Evaluation and Management of Chronic Pain

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Peter S. Staats and Sean Li

Introduction

Chronic pain is one of the greatest health-care crises affecting Americans today. It is a major cause of disability and a leading reason for physician office visits. Moreover, the indiscriminate treatment of chronic pain with systemic opiates has become a major cause of morbidity and mortality. There are close to 16,000 deaths each year attributed to the use of prescription opiates in the United States. It is crucially important for physicians to have an appropriate algorithm for managing patients with pain.

Any strategy begins with a comprehensive evaluation that leads to establishing an accurate diagnosis. To achieve an accurate diagnosis, it is important for caregivers to include a detailed history and physical examination, any necessary imaging, a psychosocial evaluation, understanding the options for patients with chronic pain, and implementing the most conservative options [1]. When the correct diagnosis is made, one can develop the safest and most effective care plan to managing pain.

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What Is Pain?

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or defined in such terms" [1]. As such, there is typically an emotional component as well as a biologic component of most human pain states [2]. The challenge for the treating physician is to assess the patient from a psychosocial as well as from a biologic perspective and come up with the most appropriate accurate diagnosis, from which a therapeutic plan can be developed.

Physicians need to recognize that pain syndromes are complex and have the ability to treat pain or organize care from a biological, psychological, and social perspective. For most physicians who are trained primarily in the biological approach, it can be challenging to evaluate a patient with severe chronic pain with comorbid psychiatric disorders. In the reverse, many psychiatrists and psychologists who are expert pain clinicians may lack the expertise to diagnose and manage the biological underpinnings. For example, specific nerve injuries can manifest with diffuse pain problems. A clinician needs to be able to recognize these problems and establish the underlying pain generator. Sometimes this will lead to a cure, while at other times the most appropriate management strategy can be achieved.

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Patients with similar injuries can present with dramatically different experiences of pain. This can occur for a variety of reasons that are not always evident. For example, some patients with psychological disorders like severe depression and anxiety will frequently present with increased pain beyond what would be expected based on the injury or objective findings. Discrete lesions can be missed, but psychological factors can amplify pain as well. Patients with negative thoughts will experience more pain compared with others with neutral and positive thoughts [3]. On the other extreme, individuals can have genetic disorders leading to lack of pain fibers and experience no pain following an otherwise traumatic injury. These patients with "congenital insensitivity to pain" truly feel no pain [4]. There are multiple gradations in between with sensitivity to nerve injuries.

Pain generally begins in the periphery at specific nociceptors and is conducted to the central nervous system via specific pathways. There is processing and neuromodulation that occurs at the dorsal root ganglion, the spinal cord, and further up the central nervous system [5]. The plasticity that occurs throughout the nervous system has been shown to modify and amplify pain in chronic pain conditions. We have recently learned that at each step along this pathway, the pain signal can be modulated. The pain physician is like a general contractor and should be facile with clinical diagnosis and with the general treatment strategies. If necessary, a pain physician will consult with "subcontractors" who are specialized in addressing focal nerve injury.

If one looks closely enough, most patients we see in clinical practice have an identifiable biologic basis for their pain. However, most patients also have an emotional component that leads to suffering. In some cases this suffering, especially if associated with some psychologic morbidities, can overwhelm the physician. A consultation with psychology should be strongly considered if there is any question of overlapping diagnoses. The job of the pain physician is not only to determine biological source of pain but also to apportion the component of pain that emanates from both the biological underpinnings and the emotional overlay. This evaluation can be quite complex and may involve a more comprehensive evaluation with psychology. In this setting a multidisciplinary evaluation of the patient with pain is recommended.

Diagnostic Workup

This chapter certainly does not attempt to make the reader an expert in all of the different disorders that can cause pain. There are entire treatises devoted to the diagnosis and management of chronic pain [6, 7]. There are no simple X-rays or laboratory tests that indicate if a patient has severe pain. Physicians should, on the other hand, do their best to establish a diagnosis and come up with the most appropriate therapeutic plan. This is achieved by taking a detailed history, performing a physical examination, and obtaining the appropriate workup.

The expectation is understanding that not all patients have a "chronic pain syndrome," and some present with pure psychological pathology. Rather, in most cases, specific biologic correlates or underpinnings can be identified that may explain a patient's pain. While most patients do have some component of emotional overlay, psychological morbidity is rarely the primary pathology. Once a diagnosis has been established, a care plan can be formulated. Whenever possible, the source of the pain should be identified, and the clinician-patient team should predetermine a treatment goal. Only with this framework can we expect to come up with an appropriate therapeutic plan.

The complete history and physical examination for all painful disorders is beyond the scope of this chapter. However, the concept of establishing a presumptive diagnosis before embarking on the therapy cannot be overstated. The visit begins with a comprehensive history and physical examination. Prior to considering implementation of a long-term strategy for chronic intractable pain, the physician should establish a diagnosis or at least a presumptive diagnosis. With a diagnosis in hand, one can come up with the most appropriate therapeutic plan [8].

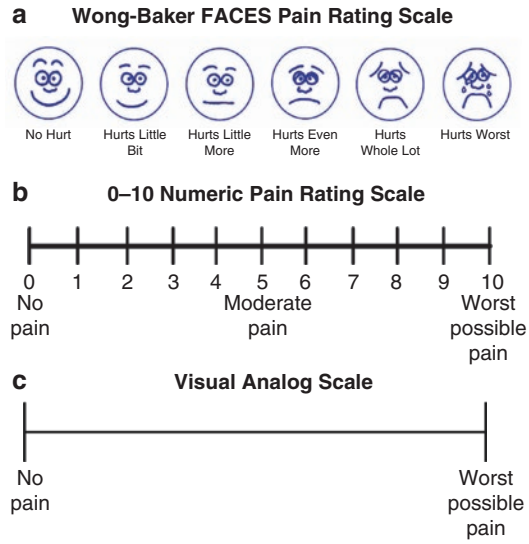

Fig. 5.1 Pain severity scales. Various tools have been developed to help patients and clinicians quantify the severity of pain. The following are examples of common pain scales: (**a**) Wong-Baker FACES Foundation (2015). Wong-Baker FACES® Pain Rating Scale. Retrieved [Date] with permission from http://www.WongBakerFACES.org. (**b**) numerical pain rating scale, and (**c**) visual analog scale (Note: for permission please see Wong-Baker FACES pain rating scale: From Wong et al. [9]. Copyrighted by Mosby, Inc. Reprinted with permission, 0–10 numerical pain rating scale: From McCaffery and Pasero [10]. Copyrighted by Mosby, Inc. Reprinted by permission, Visual analog scale and verbal pain intensity scale: From *Pain Management: Theory and Practice*, edited by RK Portenoy & RM Tanner, copyright 1996 by Oxford University Press, Inc. Used by permission of Oxford University Press)

Begin with a chief complaint. Why is the patient here to see you? What is the primary pain problem? The secret to taking a good history is being a good listener. Figure 5.1 illustrates several common pain severity scales utilized to assess pain. During an initial intake, one needs to take a history and understand the inciting events, the time course and character, and the severity of the pain. What makes the pain better or worse? Verbal descriptors of pain, e.g., "burning sensation," can help determine if the pain is neuropathic or not. Confounding variables, such as work history and satisfaction with the job, will be important as well, and the end result should be a medical documentary of the patient's pain history. The pain history should include:

1. Anatomic location (body part)
2. Severity (0–10 scale; faces; mild, moderate, severe)
3. Verbal descriptors (shooting or burning, dull or achy)
4. Time course (When is it bad? Does it wax and wane throughout the day, week, or month?)
5. Alleviating factors (What makes it better?)
6. Aggravating factors (What makes it worse?)
7. Changes in functional status caused by pain
8. Review of diagnostic workup (previous EMG, MRI, laboratory tests)
9. Review of the previous treatment (previous surgery, medication, and rehabilitation strategies)

Obtaining a past medical history is part of the comprehensive evaluation for pain. Comorbid diseases can be central in defining a differential diagnosis. Patients with a history of many disorders, including diseases such as cancer or diabetes, can develop painful conditions as a result of the disease or its treatment. A complete understanding of the patient's history thus can be helpful when trying to establish a diagnosis. For example, patients with uncontrolled diabetes may develop peripheral neuropathies that can be quite painful. The practitioner should understand that part of the treatment of the pain is to work with the primary care physician/endocrinologist to get diabetes under control. As part of the comprehensive evaluation, one should understand what treatments have been tried to date and what the outcome has been of previous treatments. Has a patient previously tried medications, injections, physical medicine modalities, or surgical interventions?

The pain practitioner typically takes a history and follows with a focused physical examination that is determined by the history. This helps the physician narrow the differential, or presumptive, diagnosis. This typically involves inspection, palpation, provocative maneuvers, and a neurologic examination. Laboratory workup can be used to help make a diagnosis or determine if it is safe to proceed with a planned course of therapy. In addition, with the use of some pharmacologic agents, specific laboratory testing may help

identify complications that can occur with treatment strategies. More commonly, laboratory workup may be used to determine if it is safe to proceed with interventional pain procedures.

The reason to obtain additional studies is to establish a diagnosis and to help guide the therapy. One should only perform the additional studies below as a guide to therapy. Plain X-rays use X-ray radiation to take a picture of the hard and soft tissue in the spine. These can be helpful in arthritic disorders and evaluating other connective tissues. Flexion-extension films of the spine are taken with patients in multiple positions to assess stability of the spine if a fracture (spondylosis) is suspected. This test also helps to determine spinal instability. In addition, by carefully orienting the patient in the correct plane, fractures and foraminal compromise can be identified and correlated with a patient's symptoms.

Computed tomography uses a series of X-ray-generated images formatted into two-dimensional and now three-dimensional images of both soft and hard tissues. Scans can help identify hard tissue abnormalities, cancer, and spinal pathology. Ultrasound images internal structures by measuring their capacity to transmit and reflect high-frequency sound waves, making them good for evaluating soft tissue abnormalities. Because of the refractive elements of bony structures, they cannot be used to visualize structures deep to the bony tissue. In the soft tissue, patterns of tears and can be seen in muscles, and abnormal activity can be seen in the soft tissue. This highly sensitivity modality is frequently used to evaluate muscle and ligamentous tears as well as soft tissue structures such as cysts.

Magnetic resonance imaging utilizes strong magnetic fields to assess soft tissues. The detailed images allow for detailed evaluation of the internal soft tissue, such as the nervous tissue or herniated disks in the spine. In the spine, there is clearer definition of the spinal cord, surrounding CSF, and extradural structures, such as disks. Moreover architecture of the disks and level of disk dehydration can be assessed by changes in signal intensity in the spine. MRI with and without contrast will help distinguish malignancy and inflammatory or scar tissues from a re-herniation.

EMG, or electromyography, measures electrical activity within muscles. Various patterns of altered activity can indicate both primary muscle pathology and denervation. Electromyography records voltage changes within a muscle by placing a needle into the muscle. Electrical activity is then recorded in the muscle and displayed on an oscilloscope. Various patterns correlate with diseases of the muscle and other pathologic processes. Nerve conduction velocity (NCV) tests help determine if there is damage along the path of specific nerves. Nerve conduction studies measure velocity and amplitude of electrical activity of the nervous tissue. Abnormalities in electrical activity and conduction can indicate pathology of the nervous tissue, and can be used to identify entrapment syndromes, lesions along the course of a nerve or intrinsic problems within a nerve. The pattern of abnormalities identified can help distinguish between radiculopathies, plexopathies, and primary nerve injuries. These patterns can be used to guide therapy.

Radionucleotide bone scanning is used to assess tissue that has high bone turnover, as seen in fractures, metastatic tumor, and infection. Because this technique is relatively sensitive, it can be used to identify subtle lesions that are missed with other techniques. Biopsy to obtain a tissue diagnosis can be helpful with some neurologic and rheumatologic pain states, visceral pain syndromes, as well as with cancer diagnosis.

In an interventional pain, physicians will also perform diagnostic blocks in order to determine if a structure is involved in pain. This involves placing low volumes of local anesthetic around a peripheral nerve. If pain relief follows a local anesthetic block, an ablative procedure is entertained [11]. For example, diagnostic blocks are frequently performed in the spine (medial branch blocks), viscera (celiac plexus block), or peripheral (specific neural structures, i.e., radial nerve) to determine if the structure innervated by that nerve or plexus is the source of the problem [12]. Table 5.1 illustrates the various types of pain and the associated characteristics. If the practitioner is not clear on the diagnosis, it is appropriate to obtain consultation with pain physicians or members of other specialties.

Treatment Strategies

All too often practitioners may have not established a diagnosis or have an inaccurate diagnosis before beginning treatment. The treatment strategy chosen should be determined after one has established a presumptive diagnosis and a treatment goal. Broadly speaking, there are several general approaches to treating patients with chronic pain. These include medical approaches, anatomic or surgical approaches, neuromodulatory approaches, psychological approaches, alternative approaches, and interventional approaches. Figure 5.2 illustrates a pain treatment ladder that was adapted from the World Health Organization's pain treatment.

Generally, the practitioner should consider conservative modalities prior to the more invasive options. One should generally have a clinical matrix in place, understanding the risks of the therapies being recommended, the likelihood of curing or managing the problem, the risks of the proposed therapy for any given patient, and the costs of the therapies over both the short and long term. If a patient presents with back pain, it is crucial to understand the pathology, as well as the patient's comorbid medical disorders, prior to making decisions on the appropriate treatment strategy. A young patient with new onset neurologic deficit, herniated disk, and classic radicular findings may benefit from a micro-diskectomy early in the treatment algorithm. Alternatively an elderly patient with comorbid medical disorders and back pain may benefit from early treatment with physical therapy, chiropractic care, or medication management. Each treatment strategy is based on the judgment of the practitioner and an understanding of the entire clinical picture for an individual patient.

Table 5.1 Types of pain

Types of pain	Characteristics
Nociceptive pain	Transient, response to noxious stimuli
Neuropathic pain	Damage or dysfunction of the nervous system
Inflammatory pain	Response to tissue damage and inflammation
Postsurgical pain	Transient pain, nociceptive, and inflammatory
Cancer pain	Associated with malignancy

Benzon et al. [13]

Medication Management

There are several classes of medications frequently used in the treatment of pain. They can be used for a variety of indications (see Table 5.2). Within each class of medication, there are multiple medications that are commonly used as well as numerous side effects and risks that define the category. The class of medication chosen is determined by the patient's disorder and side effect profile of the agent(s) chosen. For example, neuropathic pain can be most effectively treated with

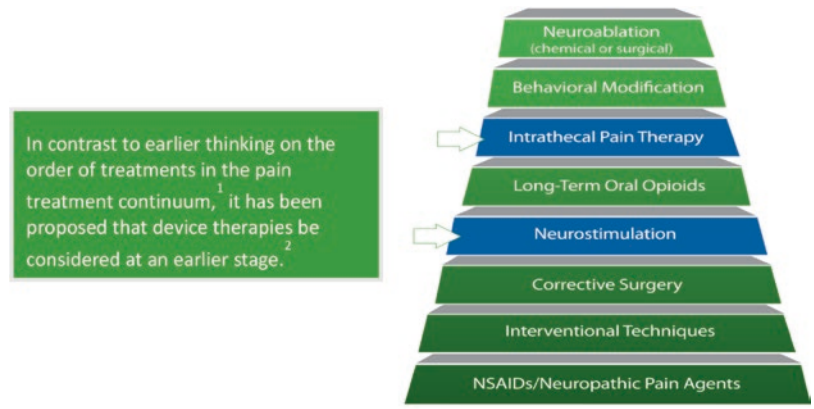

Fig. 5.2 World Health Organization pain treatment ladder. The WHO pain treatment ladder was originally devised to treat cancer pain (This is an adapted version for treating chronic nonmalignant pain (http://www.who.int/cancer/palliative/painladder/en/#, Krames [14], Stamatos et al. [15])

Table 5.2 Common pain medications and their routes of administration

Class of medication	Mechanism of action	Route	Concerns	Notes
Nonsteroidal anti-inflammatory	Inhibits prostaglandin synthesis	Oral and IV	GI Bleeding/platelet dysfunction Renal dysfunction Cardiovascular risk	Acute chronic and cancer
Acetaminophen	Central	Oral and IV	Hepatotoxicity in higher doses or chronic use	Hidden in many other combo medications and OTC formulations
Steroids	Potent anti-inflammatory	Oral IV topical	Bone Immune depression Hyperglycemia associated with GI bleeding Autologous steroid depression	Not a long-term option
Antiseizure medications	Multiple mechanisms	Oral	Gingivitis, aplastic anemia Drug-drug interactions	Neuropathic pain
Antidepressant medications	Can alter reuptake of serotonin and norepinephrine	Oral	Serotonin syndrome a rare side effect Anticholinergic effects	Neuropathic pain
Opiates	Bind opiate receptor	Oral IV, IM, intrathecal	Respiratory depression Endocrine Addiction Constipation Death	Neuropathic Nociceptive pain (Limited)
Cytokine modulators	Affects TNF-alpha	Oral intravenous	Immune suppression	Rheumatoid arthritis
Local anesthetics	Blocks Na channels	Topical Epidural and intrathecal	Seizures Tachyphylaxis	Less common oral or IV
NMDA receptor antagonists	Blocks N-methyl-D-aspartate receptor	Topical Intravenous	Hallucination Sialorrhea	May affect tolerance and
Alpha-2 agonists	Binds the alpha-2 receptor centrally and peripherally	Topical/intrathecal	Hypotension	Sympathetically maintained pain
Bisphosphonates	Inhibit pyrophosphate metabolism	Oral Intravenous	Jaw disease	Used in clinical trial for CRPS type 1 osteoporosis

Table 5.3 Antiseizure medications

Drug	Mechanism of action	Starting dose	Typical daily dose	Primary clinical use	Special considerations
Gabapentin	Binds to voltage-gated calcium channels	300 mg	1800–3600 mg	Postherpetic neuralgia (general neuropathic pain)	Start at low dose and slow titration upward
Pregabalin	Binds to voltage-gated calcium channels	50 mg	150–300 mg	Diabetic peripheral neuropathy, fibromyalgia, spinal cord injury	Start at low dose and slow titration upward
Topiramate	1. Blocks voltage-gated Na channels 2. Augments GABAA receptors 3. Antagonizes AMPA/kainate receptors 4. Inhibits carbonic anhydrase (isozyme II and IV)	50 mg per day	100–200 mg	Primary indication seizure disorder Effective in migraine prophylaxis	1. Side effect is weight loss 2. Used in bipolar disorder 3. Effective with headaches
Gabapentin enacarbil (Horizant)	Extended release gabapentin	600 mg	1200 mg	Restless leg syndrome and neuropathic pain	Different pharmacokinetic profile than gabapentin
Gabapentin (Gralise)	Extended release gabapentin	300 mg	1800 g once daily in the evening	Postherpetic peripheral neuropathy and neuropathic pain	Different pharmacokinetic profile than gabapentin
Phenytoin	Voltage-dependent block of voltage-gated sodium channels Class 1b antiarrhythmic	100 mg tid	200 mg tid	Treatment of trigeminal neuralgia (second choice to carbamazepine)	Narrow therapeutic index

antiepileptic medications and antidepressant medications. If a patient were to present with chronic burning pain and a comorbid depression, the physician may choose an antidepressant class of medication. Severe lancinating pain is more commonly treated with antiseizure medications (see Table 5.3).

Opiates require a specific discussion. Opiates can be used in chronic pain, but there is a paucity of data supporting their use in long-term administration. Lower doses should be considered at early phases as part of a rehabilitative strategy. However, not all patients with chronic pain should be placed on opiates. There are significant risks of systemic opiates that include death. Clinical guidelines support the use of opiates in certain clinical settings [16].

Opioid therapy should be reserved for patients with moderate to severe persistent chronic pain refractory to non-opioid and intervention pain management modalities to improve functioning and quality of life. This should be only started after careful assessment of the risks and benefits of opioid therapy for the individual patient. The initiation, titration, monitoring, and maintenance of opioid medications should only be carried out under the care of an adequately trained pain management specialist and mental health or addiction specialist [17]. Much of what is practiced in the prescribing of opioids for chronic pain has been adapted from experiences with treating cancer pain. The "analgesic ladder" (ref. to fig. or to other chapters) was first introduced by the World Health Organization (WHO) in the 1980s [18]. The short-term (less than 6 months) use of opioids for the treatment of non-cancer chronic pain has been shown to be effective in several systematic reviews. Furlan et al. reviewed 41 randomized trials in 6019 patients suffering from nociceptive, neuropathic, mixed, and fibromyalgia pain and concluded that opioid use over 5–16 weeks was more effective than placebo despite a 33 % dropout rate [19]. Chou and Huffman found opioids to be moderately effective in the treatment of chronic non-cancer pain compared to placebo based on study periods less than 12

weeks [20]. Interestingly, tramadol was the only pain medication to show fair evidence in the treatment of chronic osteoarthritis pain in the systematic review by Manchikanti et al. [21]. In this comprehensive systematic review of 111 trials, only four studies evaluated the effectiveness of opioid use beyond 6 months. Furthermore, Trescot et al. reviewed the efficacy of chronic opioid therapy in terms of functional improvement among chronic pain patients in addition to their pain relief. For treatment of chronic noncancer pain beyond 6 months, there is a weak evidence supporting morphine and transdermal fentanyl; there is limited evidence for other more commonly used opioids including hydrocodone and oxycodone [22].

Physical Medicine Modalities

Physical modalities include all modalities designed to modify the muscular or painful tendinous insertions. The key pillars in this treatment modality include identifying altered mechanics, promoting healing, and restoring proper mechanics and function. Complimentary treatments such as chiropractic care and acupuncture should be considered along with conventional therapies such as manipulation, physical therapy of the deep tissue including massage, exercise, heat, and cooling, and transcutaneous electric nerve stimulation (TENS) therapy. All of these approaches can be effective for various types of pain.

Psychological Approaches

Many patients with chronic pain can benefit from a comprehensive psychological evaluation. The degree of suffering and comorbid psychologic disorders can be reduced. Biofeedback can decrease arousal of pain and provide additional pain relief. Relaxation techniques such as biofeedback, guided visual imagery, and hypnosis are few of the coping mechanisms that contribute to the multimodal pain treatment strategy. The restoration of sleep in the activity-rest cycle is a key element in the psychosocial component of chronic pain. Treatment is often maintained through self-management interventions that may comprise of scheduled group sessions utilizing the social support and peer interactions.

Cognitive and Behavioral Approaches

An important aspect of treating chronic pain is bridging the gap between patient's expectations of the treatment plan and the reality of what is actually achieved. Utilizing cognitive behavioral therapy, the focus of pain relief is redirected from "the pain" itself to goal-oriented improvement of function. Negative mechanisms such as catastrophizing are replaced with adaptive and more constructive mechanisms such as self-reassurance. This cognitive restructuring focuses on the value of attitudes, beliefs, and emotional responses to pain and allows the sufferer to resume pleasurable activities and activities of daily living.

Interventional Pain Management

Interventional pain management is the discipline of medicine devoted to the diagnosis and treatment of pain-related disorders, principally with the application of interventional techniques in managing subacute, chronic, persistent, and intractable pain, independently or in conjunction with other modalities of treatment. Interventional pain management techniques are minimally invasive procedures, including percutaneous precision needle placement, with placement of drugs in targeted areas or ablation of targeted nerves, and some surgical techniques, such as laser or endoscopic diskectomy, intrathecal infusion pumps, and spinal cord stimulators, for the diagnosis and management of chronic, persistent, or intractable pain [23]. The lack of knowledge or fear of the risks of some of these techniques leads to over-prescribing of opiate analgesics. Some primary care physicians hesitate to refer out for these procedures, considering them risky or may not know of their efficacy. However, when used judiciously and in appropriate patients, it is possible to decrease the amount of opiates and the complications related

to opiates, improve the quality of life, and in some instances improve life expectancy [24, 25].

Epidural Steroid Injections

One of the classic interventional or minimally invasive approaches is epidural steroids, application of small amounts of steroids to specific sites within the epidural space [26]. Usually performed with the aid of fluoroscopic guidance, this technique involves placing a needle into the epidural space. The needle may be placed translaminarly, through the caudal canal, or transforaminally. Each technique can be performed with and without a catheter. Multiple types of steroids, local anesthetics, and contrast are used in the performance of the procedure. It is thought to decrease inflammation, improve pain scores, and function and decrease opiate consumption in patients with acute radiculopathies secondary to disk herniations. They are also infrequently performed in patients with cancer, PHN, and vascular insufficiency pain.

Epidural Infusions of Local Anesthetics

Less frequently, epidural catheters are placed to run an infusion of local anesthetics. The local anesthetic quality can be used to decrease pain and improve function in patients undergoing rehabilitation or in the immediate perioperative period following extremity, abdominal or thoracic surgery, or trauma. This technique has superior pain control over systemic opiates alone. Risks of this technique include epidural bleeding or trauma and should be considered carefully in patients who require anticoagulation.

Sympathetic Ganglion Blocks

Sympathetic blocks are used most frequently in the diagnosis and management of complex regional pain syndrome (formerly known as reflex sympathetic dystrophy or RSD), first reported by Weir Mitchell during the civil war in soldiers who suffered limb injuries. This was later named Sudeck's dystrophy with observed muscle atrophy and bone demineralization. In 1947, Evans refined the diagnosis with the term reflex sympathetic dystrophy (RSD) with assumed involvement of the sympathetic nervous system with observed abnormal activity in the periphery. It was recently in 2003, the International Association for the Study of Pain (IASP) formed a consensus group in Budapest who outlined the diagnosis criteria for complex regional pain syndrome or CRPS (see Fig. 5.3) [27]. Type I and II differ by the presence (type II) or absence (type I) of named nerve injury. Disproportionate pain is the hallmark of this syndrome that leads to peripheral sensitization and associated with sensory (allodynia), vasomotor (temperature asymmetry), sudomotor (abnormal sweating), motor (atrophy), and trophic (hair and nail growth abnormalities) changes. Variants of complex regional pain syndrome have been described to include sympathetically maintained pain and sympathetically independent pain. Sympathetic blocks are used to distinguish between the two types of the disorder. Table 5.4 describes various treatment options for CRPS including sympathetic nerve block.

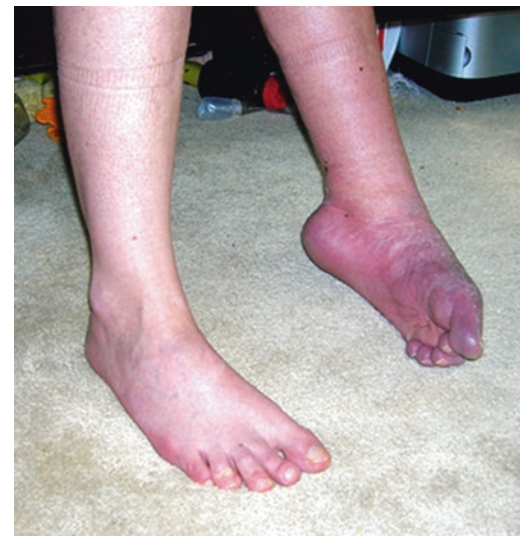

Fig. 5.3 Complex regional pain syndrome. This photo illustrates the typical syndrome of persistent disproportionate pain in the setting of sensory, vasomotor, sudomotor, motor, and trophic changes

Table 5.4 Complex regional pain syndrome (CRPS): treatment options

Psychological	Pharmacological	Physiological	Interventional
Cognitive behavioral therapy	Corticosteroids	Occupational	Sympathetic nerve block
Biofeedback	NSAIDs	Physical	Intravenous
Relaxation training	Anticonvulsants	Desensitization	Neuromodulation
Coping skills	Antidepressants		Intrathecal
	Opioids		

The use of multidisciplinary approach including diagnostic/therapeutic sympathetic nerve block strives to achieve overall goal of functional restoration in the treatment of CRPS

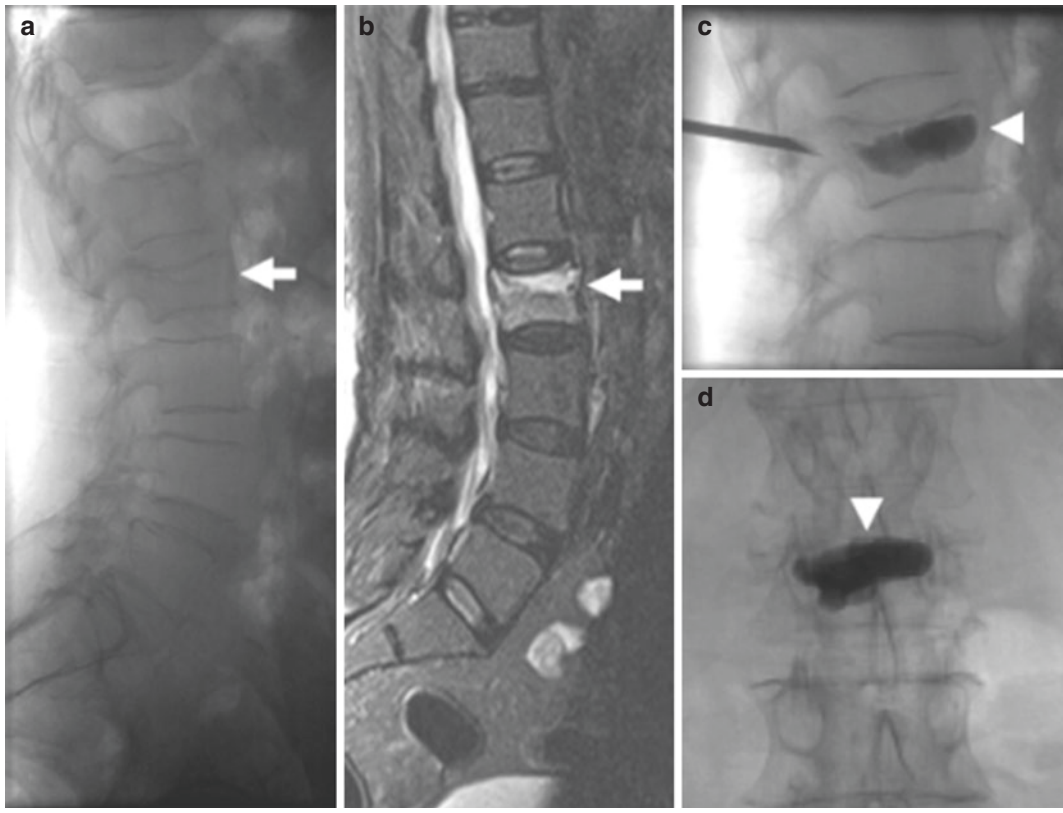

Fig. 5.4 Vertebral augmentation. Acute vertebral compression fractures can be stabilized with percutaneous vertebroplasty. The following is an example of an L2 vertebral compression fracture shown on X-ray (**a**), and MRI (**b**). There is evidence of bone marrow edema on the MRI suggesting acute inflammation. Panel (**c**) (lateral view) and (**d**) (AP view) illustrates the vertebral body after injection of bone cement via vertebroplasty. Kyphoplasty is a similar procedure that utilizes the addition of a pneumatic balloon (not shown) to create a cavity in the vertebral marrow prior to injection of bone cement

Vertebroplasty and Kyphoplasty

This therapy is indicated for patients with focal pain due to a spinal compression fracture. These are minimally invasive, fluoroscopically guided techniques to restore the structural instability of a fractured vertebral body by placing a small amount of bone cement either directly through a cannula. The compressed vertebral body height may be restored during a kyphoplasty by first placing a pneumatic balloon into the crushed vertebrae. This newly created cavity is then filled with bone cement to stabilize the augmented vertebral body. Both of these procedures have

been demonstrated to improve pain and decrease opiate consumption in patients with semi-acute and acute vertebral compression fractures (Fig. 5.4) [28].

Minimally Invasive Lumbar Decompression

Minimally invasive lumbar decompression has been recently developed to treat lumbar spinal stenosis as a result of ligamentum flavum hypertrophy. Patients with spinal stenosis present with progressive neurogenic claudication where low back and/or lower extremity pain is exacerbated with standing or walking. This is a minimally invasive, fluoroscopically guided technique for decompressing the narrowed spinal canal by removing portions of the ligamentum flavum through 5 mm trocar sites. This procedure may help chronic pain patients obtain pain relief with less risk than open spinal surgery. Numerous well-controlled trials have been performed with the level one evidence pending [29].

Neuromodulation

Neuromodulation is the field of medicine where electrical energy or medications are targeted to the nervous system through which the conduction of pain signals is modulated and reduced. The use of electricity in the treatment of pain dates back to 46 A.D. where torpedo fish were used by Scribonius Largus to treat headaches. In 1967, Dr. Norman Sheely pioneered the use of electrical leads in the dorsal epidural space to treat intractable cancer pain. This concept has evolved into sophisticated electronic devices that can help patients manage chronic pain. Targeted drug delivery to the intrathecal space was first described by Dr. August Bier in 1898 when he described the first spinal anesthetic [30]. Similarly, the delivery of specific medications has also evolved into the application of implanted computer-controlled pumps capable of delivering precise amounts of analgesic medication(s) to the intrathecal space.

Spinal Cord Stimulation

Spinal cord stimulation involves implanting electrodes into the epidural space to modify pain or disease. The therapy has been demonstrated to be more effective than repeat back surgery and then medication management in the control of pain [31, 32]. Traditional, or tonic stimulation, has been used since the 1960s and is a widely accepted approach to managing neuropathic pain. Traditional stimulation would layer a sensation of "buzzing" over an area of pain, effectively masking the painful sensation with a gentle buzzing sensation. In order to experience pain relief with traditional stimulation parameters, there was a requirement of stimulating the area of pain. Both rechargeable and non-rechargeable power sources have been used to control pain. Figure 5.5 illustrates a typical implanted spinal cord stimulator system. These therapies have been traditionally most effective for neuropathic pain of the trunk and limbs.

New frequencies are also improving the efficacy of spinal cord stimulation. High-frequency spinal cord stimulation involves utilization of frequencies in the 10,000 Hz range and requires a larger energy requirement. It is typically set subthreshold, so the patient feels no paresthesia as they typically do with traditional or tonic stimulation. High-frequency spinal cord stimulation was recently compared to traditional or tonic stimulation in a FDA clinical trial. In a non-inferiority study design, high-frequency stimulation demonstrated superior pain control for both the back and leg over traditional or tonic stimulation [33]. Burst stimulation involves utilizing novel frequencies that have bursts of electrical activity followed by a quiescent period. It is also widely used in Europe and Australia and is the subject of FDA-approved clinical trials in the United States [34].

Novel Targets and Frequencies

Newer stimulation targets or approaches may even improve on the success of traditional spinal cord stimulation. For example, DRG stimulation

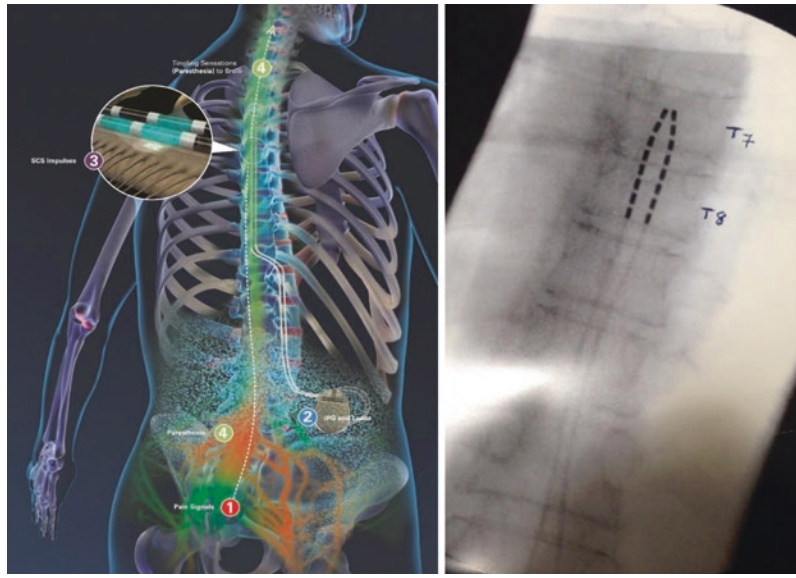

Fig. 5.5 Spinal Cord Stimulation. Chronic refractory neuropathic pain of the trunk and limb can be treated with electrical stimulation of the pain fibers within the dorsal horn of the spinal cord. Placement of electronic leads within the epidural space creates paresthesia based stimulation to the painful areas. Left panel illustrates the placement of spinal cord stimulator leads within the epidural space to modulate ascending pain signals (Image courtesy of Boston Scientific). The right panel is an example of multi-contact leads placed in the thoracic epidural space

involves placing the electrodes directly on the dorsal root ganglion (DRG) and stimulating the DRG that is presumed to be involved in the processing of painful stimuli. It appears to be superior to traditional spinal cord stimulation in certain settings [35]. Electrodes are also placed on peripheral nerves in the head and neck to modulate headaches. A novel approach approved in Europe and Australia stimulates the vagus nerve noninvasively as a prophylaxis and treatment for cluster headaches and migraines and has been approved in Europe for GI disorders, asthma anxiety, and depression [36].

Intrathecal Drug Therapy

Intrathecal therapy has been relegated to a salvage approach for most patients with severe cancer and non-cancer-related pain [37]. Intrathecal therapy involves placing a catheter into the intrathecal space and connecting it to an implantable pump to deliver analgesics including opioids. It has been demonstrated to be effective in both cancer and non-cancer populations. In the cancer population, intrathecal opiates have been shown to improve pain with less side effects and possibly improve life expectancy when compared to medical management alone [38]. In addition, when compared to the costs of systemic opiates, intrathecal therapy becomes cost-effective after 28 months. The high upfront costs of the device are offset by the lower costs of maintenance of intrathecal opiates. Furthermore, with close to 16,000 deaths attributed each year to systemic opiates, the overall higher safety profile of controlled delivery is favorable on multiple fronts [39].

In addition, the use of non-narcotics in the intrathecal space to manage severe pain is quite common. Novel agents, including intrathecal ziconotide, have been demonstrated to be effective in patients with severe pain related to cancer and AIDS and in non-cancer-related pain [40, 41]. Algorithms have been developed that guide physicians through various medications [42, 43]. The therapy is widely considered a safe therapy and is used for patients with chronic

severe pain who have failed an adequate response to other conservative therapies including low-dose opiate therapy.

Summary

There are multiple treatment strategies that are effective in the management of cancer and non-cancer-related pain. While opiates remain an important tool for physicians, it should not be considered the only tool that physicians have in managing pain. In the treatment of chronic pain, pain should be regarded as the disease state rather than a symptom. Whichever treatment strategy the physician chooses, he/she should begin with a thorough history and physical examination. Based on this, a presumptive diagnosis should be established. This diagnosis thus should lead the physician down an individualized treatment algorithm. The risks of all therapies should be evaluated when developing the appropriate therapeutic plan. All strategies, from simply ignoring the pain to complex surgical procedures, involve some risk. Understanding the treatment options should facilitate treatment with safest and most conservative option, working up in a hierarchical fashion.

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