterally. The transducer is then moved cranially following the edge of sacrum until the bony contour of the ileum comes in view. The cleft between the ileum and the lateral sacral edge represents the sacroiliac joint. A 22-gauge needle is then inserted at the medial end of the transducer and advanced from medial to lateral under direct vision in-plane with the ultrasound beam until it enters the joint

approach is the inability to visualize the needle and the injectate once the needle enters below ileum. It is difficult to assess periarticular versus intra-articular injectate spread. In a sense, this technique is not a "true" direct visualization, although ultrasound is used to guide the needle placement.

Outcome Study

Pekkafahli et al. [37] reported a feasibility and effectiveness study of ultrasound-guided intra-articular SI joint injection with fluoroscopic validation in 34 patients with sacroiliitis, 26 patients with bilateral disease, and 8 patients with unilateral disease. The synovial portion of these SI joints was injected under ultrasound guidance, resulting in 46 (76.7%) successful injections and 14 (23.3%) missed injections. The authors noted that successful intra-articular injection rate was 60% for the first 30 injections with improvement to 93.5% in the last 30 injections, suggesting a steep learning curve of this technique.

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Sympathetic Neural Blockade and Trigger Point Injections

29

Vwaire Orhurhu, Christopher Aiudi, Ivan Urits, Mark Jones, and Michael P. Zaccagnino

Key Points

- The use of ultrasound and fluoroscopy as a guide has dramatically improved the safety of sympathetic blocks. However, adequate training and knowledge of the complications associated with each block are vital.
- Sphenopalatine ganglion (SPG) block is indicated in sphenopalatine neuralgia. Other indications for SPG block include trigeminal neuralgia, headaches (cluster and migraine headaches), atypical facial pain, and many other pain syndromes not effectively treated with pharmacological agents.
- Multiple techniques have been developed to safely perform a stellate ganglion (SG) block. However, it is important to know that at C7–T1, the vertebral arteries lies anterior to the stellate ganglion until they enter the vertebral foramen at C6 where it lies posterior to the C6 transverse process. The cervical sympathetic chain lies medial to the carotid space at C6.
- The stellate ganglion also supplies some of the sympathetic innervation to the upper extremity. The ganglion receives sympathetic inputs from C7, C8, and T1 and occasionally from C5, C6, T2, and T3. Inadequate pain relief with a satisfactory stellate block may result from the inconsistent involvement of these nerves.
- Common indications for SG blocks include sympathetically mediated pain (i.e., CRPS I/II), cancer-related pain, vascular pain conditions (i.e., vascular insufficiency, Meniere syndrome, Raynaud's disease), and other conditions such as herpes zoster and postherpetic neuralgia.
- Chronic pain from malignancies in the abdomen can be difficult to treat. Celiac plexus blocks can be used as an alternative therapy from improvement and quality of life for patients with conditions like pancreatic cancer.
- Pelvic pain continues to be very challenging when conservative measures fail. Patients may present with a history of vague, dull, burning, and poorly localized visceral pain, refractory to conservative measures. These patients may benefit from blockade of the superior hypogastric plexus or ganglion impar block.
- Myofascial trigger points (TPs) are small tender nodules in taut, "rope-like" bands of skeletal muscle. They can be detected by palpation as the "spot of maximum tenderness" along the taut band that produces or increases the typical pain experiences by the patient.

Case Presentation

A 52-year-old female secretary presented to the pain clinic 6 months after a job-related injury that occurred at her place of work while using a poorly positioned computer keyboard. She was diagnosed of carpal tunnel syndrome and subsequently underwent an endoscopic carpal tunnel release surgery. She was able to return to work but developed a gradually progressive pain at her left arm and wrist. She described the

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pain as severe, sharp, and rates it a 9 out of 10. Her pain is associated with cramping and numbness. During physical examination, the temperature of her left hand was 3° lower than her right hand. There is also noted mild atrophy of her left palm and some color discoloration. She was diagnosed with chronic regional pain syndrome (CRPS) type I and was started on a multimodal regimen of occupation therapy and neuropathic pain agents including tramadol, gabapentin, nortriptyline, and celecoxib. The use of neuropathic pain medications and occupational therapy provided moderate relief, and the pain continued to persist at 7 out of 10. We discussed the use of stellate ganglion (SG) block and trial for spinal cord stimulation (SCS) while adjusting her current medication regimen. The patient held off on pursuing spinal cord stimulation therapy and wanted to try the SG block. After the SG block was performed, patient's pain score drastically reduced from 10 out of 10 to a 3 out of 10. This pain relief lasted for 7 weeks, and the SG block was subsequently repeated with good analgesic efficacy.

Introduction

The pathophysiology involved in the development of chronic pain remains multifactorial. The afferent and efferent pathways of the sympathetic nervous system have been implicated for the generation, prolongation, and treatment of various chronic pain syndromes. Sympathetic blocks have demonstrated to work by two mechanisms. First, these blocks interrupt preganglionic and postganglionic efferent nerves, which through direct and indirect coupling may interfere with primary afferent nerves [1–3]. Second, afferent nerves from deep visceral structures travel with sympathetic nerves and may be blocked due to their close proximity [4–6].

Some of the indications for sympathetic block and neurolysis include but are not limited to trigeminal neuralgia, CRPS I/II, cancer pain, abdominal pain, and pelvic pain. The goal of this chapter is to discuss some of the commonly used sympathetic nerve blocks and their anatomical location, indication, procedural technique, and complications.

Anatomy of the Sympathetic Nervous System

The autonomic nervous system, a subdivision of the peripheral nervous system, unconsciously controls and regulates functions of the digestive, respiratory, and cardiovascular systems among others. Within the autonomic nervous system, there exist two major subdivisions: the sympathetic and parasympathetic nervous systems. The sympathetic nervous system is often associated with a "fight or flight" stress response, whereas the parasympathetic nervous system is often associated with a "rest and digest" response. These two subdivisions of the autonomic nervous system interact with each other in a competitive fashion to regulate the functions previously listed.

The sympathetic nervous system will be the focus of this overview since this subdivision is a key target for interventional pain techniques. As previously mentioned, the sympathetic nervous system is involved in the stress responses which acts to produce peripheral vasoconstriction for shunting blood to large muscles, catecholamine release with subsequent enhancement of cardiopulmonary function, and intestinal function inhibition.

Sympathetic nerves travel to afferent organs involving multiple nerves and ganglia. Preganglionic sympathetic nerves, also known as general visceral efferent neurons, have cell bodies in the intermediolateral horn (lateral gray column) of the spinal cord from levels T1 to L2/3. The nerves exit the spinal cord with the ventral root of the spinal nerve of the corresponding vertebral level and then travel within the white rami communicants to eventually either synapse with a postganglionic sympathetic nerve or travel directly to affect target organs (chromaffin cells of the adrenal medulla).

Sympathetic nerves destined to synapse with a postganglionic nerve travel to paravertebral ganglia. The paravertebral ganglia, more commonly known as the sympathetic chain, run laterally to the vertebral bodies bilaterally and are subdivided into paired cervical (3), thoracic (12), lumbar (4), and sacral (4) ganglia and one unpaired ganglion impar (Fig. 29.1) [2, 8–10]. When a preganglionic nerve reaches the paravertebral ganglia chain, it can either synapse directly with postganglionic nerves, travel up/down the paravertebral ganglia chain to synapse with a postganglionic neuron at another vertebral level, or pass through and form thoracic/lumbar/sacral splanchnic nerves and eventually synapse at prevertebral ganglia. Prevertebral ganglia, also known as preaortic ganglia, are located in the head, chest, abdomen, and pelvis. If multiple ganglia are in close proximity, they are referred to as a plexus of nerves. Prevertebral ganglia include the ciliary, otic, sphenopalatine, submaxillary, celiac, superior mesenteric, aorticorenal, and inferior mesenteric ganglia [2, 9, 10]. Plexuses include the cardiac, pulmonary, celiac, superior hypogastric, and inferior hypogastric plexuses [2, 9, 10].

Postganglionic nerves then travel to innervate target organs. Postganglionic nerves from the paravertebral ganglia leave the chain via gray rami communicants to rejoin spinal nerves and then travel to innervate their appropriate structure

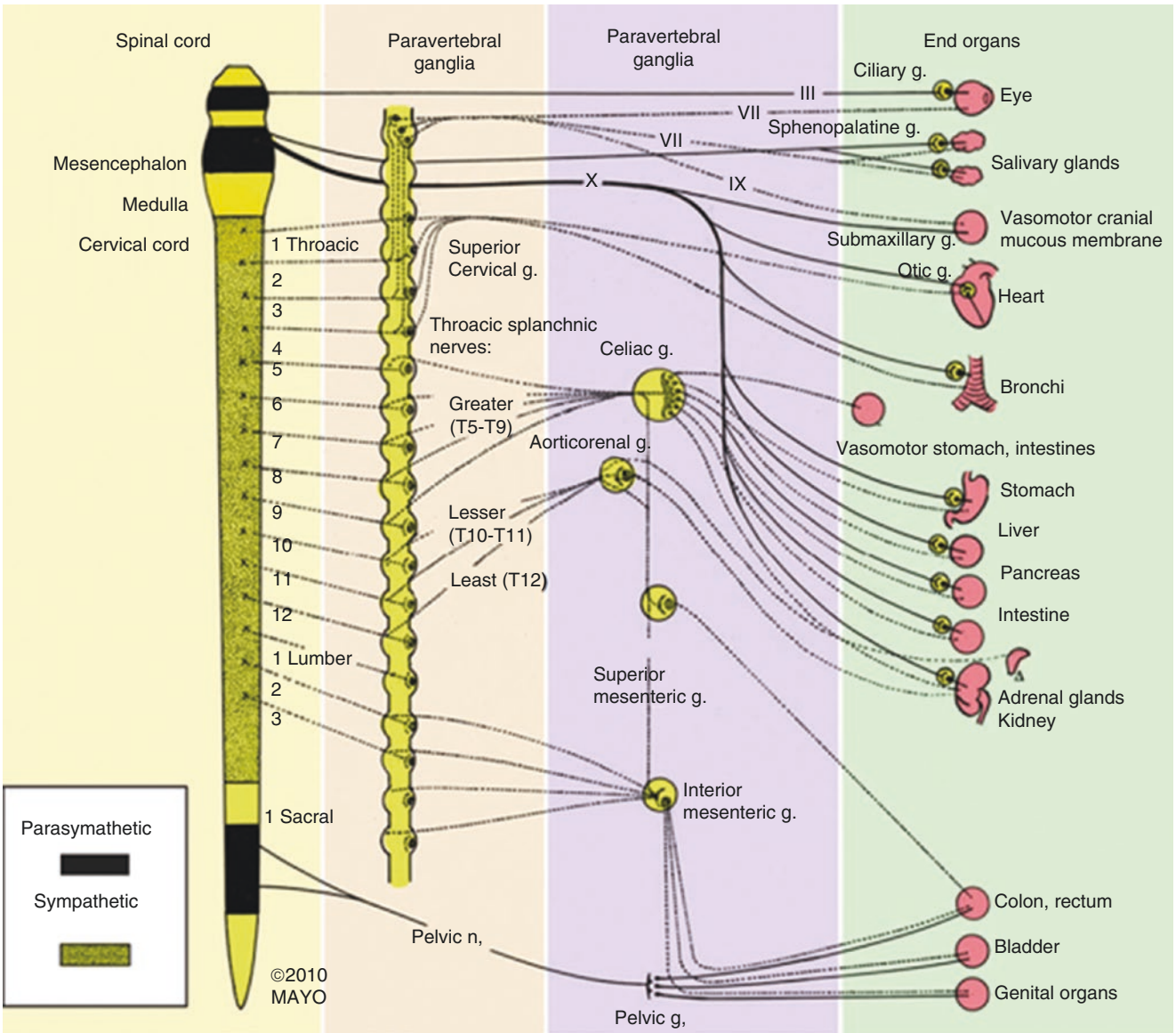

Fig. 29.1 The anatomical pathways of the autonomic nervous system. (From Lamer and Eldrige [7]; used with permission of Mayo Foundation for Medical Education and Research, all rights reserved)

such as the pupils, heart, vasculature, and sweat glands [2, 4, 8–10]. Postganglionic nerves from the prevertebral ganglia/plexus travel to innervate their structures including viscera throughout the body (see Fig. 29.1) [10].

Of note, while the gray rami communicants contain only postganglionic sympathetic efferent nerves, the white rami communicants contain both efferent preganglionic sympathetic efferent nerves and afferent visceral nerves, which carry pain signals. The anatomic contents of the white rami communicants describe the only neural traffic between the central nervous system and sympathetic nervous system [2, 9].

Sphenopalatine Ganglion Block

Anatomy

The sphenopalatine ganglion (SPG), also known as the pterygopalatine ganglion or Meckel's ganglion, is the most cephalad region of input for the superior cervical sympathetic ganglion. It resides in the pterygopalatine fossa and is bordered anteriorly by the maxillary sinus, posteriorly by the medial plate of pterygoid process, and medially by the perpendicular plate of the palatine bone [11].

The SPG contains sensory, parasympathetic, and sympathetic fibers (see Fig. 29.1). Sensory fibers include the sphenopalatine branches of the maxillary nerve and receive inputs from the nasal membrane, soft palate, and pharynx [5, 11, 12]. Parasympathetic fibers arise from the nervus intermedius through contribution from the greater petrosal branch of the facial nerve and are responsible for the secretory and vasodilatory functions of the various glands of the eyes and naso- and oropharynx. The sympathetic fibers originate from preganglionic fibers of the upper thoracic spinal cord and synapse with postganglionic fibers at the superior cervical ganglion. From here, the sympathetic nerves travel through the carotid plexus and join the deep petrosal nerve which then enters the SPG to supply the vasoconstrictor functions of the ganglion.

Indications

A SPG block is a useful technique to manage pain syndromes in the head region. These include sphenopalatine neuralgia, trigeminal neuralgia, headaches (cluster and migraine headaches), atypical facial pain, and many other pain syndromes not effectively treated with pharmacological agents [4, 8–10, 13–15].

Procedural Technique

There are several techniques for a SPG block: a topical intranasal approach, an intraoral greater palatine foramen approach, and a fluoroscopic-guided lateral approach. The SPG can be effectively blocked with local anesthetics with or without steroid, radiofrequency (RF) lesioning, and chemical neurolysis.

Intranasal Approach

The intranasal approach relies on topical application of local anesthetics that absorb through the nasal mucosa to the sphenopalatine ganglion. Pledgets containing local anesthetics are placed in an applicator device such as bayonet forceps [16, 17]. Prior to application, patients should be instructed to blow through each nostril to determine the nares with the most opening. The applicator is inserted into the affected nare until it reaches the level of the zygomatic arch. Slowly advance posterolaterally into the nasopharynx. Once in place, insert another applicator similarly with a final destination being superior and posterior to the initial applicator. The applicators are kept in place for 30–35 seconds. Unfortunately, many patients may not tolerate the insertion of pledgets. Newer techniques that use hollow-lumen cotton-tipped applicators in a similar fashion are generally better tolerated, but the applicators are usually left in place for ~30 minutes [18].

Intraoral Approach

In this technique, also known as the greater palatine foramen approach, the patient is placed in the supine position with slight extension of the neck. Using a dental needle with a 120° angle, insert it medial to the gumline of the third molar. Often, a dimple can be seen, which represents the foramen. Once inserted, advance the needle 2.5 cm superiorly and posteriorly. Because the maxillary nerve lies cephalad to the SPG, if facial paresthesias are elicited, the needle should be pulled back and redirected caudad. Fluoroscopic imaging can be used with contrast solution to obtain a proper spread and visualization of the pterygopalatine fossa. After negative aspiration for blood and cerebrospinal fluid (CSF), inject cautiously 2 mL of local anesthetic with or without steroid.

Fluoroscopic-Guided Lateral Approach

To begin, place the patient in the supine position. Using fluoroscopy in the lateral view, visualize the cervical spine and mandible. Rotate the head until the mandibular rami are superimposed, and then move the C-arm cephalad until the pterygopalatine fossa is visualized. This image is commonly described as an inverted flower "vase" just posterior to the posterior aspect of the maxillary sinus. The site of needle entry is the coronoid notch under the zygomatic bone. A standard 22-gauge, 3.5 inch spinal needle is typically used for this technique. Then administer subcutaneous local anesthetic, and using a posteroanterior (PA) view of the orbit and maxillary sinuses, advance the needle cephalad and mildly posterior to the pterygopalatine fossa. Confirm positioning near the fossa, and advance it until it's adjacent to the lateral nasal mucosa. Obtain a lateral view to confirm needle position in the fossa. After negative aspiration for blood, air, and CSF, inject up to 5 mL of local anesthetics.

Radiofrequency

Once a successful temporary diagnostic block with local anesthetics with or without steroid is observed, a potentially longer-lasting treatment with radiofrequency (RF) lesioning may be employed. Using the fluoroscopic-guided lateral approach, RF lesioning at the SPG can be performed using conventional thermal RF lesioning or pulsed RF lesioning. Typically, a 22- or 20-gauge, curved blunt-tipped RF needle with a 5–10 mm active tip is used. It is important to confirm needle positioning in the fossa to prevent damage to the maxillary division of the trigeminal nerve during RF lesioning. Once the final needle positioning is confirmed radiographically, sensory testing should occur. If the needle is correctly positioned, paresthesias should be felt at the base of the nose. Paresthesias in the upper teeth or hard palate signify inappropriate needle placement and involvement of the maxillary nerve and greater/lesser palatine nerves, respectively. If these paresthesias occur, the needle should be positioned caudally if the maxillary nerve is involved and/or posteromedially if

the greater/lesser palatine nerves are involved. Once properly positioned, one or two conventional thermal RF lesions can be made using 80 °C for 70–90 seconds, or two to three pulsed RF lesions can be made using 42 °C for 120 seconds. Since a higher temperature is used with conventional thermal RF lesioning, 1–2 mL of local anesthetic should be applied prior to treatment. The temperature is only slightly above normal body temperature with pulsed RF lesioning; therefore, local anesthetic pretreatment is not necessary.

Chemical Neurolysis

As in RF lesioning, once a successful temporary diagnostic block with local anesthetics with or without steroid is observed, if desired, a potentially longer-lasting treatment with chemical neurolysis may be employed. Using the fluoroscopic-guided lateral approach, after negative aspiration for blood and CSF, inject 1 mL of 2% lidocaine; then after adequate anesthesia, follow with 1 mL of 6–12% phenol.

Complications

Complications of a sphenopalatine ganglion block include epistaxis and hematoma formation if the nasal mucosa, maxillary artery, or venous plexus is punctured. Infection, including meningitis, can occur if aseptic technique is not properly performed. Hypoesthesia and numbness of the palate, maxilla, or posterior pharynx can occur from injury to the maxillary or mandibular nerves [19, 20]. Trauma can occur to the parotid gland or branches of the facial nerve. Impairment of the secretomotor function of the SPG may occur, leading to decreased lacrimation and/or mucus production of the nose or mouth. During RF lesioning bradycardia can occur [19–21]. If bradycardia occurs, stop the lesioning; if the bradycardia does not resolve, atropine can be used for symptomatic bradycardia.

Stellate Ganglion Block

Anatomy

The stellate ganglion is a collection of nerves formed by the fusion of the first thoracic ganglion and inferior cervical ganglion. The fusion of these two ganglia exists in 80% of the cases. Preganglionic axons from thoracic nerve roots join the sympathetic chain and travel cephalad to synapse at the stellate, middle, and superior cervical ganglia. Sympathetic innervation from the head and neck arises predominantly from preganglionic axons of the T1–T3 nerve roots, while sympathetic innervation of the upper extremity arises predominantly from preganglionic axons of the T2–T9 nerve roots.

Postganglionic fibers travel directly from their respective ganglia alongside arterial vasculature to the head and neck and brachial plexus to innervate the arm. Because postganglionic fibers control vasoconstrictor and sudomotor functions, blockade of these fibers during a stellate ganglion block results in ptosis, miosis, enophthalmos, and disruption of the face and neck sweat response.

The stellate ganglion functions as a main gateway for sympathetic innervation to the head and neck and arm via the brachial plexus. This is because most of the preganglionic fibers that serve these regions either synapse into or traverse through the stellate ganglion. However, the first three intercostal nerves can also carry sympathetic input directly to the brachial plexus bypassing the stellate ganglion, explaining why inadequate pain relief with a satisfactory stellate block may result from the inconsistent involvement of these nerves [22, 23].

The stellate ganglion is typically found anterior to the C7 transverse process and first rib, abutting the longus colli muscle anterolaterally. In roughly 20% of individuals, fusion of the first thoracic ganglion and inferior cervical ganglion does not occur. In this case, the inferior cervical ganglion can be found at the C7 level, whereas the first thoracic ganglion is found at the level of T1. At the level of C7, the vertebral artery and vein lie anterior to the stellate ganglion and depending on the stellate ganglion nerve block approach, potentially in the pathway of needle placement. Once the vertebral artery reaches the C6 level, it heads posteriorly, enters the vertebral foramen, and is shielded by the anterior tubercle of C6 (Chassaignac's tubercle).

Indications

A stellate ganglion block is indicated for painful conditions involving the head, neck, upper extremities, and upper thoracic dermatomes. Pain conditions include sympathetically mediated pain (i.e., CRPS I/II), cancer-related pain, vascular pain conditions (i.e., vascular insufficiency, Meniere syndrome, Raynaud's disease, vasospasms, accidental arterial drug injections), and other conditions such as phantom limb pain, frostbite, herpes zoster, and postherpetic neuralgia [24–26]. Rare indications include angina pectoris, hyperhidrosis of the upper extremity, and pulmonary embolism [25, 27, 28].

Procedural Techniques

There are several approaches for a stellate ganglion block: paratracheal, anterior, posterior, and oblique approaches. These approaches can incorporate imaging modalities such as fluoroscopy, CT, and ultrasound. The stellate ganglion

can be effectively blocked with local anesthetics with or without steroid, radiofrequency (RF) lesioning, and chemical neurolysis. During the procedure, resuscitative equipment should be available, including medications, suction devices, oxygen delivery systems, cardiac defibrillators, and tools needed for intubation. In all techniques, successful stellate ganglion block should result in an ipsilateral Horner's syndrome (ptosis, miosis, and anhidrosis) and an increase in temperature (greater than 3 °F) of the ipsilateral upper extremity [29]. Horner's syndrome is a result of cephalic sympathetic blockade to the head and neck; however, it does not verify upper extremity sympathetic blockade. Measuring an increase in skin temperature is the most practical way to demonstrate upper extremity sympathetic blockade. Other signs confirming a successful stellate ganglion block include Guttman's sign (unilateral nasal stuffiness) and increased facial warmth. Patients should be observed after the procedure for approximately an hour for complications. Sympathetic blockade of the upper extremity or the shoulder can also be measured with laser Doppler flowmetry, sudomotor, sweat test, or sympathogalvanic response.

Landmark-Guided Paratracheal Approach

Although this is a blind procedure, fluoroscopy can be used to confirm proper needle placement and contrast spread. To begin, the patient is placed in the supine position with slight hyperextension of the neck with or without a shoulder roll. The location of the cricoid cartilage acts as a landmark for identification of the C6 level in the adult population. Have the patient slightly open their mouth and then palpate for the C6 anterior tubercle (Chassaignac's tubercle); this is typically located at the medial border of the sternocleidomastoid (SCM) muscle a few centimeters cephalad to the sternoclavicular joint. Once the C6 tubercle has been identified, maintain pressure over the tubercle, and retract the carotid artery and SCM muscle laterally while observing and avoiding the trachea medically. Then administer subcutaneous local anesthetic, and advance a 22- or 25-gauge spinal needle in an anteroposterior direction until boney contact is made with the C6 tubercle or the junction between the C6 tubercle and vertebral body. Once boney contact is made, withdraw the needle approximately 2–4 mm. Since imaging is not employed with this technique, the specific location of needle contact is unknown. If using imaging, after negative aspiration for blood, air, or CSF, inject contrast. Once proper needle placement is confirmed and after negative aspiration, cautiously inject 0.5 mL of 1% lidocaine, and monitor for aberrant symptomatic changes. If the test dose produces no adverse events, inject 5–10 mL of 1% lidocaine or 0.25% bupivacaine with or without a steroid in an incremental fashion with frequent aspiration. The use of hand signals to confirm or deny adverse events can be beneficial. This minimizes movement of surrounding the neck muscles that may distort needle placement.

Ultrasound-Guided Approach

Ultrasound is now commonly used for the visualization of the stellate ganglion and its surrounding tissue. The benefit of using ultrasound is direct visualization of vital structures and injectate spread, thereby theoretically decreasing the incidence of retropharyngeal hematoma and vascular injections. As in the landmark-guided paratracheal approach, the patient is placed in the supine position with slight hyperextension of the neck with or without a shoulder roll, and the C6 level is located using the cricoid cartilage as a landmark. Fluoroscopy can be also used to identify the desired level. At the C6 level, just lateral to the trachea, transversely place a linear array ultrasound probe (3–12 MHz) (Fig. 29.2).

Visualization with the ultrasound will reveal structures surrounding the stellate ganglion; these include the carotid artery (an important landmark), sternocleidomastoid, internal jugular, thyroid gland, vertebral artery, esophagus, pleura, nerve roots, and the longus colli muscle (another important landmark). The target location lies in the facial plane anterior to the longus colli muscle, where the stellate ganglion is observed. After subcutaneous local anesthetic administration, using an in-plane approach, guide a 21- or 22-gauge needle to the target location. After negative aspiration for blood, air, and CSF, as well as close patient monitoring, inject 5–10 mL of 1% lidocaine or 0.25% bupivacaine with or without a steroid in small aliquots under real-time

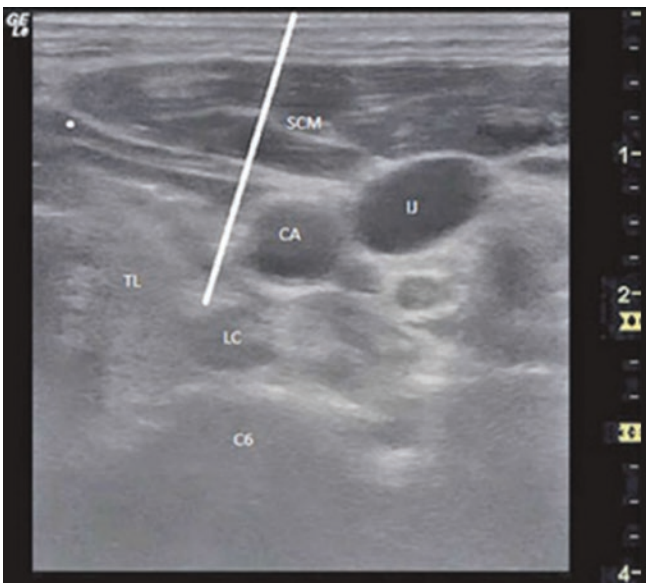

Fig. 29.2 The use of ultrasound to identify the stellate ganglion at level C6. SCM, sternocleidomastoid muscle; IJ, internal jugular; LC, longus colli muscle; TL, thyroid lobule; CA, carotid artery

ultrasonography while observing for the spread of injectate volume along the appropriate fascial plane.

Fluoroscopic-Guided C7 Anterior Approach

This approach is similar to the landmark-guided paratracheal approach except the target is the C7 anterior tubercle or the junction between C7 tubercle and vertebral body (Fig. 29.3). To begin, the patient is placed in the supine position with slight hyperextension of the neck. Using fluoroscopy in posteroanterior (PA) view, square the C7 vertebral body end plates, and identify the C7 tubercle and transverse process. Importantly, at the level of C7, the vertebral artery and vein lie anterior to the stellate ganglion, unlike at the C6 level where the vertebral artery is shielded by the anterior tubercle of C6 (Chassaignac's tubercle). To avoid the vertebral artery, the target location lies medial to the C7 tubercle between the tubercle and vertebral body junction. Administer subcutaneous local anesthetic, and advance a 22- or 25-gauge spinal needle coaxially until contact with bone is made. Then withdraw the needle approximately 2–4 mm, and confirm depth in the lateral view. After negative aspiration for blood, air, or CSF, inject contrast under real-time fluoroscopy in the PA view, and observe for optimal spread along the anterolateral borders of ~C6–T2 vertebral bodies to ensure adequate blockade of the stellate ganglion. Once proper needle placement is confirmed, cautiously inject 0.5 ml of 1% lidocaine, and monitor for aberrant symptomatic changes. If the test dose produces no adverse events, inject 5–10 mL of 1% lidocaine or 0.25% bupivacaine with or without a steroid in an incremental fashion with frequent aspiration. The use of hand signals to confirm or deny adverse events can be beneficial. This minimizes movement of surrounding the neck muscles that may distort needle placement.

Fluoroscopic-Guided C7 Oblique Approach

This approach helps avoid the anterior located vertebral artery and minimizes the risk of recurrent laryngeal nerve injury. It also enables less local anesthetic injectate volume to be used which in turn decreases the incidence of temporary recurrent laryngeal nerve and phrenic nerve blockade. To begin, the patient is placed in the supine position. Using fluoroscopy in the PA view, square the C6–C7 vertebral body end plates. Then oblique the C-arm ipsilaterally until the neural foramina are visualized. On this image identify the

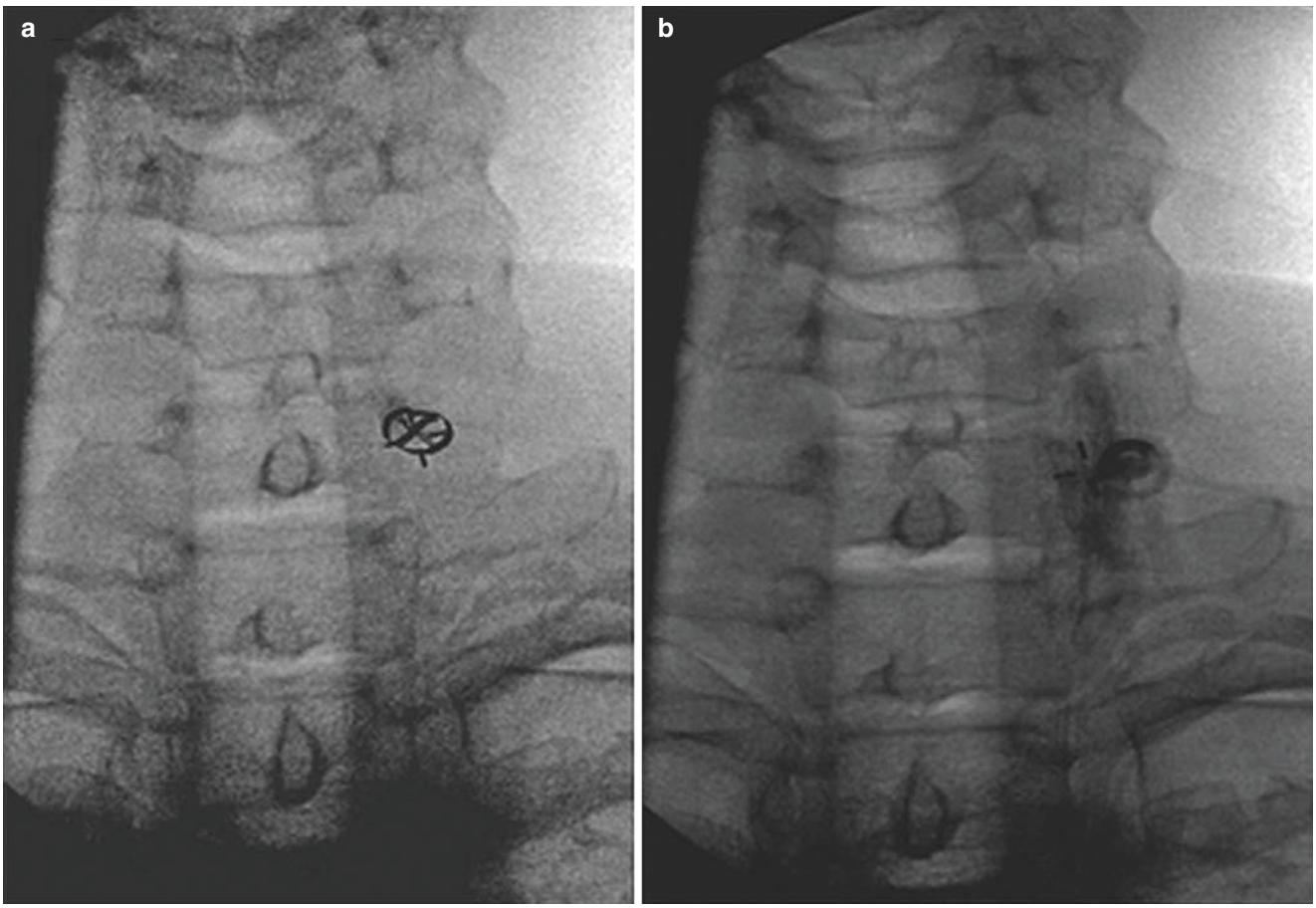

Fig. 29.3 (**a**) The initial landmark marked at point X for the anterior approach to identifying the stellate ganglion. (**b**) The spread of contrast along the anterolateral borders of C5–T1

neural foramina, intervertebral disc, and uncinate process (a superiorly projecting hook-shaped process on the lateral aspects of the superior articular surfaces of the cervical vertebral bodies). The target locations lie at the base of the uncinate process of the C7 vertebral body. Administer subcutaneous local anesthetic, and advance a 22- or 25-gauge spinal needle coaxially, making sure to stay anterior to the neural foramina, until contact with bone is made. At this point proceed with contrast, the test dose, and then the desired medications as previously described in the C7 anterior approach.

Fluoroscopic-Guided T2 Posterior Approach

The posterior approach is used when an anterior approach is contraindicated (infection, trauma, tumor prohibiting anterior access), when other approaches fail to produce a sympathetic blockade, or when a chemical or surgical neurolytic sympathectomy is desired [30, 31]. With this approach, image-guided fluoroscopy (or CT) must be employed to identify the necessary anatomical locations. The disadvantages of this approach include an increased risk of pneumothorax, accidental injury or injection into the aorta and spinal column, and trauma to the exiting spinal roots. To begin, the patient is placed in the prone position. Using fluoroscopy in the AP view, identify the T2 and T3 vertebral bodies. Next, oblique the C-arm ipsilaterally until the lateral margin of the transverse process just overlaps the lateral margin of the vertebral body, and then square the first rib. It's important to note that the more oblique the angle, the higher the likelihood of a pneumothorax. Therefore, while maintaining optimal needle placement, decreasing the obliquity may minimize this complication. The target location lies at the midpoint of the T2 or T3 vertebral body (confirmed in the lateral view). Administer subcutaneous local anesthetic, and advance a 22- or 25-gauge spinal needle coaxially until contact with bone is made. Confirm needle placement in the lateral view. After negative aspiration for blood, air, or CSF, inject contrast under real-time fluoroscopy in the AP view, and observe for optimal spread along the anterolateral borders of ~C7–T3 vertebral bodies. At this point proceed with the test dose and then the desired medications as previously described in the C7 anterior approach.

Radiofrequency

Once a successful temporary diagnostic block with local anesthetics with or without steroid is observed, a potentially longer-lasting treatment with radiofrequency (RF) lesioning may be employed. Using the fluoroscopic-guided C7 anterior approach, RF lesioning at the stellate ganglion can be performed using conventional or pulsed RF lesioning. It is important to note that RF lesioning is done at the C7 level because the probe must be in close proximity to the target structure due to the limited field distribution of conventional RF lesioning. Typically, a 22-gauge RF needle with a 5 mm active tip is used. Once the final needle positioning is confirmed radiographically, stimulation testing should occur to ensure the phrenic and recurrent laryngeal nerves are not involved. This can be done by observing for patient respiratory changes and having the patient say "EE" during stimulation. If using the fluoroscopic-guided T2 posterior approach, these two nerves will likely be avoided. Sensory stimulation is carried out at 50 Hz to determine the lowest voltage (V) sensory threshold. If performing conventional RF lesioning, motor stimulation is performed at 2 Hz for up to 3 V. Once stimulation testing is satisfactory, for conventional RF lesions, pretreat with local anesthetic (typically 2 mL of 2% lidocaine) since a higher temperature is used. With pulsed RF lesioning, the temperature is only slightly above normal body temperature; therefore, local anesthetic pretreatment is not necessary. Once the target location is adequately anesthetized (junction between C7 tubercle and vertebral body), thermal RF lesions can be made using 80 °C for 60–90 seconds [1, 12]. The RF needle tip can be slightly repositioned for additional RF lesioning sites as well. These include the medial aspect of the transverse process and the superior aspect of the junction between C7 tubercle and vertebral body. At each additional site, confirm needle placement radiographically, and perform stimulation testing, and if satisfactory, inject local anesthetic pretreatment, and repeat thermal RF lesioning. For pulsed RF lesions, the needle tip should be adjusted so that the target is slightly proximal or in front of the needle tip. This is due to the field distribution of pulsed RF. Once the RF needle is properly positioned radiographically and simulation testing is satisfactory, pulsed RF lesions can be made using 42 °C for 120 seconds. Complications of RF lesioning are similar to a stellate ganglion block.

Chemical Neurolysis

As in RF lesioning, once a successful temporary diagnostic block with local anesthetics with or without steroid is observed, if desired, a potentially longer-lasting treatment with chemical neurolysis may be employed. While RF creates small discrete lesions, chemical lesions are typically larger and less discrete. Inappropriate spread of neurolytic solution can result in permanent recurrent laryngeal nerve blockade and Horner's syndrome. Therefore, always inject a local anesthetic test dose prior, and observe for 15–30 minutes to ensure that no somatosensory or motor nerves are involved. Chemical neurolysis is typically performed using the fluoroscopic-guided C7 anterior approach or T2 posterior approach with 2–3 mL of 3–6% phenol or 50–100% alcohol. Because alcohol creates a burning dysesthesia effect, it is recommended to administer local anesthetic prior to or simultaneously with this neurolytic agent.

Complications

Major complications of a stellate ganglion block include pneumothorax, intraspinal injection, and intra-arterial injection. The use of imaging modalities, contrast spread, test dose administration, proper aspiration techniques, and methodical needle manipulation can help minimize these complications.

Common complications of a stellate ganglion block include hoarseness and globus sensation, subjective dyspnea, and temporary arm weakness. These complications are a result of local anesthetic spread to the recurrent laryngeal nerve, phrenic nerve, and brachial plexus, respectively. Other complications include temporary neuritis, persistent cough, and airway obstruction from retropharyngeal or cervicomediastinal hematomas [32–38].

Bilateral stellate ganglion blocks should not be performed since bilateral dysfunction of the recurrent laryngeal nerve or phrenic nerves can lead to respiratory compromise.

Intraspinal injections can lead to high cervical spinal anesthetics necessitating intubation and mechanical ventilation for decreased respiratory drive, as well as intravenous fluids and/or vasopressor therapy for the treatment of profound hypotension. Medications to facilitate intubation are often not necessary due to extensive laryngeal anesthesia and loss of consciousness from the misplaced injection.

Intra-arterial injections can lead to unconsciousness, respiratory compromise, seizures, and hypotension. Intravenous fluids, vasopressors, oxygen, and mechanical ventilation may be required. It is important to ensure no air is within the injection syringe, since this can lead to cerebral air embolisms [9, 38, 39].

Intravenous injections of small doses of local anesthetics do not typically cause significant complications. However, air embolisms in the venous system may result in paradoxical cerebral air emboli leading to significant consequences.

When using a neurolytic solution, a test dose with local anesthetic can be used to identify potential inappropriate neurological involvement. After injecting local anesthetic, monitor the patient for 15–30 minutes to determine if the neurolytic solution can be safely provided.

Abdomen/Thorax Sympathetic Blocks

Celiac Plexus and Splanchnic Nerve Blocks

Anatomy

The majority sympathetic innervation of the abdominal viscera is transmitted from the central nervous system (CNS) via splanchnic nerves to the celiac plexus. In return, the celiac plexus transmits the majority of nociceptive information from the abdominal viscera back through the splanchnic nerves to the CNS.

The splanchnic nerves are preganglionic sympathetic nerves that originate in the anterolateral horn of the spinal cord and exit via the ventral spinal roots from T5 to T12. They are unique in that they do not synapse in the sympathetic chain but rather pass through and synapse at the various distal ganglia that make up the celiac plexus. From these ganglia, postganglionic nerves then travel with accompanying blood vessels to each specific visceral organ.

There are three pairs of splanchnic nerves [40, 41]. The greater splanchnic nerves arise from ~T5 to T10 spinal roots, the lesser splanchnic nerves arise from ~T10 to T11 spinal roots, and the least splanchnic nerves arise from ~T11 to T12 spinal roots. Splanchnic nerves run paravertebrally in the thorax in a compartment bordered by the vertebral bodies medially, pleura laterally and dorsally, the posterior mediastinum ventrally, and the crura of the diaphragm caudally [42]. This compartment holds ~10 mL volume on each side. The splanchnic nerves then travel through the crus of the diaphragm and synapse at the celiac plexus with postganglionic nerves.

The celiac plexus is formed by various ganglia, preganglionic splanchnic nerves, preganglionic parasympathetic nerves of the vagal trunks, sensory nerves from the phrenic and vagal nerves, sympathetic postganglionic fibers, and interconnecting fibers. Ganglia of the celiac plexus include the celiac, superior mesenteric/aorticorenal, and renal ganglia, which the greater, lesser, and least splanchnic nerves each contribute to, respectively. Postganglionic nerves originating in these ganglia innervate the distal esophagus, stomach, small intestine, and ascending and transverse colon, as well as the foregut and midgut organs that include the liver, gallbladder, spleen, adrenals, mesentery, and kidneys. Thus, pain syndromes involving these abdominal viscera can be targeted for blockade. Abdominal viscera such as the descending colon, rectum, and pelvic organs are not innervated by the celiac plexus [43, 44].

The celiac plexus is anterior to the crus of the diaphragm in the retroperitoneal space. It lies on the anterolateral surface of the abdominal aorta surrounding the celiac artery. It extends from around the T12–L1 intervertebral disc to the upper portion of the L2 vertebral body and measures ~3 cm in length by ~4 cm in width. Afferent nociceptive fibers from the abdominal viscera are found throughout the celiac plexus, with majority of these fibers being transmitted back through the splanchnic nerves to CNS. Thus, either a splanchnic nerve block or celiac plexus block can be used to treat a variety of abdominal visceral pain syndromes.

Indications

Celiac plexus and splanchnic nerve blocks can be used to treat pain originating from any organ innervated by the

plexus, as previously described. These blocks are considered effective for pain management in abdominal malignancies, but are generally less efficacious for chronic nonmalignant abdominal pain [1]. They can also be used to treat severe nausea and vomiting associated with abdominal malignancies since the sympathectomy from the block allows for unopposed parasympathetic activity and the promotion of peristalsis.

Celiac plexus and splanchnic nerve blocks can be used as a diagnostic tool to determine the origin of pain in acute and chronic abdominal visceral pain syndromes [1, 42]. If an initial diagnostic block relieves the patient's pain, further treatment modalities such as radiofrequency lesioning and chemical neurolysis can be used for more durable forms of pain relief.

Procedural Techniques

There are several approaches to a splanchnic nerve block and celiac plexus block. These approaches can incorporate imaging modalities such as fluoroscopy, CT, transcutaneous ultrasound, and endoscopic ultrasound. This section will detail these approaches using fluoroscopic guidance. The celiac plexus can be effectively blocked with local anesthetics with or without steroid, radiofrequency (RF) lesioning, and chemical neurolysis.

It is important to note that the crus of the diaphragm is the anatomical determinant of whether the block is a splanchnic nerve block or a celiac plexus block. This is because the splanchnic nerves run posterior to the crus (retrocrural), while the celiac plexus lies anterior to the crus (antecrural). Since the crus attaches to the T12/L1 vertebral bodies, needle locations at the T11 vertebral body level will typically result in a splanchnic nerve block, needle locations at the T12 vertebral body level may result in either block largely depending on needle depth, and needle locations at the L1 vertebral body level will typically result in a celiac plexus block.

The retrocrural space for a splanchnic nerve block can be accessed via a posterior, transdiscal, or anterior approach. Similarly, the antecrural space for a celiac plexus block can be accessed via a posterior, transaortic, transdiscal, or anterior approach.

Classic Posterior Approach (Retrocrural and Antecrural)

To begin, place the patient in the prone position with a pillow beneath the abdomen to increase the distance between transverse processes. Using fluoroscopy in the AP view, identify the 12th ribs and T11–T2 vertebral bodies. To help with needle guidance, mark the intersection of the inferior margin of the 12th rib and the lateral border of the paraspinal muscles (typically 5–8 cm from midline) bilaterally; these will be the locations of needle entry. Then connect these marks to the upper portion of the L1 vertebral body; this will serve as a visual guidance when directing the spinal needles medially and cephalad [43, 45]. A bilateral needle method is necessary to adequately perform a splanchnic nerve block; however, a single needle method can be used successfully in a celiac plexus block. Administer subcutaneous local anesthetic, and advance a 20- or 22-gauge spinal needle that is 12–18 cm long (some prefer to use an introducer followed by a 25-gauge spinal needle). Needle projection with final location depends on the desired block (retrocrural vs. antecrural). For a splanchnic nerve block, direct the needles more cephalad to the T12 vertebral body; for a celiac plexus block, direct the needles less cephalad toward the L1 vertebral body. The needles should be projected at a ~45° angle toward midline with the goal to make contact with the desired vertebral body. As needed, confirm depth with a lateral fluoroscopic view during advancement. Once bony contact is made with the desired vertebral body, make note of the depth, and withdraw the needle a necessary amount in order to redirect the needle tip laterally to walk off the vertebral body. At this point, final depth depends on the desired block (splanchnic vs celiac plexus). For a splanchnic nerve block, advance the needles slowly in the lateral view to the anterior and lower third of the T12 vertebral body. Similarly, for a celiac plexus block, advance the needles slowly in lateral view while detecting for increased resistance during passage through the crus of the diaphragm until 1–2 cm beyond the anterior margin of the L1 vertebral body or until aortic pulsations are felt [43]. With regard to a celiac plexus block, the left needle is typically posterolateral to the aorta, whereas the right needle should be anterolateral to the aorta. After negative aspiration for blood, air, CSF, or lymph, inject contrast under real-time fluoroscopy in the AP and lateral view, and observe for optimal spread. For a splanchnic nerve block, contrast should be confined to the midline and concentrated near the anterolateral borders of the T12 vertebral body bilaterally in the AP view while having a smooth posterior contour corresponding to the psoas fascia in the lateral view. For a celiac plexus block, contrast should be seen anterior to the crus, infiltrating around the celiac axis, and lateral to the aorta. Visualization of contrast on both sides of the aorta is preferable but not mandatory. If attempting a single needle celiac plexus block, the right side is performed first; if there is lack of bilateral aortic contrast spread, then it is suggested to perform a left-sided block as well to maximize the celiac plexus blockade. Once proper needle placement is confirmed, cautiously inject 6 mL (divided bilaterally) of 2% lidocaine with epinephrine, and monitor for aberrant sign and symptoms. If the test dose produces no adverse events, inject in incremental doses 10–20 mL (divided bilaterally) of desired local anesthetics (e.g., 50:50 mixture of 1–2% lidocaine and 0.25–0.5% bupivacaine) with or without a steroid in an incremental fashion with frequent aspiration.

Posterior Oblique Approach (Retrocrural, Antecrural, and Transaortic)

This approach can be used for both a splanchnic nerve block and celiac plexus block, including a transaortic celiac plexus block (Fig. 29.4). The only difference from the classic posterior approach is the initial obliquity of fluoroscopy and the needle advancement in coaxial view. The transaortic approach involves deliberate penetration of the aorta. The elasticity of the aortic wall and tight adjacent structures allow for safe needle puncture.

To begin, place the patient in the prone position with a pillow beneath the abdomen to increase the distance between transverse processes. Using fluoroscopy in the AP view, identify the T12 vertebral body for a splanchnic nerve block and the L1 vertebral body for a celiac plexus block, and square off the superior end plate. Then oblique the C-arm to the patients left side until the tip of the respective transverse process is aligned with the anterolateral border of the respective vertebral body. Of note, for vertebral body levels above L1, aim for an oblique angle ~15° to minimize risk of pneumothorax. For a splanchnic nerve block, the target location lies at the mid to lower third of the T12 vertebral body at the anterolateral margin; often the C-arm may need to be moved caudally to move the 12th rib out of the target location. For a celiac plexus block, the target location lies just cephalad to the transverse process of L1 at the anterolateral margin of the L1 vertebral body. Administer subcutaneous local anesthetic, and advance coaxially a 20- or 22-gauge spinal needle that is 12–18 cm long (some prefer to use an introducer advanced to the posterolateral intervertebral disc space followed by a 25-gauge spinal needle). During needle advancement confirm depth with intermittent lateral fluoroscopic views. At this point, please refer to the classic posterior approach for details on proceeding with a splanchnic nerve block and celiac plexus block. To perform a transaortic celiac plexus block, continue needle advancement while detecting for increased resistance during passage through the crus of the diaphragm until aortic pulsations are felt (typically ~3 cm anterior to the L1 vertebral body) [46]. At this point, using intermittent aspiration or continuous observation of blood flow, penetrate the aortic wall, and advance the needle until negative aspiration or blood flow ceases, indicating passage through the anterior wall of the aorta. After negative aspiration for blood, air, CSF, or lymph, inject contrast under real-time fluoroscopy in the AP and lateral view, and observe for optimal spread. Contrast should be confined to the midline and concentrated along the bilateral anterior surface of the aorta infiltrating around the celiac axis in AP view while having a preaortic T12–L2 spread that is often pulsating in the lateral view. At this point proceed with the test dose and then the desired medications as previously described in the classic posterior approach. Of note, make sure to frequently aspirate to confirm the needle tip has not slipped back into the aorta.

Posterior Transdiscal Approach (Retrocrural and Antecrural)

A posterior transdiscal approach should be performed if there is a risk of renal puncture, such as with hydronephrosis. The celiac plexus or splanchnic nerves can be blocked depending on final needle positioning with respect to the crus and targeted vertebral level. For a splanchnic nerve block, the T11–T12 disc will be entered, and for a celiac

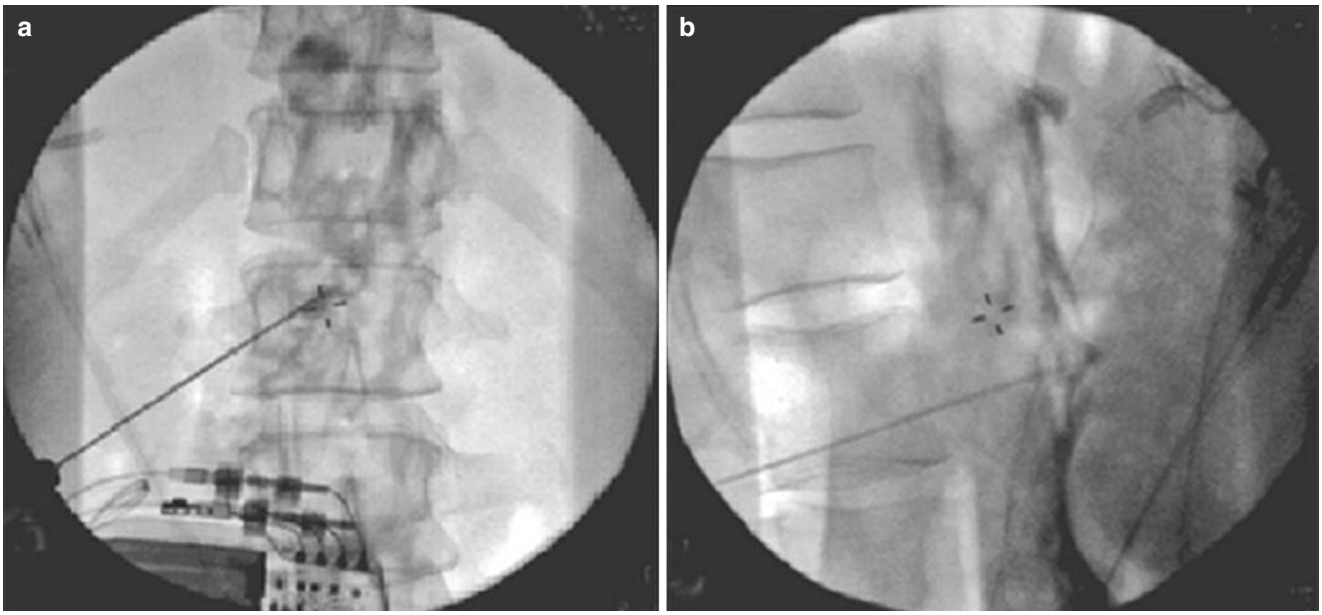

Fig. 29.4 (**a**) An AP view of the transaortic approach to access the celiac plexus. (**b**) Lateral view of the transaortic celiac plexus block

plexus block, the T12–L1 disc will be entered. Intravenous antibiotics are typically given 15–30 minutes prior to the procedure using cefazolin 1 g, gentamicin 80 mg, or ciprofloxacin 400 mg; for patients allergic to penicillin, clindamycin is an alternative. Additionally, many providers choose to administer intradiscal antibiotics within the contrast solution during the procedure using cefazolin (1 mg/mL contrast) or clindamycin (6–7.5 mg/mL contrast).

To begin, place the patient in the prone position with a pillow beneath the abdomen to increase the distance between transverse processes. Using fluoroscopy in the AP view, identify the respective vertebral body (T12 for a splanchnic nerve block and L1 for a celiac plexus block), and square off the superior end plate. Then oblique the C-arm ~15°. The target location lies just lateral to the inferior aspect of the respective facet joint. Administer subcutaneous local anesthetic, and advance coaxially a 20- or 22-gauge spinal needle that is 12–18 cm long (some prefer to use an introducer advanced to the posterolateral annulus fibrosus of the intervertebral disc space followed by a 25-gauge spinal needle). During needle advancement confirm depth with intermittent lateral fluoroscopic views, and importantly, confirm laterality in AP view making sure the needle tip does not cross the medial margin up the pedicle until past the posterior border of the respective intervertebral body. Continue needle advancement while detecting for increased resistance during passage through the annulus fibrosus of the posterolateral intervertebral disc. Once the disc space is entered, some providers confirm with contrast injection. Continue to advance the needle while checking depth until the needle tip penetrates through the annulus fibrosus of the anterolateral disc (some prefer to use a loss of resistance technique with a saline syringe to detect exiting through the disc). At this point proceed as described in the classic posterior approach with regard to retrocrural (splanchnic nerve block) or antecrural (celiac plexus block).

Anterior Approach (Transabdominal)

An anterior approach to a celiac plexus or splanchnic nerve block involves passing the needle through the abdominal wall and possibly through multiple organs including the liver, stomach, intestine, vessels, and the pancreas. New needle technology and imaging techniques have allowed for a low complication rate [47, 48]. The anterior approach requires one needle for a celiac plexus block and two for a splanchnic nerve block. This approach remains further from periosteum, nervous tissue, and paraspinous muscles which helps lead to less procedural discomfort. Patients can remain supine, which may be advantageous for patients requiring this procedure for abdominal pathology or pain. Disadvantages of the anterior approach include risk of infection, abscess, hemorrhage, and fistula formation [47].

Radiofrequency Lesioning of the Splanchnic Nerves

Once a successful temporary diagnostic block with local anesthetics with or without steroid is observed, a potentially longer-lasting treatment with radiofrequency (RF) lesioning may be employed. RF lesioning of the splanchnic nerves can be complicated due to their close proximity to the descending aorta and their position in a narrow compartment (previously described). Possible advantages of RF lesioning over chemical neurolysis include a more precisely controlled damage zone and an immediate effect (neurolytic agents could take 7–10 days) [49]. Using the posterior oblique approach, RF lesioning can be performed using conventional RF lesioning. Of note, many providers perform RF lesioning at the T11 vertebral body level, in addition to the T12 level, for broader coverage of the traversing splanchnic nerves. Typically, a 20-gauge RF needle with a 15 mm active tip is used. Once the final needle positioning is confirmed radiographically, sensory and motor stimulation testing should occur. Sensory stimulation is carried out at 50 Hz and 1.0 voltage (V) to determine adequate location of RF needle tips. Pain, pressure, or discomfort in the abdominal region (sometimes lumbar region) should be felt; if not, then the RF needle should be advanced a few millimeters anterior or posterior until proper sensory response is obtained. Motor stimulation is then performed at 2 Hz for up to 3 V to ensure that the intercostal nerve and phrenic nerve are not involved. No contractions of the intercostal muscles or diaphragm should occur; if they do occur, then the RF needle should be advanced a few millimeters anterior (away from the intercostal nerve) or posterior (away from the phrenic nerve) until contractions cease. Once stimulation testing is satisfactory, pretreat each site with local anesthetic (typically 2–3 mL of 2% lidocaine) mixed with dexamethasone (1–2 mg) to minimize thermocoagulation discomfort and post-procedural neuritis, respectively. Once the target location is adequately anesthetized, a thermal RF lesion can be made using 80 °C for 60–90 seconds [1, 12].

Neurolytic Block

As in RF lesioning, once a successful temporary diagnostic block with local anesthetics with or without steroid is observed, if desired, a potentially longer-lasting treatment with chemical neurolysis may be employed. While RF creates small discrete lesions, chemical lesions are typically larger and less discrete. Inappropriate spread of neurolytic solution can result in deafferentation pain of somatic nerves, neuritis, and paraplegia [46, 50–56]. As with any paraspinal administration of neurolytic solution, intravascular spread to the spinal cord may occur. Therefore, always confirm needle tip positioning with appropriate imaging and contrast spread, as well as a local anesthetic test dose with 15–30 minutes of observation to ensure that no somatosensory or motor nerves are involved. Chemical neurolysis of both the splanchnic

nerves and celiac plexus can be performed using any of the previously mentioned approaches. Typically, 15–30 mL of 50–100% alcohol or 6–10% phenol can be used with or without contrast solution [26, 57, 58]. Because alcohol creates a burning dysesthesia effect, it is recommended to administer local anesthetic prior to or simultaneously. While no direct comparison exists, alcohol is believed to produce a block for a longer period of time [59, 60].

Complications

Blockade of the celiac plexus, whether via a splanchnic nerve block or celiac plexus block, is considered relatively safe. Common reported adverse events are transient and include local pain (96%), diarrhea (44%), and orthostatic hypotension (38%), with the latter two being a result of sudden sympathectomy [61]. Interestingly, diarrhea is more frequently associated with an antecrural approach (65%) than the retrocrural approach (5–25%), and orthostatic hypotension is more frequently associated with a retrocrural approach (~50%) than the antecrural approach (10%). Severe complications can be quite devastating but are also rare. These include pneumothorax, retroperitoneal hematoma, aortic dissection, paraplegia, and thoracic duct injury [6, 62, 63]. Patients should receive a post-procedural chest x-ray to rule out possible pneumothorax. Studies have shown that a paraplegic presentation may be the result of either the superior spread or direct injection of neurolytic solution into the artery of Adamkiewicz resulting in thrombosis and spasms [59, 60, 62–65]. The use of the transaortic approach has been reported to increase the risk of aortic dissection [66, 67].

Lumbar Sympathetic Block

Anatomy

Preganglionic sympathetic nerves from the lower thoracic and lumbar spinal cord give rise to ~4 bilateral lumbar paravertebral ganglia of the lumbar sympathetic chain. Some preganglionic sympathetic nerves pass through the lumbar paravertebral ganglia without synapsing and form the lumbar splanchnic nerves, which travel to and synapse with postganglionic sympathetic efferent nerves of the inferior mesenteric prevertebral ganglia. The lumbar paravertebral ganglia and splanchnic nerves carry sympathetic efferent nerves and afferent sensory nerves innervating the lower extremities and lower abdominal and pelvic viscera.

As previously described at the beginning of this chapter, the sympathetic chain, also referred to as paravertebral ganglia, extends from the superior cervical spine down to the coccyx and travels as two distinct chains/ganglia along the lateral border of the vertebral column. Once the thoracic sympathetic chain passes under the diaphragmatic crura and emerges retroperitoneally, it becomes the lumbar sympathetic chain. The ganglia of the lumbar sympathetic chain are located more anterolaterally along the vertebral column and at the inferomedial margin of the psoas muscle, with the aorta lying anteromedial to the left chain and the vena cava lying anterior to the right chain. The lumbar sympathetic ganglia range from a length of 5–15 mm and typically exist between the L2–L3 and L4–L5 intervertebral disks with a propensity to cluster around the upper L3 vertebral body, thus explaining why this level is the classic target of a lumbar sympathetic block [68, 69].

Indications

A lumbar sympathetic block is indicated for painful conditions of the lower extremities and lower abdominal and pelvic viscera. Pain conditions include sympathetically mediated pain (i.e., CRPS I/II), circulatory insufficiencies in the lower extremities (e.g., arteriosclerotic vascular disease, Buerger's disease, Raynaud's disease, etc.), phantom limb pain, neuropathic pain (e.g., postherpetic neuralgia), discogenic pain with pseudosciatic radiation, and other various conditions not included in the previous categories (e.g., hyperhidrosis, alba dolens, erythromelalgia, etc.).

Procedural Techniques

There are several techniques that have been described to perform a lumbar sympathetic block in the literature. These typically describe the target location being at the L2 or L3 vertebral body level, with skin entry occurring ~5–8 cm from the midline, and needle advancement to the lateral margin of vertebral body and then walking off the vertebral body anteriorly until the needle tip is through the fascia of the psoas muscle, at which point the injectate is administered. These approaches incorporate imaging modalities such as fluoroscopy, CT, and ultrasound, with fluoroscopy currently being the most common.

This section will describe a standard fluoroscopic-guided lumbar sympathetic block technique suitable for most patients. Measuring an increase in skin temperature is the most practical way to demonstrate lower extremity sympathetic blockade; however, in patients with severe peripheral vascular disease, this may not be demonstrable. Sympathetic blockade of the lower extremity can also be measured with laser Doppler flowmetry, sudomotor, sweat test, or sympathogalvanic response.

Standard Fluoroscopic-Guided L3 Posterior Approach

To begin, place the patient in the prone position with a pillow beneath the abdomen to increase the distance between transverse processes. Using fluoroscopy in the AP view, identify the L2–L3 vertebral bodies, and square off the L3 superior end plate. Then oblique the C-arm to the ipsilateral side of treatment until the tip of the respective transverse process is

aligned with the anterolateral border of the respective vertebral body. Of note, the iliac vessels typically bifurcate at the L4 vertebral body level, increasing the likelihood of intravascular injection at the lower lumbar levels. The target location lies at the anterolateral margin of the upper third of the L3 vertebral body. Administer subcutaneous local anesthetic, and advance coaxially with a 22-gauge spinal needle that is 12–18 cm long. As needed, confirm depth with a lateral fluoroscopic view during advancement. Once bony contact is made with the desired vertebral body, redirect the needle tip laterally to walk off the vertebral body. If done carefully, a pop through the anterior psoas fascia will be felt. Advance in lateral view until the needle tip evenly contacts the anterior margin of the vertebral body. After negative aspiration for blood or CSF, inject contrast under real-time fluoroscopy in the AP view, and observe for optimal spread outside the psoas muscle along the anterolateral borders of L2–L3 vertebral bodies beneath the facet joints; if there is spread laterally, then the needle is in the psoas muscle and needs to be adjusted. In the lateral view, make sure contrast is observed along the anterior third of the L2–L3 vertebral bodies contained within the prevertebral tissue plane; if contrast spread is anterior to the prevertebral tissue plane, then the needle is in intraperitoneal space and needs to be adjusted (Figs. 29.5 and 29.6). In the lateral view, make sure contrast is observed along the anterior margin of the L5–S1 vertebral bodies contained within the prevertebral tissue plane. Once proper needle placement is confirmed and after negative aspiration, inject 3–5 mL of desired local anesthetic with or without a steroid. This procedure can be performed at the adjacent L2 and L4 levels as well.

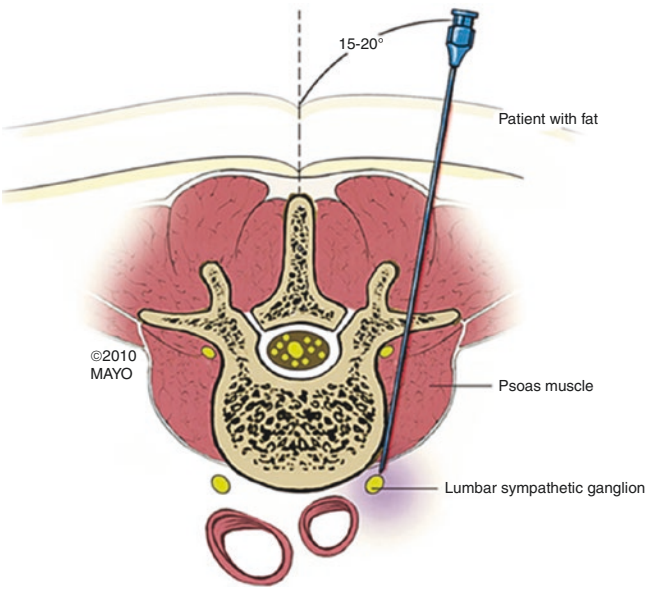

Fig. 29.5 Needle trajectory for targeting the lumbar sympathetic ganglia at L2–L3 vertebral level. (From Lamer and Eldrige [7]; used with permission of Mayo Foundation for Medical Education and Research, all rights reserved)

Radiofrequency Ablation

Once a successful temporary diagnostic block with local anesthetics with or without steroid is observed, a potentially longer-lasting treatment with radiofrequency (RF) lesioning may be employed. Possible advantages of RF lesioning over chemical neurolysis include a more precisely controlled damage zone and an immediate effect (neurolytic agents could take 7–10 days) [49]. Using the standard fluoroscopic-guided posterior approach, RF lesioning of the lumbar sympathetic chain can be performed using both conventional and pulsed RF lesioning. Regarding pulsed RF lesioning, this technique uses a lower, nondestructive temperature and appears to further minimize complications while still producing positive outcomes. To achieve adequate coverage of the sympathetic chain, RF lesions are typically performed at multiple levels – the inferior one-third of L2, the upper one-third of L3, and the middle of L4 vertebral bodies. Typically, a 20-gauge RF needle with a 10–15 mm active tip is used. Once the final needle positioning is confirmed radiographically, sensory and motor stimulation testing should occur. Sensory stimulation is carried out at 50 Hz and 1.0 voltage (V) to determine adequate location of RF needle tips. Paresthesias along the ipsilateral low back and proximal lower extremity in a dermatomal fashion should be felt; additionally, there can be a faint feeling in the abdomen. If performing conventional RF lesioning, motor stimulation is then performed at 2 Hz for up to 3 V to ensure that the spinal nerve roots are not involved. Once stimulation testing is satisfactory, for conventional RF lesioning, pretreat each site with local anesthetic (typically 2–3 mL of 2% lidocaine), and if desired, add dexamethasone (1–2 mg) to minimize thermocoagulation discomfort and post-procedural neuritis, respectively. With pulsed RF lesioning, the temperature is only slightly above normal body temperature; therefore, local anesthetic pretreatment is not necessary. Once the target location is adequately anesthetized, a conventional RF lesion can be made using 80 °C for 60–90 seconds; an additional lesion may be created with slight needle tip repositioning. A pulsed RF lesion can be made using 42 °C for 120 seconds; this is typically repeated after the rotating the needle tip 90° and/or slight repositioning for 2–3 more treatment lesions.

Neurolytic Block

As in RF lesioning, once a successful temporary diagnostic block with local anesthetics with or without steroid is observed, if desired, a potentially longer-lasting treatment with chemical neurolysis may be employed. Typically, chemical neurolysis is reserved for patients who have failed medical therapy and who are not candidates for surgical

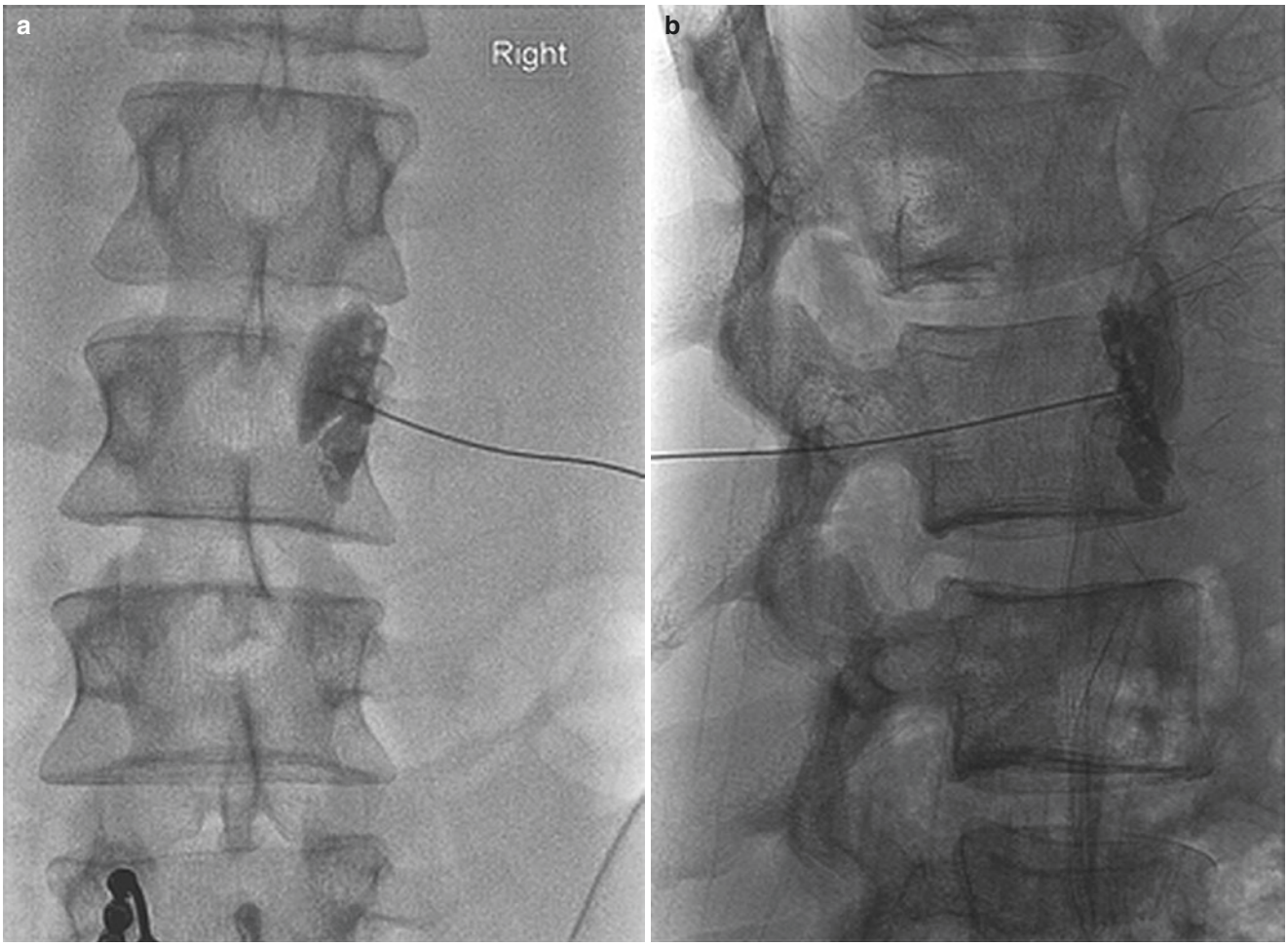

Fig. 29.6 (**a**) AP fluoroscopic view of the right lumbar sympathetic block. (**b**) Lateral view. Both images reveal contrast spread at their respective views

approaches (e.g., angioplasty). While RF lesioning creates small discrete lesions, chemical lesions are typically larger and less discrete. Inappropriate spread of neurolytic solution to a somatic nerve or nerve root can result in permanent nerve injury. The L2 nerve roots, where the genitofemoral nerve arises from, are most commonly affected. Post-neurolysis genitofemoral neuralgia has been reported in up to 5–10% of cases [70]. Also, as with any paraspinal administration of neurolytic solution, intravascular spread to the spinal cord may occur. The use of a local anesthetic test dose prior to chemical neurolysis is recommended to ensure that no somatosensory or motor nerves are involved and to ensure adequate needle tip position by observing for an increase in skin temperature within the ipsilateral lower extremity. Additionally, always confirm needle tip positioning with appropriate imaging and contrast spread. As in RF lesioning, chemical neurolysis can be performed using the standard fluoroscopic-guided posterior approach and is usually required at multiple vertebral body levels to ensure adequate neurolytic solution spread for proper therapeutic benefits – the inferior one-third of L2, the upper one-third of L3, and the middle of L4 vertebral bodies. This also enables less neurolytic solution volume administered at one location, thus theoretically decreasing aberrant neurolytic spread. Typically, lower volumes of 2–5 mL of 3–6% phenol or 50–100% alcohol are used at each level for up to a total of ~15 mL. To mitigate the burning dysesthesia produced by alcohol, it is recommended to administer local anesthetic prior to or simultaneously with this neurolytic agent.

Complications

Complications of a lumbar sympathetic block include intravascular or intrathecal injections, temporary or permanent nerve injury, hematoma, and intraperitoneal injections with visceral injury. Local anesthetic toxicity can occur if an intravascular injection occurs into the aorta, the vena cava, or the segmental radicular vessels. Nerve injury can result from needle trauma to the exiting nerve roots at the intervertebral foramen or further along the nerve pathway at the lumbar plexus within the psoas muscle. Additionally, steroid partic-

ulate or neurolytic solution injection into the segmental radicular arteries can create arterial spasms and thrombosis, resulting in spinal cord infarction with neurologic compromise, particularly if working at the upper lumbar levels where the artery of Adamkiewicz can be involved. Needle insertion into the intervertebral disc can occur and is recognized by the "Swiss cheese" tactile sensation. If this occurs, typically the needle tip is repositioned (unless a transdiscal technique is desired), and antibiotics are administered. Renal or ureteral trauma can occur if the needle entry point is more than 7–8 cm from midline. The use of imaging modalities, contrast spread, test dose administration, proper aspiration techniques, and methodical needle manipulation can help minimize these complications.

Superior Hypogastric Plexus Block

Anatomy

The superior hypogastric plexus (SHGP) is a presacral, retroperitoneal confluence of sympathetic and parasympathetic fibers. It is formed by the continuation of the paravertebral sympathetic chain from the aortic plexus and lower lumbar splanchnic nerves, as well as parasympathetic fibers from the pelvic splanchnic nerves from the S2 to S4 levels that initially enter the inferior hypogastric plexus (IHGP) and then ascend to the SHGP [26, 71]. It is located just caudal to the bifurcation of the aorta and anteromedial to the psoas muscle, overlying the anterior aspect of the L5–S1 vertebral bodies and their shared intervertebral disc, and is slightly left of midline given the leftward position of the descending aorta. The SHGP innervates and transmits pain from the majority of the pelvic viscera, including the bladder, uterus, vagina, ovaries, prostate, urethra, testes, seminal vesicles, sigmoid colon, and rectum. The nerve fibers of the SHGP converge and form bilateral hypogastric nerves which travel alongside the internal iliac arteries and veins to the paired inferior hypogastric plexuses (IHGP). The IHGP is located alongside the rectum bilaterally at the S2, S3, and S4 levels and has additional nerve fiber contributions from the sacral splanchnic nerves from the sympathetic trunk and pelvic splanchnic nerves [62, 72, 73]. Unfortunately, the inferior hypogastric plexus is intertwined with viscera of the pelvis and cannot be isolated to be blocked for therapeutic effects. Because of this, the SHGP block is used for the majority of pelvic-related visceral pain.

Indication

A superior hypogastric plexus block is indicated for gynecological pelvic pain (i.e., endometriosis, adhesions), non-gynecological pelvic pain (i.e., interstitial cystitis, irritable bowel syndrome), and pain from neoplasms of the pelvic viscera. Visceral structures may include the descending and sigmoid colon, rectum, bladder, prostate, prostatic urethra, testes, seminal vesicles, vaginal fundus, uterus, and ovaries. Many indications of a SHGP block can be collectively grouped into a general chronic pelvic pain syndrome – in females, the term is referred to as chronic pelvic pain (CPP), and in males the analogous condition is referred to as chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS). Patients with a history of vague, dull, burning, and poorly localized visceral pain, refractory to conservative measures, may benefit from blockade of the superior hypogastric plexus. Patients with a similar history may also benefit from blockade of the ganglion impar (see Ganglion Impar Block section for details).

Procedural Techniques

A superior hypogastric plexus block is similar to a lumbar sympathetic block. There are several techniques that have been described to perform a superior hypogastric plexus block in the literature. These approaches incorporate imaging modalities such as fluoroscopy, CT, and ultrasound, with fluoroscopy currently being the most common. This section will describe a standard two-needle bilateral fluoroscopic-guided SHGP block technique suitable for most patients, as well as a single needle intradiscal approach.

Standard Posterior Bilateral Fluoroscopic-Guided L5 Approach

To begin, place the patient in the prone position with a pillow beneath the abdomen to increase the distance between transverse processes. Using fluoroscopy in the AP view, identify the L5–S1 vertebral bodies, and square off the L5 inferior end plate. Then oblique the C-arm to the ipsilateral side of treatment until the tip of the respective transverse process is aligned with the anterolateral border of the respective vertebral body. Of note, the iliac vessels typically bifurcate at the L4 vertebral body level, increasing the likelihood of intravascular injection at the lower lumbar levels. If intravascular placement is encountered, typically advancing the needle tip further medially remedies this. The target location lies at the anterolateral margin of the lower fifth of the L5 vertebral body. Administer subcutaneous local anesthetic, and advance coaxially with a 22-gauge spinal needle that is 12–18 cm long. As needed, confirm depth with a lateral fluoroscopic view during advancement. Once bony contact is made with the desired vertebral body, redirect the needle tip laterally to walk off the vertebral body. If done carefully, a pop through the anterior psoas fascia will be felt. Advance in lateral view until the needle tip evenly contacts the anterior margin of the vertebral body. After negative aspiration for blood or CSF, inject contrast under real-time fluoroscopy in the AP view, and observe for optimal spread outside the psoas muscle along the anterolateral borders of L5–S1 vertebral bodies beneath the facet joints; if there is spread laterally, then the

needle is in the psoas muscle and needs to be adjusted. In the lateral view, make sure contrast is observed along the anterior margin of the L5–S1 vertebral bodies contained within the prevertebral tissue plane; if contrast spread is anterior to the prevertebral tissue plane, then the needle is in intraperitoneal space and needs to be adjusted. Typically, to encompass a complete SHGP block, bilateral needle placement is required for adequate bilateral contrast spread. Therefore, attention is diverted to the opposite side, and a similar procedure is performed. Finally, confirm proper needle placement, and after negative aspiration, inject ~5–10 mL bilaterally (totaling ~10–20 mL) of desired local anesthetic with or without a steroid.

Posterior Single Needle Unilateral Transdiscal Approach

A posterior transdiscal approach can be used safely as a speedier single needle technique, as well as a rescue for those who failed to respond from the standard two-needle bilateral technique (Figs. 29.7 and 29.8). This technique does incur the risk of discitis, disc rupture, and disc herniation, although no cases have yet been reported in the literature [74]. Intravenous antibiotics are typically given 15–30 minutes prior to the procedure using cefazolin 1 g, gentamicin 80 mg, or ciprofloxacin 400 mg; for patients allergic to penicillin, clindamycin is an alternative. Additionally, some providers choose to administer intradiscal antibiotics within the contrast solution during the procedure using cefazolin (1 mg/mL contrast) or clindamycin (6–7.5 mg/mL contrast).

To begin, place the patient in the prone position with a pillow beneath the abdomen to increase the distance between transverse processes. Using fluoroscopy in the AP view, identify the L5–S1 vertebral bodies, and square off the L5 inferior end plate. Then oblique the C-arm; however, unlike in the standard posterior bilateral approach, the degree of rotation is less and is only until 1–1.5 cm of the L5–S1 disc

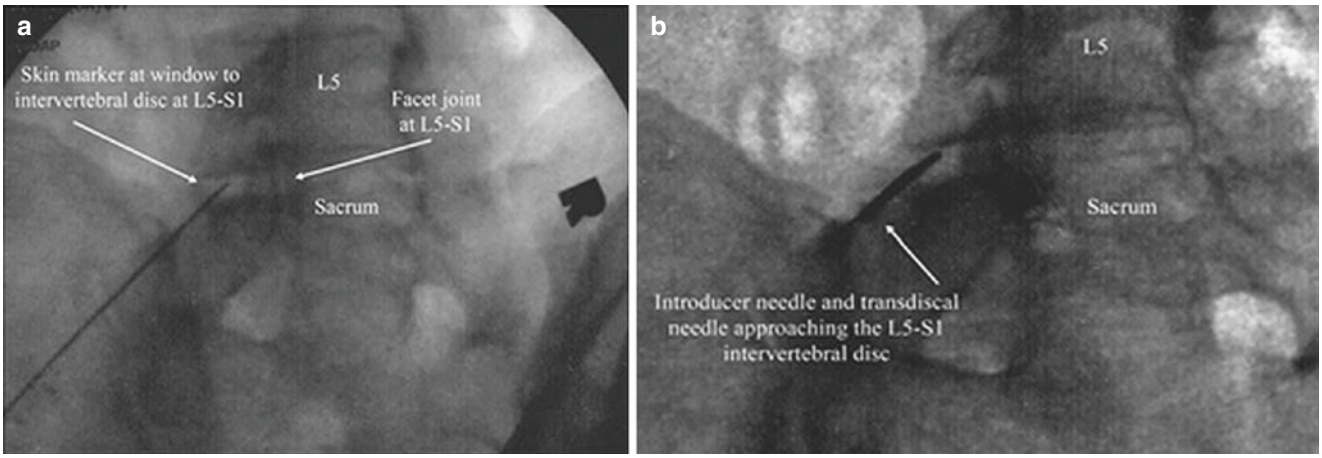

Fig. 29.7 (**a**) Oblique radiographic view of the entrance site. (**b**) Oblique radiographic view of the transdiscal needle

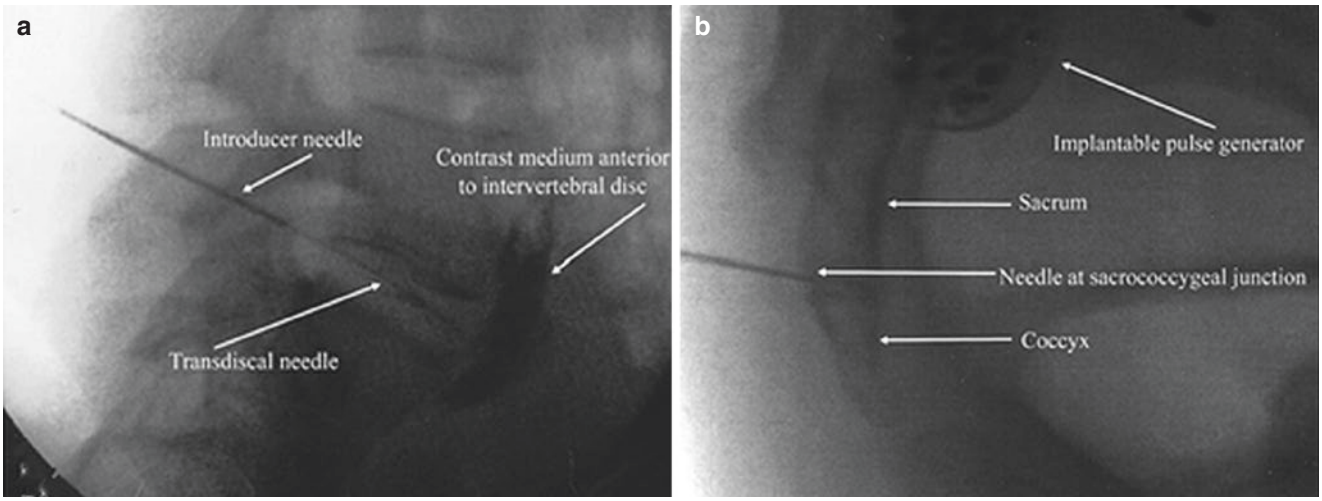

Fig. 29.8 (**a**) The lateral radiographic view of transdiscal needle. (**b**) The lateral radiographic view of the transacrococcygeal approach

is visible laterally to the superior articular process (SAP). Often, even with moderate oblique rotation, this "window" will be eliminated due to the iliac bone. The target location lies lateral to the SAP intradiscally. Administer subcutaneous local anesthetic, and advance coaxially either a single 22-gauge spinal needle that is 12–18 cm long (some prefer to use an introducer advanced to the posterolateral annulus fibrosus of the intervertebral disc space followed by a 25-gauge spinal needle). During needle advancement confirm depth with intermittent lateral fluoroscopic views, and importantly, confirm laterality in AP view making sure the needle tip does not cross the medial margin up the pedicle until past the posterior border of the respective intervertebral body. Continue needle advancement while detecting for increased resistance during passage through the annulus fibrosus of the posterolateral intervertebral disc. Once the disc space is entered, some providers confirm with contrast injection. Continue to advance the needle while checking depth until the needle tip penetrates through the annulus fibrosus of the anterolateral disc (some prefer to use a loss of resistance technique with a saline syringe to detect exiting through the disc). Ideally, the needle tip should be midline in the AP view. After negative aspiration for blood or CSF, inject contrast under real-time fluoroscopy in the AP view, and observe for optimal spread described as a loose midline appearance covering the lower third of the L5 vertebral body and extending to the sacrum. In the lateral view, make sure contrast is observed along the anterior margin of the L5–S1 vertebral bodies contained within the prevertebral tissue plane; if contrast spread is anterior to the prevertebral tissue plane, then the needle is in the intraperitoneal space and needs to be adjusted. Once proper needle placement is confirmed and after negative aspiration, inject ~10–20 mL of desired local anesthetic with or without a steroid.

Radiofrequency Ablation

Once a successful temporary diagnostic block with local anesthetics with or without steroid is observed, a potentially longer-lasting treatment with radiofrequency (RF) lesioning may be employed. Possible advantages of RF lesioning over chemical neurolysis include a more precisely controlled damage zone and an immediate effect (neurolytic agents could take 7–10 days) [49]. Using either the standard posterior bilateral approach or the posterior single needle unilateral transdiscal approach, RF lesioning of the superior hypogastric plexus can be performed using both conventional and pulsed RF lesioning. Regarding pulsed RF lesioning, this technique uses a lower, nondestructive temperature while still producing positive outcomes. Typically, a 20-gauge RF needle with a 10–15 mm active tip is used. Once the final needle positioning is confirmed radiographically and if performing conventional RF lesioning, motor stimulation is then performed at 2 Hz for up to 3 V to ensure that the spinal nerve roots are not involved. Once stimulation testing is satisfactory, for conventional RF lesioning, pretreat each site with local anesthetic (typically 2–3 mL of 2% lidocaine), and if desired, add dexamethasone (2–8 mg) to minimize thermocoagulation discomfort and post-procedural neuritis, respectively. With pulsed RF lesioning, the temperature is only slightly above normal body temperature; therefore, local anesthetic pretreatment is not necessary. Once the target location is adequately anesthetized, a conventional RF lesion can be made using 80 °C for 60–90 seconds; an additional lesion may be created with or without slight needle tip repositioning. A pulsed RF lesion can be made using 42 °C for 120 seconds; this is also typically repeated with or without slight repositioning for 1–2 more treatment lesions.

Neurolytic Block

As in RF lesioning, once a successful temporary diagnostic block with local anesthetics with or without steroid is observed, if desired, a potentially longer-lasting treatment with chemical neurolysis may be employed. While RF creates small discrete lesions, chemical lesions are typically larger and less discrete. Inappropriate spread of neurolytic solution can result in deafferentation pain of somatic nerves, neuritis, and paraplegia [46, 50–56]. As with any paraspinal administration of neurolytic solution, intravascular spread to the spinal cord may occur. Therefore, always confirm needle tip positioning with appropriate imaging and contrast spread, as well as a local anesthetic test dose with 15–30 minutes of observation to ensure that no somatosensory or motor nerves are involved. Chemical neurolysis of the superior hypogastric plexus can be performed using either the standard posterior bilateral approach or the posterior single needle unilateral transdiscal approach. Typically, a total of 5–10 mL of 50–100% alcohol or 6–10% phenol can be used with or without contrast solution [26, 57, 58]. Because alcohol creates a burning dysesthesia effect, it is recommended to administer local anesthetic prior to or simultaneously. While no direct comparison exists, alcohol is believed to produce a block for a longer period of time [59, 60].

Complications

Proper needle tip position is important to verify to avoid intravascular or intraperitoneal injections. Common complications include paraspinous muscle spasm from needle irritation, intravascular injection due to close proximity of the iliac vessels, and hematoma. More rare complications include somatic nerve injury, ureteral puncture, and gastrointestinal and sexual dysfunction from sympathetic outflow interruption [71, 75, 76].

Using an intradiscal approach increases the risk of discitis. This risk is low (1–4%), and the use of prophylactic procedural antibiotics is recommended [77, 78]. Complications of a superior hypogastric plexus block

include intravascular or intrathecal injections, temporary or permanent nerve injury, hematoma, and intraperitoneal injections with visceral injury. Local anesthetic toxicity can occur if an intravascular injection occurs into the aorta or iliac vessels or the segmental radicular vessels. Nerve injury can result from needle trauma to the exiting nerve roots at the intervertebral foramen or further along the nerve pathway. Additionally, steroid particulate or neurolytic solution injection into the segmental radicular arteries can create arterial spasms and thrombosis. Needle insertion into the intervertebral disc can occur and is recognized by the "Swiss cheese" tactile sensation and increases the risk of discitis. If this occurs, typically the needle tip is repositioned (unless a transdiscal technique is desired), and antibiotics are administered. Ureteral trauma can occur if the needle entry point is more than 7–8 cm from midline. Additional complications derive from interrupting the sympathetic outflow that can result in visceral dysfunction, including gastrointestinal disturbances and sexual dysfunction [71, 75, 76]. In women undergoing presacral neurectomy, up to 14% will have constipation, while up to 5% may have urinary urgency at 12 months follow-up [79]. The use of imaging modalities, contrast spread, test dose administration, proper aspiration techniques, and methodical needle manipulation can help minimize these complications.

Ganglion Impar Block

Anatomy

The ganglion impar (GI), also known as the ganglion of Walther or the sacrococcygeal ganglion, is the most caudal ganglion formed by the fusion of the terminal ganglia from the left and right sympathetic chains. This solitary, unpaired, midline ganglion is classically located in the retroperitoneal space, anterior to the sacrococcygeal junction, and medial to the anterior sacral foramina. However, its position can be slightly more caudal, and it has been suggested that the average location is 30% the distance from the sacrococcygeal joint to the tip of the coccyx [80]. This ganglion receives visceral afferents from the perineum, anus, distal rectum, distal urethra, vulva, and distal third of the vagina.

Indications

A ganglion impar block is indicated for diagnosing and treating gynecological, non-gynecological, and neoplastic pain from the distal pelvic, perineal, and sacrococcygeal regions. Structures may include the perineum, anus, distal rectum, distal urethra, vulva, and distal third of the vagina. There is anatomical overlap between the superior hypogastric plexus and ganglion impar. Patients with a history of vague, dull, poorly localized pain associated with burning sensations and urgency to urinate or defecate that are refractory to conservative measures may benefit from blockade of the GI. Patients with a similar history may also benefit from blockade of the superior hypogastric plexus (see "Superior Hypogastric Plexus Block" section for details).

Procedural Technique

There are several techniques that have been described to perform a ganglion impar block in the literature. These approaches incorporate imaging modalities such as fluoroscopy and ultrasound, with fluoroscopy currently being the most common. This section will describe the most common fluoroscopic technique suitable for most patients.

Posterior Transdiscal Sacrococcygeal or Intracoccygeal Approach

To begin, place the patient in the prone position with a pillow beneath the abdomen to increase the distance between transverse processes. Using fluoroscopy in the lateral view, identify the sacrococcygeal joint and the inferior intracoccygeal joints. Confirm fluoroscopy is in a true lateral view by superimposing the two great sciatic notches. Using palpation or an AP view, find the midline overlying either the sacrococcygeal joint or first or second intracoccygeal joint. Administer subcutaneous local anesthetic, and advance a 22- or 25-gauge needle that is 1–2 inches long in lateral view through the desired joint space until the needle tip is just anterior to the anterior margin of the joint space. There may be difficulty placing the needle into or through a calcified joint space; if that is the case, then reposition in another joint space. After negative aspiration for blood or CSF, inject contrast under real-time fluoroscopy in the lateral view, and observe for optimal spread along the anterior margin of the sacrum/coccyx; this is classically described as the "comma sign" (Fig. 29.9). Confirm midline placement with an AP view. Finally, after proper needle placement and negative aspiration, inject ~3–5 mL of desired local anesthetic with or without a steroid.

Complications

Complications include neuritis, nerve injury, rectal puncture, and cauda equina syndrome.

Myofascial Trigger Points

Myofascial trigger points (TPs) are small (2–5 mm) tender nodules in taut, "rope-like" bands of skeletal muscle [81–83]. They can be detected by palpation as the "spot of maximum tenderness" along the taut band that produces or increases the typical pain experienced by the patient. When palpated, the pain can be at the site of the TP and/or can be

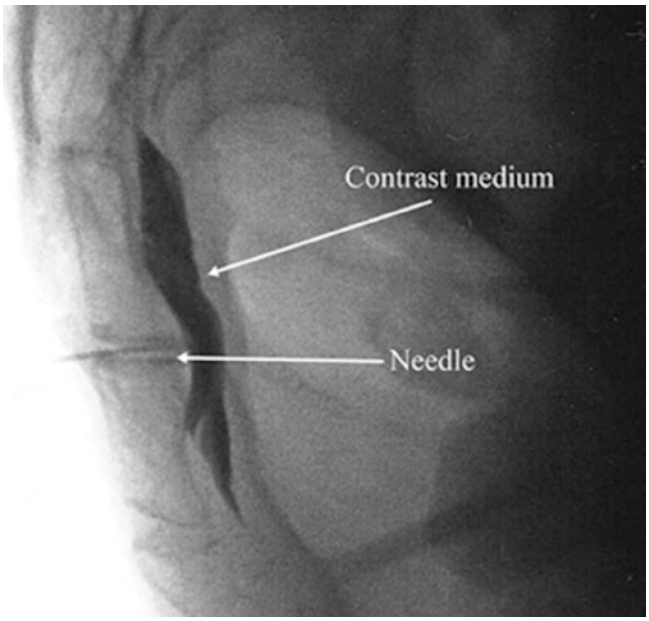

Fig. 29.9 Lateral radiographic view of contrast medium anterior to sacrum

in a referred pattern (known as the "zone of reference") with an intensity ranging from a dull ache to severe and disabling [34, 36, 37, 84]. Palpation can cause the "jump sign" (an involuntary wincing away from pain stimulus), vocal response, and/or autonomic responses including flushing, sweating, and blanching of the skin from vasoconstriction [33, 81, 85].

TPs can be active or latent. Active TPs have spontaneous pain, even at rest, and require treatment more often [37, 86–88]. Latent TPs are only painful with palpation and can be associated with weakness, stiffness, restricted range of motion, or muscle stiffening. Latent TPs do not need treatment unless the TP begins to create active TP characteristics or if the latent TP becomes activated by mechanical overload and causes prolonged muscle shortening.

The etiology of TPs has not been established. It has been theorized that TPs can be caused by underlying muscular pathology, localized neurotransmitter imbalances, and/or metabolic/vascular alterations [89]. In fact, laboratory studies have identified dysfunctional neuromuscular junctions and altered biochemical environments associated with TPs [89, 90]. These changes can result in sustained contraction of sarcomeres resulting in the restriction of blood supply, local ischemia, metabolic waste product accumulation, and increased pain signaling [91, 92]. The mechanism of trigger point injections (TPIs) has also not been established. It has been suggested that TPIs possibly inhibit the release of acetylcholine at the neuromuscular junction and decreased neurotransmitters release from sensory nerves. The inhibition of these neurotransmitters results in relaxation of the taut muscles and decreased pain signaling, respectively [93].

Trigger Point Injections for the Head and Neck

Anatomy

The bony anatomy of the neck consists of seven cervical vertebrae (C1–C7), which make up the cervical spine, support the head, and allow for a wide range of motion of the neck.

Surface Anatomy

The neck is bordered by the collarbone inferiorly, trapezius ridge laterally, and the head superiorly. There are several structures which can be palpated on the surface of the neck. Anteriorly, the identifiable midline structures from superior to inferior include the hyoid bone (below the line of the chin), thyroid cartilage, cricoid cartilage, and the trachea/thyroid gland (just superior to the suprasternal notch). Lateral to midline, the neck is divided into anterior and posterior triangles bilaterally. The sternocleidomastoid muscles separate these triangles and are the most identifiable muscles of the neck.

Other structures in the anterior neck include the common and external carotid arteries, the external jugular veins, and the spinal accessory nerves. The common and external carotid arteries can be found below the sternocleidomastoid muscle inferiorly and then along the medial margin of the sternocleidomastoid as it divides more superiorly in the neck. The external jugular veins run superficial to the sternocleidomastoid muscle in direction from the angle of the mandible to the middle of the clavicle. The spinal accessory nerve can be found at the posterior border of the sternocleidomastoid muscle at a location midway between the angle of the mandible and the mastoid process before it travels posteriorly to the trapezius. Posteriorly, the spinous processes of the cervical vertebrae are identifiable in the midline position.

Superficial Cervical Muscles

The platysma muscle is a broad sheet of muscle arising from the fascial covering of the pectoralis major and deltoid. The muscle fibers cross the clavicle and travel obliquely superomedially along the side of the neck. The anterior and posterior muscle fibers converge with muscles of the lower face and help move the lower lip and angle of the mouth laterally and inferiorly. It is innervated by the cervical branch of the facial nerve. Beneath the platysma lies the external jugular vein, which courses in the anterolateral neck, superficial to the sternocleidomastoid.

The two trapezius muscles make up the posterior superficial upper back and cervical musculature. They originate from the external occipital protuberance, spinous processes of vertebrae C7–T12, and the nuchal ligament. They extend across the neck and back bilaterally to insert on the clavicle, acromion, and spine of the scapula forming a trapezium (diamond-shaped quadrangle) to help rotate, retract, elevate,

and depress the scapula. They are innervated by the accessory and cervical nerves (C3/C4).

The rhomboid major muscles originate from the supraspinal ligaments and the T2–T5 vertebrae and insert on the inferior aspect of the medial border of the scapula. The rhomboid minor muscles originate from the nuchal ligament and spinous processes of C7–T1 and insert on the medial border of the scapula, superior to the rhomboid major. Both the rhomboid major and minor muscles are innervated by the dorsal scapular nerve (C4/C5) and help to retract and rotate the scapula while keeping the scapula fixed to the thoracic wall.

The levator scapula originates from the transverse processes of C1–C4 vertebrae and inserts onto the superior aspect of the medial border of the scapula. It is innervated by the cervical nerves from C3/C4 and often by a branch of the dorsal scapular nerve (C5). It elevates and rotates the scapula to help with glenoid cavity alignment with shoulder movements.

Lateral Cervical Muscles

The deep cervical fascia (fascia colli) is located beneath the platysma and forms sheaths for deep cervical structures, including the carotid vessels, glands, strap muscles, and paraspinous muscles.

It circumferentiates the neck and has many bony and ligamentous attachments. Posteriorly, the fascia is attached to the nuchal line of the occipital bone, the mastoid process of the temporal bone, and the body of the mandible and continues inferiorly to attach to the ligamentum nuchae and spinous process of the C7 vertebra. Anteriorly, the fascia is attached to the acromion, clavicles, and the manubrium of the sternum. From the posterior, the fascial layer travels anteriorly and invests the trapezius, ensheathes the parotid gland between the mastoid process and mandible, and covers the posterior triangle of the neck. As the fascia approaches the sternocleidomastoid muscle, it divides to invest the muscle and then reforms to create a fascial membrane that covers the anterior triangle of the neck. Anteriorly, it joins with the contralateral fascial layer at the symphysis menti and hyoid bone.

This fascial layer creates several structures and compartments through which neurovascular bundles travel. At the sternum, the fascial layer divides into anterior and posterior layer creating the substernal space. This space contains inferior aspects of the anterior jugular veins. In the neck, the fascial layer encases the carotid sheath, which contains the carotid artery, internal jugular vein, and vagus nerve. This fascial layer also creates the fibrous compartment containing the larynx, trachea, thyroid gland, pharynx, and esophagus. Superior and posterior to the clavicle, this fascia layer creates a space with the sheath of the subclavian vessels allowing the passage of the external jugular vein, the descending clavicular nerves, the transverse scapular, and transverse cervical vessels. Overall, this fascial layer is also important for maintaining the major structures of the neck in appropriate position to allow proper functioning of the cervical musculature.

Sternocleidomastoid Muscle

The sternocleidomastoid muscle originates with individual muscular heads at the manubrium of the sternum and the medial portion of the clavicle. The muscle fibers from the two heads unite midway up the neck to insert onto the mastoid process of the temporal bone and the superior nuchal line on the occipital bone. It is innervated by the spinal accessory nerve and helps with cervical rotation and flexion. When engaged unilaterally, the sternocleidomastoid muscle draws the head toward the ipsilateral shoulder and rotates the face toward the contralateral shoulder. When engaged bilaterally, they flex the cervical vertebrae and help with forced inspiration.

The sternocleidomastoid muscle divides each side of the neck into an anterior and posterior triangle. The anterior triangle is bounded by the median line of the neck, the inferior border of the body of the mandible, and the anterior margin of the sternocleidomastoid muscle. The posterior triangle is bounded by the anterior border of the trapezius ridge, the lateral clavicle, and the posterior margin of the sternocleidomastoid muscle.

Deep Muscles of the Neck

There are several complex layers of deep paravertebral muscles of the neck that are implicated in conditions amenable to TPIs. The deepest of the anterior paravertebral muscles is the longus colli. The longus colli originates on the anterior aspects of the transverse processes of C5–T3 vertebrae and inserts on the anterior arch of the atlas. It consists of three sections of muscle fibers: the superior oblique, inferior oblique, and vertical. These muscle fibers travel between vertebrae to flex the head, flex the neck, and rotate the cervical spine.

The longus capitis originates on the anterior aspects of the transverse processes of C3–C6 vertebrae and travels medially as it inserts on the basilar aspect of the occipital bone. This muscle flexes the neck at the atlanto-occipital joint and antagonizes the muscles of the posterior neck, helping to move the head back to a resting position.

Deep to the longus capitis is the rectus capitis anterior, which originates from the lateral mass of the atlas and also travels medially as it inserts anterior to the foramen magnum on the basilar aspect of the occipital bone. This muscle flexes the neck at the atlanto-occipital joint and also helps to antagonize the posterior neck muscles in a similar fashion to the longus capitis.

The rectus capitis lateralis originates on superior aspect of the transverse process of the atlas and inserts on the inferior

aspect of the jugular process of the occipital bone. This muscle stabilizes the atlanto-occipital joint and also helps with lateral flexion of the neck.

Lateral Vertebral Muscles

The lateral vertebral muscles consist of the scalene muscles, which are deep to the sternocleidomastoid muscles, innervated by cervical nerves (C2–C7), and help to elevate the first and second ribs, bend the cervical spine, and flex the cervical spine. They consist of three pairs of muscles: the anterior, middle, and posterior scalene muscles. The anterior scalene muscles are the most anterior of the scalene muscles and originate from the anterior aspects of the C3–C6 transverse processes and travel inferiorly to converse as a tendon and insert onto the first and second ribs. The middle scalene muscles originate from the posterior aspects of the C2–C7 transverse processes and travel inferiorly and insert as a broad attached onto the first and second ribs. The posterior scalene muscles originate from the posterior aspects of the C5–C7 transverse processes and insert onto the second rib.

Intrinsic Muscles of the Posterior Neck

The posterior muscles of the neck include the splenius muscles. The splenius muscles, which are innervated by dorsal rami of inferior cervical nerves, consist of the cranial and cervical portion known as the splenius capitis and splenius cervicis, respectively. These muscles originate from the nuchal ligament and spinous processes of C7–T6 and travel superolaterally to insert on the superior nuchal line of the occipital bone, the mastoid process of the temporal bone, and the transverse processes of C1–C4. When unilaterally engaged, these muscles laterally flex and rotate the head to the contralateral side. When bilaterally engaged they extend the head and neck.

Intermediate Layer of Deep Back Muscles

The longissimus muscle is the longest subdivision of the erector spinae and is divided into three parts based on the regions traversed: longissimus thoracis, longissimus cervicis, and longissimus capitis. The longissimus thoracis originates in the lumbar region where it is part of the iliocostalis lumborum and inserts on the transverse processes of the thoracic vertebrae. The longissimus cervicis originates from the transverse processes of the thoracic vertebrae and inserts on to the transverse processes of the cervical vertebrae. The longissimus capitis originates from the transverse processes of the upper thoracic vertebrae and inserts on the mastoid process of the temporal bone of the skull. These muscles are innervated by dorsal rami of spinal nerves. When unilaterally engaged, these muscles laterally flex and rotate the head and neck. When bilaterally engaged they extend the vertebral column.

The levator scapula originates from the transverse processes of C1–C4 vertebrae and inserts into the superior angle of the scapula. It is innervated by C3–C4 cervical nerves and the dorsal scapular nerve (C5). This muscle elevates the scapula and laterally flexes the head when in extension.

Other Significant Muscles for Cervical Muscle Injection

The rhomboids, which were previously described, are also sometimes considered for TPIs.

Indications for Cervical Muscle Injections

Indications for cervical TPIs include myofascial pain of the neck from arthritis, trauma, or muscular overuse. Cervical TPIs can also be used to treat pain secondary to spasticity syndromes, facet syndromes, and dystonia.

Contraindications

Contraindications for cervical TPIs include systemic or local site infections, coagulation disorders, or changes in anatomy due to cancer or previous surgery.

Identification of Cervical Injection Sites

Muscles

The location for a TPI in the neck is often identified by locating the desired musculature causing the myofascial pain. While simple physical examination can often identify the location, some providers use a portable EMG to correctly identify the muscles. Trigger point injections can be injected directly at the site of pain or in a grid pattern (Lang's method) surrounding the area of pain. Higher-risk TPIs, such as scalene muscle injections, can be performed under fluoroscopic guidance.

Procedural Technique

There are various ways to perform a TPI. The most common methods include TPIs with local anesthetic injections or simply dry needling. These methods have been shown to be equally effective. Botulinum toxin injection has also been used. For either method, locate the trigger point by finding the area of sensitivity in the taut band, and hold the trigger point between two fingers with one hand. Have the patient slightly stretch the afflicted muscle to prevent excessive movement during the injection, and insert the needle with the other hand. Redirect the needle in multiple directions, and inject local anesthetic if desired. Proper needle placement often produced a local twitch response in the afflicted muscle. Less common methods include the use of corticosteroids, phenol, alcohol, or botulinum toxin.

Complications

Pain, hematoma, and infection are recognized complications of TPIs. When an injectate such as phenol or alcohol is used, patients can experience fibrosis and nodule formation at the site. Botulinum toxin side effects are a result of toxin spread and include dysphagia, dysphonia, or transient paresis.

Trigger Point Injections for the Lower Back

Anatomy

Myofascial Trigger Points

Lower back pain caused by TPs can be superficial or deep and are often involving the iliopsoas and quadratus lumborum muscles [32].

Iliopsoas Muscle

The iliopsoas muscle originates from the iliac fossa (iliacus muscles) and the upper lumbar spine (psoas major muscle) and inserts on the lesser trochanter of the femur. This joined muscle is innervated by anterior rami of lumbar nerve roots (L1–L3) as well as the femoral nerve (L2–L4). The muscle primarily flexes the hip and is active during sitting and standing.

Quadratus Lumborum Muscle

The quadratus lumborum muscle originates on the iliac crest and inserts onto the inferior border of the 12th rib, iliolumbar ligament, and transverse processes of L1–L4 vertebrae. It is innervated by the ventral rami of thoracic and lumbar nerve roots (T12–L4). Its action includes flexion of the vertebral column and lateral flexion when unilaterally engaged.

Indications

Psoas Major Muscle

Patients with pain from iliopsoas muscle TPs typically describe pain that radiates to the sacroiliac and upper buttock region that worsens with getting up from a seated position and standing and is relieved by sitting [32]. Unilateral iliopsoas TP pain is described as a vertical pain down the spine, whereas bilateral TP pain is described as a horizontal directed pain across the lower back [32].

Quadratus Lumborum Muscle

Patients with pain from quadratus lumborum muscle TPs typically describe pain in the lower back that worsens with weight-bearing posture and is relieved by lumbar spine unloading maneuvers such as lying down [94, 95]. Patients will often complain of pain exacerbated by rolling over in bed, coughing, or sneezing. Referred pain can also be experienced and is often described as pain that radiates to the anterior thighs, to the anterior superior iliac spine, and to the superolateral aspect of the knee [94, 95].

Contraindications

Contraindications to performing a TPI of these muscles include bleeding disorders and local infection.

Procedural Technique

Place the patient in the prone position to properly visualize the targeted area under fluoroscopy.

Psoas Major Muscle

Site of needle entry is approximately 5 cm lateral to the spinous process of the L3 vertebrae. Insert the needle and advance it to the anterior one-third of the vertebral body in the lateral view.

Quadratus Lumborum Muscle

Site of needle entry is approximately 2 cm cephalad to the iliac crest and posterior superior iliac crest at the level of L3–L4 vertebral bodies. Insert the needle, and advance it until the needle tip is at the level of the neuroforamen on the anteroposterior view. In the lateral view, the needle tip should be behind the transverse processes.

Confirmation of Correct Needle Position

Psoas Major Muscle

To verify appropriate needle placement, contrast dye should be used. Using a lateral view, contrast should spread vertically over the anterior one-third of the lumbar vertebral bodies. Once confirmed, inject an 8–10 mL mixture of local anesthetic and corticosteroid into the muscle.

Quadratus Lumborum Muscle

To verify appropriate needle placement, visualize the needle posterior to the foramina at the level of the transverse processes. Once confirmed, inject a 4–6 mL mixture of local anesthetic and corticosteroid into the muscle. Botulinum toxin can be used.

Monitoring of Changes due to Procedure

Pain relief during hip flexion and extension should be experienced with both of these injections. Local anesthetic injections should provide relief within 30 minutes, whereas effects from the corticosteroids can take several days. Botulinum toxin gives relief in 2–3 days.

Complications

Complications include increased pain, infection, and hematoma formation in the muscle.

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Miscellaneous Spine Procedures: Nucleoplasty, Intradiscal Electrothermal Therapy (IDET), and Cryotherapy

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Key Points

- The general progression of treatment strategy for pain from intervertebral disc pathology includes initial conservative management of pain with anti-inflammatory medications and physiotherapy.
- Through degenerative changes or acute injuries, the integrity of the annulus fibrosis can be weakened, resulting in "bulging" or an excursion of the nucleus, thereby resulting to a protrusion that results to nerve root compression and nerve dysfunction.
- Disc nucleoplasty may be indicated for patients who have contained disc herniation and failed conservative therapy and have had radicular pain greater than 6 months.
- Discogenic pain, which refers to pain originating from the intervertebral discs, is thought to account for the pain generation in up to 40% of the patients with low back pain.
- Percutaneous intradiscal thermocoagulation therapy is a minimally invasive technique used to treat discogenic low back pain. This technique involves placing a catheter or electrode into or near the posterior annulus of the intervertebral disc to deliver heat or electricity to cause both structural modifications of the disc and destruction of nociceptive nerves.
- Percutaneous intradiscal thermocoagulation should be considered in patients who have functionally impairing discogenic low back pain, confirmed with reproducible pain on a provocative discogram, for more than 6 months and whose condition has not responded to conservative treatment.
- Cryotherapy, known as cold therapy, is a minimally invasive technique of analgesia which uses extremely low temperatures to create lesions to provide a temporary anesthetic block for pain relief.
- Given that cryotherapy employs a specialized cryoprobe that produces local temperature changes only at the tip of the device, indications for therapy include treatment for pain conditions generating from small, well-localized peripheral nerves.

Case Presentation

A 58-year-old male with a 5-year history of chronic left leg pain following a degloving injury after a pedestrian versus motor vehicle accident presents for evaluation at the pain clinic. He has a history of neuroma at the same location of his left leg pain and is status post neuroma excision.

The location of his pain is at the lateral aspect of his left leg. He describes it as dull and uncomfortable. He rates the pain a 9/10 when severe and 5/10 when mild. The pain is constant and very uncomfortable. Nothing seems to make his pain better. He has tried surgical intervention which helped but he is hesitant doing under anesthesia for another

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excision. Upon examination, a 0.5 mm by 0.8 mm scar was noted at the lateral aspect of his left leg. Pain was aggravated with palpation. No erythema, fever, chills, or recent use of antibiotics. We discussed several options including cryoablation of neuroma, medical management, and surgical referral. The patient was comfortable with a minimally invasive cryoablation and was scheduled for the procedure. Informed consent was obtained. Left lower extremity neuroma site was marked. The patient was placed in the right lateral decubitus position. Sterile prep and drape was performed with chlorhexidine. Using fluoroscopic and ultrasound guidance, the proper anatomy was identified. Local anesthetic was infiltrated subcutaneously. Using a blade, a skin nick was made. Then, a 12-gauge Angiocath was inserted through the skin nick, needle was removed, and the large 14-gauge cryo-needle was inserted through the Angiocath under fluoroscopic and ultrasound guidance. A total of six cryo-lesions were made; each lesion was 4 minutes in duration with a 40-second-deep thaw period in between lesioning. The patient tolerated the procedure well. She returned to the clinic in 8 weeks for reevaluation and possible repeat cryotherapy.

Plasma Disc Decompression and Nucleoplasty

The association between intervertebral disc pathology with low back pain and nerve compression pain syndromes (i.e., sciatica) has been long established [1, 2]. Studies have estimated that approximately 40% of lower back pain can be attributed to intervertebral disc pathology, from either acute herniation or degenerative disc disease [1, 3]. For clinicians, the decision to recommend surgical intervention versus nonsurgical conservative management has been challenging since both methods have been studied and demonstrated efficacy in treatment [2, 4–6]. When retrospectively compared to each other, surgical patients had improved pain and function [6]. However, the validity of these conclusions is restricted due to poor study design.

Currently, the general progression of treatment strategy for pain from intervertebral disc pathology includes initial conservative management of pain with anti-inflammatory medications and physiotherapy. If unresponsive, minimally invasive epidural injections or nerve blocks can be performed. Those refractory to conservative management may require surgical interventions. For patients presenting with a large uncontained disc herniation or weakness (i.e., cauda equina syndrome), open surgical intervention is attempted. However, more recently and especially for contained disc herniation refractory to conservative management, minimally invasive procedures have been developed, known as disc nucleoplasty.

Anatomy

Intervertebral discs consist of a central nucleus pulposus, a surrounding annulus fibrosis, and cartilaginous end plates. Through degenerative changes or acute injuries, the integrity of the annulus fibrosis can be weakened, resulting in "bulging" or an excursion of the nucleus pulposus beyond the normal anatomical positioning. When significant protruding occurs, nerve root compression can result causing pain and nerve dysfunction. Nerve root injury may be complete or partial. The direction and vertebral level of disc protrusion determine the affected nerve roots and degree of injury.

Indication

The postulated mechanism of pain relief from disc nucleoplasty is due to the reduction of intradiscal pressure through the dissolution/degradation and subsequent removal of soft tissue from the nucleus pulposus [7, 8]. Tissue removal results in decreased intradiscal pressure, allowing for the disc to resume a more nature configuration through protruded disc retraction, decreasing impingement on nerve roots, and improving symptoms. Identification of the etiologic level of pain source prior to disc nucleoplasty is needed. Often, patients have degenerative disc disease or prior disc herniations of multiple vertebral levels. Therefore, MRI imaging, diagnostic selective nerve root blocks, and/or pre-procedural provocative discogram should be conducted to ensure the procedure is performed on the appropriate intervertebral disc [9–11].

Disc nucleoplasty is indicated for patients who have contained disc herniation, have failed conservative therapy, and have had radicular pain greater than 6 months [11]. Since soft tissue is being removed in this procedure, the pre-procedural disc height should be greater than 50% of the original disc height. Contraindications to disc nucleoplasty include patients who require emergent open surgery for symptoms suggesting causa equina syndrome (i.e., bowel or bladder incontinence, lower extremity weakness, saddle anesthesia), uncontained disc herniations occupying greater than 33% of the spinal canal, extrusion of nucleus pulposus at the level of desired disc nucleoplasty, previous back surgery or structural deformities at the level of intervention, or pre-procedural disc height < 50% of the original disc height [11]. As always, standard contraindications such as systemic infection, site infection, or coagulopathy also apply.

Procedure

Prior to nucleoplasty, periprocedural prophylactic antibiotics (preferably 1 g cefazolin) should be administered. Sedation

is often used for this procedure. Place the patient in the prone position. Using aseptic technique, apply local anesthetic and then use a fluoroscopic oblique view for guidance. Advance a 17-guage needle using an extrapedicular posterolateral approach through Kambin's triangle, which is an anatomical right triangle consisting of the exiting nerve root (hypotenuse), superior articular process of the facet joint (height/perpendicular), and the superior end plate of the distal vertebra (width/base), proceed toward the central portion of the disc (nucleus pulposus). Once the location of the needle tip is confirmed, many clinicians perform a provocative discography by injecting contrast dye into the disc to assess annular integrity and ensure the pain etiology is the identified disc. Once confirmed, removal of tissue from the annulus pulposus is performed using the method of choice, described below. Once completed, remove the devices used to perform the procedure. Finally, inject local anesthetics into the nucleoplasty tract, external to the disc.

Disc nucleoplasty can be accomplished through thermal (laser), radiation (ablation), and mechanical means. The procedural method is similar for the various types of nucleoplasty. Percutaneous laser disc decompression (PLDD) is performed using optical fiber for transmission of the laser energy to create a high heat and radiation to the desired area to mechanically remove the soft tissue as well disrupt the normal biochemical environment of the disc, leading to reduced pain [7, 12]. Radiofrequency coblation is performed using coblation bipolar device. This method decompresses the disc by creating coblation channels using the bipolar device in ablation mode. Typically, this involves making six coblation channels by moving the device at a speed of approximately 0.5 cm/s, advancing in ablation mode and withdrawing in coagulation mode. This results in dissolving the soft tissue and then vaporizing it for removal. This method uses lower temperatures compared to PLDD, theoretically resulting in less surrounding tissue damage. Two methods of mechanical decompression include automated percutaneous lumbar discectomy (APLD) and traditional mechanical disc decompression (MCD). APLD is performed using a 2-mm probe with a side port that allows the device to cut, irrigate, and remove the soft tissue through suction [13]. Traditional mechanical disc decompression uses a rotational motor and helical probe to mechanically disrupt and remove soft tissue. Since no heat is use, nerve injury is less likely. This device also allows for disc biopsy since the disc is not modified by thermal or radiation means.

Complications

Patients should be observed for 2–4 hours post-procedurally for any complications or neurological deficits. Procedural and post-procedural complications for these minimally invasive procedures occur infrequently. The most common complications include transient paresthesia and exacerbation of the underlying back pain. These are often self-limiting. Other more rare complications include skin infections, paraspinal abscess, and discitis.

Efficacy

The use of disc nucleoplasty to reduce intradiscal pressures has been well studied and established [8, 14]. Several clinical trials have tried to determine the clinical correlation. A prospectively study evaluated the efficacy of disc nucleoplasty in patients with radicular pain secondary to disc herniation and demonstrated symptom resolution in 77% of patients at 6 months, mean reduction in pain by >50%, patient satisfaction >80%, improved disability, and decreased analgesia requirement [15]. Other studies have had similar findings [16, 17]. Several other trials have described a success rate of percutaneous disc decompression from 50% to 90% [18–20]. Unfortunately, more studies are needed since many of these studies were not randomized or controlled.

Percutaneous Intradiscal Thermocoagulation

Discogenic pain, which refers to pain originating from the intervertebral discs, is thought to account for the pain generation in up to 40% of the patients with low back pain [21, 22]. The majority of discogenic pain arises from intervertebral disc degeneration (internal disc disruption), which results in delamination/loosening of the annulus fibrosis, annular fissures, and subsequent dehydration and loss of material from the of the nucleus pulposus. These changes result in inflammatory and biochemical alterations in the microenvironment of the degenerated disc, which further leads to pain exacerbation and increases pain nociception [23–28]. Unfortunately, discogenic pain causes non-specific pain patterns, such as back, groin, and leg pain that are worse with axial loading and relieved by rest, making an accurate clinical diagnosis difficult. Imaging modalities such as MRI are used to evaluate disc integrity but cannot link disc integrity with clinical symptoms. Discography is currently the only provocative technique possibly linking clinical symptoms with MRI findings, although its predictive value has been questioned [29–32].

For those with a positive provocative test, percutaneous intradiscal thermocoagulation can be used in place of more invasive interventions, such as fusion surgery or arthroplasty [33–35]. Percutaneous intradiscal thermocoagulation therapy is a minimally invasive technique used to treat discogenic low back pain. This technique of pain relief involves placing a catheter or electrode into or near the pos-

terior annulus of the intervertebral disc to deliver heat or electricity to cause both structural modifications of the disc and destruction of nociceptive nerves [36–39]. While the exact mechanism of pain relief is unknown, theoretic explanations include changes in disc biomechanics, changes in structural integrity, and denervation [40]. Heat or electricity causes the destruction of collagen hydrogen bonds, which results in contraction of collagen fibers. This contraction tightens the laminar annulus fibrosis through annular contraction, repairs annular fissures, and improves the overall structural integrity of the disc [40–43]. At the same time, the delivered heat or electricity causes the destruction of nociceptive nerves through thermocoagulation [40–43]. The combination of these two mechanisms results in long-term and short-term pain relief, respectively.

Percutaneous intradiscal thermocoagulation encompasses two broad techniques that use different methods to generate heat in the intervertebral disc. First, intradiscal electrothermal therapy (IDET), also known as intradiscal electrothermal annuloplasty (IDEA), uses a thermal resistive coil (indirect radiofrequency) to generate heat, whereas percutaneous intradiscal radiofrequency thermocoagulation (PIRFT) uses direct radiofrequency probes to generate heat [44].

Indication

Percutaneous intradiscal thermocoagulation should be considered in patients who have functionally impairing discogenic low back pain, confirmed with reproducible pain on a provocative discogram, for more than 6 months and whose condition has not responded to conservative treatment [21]. In addition, patients should preferably have morphological changes on imaging, a preserved disc height (>50%) with a posterior annular defect, and no signs of an uncontained disc herniation (i.e., focal neurological deficits). Contraindications for this form of treatment include patients with neurological compromise, compressive lesions, or vertebral column instability since these patients may require more acute surgical interventions.

Intradiscal Electrothermal Annuloplasty (IDEA)

Pre-procedural antibiotics (cefazolin 1 g or vancomycin 1 g) are used for IDEA. In addition, light sedation is often used for patient comfort. The patient should be in the prone position with abdominal support to reduce lumbar lordosis. Obtain an oblique view with fluoroscopic imaging to determine the location of the introducer insertion site. Once determined, prepare the area using sterile technique, inject a local anesthetic, insert a 17-gauge introducer needle, and advance to the nuclear cavity of the desired intervertebral disc. Once at the desired location, obtain confirmatory views (anteroposterior and lateral) and, if satisfactory, insert a thermal catheter with a resistive coil through the needle. Advance the thermal catheter through the disc and observe its circumferential movement along the interface between the nucleus pulposus and posterior annulus fibrosis. Once the catheter is in a satisfactory position over the entire posterior annulus, begin to heat the disc using the thermal catheter. Increase the temperature in 0.5–1 °C increments every 30 seconds with a goal of 90 °C. Once at 90 °C, maintain that temperature for 4–20 minutes as specified by manufacturing recommendations. Of note, the actual temperature of the annulus ranges from 15 to 50 °C lower than the temperature of the thermal catheter probe.

Percutaneous Intradiscal Radiofrequency Thermocoagulation (PIRFT)

The pre-procedural setup for PIRFT is like that of IDEA. Pre-procedural antibiotics, light sedation, patient positioning, fluoroscopic imaging, and local anesthetics are used as described above. Advance the 17-gauge introducer needle into the center of the disc. Once the position is confirmed with imaging, place an 18-gauge RF probe into the introducer needle and then increase the temperature of the RF probe to 70 °C for 90 seconds.

Intradiscal biacuplasty, a newer form of PIRFT which uses two internally cooled radiofrequency (RF) probes positioned in the posterolateral aspect of the annulus bilaterally, is thought to allow for a larger area of thermocoagulation [45, 46]. Since these probes are internally cooled during the ablation process, they allow higher amounts of RF energy to heat the annular tissues between the probes while preventing the tissue immediately near the probe from becoming damaged, which could eventually lead to scar formation and future interference with RF energy delivery to the entire posterior aspect of the annulus [45, 46]. To perform this technique, prepare the patient as previously described. Obtain an oblique fluoroscopic view and direct two 17-gauge introducer needles (one on each side) toward the superior articular process, and enter the lower half of the intervertebral disc. Continue to advance the probes until they are aligned with the medial aspect of the vertebral pedicle in an anteroposterior fluoroscopic view. Once the position is confirmed, place an 18-gauge RF probe in each introducer needle. Reconfirm positioning prior to the application of RF. Once confirmed, increase the probe temperature over 10 minutes to 50 °C. Once at 50 °C, maintain that temperature for 5 minutes.

For all procedures previously described, patients should be observed post-procedurally for adverse effects. They should be discharged home with recommendations for physical therapy and functional rehabilitation programs. Important

aspects of this treatment option include early mobilization of tissue and functional restoration through structured core exercise programming.

Complications

The most common procedural complications include vasovagal responses and increased pain. If the patient complains of excessive pain from the heating apparatus, slow down the incremental increase until the pain has subsided. More significant but rare complications that result from improper sterile technique or inappropriate probe/device placement include infectious complications, such as discitis or spinal abscesses, hemorrhagic complications, and neurological complications, such as spinal nerve root injuries or cauda equina syndrome [47–51].

Efficacy

Initial clinical studies evaluating percutaneous intradiscal thermocoagulation, specifically IDET, suggested it may be an effective approach to improve pain and function for patients with low back pain who failed conservative management [52, 53]. While these studies demonstrated a decrease in pain severity and improved functionality, they were nonblinded and did not evaluate the long-term benefits of this procedure. Since then, there have been several randomized controlled trials conducted on the efficacy of IDET. In these trials, patients who had low back pain and positive provocative discography were randomized to either IDET or sham IDET therapy. In both trials, there was no improvement in functional status in the patients who received IDET compared to those who received sham therapy [54, 55]. While one study demonstrated a decrease in pain, this finding was not able to be reproduced [54–57]. For specific patient populations, these procedures may have some benefits. However, patients with certain preexisting conditions, such as multilevel degenerative disc disease, obesity, degenerative arthritis of the vertebral column, or inflammatory arthritis, may not benefit at all [47, 58, 59]. Clinical trials investigating the effectiveness of PIRFT have also failed to demonstrate a clinical benefit [60–62]. A systematic review in 2007 demonstrated two nonrandomized trails showing evidence for the use of IDET over PIRFT. However, this review also demonstrated IDET and PIRFT to have no difference in comparison to placebo [54]. From this review, the authors concluded the evidence did not support the use of percutaneous intradiscal thermocoagulation for discogenic pain [54].

More recently, studies have shown a benefit of the newer technique of intradiscal biacuplasty. These studies show a decrease in pain scores and improved functionality of patients up to a year after biacuplasty [63–65]. This has been postulated to be a result of decreased tissue damage surrounding the cooled RF probes as well as a decreased max temperature required during the procedure [45, 46]. Further studies are needed to assess the long-term effectiveness of this technique.

Cryotherapy

Cryotherapy, known as cold therapy, is a minimally invasive technique of analgesia which uses low temperatures to create lesions to provide a temporary anesthetic block for pain relief. The use of this technique predates modern medicine and has a long-standing history of being an effective way to produce analgesia [66, 67]. Advancements in technology and cryoprobes, which can now deliver cold temperatures to an affected site without widespread tissue damage, have allowed for cryotherapy to continue to be an effective analgesia technique in modern medicine [68–70].

Modern cryoneurolysis uses specialized cryoprobes to deliver pressurized gas (nitrous oxide or carbon dioxide) to freeze an identified nerve. As the compressed gas leaves the probe tip, it quickly expands, resulting in a rapid decrease in local temperature (the Joule-Thomson effect) to approximately −60 to −70 °C [71]. As a result, intracellular and extracellular water in the surround area freezes to form an ice ball (about 3–5 mm in diameter) on the tip of the probe and therefore directly adjacent to the intended nerve [71]. Freezing and subsequent thawing of these ice balls result in axonotmesis (disruption of the axon and myelin sheath), which leads to Wallerian degeneration of the axon but leaves the endoneurium, perineurium, and epineurium intact, allowing for nerve regeneration [71]. Since modern cryoprobes can discriminatively test for sensory and motor nerves, precise targeting can be accomplished with minimal risk to unintended nerve function.

Cryotherapy provides temporary pain relief since axonal regeneration occurs. The time course of pain relief, which typically lasts weeks to months, depends on the distance between the location of cryoneurolysis and the end organ [72, 73]. Typically, analgesia lasts longer than the time needed for nerve regeneration, which may be due to decreased neuroplastic changes, temporal relief of CNS windup phenomena, or autoimmune response at the site leading to continued nerve conduction anomalies [74–76].

Indication

Given that cryotherapy employs a specialized cryoprobe that produces local temperature changes only at the tip of the device, indications for therapy include treatment for pain

conditions generating from small, well-localized peripheral nerves. Such conditions include postoperative pain, facial pain syndromes, intercostal neuralgia, etc. Contraindications for cryotherapy include general contraindications for minimally invasive procedures, such as local/systemic infection and bleeding diathesis.

Procedure

Prior to the application of cryotherapy, many clinicians will trial multiple local anesthetic blocks to determine the location of pain generators and if the pain is potentially amenable to cryoneurolysis. Cryotherapy employs an introducer technique to ensure proper placement of the cryoprobe. Prepare the patient under sterile technique, and advance the introducer toward the desired location in a linear fashion using standard regional anesthesia techniques. Typically, 14- to 16-gauge catheters are used to allow for easy cryoprobe passage once the catheter is in place. For cryotherapy, patient awareness should be maintained to determine the location of the pain generator prior to the procedure as well as to determine if successful neurolysis is achieved during the procedure. Pain generator location can be determined by palpation, imaging modalities (fluoroscopy) with or without contrast, and nerve stimulation (motor or sensory).

Cryoneurolysis is produced by repeating cycles of freezing and thawing of the nerve. Typically, three to four cycles of freezing (−60 to −70 °C for 3–4 minutes) and thawing (30 seconds in between freezing periods) are needed. Nerve stimulation can be conducted during the thawing phases to ensure proper cryoneurolysis is achieved. Nerves surrounded by large vascular structures, such as larger arteries and veins, may require longer freezing time (4 minutes cycles instead of 3 minutes) because of more rapid thermal dissipation due to increase heat production in the local area.

Complications

The most common procedural complication includes increased pain during cryoneurolysis. This is typically a result of partial neurolysis as a result of an inappropriate distance between the ice ball formation on the tip of the cryoprobe and the nerve. Often, patients may have discomfort for the first few seconds of cryoneurolysis. This is a normal phenomenon; however, if the pain persists for longer than 30 seconds, investigation of the cause of the pain source should occur. If this occurs, allow for a thawing phase prior to moving the cryoprobe to ensure local tissue is not damaged. Once thawed, move the probe, and confirm proper positioning with pain generator location determination methods previously discussed. Often at this point, nerve stimulation should be used as a confirmatory method. Once confirmed, continue cryoablation as previously described. Pain should improve as further cryoneurolysis is conducted. Post-procedural complications include pain and swelling. It is recommended to use conservative measures such as ice and non-opioid-based pain medication regimens.

Efficacy

Cryoablation has been shown to be an effective pain management technique for nerve pain generated from peripheral nerves in the acute, postoperative, and chronic pain setting. Specifically, it has been shown to be effective for postoperative pain associated with thoracotomies and herniorrhaphies, chronic back pain, and peripheral lower extremity pain [77–83]. Unfortunately, the lack of randomized controlled trial and clinician training has prevented this technology from widespread use. Further studies are needed to demonstrate its possible extensive clinical application as well as benefits of a lower risk of deafferentation pain compared to other modern technologies used for peripheral nerve pain.

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Complications of Interventional Therapy for the Management of Low Back Pain

31

Eric J. Wang, Cameron Kluth, and Dermot P. Maher

Key Points

- All interventional pain procedures have a risk-benefit ratio that varies depending on the interaction between the medications used, the techniques employed, and patient-specific factors.
- Many interventional pain procedures share similar possible complications, but because the specific anatomy involved and the type of instrumentation required may vary greatly between procedures, the pain physician must be aware of all possible complications of each procedure he or she performs.
- Thoroughly understanding the risks of a given procedure allows the pain physician to achieve an informed and shared decision with the patient.

Case Presentation

A 63-year-old male presents with a 2-year history of low back pain (LBP) with a "lightning"-like sensation that radiates down his right leg at times. He has a history of hypertension, hyperlipidemia, and type 2 diabetes. He has a 30-pack-year history of smoking but quit 5 years ago. He takes aspirin 81 mg every day, as recommended by his cardiologist. For his back pain, he has taken over-the-counter medications including acetaminophen and ibuprofen. However, his symptoms have gradually worsened, and his pain keeps him from being able to focus while at work. His right foot also feels vaguely "weaker" than his left foot, and he reports that he has had stable, long-standing "pins and needle" discomfort in both feet. His primary care physician refers him to your office for workup for an epidural steroid injection.

Introduction

Low back pain (LBP) is a complex symptom of many different pathologic disorders. LBP is commonly reported by people of all ages and is also the single largest cause of disability on a global level [1, 2]. The financial impact of LBP is tremendous and encompasses expenditures to society as a whole, healthcare networks, and social support systems. Conservative treatment in the form of physical therapy, analgesic medications, and interventional therapy should be the initial treatments offered [3]. All treatments for any medical condition, including LBP, entail a certain ratio of potential risk to anticipated benefit. Preference is given to treatments with the lowest risk to benefit ratio.

Interventional treatments available to address LBP have grown in their variety, the types of pain that can be effectively managed, and their volume of clinical usage. Guidelines emphasizing safe and effective practices have been developed, but significant practice variation is common [4]. Continued study and refinement of interventional practices have led to many of these techniques either developing remarkable safety records or being abandoned due to unacceptable risk levels. In general, interventional therapies currently practiced carry a lower risk to benefit ratio than more aggressive therapies such as surgery without sacrificing effectiveness [4]. The epidemiology of severe complications resulting from interventional procedures is more frequently found in the form of case reports rather than large studies [5]. If these conservative modalities fail, surgery is considered an option to address ongoing symptoms, but the significantly increased risks must be considered.

Complications from interventional procedures can be divided into three broad categories: complications associated

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with all interventional techniques, complications arising from the employed medications, and complications unique to certain procedures.

Complications Associated with Medications

For most interventional pain procedures, four types of agents are administered: saline, a contrast agent, a mixture of a local anesthetic, and a corticosteroid preparation. Certain procedures make use of additional medications such as ethanol, phenol, botulism toxin, or biologically derived macromolecules. Medication-associated reactions can be either allergic or related to the pharmacologic properties of the drug. With respect to allergic reactions, there is a known incidence of allergy to all of the administered medications. True allergic reactions to medications used in pain procedures for the treatment of LBP are rare. Allergy to amide local anesthetics usually manifests as mild contact dermatitis, but it can occasionally be a life-threatening anaphylactic reaction [6]. Guidelines for the prevention and management of local anesthetic toxicity (LAST) have been published by the American Society of Regional Anesthesia and Pain Medicine (ASRA) [7] (Fig. 31.1).

Mild allergies to iodinated contrast agents are widely reported, although true anaphylactic reactions are believed to be rare [8]. Several factors have been associated with an increased risk of anaphylactic reactions to iodinated contrast. These include asthma, atopy, and advanced heart disease [9]. The risk of significant, life-threatening reactions to contrast agents can be minimized by taking a thorough history and physical examination, focusing on risk factors and personal histories of allergic reactions to iodinated contrast agents or food with iodine such as shellfish and seaweeds. Allergic reactions to gadolinium-based agents, which are often used as an alternative, are extremely rare.

Corticosteroids have been implicated as a causative agent in allergic reactions. In the United States, methylprednisolone acetate, triamcinolone acetonide, and betamethasone acetate and phosphate mixture have all been shown to be safe at therapeutic doses for interventional use. None of these medications, however, carry an FDA indication for use in interventional therapy for the treatment of chronic pain. Complications arising from the pharmacological action of corticosteroids include suppression of the hypothalamic-pituitary axis (HPA), Cushing's syndrome, osteoporosis, avascular necrosis of the osseous tissue, steroid myopathy, epidural lipomatosis, hypertension, weight gain, fluid reten-

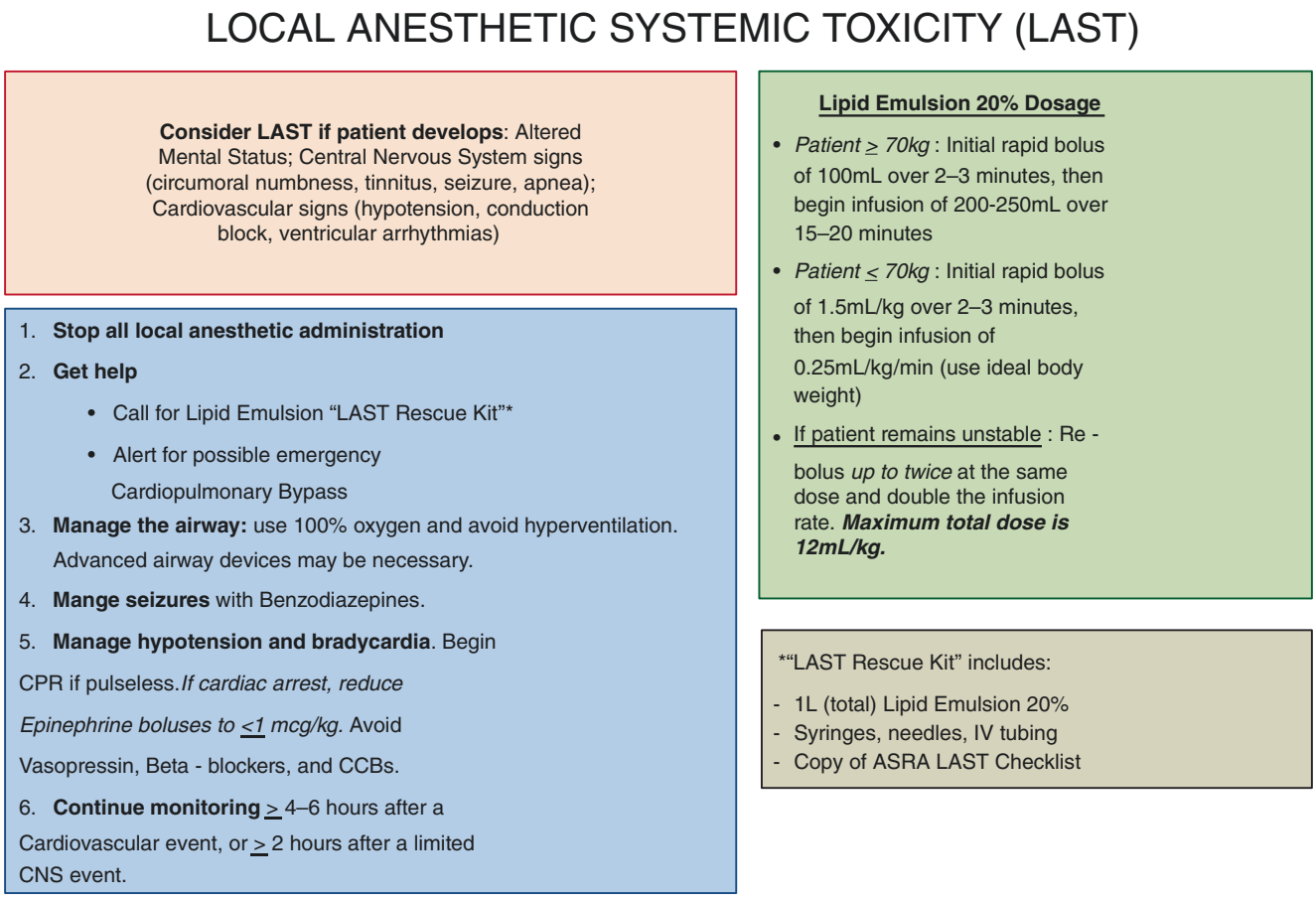

Fig. 31.1 Local anesthetic systemic toxicity (LAST)

Table 31.1 Properties of commonly injected corticosteroids

Steroid	Equivalent dose (mg)	Solubility	Serum half-life	Particle size (μM)	Size comparison to red blood cells (7.5–7.8 μM diameter)	Aggregation
Dexamethasone sodium phosphate (DMSP)	0.75	Soluble	36–54 hours	<7.6	10 times smaller	None apparent
Triamcinolone acetonide	4	Relatively insoluble	88 minutes	Varies (0.5 to ≥100)	12 times larger	Extensive and large aggregates
Betamethasone sodium phosphate and acetate	0.60	Combination	6.5 hours	Varies (<7.6 to ≥100)	12 times larger	Large aggregates
Methylprednisolone acetate	4	Slightly soluble	18–26 hours	<7.6	Usually smaller	Few but densely packed aggregates

tion, dermatologic manifestations, and hyperglycemia. A single epidural steroid injection has been demonstrated to adversely affect cortisol concentrations for up to 30 days [10]. Insulin sensitivity can be affected for up to a week following the use of steroids in interventional procedures for LBP. A single steroid injection can also cause steroid myopathy or Cushing syndrome [11]. A rapid series of three epidural injections may suppress the HPA axis for up to 3 months [12]. High-particulate steroid preparations seem particularly prone to causing thrombotic events. In terms of general recommendations, some literature recommends limiting the amount of annual steroid to 3 mg/kg of triamcinolone or the equivalent [13]. There is little prospective data that shows higher-dose steroids provide superior pain relief compared to lower-dose steroids, and therefore the lowest dose of steroids expected to yield a clinical response should be used to avoid systemic side effects.

Particulate steroids have been implicated in blockage of capillary blood flow resulting in ischemic infarctions of neural tissue. In any injection using steroids proximal to a watershed blood supply, consideration should be given to using a non-particulate steroid such as dexamethasone (Table 31.1) [14–16].

Complications of Specific Procedures

Every interventional pain procedure has risks specific to the anatomical site involved and the type of instrumentation required. The practitioner must be aware of common and rare complications in order to implement measures to avoid them, as well as quickly identify and manage them should they occur.

Epidural Steroid Injections

The goal of an epidural steroid injection (ESI) is to deposit an anti-inflammatory medication into the epidural space. The minimally invasive nature of ESIs, coupled with strong evidence of effectiveness, has made the procedure a first-line therapy offered for the treatment of back pain [8]. ESIs carry risks associated with vascular injury or intravascular injection, bleeding, infection, and direct needle trauma.

The epidural space extends cephalad from the foramen magnum to its caudal border at the sacrococcygeal ligament. The epidural space is filled with loose areolar fatty tissue and a venous plexus intended to provide cushioning and support to the spinal cord. The space is bordered by a ring of osseous and fibrous tissue anteriorly by the posterior longitudinal ligament, vertebral body, and disk, anterolaterally by the vertebral pedicles, posterolaterally by the facet joints, and posteriorly by the ligamentum flavum. The ligamentum flavum forms a tented "V"-shaped structure with an incompletely formed apex, especially in the cervical spinal regions. The ventral and dorsal nerve roots exit laterally. Radicular feeding vessels enter the spinal canal at the neural foramen, which is bordered anteriorly by the vertebral body and intervertebral disc, superiorly and inferiorly by the vertebral pedicles, and posteriorly by the superior articular process of the inferior vertebrae. The blood supply to the spinal cord consists of one anterior spinal artery, which arises from the vertebral artery and supplies approximately the anterior two-thirds of the spinal cord, and paired posterior arteries, which arise from the inferior cerebellar arteries and supply the posterior third of the spinal cord. The anterior spinal artery requires staggered reinforcement by anterior segmental medullary arteries, which are direct branches from the aorta or the vertebral arteries in the neck. In general, the cervical region has several major reinforcing arteries, whereas the lumbar region generally only has one major feeding artery. In 85% of patients, the great radicular artery (artery of Adamkiewicz) arises between T9 and L2, usually from the left, but there is a minor variant which arises from the lower lumber spine, even from as low as S1 [17]. Additional radiculomedullary arteries are found in 43% of patients [17].

The epidural space is accessed by one of the three general techniques: interlaminar, transforaminal, or caudal. With each technique, unique and often variable vascular anatomy is encountered, which can be inadvertently cannulated or injured by direct needle trauma. Vascular injury can be minimized with careful procedural technique and a complete understanding of the vascular anatomy at the intended site of epidural entry.

Complications directly from needle trauma can include vasovagal episodes, dural puncture, headache, subdural injection, intracranial air injection, spinal cord trauma, infection/abscess, hematoma, epidural lipomatosis, pneumothorax, nerve damage, brain damage, increased intracranial pressure, intravascular injection, vascular injury, embolus, and death. These have been reported from both interlaminar and transforaminal approaches. These procedures should be performed for chronic pain by trained physicians with knowledge of fluoroscopic guidance, the relevant anatomy, pharmacology, and the ability to longitudinally follow patients and address complications. Many of the possible complications discussed relating to epidural steroid injections may be applied, with procedure-specific nuances, to other neuraxial interventions.

Analysis of the American Society of Anesthesiologists (ASA) Closed Claim database found 114 claims pertaining to epidural steroid injections. Of these, 28% involved nerve injury, 24% infection, 20% headache, 10% increased pain/no relief, and 9% death/brain injury [18].

One of the most devastating outcomes of vascular trauma is an epidural hematoma. Epidural hematomas develop rapidly and clinically manifest within several hours of neuraxial needle placement. A number of estimates of the incidence have been reported for epidural anesthetics, but they are believed to be even more rare for fluoroscopically guided epidural steroid injections for chronic pain. The largest risk factors for the development of an epidural hematoma are the use of an antiplatelet or anticoagulant and/or the presence of an inherited bleeding disorder. Hematomas are rarely seen following any interventional procedure but catastrophic when they occur. The risk of epidural hematoma in patients taking antiplatelet medications or anticoagulants, such as clopidogrel and warfarin, is well established, but exactly how long patients should wait before they become ESI candidates is based largely on expert opinion. The exact time to hold each medication should be the product of a discussion between the patient, the physician providing the antiplatelet or anticoagulant, and the pain physician, with an emphasis on the risk of procedural bleeding and the consequences of an embolic or thrombotic event should the antiplatelet or anticoagulant be held. Published society guidelines should also be considered, such as the ASRA guidelines for anticoagulated patients [12, 19].

Although infection is possible with any needle or foreign body penetrating the skin, serious infections resulting from epidural needle placement are a rare event [18]. *Staphylococcus aureus* has been found to be the most commonly implicated bacterial species in epidural abscesses, suggesting that skin contamination is a common culprit [20]. Epidural abscesses initially present as back pain coupled with low-grade fevers, and patients develop subsequent progressive neurologic deficits [21]. If clinically suspected, early diagnosis with magnetic resonance imaging with gadolinium contrast and early intervention with antibiotics and possible decompressive laminectomy can improve long-term outcomes. There are also reports of infections in adjacent tissues, such as vertebral osteomyelitis and discitis, following an ESI [22].

Aseptic meningitis is a possible, although generally benign, complication that can cause burning pain, headaches, or even seizures. Several cases have occurred following inadvertent intrathecal corticosteroid injections. Arachnoiditis has been correlated with intrathecal injection of methylprednisolone [23].

Without fluoroscopy, the risk of intramuscular and inadvertent intrathecal injection may be substantially increased. Inadvertent intrathecal injections can cause significant complications including nerve injury from preservative-containing medications, adhesive arachnoiditis, aseptic meningitis, and cerebral vein thrombosis. The most common outcome resulting from dural penetration is a postdural puncture headache, which is a bilateral frontotemporal headache responsive to changes in positions. Accidental dural puncture is associated with over 50% headache incidence. Inadvertent injection of local anesthetics in the subdural space can result in profound motor weakness and analgesia. Injection of air into the subdural space (most commonly seen when loss-of-resistance technique to air is used) can result in pneumocephaly, manifesting in some cases as blurred vision and eye pain.

Cervical Epidural Steroid Injections

Extra consideration should be given before performing cervical epidural steroid injections. As with the thoracic spine, direct spinal cord injury from improper needle placement can result from either the interlaminar or transforaminal approach. Paralysis following cervical ESIs is usually attributed to anterior spinal artery syndrome, which is thought to occur from direct injury to the feeding radicular artery or embolism from high-particulate steroids into the vascular supply of the anterior spinal cord [14, 20, 22]. A second proposed mechanism is radicular artery vasospasm resulting from needle placement proximal to the artery, without direct trauma or emboli formation.

In general, the interlaminar approach for cervical epidural steroid injections is considered safer than the transforaminal approach. The multidisciplinary working group (MWG) examining the safety of cervical epidural steroid injections recommended injecting at the C7–T1 level, but no higher than the C6–C7 interspace, as the cervical epidural space is widest at C6–T1 and gaps in the ligamentum flavum occur more frequently at ascending cervical levels [8, 24, 25].

Further recommendations from the MWG for avoiding neurologic complications during cervical neuraxial injections include review of relevant imaging, using minimal or no sedation, multiple image plane fluoroscopy, and the use of contrast [25, 26].

Thoracic Epidural Steroid Injections

As with the cervical spine, thoracic epidural steroid injections carry the risk of spinal cord injury via direct trauma from improper needle placement or spinal cord ischemia from emboli or vasospasm. As the artery of Adamkiewicz supplies the anterior two-thirds of the spinal cord, injection with a particulate steroid may result in infarction of the lower thoracic spinal cord [14].

Lumbar Epidural Steroid Injections

Medicare data demonstrates that the overall growth in interventional techniques from 1998 to 2005 was 179%. In comparison, lumbar epidural steroid injections grew 271% from 1994 to 2001 [27]. The risks of lumbar epidural steroid injections are generally considered to be lower compared to that of cervical injections, but the general risks of epidural injections as described above still apply.

Facet Nerve Blocks and Medial Branch Blocks

It is estimated that 89% of people over the age of 65 have CT evidence of facet joint arthropathy [28]. The facet joints are paired structures that form by articulation of the superior and inferior articular processes on the posterolateral aspects of the spinal canal. These are true diarthrodial joints with opposing cartilaginous surfaces and synovial lining. The orientation of the facet joints dictates the type of motion allowed at each spinal level. For example, the cervical facet joints are oriented closer to the axial plane than the lumbar facet joints, allowing greater cervical spine movement in the axial plane compared to the lumbar spine.

The innervation of the lumbar facet joints is relatively consistent in the human population. The posterior rami of the spinal nerve root divides into the lateral and medial branches. The medial branch crosses the transverse process at the intersection of the superior articular process. Each medial branch then divides into two branches – an ascending branch that innervates the superior articular process at the same nerve root level and a descending branch that innervates the inferior articular process. In this way, the facet joint formed by the articulation of the L4 inferior articular process and the L5 superior articular process is innervated by the descending branch of the L4 medial branch and the ascending branch of the L5 medial branch. Both would need to be blocked for a proper diagnostic block.

The medial branches in the lumbar spine are consistently found at the confluence of the superior aspect of the transverse process and the superior articular process in the mammiloaccessory notch [29]. At the L5 level, the intended target is the dorsal ramus as it crosses the sacral ala.

The cervical medial branches have a more variable course. Starting at C5, medial branches cross the middle of the cervical articular pillars. The medial branches are higher on the articular pillar as one moves more cephalad. The third occipital nerve is a relatively large superficial branch of the C3 and runs over the articulation of the C2 and C3 vertebral bodies.

Facet joint arthropathy can be addressed by a number of different interventions, such as intra-articular steroid injections of the facet joints or diagnostic local anesthetic blocks of medial branches of dorsal rami, followed by radiofrequency ablation (RFA) of those nerves [30]. There is also a role for physical therapy, surgery, and pharmacotherapy, such as NSAIDs. For diagnostic purposes, medial branch blocks are more sensitive than intra-articular injections [31].

Reported complications of interventional procedures for facet joint pain include neurotoxicity, neurologic injury, vascular injury, disc injury, pneumothorax, infection/abscess, and pharmacologic effects of corticosteroids and other injected agents [8]. As in other interventions, most serious complications can be avoided with rational use of fluoroscopy and careful patient selection. Carefully obtained histories and physicals will aid in screening patients for potential localized infection over the site of needle entry, coagulopathy, pertinent allergies, spinal hardware, or conditions that preclude the use of fluoroscopy. The incidence of epidural hematomas and other major bleeding events following facet interventions is believed to be low, but definitive data is lacking. Postdural puncture headaches are rare but possible.

Postprocedural infections are more likely to occur in the paraspinous musculature than in the central canal or joint [32]. Epidural abscesses following facet joint injections are reported to more commonly occur via hematogenous spread rather than by direct spread from the facet joint capsule to the epidural space [33]. MRI with gadolinium contrast is the most important diagnostic tool as it can diagnose up to 90% of cases. Parenteral antibiotics are the first-line treatment. Decompression of confirmed epidural abscesses unresponsive to antibiotics with a surgical laminectomy is recommended within 36 hours, although neurologic sequelae may persist [8]. Septic arthritis has been described secondary to both cervical and lumbar zygapophyseal joint injections [33, 34]. It typically occurs unilaterally and causes widening of facet joints on plain radiographs and extra high-signal intensity on T2-weighted imaging. As with epidural abscesses, IV

antibiotics are recommended for 4–6 weeks, followed by surgical decompression if antibiotics are unsuccessful.

Unlike with intra-articular injections, diagnostic medial branch blocks are unlikely to cause exacerbation of pain. Localized tenderness, however, may occur for 24–48 hours following the procedure due to needles having penetrated the paraspinal musculature. Inadvertent intravascular injection is believed to occur in 8% of lumbar medial branch blocks, and this vascular uptake may cause a false-negative diagnostic block.

There are unique risks for procedures performed in the cervical region. During third occipital nerve blocks and cervical medial branch blocks above C5, patients may experience postprocedural ataxia due to local anesthetics blocking the upper cervical proprioceptors needed for tonic neck reflexes. This temporary sensation usually resolves within 15–30 minutes. Patients should be warned before the procedure about this potential side effect. If it does occur, the patient should be instructed to focus on horizontal objects in the room.

Facet Joint Radiofrequency Ablation

The risks of radiofrequency ablation (RFA) are similar to those of diagnostic facet nerve injections and are also reported to be very rare [8, 35, 36]. Complications unique to facet joint RFA may include a localized tenderness, exacerbation of pain for several days, dysesthesia, or allodynia. Improper needle positioning could theoretically result in thermal destruction of unintended targets, such as the ventral rami. Localized burns and motor weakness have been reported but are believed to be extremely rare. To prevent these complications, physicians can increase stimulation to at least 2 V at 2 Hz to test motor activity before starting the lesioning process. RFA has been further refined to include pulsed radiofrequency (RF) programming, which does not damage neural tissue, and water-cooled RFAs, which covers tissue over a larger surface area. As pulsed RF does not damage the nerves, exacerbations of pain, dysesthesia, and allodynia following these procedures are typically not observed.

Interventional pain physicians should be aware of the presence of an implanted cardiac pacemaker or implanted cardioverter defibrillator (ICD) when performing RFA. Electrical return pads should be positioned so that current does not pass over the device. Preprocedural consultation with a cardiologist is advisable to determine pacemaker settings and whether it needs to be set to an asynchronous mode. The defibrillating feature of ICDs should be disabled using a magnet prior to procedures to avoid accidental defibrillation during the procedure. RF devices that make use of bipolar energy will reduce, but not eliminate, some of these complications.

Dysesthesia and allodynia are more commonly observed following cervical RFA procedures and result from denervation of the lateral branch of the posterior primary ramus, which partially innervates the cutaneous tissue overlying the spinous process. Despite well-described lateral and prone approaches for cervical median branch blocks and rhizotomies, the prone technique hypothetically may provide more reliable osseous landmarks for needle placement. Studies comparing safety between lateral and prone procedures are not available.

Neuritis has been observed following RFA procedures [35]. Anecdotal evidence suggests that steroids injected at the site of denervation may decrease the incidence of postoperative neuritis.

There are few reports of infectious complications following RF ablations. It is postulated that the thermal lesioning provides a bacteriocidal effect [36]. Contrast enhancement on MRI that appears typical for paraspinal abscess, even without apparent infection, has been observed following RFA and is attributed to a noninfectious post-inflammatory process [37].

Sacroiliac Joint Injections

Interventions to sacroiliac joint (SIJ) pain are directed either intra-articularly or toward the afferent nociceptive nerves supplying the joint. The sacroiliac joints are paired structures of true diarthrodial joints with opposing cartilage and a rich overlying layer of fibrous connective tissue serving to reinforce the joint. The SIJ has limited motion in all three plains with the greatest being 1–3 degrees of motion in the x-plane [38, 39]. Weight from the upper body is transmitted through the lumbar spine to the sacrum and must then be transmitted laterally to the ilium and subsequently directed inferiorly down the femur. This abrupt change in the direction of force predisposes the SIJ to significant potential strain and possibly contributes toward the development of arthritis. The SIJ is innervated by the L5 dorsal ramus and lateral branches of the S1–S3 dorsal rami and possibly by the lateral branches of the S1–S3 ventral rami [39, 40]. As the anterior branches are largely inaccessible by percutaneous methods, they are not of major concern to most interventionalists [38].

Complications associated with intra-articular injections are uncommon. A transient, self-limited exacerbation of pain following the procedure for a few days due to distention and pressurization of the SIJ from the injectate may occur. It is recommended that only 2–2.5 ml of injectate be used to avoid excessive pain from joint distention [8]. Abscesses within the joint and presacral musculature are theoretically possible if the needle is advanced into the pelvic viscera. Bleeding complications have not been reported following intra-articular injections.

Consistent with all RFA procedures, RFA of the lateral sacral branches and lower lumbar medial branches which innervate the SIJ requires patient screening, advanced training, and fluoroscopy expertise. Possible complications of SIJ-RFA include vascular injury, hematoma, neuritis, spinal anesthesia, soft tissue and osseous burn injuries, and motor nerve injury [4].

The most common complication observed following SIJ-RFA is a transient neuritis [8]. Water-cooled RF and traditional thermal RF have been associated with a transient flare of pain as well as possible neuritis [41]. Pulsed RF does not result in neurodestruction and therefore has less incidence of local postprocedural pain but is also less effective for the treatment of SIJ pain [42]. Infections are rare following SIJ-RFA. Symptomatic bleeding has not been reported following SIJ-RFA.

Intradiscal Procedures

Discogenic etiologies of chronic back pain can be due to a disc physically occupying space within the spinal canal and causing compression of adjacent neural structures, as is the case with disc bulges, herniations, and prolapses, or from the extrusion of inflammatory mediators from the nucleus pulposus. Discogenic pain can also arise from degenerative disc disease (DDD) causing mechanical tears or fissures in the annular fibrosus of the disc, with subsequent ingrowth of afferent nerve fibers deeper into the annulus, which is usually devoid of nerves. Age-dependent desiccation of the nucleus pulposus may exacerbate DDD, causing the discs to become more brittle and vulnerable to damage. Pain from disc degeneration is usually axial, exacerbated by maneuvers that increase pressure to the disc, such as during a prolonged sitting position, and relieved by maneuvers that decrease disc pressure. Establishing which disc is causing pain can be done through noninvasive imaging, such as MRI, or provocative tests, such as discography.

The intervertebral disc is a connective tissue element between two adjacent vertebral bodies (or the sacrum in the case of the L5/S1 disc) that allows for flexion, extension, rotation, and lateral flexion of the spine. Discs are composed of an inner nucleus pulposus (NP) and an outer annulus fibrosis (AF). The disc attaches to its adjacent vertebral bodies at the vertebral end plate and to anterior and posterior ligaments. The NP is composed of type II collagen, which is approximately 80% water and creates a relatively non-distensible consistency. The AF is composed primarily of type I collagen and also has a relatively increased water content. In a healthy disc, both the AF and NP are essentially avascular, with nutrition to resident chondrocytes and fibroblasts provided by diffusion from the vertebral end plates. There is also a paucity of nerve innervation in healthy discs beyond the outer third of the AF. Desiccation of the disc can lead to weakening of the AF, allowing for its restraining forces to be overcome by hydraulic pressure from the NP. This can result in disc tears, fractures, NP herniation, and the ingrowth of nerve innervation and blood vessels into the disc.

Provocative discography uses pressurization of individual intervertebral discs under live fluoroscopic guidance to identify which discs are the sources of pain. While largely supplanted by refinement of imaging techniques, provocative discography remains unique as the only imaging modality to correlate symptomatology with imaging. The overall rate of complications, including discitis, epidural abscess, and bacterial meningitis from provocative lumbar discography, is between 0% and 2.7%, and it is around 0.6% for patients having cervical discograms. The most common serious complication is discitis, which has a reported incidence of between 1:400 and 1:30 procedures [43]. There is also evidence that trauma to the disc caused by needle entry may hasten existing disc disease or cause new disc disease [44, 45]. Significant controversy exists regarding the use of prophylactic broad-spectrum antibiotics during intradiscal procedures [46]. Injection of intradiscal steroids may result in the formation of epidural calcifications, particularly when triamcinolone is used [46, 47]. Discography procedures that involve thermal or mechanical therapeutic manipulation of the disc carry theoretically higher risks, such as thermal damage to adjacent structures. Inadvertent thermal damage to the vertebral end plate during intradisc procedures can potentially impair the passive diffusion of nutrition to the intervertebral disc.

Intradiscal electrothermal therapy (IDET) involves placing a thermal coil on the inner diameter of a torn annulus fibrosis. Radiofrequency (RF) energy modifies the collagen matrix, decreasing disc volume and ablating the small nociceptive fibers in the annulus fibrosis [48]. If the thermal coil is poorly positioned, it can transmit thermal energy to adjacent structures, such as the spinal nerves or the spinal canal. The use of moderate sedation and ensuring patient interaction can minimize the chances of such a complication going unrecognized. Flares of preexisting back pain are not uncommon following the procedure and can last several days to weeks. A rare, but catastrophic, complication of IDET therapy is damage to the nerve roots in the cauda equina, which can cause severe neuropathic pain in the lower extremities as well as potential bowel and bladder dysfunction. This is more likely when the thermal element on the posterior aspect of the disc is positioned in proximity to the spinal cord. The complication rate for IDET is approximately 0.8% [49]. Postprocedural disc herniation directly attributed to trauma from the thermal probe is rare, occurring with an incidence of 0.3% [49].

Biacuplasty uses water-cooled bipolar technology to deliver thermal energy while also protecting distal structures from thermal leakage [50, 51]. Sterile water is circulated through the thermal probes. Compared to IDET, biacuplasty uses a lower temperature (50 °C compared to 90 °C). The probes are positioned on opposing sides of the AF. Serious complications have not been reported following biacuplasty.

Nucleoplasty is an intradiscal radiofrequency intervention that reduces the volume of a herniated disc. It differs from biacuplasty and IDET in that the probe is inserted into the nucleus pulposus and not the annulus. The intention is to vaporize the NP matrix with thermal energy and subsequently remove those gases through the probe. The space generated then allows the disc to contract to its approximate original volume, thereby alleviating compression of adjacent neural structures. As the intended target is within the disc, it is rare for damage to occur to surrounding structures. The procedure typically removes about 1 mL of the nucleus pulposus. Following nucleoplasty, 76% of patients experience short-term tenderness at the needle site, 26% report mild numbness and tingling in the extremities, and 15% report increased intensity of preexisting back pain [52]. These symptoms largely resolve within 2 weeks. Among patients with residual complications, 15% experience persistent mild numbness and tingling, and 4% experience persistent back pain [53].

Percutaneous laser disc decompression has been demonstrated to be non-inferior but more cost-effective than a more invasive microdiscectomy [52]. Percutaneous endoscopic laser decompression is another directed-energy technology being refined as a surgical alternative to reduce the volume of herniated discs [54, 55].

The Disc Dekompressor is designed to physically reduce the volume of herniated discs without the use of directed energy [56]. It is placed posterolaterally into the nucleus pulposus under fluoroscopy. Similar to a nucleoplasty procedure, a negative vacuum in the center of the nucleus pulposus is created, which contracts the disc herniation and nerve root sequelae. Few complications have been reported. Clear evidence for its effectiveness is lacking [57].

Biacuplasty and IDET are contraindicated in the cervical and thoracic spine as there is not enough nucleus pulposus to accommodate the catheters. Patients with severe disc degeneration in which the disc has been reduced to 50% of its original height may also not be good candidates for the Disc Dekompressor or nucleoplasty because further disc volume reduction is inadvisable.

Other complications are usually related to instrumentation, such as breakage of the probes or catheters. Surgical removal of retained objects is warranted.

High heat exposure from IDET, biacuplasty, or nucleoplasty can damage nearby structures and cause osteonecrosis of the spine. This theoretically weakens the structural integrity of the spine and predisposes the patient to vertebral body fractures. IDET has the highest rate of these complications as it relies on proper positioning of a 5-cm-long active catheter tip.

Infectious complications following intradiscal procedures are of particular concern. The disc does not have the extensive blood supply needed to mount an effective immune response. Often these complications can be avoided with prophylactic antibiotics, treating topical infections prior to the procedure, and a strict sterile technique [58]. The most frequently identified causative bacteria in cases of discitis is *Staphylococcus aureus*. Prior to the widespread use of prophylactic antibiotics, vertebral osteonecrosis and epidural abscesses were more widely reported than discitis.

Intrathecal Drug Delivery Systems

The implantation of intrathecal drug delivery systems (IDDS), like all other neuraxial procedures, places the patient at risk for complications. This form of drug delivery provides continuous lower doses of medications administered directly into the cerebrospinal fluid (CSF) in order to mitigate many of the complications of systemic therapy. In general, the side effects of intrathecal opioids are similar to those of systemic opioids: allergy, nausea, pruritus, constipation, urinary retention, hypotension, and respiratory depression. Complications of IDDS can include iatrogenic errors, device-related infections, CSF leaks, failure to achieve adequate analgesia, granuloma formation, and device product performance events [59, 60]. IDDS has a 3.89% mortality rate within the first year following implantation, largely attributable to lack of vigilance with medications resulting in respiratory depression [59].

In the setting of IDDS, epidural hematomas are typically, but not always, associated with bleeding dyscrasias. If a spinal hematoma is suspected, immediate MRI and surgical evaluation are warranted, followed by surgical evacuation within 12 hours of the onset of symptoms. Bleeding can also occur within the reservoir pocket, possibly necessitating surgical drainage.

Infection is a frequent complication of IDDS therapy and usually occurs superficially at the pocket but can spread to deeper tissue [60–62]. If an IDDS becomes infected, constitutional symptoms suggestive of an infection generally occur within 10–14 days of implantation. Early oral antibiotics can minimize subsequent complications of infection. A reasonable therapeutic goal is to limit infectious spread into the subfascial layers via early identification and aggressive antibiotic therapy. Prompt evaluation with a contrast MRI is warranted followed by neurosurgery consultation. Explantation of the device is frequently warranted to prevent the fulminant development of meningitis or other life-threatening infections.

Needle entry below L3/L4 in adults is recommended to avoid the conus medullaris. Cauda equina syndrome has been a reported complication of IDDS placement. During the procedure, the patient is typically sedated but interactive with the physician in order to prevent unnoticed problems during needle placement. Postdural puncture headaches (PDPH) can occur from dural puncture during the needle placement. This is more likely with cutting needles and larger-gauge needles.

Catheter granulomas develop at the tip of the intrathecal catheter as an inflammatory, fibrotic, and noninfectious mass. The mass slowly develops and is more likely to occur in patients receiving high concentrations of morphine or hydromorphone. Granulomas can be investigated with a T1-weighted MRI with and without gadolinium, but routine surveillance imaging is not supported by the literature.

IDDS catheters are most likely to fracture at points of high stress, such as at the anchor point and at the junction to the reservoir [63]. If the catheter is not anchored correctly to the thoracolumbar fascia, it can migrate out of the intrathecal space, resulting in a CSF leak, headache, and ineffective analgesia. Migration into the neural foramen is also possible.

Vertebroplasty and Kyphoplasty

Percutaneous vertebral augmentation (PVA) is considered minimally invasive and thought to confer less overall risk than open surgery. Complications of vertebral augmentation procedures with either vertebroplasties or kyphoplasties are related to improper needle placement, infection, cement extravasation, and damage of adjacent structures. Patients should be screened for active infections, especially osteomyelitis or discitis. Optimal outcomes occur when vertebral body compression is limited, fractures are newer than 12 months, and T2 or STIR sequence MRI results confirm edematous bone marrow.

Bone cement is a relatively low-viscosity medium and carries the highest likelihood of extravasation when first injected, before it has reached its optimum thickness. Using cements with higher viscosity will slow their initial spread on injection. To enhance fluoroscopic visibility, the cement is frequently mixed with contrast material. Cement should only be spread under live fluoroscopy. Cement may extravasate from the intended vertebral body to spinal nerves and cause radicular symptoms or dysesthesia. Leakage into the spinal canal can cause devastating consequences such as paraplegia if not immediately addressed. If deposited in blood vessels, it can cause arterial or venous thromboses or pulmonary embolisms. Cement monomers that leak into capillaries may cause damage to the pulmonary vascular endothelium and increase pulmonary arterial pressure. Leakage incidence is estimated to be around 9% for kyphoplasties, compared with about 41% for vertebroplasties.

Pain relief is not correlated with the volume of cement injected. A meta-analysis of literature covering 1036 patients found that both vertebroplasty and kyphoplasty resulted in significant reduction in pain scores. It also found that vertebroplasty was more effective in reducing pain scores than kyphoplasty, but vertebroplasty also had a higher rate of cement leakage and new fracture [64].

Adjacent-level fractures are a potential complication of PVAs. A subsequent fracture rate of 12.4–21% is reported, with the majority being at levels adjacent to sites of prior PVA procedures [65]. Low body mass index and older age have also been identified as determinants of osteoporotic fracture complications.

Procedure-related complications for other interventions such as spinal cord stimulator, trigger point injection, and sympathetic block will be discussed in other chapters.

Summary

Primum non nocere remains the first rule of medical practice. All medical therapies for the treatment of chronic low back pain, including medications, surgery, and interventional procedures, have an anticipated risk-to-benefit ratio that must be carefully considered when recommending a specific treatment. Physicians must be aware of potential complications and how to properly address them. Compiling an exhaustive list of potential or reported complications from interventional spine procedures would prove an impossible task. However, patient care can be optimized through a thorough knowledge of complications and continued refinement of practices to avoid them.

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Regional Anesthesia in Patients with Spine Pain

32

Linda Hung and Jingping Wang

Key Points

- Regional anesthesia has many applications and is becoming increasingly popular for spine pain patients presenting for various surgical procedures.
- Regional anesthesia is a key tool in multimodal analgesia or spine pain patients, with applications preoperatively, intraoperatively, and postoperatively.
- While regional anesthesia is often used in the context of extremity-based surgeries, there is increasing evidence that it may be used as the primary anesthetic or supplemental analgesia for operations and procedures on the spine.
- Regional anesthesia for spine surgery and spine pain has traditionally involved the use of neuraxial techniques (spinal, epidural, and combined spinal-epidural anesthesia).
  - A variety of neuraxial techniques, medications, and block approaches have been described as safe and effective for spine pain patients (detailed in the text of this chapter).
  - These techniques can provide benefits over general anesthesia in many studies of spine surgery (improved postoperative pain control, hemodynamic stability, and postoperative recovery; reduced postoperative nausea and vomiting, operative blood loss, length of hospital stay, anesthesia/surgical time, and healthcare costs).
- More recently, reports of "paraneuraxial" anesthesia and other peripheral, non-neuraxial nerve blocks have been employed in patients with spine pain.
- With the increased use of ultrasound-guided regional anesthesia, neuraxial and peripheral blocks are becoming increasingly popular with expanding applications in the realm of spine surgery and spine pain.
- Further studies will continue to elucidate the optimal application, medications, dosing, and techniques for administering regional anesthesia for spine procedures.

Spine Pain Patients Presenting for Non-spine Surgery

Patients with spine pain may present for a variety of elective, urgent, or emergent, non-spine surgeries. Depending on the severity and chronicity of their spine pain, these patients may be on high doses of opioid and non-opioid analgesics and followed closely by outpatient chronic pain centers for non-pharmacologic and interventional therapies. Perioperative pain assessment and management may be challenging and require careful optimization. Ideally, in elective or even urgent scenarios, these patients should be seen preoperatively and followed during their hospital stay by an inpatient pain service. In addition, multidisciplinary input is crucial and should involve the patient's surgical and anesthesia teams, as well as nursing staff, physical therapists, occupational therapists, and case managers for discharge planning. Multimodal analgesia is also key, and perioperative pharmacologic therapy should focus on maximizing non-opioid adjuncts in addition to optimizing opioid therapy (Table 32.1).

For opioid-tolerant patients, the care team should anticipate that larger doses of opioids will be required perioperatively. When possible, existing chronic pain

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Table 32.1 Key points in perioperative management of spine pain and chronic pain patients [1–4]

1. Consider interdisciplinary management and support from a multimodal pain treatment team – including input from acute pain service, chronic pain service, physical therapy, occupational therapy, nursing, surgery, and case management
(a) Preoperative assessment of patient's current medications, risk factors, comorbidities, and devices (e.g., implanted medication pumps, spinal cord stimulators) is important. Also provide preoperative counseling, education, and reassurance regarding surgery, recovery, and analgesic planning
(b) Where appropriate, preoperative referral to pain specialists may be indicated
(c) Postoperative follow-up to adjust opioid and non-opioid medications and monitor devices is also crucial
2. Utilize multimodal analgesia. Continue preoperative non-opioid co-analgesics and add appropriate postoperative co-analgesics at the time of surgery (nonsteroidal anti-inflammatory drugs, antipyretics, neuropathic agents)
(a) Where appropriate, continue regular doses of anticonvulsants and benzodiazepines perioperatively to prevent withdrawal
3. Continue long-acting systemic opioids perioperatively to avoid opioid withdrawal (anticipate physical dependence in patients on long-term opioid therapy)
(a) For surgeries and patients in that enteral medications are to be avoided, convert long-acting oral opioids to equianalgesic parenteral form and administer parenterally
(b) Ensure patients take their regular short-acting opioid on the morning of surgery
(c) For mixed opioid agonist-antagonists (e.g., buprenorphine), consult pain service and anesthesiology for perioperative management, depending on the type of surgery
(d) Monitor closely for signs and symptoms of opioid withdrawal, adverse effects, oversedation, and respiratory depression
4. Consider intraoperative and/or postoperative ketamine infusion (opioid-sparing co-analgesic effect)
5. For certain surgeries, consider intraoperative and/or postoperative systemic local anesthetic infusions (opioid-sparing co-analgesic effect)
6. Consider regional techniques for applicable surgeries
7. Intra- and postoperatively, anticipate higher than usual opioid requirements (use equianalgesic doses appropriate to patient's degree of tolerance and provide adequate doses of opioid analgesics)
(a) Patient-controlled analgesia (PCA) at appropriate doses with or without a background opioid infusion (for opioid-tolerant patients) may be required initially following surgery. Doses should be titrated based on clinical effect
8. Consider opioid rotation if significant side effects or inadequate analgesia are encountered with perioperative dose escalation of existing opioids
9. Resume oral medication as soon as possible postoperatively to maintain steady baseline level of analgesic
10. Individualize pain management regime to specific patient rather than utilizing "conventional" or routine analgesic plans. Assess patient multiple times daily for pain control and adverse effects of pain medications. Make changes when necessary
11. Consider the impact of anxiety, mood, and fear on patient's perception of pain; consider perioperative counseling and non-pharmacologic pain management strategies
12. With postoperative recovery, anticipate gradually decreasing daily opioid requirement. Taper short-acting opioids as appropriate, back to preoperative baseline
13. Schedule close follow-up with pain physician to ensure adequate ongoing main management and opioid taper upon hospital discharge. Anticipate that chronic pain problems will not be solved in the immediate postoperative period; goals will be to help patient return to preoperative baseline and then provide ongoing chronic pain follow-up once recovered from surgery

medications should be continued in the perioperative setting. For patients who are unable to take enteral medications, efforts should be made to substitute pain medications with parenteral forms when possible, particularly for opioid-tolerant patients as abrupt cessation of both long- and short-acting opioids may lead to withdrawal. Perioperatively, the care team should also anticipate high self-reported pain scores in patients suffering from chronic pain, and treatment strategies should aim to improve perioperative function and focus on objective endpoints (ambulation, respiratory function) in conjunction with pain scores. The management of patient's and care teams' expectations is also crucial, as the primary goal of inpatient perioperative pain management is to enable the patient's recovery in the acute postsurgical setting, rather than to address or treat persistent pain concerns that were stable as an outpatient.

To this effect, regional anesthesia can be an extremely useful tool perioperatively, providing targeted analgesia to the specific surgical site in patients with chronic pain. Depending on the location of surgery, a variety of regional techniques can be used for both intraoperative anesthesia (either primary anesthetic or in conjunction with general anesthesia) and postoperative analgesia. Table 32.2 details examples of regional techniques that may be used for specific, non-spine surgeries in patients with chronic pain. The benefit of regional techniques can be prolonged for several days after surgery with the insertion of neuraxial catheters (epidural, intrathecal), truncal catheters (paravertebral, transversus abdominis plane, rectus sheath), or peripheral nerve catheters (brachial plexus catheters, lower extremity catheters). Such targeted techniques aim to block afferent pain signaling directly from the surgical site, providing optimal analgesia to reduce the potential need for high doses of systemic medications. Thus, regional anesthesia, when feasible and safe, represents an ideal method for perioperative analgesia in spine pain patients presenting for non-spine surgery.

Table 32.2 Applications of regional anesthesia to chronic pain patients presenting for various surgeries

Blocks may be performed by landmark or ultrasound-guided techniques or a combination of both
Upper extremity surgery: brachial plexus blocks (interscalene, supraclavicular, infraclavicular, axillary) and distal peripheral nerve blocks including ulnar, median, radial, musculocutaneous, and other nerve blocks of the arm, forearm, and hand
Lower extremity surgery: lumbar plexus blocks, sciatic nerve blocks (high sciatic, subgluteal, popliteal approaches), femoral nerve blocks, adductor canal blocks, distal peripheral nerve, and ankle blocks
Truncal surgery (thoracotomy, chest wall surgery, breast surgery, abdominal, and pelvic surgery): paravertebral, intercostal, pectoralis and serraturs plane blocks, quadratus lumborum, transversus abdominis plane, rectus sheath, and other truncal blocks
Neuraxial techniques: applicable to both truncal surgery (e.g., epidural) and abdominal, pelvic, and lower extremity surgery (e.g., epidural, spinal, combined spinal-epidural)

Table 32.3 General contraindications to regional anesthesia in the perioperative setting

Patient refusal and/or inability to ensure patient cooperation during procedure
Anticoagulation and/or coagulopathy (recommend consultation with American Society of Regional Anesthesia or other institutional guidelines on the use of regional anesthesia in the context of anticoagulation)
Infection at site of injection
Systemic infection and bacteremia often considered relative contraindication
Existing neurologic deficits or neurologic/neuromuscular disease in the distribution of proposed block (may include motor, sensory, or mixed deficits)
Anatomic abnormalities precluding safe use of ultrasound-guided or landmark-based techniques
Allergy to local anesthesia
Unavailable equipment specifically required for regional block
Inability to monitor patient vital signs and/or provide appropriate resuscitation from local anesthetic toxicity and other potential complications
Specific to neuraxial techniques and paravertebral blocks:
Increased intracranial pressure
Hemodynamic instability, hypovolemia, and/or fixed cardiac output lesions (potential to cause sympathectomy-related hypotension)

The appropriate anesthesia team should assess, prepare, and consent the patient for a perioperative regional technique; however, the pain consultant should be aware of general contraindications to regional anesthesia in this setting (Table 32.3).

Regional Anesthesia for Spine Surgery

An ideal anesthetic for spine surgery should provide relatively rapid onset, easily reversible effects, optimal operating conditions, hemodynamic stability without the need for blood transfusions or large doses of vasopressors, decreased recovery time, low postoperative pain scores, and low incidences of complications including nausea and vomiting and low additional anesthetic requirements. These goals can be accomplished by a variety of anesthetic techniques including general anesthesia, regional anesthesia, and even local anesthesia depending on the type of surgical intervention.

As reported by Mergeay et al. [5], the most common techniques to provide anesthesia for patients undergoing thoracic and lumbar spine surgery include general anesthesia (GA), but benefits have increasingly been reported for regional anesthesia in spine surgery. There were 24 publications that detail the intraoperative use of regional anesthesia for spine surgery, with only 5 studies being published before 2002 and the majority of those published more recently. Interestingly, many of these publications were found in the surgical literature, with only seven reports documented in anesthesia journals. As detailed in this review [5], spinal, epidural, or caudal anesthesia can be used as a primary surgical anesthetic or combined with GA for postoperative analgesia. Different techniques and medication combinations are described for these anesthetics as well. Regional anesthesia has been described for a variety of spine surgeries, including discectomy, disc surgery, decompression/laminectomy, hardware removal, and even fusion surgeries. The literature on regional anesthesia for spine surgery encompasses a variety of study designs ranging from retrospective to prospective data, cohort studies, case-control studies, and randomized controlled trials. Various patient populations and outcomes have also been studied.

Regional anesthesia for spine surgery was initially reported in 1950s and 1960s, as referenced in certain texts [6]. It is unclear exactly how widely used this technique was at the time when it was first described. Subsequent reports of the early use of spinal anesthesia for lumbar spinal disc surgery were published by Riegel et al. [7] documenting 1871 consecutive spinal anesthetics for lumbar disc surgery with no complications due to anesthesia and high patient satisfaction. Authors reported that more than 40% of these cases were done using spinal anesthesia by this specific team.

Detailed initial reports of epidural analgesia [8] were published in 1988, documenting epidural anesthesia for lumbar spine surgery. Authors performed a retrospective review of 80 patients undergoing elective lumbar spine surgery: 40 patients received a single-shot epidural with bupivacaine, matched with 40 patients receiving GA. Epidural patients were found to have lower opioid requirements, lower postoperative rates of urinary retention, and lower operative blood loss. Epidural anesthesia also allowed for intraoperative testing of lower extremity motor function. The majority of patients (38/40) who received epidural anesthesia were satisfied with the technique. Authors concluded that for patients

undergoing decompressive lumbar spine surgery, epidural anesthesia was effective and well tolerated with advantages compared to GA.

Following these early reports on regional anesthesia for spine surgery, numerous other studies have demonstrated the feasibility, efficacy, and safety of these techniques in the clinical setting. In addition, authors have explored various technical aspects of regional anesthesia for spinal surgery, including equipment, medications, patient positioning, and other specifics of performing spinals and other regional blocks. In many studies, authors have also demonstrated clinical advantages of regional anesthesia compared to general anesthesia in the setting of spine surgery. The subsequent portions of this chapter will detail the evidence for use of spinal and epidural anesthesia, benefits and drawbacks of performing a regional technique for spine surgery, technical aspects of performing these blocks, and unique reports on the use of non-neuraxial blocks and even local anesthesia for spine surgical procedures.

Evidence Regarding Neuraxial Anesthesia for Spine Surgery

In addition to separate studies on spinal and epidural anesthesia in the setting of lumbar spine surgery, review articles have examined the topic of neuraxial anesthesia for spine surgery. Specifically, Rojas et al. [9] reviewed the safety and efficacy of regional anesthesia vs. general anesthesia for lumbar spine surgery. This review identified 11 studies comparing patients who underwent general anesthesia compared to regional anesthesia for lumbar spine surgery. Four of the discussed studies were randomized controlled trials (RCTs), three were case-control trials, two were prospective cohorts, and two were retrospective analyses. Spinal anesthesia was utilized in 8 of 11 studies, and epidural anesthesia was used in 3 of 11 studies.

Regarding results, this review identified that nine studies reported on postoperative analgesic use and pain scores. Seven of the nine studies (including all four RCTs) demonstrated lower postoperative analgesic requirements and/or decreased pain scores in regional anesthesia. Seven studies reported on blood loss, and four of the seven studies showed no difference in blood loss, while three of the seven studies showed less blood loss in regional anesthesia.

All studies had recorded hemodynamic variables: seven out of seven studies recording heart rate (HR) and mean arterial pressure (MAP) showed favorable hemodynamic outcomes for regional anesthesia compared to general anesthesia, including all four RCTs (lower HR and MAP or smaller change in these outcomes for patients undergoing regional anesthesia). Generally, in patients receiving regional anesthesia for spine surgery, there was less hypertension and tachycardia compared to patients receiving general anesthesia.

Nine studies in this review reported on surgical time data. Three out of nine demonstrated decreased surgical times for regional anesthesia compared to general anesthesia, while six studies showed no difference between the two anesthetic modalities for surgical time. Seven studies reported on time in the postanesthesia care unit (PACU): two of seven studies reported longer PACU times in regional anesthesia compared to general anesthesia, while four out of seven studies reported no difference; one study showed longer PACU stays in general anesthesia. Regarding length of stay, two studies showed shorter duration of hospitalization for patients receiving regional anesthesia for lumbar spine surgery compared to general anesthesia; four studies showed no difference in hospital stay.

Regarding complications, five studies reported postoperative urinary retention as a variable. Three out of five studies noted more urinary retention in patients undergoing general anesthesia, while two out of five studies showed no difference.

Eight studies reported on postoperative nausea and vomiting (PONV): five out of eight studies demonstrated higher PONV or higher antiemetic use in general anesthesia compared to regional anesthesia (three out of four RCTs). Three out of eight studies showed no difference in PONV or antiemetic use.

Overall, this review [9] suggested that both regional anesthesia and general anesthesia are safe and effective for lumbar spine surgery. Results demonstrated that regional anesthesia may have a number of advantages and be superior to general anesthesia in some regards, particularly in patients undergoing simple lumbar decompression or for patients with high risk of general anesthesia complications.

Evidence for Spinal Anesthesia in Spine Surgery

Numerous reports have been published on the use of spinal anesthesia for spine surgery. Jellish et al. [10, 11] published an early prospective randomized controlled trial comparing the short- and intermediate-term perioperative outcomes after spinal or GA for lumbar disc and laminectomy surgery. In this study, 122 patients were randomized to standard GA or spinal anesthesia with intravenous (IV) propofol sedation. Results demonstrated that total anesthesia and surgical times were longer in the GA group (131 minutes vs. 106.6 minutes anesthetic time; 81.5 minutes vs. 67.1 minutes surgical time). The authors showed that intraoperative hemodynamics were similar between groups, but increased blood pressure was more common with GA. In addition, they noted significantly

less blood loss during spinal anesthesia compared to GA (133 mL vs. 221 mL). In terms of postoperative recovery, heart rate (HR) and mean arterial pressure (MAP) were higher in the GA group, as were pain scores (5.8 vs. 2.2) and analgesic and analgesic consumption. Furthermore, severe nausea was more common with GA, both in the postanesthesia care unit (PACU) and within 24 hours after surgery. Interestingly, there was no difference in urinary retention, length of hospital stay, and analgesic requirements after discharge from PACU between the spinal and GA trial groups.

A large retrospective chart review on spinal anesthesia for spine surgery was published by Tetzlaff et al. [12]. This study included patients presenting for elective lumbar spine surgeries, performed by a single surgeon. 803 patients were analyzed, of whom 611 received spinal anesthesia, compared to the remainder who received GA. Patients in both groups were largely similar in demographics, with the exception that patients in the spinal group had significantly higher body weight compared with those in the GA group. Retrospective data noted higher incidences of nausea and deep vein thrombosis (DVT) in patients receiving GA. In those receiving spinal anesthesia, mild hypotension and decreased HR were the most common hemodynamic changes, while hypertension and increased were more common with GA. Regarding medication use in patients receiving spinals, isobaric bupivacaine was associated with the lowest incidence of needing supplemental local anesthesia intraoperatively, compared to hyperbaric bupivacaine or hyperbaric tetracaine (see details later in this chapter for discussion of pharmacology for neuraxial technique). Authors in this retrospective study concluded that spinal anesthesia is an effective alternative to GA for lumbar surgery and is associated with a lower rate of minor complications [13].

Dagher et al. [14] performed a randomized controlled trial including 69 patients presenting for lumbar microdiscectomy, randomizing subjects to either spinal or general anesthesia. They reported on the quality of analgesia and recovery from surgery after either technique. Their data noted lower pain scores in spinal patients at 4 hours and 8 hours postoperatively, and lower total analgesic consumption in the first 24 hours after surgery. Postoperative recovery time including time to drinking, eating, and walking was faster after spinal anesthesia compared to GA. Postoperative nausea and vomiting (PONV) was higher in those receiving GA. Urinary retention was again found to be comparable between groups. Overall, authors concluded that patient and surgeon satisfaction were better in the spinal group.

Subsequent to these earlier studies, McClain et al. [15] performed a case-controlled study of 200 patients undergoing lumbar surgery, treated with spinal or general anesthesia. A total of 400 patients were matched for anesthetic class, preoperative diagnosis, surgical procedure, and perioperative protocols. All patients were treated according to protocol and recovered in the same PACU. For patients receiving spinal anesthesia for lumbar spine surgery, overall complication rates and time to discharge were lower. For patients receiving GA, total anesthetic and operative times were longer, and perioperative HR and MAP were elevated compared to patients receiving spinal. PONV and antiemetic use and urinary retention were increased among GA patients as well. Spinal patients interestingly had fewer headaches compared with GA patients, but this was not statistically significant. Authors concluded that for patients undergoing decompressive lumbar spine surgery, spinal was at least comparable to GA with respect to complications, but had major advantages in the perioperative setting. The same investigators published additional data [16], analyzing outcomes in 400 patients presenting for lumbar decompression surgery for lumbar stenosis or disc herniation with either spinal anesthesia or GA. Patients were matched for anesthesia-related class, preoperative diagnosis, surgical procedure (including procedure complexity), and perioperative treatment and recovery protocols (including analgesia). Again, anesthesia and operative times were longer for GA, and GA was associated with more nausea and antiemetic as well as analgesic requirement during recovery. Complication rates and urinary retention were lower in spinal anesthesia. No neurologic injuries were noted in either group. Interestingly, the incidence of spinal headache was lower in patients receiving spinal anesthesia (1.5% vs. 3%). Again, authors concluded spinal anesthesia was safe and effective, with many advantages compared to GA for lumbar laminectomy.

Regarding suitable patient selection for spinal anesthesia in spine surgery, Goddard et al. [6] reported a retrospective cohort of 125 patients who underwent lumbar spine surgery with spinal anesthesia. In this cohort, the median age of patients was 44 (range 20–72), median weight 82 kg, and median BMI 26.6. The study included eight patients who were ASA 3–4. The distribution of cases was such that 86 cases were microdiscectomies, 34 cases were decompressions and multilevel fusions, 4 cases were nerve root decompressions, and 1 case was hardware removal. The median OR time was 70 minutes. In this retrospective series, no spinal anesthetic failures were noted, and there were no episodes of airway compromise, desaturation, hemodynamic instability, or post-dural puncture headache. Patients reported excellent postoperative pain relief, with only 44% requiring oral analgesia.

Following this, McLain and Tetzlaff [17] compared perioperative and postoperative outcomes in 76 patients undergoing lumbar microdiscectomy for herniated nucleus pulposus with either spinal (n = 43) or general anesthesia (n = 33). The patients were drawn from a case-controlled study group, with an age range of 18–40 years and ASA class 1. For patients receiving general anesthesia, surgical and anesthesia times were longer. Urinary retention was also

more common for GA. In postoperative recovery, PACU admission times were shorter for patients receiving GA, but patients receiving spinal needed less pain medication and had less nausea/emesis. Patients in the spinal group also had a trend toward lower complication rates and a shorter hospital stay. Patients and surgeons reported high levels of satisfaction with spinal anesthesia. Authors concluded that in young, medically fit pts., spinal anesthesia had specific advantages over GA.

More recently in the literature, several RCTs have been published on the topic of spinal anesthesia for spine surgery. Sadrolsadat et al. [18] performed a prospective RCT comparing spinal and general anesthesia for elective lumbar disc surgery (laminectomy for herniated discs) in 100 patients. Investigators assessed a number of perioperative factors, including HR, MAP, blood loss, surgeon satisfaction, severity of pain, nausea/vomiting, and length of stay. Mean blood loss was not significantly different in groups (trend lower in GA), and surgeon satisfaction was higher in patients receiving GA. No major complications were noted with either spinal or GA; however, hypotension was more frequent in patients undergoing GA, while PONV was more frequent in patients who received spinal. In this RCT, authors concluded that contrary to previous studies, there was no advantage of spinal anesthesia over GA. However, in this study, authors used larger doses of bupivacaine than other studies (4 mL 0.5% isobaric bupivacaine – see later discussion for details of drug dosing).

Attari et al. [19] also performed an RCT of spinal anesthesia compared to GA for elective lumbar spine disc surgery. Their study included 72 patients randomized to spinal or general anesthesia and found that the spinal group had less blood loss, less hemodynamic changes, more surgeon satisfaction with operating conditions, lower postoperative pain scores, and less analgesic use compared to GA. Contrary to the findings of Sandrolsadat et al. [18], these authors found that spinal anesthesia was advantageous and provided better intra- and postoperative analgesia compared to GA.

More recent retrospective studies have confirmed RCT findings that spinal anesthesia is suitable for elective spine surgery. Singeisen et al. [20] performed a retrospective analysis of 473 cases of prone spine surgery (decompression, discectomy, transpedicular instrumentation). A substantial number (368 cases) of these cases were done with spinal anesthesia, while 105 cases were done with general anesthesia. Seven cases of spinal failure were noted, requiring conversion to GA. Overall, baseline characteristics between patients receiving spinal and GA were similar except that patients receiving spinal anesthesia were older (median 61 vs. 56 years). Authors found that spinal anesthesia patients required less time for induction, preoperative preparation, and closure compared to GA. Total anesthesia time was lower with spinal (by 19 minutes).

Erbas et al. [21] also reported retrospective data on posterior lumbar stabilization surgery under spinal anesthesia. Their study focused on high-risk patients with degenerative spondylolisthesis, spinal stenosis, and lumbar compression fracture. This retrospective review included 497 patients over 8 years who had spinal stabilization under spinal anesthesia. No instances of anesthetic failure occurred, and stable hemodynamics reported. The median patient age was 51 years, with an average anesthesia duration of 130 minutes and an average operative time of 85 minutes. Postoperatively, 7.2% of patients reported nausea, and 3.6% reported emesis, most resolving with one dose of antiemetic. No spinal headaches were noted. The incidence of minor urinary retention was 7.2%, all of which recovered with catheterization within 24 hours. No respiratory complications or deaths occurred, and authors concluded that spinal anesthesia is safe and effective for lumbar spine stabilization, particularly in high-risk patients.

Dagistan et al. [22] confirmed the benefits of spinal anesthesia in a retrospective study of 180 patients who underwent lumbar microdiscectomy. Their study found that total anesthetic time was longer in patients requiring general anesthesia and that less bleeding occurred at the surgical site in patients receiving spinal anesthesia. Intraoperative blood pressure was also generally lower in patients receiving spinal anesthesia, while tachycardia was higher in patients receiving general anesthesia, as was analgesic requirement in PACU. At PACU admission, HR, BP, and analgesic requirement were higher in patients receiving general anesthesia. Nausea and emesis were also more frequent in patients receiving general anesthesia. Patients receiving spinal anesthesia had an increased incidence of urinary retention. Overall, pulmonary complications requiring treatment were not significantly different in patients receiving general or spinal anesthesia, but there was a trend to more pulmonary complications in patients receiving GA. Authors concluded that spinal anesthesia was safe and effective for lumbar spine surgery, and there are a number of benefits potentially compared to GA.

Finally, most recently, Lessing et al. [23] reported on a single-institution experience with spinal anesthesia for lumbar spine surgery specifically in elderly patients. In this study, 56 patients 70 years or older underwent a variety of lumbar spine surgeries (27 decompression, 29 decompression and fusion). The mean operative time was 101 minutes, mean operative blood loss was 187 mL, and mean maximal pain score (visual analogue scale) was 6.2/10. Nausea was noted in 21% of patients, and the mean length of hospital stay was 2.4 days. There were no cases of mortality, stroke, permanent loss of function, or pulmonary embolism. In addition, there were no cases of failed spinal technique requiring conversion to GA, and all patients ambulated on the day of surgery or next morning. The oldest patient in this study was

84 years of age, and the longest surgery was 3.5 hours. Authors demonstrated in this case that lumbar spine surgery with spinal anesthesia is a safe and viable option for elderly patients (70 years or greater) undergoing spinal surgery.

In summary, currently, a considerable body of evidence exists to support the use of spinal anesthesia for lumbar spine surgery. The literature to date is heterogenous and includes RCTs, retrospective studies, and case-controlled cohort studies. Much of the literature seems to suggest that spinal anesthesia is at least a safe alternative to general anesthesia in the setting of lumbar spine surgery. In addition, some studies show that spinal anesthesia may have distinct advantages including improved postoperative pain control, less postoperative nausea and emesis, improved hemodynamic stability, less intraoperative blood loss, high patient and surgeon satisfaction, low complication rates, potentially earlier mobilization, faster postoperative recovery, and even reduced thromboembolic complications.

Evidence for Epidural Anesthesia in Spine Surgery

Similar to the existing literature on spinal anesthesia for spine surgery, a number of reports have been published on the use of epidural anesthesia for spine surgery. Among earlier reports of epidural anesthesia for spine surgery, Demirel et al. [24] published a prospective randomized controlled trial comparing perioperative outcomes in lumbar spine surgery with either epidural or general anesthesia. Sixty patients presenting for elective partial hemilaminectomy and discectomy were randomized to receive either epidural or general anesthesia. Authors found that the time to start of surgery was longer in the epidural group (36.7 vs. 25.4 minutes), but total anesthesia time did not differ. Surgical time overall was longer in the general anesthesia (GA) group (118.8 vs. 139.6 minutes). The documented heart rates (HR) and mean arterial blood pressures (MAP) of epidural patients at 15, 20, and 25 minutes after local anesthetic injection were generally lower. However, the frequency of bradycardia, tachycardia, and hypotension during anesthesia did not differ. Hypertension was more frequent in the GA group, while blood loss was less in epidural group (180 mL vs. 289 mL). In recovery, HR and MAP were both higher in the GA group. Of note, peak pain scores and nausea in the postanesthesia care unit, as well as 24 hours postoperatively, were higher in those receiving general anesthesia. There was no difference between groups in length of stay. Authors concluded that epidural anesthesia is a safe and effective alternative to general anesthesia for certain lumbar spine surgeries and that there were significant advantages including hemodynamic stability, decreased blood loss, and improved postoperative analgesia and reduced postoperative nausea.

Following this trial, Yoshimoto et al. [25] published another prospective, randomized, single-blinded study comparing epidural morphine analgesia to systemic opioid analgesia in patients receiving general anesthesia for posterior lumbar spine fusion. Twenty patients were randomized to receive preoperative epidural morphine, along with general anesthesia (total intravenous anesthesia with propofol infusion), while another 20 patients were randomized to receive volatile anesthesia with sevoflurane and intermittent intravenous fentanyl without a regional block. Authors noted that the average MAP during surgery was lower and hemodynamics were more stable in the epidural group. Blood loss in surgery was also less in the epidural group, as was the requirement for postoperative analgesics. Interestingly, visual analogue scale pain scores were lower in the systemic opioid group on the first, second, and third days after surgery. Authors also noted that it was difficult to evaluate the neurological status in five general anesthesia patients due to incomplete emergence. No patients in the epidural group had difficulties with neurological assessment.

Papadopoulos et al. [26] performed a prospective observational study of 43 patients scheduled for primary lumbar microdiscectomy. Seventeen of the 43 patients agreed to be randomized to general anesthesia vs. epidural anesthesia for lumbar spine surgery. The remaining 26 patients selected their type of anesthesia as per preference. The mean age of patients was 38 years, and by demographic comparison, the patients undergoing epidural anesthesia were "marginally order" than those receiving general anesthesia. Epidural and general anesthesia groups had no difference in surgical time, pain scores, hospital stay, or likelihood of ambulating out of bed on the day of surgery. No major complications were noted in either group. Epidural anesthesia patients had much less nausea and emesis perioperatively.

Subsequently, Yoshikawa et al. [27] performed a study examining the feasibility of epidural anesthesia for percutaneous endoscopic lumbar discectomy. They performed a retrospective comparison of three groups (28 cases with epidural, 19 with local anesthesia, 28 with general anesthesia). Patients were matched in age, surgical site, and duration of surgery. In the epidural group, no patient required a change of anesthetic technique (conversion to general anesthesia) or analgesics during surgery. The epidural group received a small amount of local anesthetic, but spent longer in the operating room compared to those receiving local anesthesia only. Epidural and general anesthesia groups had several cases staying longer in hospital (wide statistical dispersion on length of stay). No differences were noted in the dose of local anesthesia, duration of total procedure, or time to discharge between those receiving epidural versus general anesthesia. This study, nonrandomized and retrospective, seemed to demonstrate that when feasible, local anesthesia is a reasonable choice for percutaneous endoscopic lumbar discectomy. However, when

comparing epidural anesthesia to general anesthesia, there are largely no differences in complications. Epidural analgesia is a feasible and safe alternative to other modalities of anesthesia for percutaneous lumbar spine surgery.

More recently, Khajavi et al. [28] performed a randomized controlled trial involving 80 patients undergoing one- or two-level laminectomy and/or discectomy. Patients were randomized to receive general anesthesia only or combined epidural and general anesthesia. Mean arterial blood pressure (MAP), heart rate, blood loss, and anesthetic medication doses were lower in those receiving combined epidural and general anesthesia, compared to those receiving general anesthesia alone. Postoperative pain scores and total analgesic requirements were also lower in the combined epidural and general anesthesia group. In addition, fewer complications were noted in those receiving combined epidural and general anesthesia. Authors concluded that combined epidural and general anesthesia had major advantages to patients receiving general anesthesia alone for lumbar spine surgery.

Akakin et al. [29] reported on a cohort of 27 patients presenting for single-level simple microdiscectomy. All patients had epidural anesthesia with catheter placement for their surgery. The mean duration of surgery was 45.5 minutes. The mean pain score (visual analogue scale) was 0.78 immediately postoperatively, 0.52 at 4 hours, and 0.35 at postoperatively 24 hours. Three patients had nausea, one patient had emesis, and all patients were satisfied with epidural anesthesia for their surgery. Patients in this cohort all stated they would consider this anesthesia technique again for future procedures. Authors concluded that epidural anesthesia was safe and effective for lumbar microdiscectomy.

Finally, Albayrak et al. [30] retrospectively reviewed 700 cases of lumbar disc surgery with epidural anesthesia, specifically focusing on surgical outcomes in patients receiving this anesthetic technique. This review included 55% male patients and 45% female patients. Forty-two of the 700 cases involved recurrence of disc herniation, and 11 of these required reoperation for herniation. In total, 11 of the 700 cases had dural injury repaired intraoperatively by primary suture and tissue sealant. Six of the 700 cases had infection of incision site treated with antibiotics, and 22 patients out of 700 received required conversion of epidural anesthesia to general anesthesia. Microdiscectomies were done in 578 cases, and open surgery was done in 122 cases. Authors concluded that from a surgical perspective, epidural analgesia was feasible and more advantageous for some patients with less risks than some elements of general anesthesia.

In summary, many of the findings in favor of spinal anesthesia for lumbar spine surgery have, to a lesser extent, also been found in studies relating to epidural anesthesia. Generally, the literature, though less robust in epidural anesthesia, demonstrates that this technique is safe and effective either in combination with general anesthesia or alone for lumbar spine surgery. Again, advantages has been approved such as improved postoperative analgesia, less postoperative nausea and emesis, improved hemodynamic stability, good patient satisfaction, and even good surgical outcomes and decreased risk for complications.

Benefits of Neuraxial Anesthesia for Spine Surgery

Analgesia and Opioid Requirements

Numerous benefits of neuraxial anesthesia have been noted for patients undergoing spine surgery. One of the greatest advantages of this technique is the potential benefit of improved pain control postoperatively. Much of the literature has demonstrated significantly better postoperative analgesia in patients receiving neuraxial blockade, especially in patients who have existing chronic pain prior to spine surgery. Some data also suggests that sensory block often lasts longer than motor block with neuraxial and regional anesthetic techniques, providing more prolonged analgesia without limiting the opportunity for neurologic exam following surgery. Some authors suggest that decreased pain scores with the use of regional anesthesia for spine surgery may be due to regional techniques selectively inhibiting afferent nociceptive sensitization pathways [9]. There is a potentially significant effect of "preemptive analgesia" when regional techniques are initiated before surgery. If regional and/or neuraxial anesthesia is employed after incision (i.e., during a case with combined general and neuraxial anesthesia), or if local anesthesia is injected immediately after nerve root exposure, some authors postulate that the effect of preemptive analgesia and inhibition of afferent nociceptive sensitization may not be as significant. Nonetheless, single-shot neuraxial anesthesia can decrease intraoperative opioid requirements, even if combined with general anesthesia for spine surgery. This also helps lower pain scores postoperatively and decrease analgesic requirements.

Catheter-based techniques such as epidural placement can supplement intraoperative anesthesia and be used for postoperative pain control, with the catheter left in situ for a longer period of time. Epidural catheters may also be placed intraoperatively by the surgical team and used for postoperative analgesia. Catheters allow flexibility in planning intra- and postoperative analgesia, as they may be used to re-dose the regional anesthetic during surgery, removed after final injection to prolong the duration of analgesia at the end of surgery, or left in place for several days after [5].

Postoperative Nausea and Vomiting

In addition to improved analgesia, regional anesthesia for spine procedures reduces opioid-related side effects such as postoperative nausea and vomiting (PONV), as well as antiemetic use. Most studies have shown significantly lower rates of PONV in patients receiving regional anesthesia for spine surgery. Apart from the opioid-sparing effects of neuraxial anesthesia, authors note that general anesthesia with volatile agents can cause significant nausea and inhibit gastric emptying. Nitrous oxide in combination with volatile agents further predisposes to PONV. These effects are absent when spinal or epidural anesthesia is used for spine surgery. Regional techniques may be supplemented with intravenous propofol sedation (as shown in many studies), and propofol has additional potential antiemetic properties. Furthermore, some studies suggest that regional anesthesia is associated with improved gastric emptying further decreasing PONV [5].

Operating Conditions and Operative Blood Loss

Other benefits of regional anesthesia for spine surgery include the avoidance of physiologic consequences of general anesthesia in the prone position. Regional anesthesia permits spontaneous ventilation in the prone position during spine surgery, which leads to less distension of epidural veins and produces an excellent surgical field with good operating conditions. This may explain the significantly reduced intraoperative blood loss often seen with regional anesthesia for spine surgery, compared to general anesthesia (and positive pressure ventilation). Operating in lateral or sitting position can also reduce blood in the surgical field (orthostatic drainage); however, orthostatic pressure on veins and CSF in the sitting position can enhance the risk of bleeding and dural tear in non-prone positions [5].

Hemodynamic Stability

Regarding other aspects of hemodynamics, many studies allude to increased hemodynamic stability in patients receiving neuraxial anesthesia for spine surgery. Three of four RCTs in a recent review [9] reported favorable hemodynamics and less intraoperative blood loss with the use of neuraxial anesthesia. In addition, most studies comparing general and regional anesthesia for spine surgery demonstrate less perioperative hypertension, tachycardia, and blood loss in patients receiving regional techniques. In these cases, lower blood loss may be related not only to spontaneous ventilation (lower intrathoracic pressure, less distension of epidural veins) and better operating conditions but also to the sympathetic block and fewer episodes of hypertension causing bleeding with regional anesthesia. However, due to limited blood loss in general for many spine surgeries, statistical significance may not always in existing studies of this effect of regional anesthesia [5].

Despite common mild hypotension, patients were hemodynamically more stable with most regional techniques (lower heart rate, blood pressure) than general anesthesia. This mild hypotension from sympathetic blockade helps with maintaining a clean operative field, decreasing blood loss and shortening operative time. Many authors suggest that improved hemodynamic stability with neuraxial techniques may be due to inhibition of the release of stress hormones intraoperatively [9], leading to less increase and fluctuation in mean arterial pressure and heart rate. In some cases, regional anesthesia resulted in mild hypotension, which was readily responsive to vasopressor support intraoperatively. Some studies have shown that hypotension is related to position during surgery, with knee-chest position resulting in greater hypotension as blood pools in dependent extremities [5].

Given the hemodynamic benefits of regional anesthesia, some authors have studied these techniques specifically in elderly patients, with the aim to avoid general anesthesia in this group [6, 23]. In elderly patients with cardiovascular disease, lumbar spine surgery, usually for pain control, is based on extensive risk-benefit discussions. With the increased hemodynamic stability seen when using regional techniques, authors have shown benefits for elderly patients undergoing spine surgery using this mode of anesthesia. Neuraxial anesthesia may extend patient selection for lumbar spine procedures in this setting.

Postoperative Headache

Other benefits of neuraxial anesthesia for spine surgery include a surprisingly low incidence of dural-leak-related headache. Despite concerns regarding post-dural puncture headache (PDPH) related to spinal anesthesia, the incidence of this complication is very low when patients receive spinal anesthesia for spine surgery. In fact, some studies find spinal anesthesia results in a lower incidence of dural-leak headache compared to general anesthesia for spine surgery. The reason for this counterintuitive finding is thought to be related to better operating conditions seen with spinal and neuraxial anesthesia, leading to a decreased risk of surgical dural tear during the operation. Moreover, some authors suggest that surgical bleeding in area of dural puncture functions as "mini blood patch" [5] to prevent any PDPH related to neuraxial techniques. Nonetheless, some studies report significantly lower rates of headache following spinal anesthesia for spine surgery, compared to general anesthesia [5].

Positioning

There are many positioning-related advantages of spine surgery under regional anesthesia. Specifically, spine surgery under regional anesthesia does not require intubation or airway manipulation. As such, many complications associated with airway manipulation and prone positioning may be avoided (airway edema, endotracheal tube malpositioning/dislodgement, and anesthesia circuit malfunction). Positioning injuries while prone can also be minimized, as patients under regional anesthesia may self-adjust and self-position onto the operating table and then continue to make small adjustments in position when lightly sedated during the case. This reduces the incidence of serious injuries that can happen under general anesthesia related to head malpositioning, cervical spine strain, pressure injury to the face and eyes with attendant risk for vision loss, and upper extremity and brachial plexus injury.

Urinary Retention

Although urinary retention is commonly thought to be a complication of neuraxial anesthesia with local anesthetic or opioid, many studies find that the incidence of urinary retention after spine surgery is similar among patients receiving general anesthesia and spinal anesthesia (without intrathecal opioids). In fact, some studies find that urinary retention is even more common after general anesthesia.

Thromboembolic Complications

Many studies have demonstrated a lower risk of thromboembolic complications in patients receiving regional anesthesia for a variety of orthopedic procedures. These results have also been demonstrated in studies involving spine surgery. In patients receiving spinal or neuraxial anesthesia for back surgery, faster postoperative mobilization occurs compared to general anesthesia. This increased mobility, combined with modulation of the hypercoagulable state, may be responsible for reduced rates of thromboembolism noted with regional anesthesia and spine surgery [5]. Detailed studies suggest that neuraxial techniques with local anesthesia enhance fibrinolytic activity, reduce antithrombin III activity to normal levels, and attenuate increases in post-op platelet activity [5], serving to modulate the surgical stress response and hypercoagulable state after major operations.

Surgical Stress Response

In addition to many of the advantages found for neuraxial anesthesia in spine surgery, several authors have studied the beneficial effect of regional anesthesia on the surgical stress response during these operations.

Ezhevskaya et al. [31] performed a prospective RCT comparing epidural analgesia with systemic opioids postoperatively. They studied the effect of epidural analgesia on pain management and stress response in patients undergoing major spine surgery. Eighty-five patients were randomized to two groups: one group received an epidural with general anesthesia (GA) during surgery and epidural analgesia postoperatively, while the other group received GA only, with systemic opioids for analgesia after surgery. Pain, nausea, mobility, and satisfaction were measured along with levels of stress hormones (cortisol, glucose, IL-1B, IL6, IL10) during and after surgery. Patients in the epidural group had less pain, less nausea, earlier mobility, and higher satisfaction with their surgical experience. Epidural patients also had less intraoperative and postoperative blood loss, lower levels of glucose, and stress/pro-inflammatory hormones (cortisol, IL-1B, IL6, IL10) postoperatively. Authors concluded that epidural analgesia, combined with GA, produced better postoperative pain control, less bleeding, and a lower surgical stress response as measured by inflammatory hormones.

The same group subsequently published larger study on the impact of epidural anesthesia on the surgical stress response in spine surgery [32]. This study included 350 patients age 15–65 presenting for lumbar spine surgery. Patients were randomized again into two groups: (1) GA + continuous epidural analgesia intra- and postoperatively and (2) GA alone + systemic opioids after surgery. In the epidural group, patients were found to have significantly less pain, nausea, earlier mobility, and higher satisfaction than patients receiving only GA. Again, patients receiving epidural analgesia had lower plasma glucose, cortisol, c-reactive protein, IL1B, IL6, and IL10 at various stages postoperatively. Furthermore, authors found that the ratio of CD4:CD8 and B cells increased by postoperative day 3 (POD3) in the epidural group, while NK cells decreased by POD2 after surgery in epidural group. T lymphocytes (CD3) decreased in all patients but were lower in patients receiving opioids compared to epidural analgesia. Authors concluded that epidural analgesia significantly reduces the surgical stress response, stress-related immunosuppression, by suppressing deleterious inflammatory mediators and preventing postoperative lymphocyte apoptosis.

Length of Stay

Regional anesthesia also has potential advantages to reducing length of stay (LOS) for inpatients and reducing healthcare costs associated with spine surgery. Hospital stay has decreased in general for most types of surgery over the last two decades. The trend of decreasing LOS has also been noted in spine surgery, and day-case, ambulatory spine pro-

cedures have existed for a few decades (mostly involving minor surgery cases such as microdiscectomy). Regional anesthesia and optimization of postoperative analgesia are important factors in reducing LOS. Data shows a reasonably high readmission rate related to poor analgesia. Studies have noted that 72% of patients presenting with postoperative pain were discharged after being seen and 28% stayed overnight due to uncontrolled pain or hypotension. Uncontrolled pain was responsible for 18.9% of unanticipated admissions after ambulatory spine surgeries in one study [5]. Some authors suggest that regional anesthesia may help optimize postoperative analgesia and decrease unanticipated admissions and readmissions, as well as reduce hospital length of stay for spine surgery. Neuraxial anesthesia may result in faster oral intake, ambulation, and shorter hospital/postanesthetic care unit (PACU) stay and lower costs in general [5].

Cost-Effectiveness

Many studies have examined the cost-effectiveness of regional anesthesia for spine surgery and whether neuraxial techniques significantly decrease healthcare costs associated with spine procedures.

One of the earlier studies to report on the cost-effectiveness of neuraxial anesthesia in spine surgery was published by Vural et al. [33]. This study was a prospectively randomized trial involving 66 patients [American Society of Anesthesia Physical Status (ASA-PS) I-II] undergoing one-level lumbar disc herniation repair. Patients were randomized to receive spinal anesthesia or GA. In terms of clinical outcomes, authors found that spinal and GA were similar in hemodynamic stability, postoperative analgesic requirement and pain, time to first mobilization, urinary retention, and other clinical factors. However, patients in the spinal group required significantly less intraoperative opioid than those in the GA group. Interestingly, patient satisfaction was higher in the spinal group compared to GA, and specific to cost-effectiveness, total cost was higher in the GA group compared to spinal. Authors concluded that lumbar spine surgery could successfully be performed using either anesthetic technique, with potential cost-efficacy advantages in favor of spinal.

Kahveci et al. [34] also studied the cost-effectiveness of spinal anesthesia versus GA. Authors prospectively randomized 80 patients, ASA-PS I-II, to spinal anesthesia ($N = 40$) versus GA ($N = 40$). Authors found many of the aforementioned benefits in favor of spinal anesthesia: patients in the spinal group had greater hemodynamic stability (generally lower heart rate and mean arterial pressure at the end of surgery and at PACU admission) and less intraoperative blood loss (not statistically significant). Moreover, the duration of anesthesia, postoperative analgesic requirement, and anesthetic costs were higher in those receiving GA. Overall, the duration of surgery, duration in PACU, and complications were similar. Authors concluded based on this study that overall, spinal anesthesia is as clinically effective as GA for spine surgery, but more cost-effective.

Walcott et al. [35] performed a retrospective cohort study of consecutive patients undergoing non-instrumented elective lumbar spine surgery for spondylosis by a single surgeon. In this study, patients were evaluated for both GA and spinal anesthesia, and the decision regarding anesthetic technique was based on a combination of physical status, anatomy, and consensus between the patient, surgeon, and anesthesiologist. Operating room (OR) costs were calculated for patients who received GA versus those who received spinal anesthesia while blinded to clinical outcomes. In the study, 319 patients received GA, while 81 received spinal. Data found that GA cases resulted in longer OR time (175 minutes vs. spinal 158 minutes $P < 0.001$). OR costs were 10.3% higher for GA compared to spinal ($P = 0.003$). Complications of spinal anesthesia in this study were excessive movement (1), failed spinal attempt (3), intraoperative conversion to GA (2), and high spinal (1). Authors concluded that spinal anesthesia was safe for the most part and could reduce OR time, costs, and potentially complications.

Ulutas et al. [36] subsequently published a retrospective analysis of 850 lumbar microdiscectomies performed by the same surgeon, under either epidural anesthesia ($n = 573$) or GA ($n = 277$). Their analysis revealed that epidural anesthesia was a potentially more reliable technique, enabling the surgeon to communicate with the patient intraoperatively. Specific to cost analysis, patients receiving epidural anesthesia had lower healthcare and hospital costs compared to those receiving GA. The epidural group had significantly less time spent in the OR, with no difference in the duration of surgery. Authors noted that anesthetic technique had implications on cost and the efficiency of OR use. Specifically, they concluded that epidural anesthesia could decrease healthcare costs and enable more surgeries to be completed with less nerve root manipulation and more comfort to the patient, resulting in improved clinical outcomes and increased efficacy, reliability, and cost savings.

Finally, in the realm of cost-efficacy, Agarwal et al. [37] retrospectively identified 542 patients undergoing elective lumbar discectomy or laminectomy and assessed costs related to GA versus neuraxial anesthesia. They identified 364 who received spinal anesthesia and 178 who received GA and compared healthcare costs between the two groups (total cost; mean direct operating cost; indirect cost including support staff, insurance, tax, floor space, and facility; and administrative costs). After controlling for patient and procedure characteristics, authors found that spinal anesthesia had 41.1% lower direct operating cost, 36.6% lower indirect cost, and 39.6% lower total cost compared to GA. The reduced healthcare costs found with spinal anesthesia were attributable to a shorter LOS, reduced anesthesia and OR

time, and lower intraoperative blood loss. These factors together resulted in significantly lower costs associated with spinal anesthesia, while other factors were also responsible for lower OR and total costs.

Patient Satisfaction

Finally, patient and surgical satisfaction may be higher when surgery is done under regional anesthesia; however, this has only consistently been reported following spinal anesthesia.

Overall, many studies show significant advantages in the use of regional anesthesia for spine surgery including improved analgesia and reduced opioid requirements, less PONV, improved operating conditions and less blood loss, increased hemodynamic stability, reduced postoperative headache, positioning injuries, low rates of urinary retention, reduced thromboembolic complications, surgical stress response, and lower hospital and PACU LOS with potentially significant healthcare cost reductions. Though these advantages have been documented in various studies and reviews, the current literature is heterogenous, and further prospective, randomized trials are required to clearly delineate the benefit of regional anesthesia in spine surgery. Based on current data, there is no clearly superior anesthetic technique in terms of morbidity or mortality outcomes, but many studies suggest that short-term, secondary benefits exist for selecting regional anesthesia over general anesthesia for spine procedures.

Non-neuraxial and Paraneuraxial Nerve Blocks for Spine Surgery

In addition to the use of local anesthesia and neuraxial anesthesia for spine procedures, there is growing evidence for the use of newer, non-neuraxial peripheral nerve blocks for spine surgery.

Redhu et al. [38] published a case report of lumbar paravertebral block as sole anesthetic for L4-5 discectomy. Authors reported on a 72-year-old male patient with severe low back pain radiating to the right thigh and leg for 5 years. The patient was bedbound for 15 days prior to surgery and had a medical history significant for hypertension, coronary artery disease, and type 2 diabetes. His medications included amlodipine, digoxin, glyceryl trinitrate, furosemide, spironolactone, atorvastatin, and clopidogrel (stopped 2 weeks before surgery). This patient was very medically complicated, and preoperative workup included an electrocardiogram demonstrating complete right bundle branch block with ST-segment depression in the lateral leads and borderline first-degree AV block. His preoperative echocardiogram revealed a significantly dilated left atrium and ventricle with inferoposterior akinesia, significant myocardial scarring, and basal and mid-lateral wall hypokinesia. The patient's left ventricular ejection fraction was noted to be 20–25% (cardiac output was estimated at only 2 L/min).

Given this patient's significant cardiac dysfunction and limited reserve, he was stratified as very high risk for anesthesia. The neurosurgical team was keen to proceed with surgery for the patient's intractable back pain and to correct the existing neurologic deficit. In the context of this medically challenging case, the patient received bilateral lumbar paravertebral nerve blocks with 6 mL 2% lidocaine on each side at the L4 level. The left-sided paravertebral block was performed under fluoroscopic guidance, and the right-sided block was performed under ultrasound guidance, both with the patient in the prone position. The surgeon supplemented the field with local anesthesia (5 mL 2% lidocaine). Fifteen minutes after injection of the nerve block, sensory block was assessed as appropriate, and surgery was started. During the procedure, the patient reported "neuralgic pain" during manipulation of the nerve root, which resolved with an additional 2 mL of 2% lidocaine infiltration by the surgeon. The patient remained hemodynamically stable throughout the 1.5 hour surgery and had an uneventful recovery. He was discharged 3 days after surgery with a good outcome. The authors demonstrated that limited lumbar spine procedures (L4-5 discectomy) could be performed safely and effectively under bilateral lumbar paravertebral blockade with supplemental infiltration of local anesthesia in medically challenging patients.

In addition to paravertebral blocks for spine surgery, Ohgoshi et al. [39] reported on the use of a multifidus cervicis plane (MCP) block for analgesia in cervical spine surgery. This case report details the management of a 66-year-old female who underwent posterior cervical laminoplasty (C3-6) for ossification of the posterior longitudinal ligament. The authors performed bilateral MCP regional blocks for perioperative analgesia (the nerve blocks were performed after general anesthesia). For these blocks, 20 mL of 0.375% ropivacaine was injected on either side between the fascial plane of the multifidus cervicis and semispinalis cervicis muscles at the C5 level. Authors detailed their approach with ultrasound guidance to complete this block. For general anesthesia, they used propofol and remifentanil. No long-acting opioids were given intraoperatively, and no additional postoperative opioids were given (only nonsteroidal anti-inflammatory medications). In this case, good perioperative analgesia was reported with the use of these nerve blocks. Authors also reported using the MCP block in 20 patients undergoing cervical laminoplasty, with good analgesic effect perioperatively. However, they stated that the dermatomal spread of local anesthesia and exact duration of action of these blocks remain unknown, suggesting this is better elucidated with a future study.

Interestingly, and along similar lines, Matsunami et al. [40] published a case report of a successful anesthetic for posterior cervical spinal fusion using a combination of regional anesthesia (peripheral nerve blockade) and general anesthesia. In this report, authors performed a block of the frontal nerve, greater occipital nerve, and superficial cervical plexus in a patient with athetoid cerebral palsy. This patient, a 69-year-old woman (157 cm, 33 kg), was scheduled for a posterior cervical spine fusion for cervical spondylotic myelopathy. She received general anesthesia with endotracheal intubation and subsequently had regional nerve blocks of the frontal nerve, greater occipital nerve, and superficial cervical plexus using ropivacaine. General anesthesia was maintained using total intravenous anesthesia with propofol, remifentanil, and dexmedetomidine. After surgery, no pain or athetoid movement was noted. Authors concluded that this combination of peripheral nerve blocks provided excellent analgesia postoperatively for the spine procedure.

In addition, Ueshima et al. [41, 42] described the use of an ultrasound-guided thoracolumbar interfascial plane block (TLIP Block) for analgesia in lumbar spine surgery. Authors described this block as injection of local anesthetic into the fascial plane between the multifidus and longissimus muscles at the level of the L3 vertebra. They also described continuous TLIP blocks and suggest that this injection can block the ventral rami of the thoracolumbar nerves (L2-3) and provide perioperative analgesia in lumbar vertebral surgery. Authors reference previously described approaches to the TLIP block and note that in previous reports, the injection site of this block is near the incision site of surgery, carrying a risk of infection. They describe a lateral approach to the TLIP block, with injection at the fascial plane between the iliocostal muscle and longissimus muscles at the lumbar vertebra (authors suggest that compared to a conventional TLIP block, the lateral TLIP block can decrease infection risk).

They also reported on two cases of lateral TLIP for lumbar vertebral surgery. Case 1 involved a 67-year-old female who underwent laminoplasty at L2-3, with lateral TLIP blocks performed after general anesthesia. In this patient, bilateral TLIP injections of 20 mL of 0.2% levobupivacaine (40 mL total) were administered into the fascial plane between the iliocostal muscle and longissimus muscles at ~L3 using ultrasound guidance (high-frequency linear probe). General anesthesia was maintained using TIVA (propofol, remifentanil, rocuronium). Postoperatively, no additional analgesic was required, and recovery was uncomplicated. The second case involved a 70-year-old male on dialysis undergoing lumbar laminectomy at L3-4 for a herniated disc. Lateral TLIP blocks were performed in this patient, also after general anesthesia, with the same doses as case 1 (20 mL of 0.2% levobupivacaine on each side). In this patient, postoperative pain control was also adequate, and no additional analgesic was required. Authors concluded that lateral TLIP blocks were effective for postoperative analgesia in lumbar spine surgery, though further studies regarding optimal dosing, volume, and concentration of local anesthetic are required. Other authors and centers also seem to have experience with use of the continuous TLIP blocks [43] for spine surgery.

Finally, larger studies have also investigated the use of peripheral nerve blocks for spine procedures. Wang et al. [44] compared cervical plexus blocks to general anesthesia for anterior cervical decompression and fusion (ACDF). In this study, 356 patients who underwent one-level ACDF for cervical spine myelopathy were prospectively reviewed. Patients received either general anesthesia or cervical plexus anesthesia for their spine procedure. Both anesthesia induction time and postoperative recovery were longer patients receiving general anesthesia compared to those who had their procedure done under regional block. The duration of surgery and recovery stay were also longer in those receiving general anesthesia. No difference was noted in perioperative blood loss and surgeon and anesthetist satisfaction, but patient satisfaction was higher in those receiving general anesthesia. Doses of analgesic and antiemetic were higher in the general anesthesia group, as well as the anesthesia medical cost. No differences were noted in hemodynamics preoperatively, but intraoperatively, heart rate and blood pressure were higher in the cervical plexus block group. Following general anesthesia, patients had increased, highest at 8 hours, postoperatively, with pain steadily decreasing until 24 hours postoperatively when NRS pain score was 1/10. In those receiving the regional block, intraoperative pain scores were 4/10, and pain decreased starting from 4 hours postoperatively (at 24 hours after surgery, the NRS was 2/10). Severe postoperative nausea and emesis were higher in the general anesthesia group.

Similarly, Mariappan et al. [45] studied the effect of superficial cervical plexus blocks on the quality of postoperative recovery after ACDF. The authors performed an RCT double-blinded trial, enrolling adults over 18 years of age scheduled for elective single- or double-levels ACDF. Participants were randomized to superficial cervical plexus block (SCPB) with 10 mL of bupivacaine 0.25% or no block. The primary outcome was quality of recovery at 24 hours postoperatively, measured using a 40-item quality of recovery questionnaire (QoR-40). Forty-six patients were randomized (23 block, 23 no block). The median aggregated global QoR-40 scores at 24 h were higher in the SCPB group (better quality of recovery in patients receiving a nerve block compared to no block). No differences regarding mean postoperative opioid consumption were noted at 24 h, and the number of patients discharged within 24 h did not differ between groups. Authors noted that performing a superficial cervical plexus block for ACDF surgery was beneficial to patients' reported quality of recovery at 24 h after surgery in this double-blinded RCT.

In summary, several studies have examined the use of non-neuraxial peripheral nerve blocks in spine pain and spine procedures. In fact, Xu et al. [43] have suggested that the term "paraneuraxial nerve blocks" be applied to include many of the non-neuraxial truncal blocks that are increasing in popularity and may have implications for analgesia in spine surgery. Xu et al. [43] propose the term "paraneuraxial nerve blocks" to include blocks such as paravertebral blocks, thoracolumbar interfascial plane (TLIP) blocks, erector spinae blocks, retrolaminar blocks, cervical columnar interfascial plane blocks (CLIP blocks), sympathetic chain blocks, and lumbar plexus nerve blocks to target nerves just outside the neuraxis. They define these paraneuraxial blocks as targeting "the spinal nerve between the lateral margin of the spinal foramen and lateral edge of the erector spinae muscle," an area which contains roots of the spinal nerves, their ventral and dorsal branches and plexuses, the sympathetic chain, and white and gray rami communicantes [43]. Conceptually, these blocks are near but not within the neuraxis like spinals and epidurals. Though most reports and studies of these "paraneuraxial blocks" have been in the context anesthesia for truncal surgery and truncal pain syndromes (thoracic/abdominal analgesia), there may be select applications of these blocks for anesthesia and analgesia in spine pain and spine surgery, particularly if the paraneuraxial blocks are performed more proximally, closer to the neuraxis itself.

Limitations of Regional Anesthesia in Spine Surgery

Despite the benefit of regional anesthesia for spine surgery demonstrated in many studies, there are still some limitations to the use of neuraxial and regional anesthesia for spine surgery and perioperative spine pain management.

OR Time, Procedure Time, and Hospital Length of Stay

Mergeay et al. [5] noted that not all studies favor spinal or epidural anesthesia for spine surgery. In the realm OR resource usage and efficiency, some studies demonstrated that when using epidural anesthesia for spine surgery, the procedure was more time- consuming; however, epidural analgesia was able to provide longer-lasting analgesia than a single-shot spinal anesthetic. In other studies, no difference was found in procedural time between neuraxial or general anesthesia and time to mobilization out of bed. A few studies have found longer OR time or surgical time but equal total anesthesia or procedural time when comparing general anesthesia to epidural anesthesia.

In terms of hospital resource usage and postoperative recovery, depending on hospital discharge criteria, sometimes no differences were noted between general and regional anesthesia in terms of hospital LOS. Additionally, some studies show that PACU times may be prolonged after regional anesthesia, especially when long-acting local anesthetics are used and discharge depends on recovery from sensory and motor block. Occasionally, discharge from PACU may be delayed due to hemodynamic parameters (hypotension) in the setting of regional and neuraxial anesthesia [5].

Postoperative Neurologic Assessment and Neurologic Injury

When regional anesthesia is used perioperatively for spine surgery and spine pain patients, there may be an inability to immediately assess the patient's neurologic status postoperatively leading to potential delays in the diagnosis of spinal cord injury and evolving cord compression from hematoma or other processes. This is especially true when using long-acting local anesthetics or with catheter-based regional techniques, which prolong motor or sensory blockade (e.g., epidurals). Possible solutions include starting the epidural or regional catheter postoperatively, after a full, appropriate neurologic examination has been. Some authors report using this method to provide postoperative analgesia with local anesthetic via epidural catheters after ascertaining neurologic function.

Moreover, when patients receive surgery for spinal stenosis, disc herniation, or pathology with compromise of the available space within the spinal canal, there is a risk of cauda equina syndrome or spinal cord compression with any additional space-occupying volume within vertebral canal (e.g., blood, abscess, injected fluid volume such as local anesthetic epidural bolus or infusion). Non-neurosurgical cases have been reported where neuraxial block injectate was considered to be responsible for the presentation of spinal cord ischemia, compression, and/or cauda equina syndrome [5]. Interestingly, combined spinal-epidural techniques were more often found to be the culprit of contributing to and/or masking neurologic symptoms from spine and nerve root compression, than either spinal or epidural alone. In this context, theoretically, spinal anesthesia may be lower risk for spinal cord compression in patients in preexisting compressive pathology, as it involves only a low-volume injectate directly into the CSF. However, when spinal anesthesia is performed below the compressive lesion (i.e., stenosis or disc herniation), it may theoretically have less optimal spread to the areas above the lesion, resulting in block failure or even possible neural toxicity due to accumulation of local anesthesia below the level of stenosis. Some authors [5] recommend considering the safety of neuraxial

anesthesia in patients with existing spine pathology, particularly with severe stenoses, compression, and pre-existing space-occupying lesions. They recommend considering that these patients may require multiple attempts for neuraxial or regional anesthesia, as well as keeping in mind the increased risk of failure, abnormal anatomy, and accounting for previous surgeries/interventions. One study showed that patients with spine pathology can experience more than two times the increased frequency of paresthesias when receiving intrathecal injections or catheter placement.

Conversion to General Anesthesia

In addition to some drawbacks including potentially prolonged PACU stay and limited ability to assess postoperative neurologic function, regional anesthesia for spine surgery may fail intraoperatively for various reasons, necessitating urgent conversion to general anesthesia. In cases of failed spinal or epidural anesthesia, intraoperative conversion to general anesthesia may prove technically challenging, involving maneuvers such as prone airway management. Existing studies, though involving small patient numbers, note very few instances of intraoperative spinal and epidural failure. In fact, most published studies did not involve any cases of neuraxial anesthesia failure requiring conversion to general anesthesia. At our institution, for unanticipated prolongation of spine procedures attempted under single-shot spinal, cases have been documented of intraoperative supplementation of additional intrathecal bupivacaine and fentanyl by the surgical team, to extend the duration of a receding spinal block.

Surgeon, Anesthesiologist, and Patient Preference

Despite its practicality and advantages, at many centers, regional techniques are not frequently chosen for intraoperative anesthesia and perioperative analgesia in spine surgery. This may be partially due to anesthesiologist and surgeon preference, as general anesthesia has classically been the accepted method for spine surgery (ensures a secure airway prior to prone positioning, may guarantee motionless patient with neuromuscular blockade, and easily extend duration anesthetic with GA). In addition, with epidural placement, surgeons may be reluctant to allow foreign material (epidural catheter, even if sterile insertion) close to the operative site, due to the possible or theoretical risk of infection [5].

In experienced centers, these reservations regarding regional anesthesia become less significant over time and with further experience using these techniques perioperatively. For example, surgeons become familiar with operating in spontaneously breathing prone patients. Anesthesiologists develop optimal neuraxial and sedation protocols to ensure intraoperative patient comfort and minimize the risk of conversion to general anesthesia. Epidural placement and dosing are optimized to limit the risk of catheter placement within or near the surgical field. Moreover, with time, some surgical teams have developed preferences for regional techniques in spine surgery. Many studies have demonstrated better operating conditions with less venous congestion in the surgical field in spontaneously breathing patients.

In addition to anesthesiologist and surgeon preference, there are also barriers to patient acceptance of regional anesthesia, as many patients may be anxious and concerned about intraoperative awareness and "staying awake" during surgery. However, with appropriate patient counseling, preparation, and education preoperatively, many patients change their perspectives on regional anesthesia and select this method preferentially for their perioperative care, given the significant advantages. It is important to consider anesthesiologist, surgeon, patient, and institutional preferences and practices when assessing the suitability of regional anesthesia for spine surgery.

Regional Anesthesia Contraindications

Regardless of the advantages, it is important to be mindful of absolute and relative contraindications to regional techniques when selecting them for spine surgery. Most studies involving neuraxial anesthesia for spine patients have used these contraindications as exclusion criteria. Frequently cited contraindications include patient refusal, severe or multilevel spinal stenosis (risk of high block, difficulty predicting dose, spinal failure/difficult placement), history of seizures, intracranial hypertension, coagulopathy, infection at the needle site or systemic sepsis, hemodynamic instability and hypovolemia, near-complete or total myelographic block, and myelographic arachnoiditis. It is important to consider these contraindications prior to proceeding with neuraxial techniques for spine procedures.

Neuraxial Side Effects

In addition to contraindications, neuraxial and regional anesthesia may have a number of side effects when administered for spine procedures. For example, some studies have shown that neuraxial techniques increase the risk for urinary retention postoperatively, when local anesthesia, opioids, or both agents are employed. This may increase the incidence of temporary catheterization perioperatively, leading to lower patient satisfaction and a potential increased risk of urinary tract infections, though this has not been shown. Other neur-

axial side effects to be mindful of include motor impairment with local anesthesia and pruritus, sedation, and respiratory depression with neuraxial opioids. Each of these side effects may be monitored and treated appropriately and is largely transient related to intraoperative dosing of local anesthetic or opioid.

Other Pitfalls

Studies have cited other potential drawbacks to regional anesthesia in spine procedures, specifically including increased cost in some instances and failure of neuraxial catheters (rates noted of up to 37% in some studies). Mergeay et al. [5] limited duration of satisfactory analgesia (sometimes analgesia only at rest, not during mobilization), and sometimes analgesic benefit occurring too late during the postoperative period. It is important to consider these potential drawbacks when selecting regional anesthesia for spine surgery. For different types of surgeries, different anesthesia and analgesia techniques may be required. For instance, spinal fusion patients may not do as well with epidural or intrathecal anesthesia intraoperatively, due to the extensive nature of the procedure, but may benefit from postoperative epidural analgesia. These patients may have pre-existing chronic pain that makes postoperative analgesia particularly challenging, with or without epidural placement. Conversely, regional anesthesia for intraoperative and postoperative care may be ideal other procedures such as discectomy, laminectomy, or scoliosis correction, providing intraoperative anesthesia and prolonged pain control after the procedure.

Type of Surgery and Suitable Patients for Regional Techniques

Recognizing some of the drawbacks of regional anesthesia for spine procedures, there are important principles in selecting the appropriate patients and types of surgical procedures which are most amenable to regional techniques. A variety of spine surgeries and procedures have been completed under regional and neuraxial anesthesia, ranging from minimally invasive microdiscectomy to large, extensive scoliosis corrections and fusions. Spine surgeries from anterior to posterior approaches have also been reported under neuraxial anesthesia. Most studies reporting on regional techniques for spine surgery are done for lumbar surgeries and interventions. These procedures are inherently more suitable for neuraxial techniques, specifically spinal anesthesia, because dural punctures for spinal anesthesia are performed below L2 (inferior terminus of conus medullaris) [5]. However, thoracic spine procedures can be performed under regional anesthesia by using thoracic epidural catheters or even single-shot lumbar spinals with high volume and dose to increase spread to lower thoracic spine levels. When using single-shot spinals for thoracic spine procedures, despite the higher dose, these techniques should be anticipated to last a limited duration and are often combined with concurrent general anesthesia.

Generally speaking for lumbar spine procedures, the upper sensory level achieved for neuraxial block should be at or above T10 for adequate surgical anesthesia. High levels of motor block are not well tolerated in the prone position (lack of abdominal muscle strength due to epidural blockade and ability to breathe deeply – this can lead to poor respiratory mechanics when compounded with increased abdominal pressures in the prone position and intercostal paralysis from high block). Usually, surgery above T10 is not recommended under neuraxial anesthesia alone, due to cardiovascular (hypotension from extensive sympathectomy) and respiratory effects.

In addition to the location of the spinal intervention, the type and duration of surgery are important to consider when selecting regional versus general anesthesia for spine procedures. Typically, general anesthesia is preferred in long procedures (greater than 2-hour duration) or procedures with significant anticipated blood loss and need for intraoperative resuscitation (e.g., multilevel laminectomy, multilevel extensive effusions, spine distraction using rods or pedicle screws, significant hardware insertion). General anesthesia facilitates easy extension of duration of anesthetic intraoperatively and provides a secured airway in the prone position should the need for aggressive resuscitation and hemodynamic control be required intraoperatively. The most frequent and optimal surgical procedures done under regional or neuraxial alone would be lumbar microdiscectomies, discectomies, one- or two-level laminectomies, or limited multilevel fusions.

When selecting appropriate patients for regional anesthesia in spine surgery, it is important to consider specific contraindications to these techniques (referenced in previous section, Regional Anesthesia Contraindications). Moreover, previous spine surgeries and interventions (epidural blood patch, steroid injections) can affect the ease and success of neuraxial techniques administered for repeat surgeries. This effect is usually more significant with epidural anesthesia than with spinal anesthesia and can lead to increased regional failure rate and unreliable spread. Nonetheless, epidural analgesia in patients with previously instrumented epidural spaces is not necessarily different or more prone to failure compared to those who have not had previous epidural interventions. Other studies have found that labor epidurals were not at increased risk of failure in patients who have previously had discectomy.

In addition to these considerations for patient selection, other patient characteristics, including body habitus, are important when deciding to use regional or general anesthe-

sia for spine procedures. Obese patients with increased abdominal girth are more likely candidates for general anesthesia, as they may experience more respiratory complications breathing spontaneously in the prone position (poor respiratory mechanics, reduced chest wall excursion, increased abdominal pressures, respiratory compromise if reliant on spontaneous breathing). In obese patients, there may also be unpredictable spread of single-shot intrathecal anesthetics, leading to high neuraxial blockade and even the risk of total spinal. By contrast, pregnant patients may be excellent candidates for spinal surgery under regional technique, as this minimizes the risks of gastric regurgitation and instrumenting a potentially difficult airway. Furthermore, regional anesthesia in pregnant patients also allows the patient to optimize her own intraoperative positioning (patient may position self on operating table and adjust intraoperatively if needed for comfort and minimizes systemic and fetal exposure to anesthetic agents). Specifically, in pregnant patients undergoing spinal surgery with regional anesthesia, it may be important to consider non-prone positions at later stages in gestation (aortocaval compression, positioning the patient prone with a gravid uterus).

Technical Aspects of Performing Regional Anesthesia for Spine Surgery

There are many technical considerations to performing regional anesthesia for spine surgery and spine pain. The literature on regional anesthesia for spine surgery details many different approaches to regional anesthesia for spine procedures.

Spinal anesthesia has been reported as the primary anesthetic for many spine procedures including lumbar disc surgeries, single- and double-level laminectomies, and even lumbar spine fusions. Epidural anesthesia has been reported for the same surgeries but used less commonly. Less studies have been reported with epidural anesthesia, as epidurals are also more technically challenging and time-consuming to place. Moreover, epidural anesthesia may provide less optimal spread of local anesthetic in the neuraxis for spine surgeries. There are also potential drawbacks regarding the presence of foreign material (epidural catheters) in or near the operative field (infection risk, technical challenges, catheter loss, fragmentation, and/or shearing). In most reports, epidurals are often used as part of a combined neuraxial and general anesthesia technique. In some instances, epidural catheters are even placed surgically (intraoperatively by the surgical team) and then tunneled out to the skin at the conclusion of the operation. In these cases, the use of a postoperative pump to deliver ongoing local anesthesia to the surgical site has proven to be safe and effective. At our institution, these surgically inserted epidural or anesthetic catheters are often managed concurrently by the surgical and acute pain services and removed when deemed appropriate.

The use of combined spinal-epidurals (CSEs) has been described for spine procedures in one study, which found that CSEs provided consistent operative anesthesia during the spine procedure, with the benefit of additional analgesia for the postoperative period [5].

Many studies compare different regional techniques and the specifics of performing spinals, epidurals, and CSEs for spine procedure (e.g., patient positioning, local anesthetic agents used) [5].

Patient Positioning

Regional techniques for spine procedures have been performed in the lateral, sitting, or different variations of the prone position. Technically speaking, sitting position is comfortable for the patient, provides optimized positioning for administration of the neuraxial technique, but also gives the patient more opportunity to move during the administration of the block, which can make the procedure more technically challenging. In addition, due to the upright position (pooling of venous blood in dependent extremities and lower body), hypotension due to sympathectomy can be more significant after administration of a neuraxial technique in the sitting position, if the patient is kept upright. In addition, depending on the baricity of the injected local anesthesia (in spinal blocks), anesthesia may preferentially settle to lower lumbar and sacral dermatomes after a hyperbaric spinal is administered and the patient is kept sitting in the upright position for a prolonged time [5]. Some authors suggest that an epidural may be more suitable than spinal for patients remaining sitting for a prolonged time after administration of the neuraxial technique. In some cases, surgical procedures are performed in the sitting position, and this can provide improved operating conditions, but lead to the ongoing aforementioned concerns with hypotension and patient comfort/movement intraoperatively.

Most descriptions of how neuraxial anesthesia is administered involve placing the block with the patient sitting or prone and then resuming the supine position immediately after the injection of local anesthesia for a period of time (enables the block to "settle"). Patients are then placed in the operative position (sitting or log rolled prone) and allowed to self-adjust positioning of the torso and head to achieve comfort. Studies comparing prone intraoperative positioning versus knee-chest intraoperative positioning during spinal anesthesia found that knee-chest positioning results in more pulmonary restriction than regular prone positioning. The knee-chest position, as a result, is not recommended for patients with existing respiratory compromise undergoing spine procedures with regional anesthesia and spontaneous

respiration. Positioning with a special frame or non-prone positioning is frequently needed in pregnant patients undergoing spine procedures under regional anesthesia.

Regarding specific studies of patient positioning, Laakso et al. [46] performed a randomized controlled trial of different patient positions (knee-chest vs. horizontal side position) during the placement of spinal anesthesia in patients undergoing lumbar disc surgery. Authors enrolled 40 patients (ASA 1–2, ages 24–61) undergoing lumbar disc surgery with spinal anesthesia. Spinals were done with 27G needles at the L2-3 level, using 3 mL 0.5% bupivacaine. Patients were randomized into two groups: one group where spinal anesthesia was performed with the patient in the operative position (prone knee-chest) and another group in which the spinal was performed in the lateral decubitus position and then turned supine for 20 minutes before surgical positioning into the knee-chest position. In three patients in the prone knee-chest group, the spinal was initially attempted with a 27G needle, but needed to be replaced by a larger 25G needle for successful lumbar puncture. The final sensory level on the skin after administering spinal anesthesia (tested by pinprick) was T5 in prone knee-chest group and T6 in lateral decubitus group. Recovery time from spinal anesthesia was similar in both groups (average 210 minutes from injection). Mean decrease in systolic blood pressure was greater in the prone knee-chest group (30 mmHg) than in the lateral decubitus to supine group. Ephedrine was required earlier on for hemodynamic support in those receiving spinal anesthesia in the lateral position (three patients needed ephedrine all within 10 minutes of injection) vs. the prone group, where six patients required ephedrine after 15 minutes. Four patients in the prone group needed anticholinergic treatment for bradycardia compared with two patients in the lateral group. Light sedation was given to 5/20 patients in the prone group, compared to 4/20 patients in the lateral group (patients primarily received sedation for numbness and aching in the shoulder region). Authors concluded that spinal anesthesia was similarly effective in the two groups, regardless of patient positioning, but there was a tendency for more hemodynamic deterioration in the knee-chest group.

Yilmaz et al. [47] also performed a prospective study comparing perioperative hemodynamic and respiratory function in patients undergoing lumbar disc surgery under spinal anesthesia in the prone and knee-chest positions. In this study, spinal anesthetics were all injected with the patient in the lateral decubitus position, but patients were randomized to either intraoperative prone positioning or knee-chest positioning for the surgical procedure. This study included 45 patients (ASA 1–2), presenting for lumbar microdiscectomy; half of the patients ($N = 22$) were randomized to intraoperative prone positioning for the procedure, while the other half ($N = 23$) were randomized to knee-chest position. Spinal anesthesia was performed in the left lateral decubitus position with 3.5–4 mL of 0.5% hyperbaric bupivacaine via a 27G spinal needle. In each patient, the spinal was administered one to two levels above the operative area. Patients were kept lying supine for 8 minutes following the spinal injection, and pinprick test was used to determine the level of spinal anesthesia. Following administration of the spinal, patients were randomized to prone or knee-chest position. Authors noted that immediately after the spinal, blood pressure was decreased and heart rate was increased in both positioning groups. Both positions exhibited a decrease in forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1) during the surgery compared to preoperative values. The decrease in peak expiratory flow and forced expiratory flow at 25% (FEF25) was significantly more in the knee-chest position compared to simple prone position. Authors concluded that knee-chest positioning caused a greater restrictive defect in spontaneously breathing patients who had received spinal anesthesia for a spine procedure and cautioned the use of this position in those with limited respiratory reserve.

Medications for Regional Anesthesia in Spine Procedures

The most commonly used local anesthetic for regional anesthesia in spine procedures is bupivacaine (widely reported in most studies). Specific to spinal anesthesia, intrathecal doses of up to 15 mg have been documented. The use of plain (isobaric) versus hyperbaric bupivacaine solutions has been studied by different authors in the context of spinal anesthesia for spine procedures. The spread of plain bupivacaine appears to be less affected by patient positioning than the spread of hyperbaric bupivacaine. Plain (isobaric) solutions can produce unreliable or unpredictable spread, leading to inconsistent dermatomal levels of coverage and quality of anesthesia [10, 11].

Conversely, some other authors have found that plain bupivacaine is better than hyperbaric bupivacaine and tetracaine, producing a denser sensory block and better control of the sensory and motor block, with a lower incidence of incomplete block. These authors found hyperbaric bupivacaine had a faster onset for complete motor and sensory block but higher levels of upper sensory blocks and greater hypotension, with more interventions to treat heart rate and blood pressure changes, and hyperbaric solutions also required local anesthesia wound infiltration more frequently.

Tetzlaff et al. [12] conducted a study to evaluate the effects of local anesthetic baricity on the performance of spinal anesthesia for lumbar spine surgery. They enrolled 53 patients (ASA 1–2) and randomized these patients to receive a spinal with 15 mg of bupivacaine with 0.2 mg epinephrine

as either 3 mL 0.5% plain (isobaric group) or 2 mL 0.75% with 8.25% glucose (hyperbaric group). All spinals in the study were performed for patients receiving spine surgery, using a 22G Quincke needle at the L3-4 interspace. Spinals in this study were placed with the patient in sitting position. A blinded observer collected data after spinal anesthetic insertion: variables including the onset of motor and sensory anesthesia, the highest sensory level achieved, the maximal changes in heart rate and blood pressure, and the need for hemodynamic treatment were recorded. In addition, the frequency of failed blocks and need for supplemental local anesthesia to complete incision or wound closure were recorded. Authors found that the time to onset for complete motor and sensory block was longer in those receiving isobaric bupivacaine for their spinal. The maximal sensory level achieved was higher in the hyperbaric group. Maximal changes in blood pressure and interventions required to treat heart rate and blood pressure were greater in those receiving hyperbaric spinals. Two failed spinals were repeated successfully in the hyperbaric group, and the need for local anesthetic infiltration to supplement anesthesia during wound incision and closure was greater in the hyperbaric group. Authors concluded that plain bupivacaine was better than hyperbaric bupivacaine for spinal anesthesia in elective lumbar spine surgery.

In addition to this study evaluating hyperbaric versus isobaric spinal anesthetics for spine surgery, Sahin et al. [48] compared the use of levobupivacaine to bupivacaine for spinal anesthesia in lumbar disc surgery. Sixty patients (ASA 1–3), presenting for unilateral, single-level (L4-5) lumbar disc hernia surgery, were enrolled. All surgeries were performed by the same surgeon. Patients were randomized to 15 mg (0.5%) isobaric bupivacaine ($N = 30$) or 15 mg (0.5%) isobaric levobupivacaine ($N = 30$), administered intrathecally for their spinal anesthetic. Sensory and motor block dermatomes, as well as intraoperative sensory and motor block characteristics, and post-op recovery times of spinal anesthesia were tested. Surgeon and patient satisfaction were also assessed, as were intraoperative hemodynamics and postoperative complications. Authors found that the maximal sensory block (dermatomal level achieved) was higher in patients receiving levobupivacaine spinals (on average higher by about 1.6 levels). There was no difference in the onset of sensory and motor blockade and no difference in operative. The recovery time of sensory and motor block was shorter in those receiving levobupivacaine, and mobilization was earlier in this group. Patient satisfaction and intraoperative and postoperative complications were similar between the two groups. Authors concluded that block recovery time was shorter in the levobupivacaine group, resulting in a potential disadvantage for longer procedures, but allowing for earlier mobilization, postoperative recovery, and neurological assessment in shorter procedures.

In addition to the baricity and type of the local anesthetic utilized in spinal anesthesia, some authors have studied the use of various adjuncts in addition to local anesthetic for spinals used with spine procedures. Salem et al. [49] performed a prospective double- blinded randomized controlled trial of 52 patients undergoing spine surgery with spinal anesthesia. The included patients had lumbar spondylolisthesis and were presenting for instrumented one-level posterolateral lumbar spine fusion. They were randomized to group D (15 mg hyperbaric bupivacaine with 5mcg dexmedetomidine) versus group P (15 mg hyperbaric bupivacaine only). In this study, scores rating operative field quality and surgeon satisfaction were higher in group D (spinals of bupivacaine + dexmedetomidine) compared to group P (spinals with bupivacaine only, $P < 0.0001$, and $P = 0.002$). Patients who received dexmedetomidine in their spinal also had longer durations of sensory and motor blockade compared to those who had plain local anesthesia spinals. Time to first request of analgesia was longer, and total dose of ketorolac was lower in those receiving dexmedetomidine in their spinals (smaller analgesic requirements were generally noted in the dexmedetomidine group). Authors concluded that dexmedetomidine improved the quality of operating conditions, prolonged the block, and provided better postoperative analgesia with few side effects in patients receiving spinal anesthesia for spine surgery. Specific spinal dosing in this study was hyperbaric bupivacaine 15 mg (3 mL 0.5%) with dexmedetomidine added as 5mcg in 0.5 mL saline (or saline alone for those receiving plain bupivacaine blocks). Patients received premedication with 15 mcg/kg intramuscular atropine and 10 ml/kg of lactated ringers. The spinal was performed with the patient in sitting position, at L3-4 via a midline approach with a pencil point 25G needle, hole pointing upward. The patient was placed supine after spinal injection and then moved to prone shortly after the anesthesia level was established.

Detailed Technical Aspects of Spinal Anesthesia for Spine Procedures

Different authors have described a variety of ways to perform spinal anesthesia for spine procedures, with varying effects and outcomes. Below, the specific methods by which different groups have performed spinal anesthesia, including needle type and gauge, level of intrathecal injection, medications used, patient positioning, and approach, are discussed, along with effects such as duration of block, block failure requiring conversion to general anesthesia, and the need for supplemental local anesthetic infiltration.

Goddard et al. [6] reported performing spinal anesthesia with a pencil point needle and 3–3.5 mL of 0.5% plain (isobaric) bupivacaine. In their study, 118 patients received also

received intrathecal diamorphine 0.25 mg or 0.3 mg. The lumbar puncture/spinal was done in the lateral, sitting, or prone positions. In patients presenting for spinal decompression, the spinal injection site was purposefully chosen to be above the stenotic area but below the conus medullaris. In patients undergoing discectomy, a level other than the surgical level was chosen. Immediately after injection, patients self-positioned onto the Jackson spinal table or Wilson frame. If supplemental local anesthetic was required for skin incision, bupivacaine 0.5% with 1:200000 epinephrine was infiltrated in the incision site. Patients were sedated during the procedure in the prone position, using target-controlled infusions of propofol.

Erbas et al. [21] described the use of spinals for posterior lumbar stabilization. Spinal anesthetics were performed at L3-4 or L4-5, with 15 mg of 0.5% plain bupivacaine with 2 mcg of fentanyl and 0.2 mg of epinephrine. Authors reported no incidences of anesthetic failure with these spinals.

Sandrolsadat et al. [18] elected to use a larger dose of intrathecal medication for their spinals in patients presenting for spine procedures. They performed lumbar puncture at L3-4 with 25G Quincke needles and injected 4 ml 0.5% bupivacaine for the anesthetic. Patients were subsequently positioned supine for about 10 minutes until a satisfactory block of T6-T10 was achieved. Then, patients positioned themselves prone and received sedation with propofol at 25–50mcg/kg/min for the duration of the operation. Authors observed no conversions to general anesthesia in this study.

Jellish et al. [10] performed spinals with hyperbaric bupivacaine 0.75% (in 8.5% dextrose solution) and in their study, elected to administer 11 mg of bupivacaine to patients receiving spinals for spine procedures. Spinals were performed with a 25G Quincke at L4-5, or L5-S1 with patients in the right lateral decubitus position. Once the block was placed, patients were repositioned supine. When a stable level of anesthesia had been achieved (between T6 and T10), usually after ~10 minutes, patients were rolled prone and self-positioned comfortably. Supplemental oxygen was administered at 2 L/min, and sedation with propofol 25–50 mcg/kg/min was provided for the case with good effect.

Rung et al. [50] suggested the use of isobaric 0.5% bupivacaine (10 mg) when administering spinal anesthesia for spine surgery. Authors in this study suggested that isobaric bupivacaine was beneficial because dermatomal anesthesia levels were not affected by patient positioning during and after spinal injection, when using isobaric solutions. Rung et al. suggested that in this case, the injection of the spinal anesthetic could be done with patients in the prone position, after moving onto the OR table, thus saving time because patient can be prepped and draped while spinal is setting up. These authors suggested that rather than waiting 10 minutes for a hyperbaric bupivacaine spinal to "set up" described by Jellish et al. [10, 11], this could improve time efficiency. They also suggested that isobaric spinals may have a lower risk of hypotension and high spinal compared to hyperbaric solutions (highest spinal level attained is usually lower when using isobaric bupivacaine). In addition, Rung et al. also advocated for adding a small dose of fentanyl (25 mcg) for intraoperative and postoperative analgesia. At this dose, they reported no significant opioid side effects. In fact, using this technique of spinal anesthesia for single-level disc surgery, most patients in this study were reportedly discharged on the day of surgery.

Dagistan et al. [22] reported performing spinal anesthetics with a single injection at L3-4, using a 25G Quincke needle, and administering 3 mL 0.75% bupivacaine with 8.5% dextrose (hyperbaric solution). Patients in this study received propofol at 25–50 mcg/kg/min for sedation. Postoperatively, rehabilitation and physical therapy involved walking within 6–8 hours after surgery, stretching, and returning to work in 6–8 weeks. Authors reported good outcomes for these patients and recommended the use of spinal anesthesia for spine procedures.

Dagher et al. [51] described performing spinals in the left lateral decubitus position for lumbar spine discectomy. These spinals were performed one to two levels above the herniated disc, using 3–3.5 mL of isobaric 0.5% bupivacaine. This was followed by wound infiltration with 15 mL of bupivacaine with 1:200000 epi prior to surgical incision. Spinals in this study had good effect and provided adequate anesthesia for the procedure.

Detailed Technical Aspects of Epidural Anesthesia for Spine Procedures

In addition to technical aspects of spinal anesthesia for spine surgery, several authors describe the use of epidural anesthesia for spine surgery.

Greenbarg et al. [8] first described the use of a single-shot epidural for spine procedures. They documented preforming the epidural with the patient in sitting or lateral position, with 17G Tuohy needle introduced at the L2-3 interspace. In this study, authors used 6–8 mL of 0.75% bupivacaine with 1:200000 epinephrine as a single dose for the spine procedure. They reported that this technique was safe and feasible.

Demirel et al. [24] reported on the use of epidural catheters for spine procedures. Specifically regarding epidurals in this case, catheters were placed with the patient in the sitting position, using an 18G Tuohy needle and loss of resistance technique via the midline approach. The epidural was placed two levels above the herniated disc (i.e., for L5-S1 herniation, epidural at L3-4). Once the epidural space was located, a 20-gauge epidural catheter was threaded 3–4 cm beyond the tip of the epidural needle, in a cranially directed fashion.

Aspiration via the epidural catheter was negative for CSF, confirmed with a 2-mL syringe. A 3-mL test dose of 2% lido with 1:200000 epinephrine was administered and found to be negative. The catheter was then tunneled subcutaneously 7–8 cm in the cranial direction. Patients were subsequently placed supine, and if no findings of intrathecal injection were noted after 5 minutes from the test dose (i.e., no motor block), an additional 15–20 mL of 0.5% isobaric bupivacaine with 100 mcg fentanyl was given for operative analgesia. The sensory level achieved by epidural anesthesia was tested with pinprick sensation (usually between T6 and T10), once the patient had adequately self-positioned. Additional bupivacaine was given via the epidural if inadequate anesthesia was noted at the beginning of the case. In addition, 10 mL of 0.5% bupivacaine was given intraoperatively for prolonged surgery. In this study, for postoperative analgesia, 0.125% bupivacaine with 2mcg/mL of fentanyl was infused at 10 mL/hour via the epidural at the end of the case and continued for 2 days.

In this study, no complications were documented related to the epidural technique, and no patients had their epidural catheter visible in the surgical field during the operation. Moreover, there were no incidences of venous air embolus. Four patients required supplemental local anesthesia via the epidural catheter intraoperatively (given for surgery longer than 150 minutes). Intraoperative boluses via the epidural catheter produced pain relief within 5 minutes after epidural catheter injection. Two patients required additional intravenous fentanyl during the surgery, but no cases in this study of epidural anesthesia for spine surgery required conversion to general anesthesia.

Akakin et al. [29] also reported on the use of epidurals for single-level lumbar spine surgery. In this study, patients receiving epidurals were given a single injection of 20–30 mL of 2% lidocaine with epinephrine 1:200,000, as well as 100 mcg of fentanyl, injected via an epidural catheter placed at least two levels above the surgical site. Epidural injections were done at a single level, between T12 and L5, with the majority of injections being done between L2-3 and L3-4. No instances of dural puncture occurred, and no cases were converted to general anesthesia. The epidural catheter was left in place intraoperatively to supply additional anesthesia for unexpected prolongation of the procedure. Patients self-positioned prone and received propofol and midazolam for intraoperative sedation, as well as minimal supplemental oxygen in the form of nasal prongs at 2 L/min. Authors found the use of epidural analgesia to be technically safe and feasible for spine surgery.

Ezhevskaya et al. [31] described the use of combined epidural and general anesthesia for spine surgery. Authors performed the epidural three to four segments above the expected site of surgery, and the epidural catheter was left 3 to 6 cm into the epidural space. The epidural was then tested by aspiration (assessing for accidental intrathecal placement by aspirating for cerebrospinal fluid – CSF) and a test dose (administration of 2 mL of 2% lidocaine with 1:200,000 epinephrine to assess for accidental intrathecal placement – motor block or intravascular placement – tachycardia from epinephrine). After confirming appropriate epidural placement, authors administered a bolus of ropivacaine (0.375–0.75% solution, 3–10 mL in incremental doses) with 100 mcg of fentanyl. This bolus served as the initial operative anesthesia. Intraoperatively, authors maintained patients with general anesthesia (1 minimal alveolar concentration of sevoflurane with bispectral index monitoring for depth of anesthesia) and epidural infusion (0.2% ropivacaine, 2 mcg/mL fentanyl, and 2 mcg/mL epinephrine at 5–10 mL/hour).

Khajavi et al. [28] also studied combined epidural and general anesthesia for spine surgery. In this study, patients received a single-shot epidural consisting of 18 mL of 0.25% bupivacaine (45 mg) and 100 mcg fentanyl in 18 mL of distilled water. The injection was performed at the same level or one level below the planned surgical site, in the sitting position, using an 18G Tuohy. Patients subsequently received general anesthesia, and outcomes of the epidural + general anesthesia group were compared to those of a control group receiving general anesthesia alone. The general anesthesia induction in both cases was similar, consisting of thiopental, fentanyl, midazolam, and atracurium. Authors concluded that epidural anesthesia was safe and provided numerous benefits (improved analgesia, hemodynamic stability) in combination with general anesthesia.

Moreover, Yoshimoto et al. [25] described the use of epidural and general anesthesia for spine surgery. In this study, authors placed epidurals within one to two levels of the cephalad segment of the operative site. Similar to other reports, epidural catheters were inserted through an 18G Tuohy needle, with the tip confirmed in the epidural space after using loss of resistance technique. Also similar to other reports, the epidural catheter was threaded 5 cm into the epidural space, in the cephalad direction. Operative anesthesia was initiated with a bolus of 15–20 mL of 0.5% bupivacaine, along with 1–3 mg of epidural morphine. The dose of local anesthetic and opioid administered via epidural were specific to the patient's age, height, and weight. Interestingly, in this study, authors removed the epidural catheter immediately after the injection (epidural catheter was not left in place for intraoperative "top-up" of anesthesia or intraoperative boluses). No additional epidural injections were given during or after the surgery. Patients receiving epidurals in this group also received general anesthesia (total intravenous anesthesia with propofol infusion, vecuronium, and endotracheal intubation). Authors concluded this technique was safe and effective.

Several other reports exist detailing the use of epidural anesthesia for spine surgery. Ulutas et al. [36] performed

single-shot epidurals one to two levels above the operative field, utilizing an 18G Tuohy needle and loss of resistance technique. In this study, authors administered 50 mcg of fentanyl and 100 mg of lidocaine (5 mL), as well as 10 mL of 0.5% bupivacaine. Patients in this study did not receive epidural catheters and instead had their spine procedures completed under single-shot epidural anesthesia. Immediately after injection, patients were positioned horizontal, and block levels were tested. Following confirmation of adequate anesthesia levels, patients were positioned prone, and intraoperative sedation was administered using midazolam 0.03 mg/kg. Patients tolerated the spine procedures well under epidural anesthesia.

Finally, Nicassio et al. [48–52] performed a prospective study comparing lumbar microdiscectomy under epidural anesthesia in the sitting position to lumbar microdiscectomy under general anesthesia in the genupectoral position. Authors analyzed 23 patients with surgeries performed in the epidural and sitting group versus 238 patients with surgeries in the general anesthesia and prone or knee-chest position. Throughout the study, no patients experienced complications linked to epidural placement, and only one patient experienced a small dural tear as a surgical complication. Twenty of 23 patients receiving epidural anesthesia expressed satisfaction with the level of analgesia, while three patients in the epidural group reported poor analgesia. All patients found the sitting position comfortable. Authors noted that the sitting position had surgical advantages including better patient comfort, recreating spine loading conditions similar to orthostasis, and a "cleaner" operative field using gravity to drain blood. However, with operations in the sitting position, there were concerns regarding the patient developing a dural tear and CSF leak. Overall, authors found that epidural anesthesia allowed for a reduction in anesthesia and surgical times, as well as reduction in complications and length of stay.

In this study, Nicassio et al. [52] performed neuraxial anesthesia via the midline approach, with the patient sitting. Epidural injection was performed two spaces above the prolapsed disc, with a 17-gauge needle and identification of the epidural space identified with loss of resistance to air. Specifically regarding the anesthetic, 8–10 mL (depending on BMI) of ropivacaine 0.75% was injected as a single-shot bolus, and the patient remained sitting for 30 minutes. After the induction of neuraxial anesthesia, the patient was positioned on the surgical table in the sitting position, and microdiscectomy was performed in this position.

Overall, the technical aspects of epidural placement for spine procedures seem to suggest that both single-shot and catheter-based techniques are feasible, particularly when the site of epidural injection is selected to be a one to two interspaces away from the surgical site. Studies seem to report that epidural anesthesia is safe and effective as the primary or sole anesthetic for spine surgeries. Epidural anesthesia may also be combined with general anesthesia for spine procedures with beneficial outcomes.

Detailed Technical Aspects of Combined Spinal-Epidural Anesthetics for Spine Procedures

In addition to spinals and epidurals for spine procedures, some authors describe the use of combined spinal-epidural anesthesia for spine surgery. Jellish et al. [11] examined the use of combined spinal and epidural analgesia for spine surgeries. Specifically, the authors administered spinal anesthesia to patients for their lumbar spine procedures and evaluated the role of additional epidural clonidine versus additional local anesthetic (bupivacaine) infiltration at the incision site on postoperative outcomes. Authors enrolled 120 patients receiving lumbar surgery. Each of these patients received a bupivacaine spinal supplemented by either 150mcg of epidural clonidine or placebo and/or incisional bupivacaine or saline. In terms of study results, no differences were noted in intravenous fluid administration, blood loss, intraoperative hypotension, or bradycardia among all groups. Postanesthesia care unit pain scores were lower, and the demand for analgesics was lower in patients who received both epidural clonidine and subcutaneous bupivacaine in addition to their bupivacaine spinals. Patients who received epidural clonidine had improved postoperative hemodynamics. Hospital discharge, urinary retention, and other variables were not significantly different. Authors concluded that epidural clonidine was a good supplement to spinal anesthesia for spine surgery, which provides improved postoperative analgesia and hemodynamic stability with no complications.

Specific to this study [11], neuraxial anesthesia was performed with the patient in the sitting position, at L3-4 or L4-5. A 17-gauge Tuohy combined spinal-epidural needle was advanced to the epidural space, and a 27-gauge Sprotte spinal needle was inserted through the epidural needle until dura was entered and CSF visualized. For the spinal anesthetic, 1.5 mL of 0.75% spinal bupivacaine (11.25 mg) was injected into the CSF. The Sprotte spinal needle was subsequently removed, and 10 mL of study solution was injected into the epidural space (this solution was either 150 mcg of clonidine or 10 mL saline). Patients were then positioned supine until an appropriate level of spinal anesthesia was achieved and then rolled prone and self-positioned until comfortable. Oxygen was administered via nasal prongs at 2 L/min, and patients received intraoperative sedation with propofol infusion at 25–50 mcg/kg/min. Authors concluded that the addition of epidural clonidine to spinal anesthesia for spine surgery provided effective adjunctive anesthesia.

Duger et al. [53] also studied the anesthetic, analgesic, and side effects of combined spinal-epidural anesthesia for spine surgery. In this study, the authors compared the effects of spinal, epidural, and combined spinal-epidural anesthesia. The study involved 66 patients undergoing lumbar laminectomy, who were randomized into 3 groups: (1) spinal anesthesia, (2) epidural anesthesia, and (3) combined spinal-epidural anesthesia. The demographics, surgical times, and peak sensory levels achieved by neuraxial anesthesia were similar in all three groups. Hemodynamic variables (heart rate, mean arterial blood pressure) and oxygen saturation did not differ between groups. No differences were noted intraoperatively in the level of sedation between groups. Postoperatively, however, sedation scores were similar for epidural and combined spinal-epidural groups, while sedation scores were significantly lower in those receiving just spinal anesthesia. Postoperative pain scores were higher in the spinal group compared to the epidural and combined spinal-epidural groups; however, the time to use of first PCA was similar in all groups. Total use of morphine and postoperative nausea and vomiting over the 24-hour study period were higher in those who received spinal anesthesia compared to those who received epidural or combined spinal-epidural anesthesia. However, patients receiving spinal anesthesia had a lower rate of pruritus than those receiving epidural and combined spinal-epidurals. Authors concluded that all three techniques of neuraxial anesthesia are adequate and effective for lumbar laminectomies, but epidural and combined spinal-epidural techniques may be more effective than spinal anesthesia alone for postoperative analgesia, with less side effects.

Local Anesthesia for Spine Surgery

In addition to neuraxial anesthesia, there are some reports of local anesthesia and even peripheral nerve blockade for spine procedures and spine surgeries.

Chen et al. [54] reported on the use of local anesthesia for endoscopic discectomy for L5-S1 disc herniation with an interlaminar approach. The authors performed a prospective, randomized controlled trial of general anesthesia versus local anesthesia for endoscopic discectomy. In this study, 123 patients with L5-S1 disc herniation were enrolled and received endoscopic interlaminar lumbar discectomy. The surgeries were performed by two surgeons with different anesthesia preferences (local anesthesia vs. general anesthesia) in two medical centers. Back pain, leg pain, and functional status (Oswestry Disability Index) were improved after surgery in the patient group as a whole; however, mean hospital length of stay was shorter in patients receiving local anesthesia compared to those receiving general anesthesia. Complications included one case of dural tear and three cases of disc herniation recurrence within 1 month, requiring open or redo endoscopic surgery. Authors concluded that general anesthesia and local anesthesia were both effective and safe for this procedure; however, local anesthesia appeared to be better than general anesthesia for length of hospital stay.

Sairyo et al. [55] also reported on local anesthesia for spine procedures. These authors focused on patients receiving minimally invasive percutaneous endoscopic discectomy with a transforaminal approach under local anesthesia. This study has described the use of local anesthesia for this minimally invasive procedure and also noted that Japanese authors had previously used the technique since 2003, presenting three successful cases.

Moreover, Jha et al. [56] also reported the use of local anesthesia for percutaneous endoscopic lumbar discectomy for a large herniated disc causing cauda equina syndrome. In this case report, the lumbar disc herniation was resected endoscopically through a transforaminal approach in an awake patient under local anesthesia. Authors suggested that percutaneous endoscopic discectomy under local anesthesia was superior to open surgery, faster to perform, and provided the ability to undertake immediate intervention in a patient threatened with cauda equina syndrome. Furthermore, authors hypothesized that the local anesthetic technique would be associated with less perioperative complications and morbidity, minimized soft tissue damage, and allowed for early mobilization with better outcomes and greater patient satisfaction compared to traditional general anesthesia techniques. Authors concluded that the use of local anesthesia for this minimally invasive technique was effective and feasible and allows more options for subsequent surgeries and spine procedures in the future, whether open or minimally invasive.

Numerous other case reports of local anesthesia for spine surgeries also exist. Teifeian et al. [57] presented a case of transforaminal endoscopic surgery under local anesthesia for a ventral epidural thoracic spinal tumor resection.

Yamashita et al. [58] described the use of local anesthesia for a percutaneous endoscopic discectomy (minimally invasive technique) for resection of a repeat herniated nucleus pulposus. In this case, the patient had previously undergone transforaminal percutaneous endoscopic discectomy (PED) under local anesthesia 2 years prior and suffered a recurrent right-sided disc herniation. The authors performed another transforaminal PED using the same previous route, removing a small adhesion around the L5 nerve root, successfully removed the mass and performed surgery under local anesthesia. The use of local anesthesia was able to provide good postoperative analgesia, less postoperative pain, earlier discharge, and a faster return to function and sport activities in this patient. Authors concluded that local anesthesia was safe and effective for minimally invasive PED.

Wang et al. [59] presented a case series of endoscopic technique for interbody fusion combined with percutaneous screw fixation. In this series, authors documented that there was no requirement for general anesthesia in this spinal procedure. Ten consecutive patients undergoing this procedure were followed for 1 year with good outcomes. Endoscopic access was used for neural decompression, discectomy, endplate preparation, and interbody fusion. Authors also reported that pedicle screws and connecting rods were placed percutaneously in cases of spine stabilization. In this series, authors used liposomal bupivacaine for long-lasting analgesia and combined local anesthesia with sedation for patient comfort. No narcotics or regional anesthetics used (only local anesthesia), and all patients had their spine procedures successfully completed endoscopically, with no conversion to open surgery. Mean operative time was 113.5 minutes, and mean blood loss was 65 mL, while the mean length of hospital stay was 1.4 days. No complications and no cases of no non-union were reported on follow-up. Authors concluded that in the case of these new minimally invasive and percutaneous techniques for spine surgery, local anesthesia could be the anesthetic of choice and provide significant benefits.

With growing evidence to support the feasibility and efficacy of using local anesthesia for spine procedures, Sanusi et al. [60] conducted a 2-year retrospective assessment of patients who underwent transforaminal endoscopic discectomy under local anesthesia. This review was conducted at a tertiary neurosurgical center in the United Kingdom and involved procedures done by a single surgeon. A total of 201 patients underwent endoscopic discectomy, with a mean age 41 years, male/female ratio of 1.3:1, and most common level of operation being L4-5. All discectomies were done under local anesthesia in this review, with the average operative time being 110 minutes. In this review, 95% of patients were discharged within 7 hours postoperatively. Pain scores (visual analogue scale – VAS) dropped from 7/10 to 0–1/10 in 95% of the patients 2 weeks postoperatively. About 87% of patients returned to activities of daily living shortly after surgery. There were no instances of CSF leak, hematoma formation, or surgical site infection. About 1% of patients in the study had nerve root injury, while 6% had recurrent herniation and required microdiscectomy. This review adds to the growing evidence that minimally invasive spine procedures are feasible and safe under local anesthesia.

Fang et al. [61] published a study comparing epidural and local anesthesia for lumbar transforaminal endoscopic surgery. The authors of this study noted that percutaneous endoscopic lumbar discectomy for lumbar disc herniation has largely been done under local anesthesia. However, some patients experience pain and have difficulty tolerating the surgery during intervertebral foramen expansion. Thus, authors undertook a retrospective analysis of lumbar transforaminal endoscopic surgery at a single center, reviewing 286 cases, 121 using local anesthesia and 165 using epidural anesthesia. For lumbar transforaminal endoscopic surgery, the authors found no difference between neurologic complications between the two groups and no difference in postoperative outcomes or intraoperative radiation exposure. Patient satisfaction was 73.6% in local anesthesia group and 91% in the epidural group ($P < 0.001$). Authors concluded that epidural anesthesia was feasible and safe and that there was no broad difference between local anesthesia and epidural anesthesia in terms of neurologic complications. Interestingly, even for this minimally invasive procedure, authors noted that patient satisfaction was higher in those receiving epidural anesthesia compared to local anesthesia. Epidural anesthesia may be an excellent alternative to local anesthesia in patients presenting for minimally invasive lumbar spine surgery.

Finally, many reports exist regarding the use of local anesthesia for vertebroplasty, kyphoplasty, and other minimally invasive vertebral body procedures. These procedures may be performed under local anesthesia or general anesthesia. Emre et al. [62] assessed outcomes of vertebroplasty under local anesthesia in patients deemed high risk for general anesthesia. In this study, vertebroplasty was done under local anesthesia in 62 cases of patients with osteoporotic vertebral fractures. No patients had a history of trauma, and all were classified as ASA-PS III. The average age of patients in this study was 77.5 years, and the mean VAS pain score before surgery was 7.52. On the first day after surgery, the mean VAS pain score was 3.55, followed by 2.03 in week 1 after surgery, and 0.87 a month after surgery. No major complications were noted in patients undergoing vertebroplasty with local anesthesia (one asymptomatic cement embolus was documented). Authors concluded that vertebroplasty under local anesthesia was safe and effective, providing adequate pain control and allowing for early ambulation.

Overall, there is growing evidence to suggest that local anesthesia, in addition to regional techniques and neuraxial blocks, is safe and effective for lumbar spine procedures, specifically for minimally invasive surgeries.

Summary

The use of regional anesthesia for spine pain and spine procedures has dramatically increased in recent years. Regional and local anesthesia can be used as the primary anesthesia for spine surgeries and procedures and also provide analgesia for spine pain and improve pain control following spine procedures. Regional anesthesia for spine surgery and spine pain has traditionally involved the use of neuraxial techniques (spinal, epidural, and combined spinal-epidural anesthesia). These techniques can provide benefits over general anesthesia in many studies of spine surgery (improved postoperative pain control, hemodynamic stability, and postop-

erative recovery; reduced postoperative nausea and emesis, operative blood loss, length of hospital stay, anesthesia/surgical time, and healthcare costs). However, in recent years, these techniques have been expanded to include growing reports of "paraneuraxial" anesthesia and other peripheral, non-neuraxial nerve blocks. With the advent of ultrasound-guided regional anesthesia, neuraxial and peripheral blocks will continue to become increasingly popular, safe, and effective, with expanding applications in the realm of spine surgery and spine pain. Further studies are required and will continue to elucidate the optimal dosing, use, and techniques for administering regional anesthesia for spine procedures.

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Radiation Therapy for Oncologic Spine Pain

33

Brent D. Cameron, Christien A. Kluwe, and Albert Attia

Key Points

- Safe, effective treatment
- Provides durable palliation
- Can be done in as little as one session
- May be repeated, dependent on clinical scenario

Case Presentation

JS is a 78-year-old male with an oncologic history significant for intermediate-risk prostate cancer initially treated with surgical resection, now with biochemical recurrence. He is currently managed with anti-androgen therapy. At routine follow-up, he describes a dull, aching pain in his low back that has progressively worsened over the last several weeks. He denies any abnormal paresthesia such as tingling or numbness about the abdomen. His motor functions are intact and he does not have difficulties with voiding. A 99Tc-MDP radionuclide bone scan demonstrates increased radiotracer uptake in several ribs bilaterally as well as a focus of intense activity in the L2 vertebral body. Subsequent MRI demonstrates a marrow-replacing enhancing mass in the vertebral body without cortical breakthrough or loss of vertebral height; there is no evidence of abnormal spinal cord signal (Fig. 33.1). The patient's pain initially responded to opioids, but opioids have since been discontinued due to intolerable constipation and dizziness. The patient's medical oncologist inquires about possible radiotherapy options.

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Introduction

Metastases to the bone are a common occurrence in solid malignancies, with approximately a half of all patients developing these bone metastases during the course of their disease [1, 2]. This is particularly true for patients with breast, prostate, and lung cancers with incidence rates of 65–75%, 65–75%, and 30–40%, respectively [3]. Though all bone metastases can cause morbidity in the form of pain and limited function, tumor deposits in the spine are of exceptional concern: not only does the location in the axial spine increase the propensity for pain with daily activities, extraosseous extension can impinge nerves, and destruction of vertebral bodies can result in extremely painful compression fractures with concomitant damage to the spinal cord. Furthermore, patients who develop paralysis from cord compression are at increased risk for death, with a 6-month survival of 31% vs. 71% for ambulatory patients [4]. For this reason, the development of bony pain in a patient with a known metastatic disease should be aggressively managed in a multidisciplinary manner.

Clinical Indications

While the absolute criteria for initiation of palliative radiotherapy for spinal metastases vary by institution and physician, several factors must be considered. Oncologic pain is heterogenous and diffuse in nature and is initially managed with pharmacologic therapy at many centers. When medical management fails to adequately improve the patient's quality of life or is poorly tolerated, more invasive means of resolving pain are introduced. In addition to symptomatic presentation, surveillance and diagnostic imaging may discover asymptomatic lesions that present risk for subsequent pathologic fracture. For spinal disease, the Spinal Instability Neoplastic Score (SINS) has been developed to better triage which patients may benefit from surgical intervention and which may be managed nonoperatively (e.g., with radiother-

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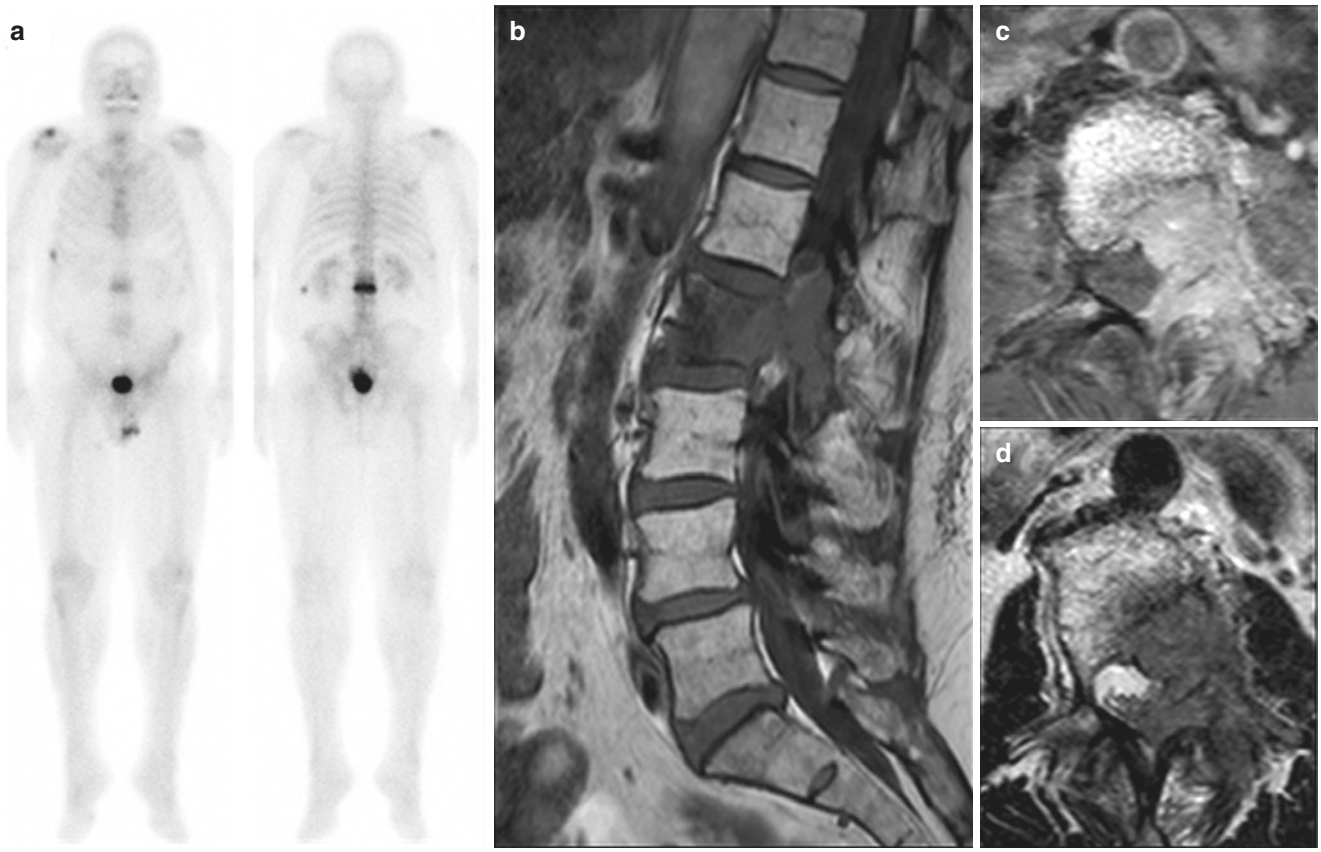


Fig. 33.1 (**a**) 99Tc-MDP radionuclide bone scan shows intense uptake in L2. (**b**) T1-weighted MRI L-spine showing marrow-replacing process involving the entire vertebral body of L2 without significant height collapse. (**c**, **d**) T1 + c- and T2-weighted images, respectively, demonstrating involvement of the posterior elements with limited extension into the epidural space – the thecal sac is displaced though CSF is unobstructed

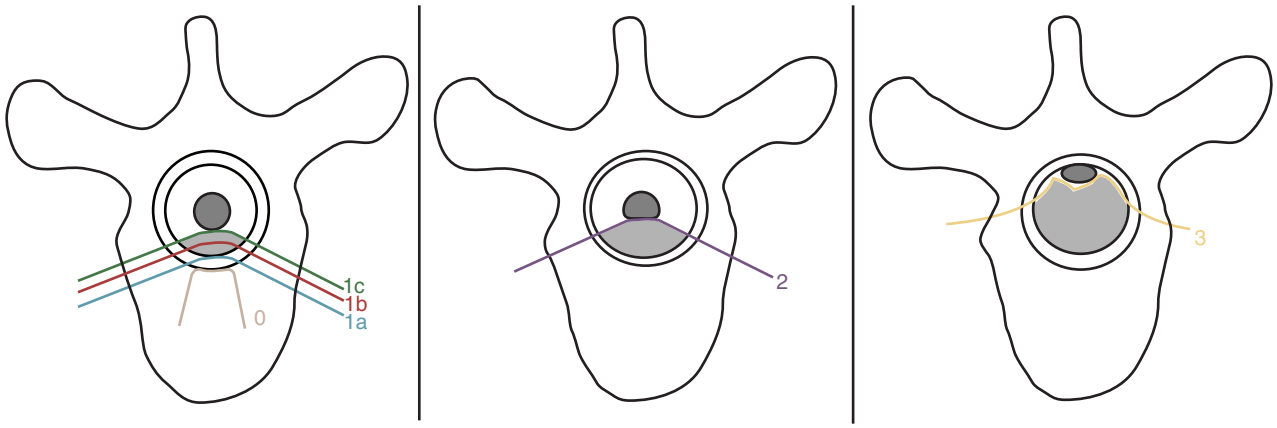
Table 33.1 The Spinal Instability Neoplastic Score (SINS) grades tumor-related instability of the vertebral column with good intra-observer reliability and may guide physicians on management of spinal metastatic disease. Posterolateral involvement refers to fracture or tumor replacement of the facet, pedicles, or costovertebral joint

	0	1	2	3
Location	Rigid (S2-S5)	Semirigid (T3-T10)	Mobile (C3-C6, L2-L4)	Junctional (O-C2, C7-T2 T11-L1, L5-S1)
Mechanical pain		Pain-free	No	Yes
Bone lesion	Blastic	Mixed	Lytic	
Radiographic alignment	Normal		Deformity (kyphosis/scoliosis)	Subluxation (4 points)
Vertebral body collapse	None	>50% involved with no collapse	<50%, collapsed	>50%, collapsed
Posterolateral involvement	None	Unilateral		Bilateral
Score				
1–6	Stable			
7–12	Potentially unstable			
13–18	Unstable, operative management indicated			

Adapted from Fisher et al. [5]

apy) (Table 33.1) [5]. Alternatively, the Mirels criteria can be used to base decision-making; however this is more commonly utilized in peripheral lesions of weight-bearing bones (e.g., femoral metastases) [6].

In a fraction of spine disease, tumor may have broken through the cortex of bone and expanded into the spinal canal. A common nomenclature has been generated to grade the significance of this extension (Fig. 33.2). Depending on the



Bilsky Grade	Ryu Grade Correlate
0: bone only disease	0: bone only disease
1a: epidermal impingement w/o deformation of sac	I: epidural disease w/o sac compression
1b: deformation of sac w/o abutment of cord	II: involvement of sac with mild compression
1c: deformation of sac w/abutment of cord	III: tumor impingement to spinal cord
2: spinal cord compression with visible CSF	IV: spinal cord displacement with visible CSF
3: spinal cord compression with no visible CSF	V: spinal cord compression with no visible CSF

Fig. 33.2 Radiographic grading of epidural spinal cord compression as described by Bilsky et al., with correlates as described by Ryu et al. A higher grade (Bilsky 2–3 or Ryu IV–V) indicates increased risk of cord compression and may require surgical decompression prior to radiotherapy. (Reprinted with permission from, Bilsky et al. [10, 11])

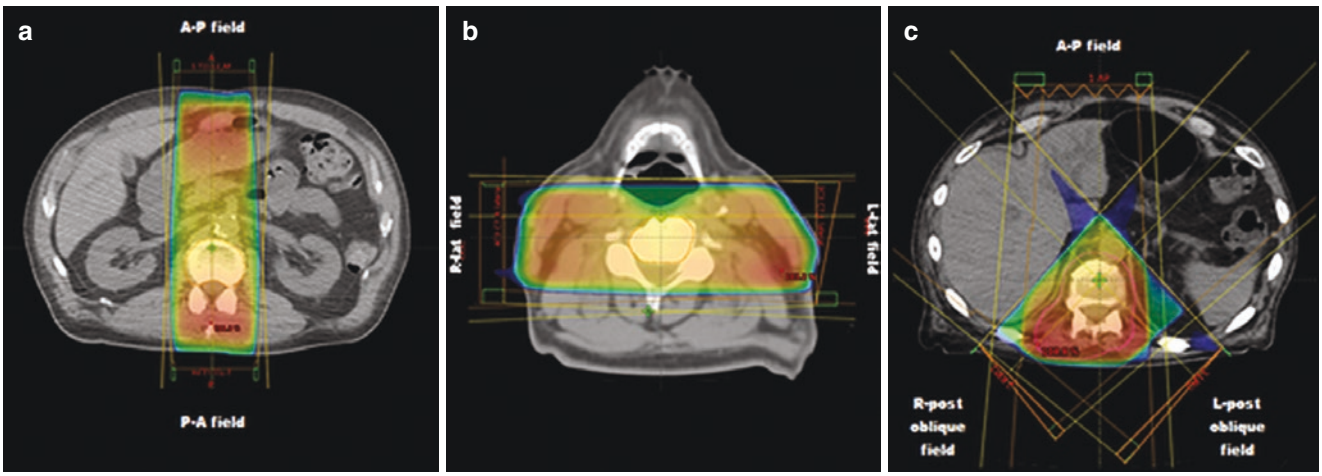


Fig. 33.3 3D conformal spinal radiotherapy. (**a**) Representative "AP-PA" lumbar spine plan. (**b**). An "opposed lateral" beam arrangement for treatment of cervical spine. (**c**). Conformal 3D plan with posterior wedge pair beam arrangement to limit normal tissue toxicity

extent and acuity of spinal cord compression, surgical management may be indicated. Malignant cord compression can be identified by a loss of T2-weighted CSF signal within the thecal sac at any level with associated cord edema. It should be noted that radiotherapy cannot alleviate cord compression immediately (this takes several days) and may only be indicated when neurologic compromise is irreversible and pain control becomes a paramount concern. In several retrospective series, duration of paresis <48–72 hours is correlated with regaining ambulation [7–9]. Thus, patients with a neurologic deficit >72 hours are considered unlikely to regain function.

3D Conformal Radiotherapy

The mainstay of radiation therapy to the spine has been traditional external beam radiotherapy. Historically, nearly any spinal level can be treated with the limiting factor being the maximally tolerated spinal cord dose before the risk of myelopathy becomes unacceptable. Short- and long-term toxicity from 3D conformal therapy over 1–2 weeks is generally well tolerated. This is due in part to the limited amount of normal tissue that is treated in most standard plans (Fig. 33.3).

The patient may be positioned in whatever manner is most comfortable, typically lying flat on a pad on the treatment table. The simplest plan utilizes two opposed beams of radiation, commonly called an "AP-PA approach." In this scenario a homogenous dose is delivered across the axial plane of the patient (see Fig. 33.3a), delivering the therapeutic prescription to both the spine and internal organs within its path. This may result in acute toxicity, manifesting as intermittent diarrhea, nausea, or esophagitis depending on the affected organs. In the cervical spine, opposed lateral fields may be used in the limited region between the shoulders and base of skull. This allows for delivery of dose while avoiding radiation through the jaw and esophagus (Fig. 33.3b). In cases where it is imperative to minimize toxicity to thoracoabdominal organs (e.g., acutely damaged from recent chemotherapy, prior irradiation, intractable nausea, etc.), additional convergent beams can be utilized to minimize dose to normal tissues. In this "three-field approach," an AP field is opposed by a pair of posterior oblique beams. Such an arrangement greatly reduces the dose delivered to centrally located organs while also avoiding critical structures such as the kidneys (see Fig. 33.3c).

Though many clinicians are aware of the efficacy demonstrated by radiotherapy, few outside the discipline are familiar with the timing of anticipated response. In a prospective trial by Nomiya and colleagues, 91 patients were evaluated for timing and extent of pain response after irradiation [12]. Complete pain relief occurred in 49% of cases, while 91% experienced a greater than 50% reduction in pain scores. The average time to achieve a 50% response was 13 days, while a complete response occurred by 24 days on average. In our clinic, we counsel patients that a pain response may be noted in the first 72 hours and that this will progressively continue for approximately 4 weeks, at which point a new pain baseline may be established.

Duration of treatment has typically been at the discretion of the treating physician, and schedules ranged from single days to 3 weeks long. A randomized trial sought to compare short- and long-course radiotherapy utilizing two popular fractionation schedules: 8 Gy in a single fraction vs. 30 Gy in 10 fractions [13]. In those patients with breast or prostate cancer, overall response rate based on the Brief Pain Inventory was not different between the two treatment groups at 3 months. The long course was associated with more acute toxicity, while long-term toxicity was rare and comparable between the two groups. Of note, the short-course group did require retreatment at double the rate of the long course (18% vs. 9%). However, one out of three patients no longer required narcotic pain medications at 3 months. While this trial was not limited to painful spine metastases, they were included and comprised a majority of the treated sites.

As tumor cells respond to cytotoxic radiotherapy, local inflammation can acutely worsen symptoms. A prospective symptom assessment trial by Loblaw et al. in 2007 established the incidence of pain flare after radiotherapy to bone metastases, particularly in those receiving a short course of 8 Gy × 1 [14]. Subsequent interventional investigation by Chow et al. demonstrated reduction in incidence of pain flare from 35% to 26% when patients were pre-treated with corticosteroids [15]. In our practice, we balance benefit versus the risks of steroid therapy. When indicated, patients are prescribed a 4-day course of 8 mg dexamethasone daily to start on the first day of radiation. Patients must be counseled about the risk for gastric ulcer, especially those with previous history of bleeding gastric ulcer. Prophylactic proton pump inhibitors may be prescribed. Furthermore, diabetic patients should be advised to closely monitor blood glucose levels and adhere to a diabetic diet.

Stereotactic Radiotherapy (SRS)

Stereotactic ablative body radiotherapy (SABR) involves the delivery of highly conformal radiation in doses that exceed conventional dose ranges – some applications deliver as much as 2400 cGy in a single fraction compared to the traditional 200–800 cGy fractions. High-dose radiotherapy is delivered in one to five treatments and is thought to be directly ablative to tumor cells while limiting dose to surrounding normal tissues. Operationally, SRS is limited to single-fraction delivery and SABR may be up to five fractions. Furthermore, treatment with 8 Gy × 1 has not been delivered in a manner consistent with SRS setup and delivery, and the dosimetric parameters are quite different such that 8 Gy delivered in a single session should not be considered SRS. Historically SRS/SABR has been reserved for treatment in the re-irradiation setting. However, upfront treatment of patients with first-line SRS/SABR is an evolving paradigm where patients with oligometastatic disease or those known to have targetable mutations with systemic therapy are now being considered.

In a Phase 1–2 trial utilizing SABR for spinal metastases, Wang et al. enrolled 149 patients on the trial that delivered 27–30 Gy in three fractions to the spine [16]. Their primary endpoint was the frequency and duration of pain relief. At a median follow-up of 15.9 months, 54% of patients reported no pain at 6 months post-SABR compared to 26% of patients pre-SABR. A significant decrease in opioid use at 6 months was also observed. Similarly, the RTOG (Radiation Therapy Oncology Group) conducted a Phase II/III study of image-guided SABR for localized spine metastases (RTOG 0631). Eligibility criteria included localized spine metastases to either one level, two adjacent levels, or a maximum of three sites, minimum of 3-mm gap between the spinal cord and the epidural lesion. Patients were ineligible if there was a compression fracture resulting in >50% spinal height. The trial

Fig. 33.4 Immobilization devices for SABR directed to the spine. (**a**) Alpha cradles (Smithers Medical Products) are single-use custom fitted bags filled with a foam that hardens when activated. (**b**) Multiuse vacuum bags filled with polystyrene beads can be molded to the patient before evacuation of air to lock the beads into place (Vac-Lok, CIVCO Radiotherapy). (**c**) External fixation devices can be coupled with the custom cradles to improve positioning and reproducibility (Body Pro-Lok, CIVCO Radiotherapy)

required an MRI within 4 weeks of treatment initiation to monitor for acute and long-term changes to both the bone and spinal cord. Though this trial is ongoing, initial Phase II data demonstrates the feasibility and safety of SABR in this setting [17]. The Phase III comparison will be 8 Gy × 1 versus 16–18 Gy in a single fraction with pain control as a primary endpoint; secondary endpoints include rapidity and duration of pain response, quality of life, and incidence of adverse events. Accrual has closed with results anticipated in early 2022.

Beyond palliation of pain, SABR can also provide excellent local control of disease, a particularly important concept now that patients are living much longer with oligometastatic disease. In a single-institution, prospective, non-randomized cohort of 500 cases at the University of Pittsburgh Medical Center, SABR demonstrated long-term tumor control rates of 90% when used as the primary therapy. When including re-irradiated fields, long-term control approximated 88%. Most notably, long-term control was demonstrated in all breast, lung, and renal cell carcinoma metastases but only 75% of melanoma metastases (a notoriously radioresistant pathology) [18].

Patient position and immobilization are of critical importance for SRS/SABR given the higher doses per fraction and the highly conformal radiation delivery. For the above trials, supine position was required. Depending on the spinal region to be treated, a variety of immobilization devices can be considered including vacuum bags, alpha cradles, or SRS frames (Fig. 33.4). For treatment of the cervical spine, a rigid head/neck immobilization device is highly recommended. Daily pre-treatment onboard imaging should be performed to allow for target localization, preferably with a cone beam CT. This facilitates high-fidelity dose delivery by matching bony landmarks on planning scans with real-time data and ensures vital organs are safely avoided. Using these systems, treatment delivery can be done with 1-mm accuracy.

Physicians considering SABR for their patients should be aware that a pain flair can be common and counsel their patients appropriately. Chiang and colleagues found that 68% of steroid-naive patients had a pain flare after SABR [19]. This most commonly occurred the day after treatment and was rescued with dexamethasone. Careful consideration must also be given to the risk of fracture. One group has reported that the post-SABR fracture progression may be as high as 39% [20]. Lytic lesions involving >40% of the vertebral body and involvement of vertebral bodies below T10 appear to confer the highest risk for fracture progression. Alternatively, the physician must weigh the risks of possible tumor progression which will inevitably lead to fracture progression. Table 33.2 lists suggested characteristics of patients who would most benefit from SABR to the spine.

Table 33.2 Suggested characteristics of patients who would most benefit from SABR to the spine

Ideal candidates for spine SABR
Good KPS (70–100)
Recent spinal MRI at level to be treated
One to three involved sites (oligometastatic disease)
No compression fracture at the treating level
No bony retropulsion into the spinal canal or acute neurologic compromise
Prior radiotherapy to the involved spinal level

Re-Irradiation for Recurrent or Persistent Pain

Re-irradiation of spinal metastases has recently become a topic of interest in palliative care research. Long considered too high risk for causing radiation myelopathy, the development of IMRT initiated the treatment of vertebral bodies without heavy dose overlap on the spinal cord (intensity-modulated radiation therapy, a technical precursor to SRS/SABR that allowed for more conformal treatment volumes). In an early retrospective review of 23 patients at Shizuoka Cancer Center in Japan who underwent IMRT re-irradiation, 1-year local control rates were 88%, pain relief occurred in 65%, and most importantly no late toxicities including radiation myelopathy

or compression fractures occurred [21]. A larger retrospective analysis of 237 spine lesions re-irradiated with SRS at Henry Ford Hospital confirms these early findings. Pain response was achieved in 81% of patients with radiographic tumor control in 71%. Only one patient experienced radiation myelopathy (though this patient also underwent surgical manipulation after completing radiation therapy), and 9.3% developed compression fractures [22].

While SRS/SABR after prior 3D conformal radiotherapy is now generally accepted as safe, there is limited data on repeated courses of stereotactic therapy. While there is no Level 1 evidence, a single-institution retrospective study from the Henry Ford Hospital may provide some guidance. In a 49-patient cohort with 60 tumors re-irradiated with SRS, overall pain response rate was 86%, while radiographic tumor control was seen in 72.5%. Eight patients (21%) experienced adverse effects including myelomalacia, neurologic weakness, and radiculopathy. Of the 83 vertebral bodies re-irradiated, 56 developed compression fractures, 21 (25%) of which were attributed to toxicity. Thus, while repeat courses of SRS may be effective, toxicity risks may be significant, and caution should be exercised [23].

Treatment-Related Toxicities

Radiation myelopathy is the most debilitating and potentially lethal toxicity which radiation oncologists should concern themselves. Historically, dose constraints have been very conservative to avoid the rare case of myelopathy. This typically has led to underdosing of tumor near the spinal cord which theoretically may spare tumor tissue that is then capable of regrowth. Recent Phase 1 data has emerged that shows dose constraints for the spinal cord in those patients who are not operative candidates and are radiation-naive may be unnecessarily low [24]. The four investigational arms of the study were a Dmax (dose to 0.01 cc) of 10Gy, 12Gy, 14Gy, and 16Gy. With median follow-up of 17 months, the authors estimated a 1-year local control rate of 84%. Notably, there were no radiation myelopathies. Dose constraints must be selected based on the capabilities of the facility including the pre-planning image registration, conformality of delivery, onboard imaging capabilities, and the ability of the patient to present for routine follow-up.

Concurrent Chemotherapy

Traditional chemotherapies such as platinum agents, taxanes, antimetabolites, 5-FU, and gemcitabine are typically not given with concurrent palliative therapy – the cytotoxic effect of radiotherapy can be amplified by these agents. Generally, a period of 7 days is allowed to "wash out" the chemotherapy. There is little clinical data on this, with the duration largely dependent on the pharmacokinetics and clearance of the drug in question. Most palliative courses of radiotherapy can be coordinated in between cycles of palliative chemotherapy. For tissues such as the spinal cord however where myelopathy can be a life-threatening event, an overabundance of caution is used to minimize the likelihood of toxicity. Additionally, the choice of conformal techniques such as SBRT or SRS can be utilized to minimize the contribution of radiation to nearby healthy tissues and shrink the overall time period of exposure (one to three fractions as opposed to a more protracted 2-week course).

The contribution of newer therapies such as kinase inhibitors and immune-modulating antibodies to toxicity is poorly understood. First- and second-generation tyrosine kinase inhibitors (erlotinib, crizotinib, afatinib, gefitinib) are notable for poor CNS penetration and typically considered "safe" for concurrent therapy. Newer agents such as osimertinib have demonstrated increased CNS penetration [25]. Though osimertinib preferentially targets mutant EGFR (T790M), wild-type EGFR is still affected, indicating that further studies should be undertaken to assess clinical risk before it is considered a "safe" agent. Likewise, vemurafenib is a BRAF inhibitor that specifically targets V600E variants and has demonstrated increased toxicity when given concurrently with radiotherapy [26].

Concurrent administration of immunomodulatory drugs presents an interesting challenge. Immune checkpoint inhibitors (ICIs) function through blocking signals that downregulate immune responses. Cytotoxic T-lymphocyte-associated protein 4 (CTLA4) is expressed on activated T cells and facilitates a negative modulatory signal; ipilimumab (Yervoy, Bristol-Myers Squibb) blocks this interaction, allowing patient T cells to target a broader variety of antigens [27]. Many cancers secrete ligands for programmed cell death protein 1 (PD-1), which is expressed on lymphocytes and induces apoptosis to promote immune tolerance in the tissue. Monoclonal antibodies such as nivolumab (Opdivo, Bristol-Myers Squibb) block the cell surface receptor PD-1, whereas others such as atezolizumab (Tecentriq, Roche Genentech) inhibit the binding function of PD-L1. Together these agents inhibit the immune-suppressive environment in some tumors, allowing the immune system to target tumor neoantigens. Radiation is particularly relevant in this context as it contributes to local inflammation and can induce neoantigens. Thus, there may be a synergistic effect, and concurrent immunotherapy would be desirable as a means to boost an abscopal response (the response of out-of-field tumor to localized radiotherapy) [28, 29]. Though neurologic adverse events are typically rare with ICIs, this is likely due to the inability of the antibodies to cross the blood-brain barrier. Local inflammation through radiotherapy increases the permeability of the

blood-brain barrier and may facilitate an increase in neurotoxicity from ICIs. What little clinical data exists is retrospective in nature and offers limited guidance in these scenarios. At our institution, concurrent immunotherapy is not actively suspended. Caution should be practiced and patients closely monitored.

Conclusion

In conclusion, metastatic disease to the spine can be a debilitating disease process. Radiation therapy offers an effective and durable option for pain control in these patients with limited toxicity. Patients may be treated with standard external beam radiation in as few as a single treatment to 8 Gy. For a select population of patients, spinal SRS/SABR can be considered as a viable treatment option (Fig. 33.5) for radiation dose distribution. Patients can experience pain flairs during or immediately after completion of therapy, but this often responds to steroids. In most cases, standard chemotherapy should be suspended at least 1 week prior to and during radiotherapy. There is limited Level 1 evidence for targeted agents and immunomodulatory agents during irradiation of the spine. Emerging retrospective data suggests that concurrent radiation therapy with other therapies such as immunomodulatory therapy or chemotherapy may be safe, or even synergistic, but physicians should use caution in this setting.

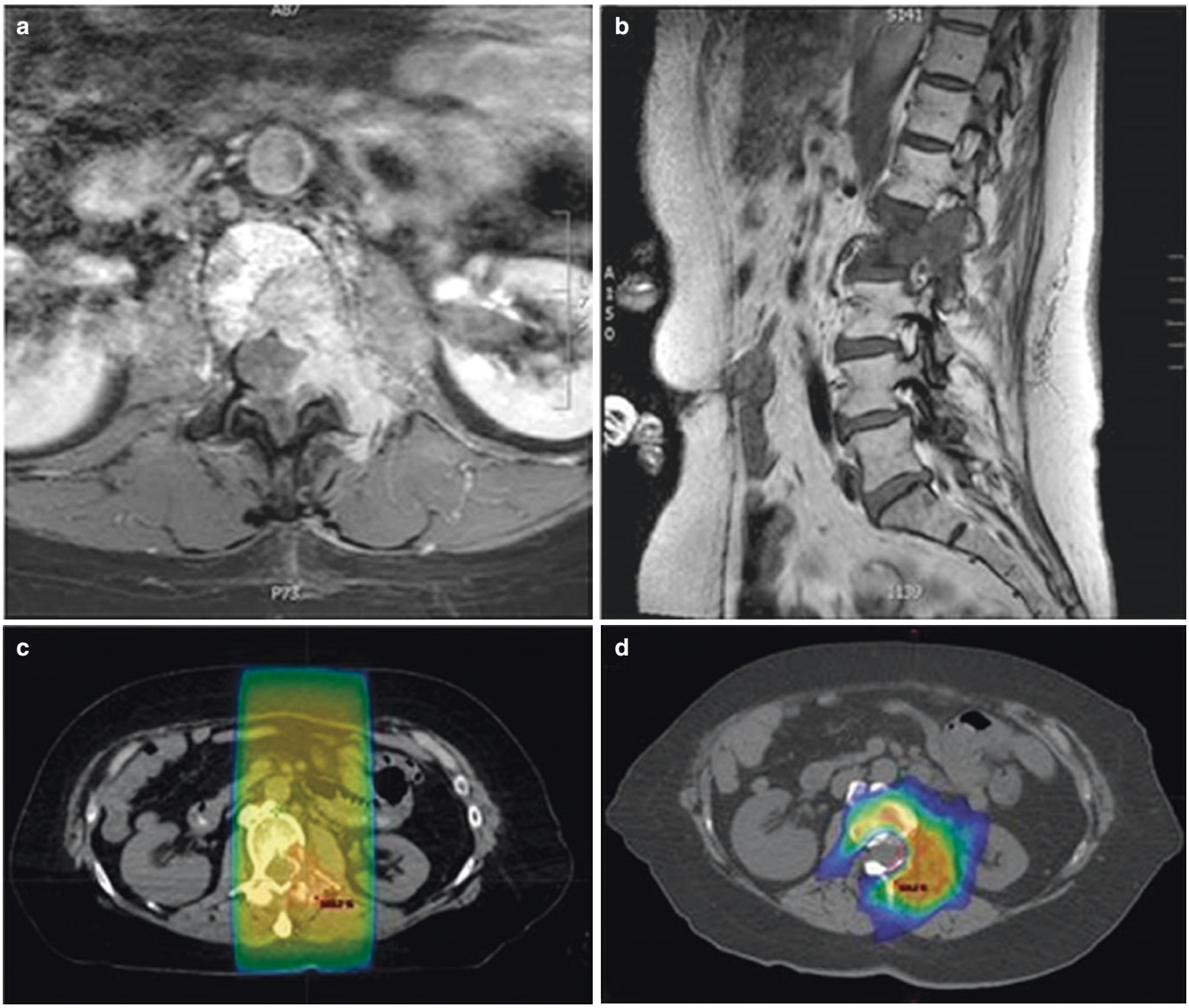


Fig. 33.5 (**a**) Representative axial MRI slice of a patient treated initially with conformal 3D radiation therapy (RT). (**b**) Representative sagittal slice of lesion. (**c**) 3D RT plan for the patient represented in (**a**, **b**). Blue represents 50% isodose line. (**d**) SBRT plan for the same patient in (**a**, **b**) treated several months after treatment in (**c**)

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Rehabilitation Approaches to Spine Care: Physical Therapy, Occupational Therapy, and Aquatic Therapy

34

Elliot W. Yoo, Eve Kennedy-Spaien, and Mark Lueck

Key Points

- Interdisciplinary approach
- Treatment approaches for neck and low back pain
- Treatment tools and modalities
- Aquatic therapy
- Occupational therapy
- How to write a therapy prescription
- Patient education and counseling

Introduction

Spine care can be complex and involve many disciplines. The terms multidisciplinary and interdisciplinary have been utilized interchangeably over the years. There are, however, subtle differences between these two terms. A multidisciplinary approach implies that there are multiple health-care providers involved in the care of a patient's illness. For example, a typical patient with low back pain may first see a primary care physician and receive a prescription to see a physical therapist. If pain persists, they may be referred to a physiatrist, pain management specialist, or a surgeon. The patient may separately be seeking care from a massage therapist, acupuncturist, or a chiropractor. The patient often progresses through the health-care continuum in a fragmented manner developing divergent goals and receiving conflicting messages. An interdisciplinary approach, however, implies that these disciplines work in synchrony with shared objectives and toward common goals. Physical and occupational therapists are critical members of this interdisciplinary team. The primary goals of therapy include reducing pain as well as optimizing function. Treatment plans can vary depending on the treatment preferences and biases of both the patients and therapist, functional goals, as well as the treatment tools available. This chapter is meant to help the practicing clinician better understand the role of physical therapy, occupational therapy, and aquatic therapy in an interdisciplinary approach to spine care.

Physical Therapy for Spine Care

Physical therapists, also known as physiotherapists, play a vital role in spine care. A physical therapist can help patients identify mechanical deficiencies and restore and improve movement, activity, and functioning, thereby decreasing pain and enabling optimal performance. Clinical practice guidelines (CPGs) for the treatment of cervical and lumbar pain have been released by the American Physical Therapy Association (APTA) in 2017 and 2012, respectively. These guidelines allow the physical therapist to develop an impairment/function-based diagnosis to more appropriately tailor treatments to a specific subgroup of patients with neck or low back pain. Additionally, physical therapists may use clinical prediction rules (CPRs) that have variable levels of validation to help guide their treatment plans. As physical therapy has adopted a more evidence-based approach to care, the use of passive modalities such as ultrasound and electrical muscle stimulation has decreased, while the role of manual therapy and therapeutic exercise has increased. The goal is to get patients as active as possible in their own treatment, and passive modalities may hinder that goal by promoting dependency on the physical therapist. Physical therapists have a variety of tools available to them for the care of patients with neck and back pain, and some of these treatments and modalities will be reviewed in this chapter.

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Spinal Manipulation and Mobilization

Spinal manipulation and mobilization are widely utilized interventions for low back pain symptoms. Manipulation is a technique which uses a high-velocity, low-amplitude manual thrust to the spinal joints at or near the end of the passive range of motion. Mobilization utilizes small- to large-amplitude, low-velocity passive oscillatory motions to improve ROM at a specific spinal segment. The goals of spinal manipulation and mobilization are to improve joint motion, reduce pain, and improve function. The utility and effectiveness of these therapies have come under dispute in recent years.

Low Back

A Cochrane review by Rubinstein et al. demonstrated that spinal manipulative therapy was relatively safe compared to other therapeutic interventions. However, it did not provide more benefit in acute low back pain patients when compared to sham or alternative interventions and did not offer an additional benefit when added to another intervention [1]. The authors did note that a small number of studies limited the review. Other limitations include heterogeneity in outcomes, comparison groups, and follow-up intervals. The authors note that future research is warranted. Another systematic review by Rubinstein and colleagues concluded that spinal manipulative therapy had a small and statistically significant but not clinically relevant, short-term effect on pain relief and improving function in patients with chronic low back pain compared to alternative therapy interventions [2].

There is, however, some evidence that demonstrates manual therapy to be effective when utilized in particular subgroups of low back pain. Clinical practice guidelines for low back pain from the American Physical Therapy Association (APTA) suggested considering thrust manipulative procedures to reduce pain and disability in patients with low back pain with duration of symptoms less than 16 days and for symptoms that do not extend beyond the knee citing studies from Flynn et al. which were further validated by Childs et al. [3, 4]. Childs et al. also demonstrated the increased efficacy of spinal manipulative therapies in patients who demonstrate lumbar hypomobility on physical examination [4].

Neck

The evidence for the utilization of manipulation and mobilization in neck pain is conflicting. When manipulation and mobilization techniques were contrasted against an inactive control and other active treatments, a Cochrane review by Gross and colleagues showed that:

1. There was low-quality evidence showing a single cervical manipulation versus inactive control relieved pain at immediate follow-up but no relief at short-term follow-up.
2. Multiple sessions of cervical manipulation provided similar relief in pain and improvement in function as multiple sessions of mobilization at immediate-, short-, and intermediate-term follow-up in acute and chronic neck pain.
3. Cervical manipulation was more effective than some medications at short- and long-term follow-up.
4. Cervical manipulation was more effective than massage therapy at short- and intermediate-term follow-up for cervicogenic headaches.
5. Mobilization as an isolated treatment may not be effective in reducing pain against inactive controls or when compared to passive therapies including ultrasound, transcutaneous electrical nerve stimulation (TENS), acupuncture, and massage in subacute and chronic pain [5].

Rare but serious adverse effects including disc herniation, strokes, and neurologic deficits are reported in the literature. The prevalence of these complications is unclear as adverse effects are often not reported in studies. Further studies to determine these risks are warranted.

Strengthening, Coordination, and Conditioning

Strengthening, coordination, and conditioning of the core muscles are commonly referred to in the literature as spinal stabilization exercises or motor control exercises (MCE).

Low Back

The goals of MCE include restoring coordination and control of the deep trunk muscles which include the transverse abdominis, lumbar multifidus, and the pelvic floor muscles. A Cochrane review evaluating MCE for acute nonspecific low back pain concluded that while there is some literature indicating MCE was not superior to alternative treatments, more research was needed to determine the utility of MCE in acute and subacute low back pain [6]. A systematic review by Bystrom et al. reviewing MCE's effect on pain and disability demonstrated the superiority of MCE when compared with general exercise in regard to pain in the short and immediate term and during all time periods for disability. MCE was more effective than manual therapy with regard to disability but not pain. MCE was superior to minimal intervention with regard to pain and disability [7]. Core strengthening exercises remain a vital part of rehabilitation efforts in the recovery of acute, subacute, and chronic low back pain and should be a part of a comprehensive treatment plan.

Neck

A Cochrane systematic review by Gross and colleagues, which included 27 trials, demonstrated moderate-quality

evidence to support the use of cervico-scapulothoracic and upper extremity strengthening, conditioning, and stretching exercises for patients with chronic mechanical neck pain. There was also moderate-quality evidence to support the use of cervico-scapulothoracic strengthening and endurance exercises for chronic cervicogenic headaches at long-term follow-up. There was low-quality evidence demonstrating a small benefit from these exercises for acute radiculopathy symptoms [8]. Stretching and strengthening of the cervical, periscapular, thoracic and upper extremity muscles should be included in most treatment plans when addressing neck pain as well as cervical radiculopathy symptoms.

Directional Preference Exercises

Directional preference management, also commonly referred to as the McKenzie method, is a standardized approach for the classification and treatment of spine and musculoskeletal pain symptoms. The McKenzie approach aims to correlate specific planes of movement with worsening and reduction in pain symptoms. When a directional preference is identified (flexion, extension, or lateral shift and rotational movements), the physiotherapist guides the patient through a series of exercises which include repeated ROM biased toward the direction in which the patient experiences pain relief with the goal of centralizing pain symptoms from the periphery to the core and midline of the body.

Low Back

A randomized controlled trial by Long and colleagues included 312 participants, and of those participants, 74% had a directional preference [9]. Of the 230, 83% of the participants had an extension preference, 7% flexion, and 10% lateral. These patients were randomized into three groups: (1) exercises which matched their directional preference, (2) exercises opposite to their directional preference, and (3) nondirectional exercises. Patients who were randomized into the exercise group which matched their directional preference experienced a significant decrease in their pain, decrease in medication use, and reduction in disability. A third of the participants in the other two groups dropped out of the study due to limited benefit or worsening symptoms from the exercises provided to them. After an extensive review of the literature, the APTA provided an A grade recommendation supporting the consideration for utilizing directional preference exercises to promote centralization in patients with acute low back pain with radicular symptoms as well as patients with low back pain with mobility deficits [10].

Neck

The literature for directional preference and centralization is less robust for neck pain symptoms. A multicenter study by Edmond et al. found that prevalence for directional preference and centralization in neck pain was 0.7 and 0.4, respectively [11]. In this study, a directional preference classification when combined with matched exercises predicted an improvement in function but not pain. More studies are needed to validate the utility of directional preference classification in neck pain.

Flexion-Based Exercises for Lumbar Spinal Stenosis

Flexion-based lumbar exercises also commonly referred to as Williams flexion exercises are a set of exercises that work to enhance flexion and diminish excessive lumbar extension with the goal of opening the central and foraminal canals and decreasing pressure over the apophyseal joints. Williams theorized that humans had redistributed body weight to the posterior spinal column and discs while evolving to standing upright on two legs. Flexion-based exercises have been used as a standard treatment for lumbar spinal stenosis for many years. While there is some literature to support the use of flexion-based exercises for lumbar spinal stenosis [12, 13], more evidence is still needed. Per the APTA, clinicians could consider these exercises in conjunction with other standard rehabilitation measures to improve pain and disability in patients with low back pain with radicular symptoms [10].

Traction

Spinal traction has been utilized for the relief of pain for thousands of years [14]. The exact mechanism of spinal traction is unclear. However, explanations for pain relief include separation and a decrease in pressure between the intervertebral spaces, suction of disc protrusions, distraction of the facet joints, tension of the spinal ligament structures, and stretching of the paraspinal muscles. There are various approaches to spinal traction. Mechanical traction is the use of a device which involves a table with two sections and a harness positioned at the lower edge of the rib cage and iliac crest to produce a specific amount of tension with a motorized pulley system. Autotraction also involves a sectioned table, but the patient delivers their own traction pushing with their legs and pulling with their arms. Manual traction is usually performed by a physiotherapist. There is also a multitude of devices in the market utilizing gravitational forces to provide spinal traction.

Low Back

Despite increasing popularity of the use of traction over the last several decades, the evidence behind its use is conflicting. A Cochrane review by Wegner and colleagues concluded

after a review of 32 randomized control studies that traction alone or in conjunction with other treatments has minimal impact on pain intensity, functional status, or return to work in patients with low back pain [15]. The APTA clinical practice guidelines for low back pain also mention that there is moderate evidence to suggest that traction is not effective for reducing pain symptoms in patients with nonradicular low back pain symptoms [10]. The APTA guidelines did, however, mention that there was preliminary evidence to support the use of mechanical traction for a subgroup of patients with low back pain with radicular symptoms with peripheralization of symptoms and a positive cross straight leg raise on physical examination [16].

Neck

A Cochrane review by Graham et al. concluded that more evidence was needed to either support or refute the efficacy of traction for neck pain with or without radicular symptoms [17]. The APTA clinical practice guidelines for neck pain cite moderate evidence to support the use of a multimodal approach for chronic neck pain with mobility deficits which include manual traction. There is moderate evidence to support the use of intermittent mechanical traction combined with other treatment measures including stretching and strengthening for chronic neck pain with radicular symptoms [18]. More research is needed. Table 34.1 includes a list of contraindications to spinal traction.

Thermotherapy and Cryotherapy

Thermotherapy and cryotherapy are relatively safe and cost-effective adjunct treatment options for neck and back pain symptoms. While both treatment modalities facilitate a decrease in pain and muscle spasms, it is important for the clinician to consider additional variables when choosing between these modalities as they have opposite effects on blood flow, edema, inflammation, tissue metabolism, and extensibility. Thermotherapy increases these effects, while cryotherapy does the opposite [19]. Due to these effects, the clinician must take into consideration the patient's comorbidities and current clinical condition when choosing either of these modalities. Thermal modalities are most effective when they are used proactively. It is recommended that the patient use them before pain levels become too high—at least three times daily. Tables 34.2 and 34.3 describe pertinent heat and cold therapy modalities and their mechanisms, respectively. Tables 34.4 and 34.5 outline indications and contraindications when considering using heat and cold therapy modalities, respectively.

Table 34.1 Contraindications for spine traction

Instability of spine segment
Vertebral fracture
Respiratory and cardiovascular disease
Acute sprains or strains
Extruded disc fragment
Pregnancy
Hiatal hernia
Spinal malignancy
Rheumatoid arthritis
Hypermobility and ligamentous strain
Osteoporosis
Additional contraindications for inversion tables
Glaucoma
Retinal detachment
Recent stroke, TIA
Obesity
Uncontrolled hypertension

Transcutaneous Electrical Nerve Stimulation

Transcutaneous electrical nerve stimulation (TENS) is a commonly utilized adjunct modality for various musculoskeletal pain diagnoses. The mechanism of action is generally thought to be twofold. (1) The first is through the gate

Table 34.2 Heat therapy modalities and mechanisms

Mechanism and indications		Treatment modality
Heat therapy Increases local blood flow and local edema Can increase inflammation Increases local metabolism Increases tendon extensibility Decreases pain and muscles spasms	*Conduction*: transfer of heat through direct contact	Heat packs Heating pads
	Convection: transfer of heat through air or fluid	Hydrotherapy: whirlpool
	Conversion: transition of one energy form (sound waves, light) into another (heat)	Superficial heat Heat lamp Deep heat Ultrasound Diathermy (shortwave, microwave)

Table 34.3 Cold therapy modalities and mechanisms

Mechanism		Treatment modality
Cold therapy Decreases local edema Can reduce inflammation Decreases local metabolism Decreases tendon extensibility Reduces pain and muscles spasms and spasticity	*Conduction*: transfer of heat through direct contact	Cold packs Ice massage
	Convection: transfer of heat through air or fluid	Hydrotherapy: cold baths
	Evaporation: transfer of heat as fluid transitions into a gaseous phase	Vapocoolant spray

Table 34.4 Precautions and contraindications for heat therapy modalities

Indications for heat	Precautions and contraindications
Muscle spasms	Impaired sensation
Joint stiffness	Local malignancy
Myofascial pain	Pregnancy
Arthritis	Limb ischemia: heat increases local metabolic requirements
Subacute to chronic pain processes	Caution with patients with multiple sclerosis Hydrotherapy: skin infection
	Ultrasound: near tumors, laminectomy, infection, pacemaker, total hip or knee prosthesis sites. Skeletal immaturity
	Shortwave diathermy: near pacemaker, metal items. Skeletal immaturity
	Microwave diathermy: moist skin, blisters, edematous tissue. Skeletal immaturity

Table 34.5 Precautions and contraindications for cold therapy modalities

Indications for cold	Precautions and contraindications
Muscle spasms	Impaired sensation
Myofascial pain	Arterial insufficiency
Neuropathic pain	Open wounds
To reduce acute inflammatory reaction	Limb affected by Raynaud's
To reduce UMN limb spasticity	Paroxysmal cold hemoglobinuria, cryoglobulinemia
Arthritis	Caution with patients with multiple sclerosis
Acute pain processes	

control theory whereby electrical stimulation activates the large-diameter Aβ sensory fibers, therefore exciting the inhibitory cells and decreasing transmission of pain signals from the small-diameter C fibers. (2) Electrical stimulation activates the Aδ fibers which stimulate the release of endogenous opioids in the spinal cord decreasing transmission of pain signals at the spinal cord level. The Aβ fibers are thought to be stimulated at a higher frequency (90–130 Hz) and Aδ fibers at a lower frequency (2–5 Hz). The evidence for TENS for low back pain is conflicting; however, given its relatively low-cost burden and general safety profile, it may be considered as a treatment option for patients with neck and back pain. See Table 34.6 for precautions and contraindications when considering TENS therapy.

Ultrasound

Ultrasound utilizes sound waves to deliver thermal energy into the underlying soft tissue and used as a deep heating modality. It is also thought to facilitate tissue repair. A

Table 34.6 TENS precautions and contraindications

Over malignancy
Open wounds, infections
Directly over the spinal column
Pacemaker
Caution during pregnancy
Caution with patients with epilepsy
Insensate skin
Caution with patients with cardiac conditions, arrhythmia
Avoid head, eyes, anterior neck/carotid sinus region, a region of skeletal immaturity, transthoracic electrode placement

Cochrane review by Ebadi and colleagues reviewed seven small studies to evaluate the efficacy of ultrasound treatment for patients with nonspecific low back pain. While there was some evidence demonstrating an improvement in low back function in the short term, high-quality evidence to support the use of ultrasound for nonspecific low back pain was lacking [20]. See Tables 34.4 and 34.5 for indications and contraindications in the use of ultrasound therapy.

Biofeedback-Assisted Neuromuscular Reeducation

Patients living with ongoing chronic spine pain frequently develop fear avoidance movement patterns. Kinesiophobia has been shown to adversely affect the quality of life and limit physical activity of patients with chronic low back pain [21]. Patients develop guarded movement patterns that can ultimately result in more pain. Patients with low back pain frequently demonstrate suboptimal flexion relaxation patterns during forward lumbar flexion [22]. Occupational and physical therapists utilize surface EMG neuromuscular reeducation to help patients normalize movement patterns. The patient visualizes muscle firing patterns on the screen and monitor for asymmetric movement patterns and inappropriate guarding. Visual feedback allows the patients to correlate what they see on the screen with what they are feeling in their body. This can provide an additional anchor for patients as they learn to build muscle memory and develop adaptive movement patterns. Combining surface EMG retraining on the lumbar paraspinal muscles and functional restoration has been shown to have positive effects in restoring flexion relaxation patterns [23]. This, in turn, has also been shown to have positive correlations with self-efficacy, reducing fear avoidance, and improving function [24]. Surface EMG biofeedback-assisted neuromuscular reeducation may be helpful for chronic neck and shoulder pain as well. Biofeedback can be useful in retraining cervical paraspinal and upper trapezius muscles during computer and upper extremity activities to help reduce neck pain and improve postural alignment.

Aquatic Therapy

Aquatic therapy is an alternative or adjunct approach to treatment when a land-based approach is prohibitive. Treatments are performed with the patient in a pool setting with exercises guided by either a physical or occupational therapist. Therapy in an aquatic environment may offer additional benefit to the patient with back or neck pain as buoyancy can reduce the effects of gravity on painful muscles and joints while hydrostatic pressure may help stabilize and support patients with balance impairments. In addition to this, the viscosity of water can offer natural resistance to the whole body and aid in conditioning weak muscle groups. A systematic review by Waller et al. reported that while aquatic therapies were no better than alternative land-based therapies, there was sufficient evidence to suggest that aquatic-based therapies could be beneficial for chronic and pregnancy-related low back pain symptoms [25].

Aquatic therapy treatments can vary significantly depending on the approach used. Techniques include the Ai Chi, Watsu, Halliwick, Bad Ragaz Ring, and Burdenko methods among others. While each method will not be reviewed in this chapter, it is important for the referring clinician to be aware of the wide array of treatment approaches even in aquatic therapy when referring your patient for treatment.

Occupational Therapy

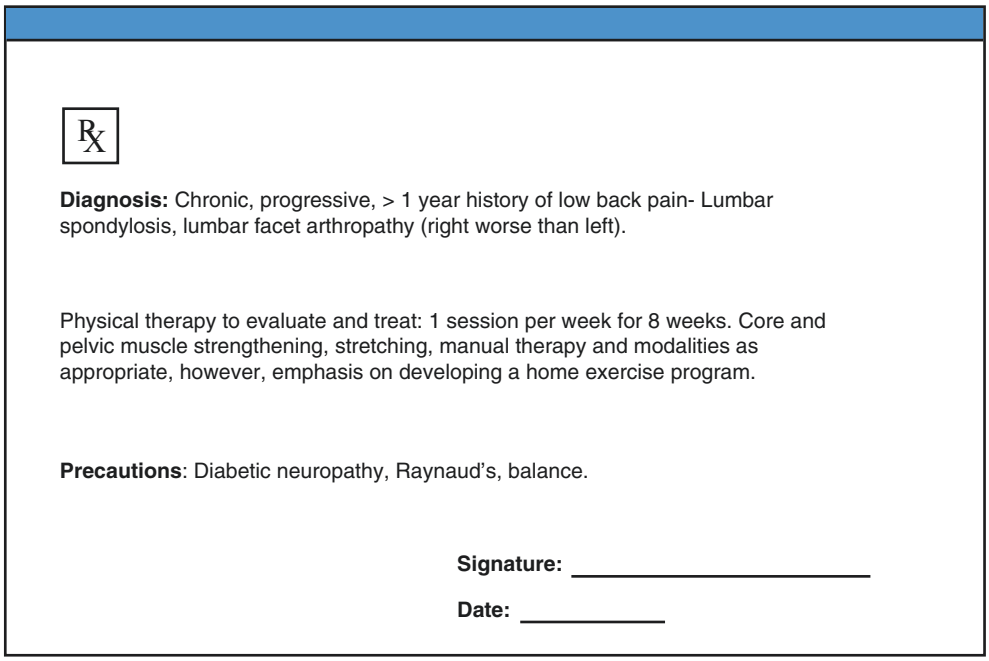
Occupational therapy (OT) practitioners bring a unique perspective to the patient with neck and back pain. For many patients, pain can take control over many, if not all, aspects of daily life. Occupational therapists help patients return to activities that are meaningful to them by introducing and training patients to utilize specific tools to enable occupation. An occupational therapist who specializes in pain management begins by discovering the client's functional goals and priorities. They assess the patient's ability to perform activities of daily living (ADLs). The OT looks at whether the person can perform a task but also assesses how they are completing it. The therapist evaluates movement patterns during activity, muscle guarding, and use of pain coping techniques. The OT works with patients to identify functional goals and develop a plan to help them get back to the activities they value without increasing their pain. Occupational therapists evaluate activity demands and teach clients how to perform each task using the safest body mechanics for the individual. An activity analysis for each problematic activity allows the therapist and patient to find an optimal biomechanical strategy to perform it without increased pain or injury. Commonly, therapists find that patients avoid engaging in activities due to fear of pain. Fear avoidance has been shown to predict disability [26] and can be a significant barrier to improving activity levels in patients with chronic pain. With practice, the patient's confidence in his or her ability to safely complete activities (self-efficacy) is gained. Patients practice body mechanics within the home, clinic, and community. If appropriate, worksite assessments are completed to optimize ergonomics on the job.

Therapy Prescription

Treatments offered to patients can vary depending on the components included in a physical therapy prescription. Therapists are often provided minimal information when receiving a patient from the prescribing physician. An effective therapy prescription should consist of pertinent details including working diagnosis, history, and treatment approaches that might be best suited for a patient. The different components of physical therapy prescription are outlined in Table 34.7. A sample physical therapy prescription is shown in Fig. 34.1.

Table 34.7 Components of a physical therapy prescription

Components of a physical therapy prescription	Considerations
Diagnosis and brief history	Pertinent details including mechanism of injury, chronicity, progression, and diagnoses being treated should be included
To "evaluate and treat"	Allows therapist to use discretion in choosing a therapeutic approach
Frequency and duration	Acuity of symptoms may guide frequency and duration of therapy sessions. More acute symptoms may benefit from a higher frequency of therapy sessions, earlier on (e.g., 3 days a week for 3 weeks). Patients with more chronic symptoms may benefit from a lower frequency at a longer duration. Frequency and duration should also be guided by the complexity of the diagnosis and function deficits as well as the availability of the patient
Treatments	If a specific approach to therapy is warranted, you may specify the approach and treatment modalities in the prescription For example, manual therapy, myofascial release, stretching, ROM, strengthening, approach (directional preference exercises, flexion-based exercises, etc.), modalities, home exercise program
Safety precautions	The prescribing physician should notify the therapist if there are comorbidities or therapy restrictions that should be taken into consideration when formulating a treatment plan. These considerations include but not limited to weight-bearing restrictions, range of motion restrictions, fall risk, recent surgery, kinesiophobia, cardiovascular or respiratory concerns
Signature and date	From ordering physician



℞

Diagnosis: Chronic, progressive, > 1 year history of low back pain- Lumbar spondylosis, lumbar facet arthropathy (right worse than left).

Physical therapy to evaluate and treat: 1 session per week for 8 weeks. Core and pelvic muscle strengthening, stretching, manual therapy and modalities as appropriate, however, emphasis on developing a home exercise program.

Precautions: Diabetic neuropathy, Raynaud's, balance.

Signature: _____

Date: _____

Fig. 34.1 Sample physical therapy prescription

Patient Education and Counseling

Patient education and counseling is a critical component of providing excellent care for patients with neck and back pain. The quality of physician to patient communication is positively correlated with improved patient adherence to recommended treatment plans [27].

Validation and Empathy

Back and neck pain has been managed within a biomedical model for years. We now know that psychosocial factors also play a significant role in patient's perception and impact on pain. Pain can affect patient's sleep, function, work, and overall quality of life. Acknowledging this impact through careful listening can help establish trust between the patient and physician and aid in developing realistic and meaningful functional goals with the proposed treatment plan.

Goal Setting, Coaching, and Prevention

Physicians play an important role in helping their patients develop realistic and meaningful short-, intermediate-, and long-term functional goals. They also play a vital role in coaching a patient on their journey to recovery. Physicians are recommended to take an inventory of the patient's work requirements, passions, and hobbies and familiarize themselves with the types of exercises and sporting activities that the patient enjoys. A Cochrane review by Choi and colleagues reviewed 13 articles covering 9 interventions which demonstrated moderate-quality evidence to support posttreatment exercises were effective for reducing the rate of recurrence at 1 year [28]. While it was difficult to specify the contents of a post-rehabilitation exercise program, maintaining a combination of general exercises which include stretching, muscle strengthening, and endurance training could be effective in reducing the frequency of recurrences of low back pain. Clinicians and therapists can leverage the patient's goals and preferences to help the patient remain focused and compliant as they progress through their rehabilitative treatment program and attempt to prevent future recurrences.

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Psychological Assessment and Behavioral Management of Spine Pain

35

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Key Points

- Psychosocial comorbidities are typically encountered with chronic spine conditions. Common comorbidities may include a wide range of symptoms associated with anxiety disorders and PTSD, fear-avoidance of activity, catastrophizing, somatization, substance misuse and abuse, and disability.
- Early assessment and management of behavioral symptoms can optimize outcomes for spine treatments, including reduction of disability, improvement of functional outcomes, reduction of substance misuse and abuse, and reduction of the psychological sequelae of persistent pain.
- Applying time-limited behavioral strategies such as cognitive behavioral therapy (CBT), acceptance and commitment therapy (ACT), mindfulness-based stress reduction (MBSR), and operant therapies have been shown to improve outcomes for acute and chronic spinal conditions.
- Multiple validated assessment instruments are available and are useful for patient screening, goal setting, and measurement of treatment outcomes.
- Certain patient populations may require more complex assessment and care, including patients presenting with elevated risk for substance use, those with work-related disability, and those at risk for overutilizing medical services.
- Efforts should be made to reduce barriers to access to specialized behavioral healthcare; integrating behavioral services into the multidisciplinary care model and universally applying a biopsychosocial approach to pain assessment and management can improve treatment outcomes.

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Introduction

Psychological factors and comorbidities are well-known to impact outcomes for acute and chronic spine pain, predicting treatment resistance as well as associated disability [1–6]. Psychosocial factors also predict poor adherence to treatment recommendations and a complicated course of treatment [1, 4, 7–9]. Although much research has focused on identifying psychological factors associated with low back pain, similar findings have been documented in patients presenting with acute and chronic neck pain [3]. Some investigators have offered an extensive list of clinical risk "flags" which may predict subsequent disability and have argued that identification and early intervention may offer the best outcomes [10] (see Table 35.1 for risk "flags" for delayed recovery with spinal pain). To address these issues clinically, Block and Sarwer [11] provide an evidence-based template for presurgical psychological screening and management of

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Table 35.1 Psychosocial risk "flags" for delayed recovery from spinal pain conditions

Severe anxiety or posttraumatic stress disorder
Substance misuse or substance use disorder
Clinical depression
Excessive somatization, multiple pain/somatic complaints
Fear-avoidance of activity and pain
Catastrophizing, e.g., worry that the increase in pain is causing "harm"
Severe job-related concerns, e.g., supervisor dissatisfaction, perception of unpleasant work, poor work history
Threats to financial security
Adversarial relationships with stakeholders (e.g., contested worker compensation claims, challenges to the severity of symptoms by treating clinicians and family)
Preference for passive treatments
Poor social supports
Significant other reinforces disability and somatic overconcern
Absence of clear, measurable goals, e.g., "I just want my life back"
Satisfaction with disabled role

patients with persistent spine pain, with practical clinical recommendations largely based on their work at the Texas Back Institute.

For patients with acute spine pain, early behavioral and rehabilitative interventions have some demonstrated success, although the data is not as robust as for chronic pain conditions. It is important to recognize that patients with acute low back or neck complaints represent a heterogeneous population, so individualized interventions will likely yield more favorable outcomes. Patients may present with a myriad of risk factors such as anxiety, depression, job dissatisfaction, catastrophizing about pain and injury, or fear-avoidance of activity. Behavioral interventions that fail to differentiate patients by risk factors have shown less robust effects than those that screen and target-specific psychosocial factors [12]. For example, Archer et al. [13, 14] specifically screened for fear-avoidance of activity and found that structured cognitive behavioral therapy combined with directed rehabilitation significantly reduced pain and disability. Although most patients with chronic spine complaints will have one or more psychological risk factors, screening the acute patient for risk "flags" may offer an opportunity for targeted behavioral intervention early in treatment to reduce the risk of delayed recovery and development of chronic disability.

Behavioral interventions are most effective when the patient with chronic pain is treated by a multidisciplinary team [1, 7, 15, 16], consistent with a biopsychosocial approach to assessment and treatment. Effective management of the complex chronic pain patients also requires ongoing and consistent messaging from various team members and the consistent support of clinicians working with the patient in order to achieve measurable goals. For less complex patients, multiple studies report positive outcomes with stand-alone psychotherapy interventions, such as individual and group cognitive therapy and also with interventions that include mindfulness training and acceptance/commitment therapies [10, 17, 18, 20]. Despite the importance of an individual role for behavioral pain clinicians, working within a multidisciplinary team remains the best practice.

Behavioral Evaluation of Pain

Patients may be referred to mental health clinicians for psychological "screening" prior to interventions such as lumbar fusion or spinal column stimulation or may be referred for "opioid risk stratification." However, such limited screening efforts may offer the patient and the referring clinician little practical advice for improving outcomes. Ideally, psychological assessment of the patient with persistent spine pain should consider the wide range of psychosocial factors that may impact the patient's long-term prognosis [21]. Beyond risk assessment screening, it is important for the psychological assessment to identify realistic pain treatment goals, address patient expectations, facilitate communication between various care providers, and consider the need for adjunctive therapies, such as structured behavioral or rehabilitative treatments.

The scope of the psychological evaluation should include a detailed description of all pain complaints; Kamaleri [22] found that 80% of the variance in disability was directly related to the number of pain sites reported by the patient. A subspecialist may selectively focus on leg or neck pain, inadvertently ignoring multiple other complaints documented in the patient's record that may impact prognosis. A thorough pain history is essential and should probe for details regarding pain onset, understanding that the patient may identify a specific cause of his or her pain while inadvertently leaving out additional history of other pain complaints and the relevant factors that have precipitated or maintained them.

It is also imperative to delineate the specific areas of perceived functional limitation secondary to the pain, e.g., inability to sit for more than 30 minutes, difficulty lifting a gallon of milk, or problems engaging in sexual activity. "Secondary gain," or social/financial factors that reinforce somatic concern or disability, should be respectfully explored, and interviewing the patient with a significant other may help the clinician to better understand of the potentially relevant factors. Early investigations by Block

[11] and others showed that spousal "solicitousness" can be a predictor of excessive somatic concern, higher pain rating, and disability. Out of concern and desire to provide support, the highly attentive spouse may caution the patient about re-injury or exacerbation of back pain, discouraging engagement in common household tasks or work activities. In severe cases, a role reversal may develop in which the patient with chronic back pain spends much of the day in bed, while the spouse overcompensates for this diminished activity. Even in the absence of serious underlying medical pathology, the patient may respond with increasing withdrawal from daily activities, contributing to hopelessness and depression. The patient may become more concerned and preoccupied about his or her symptoms and may display severe pain behaviors including increased complaints of pain or reliance on unnecessary assistive devices such as braces, crutches, or wheelchairs. Clinicians must avoid unwittingly reinforcing these dysfunctional and potentially destructive patterns.

Fear-avoidance of activity, comorbid anxiety and affective symptoms, sleep disturbance, and suicidal thinking [23–25] may accompany spine pain that persists for more than a few months. Anxiety commonly manifests as fear-avoidance, a pattern in which the patient avoids engaging in activities that are critical to overall functional improvement due to fear of exacerbating the underlying condition. Similarly, anxiety may manifest as "catastrophizing" about one's health status, such as the unrealistic fear of "herniating another disc" or "causing the fusion to become unstable," even though months may have passed since surgical recovery and despite reassurance that there is no evidence of new underlying pathology.

While anxiety symptoms are commonly associated with acute spine pain conditions and often present in chronic pain states, a history of trauma or the diagnosis of posttraumatic stress disorder (PTSD) has been found to be predictive of poorer outcomes with spinal treatments and postsurgical rehabilitation, especially when the patient perceives a loss of control over his or her environment. The presence of these risk factors should prompt the clinician to seek psychological assessment and recommendations for management. A full assessment should include inquiring about history of flashbacks, dissociative episodes, and other PTSD-related symptoms.

Depression is a common consequence of persistent pain and an added risk factor for developing treatment-resistant pain conditions [26], and early assessment and management of mood symptoms from a behavioral and pharmacological standpoint often is necessary. Within 5 years of pain onset, 50% or more of patients develop symptoms of depression, and the clinician must address these symptoms independently from the pain condition, as severe depression does not necessarily resolve even after improvement of persistent pain. Symptoms and signs of depression are commonly missed by clinicians (and patients) due to the singular focus on pain complaints, and careful attention to periodic assessment of affective symptoms should be included as an independent health issue. Assessment also must include ongoing periodic evaluation of suicidal thinking, including risk factors as well as protective factors that may mitigate suicide risk. Depression and suicide risk deserve increased attention in the patient with any chronic medical condition, and the person with persistent pain may require added care given the prevalence of psychiatric comorbidities. Brief screening questionnaires such as the PHQ-9 are useful tools to provide the clinician with a structured way to identify symptoms (Table 35.2).

Emotional responses to prior surgeries or spine procedures may also help predict outcomes and provide clues to more effective management. For example, if the patient had a prior surgery that led to escalating opioid use and a difficult taper or nonadherence with postsurgical rehabilitation due to activity fear-avoidance, knowing this history in advance will provide the clinician valuable insights for postsurgical treatment planning. A careful history, data collection from family and caregivers, review of prior records, and discussion with past clinicians who took care of the patient can help uncover this important history.

Questionnaires and Observational Measures

Multiple validated screening questionnaires are available to assist with chronic pain assessment [40]. Chiarotto et al. [61] provided a comprehensive review of more than 20 measures, including those addressing outcomes with low back pain, and most measures included significant psychosocial elements. There are few psychological and disability measures specifically related to neck pain, but several have been widely studied, including the Neck Disability Index [36]. Recent reviews include the patient-reported outcome measures (PROMs), a self-report measure addressing emotional and physical functioning that may be used with disease-specific populations [32, 41]. Despite widespread use, some have argued that the PROMs may not be as valuable for clinical decision-making and planning [41]. General measures (not disease-specific) such as the World Health Organization Disability Assessment Scale (WHODAS-2) [37] have received increased attention; scoring is relatively

Table 35.2 Brief screening and outcomes measures/procedures for clinical practice

Domain	Measure	Comment
Emotional functioning	GAD7 (anxiety) [23]	Brief, 7-item generalized anxiety screening, extensively studied with multiple populations including low back pain
	PHQ-9 (depression) [23, 24]	Brief, 9-item depression screening, extensively studied with multiple populations including spinal pain. Also addresses suicidal ideation
Fear-avoidance/ pain catastrophizing	Tampa Scale of Kinesiophobia [25, 26]	17-item scale addressing fear-avoidance of activity, predicting of other disability measures, used in low back and neck pain
	Pain Catastrophizing Scale (PCS) [19, 20, 27]	13 items, one of several scales available to address this construct, with the PCS frequently used with spine conditions. Constructs addressed include rumination, somatization, and helplessness
Somatization	PHQ-15 [23]	Most widely used 15-item self-report measure for somatization, normative data available for spine populations, may not be sensitive to somatic overconcern when patient only endorsed pain-related symptoms
Disability/ functional	PROMIS-PF-4 [56]	Brief screener, several versions available, recommended by the NIH Task Force on research standards for low back. Limited use in studies in contrast to RMDI and ODI
	Oswestry Disability Index (ODI) [27–31]	10 items listing degrees of severity for each domain, extensively studied with low back pain, addressing mostly functional variables such as sitting, standing, sitting, but also social and sexual activity impacted by disability
	Roland Morris Disability Inventory (RMDI) [29, 31]	24-item, extensively studied in a broad range of low back pain populations, covers similar disability domains as ODI, including psychosocial areas, but less sensitive as a measure of severe disability than the ODI
	Neck Disability Index (NDI) [32]	10-item widely used measure that correlates with quality of life and other emotional function measures. Also shows predictive validity with self-report (ODI) and objective measures of function
	Whodas-2 [33–35]	36-item self-report questionnaire which addresses 6 domains of functioning: (i) cognition (understanding and communication); (ii) mobility (ability to move and get around); (iii) self-care (ability to attend to personal hygiene, dressing, and eating and to live alone); (iv) getting along (ability to interact with other people); (v) life activities (ability to carry out responsibilities at home, work, and school); and (vi) participation in society (ability to engage in community, civil, and recreational activities). Not intended as a brief screening in the patient needs to complete 36 items but well- established validity and reliability with normative data and utility for assisting the patient with goal setting
Substance use/ misuse	National Institute on Drug Abuse (NIDA) Quick Screen [36]	4-item *clinician administered* screening instrument for substance use, including prescription medication use, demonstrated efficacy in changing provider assessment behavior and identifying at-risk patients. Standardized and available by web application when evaluating the patient, guiding the clinician through brief assessment, counseling and referral. Easily integrated in most e-record platforms
	Current Opioid Misuse Measures [37–39, 57]	17-item brief screening for patients currently using chronic opioids addresses risk for current/future aberrancy. Not intended for stand-alone use, but part of comprehensive opioid risk assessment. Validated short form available, as well as computer-based applications

simple, the categories cover specific emotional and physical functioning domains relevant for patients with spinal conditions, and comparisons can be made across patient populations. Specific scale items may also be used clinically to facilitate patient-clinician dialogue regarding goal setting and can be used to track specific objective changes over time. Debate continues over the development of condition-specific measures versus those that may be used more generally across pain conditions. Although many psychological measures have been created specific to low back pain and that permit comparisons with normative data, chronic pain is not a disease-specific entity, and it encompasses common psychological and disability factors regardless of the location of the chronic pain condition. Once a pain condition persists for more than 3 months, there are more similarities across conditions than there are differences. With respect to psychological and disability variables, a patient with persistent pain of more than 3–6 months has less in common with an acute spine patient than with an individual who may have chronic pain located at a different site. Hence, assessment protocols for chronic pain conditions are similar, as are the treatments most likely to result in a positive outcome.

The measures listed in Table 35.2 do not require assistance from a psychologist or psychiatrist, are relatively easy to score and evaluate, and may be used to provide a baseline for symptom monitoring. They may be repeated over time to track outcomes, and each measure has robust normative data for spine populations. Scales may be easily integrated into the electronic medical record; some use a computerized scoring system that limits the number of items presented

to the patient if scoring reaches a certain threshold, i.e., a stochastic curtailment process [62]. As a result, patient time and clinician burden can be reduced, especially compared to lengthy psychological assessment instruments (such as the 500+ item Minnesota Multiphasic Personality Inventory-2) used in the past.

Goal Setting and Patient Expectations

Collaborative goal setting is critical to psychological assessment and behavioral treatment, but it is an area of treatment planning often overlooked by physicians and mental health providers alike. Subjective pain relief may be the primary goal for the patient, but objective measures of physical and social/emotional functioning may be more attainable and prove to be better indicators of long-term treatment outcomes. It is best to define objective goals within specific timelines. Examples of specific and measurable goals include return to work in 6 weeks, return to a specific recreational activity once per week, gardening 1 h per day, or walking 60 minutes per day. Goal setting is of such importance that the absence of identifiable goals should be considered a risk factor for poor outcome. Inadequate goal setting may lead a patient to state, "I'll never exercise again," "I could never return to work, " or "My doctor told me I need to be on this (opioid) for life." Vague, poorly measurable, or unrealistic goals should be challenged, negotiated, and revised. "My only goal is to get my life back," is a goal that offers little direction or options for measuring change for the treating clinician or the patient. Such statements are a flag that directed behavioral counseling is indicated.

Similarly, evidence of fear-avoidance and catastrophizing about the pain and the consequences of the pain should be carefully assessed. The patient may feel that any "flare-up" of pain implies new tissue damage, leading him or her to insist on additional consultations, medication, and imaging. Helping the patient understand the difference between "hurt" and "harm" when a pain exacerbation occurs is a necessary clinical intervention. An unrealistic and unattainable goal, such as the patient's request to "just fix me," represents a flag that the proposed intervention or surgery will be unsuccessful, especially if the underlying pain condition is chronic. Each of these examples may predict to a problematic outcome, but behavioral interventions can provide practical guidance and assistance to both the patient and the treatment team, particularly when the behavioral care is integrated into a multidisciplinary setting.

Finally, predictors of poor future adherence require attention. The World Health Organization [42] notes "increasing the effectiveness of an adherence intervention may have far greater impact on the health of the population than any improvement in specific medical treatments." Rates of adherence to treatment recommendations typically plummet when the patient presents with chronic psychiatric comorbidities, encounters complex treatment recommendations, or holds beliefs or expectations about treatment outcomes that differ from those of the clinician [43, 44]. Adherence rates to prescribed treatments are generally low, about 50% for patients leaving a physician's office, and rates worsen if comorbid chronic medical or psychiatric conditions are present. Early integration of behavioral assessment and treatment may help maximize adherence and improve outcomes [43, 44].

Assessment and Optimization for Specific Spine Interventions

Spinal cord (column) stimulation (SCS) treatment protocols typically require psychological assessment. Early psychological screening models were largely generated by industry, and the threshold for accepting patients was low. Standardized protocols for screening remain lacking, although there is an emphasis on patient assessment for the purpose of optimizing the intervention for the patient, rather than simply "screening." The first step should include close scrutiny of the patient's goals as well as working with the patient to establish realistic and measurable endpoints. Examples of unrealistic goals might include relief of total body pain, a reduction of high-dose chronic opioids in the absence of structured tapering program, or a return to work after years of disability. If ongoing severe psychiatric symptoms are present, such as those attributable to PTSD or major depression, it is prudent to establish behavioral and/or psychopharmacologic treatments prior to embarking on SCS. Some centers also prefer to taper opioids and other controlled substances prior to SCS to help better position the patient to set appropriate goals. Reasonable goals post-SCS might include decreased pain, improved sleep, or return to specific, measurable activities. Prior to implantation, the clinician should address goal setting directly and review progress toward shared goals during follow-up visits. Re-administering questionnaires such as the WHODAS-2, PHQ-9 depression scale, and the Tampa Scale of Kinesiophobia should be considered. There are no standardized protocols for choosing the best self-report questionnaires for SCS, and Table 35.1 lists commonly used assessment instruments. Ideally, testing should address multiple domains including depression and anxiety, self-reported disability, substance use risk, somatization, and fear-avoidance of activity. Goal setting using objective measures of function, such as commercial digital activity monitoring devices, can provide an excellent opportunity to engage the patient to return to desired activities.

Psychological evaluation prior to procedures such as indwelling pump implantation may require extra attention, as these procedures may be more involved than SCS

treatment. In cases of extensive spine surgery such as multi-level lumbar spine fusion, adherence to postsurgical rehabilitation is critical for a good outcome. Some patients may require psychological preparation for the rehabilitation process, including structured support from a rehabilitation specialist and mental health provider familiar with the details of their care.

Special Populations

Patients Taking Opioids

Opioid risk stratification, management, and tapering are challenging and controversial areas of treatment with spine pain conditions. There has been increased focus on reducing opioids prior to spine surgery, as the presence of high-dose opioids has been shown to predict poorer outcomes [45]. Using high-dose opioids is also associated with the presence of mental health comorbidities, including risk for substance use disorder. Substance use disorder is a predictor of poor outcomes for spine surgery as well as a range of other conservative and interventional treatments for spinal conditions. Smoking has historically received the most attention by orthopedic surgeons due to related wound healing issues [46], and tobacco use has also been shown to be a predictor of poor outcome with opioid therapy [47]. A history of excessive alcohol use also predicts to poor outcome with spine surgery and other spinal treatments, as does abuse of controlled substances, particularly opioids and benzodiazepines [46].

Substance use screening is now routine in many healthcare settings; additional data from state prescription drug monitoring program (PDMP), urine toxicology screening, review of prior medical records, and standardized screening questionnaires are all useful risk assessment tools (see Table 35.2). However, screening questionnaires alone are insufficient as a measure of risk, and an interview-based comprehensive assessment that includes other risk factors should always be included as part of the overall patient assessment.

The number of states requiring prescribers to check PDMP data is increasing. These programs do not merely address diversion but also create an opportunity to have a conversation with the patient about their other conditions and open the door to a discussion regarding their risk for substance use disorder. Review of the PDMP early in the assessment phase of care (rather than reviewing a PDMP only at the time a controlled substance is written) provides an opportunity for advance planning and management of the complex spine pain patient. Urine toxicology should also be considered at an early stage of evaluation if risk factors are present and the management of controlled substances appears that it may be a potential challenge.

The behavioral treatment component of tapering any controlled substance is critical to a positive outcome. Patients are almost universally fearful about the perceived consequences of reducing opioids or benzodiazepines, especially if these medications have been used chronically. Improved spine surgery outcomes have been reported after tapering, although few studies offer specifics regarding the structure of the tapering intervention [46]. Berna et al. [48] provided a detailed template for tapering and emphasized the importance of frequent visits, short-term treatment, and implementing strategies to reduce the individual's anxiety and improve adherence.

Injured and Disabled Workers

The injured and disabled worker populations have notoriously poor outcomes with spine treatment [1, 5, 7, 49]. Although financial incentives may complicate recovery, other factors are likely to play a more important role, including fear of pain or re-injury and fear of employment termination. Studies dating to the early 1990s have found that dissatisfaction with one's supervisor predicted development of low back pain, and multiple subsequent studies suggest that physical job demands may be less predictive of outcome than psychosocial demands [50]. If the patient was injured at work, discussions between various stakeholders can become adversarial, and the patient may become demoralized, depressed, and hopeless in the process. Clinicians working with this population need to have some knowledge of disability law, as most state compensation systems do not provide access to occupational medicine specialists. Pain or rehabilitation psychologists can assist and guide the treatment team to shape a successful care plan for the disabled worker. Failure to address barriers and reluctance to delineate an early plan for return to a job are the strongest predictors of poor long-term outcome with disabling chronic spine conditions [10].

Patients with Multiple Pain Conditions

The patient with multiple pain conditions may display excessive somatization, preoccupation with numerous physical complaints that cannot be fully attributed to an organic cause [51]. Although it is common for patients to be anxious and worry about persistent pain, conflicting diagnoses, and multiple treatment recommendations, there is a subset of individuals who display a more long-standing picture of somatization and relatively extreme somatic overconcern. Although the term "symptom magnification" has been used in some occupational medicine settings [52], this term may erroneously imply intent to

deceive caregivers. A patient with marked somatization may tailor the description of various pain complaints to the specialty of the physician, complaining about diffuse symptoms to the rheumatologist, back pain to the orthopedic surgeon, and multiple unexplained GI complains to the gastroenterologist. Preoccupied by minor bodily concerns, the somaticizing patient may consult multiple clinicians and subject themselves to unnecessary diagnostic studies and interventions in an effort to validate the seriousness of their complaints. Electively seeking medical treatments for each body part or complaint can further complicate the problem, as each specialist clinician provides a new and ominous-sounding diagnosis. In this way, a diagnosis of degenerative disc disease associated with normal aging can become a crippling condition.

Patients with somatization may be particularly resistant to psychological referral, and they rarely are adherent to treatment in general mental health clinics due to this recalcitrance. Although some data show somatization may respond to structured behavioral treatments, patients' complaints are often best managed with frequent primary care visits to offer reassurance and guidance that will minimize multiple unnecessary tests and avoid iatrogenic complications. Behavioral programs that focus on ignoring or decreasing focus on somatic symptoms and improving function despite pain may be helpful, although long-term management will often be necessary. A key to good patient outcomes involves identification of the patient with somatization as early in the treatment process as possible. Screening questionnaires such as the PHQ-15 may help [53], but a comprehensive interview remains the gold standard of assessment of this complex patient population.

Behavioral Treatments to Optimize Outcome

Behavioral treatment remains a mainstay for optimizing outcomes for spinal treatments. Short-term behavioral interventions should focus on establishing realistic and measurable treatment goals, encouraging adherence with medication or rehabilitation treatments, reducing comorbid symptoms of anxiety and depression, addressing functional sleep disorders, managing substance use risk, navigating work-related barriers, and addressing unhelpful behaviors of family members. Many studies of behavioral pain management interventions overlap in focus [54]; the literature does not support the efficacy of one intervention over another [49], although individualizing treatment to specific goals is important for successful outcomes. Cost-effective group therapy approaches and delivery of services by nonmental health providers also have received growing attention to provide access to care when individual services are unavailable or financially beyond the patient's reach.

Cognitive behavioral therapy (CBT) for chronic pain is based on the concept that pain and its associated functional impairment are influenced not only by physical pathology but also by the individual's emotional states, thoughts about their pain, and behavioral responses to pain. CBT interventions aim to reduce pain by modifying the associated cognitive and emotional distress as well as improving function and quality of life. Typical approaches used in CBT for chronic pain include goal setting, psychoeducation about pain perception, relaxation training and stress management strategies, time-based activity pacing (and/or quota-based activity), and cognitive restructuring of maladaptive thoughts, beliefs, and attitudes [55].

Psychoeducation includes helping the individual understand the pathophysiology of pain while highlighting the impact of physical, cognitive, emotional, behavioral, and social factors on the patient's pain experience. *Relaxation strategies*, such as diaphragmatic breathing and progressive muscle relaxation, can help patients cope more effectively with pain and the associated anxiety and stress by reducing muscle tension, increasing self-efficacy, and reducing the intensity of pain. *Time-based activity* (activity pacing) interventions help patients to maintain consistent levels of day-to-day activity instead of pushing through tasks to the point of excessive pain and subsequent disability. *Operant approaches*, in contrast to activity pacing, teach patients to engage in an activity for a predetermined amount of time despite their experience of pain. Some studies suggest that this approach may be more effective than activity pacing, as the patient "works through" the pain and becomes less fearful of its occurrence. *Cognitive restructuring* teaches patients to identify and challenge their distorted assumptions or maladaptive thoughts (e.g., black- and white-thinking or overgeneralizing) and practice more realistic or adaptive alternative ways of thinking about their pain. A meta-analysis of 22 studies showed CBT for back pain resulted in improvements in reported pain, pain-related interference with activities, health-related quality of life, and depression [6].

Although meditation has a long history in the treatment of chronic and acute pain, *mindfulness-based stress reduction (MBSR)* was first introduced in the late 1970s and offers a structured, group-based approach to mindfulness training in western healthcare settings. In this now well-studied model, the concepts underlying *mindfulness* are taught by first normalizing the ways in which we habitually practice *mindlessness*, most notably, by spending significant portions of our time focused on thoughts about the past, future, and ourselves; by judging our experiences (internal and external) as pleasant, unpleasant, or neutral; and by quickly reacting to experiences based on these judgments (moving toward, avoiding/escaping, or ignoring). Patients are then taught various mindfulness techniques, including focusing the

attention on present moment experiences (e.g., the senses, the breath, or other bodily sensations), embracing attitudes of acceptance and non-judgment, and refraining from habitual, avoidant reactions to pain or related distress. MBSR therefore promotes the repeated practice of acceptance and non-reactivity each time a challenging emotion or sensation (including pain) arises. As this attitude is practiced through the MBSR program, it then generalizes to experiences of pain and distress at other times. A systematic review of MBSR for low back pain found improvements in pain intensity and physical functioning [18], and a study comparing MBSR to CBT for chronic low back pain showed the two interventions to be similarly effective, with improvements in pain catastrophizing, self-efficacy, mindfulness, and acceptance [56]. Mindfulness training can be an effective, stand-alone intervention for chronic pain and can also be incorporated into other behavioral treatment approaches.

Acceptance and commitment therapy (ACT) is a form of cognitive therapy that combines acceptance and mindfulness practices with commitment and behavior change processes to increase psychological flexibility. Rather than trying to directly change the *content* of difficult thoughts, emotions, and physical sensations (as in traditional CBT), the goal of ACT is to create a psychological *context* (psychological flexibility) in which pain sensations and associated thoughts and emotions can occur without dictating the patient's function and quality of life. Psychological flexibility can be defined as "the ability to be in the present moment with full awareness and openness to our experience, and to take action guided by our values" [63]. Cognitive defusion techniques allow patients to gain distance from their thoughts and view them as simply words, sounds, or images that may or may not warrant a behavioral response. Examples include adding the phrase "I notice I am having the thought that…" before an unhelpful thought or using formal mindfulness practice with an emphasis on acknowledging thoughts without getting caught up in them, then returning focus to some other objects of attention, such as the breath. ACT for chronic pain has similar effectiveness as traditional CBT approaches. A systematic review of ten randomized control trials of ACT for pain [19] concluded that ACT led to improvements in pain intensity, sick leave usage, pain disability, physical function, depression, anxiety, and life satisfaction. There has been only one study that compared traditional CBT approaches to ACT for chronic pain patients, and both groups showed similar improvements in function, mood, and anxiety, with ACT participants expressing greater satisfaction with care [57].

The "acceptance" component of ACT interventions makes this intervention consistent with operant approaches in which pain itself is not targeted as an outcome variable. The patient is taught to "accept" the variability of pain experiences and to focus instead on goal setting around function "despite" the pain. *Operant approaches* for chronic spinal pain gained popularity in the early 1980s with the early work of Wilbert Fordyce (1976) and a classic text that was reissued by Main et al. [64] that provided a model for operant treatments within the context of interdisciplinary care. The 1990s saw a parallel development of operant treatment programs developed by Thomas Mayer and associates, with efforts to commercially develop "functional restoration" outpatient spine rehabilitation programs throughout the country [58]. Subsequent Cochrane reviews addressing this focus of interdisciplinary care provide support for this approach [15] although problems include reimbursement barriers and programs marketing the "functional restoration" approach while failing to adhere to learning theory principles.

Main et al. [64] and Gatchel et al. [50] offer detailed templates for establishing an operant pain rehabilitation treatment protocol. Using a structured rehabilitation approach, patients establish a clear set of functional goals and identify "pain behaviors" (such as complaints of pain, stopping activity because of pain, using PRN medications, or utilizing passive relief strategies and devices). Patients are taught that "hurt" does not equal "harm," and they are expected to increase specific physical and recreational activities with a pre-set quota, regardless of their pain experience. This approach is consistent with the ACT and mindfulness models in which the patient "accepts" the presence or exacerbation of pain without fighting or panicking while continuing to work toward functional, value-driven goals. Setting the goal of pain relief is specifically avoided in the operant model, as the patient works toward improving function despite the presence of pain. A recent study demonstrated that gains in aerobic exercise tolerance may be an insufficient measure of improvement, and importance also must be placed on gradually exposing the patient to situations that elicit fear of movement.

Figure 35.1 illustrates the relationship between pain and activity for the patient who develops chronic pain. Pain may start with an acute injury or pain "flair," and the patient seeks acute treatment while temporarily reducing activity. Over time, "pain-contingent" treatments get added, and the patient's escape from activity or sedentary behavior is rewarded. As illustrated in Fig. 35.2, the individual ultimately becomes deconditioned and disabled with prolonged periods of inactivity. Iatrogenic problems may develop in response to new, diffuse pain complaints. Multiple treatments are often added, including surgeries and medications, with "pain behaviors" reinforced with each transient reduction in pain. Concomitant psychological symptoms typically appear, including anxiety, depression, and sleep disorder. Clinicians may unwittingly reinforce the pain and disability behaviors in the struggle to offer the patient pain relief. An operant approach paradoxically targets specific

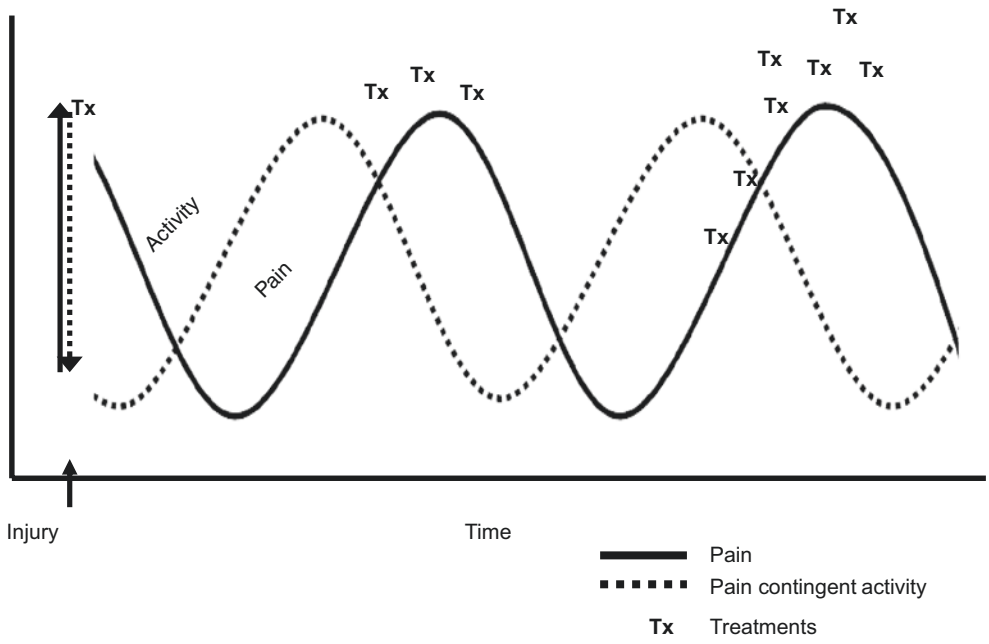

Fig. 35.1 Initial development of chronic pain with pain-contingent activity. (Adapted from [17, 61])

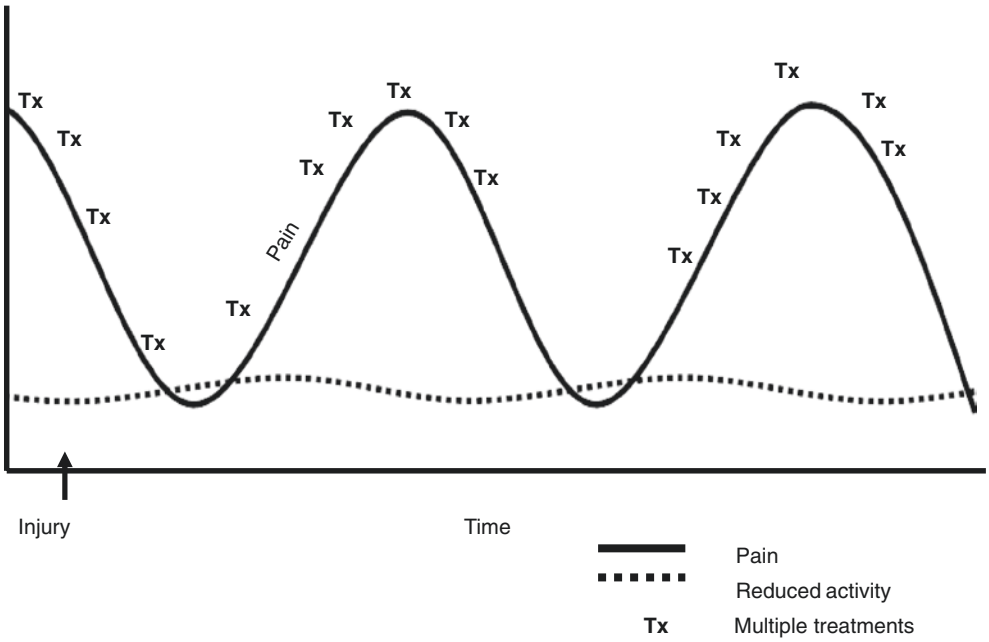

Fig. 35.2 Development of disability and chronic pain. (Adapted from [17, 61])

functional goals that are pursued despite the experience of pain, and the use of pain-contingent or "pain relief" strategies is abandoned. Figure 35.3 illustrates the introduction of a progressive activity program, such as timed walking increased at 1-minute increments per day despite pain. Most importantly, activities are tied to quantifiable goals, e.g., visiting the grocery store at week 3, returning to part-time work by week 7, etc. Not all patients with chronic pain are ideal candidates for this approach, although those individuals who recognize that their lives have become overtaken by pain limitations and multiple pain treatments may be reasonable candidates for this intervention.

Barriers to Behavioral Assessment and Care

There exist numerous barriers to behavioral interventions including cultural factors and stigma, and patients with chronic pain typically do not seek out behavioral assessments on their own [59]. Many are only referred when a crisis arises,

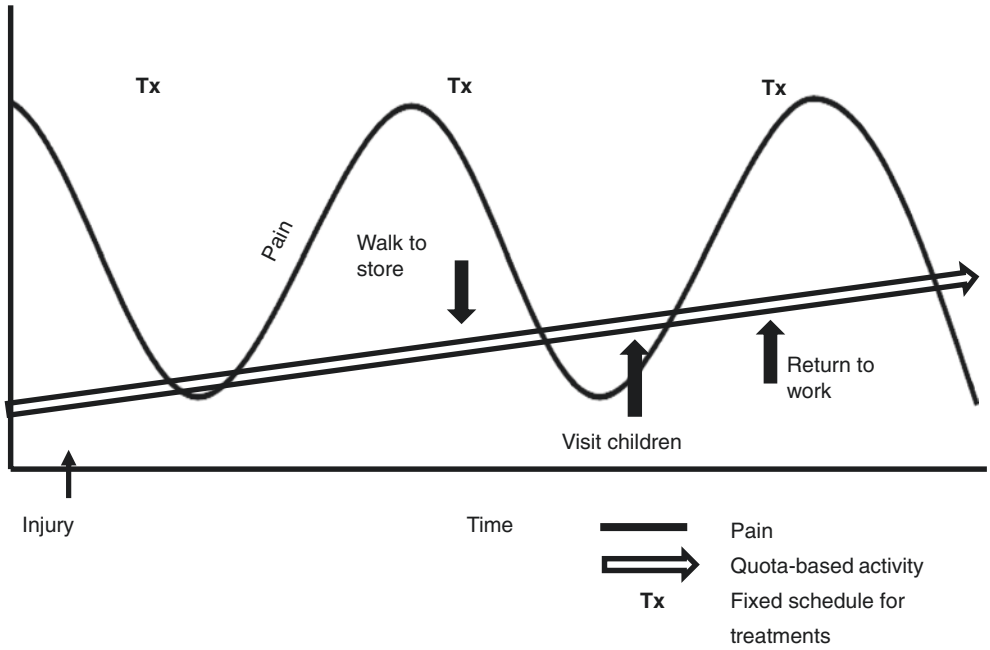

Fig. 35.3 Increasing quota-based activity and achieving goals despite pain. (Adapted from [17, 61])

and the patient may perceive the referral as a message that the clinician "thinks it's all in my head" or "thinks I'm an addict." Clinicians themselves may be reluctant to directly address psychosocial barriers, sometimes avoiding direct confrontation of resistance by simply referring the patient to a pain clinic ("I never refer them directly, they can get psychological help when they get there."). However, including a pain psychology assessment early in the evaluation process and normalizing referrals for behavioral interventions may reduce patient anxiety and improve adherence. Embedding a psychologist within spine and pain centers also may help reinforce that mental health services are readily available within the multidisciplinary pain setting. Acknowledging patients' concerns and discussing these approaches openly with the patient and family also can help overcome resistance. Another barrier may include limited reimbursement for behavioral services; although national healthcare parity laws have attempted to address this issue, insurance-related barriers to care continue to be a significant problem. Some pain care facilities include the services of an experienced behavioral pain clinician as part of routine care, recognizing that any financial losses from poor reimbursement may be more than offset by the psychologist's time investment freeing up the schedule of pain physicians and surgeons.

Another barrier is the limited number of psychologists and psychiatrists with expertise in pain assessment [65]. Currently there is no board certification for pain psychology. Referring clinicians often must delegate assessment and treatment responsibilities to off-site mental health clinicians who may have little or no specialized experience in the field. There has been pushback against referrals that "rubber stamp" behavioral screenings for procedures such as spinal column stimulation, with payers refusing to reimburse for care unless the clinicians meet a minimum standard of training [60, https://www.mass.gov/files/documents/2016/08/tp/cl-340.pdf].

Summary

Psychological assessment and management are critical elements of comprehensive care for the patient suffering from persistent spinal pain conditions. To optimize patient outcomes, psychological assessment should ideally occur early and be integrated within the comprehensive care plan for the patient. Although it is ideal to include a pain psychologist on the spine or pain treatment team, outside referrals should be directed to clinicians with specialized training and expertise assessing and managing chronic pain, disability, and the common psychosocial concomitants of pain. Finally, psychological care should not be restricted to an initial assessment; for some patients, ongoing integrated behavioral follow-up is critical to maximize functional gains. Standardized self-report or other objective measures of function should be used to document progress over time, as many patients with persistent spine pain will not maintain their gains. Behavioral interventions provide valuable opportunities to optimize patient outcomes when the treatment team recognizes and adequately addresses the numerous psychosocial factors impacting the care of the patient with spine pain. Early recognition and management of psychosocial factors predict better outcomes for acute pain, and when the pain becomes chronic, the standard of care requires adequate assessment of behavioral issues to ensure optimal care management, reduced patient suffering, improved function, and reduced overall cost of care.

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Integrative Medicine

36

Peter I-Kung Wu and Lucy Chen

Key Points

- *Integrative medicine*, which is a discipline that combines conventional therapies with complementary and alternative therapies, has become part of medical practice and may have a unique role in clinical pain management because of the multidimensional nature of pain experiences that often requires multimodal approaches for successful management.
- *Complementary medicine* refers to unconventional healthcare systems, practices, and products that are used in combination with conventional medicine, while *alternative medicine* refers to those that are used independently in place of conventional medicine.
- Approximately 38% of adults and 12% of children in the United States use complementary and alternative medicine (CAM). In 2007, 3.2 million clinical visits were for acupuncture treatment. The other most commonly used CAM therapies include natural products, deep breathing, meditation, chiropractic or osteopathic practice, and massage therapy. Low back pain is among the most common medical conditions treated by CAM. With increasing demand for CAM therapies, the majority of medical schools in the United States have incorporated coursework on integrative medicine.
- Acupuncture is perhaps the most studied both preclinically and clinically and is one of the most commonly practiced among the five major categories of CAM: whole medical systems, mind-body medicine, biologically based practices, manipulative and body-based practices, and energy therapies.
- The safety, efficacy, and cost-effectiveness of acupuncture are gaining appreciation and support, and the neurohumoral mechanisms are beginning to be understood.
- With the aging population and ever-growing cost of healthcare in the United States, more emphasis is being placed on preventive and alternative measures. Many CAM therapies may add value as primary treatments or as useful adjuncts to conventional treatment to allow us to reach the goal of maintaining health, reducing costs, and improving patient satisfaction.

Case Presentation

A 45-year-old construction worker with a 5-year history of intermittent axial low back pain and recent acute onset of left-sided low back pain associated with occasional numbness in the left first toe is referred to the Pain Clinic by his primary care physician. Back pain had progressed over the past year despite pain medications and physical therapy. Pain is described as a dull, throbbing ache in the lumbosacral area with episodic numbness and tingling in the left first toe, worsened with prolonged standing, sitting, and lifting. While findings from his neurologic examination and straight leg raise test are normal, magnetic resonance imaging (MRI) of his lumbar spine shows evidence of moderate degenerative disc disease at the L4–L5 and L5–S1 levels along with a small left paracentral disc herniation at L5–S1 with minimal neural foraminal narrowing. The patient would like to avoid injections and inquires whether acupuncture would be beneficial.

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Introduction

Integrative medicine, as defined by the American Board of Integrative Medicine and the Consortium of Academic Health Centers for Integrative Medicine, "is the practice of medicine that reaffirms the importance of the relationship between practitioner and patient, focuses on the whole person, is informed by evidence, and makes use of all appropriate therapeutic approaches, healthcare professionals, and disciplines to achieve optimal health and healing [1]." Integrative medicine combines conventional medicine with select practices from complementary and alternative medicine (CAM), for which there is some high-quality, scientific evidence for safety and efficacy, in order to facilitate the body's innate healing response, accounting for factors that influence the whole health and wellness of the patient – including mind, body, and spirit – and applying the broad concepts of health promotion, illness prevention, and healthy living. While the development of integrative medicine was influenced in part by CAM practitioners, its practice is not "alternative" but driven by exploring and scientifically validating new paradigms of treatment. The discipline embraces the form of treatment that is best suited to optimize health and healing, bringing together both conventional and complementary approaches in a coordinated way, commonly considering less invasive and less harmful interventions when possible, to treat the whole person rather than solely alleviating symptoms. Integrative medicine has become part of medical practice, taught in many medical schools and through residency and fellowship programs since the 1990s [2]. Integrative medicine may have a unique role in clinical pain management because the multidimensional nature of pain experiences often requires multimodal approaches for successful management.

In contrast to conventional medicine as practiced in the United States by holders of M.D. (medical doctor) or D.O. (doctor of osteopathy) degrees and by their allied health professionals such as physical therapists, psychologists, and registered nurses, CAM encompasses a group of diverse healthcare systems, practices, and products arising from various origins that are not generally considered to be a part of conventional Western medicine. *Complementary medicine* refers to such treatment modalities that are used in combination with conventional medicine, while *alternative medicine* refers to treatment modalities used independently in place of conventional medicine. See Table 36.1 for major categories of complementary and

Table 36.1 Major categories of complementary and alternative medicines

Whole medical systems: based on complete systems of theory and practice that often have evolved apart from and earlier than the conventional medical approach used in the United States	
Homeopathy	Seeks to stimulate the body's ability to heal itself by giving very small doses of highly diluted substances that in larger doses would produce illness or symptoms, based on the theory that any substance that can produce symptoms of disease or illness in a healthy person can cure those symptoms in a sick person. Remedies are derived from many natural sources, including plants, metals, and minerals [6]
Naturopathy	Proposes that a healing power in the body establishes, maintains, and restores health. Treatments aim to support the body's ability to heal itself through the use of dietary and lifestyle counseling and modification, dietary supplements, medicinal plants, exercise, massage, homeopathy, and treatments from Traditional Chinese Medicine
Traditional Chinese Medicine (TCM)	A whole medical system that originated in China based on the concept that disease results from disruption in the flow of Qi (body's energy) and imbalance in the forces of Yin and Yang. Practices such as herbs, meditation, massage, and acupuncture seek to aid healing by restoring the Yin-Yang balance and the flow of Qi
Ayurveda	A whole medical system that originated in India that aims to integrate and balance the body, mind, and spirit to lead to contentment and health and prevent illness. A chief aim of Ayurvedic practices is to cleanse the body of substances that can cause disease. Therapies used include herbs, massage, and yoga
Mind-body medicine: involves techniques designed to enhance the mind's capacity to affect bodily function and symptoms	
Meditation	A group of techniques in which a person learns to focus the attention and suspend the stream of thoughts that normally occupy the mind to achieve greater physical relaxation, mental clarity, emotional calmness, and psychological balance to reduce stress, anxiety, depression, and pain [7]
Relaxation techniques	Any method, process, or activity that helps to relax, increase calmness, or reduce pain, anxiety, stress, or anger, along with providing health benefits including decreased muscle tension, lower blood pressure, and slower heart and respiratory rates, including guided imagery, meditation, progressive relaxation, and deep breathing exercises
Prayer	The practice of petitioning for physical healing through prayer, faith, mental practices, spiritual insights, or other techniques that enlist religious or spiritual means in an effort to prevent illness, cure disease, relieve pain, or improve health
Mental healing	A practice that emphasizes the interrelationship between mind and body and uses the power of thought to affect the body by removing deeply held thoughts and conceptions, releasing unexpressed emotions that negatively influence health or predispose to disease, and promoting positive thinking that fosters improved health
Yoga	A practice that combines physical exercise through specific movements and poses, mental focus through meditation, and breathing exercises to improve posture, flexibility, and strength; to calm the nervous system; to balance the body, mind, and spirit; and to lower stress, anxiety, and pain

Table 36.1 (continued)

Pilates	A movement therapy that emphasizes core strengthening and control, body alignment, posture, and coordination with controlled whole-body movements by the use of specific equipment, along with coordination of breathing and concentration, to promote both physical and mental health
Tai Chi	A mind-body practice that originated as a Chinese martial art based on performing routines of slow, graceful, continuous movements coordinated with breathing deeply to enable meditation, sometimes called "moving meditation," which is thought to facilitate and balance the flow of Qi throughout the body and promote physical and psychologic well-being [8]
Art therapy	A therapeutic technique that originated in the fields of art and psychotherapy focusing on the creative art-making process itself as an outlet to relax the mind and body and distract from stress and pain or on the analysis of self-expression communicated in the art itself to reconcile cognitive and emotional conflicts and foster self-awareness and personal growth
Music therapy	An expressive therapy in which a music therapist uses music and all of its facets – physical, emotional, mental, social, aesthetic, and spiritual – to help patients improve their physical and mental health. Therapy is catered to the individual and can use either active music experiences, such as free improvisation, music creation, dance, and discussion of music, or passive music experiences, such as listening, drawing, or meditating to music to achieve treatment goals such as reducing anxiety or distracting from pain
Dance/movement therapy	An expressive therapy that uses the correlation between movement, especially dance, and emotion for psychotherapeutic purposes and physical therapy to support intellectual, emotional, and motor functions of the body
Aromatherapy	A therapy in which the scent of essential oils from flowers, herbs, and trees is inhaled to promote health and well-being
Biologically based practices: use substances found in nature	
Dietary supplements Herbal supplements	Products taken orally that can contain vitamins, minerals, herbs or other botanical products, amino acids, enzymes, organ tissues, metabolites, extracts or concentrates, and/or other dietary ingredients intended to supplement the diet. These may also include other so-called natural but as yet scientifically unproven therapies, such as using shark cartilage to treat cancer. Among the most popular supplements are *Echinacea*, *Ginkgo biloba*, ginseng, feverfew, garlic, kava kava, and saw palmetto
Manipulative and body-based practices: based on manipulation and/or movement of one or more parts of the body	
Spinal manipulation (both chiropractic and osteopathic)	The application of controlled force to a joint and/or movement of one or more parts of the body in an effort to aid in restoring health. Manipulation may be performed as a part of other therapies or whole medical systems and combined with physical therapy and instruction in proper posture. Chiropractic manipulation applies hands-on therapy focusing on the relationship between the body's structure, primarily the spine, and its function. Osteopathic manipulation applies a full-body system of hands-on techniques to alleviate pain, restore function, and promote health and well-being
Massage	The manipulation of muscle and connective tissues of the body by pressing, rubbing, and moving using the hands and fingers to enhance function of those tissues, increase the flow of blood and oxygen to massaged areas, and promote relaxation and well-being
Energy therapies: affect energy fields that purportedly surround and penetrate the body and channel healing energy into the body to restore a normal energy balance and, therefore, health	
Qigong	A component of Traditional Chinese Medicine that combines gentle physical movements, meditation and mental focus, and controlled breathing with the intent to improve the flow of blood and Qi
Reiki	A therapy in which practitioners seek to transmit a universal energy to a patient, either from a distance or by placing their hands on or near that person, with the intent to heal the spirit and thus the body
Therapeutic touch	A therapy in which practitioners pass their hands over a patient's body with the intent to use their own perceived healing energy to identify energy imbalances and promote health
Bioelectromagnetic therapy	Therapies that involve the unconventional use of electromagnetic fields, such as pulsed fields, magnetic fields, or alternating-current or direct-current fields to influence bioelectromagnetic fields in the body for healing

alternative medicines based on the National Center for Complementary and Integrative Health (NCCIH; formerly the National Center for Complementary and Alternative Medicine) [3–5]. While different types of CAMs have been practiced since ancient times, appreciation and incorporation of these medicines in Western disciplines did not occur until the 1970s. Since then, advancements in both basic science and clinical research involving these medicines have substantially increased awareness of CAM modalities in Western countries.

Current Use of CAM

The use of integrative approaches for health and wellness has grown within care settings across the United States. According to results from a nationwide survey in 1998, alternative medicine use and expenditures increased dramatically from 1990 to 1997, with roughly 629 million office visits to practitioners of alternative therapies in 1997, amounting to 1.6 times the total number of visits to primary care physicians. The total out-of-pocket expenditures related to alter-

native therapies in 1997 were comparable to that for all US physician services, conservatively estimated at $27 billion [9]. From the National Health Interview Survey (NHIS) in 2012, approximately 33.2% of US adults (ages 18 years and older) and 11.6% of children (ages 4–17 years) used CAM therapies. Among them, 3.5 million adults sought acupuncture alone, demonstrating a steady increase in use from 2002 to 2012. The most commonly used CAM therapies were natural products (dietary supplements other than vitamins and minerals) – with 17.7% of adults and 4.9% of children using such products – followed by deep breathing, yoga/Tai Chi/Qigong, chiropractic or osteopathic manipulation, meditation, and massage. The percentage of adults who practice yoga also increased substantially, from 5.1% in 2002 to 6.1% in 2007 and 9.5% in 2012. About 59 million Americans spend out-of-pocket money on CAM approaches, with their spending adding up to $30.2 billion a year, representing 9.2% of all out-of-pocket spending on healthcare and 1.1% of total healthcare spending. Third-party reimbursements for alternative therapies have also increased at patients' requests [10]. In the United States, some of the most common medical reasons for which CAM therapies are sought are neck and back pain [11–13]. Those suffering from chronic pain, especially back pain, are more likely to use CAM therapies than those without chronic pain [9, 11, 14].

Due to the diversity of CAM therapies and goals for this chapter, rather than review every modality, we will focus our discussion on acupuncture as it is perhaps the most studied CAM modality, both preclinically and clinically. We will review the most current medical evidence on acupuncture and discuss its utility as a therapeutic option for comprehensive pain management.

Acupuncture

Acupuncture is one of the most commonly practiced CAM modalities. With the ever-growing demand for acupuncture, the US Food and Drug Administration (FDA) removed acupuncture needles from the category of "experimental medical devices" in 1996 and classified them as Class II medical devices under "acupuncture needle," 21 C.F.R. § 880.5580 (1996), subject to the same single-use standards of sterility and good manufacturing practices as medical needles, hypodermic syringes, and surgical scalpels [15]. At a 1997 Consensus Development Conference on Acupuncture organized by the National Institutes of Health (NIH), acupuncture was recognized as a modality used by millions of US patients and extensively practiced by medical physicians, dentists, non-MD acupuncturists, and other practitioners for relief or prevention of pain and a variety of medical problems [16]. In 2007, the American College of Physicians recommended in evidence-based clinical practice guidelines the use of non-pharmacologic therapies with proven benefits, such as massage, acupuncture, yoga, and spinal manipulation, as options for treating subacute (duration >4–8 weeks) to chronic low back pain, citing fair evidence that acupuncture had moderate benefit [17]. In May 2017, amid increasing concern about prescription pain medication overuse in the United States, the FDA proposed changes to its blueprint on educating healthcare providers involved in the treatment and monitoring of patients with pain, recommending that providers be knowledgeable about the range of available non-pharmacologic treatments, including complementary therapies such as acupuncture and chiropractic care, when they may be helpful, and when they should be used as part of a multidisciplinary approach to pain management in order to help patients avoid opioids [18]. By January 2018, the FDA finalized this update to the opioid analgesic risk evaluation and mitigation strategy education blueprint for healthcare professionals in pain management, encouraging comprehensive pain management that incorporates the use of non-pharmacologic and self-management options, including complementary therapies, to manage musculoskeletal and chronic pain in order to mitigate opioid overprescribing, misuse, and new addiction [19].

Acupuncture Theory

Acupuncture is a therapeutic intervention that originated in China and has been practiced for over 4000 years as an integral part of traditional Chinese medicine. Based on the theory and practice of traditional Chinese medicine, human health is the result of harmony between body and nature and is maintained through a delicate balance of two opposing but inseparable forces, or elements, in the body: Yin ("cold, slow, and passive" elements) and Yang ("hot, exciting, and active" elements). Accordingly, internal "organs" in the human body are divided into Yin and Yang organs. The balance of Yin and Yang influences the flow of the body's life-force, or vital energy known as *Qi* (pronounced "chee"), along specific pathways, or meridians, in the human body to influence health. The human body consists of 12 main meridians and 8 secondary meridians. Any imbalance between Yin and Yang disrupts or blocks the flow of *Qi*, leading to disease or pain, which can manifest as tenderness on palpation. Acupuncture was developed to prevent illness and has also been useful in managing disease symptoms by restoring the balanced flow of *Qi* [20, 21].

The practices of acupuncture in the United States, which first gained public and professional attention in the 1970s [22], incorporate medical traditions from China, Japan, Korea, and other countries and encompass a set of procedures involving stimulation of anatomical points using a variety of techniques. The acupuncture technique that has been most

studied scientifically involves inserting sterilized, fine, solid, metal needles into the skin at specific points (called acupuncture points or acupoints) that are primarily located along the meridians. Other means of stimulating acupoints include the use of heat (moxibustion), mechanical pressure (acupressure), electrical stimulation (electroacupuncture, EA), or laser light (laser acupuncture) [23]. Acupuncture treats a disease condition or pain through strengthening weakened *Qi*, releasing excessive *Qi*, and/or removing blockage from the flow of *Qi* in order to restore the normal balance of the Yin and Yang system [24].

Mechanisms of Acupuncture

The biological effects and mechanisms of action of acupuncture have not been fully elucidated in terms of the principles of understanding in Western medicine. While research continues, a number of studies have revealed acupuncture produces a variety of effects on the peripheral and central nervous system (CNS) as well as influences neurohumoral factors, neurotransmitters, and other chemical mediators as part of its overall therapeutic effect.

Peripheral and Central Nervous System

Acupuncture points have been reported to correspond to focal cutaneous areas with distinct electrophysiologic characteristics, such as reduced electrical impedance, and histologic differences compared to adjacent tissue [25, 26], while meridians have been found to locate to intermuscular or intramuscular connective tissue planes, or fascial planes [27, 28]. Within this fascial network, acupuncture points and meridians have both been found to map to and overlie neuronal structures, such as the median, peroneal, trigeminal, and facial nerves, among others [29], with type II afferent nerves involved in mediating acupuncture analgesia [30]. Analgesic effects have been thought to be mediated in part by temporary stimulation of inhibitory nerve fibers to reduce transmission of pain to the brain via the gate control theory [31–33]. Infiltration of local anesthetic around an acupuncture point can abolish the analgesic effect of acupuncture; however, vascular occlusion of the upper arm could not prevent acupuncture analgesia in the hand, suggesting that neurologic connectivity mediates acupuncture analgesia to some degree [34].

Meridians correlating to specific internal organs as defined by traditional Chinese medicine theory have been found to be associated with the organ representation area in the cerebral cortex corresponding to the specific organ, within which acupoints associate to cortex areas with increased concentration of neurotransmitters, such as serotonin [35]. Positron emission tomography (PET) scan and functional magnetic resonance imaging (fMRI) studies of the brain have further revealed the effects of acupuncture on neuronal changes in the CNS. PET studies have found that acupuncture over 4 weeks compared to sham in chronic fibromyalgia patients can induce both short- and long-term upregulation of μ-opioid receptor binding availability in multiple pain and sensory processing brain regions, such as the cingulate, caudate, and amygdala, which are associated with clinically relevant reductions in pain [36]. Acupuncture attenuates the neuronal response to nociceptive stimuli in the periaqueductal gray, thalamus, hypothalamus, somatosensory cortex, and prefrontal cortex [37, 38]. While acupuncture effects have been found to commonly associate with modulation of the sensorimotor cortical and limbic-paralimbic-neocortical networks [39, 40], stimulation at different acupuncture points can induce different patterns of neuroimaging signal change in various areas in the CNS [41]. For example, EA (at low frequency) at a particular acupoint has been shown to produce more widespread fMRI signal changes in the anterior insula area as well as both limbic and paralimbic structures than manual acupuncture does [42], while EA at a different acupoint produces fMRI signal increases in the precentral/postcentral gyrus and putamen/insula, as compared to manual acupuncture that produces fMRI signal decreases in the posterior cingulate, superior temporal gyrus, and putamen/insula [43].

Humoral Factors and Neurotransmitters

Locally, acupuncture can induce the release of adenosine, a neuromodulator with antinociceptive properties, at the site of needle stimulation [44]. However, systemic acupuncture-induced analgesia may rely on inducing the release of humoral factors into the cerebrospinal fluid (CSF) and plasma, a notion supported by a cross-perfusion experiment in which analgesic effects were rendered in recipient rabbits infused with CSF from donor rabbits that received acupuncture [45], animal studies that showed acupuncture-induced increase of met-enkephalin in the cervical spinal cord and medulla [46], as well as clinical studies in which acupuncture triggered the production of endorphins in CSF and plasma [47–49]. It has also been shown that acupuncture significantly increases endorphin and anandamide (an endogenous cannabinoid) levels, with analgesia that can be blocked by the opioid receptor antagonist naloxone [50–52] or by a specific cannabinoid (CB2) receptor antagonist (AM630) [53]. EA at different frequencies can further differentially affect the synthesis and release of endogenous opioids in the CNS [54], such that analgesia from lower frequencies (2 and 15 Hz) is mediated by enkephalin, β-endorphin, and endomorphin, via μ- and δ-opioid receptors, while analgesia at higher fre-

quencies (100 Hz) is mediated by dynorphins with κ-opioid receptors [55–57]. As such, a μ-opioid receptor antagonist or antiserum against endorphin can block EA-induced analgesia at 2 Hz but not at 100 Hz [58, 59]. Different frequencies of EA can further differentially induce the release of other neuropeptides involved in pain modulation, including cholecystokinin, an anti-opioid peptide [60], orphanin, substance P, and angiotensin II, which has anti-opioid activity [55], indicating the selective activation of different supraspinal structures by different EA frequencies.

Animal research has found that EA can further modulate the release of dopamine, serotonin, epinephrine, norepinephrine [61–64], γ-aminobutyric acid (GABA, inhibitory neurotransmitter) [65, 66], adrenocorticotropic hormone, and cortisol [67]. Acupuncture further increases the release of nitric oxide [68] and downregulates the expression of pro-inflammatory cytokines interleukin (IL)-6 and IL-1β [69]. Studies have shown that analgesia induced by EA at different frequencies (2, 10, or 100 Hz) can be partially blocked by a serotonin receptor antagonist, suggesting serotonin may be a prominent mediator of acupuncture-induced analgesia [70].

Clinical Data

Despite the growing popularity and use of acupuncture among patients and medical professionals, debate remains over its utility and overall efficacy given explanations of its mode of action are based on ancient philosophy. Both early studies and ongoing efforts with randomized controlled trials (RCTs) seek to replace anecdotal case reports of therapeutic benefit with evidence to clarify the role of acupuncture in clinical pain management. Challenges in acupuncture studies relate to not only placebo control, crossover design, and individualization [71], but also issues unique to acupuncture. In particular, acupuncture has been shown to activate peripheral nerve fibers of all sizes, rendering systematic responses that are complex to study. And, effects of the acupuncture experience can be influenced by the psychosocial context, expectations, and beliefs [72, 73].

Low Back Pain

Low back pain is one of the most common health problems. It is associated with substantial morbidity and disability, affecting up to 70% of persons in Western industrialized countries at some point in their life, amounting to one of the most common reasons for visits to a physician in the United States and accounting for more than $90 billion annually in medical expenses [74]. Acupuncture has become one of the most frequently used CAM therapies for treating low back pain given its limited side-effect profile.

Several clinical trials have evaluated the efficacy of acupuncture for chronic low back pain. Findings from a 2002 RCT involving 131 patients with non-radiating low back pain for at least 6 months who were randomized into one of three groups for 12 weeks of treatment – (1) control (received only physical therapy) or 20 sessions of either (2) acupuncture or (3) sham acupuncture in addition to physical therapy – indicated that acupuncture was superior to physical therapy by the end of treatment for reducing pain, pain-related disability, and psychological distress. Compared with sham acupuncture, acupuncture was superior in reducing psychological stress [75]. A 2006 RCT of 3093 patients with chronic low back pain who were randomly assigned to receive either acupuncture or no acupuncture in addition to routine care showed that acupuncture plus routine care was associated with significantly greater improvement in back function (Hannover Functional Ability Questionnaire) at 3 months than routine care alone, and it was relatively cost-effective [76]. While further RCTs also indicate a superiority of verum acupuncture over sham acupuncture at non-acupuncture points for reducing low back pain intensity and bothersomeness [77, 78], others have shown no difference in benefit between verum and sham even while both are superior to usual care. For example, in a 2007 study of 1162 patients with chronic low back pain, the effectiveness of verum Chinese acupuncture (47.6%) was similar to sham acupuncture with superficial needling at non-acupuncture points (44.2%) for improving pain by 33% or more or back function by 12% or more 6 months after treatment; however, both treatments were nearly twice as effective as conventional therapy of a combination of medication, physical therapy, and exercise (27.4%) [79]. Thus, the benefit of acupuncture beyond placebo has been questioned [80, 81], as well as the validity of sham acupuncture to serve as a control with different effects from verum acupuncture [82], given that needling at non-acupuncture points may have nonspecific effects [83] or analgesic activity [84] based on diffuse noxious inhibitory control phenomena [85], a mechanism also proposed to underlie acupuncture analgesia independent of topographic specificity for acupoints [86, 87].

Further trials continue to evaluate efficacy. A 2008 meta-analysis of 23 RCTs (n = 6359) evaluating the use of acupuncture for nonspecific low back pain showed that while there is strong evidence of no significant difference between acupuncture and sham acupuncture, there is moderate evidence that acupuncture is more effective than no treatment for short-term pain relief and strong evidence that acupuncture can be a useful adjunctive measure to conventional therapy for treating low back pain [88]. A separate 2010 systematic review of eight acupuncture RCTs showed similar findings [89]. However, a most recent meta-analysis in 2013 demonstrated acupuncture was superior to self-care with a moderate significant difference in pain reduction and a large

significant difference in functional improvement; and acupuncture was clinically more effective than sham acupuncture in reducing pain up to 3 months following intervention, but no more effective than sham acupuncture in improving function [90]. Studies continue to evaluate the appropriateness of sham or placebo acupuncture to serve as controls in acupuncture studies [84].

Overall, joint clinical practice guidelines from the American College of Physicians and the American Pain Society recommend physicians consider acupuncture as a cost-effective [91] treatment option with proven benefits for management of low back pain [17, 92]. Studies have sought to determine the relative benefits of acupuncture compared to other therapy options. Comparative effectiveness evaluation of acupuncture versus transcutaneous electrical stimulation (TENS) showed that both provided clinically significant reduction in pain intensity and analgesic medication use after 4 weeks of treatment; however, acupuncture appeared to be more effective than TENS in improving lumbar spinal flexion range of motion [90, 93]. Acupuncture provided a somewhat greater improvement in functional activity and medication use (NSAIDs, muscle relaxants, analgesics) [90]. Acupuncture with manual stimulation of applied needles provided greater relief of low back pain than local injection of dibucaine, with both immediate and sustained effect 4 weeks after treatment [94]. While one study found acupuncture to be more effective than Thai traditional massage in reducing myofascial back pain when affective aspects are considered (McGill Pain Questionnaire) [95], another comparative study found massage therapy to be more effective than acupuncture in reducing pain and disability for chronic low back pain [96]. Thus far, there has been insufficient evidence regarding the relative benefits of acupuncture compared with either structured exercise or spinal manipulative therapy for treating chronic low back pain [97]. There are also limited data to draw conclusions on the effectiveness of acupuncture for treating acute low back pain [98].

Furthermore, it remains unclear as to which mode of acupuncture and means of its application are most effective. The duration of an acupuncture session appears to be an independent parameter to treatment outcome. For example, 30- and 45-minute EA treatment durations resulted in similar improvements in pain, physical activity, quality of sleep, and oral analgesic use; and outcomes for both durations were better than 0- (no treatment) and 15-minute treatment durations [99]. Both individualized acupuncture treatment and standardized acupuncture provided similar improvements in pain and function, and both were found to be more effective than usual care [100]. Motion style acupuncture, which requires a part of the patient's body to move passively or actively while acupuncture needles are retained, was found to reduce pain and improve function (Oswestry Disability Index) more than diclofenac injection to treat acute low back pain, with effects lasting 4 weeks after treatment [101]. *Hegu* acupuncture, which involves manipulation of the needle and needling in a fan-like pattern in relation to the meridian at an acupoint, was found to provide significantly greater pain reduction and functional improvement than standard acupuncture for chronic low back pain, with greater benefit lasting up to 48 weeks [102]. Electrical heat acupuncture, involving the application of heat over inserted needles, provided significantly greater pain relief of chronic low back pain than did EA; however, EA provided significantly greater functional improvement [103]. Time method acupuncture, which involves adding confluent acupoints related to the time of day to regular acupuncture, based on the traditional Chinese medicine principle that the environment affects systems in the body, can enhance pain reduction and reduce pain relapses compared to standard acupuncture for chronic low back pain [104].

Neck and Shoulder Pain

Studies demonstrate promising results for the use of acupuncture to treat chronic neck and shoulder pain. Several clinical trials of acupuncture for chronic neck pain with sample sizes spanning 115–177 patients have demonstrated that acupuncture was superior to controls in reducing neck pain and improving overall range of motion [105–109]. For neck pain from cervical spondylosis, an RCT of 106 subjects randomly assigned to either verum or sham acupuncture showed the verum acupuncture group had a 75.5% effectiveness to reduce pain compared to 52.8% in the control group ($P < 0.05$) [110]. In another study, acupuncture treatment reduced chronic neck and shoulder pain for at least 3 years with concomitant improvements in depression, anxiety, sleep quality, pain-related functional impairment, and quality of life [111, 112].

As it can be for low back pain, acupuncture can be a useful adjunctive therapy to conventional management to treat neck pain. The combination of acupuncture plus physical therapy was found to be more effective than physical therapy alone in improving pain and function in tension neck syndrome, and the combination was more effective than either acupuncture or physical therapy alone in improving neck muscle strength after 10 weeks of treatment, with sustained effect 6 months after treatment [113]. A multicenter RCT investigated the effectiveness of acupuncture in addition to routine care compared to that of routine care alone in 14,161 patients with chronic neck pain (duration >6 months). Subjects were randomized to an acupuncture group (1880 subjects, 15 acupuncture sessions over 3 months) or a control group receiving no acupuncture (1886 subjects). Findings demonstrated superiority of the addition of acupuncture to routine care over rou-

tine care alone to provide significant improvements in neck pain and disability ($P < 0.001$) after 3 months of treatment, with benefit maintained through 6 months [114].

Chronic myofascial neck pain is frequently treated with physical therapy or trigger point injections applied using either local anesthetics or dry needling. In one study of neck myofascial pain, acupuncture needling of the trapezius was as good as injection of 0.5% lidocaine at improving pain and neck range of motion, with benefits lasting up to 4 weeks after treatment [115]. A prospective, randomized, double-blind, sham-controlled crossover study compared acupuncture at distant points, sham laser acupuncture, and dry needling of local myofascial trigger points in patients with chronic neck pain and limited cervical spine function. Acupuncture provided significantly greater reduction of motion-related pain and improvement in range of motion compared to both sham and local dry needling [116]. While acupuncture and myofascial trigger point needling frameworks differ significantly, the correspondence between trigger points and acupoints, in particular Ashi points (tender points that are not necessarily acupoints in traditional Chinese medicine theory), has been studied [117], and based on the use of the same types of needles, similar stimulation points, similar needling techniques, and similar therapeutic effects, experts have argued that trigger point injection or dry needling is in fact a contemporary development of a simplified form of Ashi point acupuncture to treat myofascial pain, with some in the literature who refer to dry needling as trigger point acupuncture [118, 119].

Two meta-analyses have evaluated results from 10 and 14 clinical trials for the effectiveness of acupuncture for treating neck pain. There was moderate-quality evidence that suggests acupuncture is more effective than sham or inactive controls for relieving pain both immediately after treatment and at short-term follow-up. Overall, acupuncture demonstrated short-term effectiveness and efficacy in reducing neck pain [120, 121]. Similar findings were reported in a more recent meta-analysis [122]. Furthermore, a cost-effectiveness analysis involving a total of 3451 patients (1753 acupuncture group, 1698 control group) showed that treating patients with chronic neck pain with acupuncture in addition to routine care resulted in a marked clinically significant benefit and was relatively cost-effective [123].

Headaches

Many patients are refractory to current pharmacologic and conservative treatments for headache disorders such as migraine and tension headaches and seek CAM therapies like acupuncture for relief. A large, multicenter randomized trial of acupuncture for migraine (ART Migraine) involving 302 patients with migraine headache who were randomized into three groups (standard acupuncture, minimal acupuncture, and waiting list) found a significant therapeutic effect in those treated with acupuncture and minimal acupuncture as compared to those on the waiting list [124]. Many other studies of acupuncture for migraine [125–128], tension-type headache [129–132], and chronic headache [133, 134], with sample sizes from 50 to 2022 patients, have also shown similar results, and analyses indicate acupuncture is a cost-effective treatment for headache [135, 136]. More recent studies continue to show the superiority of verum acupuncture over sham acupuncture for relieving pain and reducing the use of medications for acute migraine attacks [137, 138].

The effectiveness of acupuncture compared to established pharmacologic management has also been studied. As a prophylactic treatment for migraine without aura, 2–4 months of acupuncture treatment was found to provide significantly greater reduction of the number of migraine attacks after 2 and 4 months of therapy, analgesia consumption at 2 months, and pain intensity compared to oral therapy with flunarizine, with significantly less frequent side-effects [139]. For early treatment of an acute migraine attack, acupuncture was as effective as sumatriptan in preventing a full migraine attack, with a superior side-effect profile compared to sumatriptan; however, sumatriptan was more effective in relieving headache when an attack could not be prevented [127]. Acupuncture was associated with a significantly greater reduction in the mean number of moderate or severe headache days per month compared to medical prophylaxis with topiramate, and adverse events occurred in only 6% of the acupuncture group compared to 66% of the topiramate group [140]. Compared to botulinum toxin A injection, acupuncture demonstrated significantly greater effectiveness at reducing pain severity of chronic migraine; and while both groups reduced the number of migraines per month, absence from work, and medication use, acupuncture did so with fewer side-effects [141].

Most recently, a 2016 Cochrane systematic review of the effectiveness of acupuncture for migraine prophylaxis analyzed 22 RCTs involving 4985 participants that compared an active acupuncture intervention of 8 or more weeks to one or more other interventions, including sham acupuncture, routine care only, and proven pharmacologic prophylaxis. Meta-analyses demonstrated acupuncture was associated with statistically significant improvement in both headache frequency and response when compared to routine care only up to 6 months following treatment, as well as when compared to pharmacologic treatment at 2 months but not at 3–4 months or 5–6 months following treatment. Acupuncture interventions had fewer participants drop out due to adverse effects compared to pharmacologic management, and acupuncture had statistically significant effects over sham at the end of treatment and at follow-up, leading to the conclusion that acupuncture should be considered a treatment option for migraine patients having frequent, inadequately controlled migraine attacks or adverse effects from medications [142].

Another 2016 Cochrane systematic review of the effectiveness of acupuncture for tension-type headache analyzed 12 RCTs involving 2349 participants that compared active acupuncture to sham, routine care only, and physiotherapy, massage, or relaxation. Meta-analyses demonstrated acupuncture was significantly superior to both routine care and sham acupuncture for both response and reduction in the number of headache days up to 6 months following treatment, suggesting acupuncture should be considered for treating frequent episodic or chronic tension-type headache [143].

Acupuncture is an effective and valuable option for patients suffering from migraine or frequent tension-type headaches. There are fewer adverse effects associated with this therapy compared with many standard drug treatment regimes used for headache management.

Other Pain Conditions

Acupuncture has been evaluated for treating many other pain conditions. There is low- to moderate-level evidence that acupuncture improves pain and stiffness in patients with fibromyalgia compared to no treatment or standard therapy [144], with associated increase in serum serotonin and decrease in serum substance P levels and improvements lasting up to 3 months [145]; however, there is moderate-level evidence showing that acupuncture does not differ from sham in reducing pain or fatigue. EA may be superior to manual acupuncture for improving fibromyalgia pain and function with effects lasting up to 1 month [144].

Similarly, earlier studies suggest that EA may be beneficial to reduce rheumatoid arthritis knee pain 24 hours and 4 months posttreatment compared to placebo [146]; bee venom acupuncture can reduce rheumatoid joint pain, stiffness, tenderness, and swelling compared to placebo [147]; and acupuncture may benefit gouty arthritis [148]; however, some studies also find that verum acupuncture is no better than sham, and the utility of acupuncture in treating rheumatoid arthritis has not been demonstrated in large RCTs [149].

Several studies have demonstrated results in favor of acupuncture for treating knee osteoarthritis (OA) [150], with fewer studies available for treating hip OA [151]. Acupuncture may provide pain relief lasting 12 weeks after administration [152], and moxibustion (involving the burning of moxa, the herb *Artemisia vulgaris*, at acupuncture points as a form of stimulation) can improve pain and function with effects lasting 18 weeks after treatment [153]. There is moderate-level evidence of superior or equivalent effects of moxibustion compared to sham, oral drug therapies, intra-articular injection, or topical drug therapy for improving pain and function in knee OA [154, 155]. Laser acupuncture can reduce periarticular swelling when compared to placebo laser [156]. For other musculoskeletal pain disorders, limited data show acupuncture may be superior to oral steroid for carpal tunnel syndrome, superior to exercise for Achilles tendinopathy, and no better than no intervention for patellofemoral pain [157]; but there is limited evidence to demonstrate the utility of acupuncture for treating lateral epicondyle tendinopathy [158, 159], acute ankle sprains [160], and shoulder pain [157, 161–163].

There is insufficient evidence to support or refute the overall use of acupuncture for neuropathic pain, when compared with sham acupuncture or other active therapies [164]. Some studies indicate that acupuncture provides benefit as adjunctive treatment for chemotherapy-induced peripheral neuropathy [165–167], phantom limb pain [168], lumbar radicular pain from disc herniation [169–171], and postpartum sciatica [172]. Some case reports also show the effect of acupuncture for treatment of cervical radicular pain [173] and complex regional pain syndrome [174–177].

Some studies also show benefit of acupuncture for reducing symptom burden in multiple myeloma patients undergoing stem cell transplantation with reduction of pain medication use compared to sham [178], and as adjunctive therapy for reducing cancer pain [179, 180], in particular, malignancy-related and surgery-induced pain in cancer [181].

Studies of acupuncture treatment for labor pain have shown that it can significantly reduce the experience of pain and need for epidural analgesia, with a better degree of relaxation, without adverse effect on delivery as compared with a control group [182, 183], and increased satisfaction with pain management; however, further studies are required [184]. Limited data suggest the efficacy of acupuncture for treating pain from chronic prostatitis [185]. There is insufficient evidence to demonstrate the effectiveness of acupuncture or acupressure for treating primary dysmenorrhea [186] or endometriosis [187].

Several studies have shown that patients who received acupuncture prior to surgery had a lower pain level, less opioid requirement during and after surgery, and a lower incidence of postoperative nausea and vomiting and sympathoadrenal responses [188–193]. Transcutaneous electrical acupoint stimulation may provide greater immediate postoperative pain relief and less opioid analgesia use compared to standard acupuncture [194].

Acupuncture has shown immediate analgesic effects, significantly greater than sham or analgesic injection [195]. Auricular acupuncture is a form of evolved traditional Chinese medicine known as microsystem acupuncture that uses particular somatotopic maps of acupoints situated at circumscribed parts of the body like the ear, scalp, mouth, and

hand that reflect organs and functions in the rest of the body in a somatotopic homunculus and aligns with the concept of somatic reflexology to influence the entire body. Auricular acupuncture has been shown to be a powerful tool to provide significant relief of not only chronic pain [196, 197] but also acute pain conditions in a variety of settings [198], including the emergency department [199–201].

Adverse Effects

A major reason that patients seek acupuncture is its remarkably low incidence of adverse effects compared to that of many medications and accepted medical procedures, making it a relatively safe treatment modality. A review of prospective surveys of adverse events associated with acupuncture showed that the most common adverse effects were needle pain (1–45%), tiredness (2–41%), and bleeding (0.03–38%); less common were fainting and syncope (0–0.3%), and rarely was pneumothorax (0.0008%) [202]. In a prospective large-scale survey with 34,407 acupuncture treatments in the United Kingdom, no serious adverse events were reported that required hospital admission, prolonged hospital stays, or caused permanent disability or death. A total of 43 minor adverse events were reported (0.13%), including severe nausea and fainting; unexpected, severe, and prolonged aggravation of symptoms; prolonged and unacceptable pain and bruising; and psychological and emotional reactions. Local reactions at the site of acupuncture included mild bruising, pain, and bleeding [203]. Another survey conducted in the United Kingdom also found a similar rate of adverse events, 14 per 10,000 treatments (0.14%) [204]. However, since acupuncture is an invasive medical intervention, more serious complications such as pneumothorax, cardiac tamponade, and spinal cord injury may occur if treatment is administered improperly [205]. A review of acupuncture-related serious adverse events reported in the literature from 1994 to 2004 that included 715 reports and data from 12 prospective studies that surveyed more than a million treatments demonstrated the risk of a serious adverse event with acupuncture to be 0.05 per 10,000 treatments and 0.55 per 10,000 individual patients, which is considered very low. Infection was the most common serious adverse event. Of these cases, over 60% were hepatitis B, followed by external ear infection from auricular acupuncture. After infection, there were far fewer cases of pneumothorax, followed by even fewer reports of CNS injury [206]. These more serious complications generally occur in elderly and more fragile and debilitated patients with complex comorbidities or in the hands of less skilled practitioners. Thus, it is imperative that acupuncture licensing regulations mandate training standards with strict requirements for knowledge of anatomy and sterile techniques.

Perspectives and Future Directions

Increasing awareness and popularity of CAMs have fostered the rapid growth of integrative medicine and the incorporation of therapies such as acupuncture into clinical practice. Many medical schools in the United States have already introduced integrative medicine into their curriculum [207]. To face ever-growing healthcare costs in the United States, health insurance providers have begun to emphasize preventive and alternative therapies based on their proven benefits for pain management.

Studies so far not only show the promise, but also demonstrate the effectiveness of CAMs such as acupuncture in treating a variety of pain conditions [208]. However, acupuncture is not a standardized therapy, and many variables can affect its potential effect, including chosen acupoints, needling technique, treatment duration, number of sessions, stimulation used, practitioner experience, and patient expectations. Ongoing and future studies continue to evaluate the efficacy and effectiveness of acupuncture to relieve pain from conditions such as cervical spondylosis [209], lumbar radiculitis [210], laparoscopic surgery [211], total knee arthroplasty [212], spondylolisthesis [213], vertebral compression fracture [214], neuropathic pain [164], cancer [215], and endometriosis [216]; and of different forms of acupuncture for treating pain disorders, including thread acupuncture for musculoskeletal pain [217], moxibustion for nonspecific lower back pain [218], bee venom acupuncture for rheumatoid arthritis [219], and EA for diabetic neuropathy [220] and chemotherapy-induced peripheral neuropathy [221]. Other studies further investigate the effectiveness of novel acupuncture-like stimulation devices [222]. NCCIH (National Center for Complementary and Integrative Health) of NIH continues to support research that builds the scientific foundation for complementary and integrative interventions in order to guide healthcare decision-making. Efforts continue to be made to introduce appropriate control treatments and blinding to improve the validity of acupuncture RCTs [223–225].

The advantage that acupuncture provides in relieving pain with minimal adverse effects offers a powerful, evidence-based, safe, and cost-effective alternative to pharmacotherapy for managing acute and chronic pain and a unique opportunity to decrease dependence on analgesic medications in the present climate of opioid overuse [226, 227]. Practical barriers still challenge access to acupuncture as a tool for pain management, including provider and patient perceptions and insurance plan coverage [228]. Numerous federal regulatory agencies have advised or mandated that healthcare systems and providers offer non-pharmacologic treatment options for pain. Acupuncture stands out as the most proven and immediate choice to address opioid overuse given not only its utility to improve symptom control and reduce opioid consumption [192, 229–231], but also its potential to directly address opi-

oid overuse disorder through the use of auricular acupuncture, as promoted by the National Acupuncture Detoxification Association [232, 233]. It is anticipated that CAMs such as acupuncture are likely to continue to play a growing and positive role in pain management.

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Organizational and Nursing Issues Related to Spine Pain Care

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Paul Arnstein

Key Points

- Back or neck pain is highly prevalent, and a most costly, disabling condition across the lifespan.
- Unrealistic expectations predispose patients to dissatisfaction and may lead to unreasonable demands for test and treatments.
- A comprehensive biopsychosocial assessment is the basis for an individualized multimodal treatment plan.
- Expanding the team to treat its biopsychosocial impact prevents the harm of discharging patients before they are fully treated.
- Increasing team efficiency begins with understanding the limits, overlapping skill set, scope of practice, and the value-added contribution of each member.
- Nurses are an often underutilized resource with a range of skills capable of helping patients, caregivers, and teams across the continuum of care.
- Effective nurse leaders foster a culture of quality and safety that balance concerns for pain reduction, improved biopsychosocial functioning, and avoidance of harm.
- Pain registries may improve efficient, equitable, evidence-based care that benefits patients, professionals, and the population served.
- Improving communication systems is essential to prevent gaps, duplication, delays, and fragmentation of care.

Introduction

Pain is a leading reason why patients seek healthcare [1]. Pain is also triggered by many diagnostic, treatment, and rehabilitative activities. Over 50 million Americans are admitted for major trauma or surgical procedures annually with over 100 million estimated to live with chronic pain [1–3]. Approximately 23 million Americans endure high-impact chronic pain that substantially restricts their ability to participate in work, social interactions, and self-care activities [4, 5]. The cumulative economic burden of chronic pain is considerable, incurring $10,000 per person and an annual national cost to the USA estimated at $600 billion in 2010 [1, 6].

Pain originating in the low back or neck makes up a significant proportion of these common and costly health problems. Low back pain typically is first seen in school-age children, which becomes increasingly common until 18 years of age, when its prevalence approximates that of adults [7]. When pediatric low back pain persists for weeks, up to 40% of these children have spondylolysis, and an MRI should be considered with a history of athletic activity. Identifying the stress fractures of the pars interarticularis is important given spinal immaturity that makes these fractures vulnerable to progression that may be a source of chronic pain throughout adulthood [8].

Back pain afflicts 12% of the population at any given time, with a monthly (23%), annual (38%), and lifetime (80%) prevalence exceedingly common [9, 10]. The prevalence of neck pain is similarly high, affecting 23% of the population, with wide variations noted based on age, gender, and occupation [11]. Although peak point prevalence is during middle-aged adulthood, the incidence of severe spinal pain increases with age making it the third most frequently reported symptom among adults over age 75 seeking healthcare services [10]. People with chronic low back pain have a tenfold higher rate of healthcare visits and often have comorbidities, disability, and limited financial resources that impede access to healthcare [12].

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Understanding pain that originates in the spine is particularly important because globally it consistently tops the list of disabling conditions. Large international databases containing over 300 diseases are analyzed to calculate a "Global Burden of Illness" representing the number of person years lived with a disability [6, 13]. For the past three decades, low back and neck pain have ranked as the most burdensome cause of disability accounting for over 57 million years lived with disability globally. Back and neck pain accounts for more cost and disability than cancer, heart attacks, opioid use disorder, and diabetes combined [13]. This costs an estimated 1.5–3.0% of the gross domestic product in developed nations [6].

Out of 27 million office visits for back pain each year, 42% are seen by primary care providers or chiropractors, 28% are seen in the emergency room, and 20% are seen by specialists [14]. These different providers are often wedded to their own, rather than evidence-based approaches [15]. Even within disciplines, the specific beliefs of individual providers (e.g., elevated fear-avoidance beliefs) can influence patient beliefs, treatments offered, and outcomes [16].

Patient beliefs may include unrealistic expectations that demand unnecessary or expensive treatments. Patients might expect to be "fixed" after a visit or two even though no such treatment for back pain exists [17]. Demand is also shaped by patients' past experiences of back pain and provider interpretations of their preferences [18]. Unrealistically optimistic perspectives ultimately lead to disappointment and dissatisfaction. Providers should discuss with patients where expectations overlap or differ at baseline and after treatment is initiated [19].

Many patients hesitate, or fail to disclose they have pain, which is perceived as a sign of weakness or vulnerability. Many are shamed if their reports of pain are met with laughter, disapproval, disbelief, or disparaging labels. Their motivations as a drug-seeker, wanting attention, or other secondary gains are often questioned [20]. Adding to the stigma is a barrage of media reports on opioid addiction and overdose deaths that vilify pain treatments without distinguishing nonmedical from therapeutic use or prescribed from illicit drugs.

This unbalanced reporting of the problem persists despite large studies revealing that most prescribed opioids are not misused, and with long-term use, an estimated 2% develop an addiction and 0.02% have a fatal overdose [21, 22]. Any iatrogenic case of addiction or overdose is a serious unacceptable outcome; yet so is untreated pain, which can predispose patients to drug misuse or suicide [22–25]. Direct to consumer advertising of non-opioid medications portrays monotherapy with acetaminophen, NSAIDs, gabapentinoids, or topical therapies as being able to improve pain, mood, and functioning. This claim is not supported by the best available research [26–29]. These inaccurate portrayals set up the majority of people with chronic back pain who don't respond in these ways to be further stigmatized [20, 30]. Like other stigmatized groups, those with persistent pain are often blamed for their condition and rendered silent. This fosters misuse of alcohol or other substances rather than seeking appropriate care [25].

Conversely, patients may have had pain effectively managed by opioids in an acute care setting, expecting persistent pain to respond in the same manner. There is more evidence, however, that escalating opioid doses for chronic back or neck pain does more harm than good [31, 32]. Although there is a perceived safety in using non-opioid alternatives, evidence of harm from their persistent use is mounting [33–43].

When prior treatments have failed or created more problems than benefits, many patients seek spine surgery to relieve the pain [44]. In 2011, there were nearly a million back surgeries performed in the USA, almost evenly split between spinal fusion and laminectomy procedures [45]. Nearly 150,000 neck surgeries are performed annually in the USA with costlier anterior cervical discectomy and fusion procedures far outnumbering cervical disc arthroplasty, which has a higher revision rate [46, 47].

For decades published clinical guidelines delineated strategies to close the gap between research and practice by using the best available diagnostic and treatment approaches for back pain while calling for the development of new treatments [48–50]. The goals of closing that gap and developing better treatments remain unfulfilled. Given this failure to yield a real-world reduction in the prevalence, cost, and suffering attributed to spine pain, a major transformation is needed in the way health professionals, educators, researchers, and the public understand and deal with it. This requires pain management become more personalized, patient-centered, team-based, multidisciplinary, and available to those who need it [5].

Further characterization of pain by some professionals as a somatoform type of mental illness further contributes to misdiagnosis, undertreatment, and unnecessary stigma [51]. Often these attitudes stem from the lack of training addressing core concepts and competencies in assessing, understanding biopsychosocial components, and treating pain [52, 53]. Given that pain is the primary reason why people seek healthcare and that treatments often induce pain, it is unfathomable that health professionals lack consistent high-quality training in preventing and alleviating pain. The resultant poorly managed pain is viewed globally as "poor medicine, unethical practice, and an abrogation of a fundamental human right" [1].

When clinical decisions are made to use opioids to treat pain, prescribers are scrutinized, and their judgments questioned. This scrutiny leads many prescribers to base clinical decisions on legal protections rather than the treatment that

best reduces the patient's pain and improves their functioning [54]. Resistance to prescribe opioids for pain when medically indicated may be partially due to fear of losing practice privileges, tarnishing one's reputation, or being exposed to legal actions not covered by malpractice insurance [55, 56].

Compliance with applicable state and federal laws/regulations and national standards should stand up to the scrutiny regarding appropriate prescribing and monitoring practices [57]. In recent years however, regulations and payer policies have been following selective recommendations of clinical practice guidelines. Even when professionals are familiar with guidelines that delineate best practices, they believe these publications are overly prescriptive, hamper judgment, or limit professional autonomy. Those with rigid recommendations are at odds with individual patient needs, while failing to acknowledge the role of limited time, resources, and barriers encountered, which detract from the credibility of practice guidelines [58].

Another barrier to applying best practices is the plethora of guidelines. A quick search of the National Guideline Clearinghouse (https://www.guideline.gov/) on March 10, 2018, using the term "back or neck pain" revealed over 700 clinical practice guidelines were published on the topic in the past 10 years for a variety of conditions, specialties, populations (e.g., pediatric, veterans, elderly, etc.), and specific (e.g., pre-hospitalization, critical care, outpatient, hospice, etc.) settings. The most influential guideline identified in that search was the 2016 CDC guideline for prescribing opioids for chronic pain, because of the national push to integrate them into mandated education, regulations, and payer policies [59].

Although some studies on low back pain were cited, the focus of these guidelines was based on "contextual" epidemiologic data on opioid-related harm that could not distinguish medical from illicit drug use [59]. The unbalanced "expert panel" favored addiction specialists and those who have led FDA or state-based initiatives to restrict access to opioids. Of a dozen recommendations, only one (to treat addiction) was deemed to have moderate-quality scientific evidence. The others were based on low- or very low-quality evidence from studies with notable or major limitations. Despite the dearth of credible clinical trials reviewed, all recommendations were strong and should "apply to all persons" except for urine drug testing, where clinical judgment was advised [59]. The guidelines detailed risk assessment and mitigation strategies, including suggested daily dose limits, duration limits for acute pain, and criteria for deeming therapy successful enough to continue opioids for chronic pain. These added elements were not supported by clinical research, and no drug or nondrug therapy listed as preferred over opioids has scientific evidence of efficacy meeting the high bar set for continuing opioid therapy [60]. This justifies concerns professionals express about the lack of credibility of guideline-mandated practices [58].

In a typical primary care encounter, providers have limited time to address pain as one of many clinical issues assessed and treated. Capitation payments incentivize a minimalist approach that limits access to physical therapy, psychosocial counseling, and complementary therapies [5]. Furthermore, insurance companies create barriers such as single modality coverage, "fail first" rules for medications, limited number of visits, and prior authorizations. Although most generic medications are readily available, abuse-deterrent medications and non-pharmacological interventions are generally not covered.

Calls to further restrict opioid prescriptions continue, despite substantial declines in prescribing, while opioid overdose deaths (primarily due to illicit drugs) are skyrocketing [61–63]. Regulations and payer policies would do better to support a balanced approach to treating back and neck pain based on clinical rather than public health data to promote pain reduction, functional improvement, and avoidance of harm while working to overcome stigma and overriding professional judgment.

Assessment of the Safety and Effectiveness of Pain Management

All healthcare professionals have a dual obligation to provide competent care that benefits patients and prevents harm to the individuals and populations they serve. Therefore a knowledge of community-based health problems is useful background information to consider as part of a comprehensive patient assessment. Best approaches to pain assessment include evaluating its biopsychosocial impact, as well as a history of mental illness, including the nonmedical use of prescribed or illicit drugs [57]. For complex persistent pain however, monotherapy is insufficient to help patients achieve the best balance of pain reduction, functional improvement, and avoidance of treatment-related harm. Therein lies the value of interprofessional collaboration to sort out multiple simultaneous and possibly competing priorities, to develop a thoughtfully tailored multimodal treatment plan. This process can also untangle the ethical conflicts that arise when goals of the patient, family, and professionals are not aligned [1].

Relative risks of therapeutic options need to be determined on an individual basis because overuse of opioids and other types of non-opioid pain treatments hospitalizes or kills an increasing number of people [37, 38, 64–68]. Thus, to avoid harm, professionals need to consider all medications, non-prescribed substances, interventional approaches, and comorbid states to avoid unintended harm from pain treatments [69]. In addition to balancing the need to help without harming patients, resolving injustices related to disparities in care access and delivery needs attention. Treatment

disparities based on age, race, gender financial resources, or other factors are unethical because untreated pain can lead to physical, mental, and/or socioeconomic harm [1].

All professionals have a clinical responsibility to take the patient's report of pain seriously and either treat or refer the patient to an appropriate professional for help [1]. Even if the diagnostic work-up is unable to explain the pain, professionals should treat it based on professional standards and best practices informed by guidelines and their clinical judgment. The invasion of cost-cuting business practices and restrictive policies has eroded therapeutic relationships, teamwork, and the ability to provide education and counseling about self-management strategies [69]. Our dispassionate system limits the ability to achieve the best possible outcomes delivered by team-based, interprofessional care [70–72]. This conflict in values between what health professionals believe will help and what they can deliver can be a source of moral distress and burnout.

Professional Duty to Alleviate Pain

Media attention villifying prescription opioid has fueled legal and political actions without acknowledging that judicious use in selected cases has benefitted many people. The resultant stigma and scrutiny of patients and practices that use opioids as part of a pain treatment plan have had a detrimental effect on the way pain is treated [30]. Urine tests, prescription monitoring programs, and patient provider agreements are fallable and can yield results that abandon beneficial treatment or continue inappropriate therapy. The growing trend of discharging patients on the basis of unexpected urine tests or patient provider agreement violations is concerning, because this can result in harmful self-medication behaviors [25, 73]. In these challenging cases, it is especially important to expand the treatment team rather than discharge the patient.

Pain that persists despite multiple failed treatments is a multidimensional and complex phenomenon that benefits from comprehensive, ongoing assessments, effective management, and the engagement of patients with realistic expectations. An interprofessional approach to assessment and management that is communicated with clear, consistent, agreed-upon goals is advantageous, but not practiced in most settings. Currently, health team members focus on serving the patient by offering their perspective and value-added contribution to their own treatment plan. Often professionals skilled at administering interventional or physical modalities are selected when pain interferes with functioning, as are psychosocial modalities like cognitive behavioral therapy or counseling when mental comorbidities or significant mood disorders co-occur. This Cartesian split fails to appreciate the biopsychosocial nature of pain that benefits from an integrated approach.

Treatment that lacks coordination creates gaps, duplication, or missed opportunities that waste time and resources and yield suboptimal outcomes. When severe pain, problematic behaviors, or comorbidities persist despite sequential specialty consultations, an integrated interprofessional team-based approach to therapy is warranted. The interprofessional team model has different disciplines with expertise in pain working together to best plan and treat pain. In this collaborative model, healthcare professionals share their different understandings, assessments, and critical thinking about pain to best serve patients [74]. Synchronized interprofessional teams develop a shared patient-centered treatment plan and coordinated therapies to produce better outcomes in a more efficient, cost-effective way [75].

This team-based approach is not yet a standard of practice as interprofessional education and reimbursement to maintain the clinical structure needed are not widely available. The Centers of Excellence in Pain Education (CoEPEs) are facilitating development and testing of these types of programs beginning with students in the prelicensure phase of their development. Teams of at least four different disciplines develop core competencies of understanding and assessing the multidimensional nature of pain while collaboratively planning safe, effective treatment strategies across the continuum of care [53]. Standardized, publicly available interprofessional case studies have been developed to guide classroom content, followed by interprofessional seminars to develop collaboration and critical thinking skills [76].

Interprofessional Team Members

In practice settings, an important starting point to increase the efficiency of team-based care is to understand the limits, overlapping skill set, scope of practice, and the value-added contribution of other disciplines. A brief synopsis of disciplines is provided here.

Physicians have in-depth knowledge and critical thinking skills to analyze patient reports of pain as one component of the diagnostic reasoning process. Physicians also examine quality-of-life issues, such as how pain interferes with biopsychosocial functioning, work, and meaningful activities. Physicians' wealth of knowledge of disease states and therapeutic options is critical for developing a safe, effective treatment plan. Primary care providers and specialists are essential members of the healthcare team skilled at implementing treatments, monitoring therapeutic responses, and coordinating care.

Nurses have frequent contact with patients in a variety of settings, which uniquely positions the nurse to evaluate responses to pain and therapy over time. Nurses address biopsychosocial aspects of pain; barriers to effective pain control; common pain conditions; pain assessment methods

based on age, ability, and culture; and a range of treatments (e.g., pharmacologic, interventional, nondrug) used to relieve pain. Nurses provide patients and family members with information about a variety of pain management interventions and collaborate with the interprofessional team to develop a patient-centered pain treatment plan with realistic, desirable goals established with patients and caregivers. Advanced practice nurses use their diagnostic reasoning and therapeutic decision-making to develop thoughtful treatment plans that balance these concerns.

Pharmacists' central role and responsibility helps promote the safe and effective use of medications to control pain. They may be the first point of contact for patients seeking nonprescription analgesics and provide information about prescription analgesics in the community. They understand pain mechanisms, frequently encountered pain conditions, and variables that influence patient response to pain medications. This includes risk mitigation strategies for analgesics based on the patient's age, genetic influence of metabolic pathways, medical condition/comorbidities, and other prescription or nonprescription drugs the patient is taking, including nutritional supplements. Pharmacists have an important role in monitoring the prescribing and dispensing of opioid medications and to question concerning patterns of opioid use. Pharmacists are in an ideal position to discuss with patients the safe use, secure storage, and timely disposal of any unused portion of the drugs dispensed.

Psychology professionals are skilled at conducting interviews, interpreting behaviors, and opening lines of communication while helping patients and caregivers cope with emotionally difficult situations. They help the team understand motivations, thoughts, feelings, and behaviors that affect the sensory and affective dimensions of pain, especially with comorbid mental health disorders affecting cognition, mood states, and/or substance use. Working directly with patients, psychology professionals help modify maladaptive thinking patterns and facilitate the mastery of coping strategies through cognitive behavioral therapy, hypnosis, and other modalities. They use specific motivational strategies, strengthen patient commitment to change, and guide the interprofessional team to consistently reinforce desired behaviors.

Physical therapists work with people in pain to promote comfort and improve function, overall health, and well-being. They engage patients to become active participants in their pain management by teaching and motivating them to improve strength, stamina, flexibility, and agility. Physical therapists' expertise in anatomy, physiology, and movement science makes them a great asset to the interprofessional team by establishing/implementing plans to maximize functional capacity and rehabilitation potential. In addition to therapeutic exercise, physical therapists provide manual therapy (massage/soft tissue techniques, manipulation, mobilization) and use therapeutic modalities (ultrasound therapy, electric stimulation, laser/infrared therapy, and hot/cold therapy), biofeedback, and relaxation therapies to reduce pain and related disability.

Occupational therapists focus on the impact of pain on life activities such as occupation, valued role functioning, current habits, and existing routines at home and workplace, as well as in schools and the community. The education and training occupational therapists receive in psychosocial engagement, performance patterns, and skills provide the foundation for collaborating with the patient to manage pain while facilitating participation in desired occupations. Occupational therapists combine psychosocial approaches (cognitive behavioral therapy, relaxation techniques, self-expression techniques, and problem-solving methods) and energy-conservation strategies (environmental evaluation and adaptation), along with assessment and training in the use of selected assistive devices/equipment (e.g., splints) to protect, preserve, and optimize functioning while managing pain [77].

Radiation therapy professionals use diagnostic imaging, aid in the delivery of precision targeted interventions, and administer ionizing radiation, if appropriate, to treat the pain source. External or internal radiotherapy can reduce pain caused by a growing tumor pressing on bones, nerves, or organs. In interventional radiography, technologists work closely with physicians or surgeons to perform minimally invasive fluoroscopy procedures to deliver epidural steroid injections, nerve blocks, or thermally based remedies directly to the source of pain in the neck, shoulders, arms, and upper or lower back.

Massage therapists provide services that can be an effective part of pain relief and management. A growing body of research shows that massage therapy is effective for providing relief to patients with spine pain. It also promotes relaxation and alleviates the perception of pain and anxiety for hospitalized patients with cancer. Meta-analyses have shown the value of different massage types for a variety of conditions that produce acute, chronic, or cancer pain [78–81].

Speech-language pathologists have expertise in the anatomy and physiology of the neuromuscular mechanisms for respiration, phonation, speech, resonance, and swallowing. They understand the integrated function of these systems and perform extensive assessments to pinpoint dysfunctions affecting swallowing, voice quality, articulation (motor speech), and fluency of speech. They work with patients who have tracheostomies, laryngectomies, dissections of the tongue due to cancer, clefts of the lip and palate, and other oral and facial anomalies. They identify signs of cognitive and language dysfunction that can be altered from medications and work collaboratively with other professionals to address pain during therapy.

Registered dietitian nutritionists have expertise in matters of food and nutrition. The registered dietitian nutritionist can

address how to best achieve optimal body weight and how certain food types ultimately affect pain through inflammation, vitamin/mineral deficiencies, gastrointestinal or immune system functioning, and mood. They can also provide advice on how to deal with food issues when in pain, such as shopping, preparing, and cleaning up after meals.

Other healthcare professionals and providers of complementary therapies who add value to the treatment team are consulted as needed.

Pain Management Nursing Scope and Standards of Practice

Nurses represent the largest component of the healthcare workforce and may be an underutilized resource to strengthen coordination of team-based care across care settings and providers [82]. Nurses can play a central role in pain management given their frequent contact with patients and their families, providing care in a way that addresses biopsychosocial and spiritual needs.

The broad professional nursing role includes protection, promotion, and optimization of patient health and biopsychosocial functioning. This includes prevention of illness or injury, education, counseling or advocacy activities, and performing necessary activities on the patients' behalf to achieve optimal health, recovery, or a dignified death. Internationally, each nurse has the responsibility to alleviate suffering [83]. As such nurses have a duty to prevent and relieve pain or other sources of suffering; prevent complications that may result from unrelieved pain or its treatment; and work collaboratively with a patient-centered team of healthcare professionals to achieve comfort/function goals. Mutually establishing these goals with the patient is important so they are aligned with their values, are realistic, and command adherence to the follow-up plan. Often nurses develop an understanding of what the patient values, especially regarding proposed medical interventions and possible outcomes. When patients fail to speak up, or are not present when important treatment planning decisions are made, the nurse often gives voice to the patient's perspective, values, and preferences.

To fulfill these responsibilities, the nurse uses refined pain assessment methods that are easy and meaningful to the patient based on culture, ability, and age. Familiarity with the range of treatments used to relieve pain is necessary for them to fulfill their role [84]. Additionally, nurses often have a skill set of providing comfort through a range of nonpharmacologic interventions they are qualified to administer. States and organizations vary widely regarding which of these measures nurses can implement independently. For example, therapeutic communication to reframe cognitive distortions, positioning for comfort, applying topical heat, and facilitating the use of music or other distractions are generally not restricted. Providing a massage, aromatherapy, reiki, self-hypnosis, transcutaneous electric nerve stimulation (TENS), or other modalities may be restricted to certain disciplines or license/certification prerequisites.

Nurses have a duty to understand the potential hazards of treatments, protect patients from harms based on a risk assessment, and discuss concerns with prescribers or interventionalists before the treatment is initiated. This includes knowing current federal and state regulations pertaining to prescribing, dispensing, administering, and destroying unused controlled substances. During and after therapy is initiated, nurses monitor for both the desired and undesired effects of treatment, documenting their findings and raising concerns with the appropriate provider. They ensure infusion pumps and monitoring devices are functioning properly. Nurses are responsible for providing culturally sensitive education that respects the patient/family autonomy, including how the patient's medical condition, medication use, and other therapeutic interventions may affect their safety.

Pain Management Nurse Specialty

Pain management nursing was recognized as a specialty within nursing in 2005, complete with role delineation, standards of practice, and a national certification examination administered by the American Nurse Credentialing Center [85]. Certified pain management nurses have demonstrated expertise in the multidimensional assessment and management of pain across the lifespan. They are also knowledgeable about strategies to improve the way pain is managed within organizational structures. Nurse practitioners, clinical nurse specialists, nurse midwives, and nurse anesthetists with advanced knowledge and skills related to pain have received formal recognition nationally since 2014 as Advanced Practice-Pain Management Nurses. With postgraduate training in pain, these advanced practice nurses are prepared to serve as a clinical resource, consultant, and mentor for managing patients with complex pain problems. Their training prepares them to serve as a leader, consultant, and change agent for pain-related matters; lead interprofessional pain management teams; educate staff about pain; and participate in pain-related research or quality improvement activities, including the design, implementation, and evaluation of pain programs [85].

Nurses Leaders

Nurses in leadership positions are accountable to ensure that policies, procedures, and documentation systems include information to guide sound decisions. This requires ongo-

ing communication regarding evidence-based, best practice approaches to treat patients with pain, as well as the safety guardrails in place to protect them. This may include balancing concerns about the use of monitoring equipment to expediently detect a deteriorating patient condition, with available resources while preventing alert/alarm fatigue [86]. Effective leaders in nursing foster a culture of safety by creating a work environment that empowers nurses to question unsafe or inappropriate practices without fear of retaliation. Nurse leaders can also set the tone by valuing pain relief activities. When resources are devoted to developing pain champions, such as a "Pain Resource Nurse" program, they help create a culture that supports effective pain management [87]. These pain champions identify and work to overcome organization-related challenges and barriers to pain management, including the development of a forum for collaborative, multidisciplinary teamwork and communication.

Nurse leaders may also function in administrative roles, ensuring optimal staffing levels, being fiscally responsible for reimbursement of pain interventions, and evaluating pain-relieving products. Given the complexity of pain management care along with the rapidly changing landscape of emerging therapies, evidence-based standards of practice, and regulations shaping care delivery, practice environments must change accordingly. Strong leadership is needed to stay abreast of these developments, update training and organizational policies, effectively communicate them, and monitor post-implementation adherence to required changes. This process entails engagement and collaboration with interprofessional and administrative teams.

Delivering Pain Services in Hospitals and Clinics

In outpatient settings significant variation exists in the diagnosis and treatment of patients with new onset, recurrent, or chronic back/neck pain. The dramatic increase in costly interventions with uncertain benefits and rare but catastrophic adverse effects has come under scrutiny, as changes in payer policies demanding hospitals and clinics examine their practices to justify such increases [88]. Many patients with spinal pain lack identifiable sources of their pain despite expensive imaging and tests, which may not accurately inform clinicians of specific treatment targets. Early identification of subgroups of patients and getting them on the right treatment path early is critical. Financial incentives and practice guidelines have had limited success in reducing inappropriate care and costs [89]. In hospitals, quality improvement program has focused on patients admitted for back pain but fail to address patients who have chronic back pain in addition to their primary condition. Additionally, neck or back pain may develop in the hospital because of extended time in bed, awkward positioning, disuse and deconditioning, or hospital-acquired conditions such as falls or infections.

Current standards of high-quality care have been established by The Joint Commission which requires hospitals to identify a leader or leadership team that is responsible for developing and monitoring performance improvement activities related to pain management. Part of this standard requires organizations to provide monitoring equipment for the early identification of adverse outcomes (e.g., respiratory depression) in high-risk patients and examine opioid prescribing practices. For patients at risk for opioid use disorder, this entails ensuring easy access to prescription drug monitoring information and opioid treatment programs.

An important part of the treatment planning process is establishing realistic expectations and measurable goals with the patient, including how the safety and effectiveness of treatments will be measured. This includes discussions about balancing concerns for pain reduction, improved physical and psychosocial function, and avoidance of treatment-related harm. When medications are prescribed, specific information about safe use, secure storage, and proper disposal of these drugs must be documented. In addition to detailing side effects of pain treatments, a discussion about any required modification of the home environment or daily routines to promote the safety and effectiveness of treatments should be addressed.

While The Joint Commission recognizes that the evidence supporting nondrug therapies is mixed and/or limited, professionals should discuss and provide these therapies to patients. Physical modalities (e.g., acupuncture, chiropractic therapy, osteopathic manipulative treatment, massage therapy, or physical therapy) and psychosocial approaches (e.g., patient education, relaxation therapy, and cognitive behavioral therapy) are examples of commonly provided nondrug approaches [90]. When a patient is interested in exploring safe nondrug therapies that are not provided at that setting, a system needs to be in place to educate the patient on where the treatment may be accessed.

Professionals (staff and prescribers) also must be educated by the organization. Providing accessible educational resources to improve pain assessment and treatment safety based on the identified needs is one form of education, given the limited impact that attending lectures alone has on changing practice [91]. Targeted reviews of pain assessment and treatment principles appropriate to their specialty or case-based huddles to best deal with a specific clinical situation are also effective strategies. Addressing known or suspected disparities in care within patient subgroups (e.g., age, language, race, ethnicity, comorbidity, etc.) is another topic worth exploring. Organizations also need to recognize patients with complex pain management needs and refer them when the capacity of a given provider or setting exceeds their ability to provide required services [90].

Meeting the Needs for Improvement

An abundance of research and sound clinical practice guidelines delineates the safest, most effective, and economical approaches to evaluating and treating spine pain [50, 92, 93]. In practice, there remains an overuse of imaging, rest, opioids, spinal injections, and surgery which has not predictably improved long-term outcomes. Current inconsistent use of best practices often fails to control persistent symptoms, impaired biopsychosocial functioning, and iatrogenic complications and is an inefficient use of valuable resources that drive costs up. Strategies have emerged that can be implemented in different settings (primary care, specialty ambulatory settings, hospitals, academic centers, etc.) that chart pathways for improved outcomes. These are better aligned with the evidence along a continuum of primary prevention, preventing the transition from acute to chronic pain and if chronic high-impact spine pain is present, reducing disability and its impact on costs and quality of life [94]. This approach balances multiple priorities of providing high-quality, safe, efficient, effective, timely, patient-centered, and equitable care while meeting the needs of the larger population served in a fiscally responsible way. When this approach is effective, morbidity, mortality, disability rates, and per capita costs are reduced, while system efficiency and provider and patient satisfaction are optimized [95].

Efforts to improve spine care services can be made at the public policy and payer level or by service-level decision-makers (e.g., clinicians, managers of a multi-specialty clinic), which can be influenced by consumer-level demand. Beyond individual clinicians moving to improve their own professional practice, organizations where healthcare is delivered can improve the standardization and quality of care by the Donabedian approach of targeting its structures, processes, and/or outcomes [72, 96]. Potential structural elements include factors such as the environment of care, equipment, workforce (administration, professional and support staff), training and professional development resources, and financial systems. Opportunities to improve processes include all activities relating to how healthcare is delivered. These can include prevention, diagnosis, treatment, patient education, and engaging patients in self-management activities. The outcomes evaluate the impact those structures and processes have on patients, the population served, and financial viability.

Regulators and payers have required ongoing quality improvement activities be in place, with modest penalties or bonuses reinforcing their use for organizations with ten or more clinicians. These Value-Based Payment Modifiers and Merit-Based Incentive Payment Systems have largely failed to improve cost, quality, and outcomes as intended and may have inadvertently increased both disparities in care and practices that "game" the system [97]. For example, the Medicare and Medicaid patient satisfaction scores (per Hospital Consumer Assessment of Healthcare Providers and Systems [HCAHPS] surveys) penalized hospitals for failing to improve the patient's perception that "Pain was well controlled." Amid reports that some organizations tried to boost reimbursement rates by liberalizing their prescribing of opioids, this linkage between pain control and reimbursement was removed. In 2018 the questions were changed to satisfaction with "talking about pain" and "talking about treatment," and in 2019, questions about satisfaction with pain control were eliminated.

Improvement Types

Most organizations have developed an infrastructure for continuous improvement. The most common methodologies to improve quality are Continuous Quality Improvement, Six Sigma, Total Quality Management, Plan-Do-Check-Act cycles, Statistical Process/Quality Control, and Lean techniques. These methods were initially developed for other industries but have been modified to align with the altruistic missions and professional standards within healthcare settings. These have been successfully used for processes like increasing operating room efficiency to outcomes such as reduced infection rates [98].

Pain registries have been developed to promote standardization and minimize discrepancies between evidence-based protocols for managing spine pain and clinical practices. These registries are also advancing knowledge by providing clinicians with decision support and measuring how variability in care affects specific populations served. Tested prototypes have provided clinicians with real-time treatment recommendations through immediate online feedback. Additional in-depth analysis of the database can then compare patient-reported outcomes across sites to ultimately refine decision support recommendations. An electronic knowledge library linked to the health record provides succinct summaries on best practices based on treatments chosen [99]. One quality initiative example is the Michigan Spine Surgery Improvement Collaborative that has made significant improvements in the quality and cost-effectiveness of care throughout the state. As a registry, its database serves as a platform to identify, plan, and implement future initiatives to improve quality and lower costs. Its partnership with payers ensures the sustainability of these ongoing improvements [100].

Inpatient examples also exist. Although not focused specifically on inpatients with back pain or spine surgery, an international team developed a system called "PAIN OUT" that engaged clinicians, researchers, and computer scientists to improve clinical decision-making. Their methodology allows for comparative analysis of quality of care at 17 insti-

tutions in 9 countries through audit, feedback, and benchmarking. This program built an electronic knowledge library based on succinct evidence summaries on the best practices to assess and manage post-operative pain [99].

Electronic health record optimization is an important target for both inpatient and outpatient settings, as shortfalls in current systems have been linked to safety events. Interoperability efforts should prioritize the integrations of pharmacy, laboratory, and radiology system interfaces, so providers have the clearest information to support diagnostic and therapeutic decision-making [101]. Additional technologies being refined include viral marketing campaigns using online platforms such as Google AdWords, Facebook, and Twitter; smartphone apps; exercise programs on YouTube; sending patients educational materials by email or text; meeting over Skype or Facetime; or videoconferencing.

Structure

Key structural elements to improve the quality of pain services often include having an interprofessional workgroup, written policies, procedures, and standards of assessing/treating pain. Additional structural elements include clearly defining the accountability for pain management and having educational resources available for patients, families, and professionals about pain. Information about pain needs to be part of the basic orientation of new clinicians with additional continuing education on pain provided. A periodic needs assessment and ongoing process to evaluate the quality of care provided should guide the topics to be covered. Increasingly, organizations expand the focus beyond a single discipline, assessment, or treatment approach to include interprofessional, multidimensional measures that reflect the complexity of pain and its treatment [96].

Team-based, patient-focused care benefits patients with severe, complex pain problems given its multidimensional biopsychosocial nature. Hospitals can promote a broad understanding of this perspective across disciplines by having the ability to gain interprofessional input into the treatment planning process to improve outcomes. Thus, improving communication systems between departments, the professional team (physicians, nurses, therapists, specialists, etc.), and patients/families is essential to prevent gaps, duplication, delays, and fragmentation of care. In settings lacking resources, Telehealth programs, like TelePain and the ECHO project, have been successfully implemented in ways that expedite access to interdisciplinary consultation with minimal burden for patients or added costs to the system [102, 103].

To overcome some barriers to guideline/best practice implementation and change provider behavior, it is often necessary to change clinical systems and/or create financial incentives.

Evidence exists for the effectiveness of electronic clinical decision support systems that significantly improve clinician adherence in 57% of studies conducted in hospital settings [104], with an even greater impact in other clinical settings [105]. Systems that adopted computer-based decision support providing real-time feedback at the point of care that is integrated into the clinician's workflow appear to be successful at supporting guideline adherence [105]. These systems may not be transferable to different setting; therefore having end-users evaluate the content and functioning of clinical decision support in a form that is understandable to users before it is implemented should be done. This provides useful information about current practice and workflow so the system can support, rather than be a hindrance to practice. This added step will facilitate its acceptance and use [106].

Useful templates for evidence-based order sets are available to help providers more effectively manage patients with acute low back pain [107]. Decision support tools can be particularly effective in changing ordering practices for advanced imaging. "Point-of-order" strategies that prevent providers from ordering imaging until appropriateness criteria are met have been more effective than educational interventions and are easier to implement than the more common pre-authorization approach [108]. One study found that requiring clinicians to personally order (rather than delegate ordering to support staff) exams substantially reduced the number of costly low-yield exams [109].

Process

Often pain can be managed at home by simple self-initiated nondrug methods or treated in primary care settings with or without the support of specialists. When those efforts fail and pain interferes with functioning, expedient treatment by a multidisciplinary team with expertise in pain management will usually help. If however the pain persists and is complicated by comorbidities that limit treatment options, a team-based, interprofessional approach to therapy is warranted. Interdisciplinary pain centers have demonstrated the feasibility of concurrently addressing physical, psychosocial, and functional aspects of care in a coordinated fashion that can be tailored to individual needs.

Within settings, quality improvement processes begin with identifying the opportunities for improvement, key stakeholders (patients, professionals, payers), and the person/team that will lead the initiative. Additionally, the scope and location of improvement efforts, a timeline, desired outcomes, and resources are delineated. The first step is to clarify the opportunity for improvement or problem-prone processes that need improvement through available data,

root cause analysis, or healthcare failure mode and effect analysis processes. Administrative sponsors are needed to ensure the program is appropriately resourced.

Once the scope is delineated and supported by administration, further needs assessments and gap analyses are conducted with input from people doing the target activity. A detailed plan is then developed with a breakdown of tactics, responsible persons/teams, and timelines. Once set, the project is implemented with the change component, a risk mitigation strategy, ongoing monitoring, and frequent status updates. When implementing evidence-based changes in the hospital setting, it is best to translate desired changes into pragmatic care bundles that are easily integrated into usual workflow to yield more consistent adoption of new practices designed to improve pain management and therapeutic outcomes [110].

Effectively changing professional practice requires a multidimensional approach, including:

- Identification and removal of implementation barriers
- Targeted, active implementation strategies, such as decision support systems
- Educational outreach with available interactive educational strategies
- Reminder systems
- Clinical practice audits with timely feedback
- Patient education to align expectations with current practices
- Mechanisms to review cases where professional judgment or patient needs raise questions about the appropriateness of the new process

Sometimes, even if not aligned with guidelines or clinical judgment, fulfilling reasonable patient demands enhances trust and the therapeutic relationship needed to make meaningful long-term changes [58].

During the monitoring stage of the process improvement, adjustments are made with real-time feedback until milestones are reached. Lessons learned are disseminated, and changes ultimately become the new practice standard [111]. Continued post-project monitoring is needed to sustain changes and/or identify problems, underlying causes or risks that need to be further addressed.

Outcomes

Patient-level outcomes could include changes in symptoms, biopsychosocial functioning (including health, healthcare utilization, and employment status), behavior or knowledge, as well as patients' satisfaction and health-related quality of life. Psychological factors such as distress, anxiety, depression, and pain behavior have been shown to intensify, prolong, and worsen the impact of back pain. Thus, standardized measures should routinely include these elements to evaluate outcomes for these patients [9].

Payment structure incentives linked to back pain diagnostic tests and treatments (e.g., required criteria before imaging, spinal injections, and/or spinal surgery) have reported better outcomes [9]. This includes more support for patients with complex back pain who require rehabilitative services. When initial and conservative management programs fail to lower pain and improve physical, mental, and social functioning, a multidisciplinary pain program approach should be used to optimize independence and quality of life. These programs typically include self-management education, medical treatment, behavioral therapy, and physical reconditioning [112].

If, however, pain persists and is complicated by comorbidities, multimodal therapies through an interdisciplinary pain center that include medication management and physical, psychosocial, rehabilitative, and complementary care in a coordinated fashion are an effective next step [113, 114]. Unfortunately, limited access is a major barrier to this best practice approach. Payer policies may reimburse for a consultation visit at many centers, but most require high out-of-pocket payments to receive the recommended services [115]. Creation of incentives that reimburse primary care providers adequately for delivering integrated pain care along with covering specialist-recommended services in accredited pain programs would help alleviate many of the current problems that limit access to care. Emerging evidence suggests that low-resource settings may use mobile apps to overcome these access problems which can yield beneficial outcomes [116]. This literature is heterogeneous and predominantly has included middle-aged, educated white women, which raises questions about its transferability to other populations [117].

Summary

Because the nature of pain is multidimensional, every healthcare professional, regardless of discipline or specialty, must have a working knowledge of how to assess pain in a consistent measurable way, have a basic understanding of drug and nondrug treatments of pain, and know how to approach pain treatment in a collaborative way. Knowledge that over- or undertreated pain has harmful consequences must be broadly disseminated, as does the need to tailor pain treatment plans to individual responses. Given the moral and clinical imperative to address pain, ethical conflicts often arise demanding balancing concerns for helping without hurting, advising without dictating, and doing what is best for the individual with that of the community. Pain is a challenge that no single professional group can master, but together we can explore ways to prevent needless pain and suffering for individual and societal good.

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Part VI

Challenges and Future Directions

Basic Research for Pain

38

Yong Luo and Shiqian Shen

Key Points

- Stem cell therapy provides promise for treating discogenic pain.
- Targeting CGRP(R) with monoclonal antibodies represents a breakthrough in migraine prophylaxis. Other monoclonal antibodies under development may prove effective for spine pain.
- Innovative imaging modalities facilitate pain diagnosis and treatment.
- Gut microbiome is a new frontier in pain research, which offers unique opportunities in probing the complex relationship between dietary/environmental factors and pain.

Introduction

Pain is a pathophysiological state defined by the International Association for the Study of Pain as "unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such" [1, 2]. Pain can be either acute or chronic based on its duration. Pain often becomes chronic when the duration is beyond 3 months for nonmalignant pain. With more than 100 million Americans suffering from chronic pain, the economic costs of pain in the United States are enormous. It is estimated that the annual cost of chronic pain is as high as $635 billion a year, which is more than the yearly costs for cancer, heart disease, and diabetes [3, 4]. Despite the high annual cost of chronic pain, in 2017 only $516 million was funded by NIH for pain research, which is way far less than the funds for cancer, heart disease, and diabetes research ($5980 million, $1370 million, and $1108 million, respectively). The limited funding in pain research is partially due to the lack of recognition of the importance of basic research on the advancement of pain treatment clinically. As it was recently emphasized by the American Academy of Pain Medicine, pain is the driving force for progress of pain treatment [5]. In this chapter, our goal is to review, summarize, and discuss the recent basic research findings that have advanced or will likely advance future pain treatments. We will focus on (1) stem cell therapy, (2) monoclonal antibody-based pharmacotherapy for chronic pain, (3) new imaging modality for the detection of pain signal and its response to treatment, and (4) gut microbiome modulation of neuropathic and inflammatory pain.

Stem Cell Therapy

Pain can be caused by degenerative diseases, such as herniated disc, osteoarthritis, and ligament injury, and by nerve damage, such as postherpetic neuropathy and diabetic neuropathy; therefore, the idea of using stem cells to regenerate the degenerated materials and even re-establish normal innervation becomes appealing to researchers. The majority of the stem cells used in research are mesenchymal stem cells (MSCs) derived from bone marrow. MSCs have the capacity of self-renewal while maintaining multipotency. They can be differentiated into osteoblasts and chondrocytes under neurons under appropriate induction conditions.

Discogenic pain has been a common but difficult to treat pain condition secondary to degeneration. Recently, stem cell therapy started to emerge as a new modality to treat discogenic pain. In a pilot study in 2011, ten patients with chronic pain due to lumbar disc degeneration were treated by intra-disc injection of autologous expanded bone marrow MSCs. Both safety and efficacy were demonstrated in this study. Nine out of ten patients experienced pain and disability reduction by 61.5% and 48%, respectively, at 3 months and continued to improve at 6 and 12 months [6, 7]. Although this was not a controlled randomized study, it still proved the safety of autologous MSC injections for discogenic pain. A comparison study in 2015

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with 26 patients again demonstrated the safety and efficacy of autologous MSC injections for discogenic pain. In this study, patients were divided equally into two groups. One group received one level of intra-disc injection of autologous MSCs, and the other group received two levels of autologous MSC injections. Significant decrease in both pain and disability scores was similarly observed in both groups. No significant side effects were observed [8]. Nonetheless, the efficacy of MSCs injections for discogenic pain is still awaiting for data from large multicenter randomized controlled trials.

Monoclonal Antibody-Based Pharmacotherapy for Chronic Pain

Monoclonal antibodies represent major breakthroughs in modern medicine, particularly in the treatment of cancers with anti-PD1/PDL1 and anti-CTLA4 antibodies [9, 10]. Similarly, pain treatment using monoclonal antibodies has made significant progress recently, particularly in migraine prevention. In 2018, the US Food and Drug Administration approved two monoclonal antibodies targeting calcitonin gene-related peptide (CGRP): anti-CGRP receptor mAb (erenumab, Novartis, Amgen) and anti-CGRP mAb (fremanezumab, Teva; galcanezumab, Eli Lilly) for migraine prevention [11–14]. These antibodies exert their function by targeting the trigeminovascular unit and decreasing neurogenic inflammation. In double-blinded clinical trials, these antibodies reduce the days with headaches by about 40% versus about 20% with placebo treatment.

Other monoclonal antibodies, particularly those targeting inflammatory cytokines, such as TNF-a, IL-17, and IL-23, are originally designed and aimed to treat autoimmune diseases, such as Crohn's disease, rheumatoid arthritis, and psoriasis [15–18]. Pain is one of the major clinical presentations in these conditions. Clinical use of these antibodies for treating autoimmune conditions and associated pain symptoms has gained popularity. Humira, a fully humanized anti-TNFα monoclonal antibody used for rheumatoid arthritis and Crohn's disease, is one of the best-selling drugs globally, with $19.94 billion of revenues generated in 2018 for its manufacturer. Monoclonal antibodies not only treat joint pain/arthritis in the setting of autoimmune diseases but also induce arthritis pain in some cases. For example, in the aforementioned cancer immunotherapy (checkpoint therapy) with anti-PD1/PDL1 and anti-CTLA4 antibodies, immune-related inflammatory arthritis has been recognized as a side effect that affects many different joints with concurrent pain complaints [19].

There is currently no monoclonal antibody that is primarily used for chronic pain except for migraine. However, monoclonal antibodies against nerve growth factor (NGF) have gained significant considerations as new potential pain treatment modalities. NGF is a neurotrophic factor involving in neuron growth, differentiation, and survival [20]. Numerous researchers have repeatedly demonstrated that NGF level is elevated in chronic pain conditions such as diabetic neuropathy, cancer pain, and chronic pancreatitis, suggesting its important role in chronic pain signaling [21–23]. Upon tissue damage caused by noxious stimuli, inflammatory factors such as IL-1 and TNFα are released, which increases the production of NGF. NGF binds to trkA (tropomyosin receptor kinase A) at terminal A-delta and C nerve fibers. The interactions between NGF and trkA initiate a serial of downstream pain signaling pathways involving pain initiation, maintenance, and modulation [22]. Because of NGF's important role in initiation and maintenance of pain signaling, anti-NGF antibody has been developed and underwent clinical trials targeting the NGF signaling pathway as a potential promising treatment for chronic pain conditions. Tanezumab, a humanized IgG2 anti-NGF monoclonal antibody, has been demonstrated efficacy in treating arthritic pain in several clinical trials. In a clinical trial that involved 444 patients by Lane et al. in 2010, tanezumab up to 200 ug/kg improved pain from knee arthritis by 45–62% [24]. Improvement in stiffness and limitations in physical function were also reported over 16 weeks following treatment. The most common adverse effects reported are headache and paresthesia. In a similar randomized, double-blind, placebo-controlled clinical trial with 690 patients, tanezumab treatments at different doses of 2.5 mg, 5 mg, and 10 mg on day 1, 57, and 113 improved arthritic knee pain by 51–62% using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and numerical rating scale (NRS) [25]. Again, the most common reported side effects are headache and paresthesia. The efficacy of tanezumab in treating chronic low back pain was demonstrated in a randomized, double-blind, placebo-controlled trial involving 217 patients in 2011 by Katz et al. [26]. Treatment with 200 μg/kg of tanezumab for 6 weeks was associated with 52% improvement in pain intensity and greater improvement in Roland-Morris Disability Questionnaire and Brief Pain Inventory scores. Additional research and phase III clinical trials of tanezumab on various pain conditions are necessary to characterize the mechanisms of action, safety, and efficacy.

New Imaging Modality for the Detection of Pain Signal and Its Response to Treatment

Imaging studies are commonly performed to aid the diagnosis of pain and to guide clinical treatment. However, correlation between radiologic structural abnormalities and clinical symptoms in low back pain patients is poor. For example, in population study, it has been shown that about 40% of people under age of 30 years old display lumbar intervertebral disc degeneration on the MRI, with no clinical symptoms of back pain. Lumbar disc degeneration on MRI is seen in 90%

of individuals older than 50–55 years of age [27]. A recent study examined 200 subjects and found that combined MRI changes in lumbar spine do not correlate with pain intensity, depressive and anxiety syndromes, and quality of life in patients with low back pain [28]. Significant efforts have been devoted to improving the imaging techniques for better diagnosis and treatment.

The dynamic nature of the spine and its mobility across multiple segments is difficult to depict with any single imaging modality. To circumvent this limitation, dynamic MRI has been advocated [29]. Conventional MRI is usually performed in a supine position, at rest, which may not reveal the underlying pathology which is only evident when some extent of spine loading is present. MRI in upright standing position and flexed and extended position provides additional information that is not revealed by MRI in supine position. More recently, weight-bearing MRI particularly those with a side-bending task has been investigated. Pilot study indicates that intervertebral rotations and translations have good reliability when validated against participant-specific three-dimensional models [30]. Current dynamic MRI techniques need to be further developed to optimize its speed and diagnostic accuracy. Its eventual clinical use may improve assessment of in vivo spine stability and examination of outcomes of surgical and nonsurgical interventions applied to manage pathological spine motion.

Chronic pain involves complex brain processing pathways that have gained considerable research interests. Accumulating evidence using functional MRI has suggested altered corticostriatal processing is implicated in chronic pain [31]. In patients with fibromyalgia, there is reduced mPFC activity during gain anticipation, possibly related to lower estimated reward probabilities as well as dramatically heightened mPFC activity to no-loss (nonpunishment) outcomes. Moreover, fibromyalgia patients demonstrate slightly reduced activity during reward anticipation in other brain regions, which included the ventral tegmental area, anterior cingulate cortex, and anterior insular cortex [31]. Heightened anticipation and fear of movement-related pain have been linked to detrimental fear-avoidance behavior in chronic low back pain. Fear of pain demonstrates significant prognostic value regarding the development of persistent musculoskeletal pain and disability. There are significant fear constructs that are implicated in pain processing [32].

Spinal manipulative therapy has been proposed to work partly by exposing patients to nonharmful but forceful mobilization of the painful joint, thereby disrupting the relationship among pain anticipation, fear, and movement. Using functional MRI, patients with chronic low back pain have been found to demonstrate high blood oxygen level-dependent signal in brain circuitry that is implicated in salience, social cognition, and mentalizing. The engagement of this circuitry is reduced after spinal manipulative therapy [33]. Pain assessment with pain intensity score and facial expression have both been used clinically. Pain facial expressions are mainly related to the primary motor cortex and completely dissociated from the pattern of brain activity varying with pain intensity ratings. Stronger activity has been observed in patients with chronic back pain specifically during pain facial expressions in several non-motor brain regions such as the medial prefrontal cortex, precuneus, and medial temporal lobe. In contrast, no moderating effect of chronic pain was observed on brain activity associated with pain intensity ratings. Therefore, pain facial expressions and pain intensity ratings may reflect different aspects of pain processing and suggest that distinctive mechanisms are involved in different aspects of chronic pain [34].

Recent progress has been made to image neuroinflammation, considering there is ample evidence that chronic pain, including neuropathic chronic pain, has components of heightened immune activation [35–40]. Novel contrast agents or radioligands offer promising properties in identifying neuroinflammation with MRI or positron emission tomography-MRI (PET/MRI). A molecular biomarker, the sigma-1 receptor (S1R), has been shown to be implicated in neuroinflammation and nerve injury. [18F]FTC-146 (6-(3-[18F]fluoropropyl)-3-(2-(azepan-1-yl)ethyl)benzo[d] thiazol-2(3H)-one) is a radioligand that is selective for S1R and is able to locate the site of nerve injury in a rat model with PET/MRI [41]. Using similar PET/MRI technology, patients with chronic low back pain demonstrate brain glial activation in the thalamus and putative somatosensory representations of the lumbar spine and leg, revealed by radioligand (11)C-PBR28 that binds to brain translocator protein TSPO [42]. In human lumbar degenerative disc disease, several levels of degeneration are commonly present, and to diagnose the "culprit" level that is responsible for clinical symptoms could be challenging. A recent study employed ferumoxytol, a nanoparticle formulation of iron, to image the neuroinflammation around nerve roots that might be key for lumbar radiculitis [43]. Ferumoxytol is approved by the US Food and Drug Administration to treat iron-deficiency anemia. Nanoparticles are captured by the monocytes-macrophages, which are also critical components of the immune system. In a human subject with lumbar disc degeneration at several levels, nerve root inflammation was successfully identified with ferumoxytol-contrasted MRI at the level that was concordant with clinical pain symptoms.

Gut Microbiome Modulation of Neuropathic and Inflammatory Pain

Gut microbiota is the consortium of microorganisms in the gastrointestinal tract. Gut microbiota is essential to human health and is critical for the homeostasis of multiple key systems, including the immune system, the endocrine system, and the nervous system. In fact, gut microbiota plays a

major role in the bidirectional communication between the gut and the brain. Recently, evidence points to an intriguing association between gut microbiota and neuropsychiatric disorders such as schizophrenia, autistic disorders, anxiety disorders, and major depressive disorders. There is also a critical role for gut microbiota in the pathogenesis of many pain conditions.

Chemotherapy-induced peripheral neuropathy is present in about one third of patients undergoing therapy and is a major dose-limiting side effects of treatment. Limb and perioral area numbness, paresthesia, and pain are the cardinal symptoms of chemotherapy-induced peripheral neuropathy. With the rapidly increasing numbers of cancer patients and survivors, chemotherapy-induced pain has become a major factor negatively impacting quality of life in cancer patients. In a recent research study, using a mouse model of oxaliplatin-induced pain, it has been shown that gut microbiota eradication using a cocktail of wide spectrum of antibiotics prevents the development of chemotherapy-induced pain. Similarly, germ-free mice, which do not harbor endogenous gut microbiota, are protected from developing chemotherapy-induced pain. Gut microbiota restoration using fecal transplantation reverses the protection mediated by the germ-free status. From a mechanistic standpoint, chemotherapy triggers gut inflammation and epithelial barrier leakage, which promotes bacteria translocation, transient bacteremia, and shedding of bacterial products into the bloodstream, including lipopolysaccharide. Toll-like receptor 4, the receptor for lipopolysaccharide, mediates some of the impact of gut microbiota on the development of chemotherapy-induced pain. Besides neuropathic pain, germ-free mice demonstrate attenuated acute inflammatory pain as well.

One area that has received considerable consideration is visceral pain. Given the anatomical location of gut microbiota in the gastrointestinal tract, it is natural to relate it directly to many diseases in the digestive tract, such as inflammatory bowel disease, colon cancer, etc. Irritable bowel syndrome presents with episodes of constipation, diarrhea, and abdominal pain. In a Danish population study, antibiotics were found to be a risk factor for asymptomatic irritable bowel syndrome [44]. It is plausible that the gut microbiota changes secondary to antibiotics are associated with the development of irritable bowel syndrome. In diarrhea-dominant irritable bowel patients, the abundant phyla *Firmicutes* is significantly decreased, and *Bacteroidetes* is increased. Moreover, the alterations of predominant fermenting bacteria such as *Bacteroidales* and *Clostridiales* might be involved in the pathophysiology of diarrhea-dominant irritable bowel syndrome [45]. In an Australian study of patients with irritable bowel syndrome, depression was negatively associated with *Lachnospiraceae* abundance. Patients exceeding thresholds of distress, anxiety, depression, and stress perception showed significantly higher abundances of *Proteobacteria*. Patients with anxiety were characterized by elevated *Bacteroidaceae*. These microbial changes might underscore the psychological distress which is a key pathogenic factor in irritable bowel syndrome [46].

Therapeutics based on gut microbiota to treat irritable bowel syndrome so far have led to inconclusive results [47]. A multi-strain probiotic regimen for 8 weeks increased beneficial bacteria and decreased harmful bacteria in the microbial stool analysis. The small intestine bacteria overgrowth prevalence also decreased at the end of treatment. However, the average levels of fecal calprotectin showed a decreasing tendency, without reaching statistical significance [48]. In a recent meta-analysis, 53 RCTs of probiotics, involving 5545 patients, were analyzed. Particular combinations of probiotics, or specific species and strains, appeared to have beneficial effects on global irritable bowel syndrome symptoms and abdominal pain, but it remained difficult to draw definitive conclusions about their efficacy [47].

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Chronic Low Back Pain: Improving Approach to Diagnosis and Treatment

39

Ping Jin, Lisa A. Tseng, and Yi Zhang

Key Points

- Chronic low back pain is a constellation of symptoms and signs, reflecting a group of heterogeneous pathologies.
- Studies of spinal intervention often suffer from the less stringent diagnostic and inclusion criteria, providing inconsistent results.
- There is a lack of evidence to guide the choice of spinal intervention in real-world clinical practice.
- Large-scale clinical registry has proven to provide high-quality evidence with better generalizability.

Introduction

Among all chronic pain problems and spinal pain conditions, low back pain (LBP) is the most common clinical and public health problem [1]. It is the leading cause of limited activities and absence at work throughout much of the world. In a 2012 review of the worldwide prevalence of low back pain, the mean point prevalence was estimated at 11.9%, the 1-month prevalence at 23.2%, and the lifetime prevalence at 39%, with the highest prevalence among females and those aged 40–80 years [2]. Therefore with aging populations, the actual number of people with low back pain is likely to increase substantially in the coming years. Low back pain is more prevalent in countries with high-income economies. It is a major healthcare burden. In the Global Burden of Disease 2010 Study, out of all 291 conditions studied, LBP ranked the highest in terms of disability and sixth in terms of overall burden [3].

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In the United States, there are up to 300,000 patients per year that undergo surgical management for medically refractory spinal pain. A study of Medicare beneficiaries found that the rate of complex surgery for spinal stenosis rose 15-fold from 2002 to 2007 [4]. The type of surgical procedures performed for the same diagnosis was found to be variable (Fig. 39.1) [5]. Demographically, there was a nearly eightfold variation in regional rates of lumbar discectomy and laminectomy between 2002 and 2003 [6]. In the case of lumbar fusion, there was nearly a 20-fold range in regional rates among Medicare enrollees (Fig. 39.2) [6]. These data suggest that there is a lack of evidence and consensus on the indication and efficacy for these surgical procedures. The utilization of spinal injection procedures also dramatically increased in the past decades. Manchicanti et al. examined the utilization of interventional spine procedures among Medicare beneficiaries. From 2000 through 2013, in fee-for-service Medicare beneficiaries, the overall utilization of spine injection services increased by 236%, whereas the per 100,000 Medicare population utilization increased by 156% with an annual average growth of 7.5%. Among these procedures, facet joint and sacroiliac joint injections increased by 417%, whereas the rate per 100,000 fee-for-service Medicare beneficiaries increased by 295% with an annual average increase of 11.1% (Fig. 39.3) [7]. The constant introduction of new technologies and the lack of scientific evidence, market drive, and potential financial incentives could all contribute to the growth in the utilization of spine interventions.

There remains considerable debate as to the efficacy and effectiveness of spine interventions. Evidence of randomized controlled trials showed inconsistent results, depending on the setting of the study [8–15]. The data from such studies are then used to provide very different treatment recommendations and guidelines by various specialty organizations. There are multiple factors contributing to this reality. Diagnosis of spinal pathology that underlies clinical LBP often is difficult to ascertain. Correlation between anatomic pathology and clinical symptoms is weak. There are extensive overlapping symptoms among

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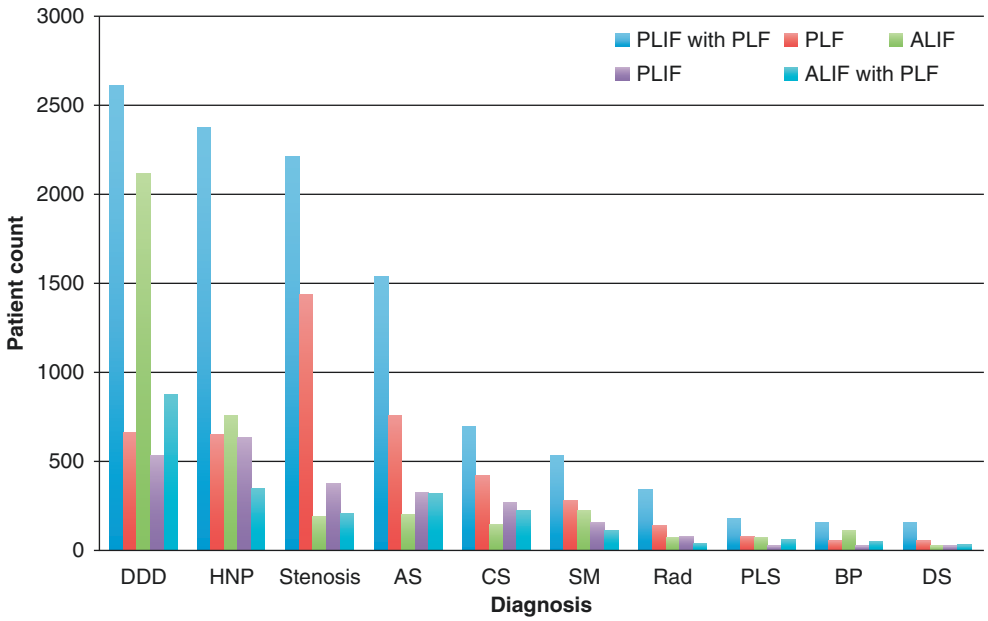

Fig. 39.1 Breakdown of lumbar fusion types according to diagnosis. *ALIF* anterior lumbar interbody fusion, *AS* acquired spondylolisthesis, *BP* back pain, *CS* congenital spondylolisthesis, *DDD* degenerative disc disease, *DS* disorders of the sacrum, *HNP* herniated nucleus pulposus, *PLF* posterolateral fusion, *PLIF* posterior lumbar interbody fusion, *PLS* post-laminectomy syndrome, *Rad* radiculopathy, *SM* spondylolysis without myelopathy [5]. (Reprinted with permission from Pannell et al. [5])

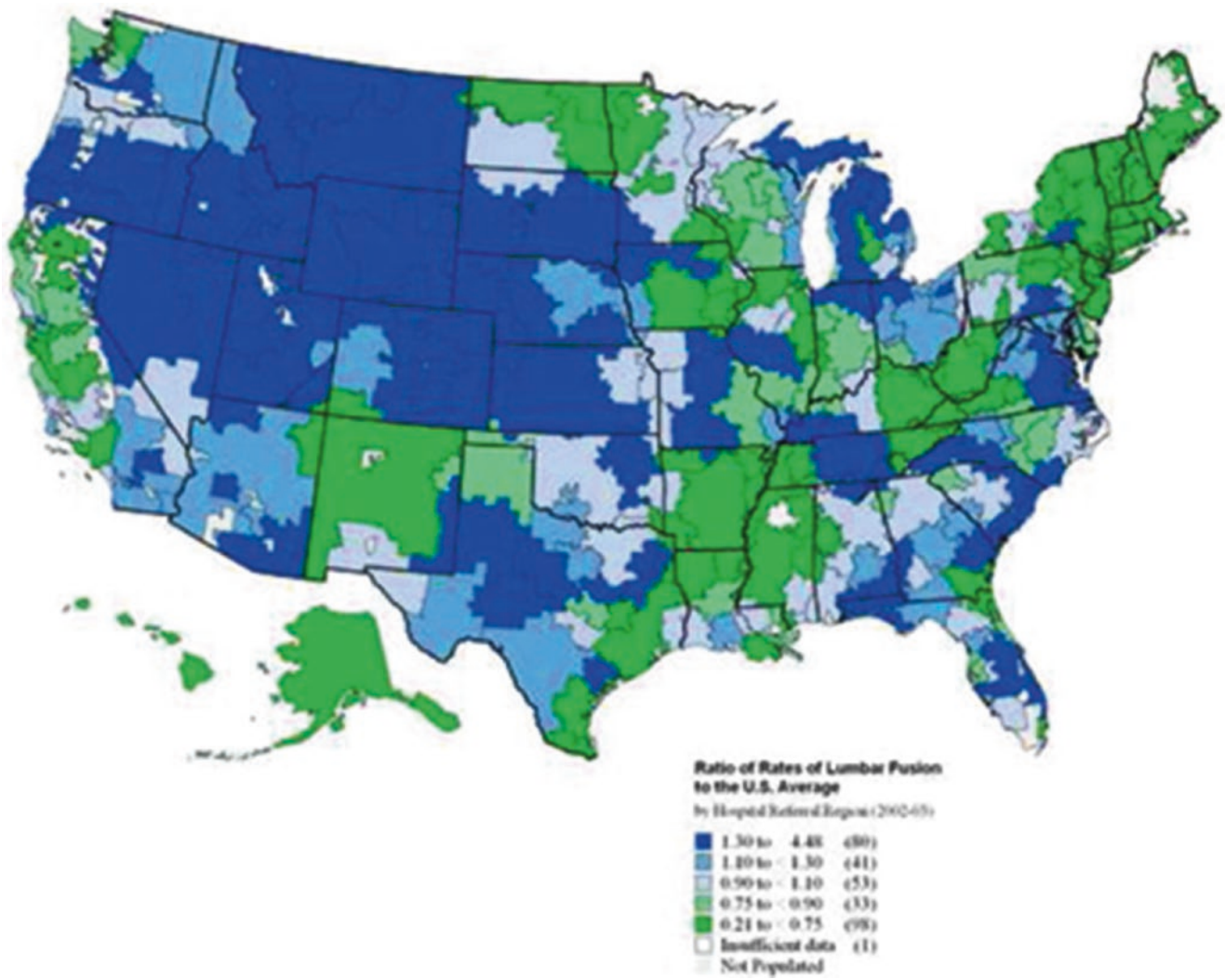

Fig. 39.2 US regional variance in the rate of lumbar fusion surgery 1992–2003 [6]. (Reprinted with permission from Weinstein et al. [6])

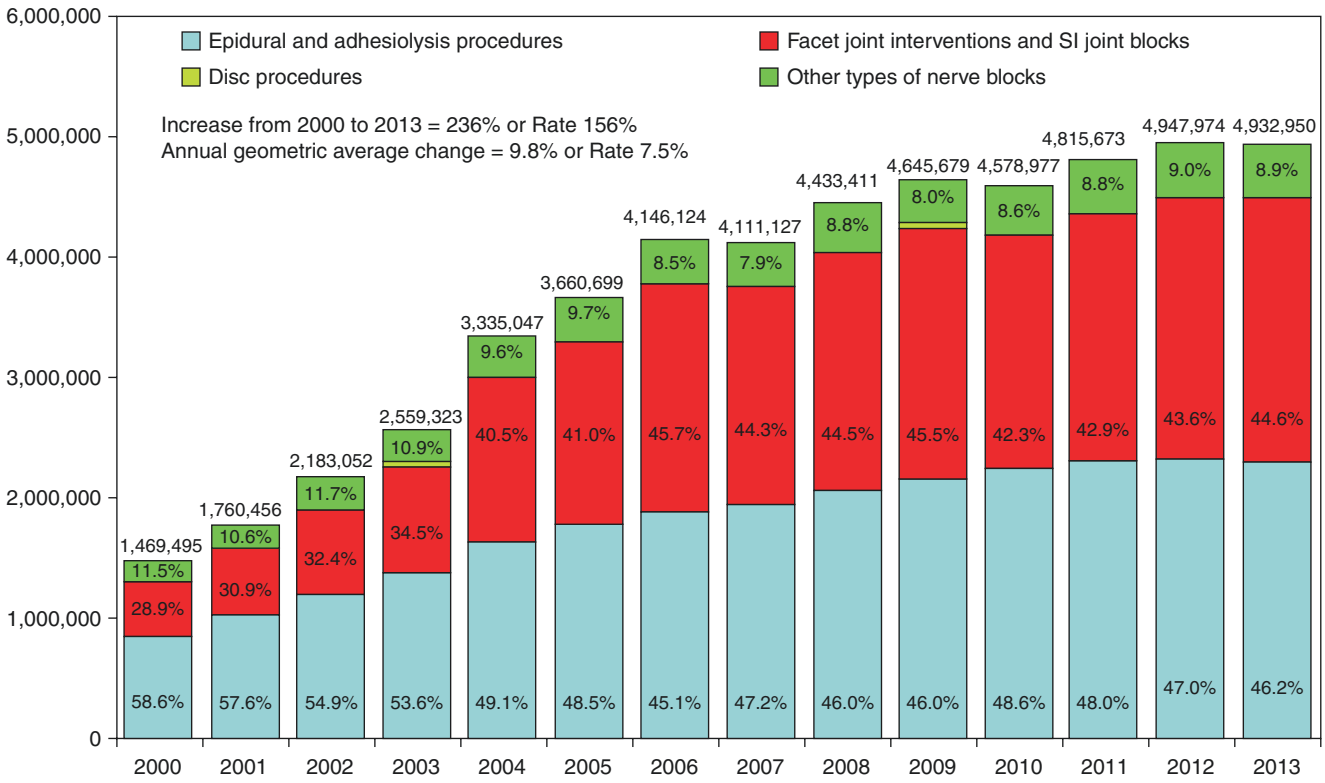

Fig. 39.3 Distribution of procedural characteristic by procedure type. (Reproduced with permission from Manchikanti et al. [7])

distinct spinal pathologies. As such, RCTs (randomized controlled trials) in the spine intervention field suffer from less restrictive inclusion criterion (inevitably) such that treatment effects may be diluted due to the heterogeneity of study subjects below the statistical power of many RCTs. Meanwhile the subjective nature of spinal pain and the frequent presence of comorbid psychological and social dysfunction render clinical diagnosis and assessment rather difficult.

In this chapter, we will review (1) the anatomic base of spinal pain, focusing on low back pain, discussing some of the common potential "pain generators," and their overlapping symptomology; (2) the prevalence and characteristics of neuropathic pain in chronic LBP, emphasizing the change of somatosensory function and central neural processes in individuals with chronic LBP; and (3) the comorbid psychological dysfunction in chronic LBP patients and its various penetrance in individual patients as it relates to treatment outcomes. We will highlight some of the key findings of several representative RCTs and elaborate on remaining issues and questions. Finally, we propose a chronic LBP-focused registry to collect relevant information across the biopsychosocial domains of pain and outcome measurements, to guide individualized treatment.

Anatomy of Chronic LBP

Chronic LBP may originate from one or more lumbar spinal levels and different anatomic structures in the anterior, middle, and posterior spine columns. As the details of spine anatomy are provided in other chapters, we will briefly review several potential pain-generating structures, their neural innervation, and clinical symptomology.

Intervertebral Disc

The intervertebral disc is an avascular fibrocartilaginous structure, composed of the cartilaginous endplates, nucleus pulposus, and annulus fibrosus. The principal function of the disc is to act as a shock absorber between adjacent vertebral bodies. The sinuvertebral nerve, formed by branches of the ventral nerve root and by the sympathetic plexus, innervates the outer 1–2 mm of the annulus fibrosus in nondegenerated discs [16, 17].

Intervertebral disc is a source of low back pain, whereby painful discs are characterized by innervation, inflammation, and mechanical hypermobility [18, 19]. It is hypothesized that discogenic pain arises because nociceptive nerve fibers grow into areas of the disc that previously had no

neural supply [20, 21]. The inflammation mechanism of discogenic pain is based on its association with degenerated intervertebral discs and the observation of upregulation of pro-inflammatory molecules in degenerated discs [22, 23]. Estimated prevalence of discogenic pain ranges 26–39% [24]. Symptom exacerbation with sitting or lumbar flexion often suggests discogenic back pain. CT or MRI tends to be nonspecific; therefore, the most reliable tool for diagnosis of discogenic pain is still lumbar provocation discography [24].

Vertebral Body Endplate

In comparison to pathologic intervertebral discs, vertebral endplate pathologies are more innervated [25]. Based on vertebral body innervation patterns and due to the anatomical proximity of the intervertebral disc and vertebral body endplate, it has been suggested that some forms of pain previously attributed to intervertebral discs may arise from the vertebral endplate [26].

The vertebral body endplate is a bilayer of cartilage and bone that serves as an interface between the intervertebral discs and adjacent vertebral bodies. The superior and inferior endplates are innervated by basivertebral nerve trunk, which enters the posterior vertebral body through the basivertebral foramen along with nutrient arteries. These nerve fibers presumably originate from the sinuvertebral nerves [17, 26], which in turn originate from the sympathetic trunk [16]. Endplate lesions and MRI Modic vertebral endplate changes are common. In a cadaveric study, endplate lesions were found in 45.6% of lumbar vertebral endplates [27]. A meta-analysis showed the median prevalence of Modic changes in patients with low back pain to be 43% compared to 6% in an asymptomatic population [28].

There is growing evidence that the endplate may represent a pain generator of axial back pain. Theoretical basis for provocation discography, i.e., pain triggered by mechanical stimulation of chemically sensitized nociceptor within the outer annulus of the disc, may also apply to chemically sensitized nociceptor within endplates weakened by damage [29]. Endplates in patients with chronic back pain show greater innervation in areas of endplate damage [25, 30] and are sensitive to direct mechanical stimulation [31]. In addition, there is evidence to support the role of endplate defects in axial back pain in that damaged endplate regions facilitate communication between the inflammatogenic intervertebral disc nucleus and vertebral body bone marrow [32]. Studies have also shown an association between low back pain and vertebral bone marrow lesions seen on MRI described as Modic changes [33–35]. Endplates associated with Modic changes show increased endplate innervation [36].

Although Modic changes are one of the most specific predictors of low back pain, they are not very sensitive [37, 38]. This may be explained by the finding that many innervated endplate pathologies are not detectable on MRI [25, 39]. Therefore, current diagnostic tools are unable to detect endplate pathologies associated with increased innervation, potentially resulting in the under-appreciation of the clinical significance of endplate damage in axial back pain.

Facet (Zygapophyseal) Joint

The facet or zygapophyseal joints are paired, planar, synovial joints formed by the articulation of the inferior articular process of one vertebra with the superior articular process of the adjacent vertebra. In general, the facet joints are innervated by the medial branches of the dorsal rami from the dorsal root ganglion. The prevalence of facet joint pain in patients with chronic LBP has been reported to be 31–55% [40].

Since facet joints have classic synovial joint features, facet joint degeneration may result from abnormal motion associated with disc degeneration and arthritis, similar to other synovial joints [41]. Other mechanisms proposed for the role of facet joints as a spinal pain generator include excessive stretching damaging the facet joint capsules [42], mechanical impingement or displacement of innervated intra-articular folds of synovial membrane [43, 44], and release of inflammatory substances [45].

Studies have demonstrated that cervical, thoracic, and lumbar facet joints are capable of causing pain in the neck, upper and mid back, and low back with pain referred to the head or upper extremity, chest wall, and lower extremity, respectively [46–48]. Facet joints have also been shown to be a source of pain in patients with chronic spinal pain using diagnostic techniques and therapeutic interventions [49, 50]. A common clinical presentation is pain localized to the midline exacerbated by standing, sitting, extension, and lateral bending. However, no consistent history, physical examination, or image findings have been found that correlated with positive diagnostic block responses.

Sacroiliac Joint

The sacroiliac joint is a synovial, diarthrodial joint between the sacrum and ilia. The anterior portion is considered a true synovial joint, whereas the posterior connection is a syndesmosis consisting of the ligamenta sacroiliaca, the musculus gluteus medius and minimus, and the musculus piriformis [51]. Although anatomic studies describe variable innervation, generally accepted innervations of the posterior sacroiliac joint include the L5 dorsal ramus and S1–S3 lateral branches [52, 53].

Diagnostic sacroiliac joint injections are currently the most commonly used method of distinguishing symptomatic

from asymptomatic joints [54]. Unfortunately, there exists a high false-positive rate due to extravasation through capsular tears or communication with the dorsal sacral foramina, lumbar epiradicular sheath, and lumbosacral plexus [55]. Reported prevalence of sacroiliac joint pain is also variable ranging from 2% to 60%; however, the majority of studies suggest a prevalence of 25% [56, 57]. Maximum pain below L5 coupled with pain being pointed to the posterior superior iliac spine or tenderness just medial to the posterior superior iliac spine (sacral sulcus tenderness) has been reported to be highly predictive of sacroiliac joint pain [58].

In contrast to the facet joint, the sacroiliac joint is surrounded by thick supporting ligaments including the iliolumbar ligaments, dorsal and ventral sacroiliac ligaments, and sacrospinous and sacrotuberous ligaments. Therefore sacroiliac joint pain may originate from the joint itself or extra-articular ligamentous sources or both [59]. Studies suggest that interventions targeting sacroiliac joint pain should employ extra-articular and intra-articular approaches [60, 61].

In summary, chronic spinal pain may originate from one or more spinal levels and different bony structures within the spine. Accurate diagnosis of the primary pain generator may prove to be challenging given the considerable overlap in anatomic structures. Clinical diagnosis based on physical exam may be unreliable. Single clinical test is often not useful, but positive and negative likelihood ratios could be optimized with a cluster of tests [62]. Although imaging modalities are helpful in diagnosis, current radiological diagnostic tools are not able to reliably detect or differentiate a painful pathology from a pathology that is not a pain generator. It remains a challenge to reach an anatomic diagnosis in many spinal pain conditions, making it difficult to develop sensitive and specific treatment pathways for spine pain/LBP.

Neuropathic Pain in Chronic LBP

Despite the high incidence and prevalence of LBP, little is known about the underlying neural mechanisms. LBP is often associated with leg pain, which is clinically diagnosed as either radicular pain/radiculopathy or referred pain. Radicular pain/radiculopathy is characterized by leg pain that radiates along specific dermatomes, and it often radiates below the knee. It may be accompanied by muscle weakness, reflex change, and/or sensory abnormalities. The referred leg pain tends to be in the thigh and is thought to have pain origin in the lumbar spine.

Low back pain can present with nociceptive, neuropathic, or mixed pain components [63–67]. Although radiculopathy is considered neuropathic in nature, axial low back pain and referred leg pain may have coexisting neuropathic and nociceptive mechanisms. Identifying the presence of neuropathic pain in LBP is important, since this often presents as a challenging management issue. Neuropathic pain is typically associated with low rates of treatment success. Patients with acute LBP may show neuropathic pain symptoms similar to those of chronic LBP. If left unrecognized and subjected to suboptimal treatment, the acute pain condition may persist and become subacute and chronic.

Categorizing LBP as either nociceptive or neuropathic is not always straightforward. There are symptomatic characteristics of neuropathic pain that provide the first clinical impression (Table 39.1) [68]. In addition, multiple evaluation instruments have been developed, such as the painDETECT questionnaire (PDQ) [69–71], the Neuropathic Pain Questionnaire (NPQ) [72], the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) [73], and the

Table 39.1 Characteristics of neuropathic pain vs. nociceptive pain[a]

Clinical characteristic	Neuropathic pain	Nociceptive pain
Cause	Injury to the nervous system, often accompanied by maladaptive changes in the nervous system	Damage or potential damage to tissues
Descriptors	Lancinating, shooting, electric-like, stabbing pain	Throbbing, aching, pressure-like pain
Sensory deficits	Common—for example, numbness, tingling, pricking	Uncommon; if present they have a non-dermatomal or non-nerve distribution
Motor deficits	Neurological weakness maybe present if a motor nerve is affected; dystonia or spasticity may be associated with central nervous system lesions and sometimes peripheral lesions (such as complex regional pain syndrome)	May have pain induced weakness
Hypersensitivity	Pain often evoked by non-painful (allodynia) or painful (exaggerated response) stimuli	Uncommon except for hypersensitivity in the immediate area of an acute injury
Character	Distal radiation common	Distal radiation less common; proximal radiation more common
Paroxysms	Exacerbations common and unpredictable	Exacerbations less common and often associated with activity
Autonomic		
signs	Color changes, temperature changes, swelling, or sudomotor (sweating) activity occur in a third to half of patients	Uncommon

[a]Reproduced from BMJ, Cohen SP, Mao J, 348, f7656, Copyright 2014, with permission from BMJ Publishing Group Ltd

Douleur Neuropathique 4 (DN4) [74], which can be used to screen for the presence of neuropathic pain in LBP patients. These screening instruments have various levels of validity and sensitivity. To further assess the neural processing of nociceptive information, quantitative sensory test (QST) has been extensively used in the preclinical settings [75]. However due to its significant requirement of personnel resource and patient participation, it has not been adapted in everyday clinical practice. Nevertheless, QST results in chronic LBP patients have demonstrated alternated neural processing of nociceptive stimuli [76–78].

The extent of neuropathic pain in LBP patients is extensively debated, with reported prevalence rates being in the range of 28.1–71.2%. In a recent meta-analysis, the pooled prevalence of neuropathic pain in LBP patient is 47%. The pooled prevalence rate of neuropathic pain was only marginally higher in chronic LBP patients than that in patients affected by acute/subacute LBP. Significantly higher prevalence rate of neuropathic pain was associated with leg pain as compared to those conditions without an associated leg pain [63]. A Japanese Society for Spine Surgery and Related Research (JSSR) study reported an overall neuropathic pain prevalence of 53.3% in spinal conditions, and 29.4% in these patients suffering from LBP. It was relatively high in patients with cervical myelopathy (77.3%), as compared to those with low back pain (29.4%). Risk factors for having neuropathic pain were identified to be advanced age, severe pain, long duration, and cervical lesions [66]. When pain location was considered in a subsequent analysis, it was found that the pain is more likely nociceptive if lumbar back pain is the primary symptom, whereas neuropathic pain is more dominant if the patient has buttock and/or leg pain [65].

Altered Somatosensory Function in Chronic LBP and QST

Quantitative sensory testing is a psychophysical method used to quantify somatosensory function in healthy subjects and patients [75, 79]. It is based on measurements of responses to calibrated, graded innocuous or noxious stimuli (typically mechanical or thermal). QST has been used for decades in the research setting, particularly for diagnosing, assessing, and monitoring sensory neuropathies and pain disorders. It supplements the conventional bedside electrophysiological tests (Table 39.2), and, as it can be influenced by higher cognitive function, it can reflect changes in the central neural processing as well (Fig. 39.4).

In a systematic review of studies on early changes in somatosensory function in acute and subacute spinal pain (7 days to within 12 weeks), Marcuzzi et al. reported that there is evidence for hyperalgesia to mechanical and electrical stimuli in the early stages of LBP [78]. Pressure pain hypersensitivity occurs in subacute LBP locally at the spine and remotely at sites with suprathreshold stimuli. This corroborates results in patients with chronic LBP showing that widespread pain hypersensitivity exists and is associated with augmented central pain processing. For example, in a prospective study of a cohort of patients with degenerative lumbar spine disorders scheduled for surgery, including LBP for more than 3 months, 22% of the patients showed altered somatosensory profiles in two or more body regions, including a non-affected region, indicating disturbed somatosensory function [80]. These patients had mostly loss of sensory function and reported worse pain and mental health condition.

The distinct, individual QST profiles have the potential to be used for subgrouping of LBP patients. In a cohort of primarily axial LBP patient, Rabey et al. were able to show three clusters of somatosensory characteristics [81, 82]. Cluster 1 (31.9%) was characterized by average to high temperature and pressure pain sensitivity. Cluster 2 (52.0%) was characterized by average to high pressure pain sensitivity. Cluster 3 (16.0%) was characterized by low temperature and pressure pain sensitivity (Fig. 39.5). Temporal summation occurred significantly more frequently in cluster 1. Clusters 1 and 2 had a significantly greater proportion of female participants and higher depression and sleep disturbance scores than cluster 3. These findings suggest possible distinct neural mechanisms for seemingly homogeneous group of LBP patients.

Table 39.2 Difference between quantitative sensory testing and conventional electrophysiological tests

Characteristics	Electrophysiological techniques: NCS and SEP	Quantitative sensory testing
Type of information obtained	Function of large myelinated sensory fibers	Function of small and large sensory fiber
	Localization along neuroaxis, of entire length for SEP and peripheral nervous system for NCS	Do not localize of lesions
		Differentiate between sensory loss and sensory gain
	Do not assess positive phenomena	
	Do not assess small fiber	
Nature of subject participation	Do not require response from subject	Require response from subject
	No active cooperation required	Clear influence of attention, motivation, cognitive impairment
Need for training	Required for investigator, but not for subject	Required for both investigator and subject
Normative data	Mostly available	Generally lacking

NCS nerve conduction study, *SEP* somatosensory evoked potential
Modified from Backonja et al. 2013 [75]

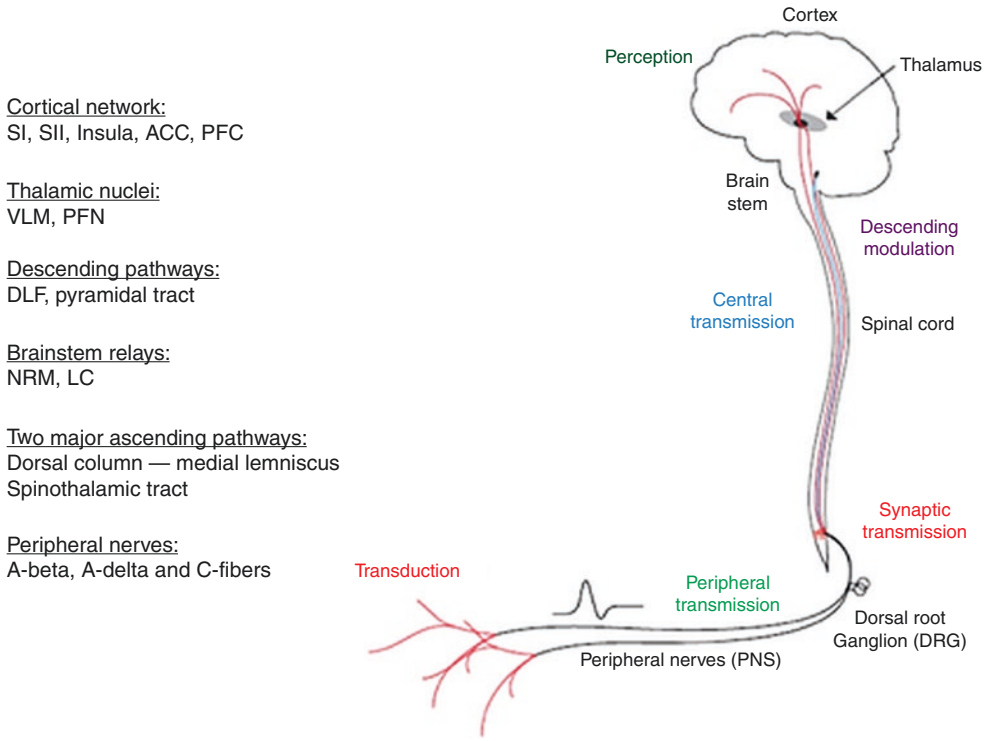

Fig. 39.4 Schematic drawing of the neural processes of nociception and pain [75]. (Reprinted with permission from Backonja et al. [75])

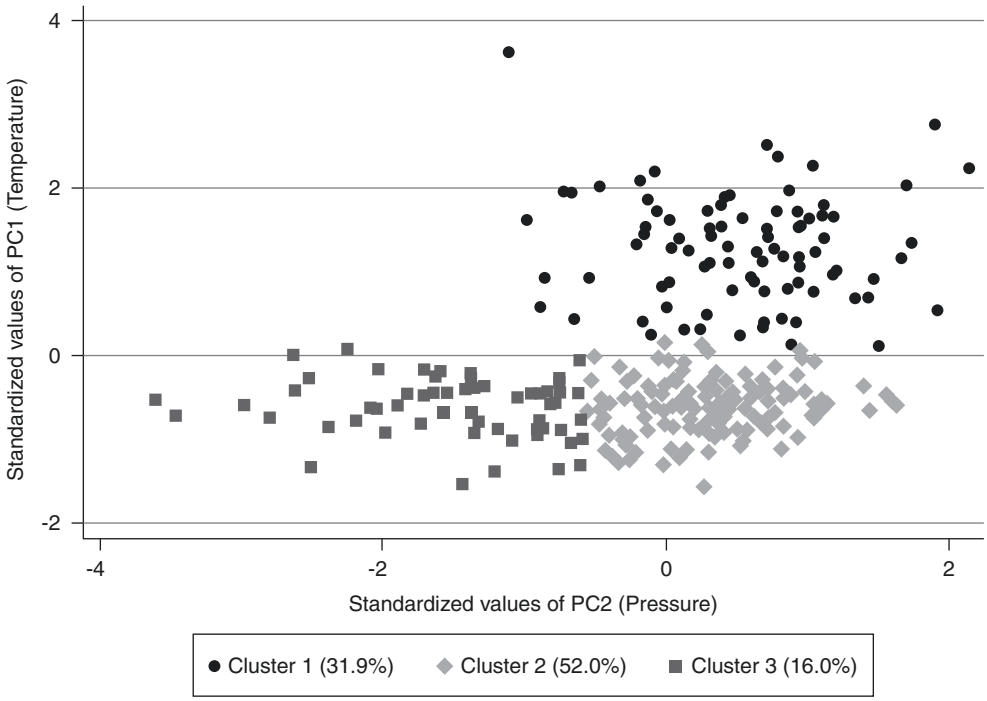

Fig. 39.5 Latent class analysis showing three clusters derived from thermal and pressure principal component scores. PC1, principal component 1 (from wrist and lumbar heat and cold pain thresholds); PC2, principal component 2 (from wrist and lumbar pressure pain thresholds). (Reprinted with permission from Rabey et al. [82])

However, there is very limited evidence of the predictive value of somatosensory characteristics in treatment response. In a randomized, double-blinded study comparing the analgesic effect of imipramine and oxycodone to placebo, thermal QST was shown to have the potential to predict imipramine effect in chronic low back pain. In contrast, the effect of oxycodone could not be predicted by any of the selected QST characteristics [83]. Maher et al. examined the prognostic value of QST in patients with unilateral lumbar radicular pain receiving epidural steroid injection. They found that the non-responders to ESIs have increased detection threshold to heat pain and

warm sensation, suggesting a preexisting dysfunction in the C fibers [84]. In a small study of patients with unilateral lumbar radicular pain undergoing pulsed radiofrequency treatment of the DRG, it was shown that the reduced pressure pain threshold normalized with treatment, while the reduced conditioned pain modulation (a parameter reflecting the function of the descending pain modulation pathway, Fig. 39.6) remained decreased [85].

Psychological Comorbidity in Chronic LBP

Chronic low back pain is highly comorbid with other pain conditions, other chronic diseases, and mental disorders. High level of negative affect is the most frequent presenting symptom of comorbid major depression or anxiety disorder, which afflicts 30–50% of patients with chronic LBP [81, 86–88].

In a cluster analysis of chronic LBP patients, Rabey et al. identified three psychological clusters from a broad range of psychological measures [81]. Cluster 1 (23.5%) was characterized by low cognitive and affective questionnaire scores, with the exception of fear-avoidance beliefs. Cluster 2 (58.8%) was characterized by relatively elevated thought suppression, catastrophizing, and fear-avoidance beliefs but lower pain self-efficacy, depression, anxiety, and stress. Cluster 3 (17.7%) had the highest scores across cognitive and affective questionnaires. These psychologically derived clusters correlated with distinct profiles of pain and disability. Cluster 1 had the most localized pain, lowest pain intensity (5.1/10 on a 0–10 numeric pain scale), and lowest disability levels (Roland–Morris Disability Questionnaire: RMDQ score = 6). Cluster 2 had more widespread pain and higher pain intensity (6.0/10) and intermediate levels of disability (RMDQ score = 9). Cluster 3 had higher pain intensity (6.2/10), the most widespread pain, and greatest disability (RMDQ score = 12).

Presence of worse psychological comorbidities is associated with higher levels of pain, poor functioning, and worse treatment outcomes, such as with spine surgery, nerve blocks, physical therapy, or medications [87–94]. In a prospective cohort study of oral opioid therapy in 81 chronic LBP patients with low, moderate, and high levels of negative affects (NA), Wasan et al. found that high NA and low NA groups had significantly different responses to opioid therapy, with an average 21% versus 39% improvement in pain, respectively. The high NA group also had a significantly greater rate of opioid misuse and significantly more and intense opioid side effects [87]. Psychological dysfunction is also associated with poor surgical outcome. Meta-analysis identified a number of psychological variables that are associated with a poorer outcome with lumbar spinal fusion. Higher levels of depression and lower scores on the SF-36 are the most commonly implicated.

Current Evidence of Spinal Interventions

In order to rigorously evaluate trials of therapeutic intervention targeting a particular pain generator, several cardinal issues need to be considered. These include symptomology, diagnosis, rationale for treatment, consequent appropriate selection of patients, outcomes assessment, and the need for rigorous control of technical performance of the therapeutic intervention [95]. Here we review some examples of "landmark" trials and highlight potential issues on how results were interpreted.

Intra-disc Interventions

It is a difficult clinical situation with discogenic low back pain. Although the majority of patient with discogenic low back pain recovers with time, there is very limited treatment

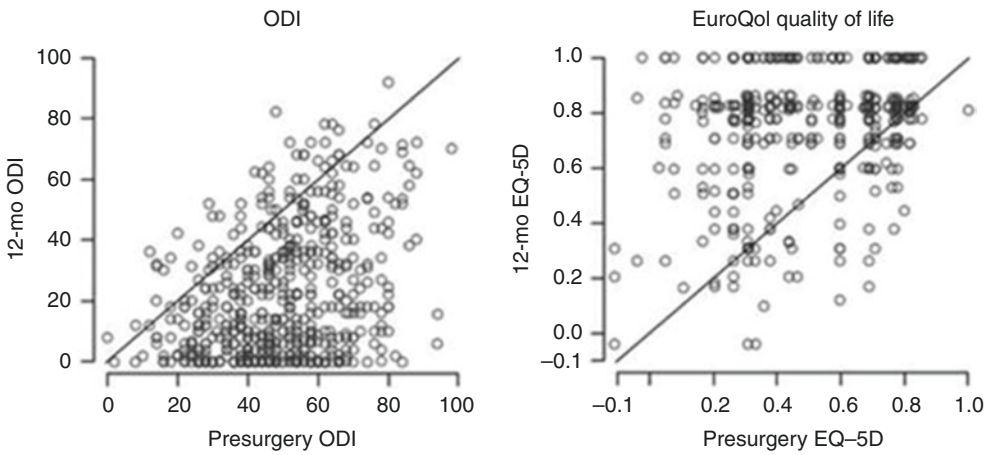

Fig. 39.6 Variation in 12-month reported outcomes at the individual patient level (lumbar disc herniation). *ODI* Oswestry Disability Index, *EQ-5D* EuroQOL Quality of Life. (Reproduced with permission from Asher et al. [127])

option for those with persistent low back pain with underlying disc abnormalities. Intra-disc interventions such as intradiscal electrothermal therapy (IDET) and radiofrequency annuloplasty could be a potentially effective treatment for discogenic pain but only in properly selected patients [96, 97]. For example, the study by Pauza et al. used very strict inclusion criteria: only patients with less than 20% disc height narrowing and a discrete posterior annular tear were included in their study [96]. Patients with radicular pain, vertebral canal stenosis or scoliosis, intervertebral disc herniation greater than 4 mm, or worker's compensation, conditions frequently seen with chronic LBP, were excluded. There were only 64 patients found suitable for randomization (out of 1360 initially considered eligible based on interview and physical examination). In this highly selected group, the results showed modest overall benefit; approximately 40% of the patients achieved greater than 50% relief of their pain, with 50% of patients having no benefit.

Freeman et al. conducted another RCT in South Australia to assess the efficacy and safety of IDET for the management of internal disc disruption in the lumbar spine [9]. Fifty-seven patients met inclusion criteria including symptoms of LBP of at least 3 months, evidence of degenerative disc disease on MRI, and presence of one- or two-level symptomatic disc degeneration as determined by provocative discography. Successful outcome was defined meeting all the following criteria: no neurologic deficit resulting from the procedure, an improvement in the Low Back Pain Outcome Score (LBOS) of 7 or more points, and an improvement in the Short-Form 36 General Health questionnaire (Australian version SF-36) subscales of bodily pain and physical functioning of greater than 1 standard deviation from the mean. At 6 months follow-up, no subject in either group met criteria for successful outcome. The authors concluded that the IDET procedure appeared safe with no permanent complications and that there was no significant benefit from IDET over placebo.

As pointed out in a commentary on the Freeman study, patients unlikely to benefit from IDET include those with severe multilevel disc degeneration, overweight patients, and those receiving workers' compensation benefits [8, 98]. More than 50% of the subjects in both groups in the Freeman study were recipients of workers' compensation. Studies have shown that those receiving workers' compensation benefits are unlikely to benefit from IDET [99, 100]. It is then reasonable to suspect that lack of benefit of IDET over placebo may be partly explained by the fact that the majority of subjects in that study were recipients of workers' compensation. The IDET procedure is considered more appropriate in the acute phase of injury, with pain localized to the annulus and not the endplates or facet joints, as commonly occurring with advanced disc degeneration, which would not be effectively treated with IDET [8].

Epidural Steroid Injection

The use of epidural steroid injections in the treatment of sciatica has also been the subject of many randomized controlled trials. In a multicenter, Lumbar Epidural Steroid Injections for Spinal Stenosis (LESS) trial, the effectiveness of epidural injections of glucocorticoids plus lidocaine was compared to lidocaine alone in patients with lumbar spinal stenosis. Primary outcomes included physical disability based on Roland–Morris Disability Questionnaire (RMDQ) and intensity of leg pain (on a scale from 0 to 10) [13, 101]. A total of 400 patients with CT or MRI confirmed lumbar central spinal stenosis were randomized and analyzed an intention-to-treat strategy. At 3 weeks, the glucocorticoid–lidocaine group had greater improvement than the lidocaine-alone group, but the differences were clinically insignificant. At 6 weeks, there was no significant difference between the two groups with respect to pain-related functional disability (as measured by the RMDQ) or pain intensity [13]. In a systematic review with meta-analysis of randomized controlled trials, Pinto et al. concluded that there was high-quality evidence showing that epidural corticosteroid injections have small, short-term effects on leg pain and disability compared with placebo in patients with sciatica but no effect in the long term [102]. In contrary, several systematic reviews and meta-analysis showed epidural steroid injection has moderate, short-term efficacy in treating lumbar radicular pain [103–106].

The inconsistence in these reports reflects several issues. In the LESS trial, patients were included with lumbar central canal stenosis and "pain in the lower back, buttock, leg, or a combination of these sites on standing, walking, or spinal extension in the past week; worse pain in the buttock, leg, or both than in the back" [13]. However, there is no consensus on lumbar spinal stenosis symptoms [95]. Neurogenic claudication is a commonly agreed upon symptom of lumbar spinal (canal) stenosis [107]; however, the actual presence of neurogenic claudication was used as eligibility criteria in only 71% of studies with a definition that varied considerably across studies [108]. The similarity in clinical presentation of lower extremity pain due to radicular pain caused by disc protrusion and neurogenic claudication caused by spinal stenosis contributes to the challenge of accurately diagnosing underlying pain generator. Imaging studies are commonly used to help diagnose lumbar spinal stenosis. However, 21% of asymptomatic subjects over age 60 have significant radiographic findings of lumbar spinal stenosis [109]. Several design issues have also been raised with the interventions used in the LESS trial including the medication selection, procedural approach, and absence of a placebo or sham injection. There is no evidence for inflammation in lumbar spinal stenosis [95], raising the question whether the epidural use of glucocorticoids plus lidocaine or lido-

caine alone should be compared. Unfortunately, a true placebo or sham epidural injection may be difficult to design. Therefore, extrapolation of these results should be avoided to answer the question of whether epidural injections are effective therapeutic interventions for lower extremity pain due to lumbar spinal stenosis.

In the Pinto study, there are significant variations in procedural technique including fluoroscopically guided caudal, interlaminar, and transforaminal approaches, as well as blind injections. By analyzing these heterogeneous trials together, it incorrectly assumes that the procedures and its associated evidence are similar [110, 111]. In addition, the average of pain severity rating may not be the best measure of efficacy. As shown previously, if the distribution of pain severity rating does not conform to a normal distribution within the study population, use of categorical data may have been more reflective of clinical applicability [111]. For instance, in a study comparing the efficacy of transforaminal injection of steroids for lumbar radicular pain, the superiority of transforaminal injection of steroids was demonstrated when categorical outcomes were calculated. In contrast, group average data showed no statistically significant change in pain scores [103], which suggests that group average may obscure an intervention's true efficacy on individuals.

Radiofrequency Ablation

There remains considerable debate as to the effectiveness of radiofrequency neurotomy in treating chronic low back pain (with an origin of lumbar facet joint or sacroiliac joint) [15, 50, 112, 113]. A recent RCT ignited further discussion on this topic [14]. The Cost-Effectiveness of Minimal Interventional Procedures for Patients with Chronic Low Back Pain (Mint) study was a non-blinded, RCT conducted in 16 multidisciplinary pain clinics in the Netherlands to evaluate, fairly broadly, the effectiveness of radiofrequency denervation of facet joint, sacroiliac joint, or the intervertebral disc. Primary outcome was numerical rating scale (numeric pain scale from 0 to 10). A total of 681 patients were randomized (251 in the facet joint trial, 238 in the sacroiliac joint trial, and 202 in the combination trial) and analyzed using an intention-to-treat strategy. Patients were enrolled into either facet joint trial or sacroiliac joint trial based on diagnostic blocks. At 3 months, the mean difference in pain intensity between the radiofrequency denervation and control groups was −0.18 in the facet joint trial, −0.71 in the sacroiliac joint trial, and − 0.99 in the combination trial. The authors concluded that the findings do not support the use of radiofrequency denervation to treat chronic low back pain originating in the facet joints and sacroiliac joints or a combination of facet joints, sacroiliac joints, or intervertebral discs.

The diagnostic criteria used in the Mint trial were less stringent than those in previous studies. The Mint study utilized single diagnostic block that was considered positive if the participant reported 50% or more pain reduction, whereas previous studies used controlled, double block and > 80% pain reduction to establish the diagnosis. Single diagnostic block has been shown to have a false-positive rate of 38% and positive predictive value of 31% [114]. Moreover, radiofrequency ablation of lumbar medial branches has been shown to be effective when diagnostic block criteria are set at 80% or 100% pain relief after comparative diagnostic blocks [15, 112]. There are also variations in the interventional technique among these studies. In the Mint trial, a 22-gauge needle was used, which may result in a smaller lesion and consequently incomplete or failed facet joint denervation [115, 116]. These technical issues became even more problematic with regard to sacroiliac joint denervation, where radiofrequency denervation techniques included cooled radiofrequency denervation, or the Simplicity III device. Given these issues around the precision of diagnosis, technical variance, results of the Mint study and previous trials should be evaluated and interpreted with appropriate caution.

Spinal Cord Stimulation

Since its introduction in the early 1960s, spinal cord stimulation (SCS) has been successfully used to treat a variety of pain conditions, including post-laminectomy low back pain. Its efficacy was consistently demonstrated in several RCTs [117–120]. The more recent development in the technology, particularly the introduction of high frequency and burst stimulation, has broadened the application of this treatment modality.

Al-Kaisy et al. conducted a prospective study of the efficacy of high-frequency SCS [120]. Patients who had failed to respond to conventional treatment and have a primary diagnosis of chronic low back pain with or without leg pain were included. Of the 83 patients enrolled, 82 completed the trial phase, and 72 had a successful trial and proceeded to implantation with 65 available for follow-up at 24 months. The mean back pain VAS (visual analog scale) score of 8.4 was reduced to 3.3 at 24 months. The mean baseline leg pain VAS score of 5.4 reduced to 2.3 at 24 months [120]. In a subgroup of the study population, which consisted of 14 patients who have previously failed traditional SCS, 11 (79%) of these patients had a successful trial with statistically and clinically significant reduction in back and leg pain at 24 months. It has been observed that benefits of traditional SCS diminish with time [121]. Al-Kaisy et al. also noted that an increase in back pain score from 6 to 24 months.

The SENZA trial was a prospective RCT in the United States to assess primarily non-inferiority and secondarily superiority of HF10 therapy as compared with traditional low-frequency SCS in patients with chronic low back and leg pain [122]. Primary outcome of the study was the percentage of subjects who respond to SCS therapy (≥50% reduction in back pain VAS score). A total of 198 patients were randomized to HF10 or traditional SCS. Of the 101 subjects assigned to HF10 therapy, 85 were available for follow-up at 24 months. Of the 97 patients assigned to traditional SCS, 71 were available for follow-up at 24 months. Responder rate for back pain with HF10 at 12 and 24 months was 78.7% and 76.5%, compared to traditional SCS of 51.3% and 49.3%, respectively. Similarly, responder rate for leg pain with HF10 at 12 and 24 months was 80.9% and 72.9%, compared to traditional SCS of 50.0% and 49.3%, respectively [122].

A potential explanation for the treatment response heterogeneity and non-responder rate observed in these trials may be due to the heterogeneity in pain diagnoses. Examining the baseline demographics in these studies, there were ten different pain diagnoses originating from different anatomical pain generators. Even though 75–80% patients in these trials carried the diagnosis of failed back surgery syndrome, this diagnosis is comprised of heterogeneous spine pathology. Further evaluation of subgroup's response may assist in identifying traits that characterize poor or non-responders to the SCS treatment.

Spinal Surgery

The landmark Spine Patient Outcomes Research Trial (SPORT) was a randomized clinical trial in 13 multidisciplinary spine clinics in 11 states in the United States to compare the outcomes of surgical and non-operative treatment for lumbar intervertebral disc herniation, spinal stenosis, or degenerative spondylolisthesis. Primary outcome measures were health-related quality of life measured by SF-36 Health Status Questionnaire and Oswestry Disability Index [123].

Patients were eligible for the SPORT intervertebral disc herniation trial if they have radicular pain despite some non-operative treatment for at least 6 weeks, physical exam evidence of nerve root compression, and confirmatory imaging study (MRI or CT) showing disc herniation at a level and side corresponding to the clinical symptoms. A total of 501 patients were randomized to non-operative care or surgical decompression of the involved nerve root by a standard discectomy. At the end of the 2-year period, patients in both non-operative and surgery groups demonstrated improvements with no statistically significant treatment effects on measures of health-related quality of life including pain, physical function, and disability [124].

The symptom heterogeneity of patients recruited into SPORT is a major limitation. Lumbar disc herniation is a heterogeneous condition ranging from asymptomatic to functionally debilitating. In contemporary clinical practice, patients with mild or improving symptoms are typically managed non-operatively since most symptomatic herniated lumbar discs follow a benign, self-limiting course. Surgery is indicated for patients with severe pain despite conservative care or progressing neurological deficit. Symptom severity is one of the prognostic factors for surgical outcome in that patient with severe pain was more likely to benefit from surgical intervention [125]. Approximately 20% of patients randomized into surgery group reported that their symptoms were "getting better" on baseline self-assessment – their outcome would have been credited to surgery irrespective of whether they underwent surgery or not. On the other hand, nearly 80% of patients randomized into non-operative group reported their symptoms were "getting worse" on baseline self-assessment – these patients preferentially cross over to surgery, but the surgical benefit would be attributed to non-operative treatment because of the intent-to-treat analysis. Poor adherence to treatment assignment was also of major concern. One half (50%) of the patients assigned to surgery received surgery within 3 months of enrollment, while 30% of those assigned to non-operative treatment received surgery in the same period. Due to the planned intent-to-treat analysis and this high crossover rate, the net effect would be diluted and likely underestimate the true benefit of surgery and overestimate the benefit of non-operative management. As-treated analyses based on treatment received were performed with adjustments for the time of surgery and factors affecting treatment crossover and missing data. These analyses yielded far different results than the intent-to-treat analysis, with strong, statistically significant advantages seen for surgery at all follow-up times through 2 years [126].

Discussion

There remain substantial questions about chronic LBP. For example, is our current approach to identify specific anatomic "pain generator," such as intervertebral disc or facet joint abnormalities, adequate to guide effective treatment? To what extent do the comorbid psychosocial factors contribute to the individual perception of pain? Are there mechanistically distinct types of low back pain that entail very different treatment approaches? The current diagnostic classification of low back pain patients, primarily relying on presenting signs/symptoms and radiographic abnormalities, almost certainly does not capture all underlying mechanisms of chronic LBP.

A recurring theme in the scientific literature and in clinical practice is that chronic LBP is a collection of heterogeneous conditions. Clinical symptoms of distinct anatomic pathologies overlap. There are variable degrees of comorbid psychological/brain dysfunction. These all affect the way in which chronic LBP is diagnosed, classified, and treated. The data from several international spine registries clearly demonstrated this nature of heterogeneity of chronic LBP. In the US N^{2}QOD spine registry data, although cohort averages demonstrated an overall improvement in mean disability and QOL (quality of life) after spinal surgeries, a wide variation in the preoperative disability, 12-month postoperative disability, and extent of 1-year improvement was observed at the patient level (see Fig. 39.6) [127, 128]. Similar scatter plot patterns were observed for all diagnoses, in all procedures, and for all patient-reported outcomes. There are patients who achieved remission, while some progressed worse, despite being treated with the same surgery.

Although randomized clinical trials have long been the "gold standard" for efficacy evidence, they are generally costly and time-consuming. Furthermore, findings from randomized controlled trials do not always translate into real-world practice outcomes [129]. In fact, to demonstrate efficacy and maximize internal validity, randomized controlled trials are typically conducted in a relatively homogeneous group of patients, usually the most severely ill, who have strong potential to benefit from treatment. On the other hand, in a more inclusive trial, those who could benefit only minimally from the treatment are included, thus diluting the average effect size and reducing the power for the trial if the sample size does not accommodate the diversity of the patients. In the low back pain research literature, the latter tended to be the case. Although a broader, more inclusive group of patients may be more representative of the target population, they may also have differential responses to the same treatment, resulting in the heterogeneity of treatment effects (HTE), defined by Kravitz and colleagues as the "magnitude of the variation of individual treatment effects across a population." More specifically, this definition includes different responses by patients with different characteristics [130]. Those characteristics can include severity of the disease, social demographic characteristics, genetic characteristics, and health-related behaviors. If there were a substantial interaction between a treatment and specific patient characteristics, the average effect observed across patients in a trial would not apply to the subgroup of patients in the trial with different levels of those characteristics. For example, in the Ghahreman study of transforaminal epidural steroid injection, there are clearly two subgroups of patients with very different response, and there is no patient reporting the "average" pain level (Fig. 39.7a) [103]. Similarly, the duration of analgesic effect after lumbar DRG (dorsal root ganglion) radiofrequency lesion showed a wide scattering/polarization (Fig. 39.7b) [113].

Yet, in the effort to summarize clinical trials to help practitioners make the best "evidence-based" decisions (most appropriate treatment pathways) in routine practice, systematic reviews and meta-analysis used the "averaging" of treatment effects across trials. Without differentiating treatment effects for subgroups within trials, this higher-order averaging of effects (average the "average") is then used as the basis for the development of guidelines

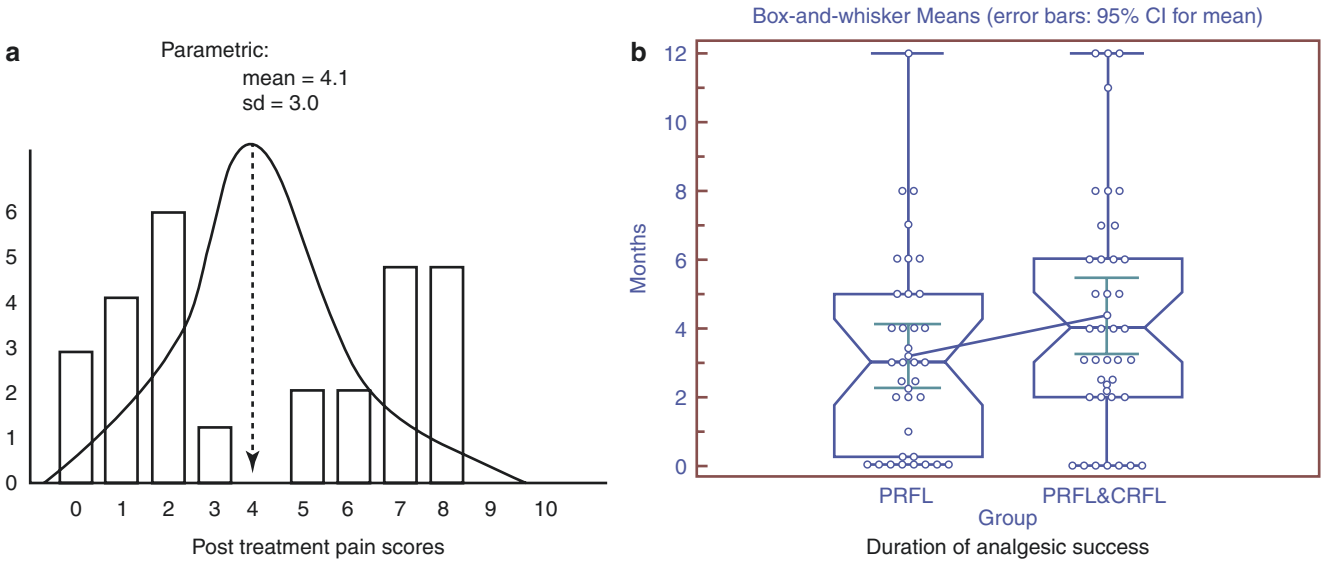

Fig. 39.7 Examples of heterogeneous treatment response. (**a**) Posttreatment pain levels after transforaminal epidural steroid injection. (Reproduced from Engel et al. [95], by permission of Oxford University Press). (**b**) Duration of pain relief after radiofrequency lesion of lumbosacral DRG. (Reproduced with permission from Simopoulos et al. [113])

for clinical practice and for quality assurance in clinical practice. The continuing acceptance of average effects may have adverse impacts on patients whose treatments are not paid for or recommended by "evidence-based medicine guidelines" (e.g., decompression of lumbar intervertebral disc for contained disc protrusion and radicular pain [131]). On the other hand, the attempt to generalize positive trial results to patients who have been excluded from those trials may result in overtreatment of those who could not benefit (e.g., lumbar fusion for multilevel degenerative disc disease [132]). Strategies to overcome the problems caused by this heterogeneity should be pursued and will increase the usefulness of trial results.

Clinical registries are increasingly used to generate evidence and ascertain the effectiveness of clinical interventions in routine practice. Registries can also be used to identify patient characteristics or healthcare delivery system factors that are related to clinical outcomes. Registry data could also been used to study the more fundamental mechanisms of disease that could be driving such outcomes.

Several major international registries of spinal surgery over the past decade demonstrated how best this should be conducted and how the data can be analyzed. The Swedish Spine Registry (SweSpine), which started in 1993 with eight contributing centers, has since grown to a major nationwide comprehensive data-gathering tool encompassing 45 centers. As an example, when the effectiveness of balloon kyphoplasty for vertebral compression fracture was examined in its data set, a very similar efficacy to that shown in the FREE randomized controlled trial was demonstrated, supporting the generalizability for the trial results [10, 11, 133, 134]. Staub et al. compared the surgical outcome between cervical total disc arthroplasty (TDA) and anterior interbody fusion (AIF) in the Eurospine's Spine Tango registry [135]. In a design similar to RCT, they retrospectively matched cohorts of patients that underwent TDA and AIF and showed similar surgical outcome. In addition, similar efficacy of TDA and AIF was shown in the excluded cohort. The results of this observational study were in accordance with those of the published RCTs. The analysis of atypical patients suggested that, in patients outside the spectrum of clinical trials, both surgical interventions appeared to work to a similar extent to that shown for the cohort in the matched study. However, since this is from registry data, it has the improved generalizability to real-world practice. This study, as an example, demonstrated how registry data could be used to supplement the evidence from RCTs.

We are in need of such a comprehensive registry with a focus on chronic LBP. The goal of this registry would be the collection of data in the biopsychosocial domains of chronic pain, the technique details of an intervention-heavy spinal pain care specialty, and the outcome measurement (Fig. 39.8). Specifically, clinical information in these areas should be systematically collected:

1. Presenting symptoms and signs, including associated neuropathic pain and psychological profiles. Validated instruments could be used to quantify some of these characteristics.

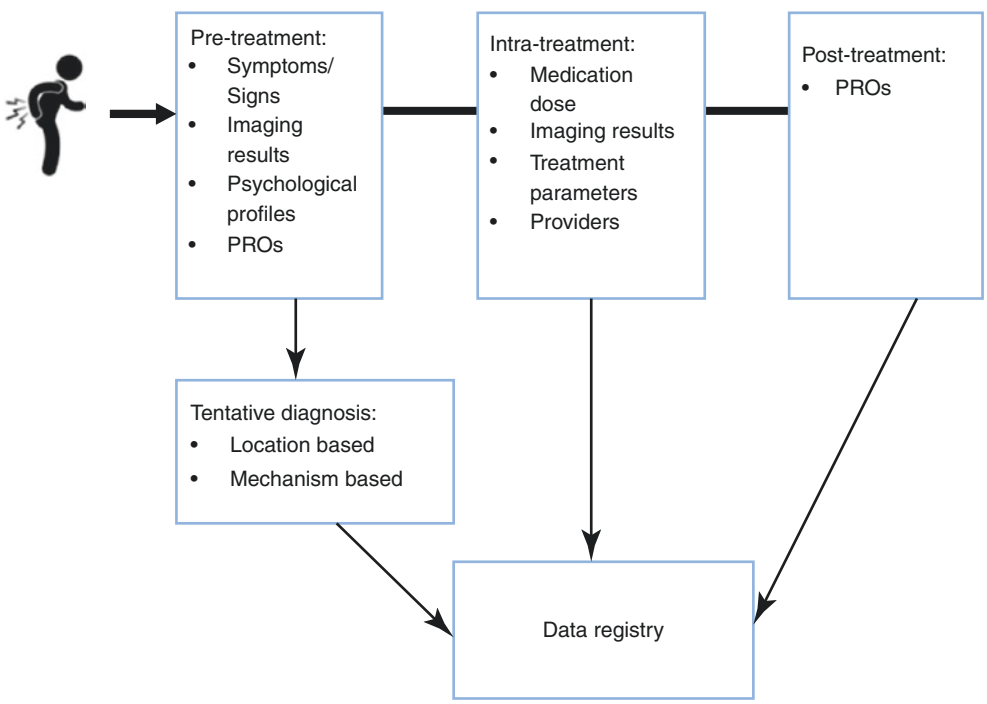

Fig. 39.8 Proposed chronic LBP registry. PROs, patient-reported outcomes

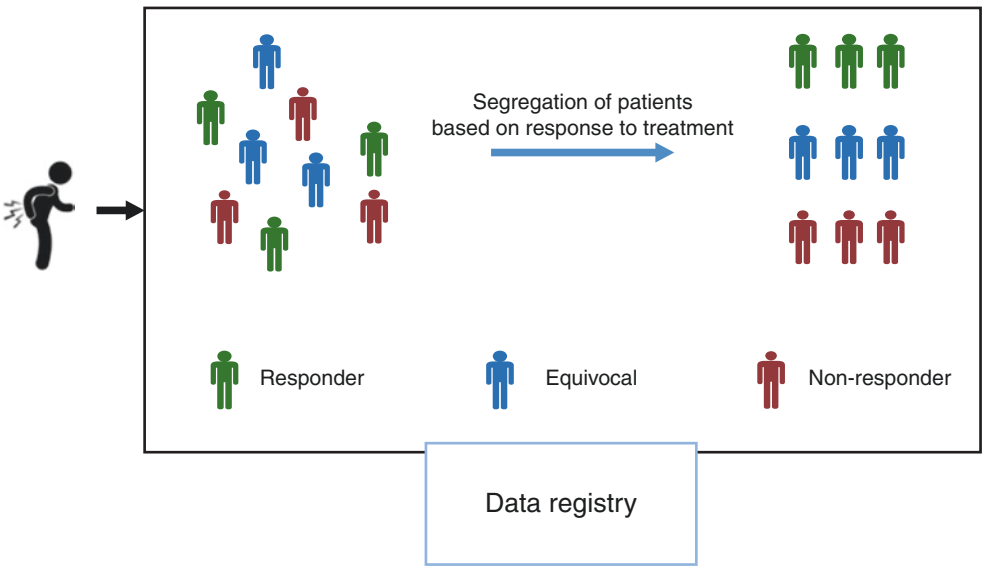

Fig. 39.9 Use of registry data to improve diagnosis of chronic LBP and to guide individualized treatment

2. Relevant radiographic findings, such as vertebral endplate abnormality, intervertebral disc height, and type and severity of spinal stenosis.
3. Technical details of intervention, such as medication dosage and intravenous contrast spread pattern in epidural injection, positioning, and temperature parameters in radiofrequency lesion of spinal nerves.
4. Routine, reliable follow-up assessment, using validated, reliable, and responsive instruments.

Registry is an efficient instrument to capture large amount of meaningful data in a relatively short period of time. The data could be used to identify subgroups and confirm differences in treatment effects for subpopulations. Several of the prominent questions regarding chronic LBP could be addressed, for example, (1) how do we diagnose chronic LBP that has better prognostic value for outcome? and (2) how do we measure the clinical pain experience that would be better and more reliable to reflect the disease burden?

Chronic LBP is a constellation of symptoms of distinct underlying conditions; it is also a disease entity by itself, reflecting altered both peripheral and central neural processing. The heterogeneity in patient characteristics, and how it moderates treatment response, could not be overestimated. If we could identify patient-specific factors that can be used for more precise diagnosis and to better predict treatment response, we will progress from the current "evidence-based" medicine to a more "outcome-based" personalized medicine (Fig. 39.9).

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