Evaluation and Management of Chronic Pain for Primary Care

A Pocket Guide for the Primary Care Provider

Bonnie Huang Hall
Editor

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This book is dedicated to my spouse (CGH) and extended family whose love, patience, and support during the difficult time of writing has been without limits. Special thanks to S.C. who persuaded me to submit a book proposal. The result has been providential.

And to those who ask, "What if I fail?"

A good friend will answer, "What if you succeed?"

Preface

This book is written by a primary care provider for primary care providers. Its chief focus is on a systematic evaluation and management of chronic noncancer pain. It is meant to be a practical guide for providers, residents, and students.

The principles emphasized in this book were derived from various sources. Besides evidence based medicine, many of the tenants espoused in this book are rooted in my own clinical experience. For example, when I joined an already established healthcare institution, I inherited a variety of chronic pain patients from previous providers. I had to quickly find information (in an often unwieldy electronic medical record system) and go through a mental checklist of what has been done and what hasn't been done for the patient. I had to evaluate for myself the previously established diagnosis causing the chronic pain, if it was even mentioned at all. I also had to battle with deciphering between those who had exhausted the medical system and treatment options and were justifiably on opioids, to those who were unfortunately opioid dependent or seeking the opioid prescription for possible financial gain. In addition, the institutions I worked at fortunately had systems in place to help the primary care provider. I was fortunate enough to serve as a chronic pain adviser, which was an invaluable learning experience. One advantage of having a systems based approach in place for chronic pain management was that the primary care provider was empowered with not only knowledge to make hard decisions about chronic pain management, but had a safe and non-threatening environment in which to seek guidance and help on these complex cases. Lastly, as a volunteer assistant clinical professor

at a family medicine residency program, I was fortunate enough to find young trainees who wanted to get a better grip on how to evaluate and manage noncancer chronic pain. Through this teaching experience, I was able to hone my skills and solidify my mental framework of chronic pain evaluation and management.

Lastly, I would like to share my personal journey into taking care of chronic musculoskeletal pain. One of my close relatives struggled for years with chronic pain. Besides pain, she was emotionally hurt by healthcare system for not only causing some of her pain, but for not relieving her pain. She started missing family outings that she traditionally attended. Pain was separating her from our lives, and it struck me, that although I prefer to avoid treating my relations and close friends, I needed to get involved. I began to listen, evaluate, and treat her chronic pain the way she wanted to be treated. She introduced me to the concept of myofascial trigger points through a book she had, but did not understand. I did not believe trigger points could cause her chronic pain, but she had already exhausted the medical system. There was nothing else she could try besides surgery and interventional procedures. Consequently, after considering the possibility of trigger points in her muscles and attempting to relieve her trigger points, she began to slowly conquer her chronic pains. I soon began to advise these non-invasive treatments to my patients. After watching them overcome their chronic musculoskeletal pains, I became inspired to write this book so that others can consider carefully the root causes of chronic noncancer pain and truly help their patients.

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Abbreviations

ACOG	American College of Obstetricians and Gynecologists
ACP	American College of Physicians
C	Centesimal dilution. At each stage of dilution, the substance is diluted by a factor of 100 CBD cannabidiolcannabidiol
CBT	cognitive behavioral therapy
CDC	United States Centers of Disease Control
CME	continuing medical education
CMS	Centers for Medicare and Medicaid Services
CN	cranial nerve
CNCP	chronic noncancer pain
COT	chronic opioid therapy
COX 2	cyclooxygenase-2
CV	cardiovascular
CT	computed tomography
DM	diabetes
GI	gastrointestinal
GYN	gynecology
EGD	esophagogastroduodenoscopy
EMR	electronic medical record
EKG	electrocardiogram
F	female
FDA	US Food and Drug Administration
HTN	hypertension
HLD	hyperlipidemia
JAMA	Journal of the American Medical Association
L	left
M	male

MRI	magnetic resonance imaging
MSK	musculoskeletal
NIH	National Institute of Health
NMDA	N-methyl-D-aspartate
NNTB	number needed to treat for an additional beneficial outcome
NNTH	number needed to treat for an additional harmful outcome
NEURO	neurological
nm	nanometer
NSAIDS	nonsteroid anti-inflammatory drugs
PCP	primary care provider
s	seconds
PDMP	prescription drug monitoring program
PPI	proton pump inhibitor
PQRST	Mnemonic used to recall descriptors of pain: Provoking factors, Quality, Radiation, Severity, Timing
PT	physical therapy
QD	daily dosing
QI	quality improvement
QT	QT interval on an electrocardiogram
QTc	corrected QT interval on an electrocardiogram
R	right
ROM	range of motion
SLR	straight leg raise
SNRI(s)	serotonin norepinephrine reuptake inhibitor(s)
SSRI(s)	selective serotonin reuptake inhibitor (s)
TCA(s)	tricyclic antidepressant(s)
THC	delta-9 -tetrahydrocannabinol
TID	three times a day dosing
TSH	thyroid stimulating hormone
UK	United Kingdom
US	United States
yo	year old
X	Decimal scale dilution. At each stage of dilution, a substance is diluted by a factor of 10.

Check List

Evaluation Check List

[ ] *Thorough History*: Thorough description of pain (OPQRST). Review past medical history, surgeries, medications past and present, and psychiatric comorbidities. History of drug use, alcohol, and abuse. Get records if needed.

[ ] *Physical Exam*: Focus especially on area of pain. Carnett test for abdominal pain. Muskulosketal and Neurological exam.

[ ] *Diagnostics*:

    Laboratories: Neuropathy evaluation, thyroid, diabetes, rheumatological

    Imaging: U/S, CT scans or MRI's

[ ] *Specialist evaluations*: Endoscopies for GI/ENT related pain, rheumatology, orthopaedics, OBGYN for pelvic pain, neurology for neuropathic pain

[ ] *Diagnosis*: What is causing chronic pain syndrome. Be specific. (Example, osteoarthritis, degenerative disc disease, diabetic neuropathy)

Management Check List

Medication:
[ ]   On appropriate medications for specific diagnosis?
[ ]   Step wise escalation: adding pain medication depending on neuropathic pain or nociceptive. Consideration of opioids if benefits outweigh risks, and continuation dependent on benefit. Consider opioid reversal agent.
[ ]   Pain Agreement: if on chronic opioid therapy. Make sure updated regularly.
High risk behavior:
[ ]   Check controlled substance database
[ ]   Urine Toxicology at regular intervals, alcohol
[ ]   Depression /suicide screen
Multimodal therapy:
[ ]   Physical Therapy
[ ]   Pain Management Procedures
[ ]   Surgery if recommended
[ ]   Specialist treatments
[ ]   Consider CAM
Patient Goals:
[ ]   consider patient goals for treatment

Introduction

Chronic pain in this work refers to chronic noncancer pain, usually of at least 12 weeks duration. Many have defined it as pain that persists beyond reasonable tissue healing time. In our society, chronic pain is widespread. In 2016, the United States Centers of Disease Control (CDC) found that 20.4% of Americans have chronic pain [1]. This figure does not include important sub-populations such as children and adolescents, active duty service members, prisoners, nor residents of long-term care facilities. The majority of chronic pain in the USA is treated by primary care physicians [2].

Chronic pain is costly. In recent years, the price of this epidemic is staggering. Medical costs, disability programs, and lost productivity attributed to chronic pain cost the US economy approximately 560 billion dollars. These direct and indirect costs due to chronic pain exceeded that of heart disease, diabetes, and cancer combined [3].

Chronic pain is challenging. Many primary care physicians voice frustration over the care of these complex patients. Primary care physicians encounter few hard and fast rules in chronic pain management to make clinical decisions easy. They also have varied clinical training, knowledge, and institutional or systems-based support concerning chronic pain [4]. In addition, they face the all too common challenge that arises from seeing approximately 50% of all physician visits in the USA [5], namely time. Not to mention, the prevalence of chronic pain is higher in the elderly, unemployed, poverty stricken, rural, and publicly insured populations [1].

Furthermore, as physicians and primary care providers we are often trying to differentiate those with true chronic pain, opioid use disorder, or psychiatric diagnoses [4]. And, to confuse the clinical picture even more, the patient may actually have all of the above. All these trying social economic health factors add another layer of complexity to the already mentioned difficulties associated with management of these patients.

Consequently, the aim of this book is to provide a framework to evaluate and treat chronic noncancer pain in the primary care setting. It is a practical guide with checklists, online resources, and example cases. This book also features sections on Complementary and Alternative Medicine (CAM), since chronic pain is the most common reason why patients seek CAM [6]. In addition, it also includes a special section on chronic musculoskeletal pain, which has been identified by the CDC as a national public health concern [7]. This book is meant to empower the primary care physician by equipping them with tools and resources to tackle this often overwhelming health issue in an efficient manner.

How to Use This Book

When reading this book, it is often helpful to get an overview first. Look over the systematic checklists. For those who quickly want to get to the punch line, there are abstracts and helpful tips found in the beginning of the chapter. Chapters are organized by specific topics, and for deeper understanding of areas where the provider would like more knowledge, read these chapters first. Lastly, read the book in its entirety to get a bigger overview of chronic pain, from evaluation to management.

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Part I
General Evaluation
and Management
of Chronic Noncancer Pain

Chapter 1
History Taking for Chronic Pain

Bonnie Huang Hall

Helpful Tips

1. Obtain a detailed description of pain ("OPQRST") and document it
2. Form a differential diagnosis for the cause of the chronic pain in terms of large, systematic categories (Neoplastic, Autoimmune, Neuropathic, Endocrine, Musculoskeletal, etc.)
3. Ask about medications tried, side effects, psychiatric history, opioid risk factors when opioids are under consideration
4. Chronic pain patients requiring opioid medications require detailed documentation of benefits and side effects of their opioid dosages, whether there is the presence of a health jeopardizing psychiatric diagnosis or substance abuse, and whether there is diversion of opioid prescriptions. Taking this detailed history will provide justification for the current opioid treatment plan.

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Introduction

Chronic non-cancer pain has been widely defined as pain existing for more than 12 weeks, which is beyond normal tissue healing time. This, however, does not mean that this pain has no organic cause or that its etiology cannot be narrowed down. Consequently, taking a history of chronic non-cancer pain must be approached with the same scrutiny as with other serious conditions such as dyspnea on exertion or chest pain. It is not acceptable to solely write in the history of present illness, that the patient has chronic pain and desires refill of medications. Without taking a proper pain history, one opens the door for litigation as standard of care has not been followed. Multimillion dollar judgments against healthcare professionals and institutions have resulted from neglecting to obtain a satisfactory pain evaluation [1].

Most importantly, however, a thorough history will enable the clinician to obtain a reasonable diagnosis and thus a targeted, often more effective treatment plan. As an internal medicine intern, it was ingrained in me that 90% of the time, a correct diagnosis can be obtained from history alone. This rule may not be so widely successful in chronic pain patients, but the principles and thought processes can still apply. For example, a complete history can help elucidate a chief cause for the pain. It can provide clues to decide if the pain is primarily neuropathic in nature or nociceptive. In addition, one can also determine if the medications prescribed are indeed benefiting the patient or not. Furthermore, a thorough history can help risk stratify a patient if opioids are under consideration.

Thorough Description of Pain

To begin with, a thorough pain history includes a thorough description of the pain. Recall the mnemonic: "OPQRST"

• Onset
• Provocation and Palliation

- Quality
- Radiation and Region
- Timing

How did the pain start? Was there trauma, motor vehicle accident, or repetitive injury that preceded the pain? What makes it better or worse? Is it burning? Does it radiate? Are there associated symptoms such as fever, diarrhea, etc.? How long does it last, and when does it occur – with meals, with movement, with stress?

Formulating a Differential Diagnosis

In addition, the aim of history taking is to formulate a differential diagnosis, if not reach the actual diagnosis causing the pain. *Remember, pain comes from somewhere.* (Albeit, the pathophysiology of chronic non-cancer pain is complex and beyond the scope of this book. For detailed, but brief overview of the mechanisms of pain, refer to Abd-Elsayed 2019 [2].) A systematic organized method of obtaining a differential diagnoses relies on categorizing diagnoses from a systems, etiological point of view. The origin of pain, like other chief complaints, can be thought of in terms of large systems-based/etiological categories such as:

- Neurological
- Rheumatoid/autoimmune
- Infectious
- Traumatic
- Musculoskeletal
- Neoplastic
- Endocrine
- Internal organ derangement: Gastrointestinal, Gynecological, Renal, Pulmonary
- Vascular/Cardiac
- Psychiatric
- Toxins: drugs, alcohol, medication, poisons

The purpose of utilizing this process is so that one can consider a comprehensive differential diagnosis and have an organized method of accomplishing this [3]. But practically speaking, it is impossible to retain a complete list of differential diagnoses for every pain complaint encountered. For example, this is a list of differential diagnosis for anterior knee pain derived in part from a recently published, reputable, peer-reviewed journal [4]:

• Articular cartilage injury
• Bone Tumor
• Chondromalacia patellae
• Hoffa disease
• Iliotibial band syndrome
• Loose bodies
• Lateral patellar compression syndrome
• Osgood-Schlatter disease
• Osteochondritis dissecans
• Patellar instability/subluxation
• Patellar stress fracture
• Patellar tendinopathy
• Patellofemoral pain syndrome
• Pes Anserine bursitis
• Quadriceps tendinopathy
• Referred pain from lumbar spine or hip joint pathology
• Saphenous neuritis
• Sinding-Larsen-Johansson syndrome
• Symptomatic bipartite patellae

There are almost 20 different diagnoses listed, some of which are not as frequently encountered or used in primary care. Now, these same diagnoses are reorganized in broader etiological categories as seen in Table 1.1.

As evidenced by the table above, only a few etiological categories are needed to cover the almost 20 diagnoses. One may not remember all the diagnoses in the musculoskeletal and traumatic pain categories, but many of them can be summarized by broad terms such as "bursitis, tendinopathy, muscular issue, bone fracture and abnormalities." Once the

Table 1.1 Anterior knee pain etiologies arranged in systems based categories

Etiological category	Differential diagnosis
Neurological	Referred pain from lumbar spine, saphenous neuritis
Rheumatoid/ autoimmune	
Infectious	
Traumatic	Articular cartilage injury, prepatellar bursitis, pes anserine bursitis, chondramalacia patellae
Musculoskeletal	Patellar tendinopathy, Osgood-Schlatter disease, iliotibial band syndrome, loose bodies, patellar stress fracture, patellofemoral osteoarthritis, lateral patellar compression syndrome, patellar instability/subluxation, quadriceps tendinopathy, bipartite patella, Sinding-Larsen-Johansson syndrome, patellofemoral pain syndrome, plica syndrome
Internal organ derangement	
Neoplastic	Bone tumors
Endocrine/ metabolic	
Internal organ derangement	
Vascular	

etiology has been narrowed down, further history, physical exam, or investigations can narrow down the differential.

And as an added bonus, if the differential diagnosis is generated through larger etiological categories, other diagnoses can also be added that were previously missed (Table 1.2). Items in italics show differentials that were added *in addition*

Table 1.2 Differential diagnosis of anterior knee pain generated using larger etiological categories

Etiology	Differential diagnosis
Neurological	Referred pain from lumbar spine, saphenous neuritis
Rheumatoid/ autoimmune	*Rheumatoid arthritis, fibromyalgia*
Infectious	*Joint space infection, soft tissue infection*
Traumatic	Articular cartilage injury, prepatellar bursitis, pes anserine bursitis, chondramalacia patellae
Musculoskeletal	Patellar tendinopathy, Osgood-Schlatter disease, iliotibial band syndrome, loose bodies, patellar stress fracture, patellofemoral osteoarthritis, lateral patellar compression syndrome, patellar instability/ subluxation, quadriceps tendinopathy, bipartite patella, Sinding-Larsen-Johansson syndrome, patellofemoral pain syndrome, plica syndrome
Internal organ derangement	*Renal osteodystrophy/bone disease*
Neoplastic	Bone tumors, *muscle tumors*
Endocrine/ metabolic processes	*Thyroid abnormalities, gout*
Vascular	*Ischemia, peripheral artery disease*

to those listed above once larger etiological categories were used in generating a differential.

In order to facilitate the recall of the above categories (and others such as congenital or toxin), various mnemonics have been suggested [3]. Furthermore, it may be helpful to develop checklists to reduce diagnostic errors [5, 6].

Of course, making the right diagnosis is not solely reliant on history and physical exam alone: it often relies on a team

of healthcare providers and specialists, obtaining past records and tests, reducing barriers in effective communication, and improving health literacy [7].

In addition, a pain history will include medications or interventions that have helped in the past and any side effects the patient experienced. Furthermore, it is also important to obtain a psychiatric history including depression, suicidal ideation or attempts, and substance abuse. There are opioid risk stratification tools that may be helpful when contemplating whether a patient is an appropriate candidate for chronic opioid therapy.

Patients Managed with Opioid Medication

Prior to the Visit

If a chronic pain patient on opioid medication is new to your practice, it may be helpful to have the front office staff ask the patient to sign a release of records form, or bring all records in prior to the appointment if they are wishing to obtain an opioid prescription. Indeed, it may be helpful to require the presence of prior records as a standard office policy prior to even having an appointment. In addition, proper expectations for this initial consultation should be set. The appointment will be for initial pain evaluation and management, including the *consideration* of opioid medication refill. It may be prudent to inform the patient that the purpose of the visit is to evaluate the appropriateness of their current treatment regimen. The evaluation may or may not result in a refill of opioid medication, and if refilled, the dosage maybe adjusted. See Chap. 9, the opioid requiring patient: office level management for further details.

Initial Evaluation

The initial evaluation should include discussions concerning goals of treatment, referencing the controlled substance pre-

scription database, and discussions of risks and benefits of opioid use [8]. A signed "pain contract" or perhaps, less punitively, "Pain Treatment Agreement" between the provider (and his associates) and the patient can be used to document the discussion of the risks and benefits, purposes of opioid medication, expectations and goals of treatment, and terms for discontinuation of medication [9].

If a patient is already on opioid medication and has already had a thorough evaluation already, history taking can then focus on several factors that will enable you to determine if continuation or adjustment of opioid medication is necessary [8].

1. Level of pain prior to opioid dosage, description
2. Level of pain post opioid dosage
3. Activities of Daily Living (ADLs) increased or decreased with opioid medication
4. Side effects of opioids
5. Aberrant behavior
6. Depression

Quantification of Pain

It is important to document the efficacy of opioid medication given there is little evidence to support its use long-term in noncancer chronic pain. Consequently, quantifying the nature (burning, achy, duration, etc.) and level of the pain (e.g. scale 1–10) before and after opioid medication administration can help support your reasons for either continuing the opioid medication or adjusting its dosage. Discontinuation of opioid medication can be supported with a history of the opioid medication being not helpful in controlling pain (e.g. no change in pain scale, or nature/duration of pain). In addition, increasing opioid medication may be reasonable if despite maximum dosages of other classes of analgesics, pain is still not well controlled. Consequently, it is important to also document in the history whether the patient continued to take other pain medications and their effect as well.

ADL's and Side Effects

In addition the benefits and side effects of opioid medication usage should be documented to substantiate your clinical decision. Patients may have an increase in ADL's from taking opioid medication with little side effects. This may help to support the decision to continue opioids. On the other hand, if the patient is suffering from sedation and constipation while gaining little in function, it may be wise to reconsider the current opioid dosage.

Aberrant Behavior and Depression

Lastly, a complete history also requires evaluating for the presence or absence of behavior that would jeopardize the health of the patient. For example, diversion of opioid prescriptions (e.g. sharing or selling opioid prescriptions) is illegal. In addition, it is recommended that there be documentation of the absence of concurrent alcohol or other substance use. Marijuana is legal in some states, but is a schedule 1 drug under United States federal law. Consequently, it is up to individual healthcare systems to decide whether recreational marijuana is considered behavior that could lead to jeopardizing the patient's health while taking opioid medications. Please see chapter on "Marijuana" and chronic pain later in this book for further guidance. Finally, it is often prudent to document the presence or absence of depressive symptoms as opioid medication can be ingested in lethal quantities. For a more in depth discussion of managing the opioid requiring patient, see Chap. 8.

Helpful Links

- CDC opioid checklist. https://www.cdc.gov/drugoverdose/pdf/pdo_checklist-a.pdf
- CDC prescribing opioid guidelines summary. https://www.cdc.gov/drugoverdose/pdf/Guidelines_Factsheet-a.pdf

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Chapter 2
Physical Examination for Chronic Pain

Bonnie Huang Hall

Helpful Tips

1. Examine from a systems point of view in order to narrow down a wide range of diagnoses (infectious, inflammatory, autoimmune, musculoskeletal, neurological, metabolic, etc.).
2. When examining an orthopedic pain, always check joints above and below.
3. Bear in mind that both internal organ and muscle dysfunction can be the source of pain.
4. Impingement on nerves anywhere along their path from brain to spinal cord and down to target end organ can cause pain.
5. If there is limited ROM and pain, consider not only the nerves and muscles that perform the motion, but also that the etiology may also be a tight painful muscle that counters (and therefore limits) that motion.

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Introduction

The goal of history taking is to generate a list of differential diagnosis. The goal of the physical exam is to examine the patient in the light of this list and make conclusions as to what are the most likely causes of the patient's chronic pain. Consequently, the physical exam is often targeted to the systems of interest [1]. However, whether the systems in question are neurological, abdominal, musculoskeletal, rheumatic, or a combination – always begin by assessing the vitals.

Vitals

Vitals include temperature, blood pressure, pulse, height and weight. (Pain quantification has already been discussed in history.) A patient who is hypertensive may be experiencing chronic daily headaches. Abnormalities in pulse can be a sign of thyroid disease. Acute pain itself can manifest as tachycardia and hypertension. Fever may disclose an underlying infection or belie a rheumatic illness.

Targeted Physical Exam

Although a full review of physical exam techniques for each system is out of the scope of this book, a discussion of useful "clinical pearls" categorized by physical exam technique will be given instead.

Inspection

Start first with inspecting the area of concern. Inspection can help determine if there are dermatological problems causing pain, or infectious etiologies. There may be neuromuscular problems as evidenced by atrophy, hypertrophy, and asymmetry. Deformities may provide evidence for inflammatory/arthritic processes or orthopedic issues.

Palpation

Palpation is one of the most valuable tools in chronic pain physical assessment. When palpating the area the patient experiences pain, keep in mind the systems based differential: for instance, examine for masses, arthritic/rheumatic changes, warmth and inflammation, and tense musculature. In addition, palpate with both light and deep touch. Neuropathic pain often can be elicited with just light touch. In addition, examine for pain caused by nearby structures, or referred pain. For example in knee pain, examine above and below the joint: hip, thigh, lower leg, ankle, and feet. Again, this section is not meant to be a thorough treatise on physical examination techniques, but a listing of a few "clinical pearls". This collection of lesser known or more helpful physical examination techniques have proven to be quite useful in aiding the diagnosis of chronic pain. A few of these techniques and considerations will be given for each region of the body in the following sections.

Head and Neck

Although there are other causes of pain in this region, such as neuropathic (trigeminal neuralgia) and infections (chronic sinusitis), key sources of chronic pain in this region can be musculoskeletal in origin. Palpation of tender muscles located in the back of the head can be invaluable in helping to identify a musculoskeletal component to migraines. These muscles are called the suboccipital muscles. Palpation can reproduce the patient's symptoms. Refer to the chapter on myofascial trigger points for information on treatment.

In addition, inclusion of temporal mandibular joint disorders (TMJ) in the differential is often very helpful in evaluating pain in the head and neck region. In one study 96% of TMJ patients had facial pain [2]. In addition, 50% of TMJ is manifested as only myofacial pain [3]. Consequently, palpation of the muscles of mastication (masseters, pterygoids,

temporalis) is also emphasized in a patient with chronic head/neck pain. TMJ can be divided as articular (muscle, joint) or nonarticular (arthritis, gout, infectious, etc.) in origin. One particular physical diagnosis technique is palpation of the temporomandibular joint via the external auditory canal.

TMJ Palpation

1. Provider places gloved fifth finger in patient's bilateral external auditory canal
2. Ask patient to open and close mouth slowly

Interpretation: Feeling a click anteriorly (the location of temporomandibular joint) can confirm articular dislocation and relocation.

TMJ Musculature Palpation

1. Palpate muscles of mastication with thumb inside mouth and second and third finger on the exterior (gentle squeezing of muscles of mastication between thumb and second and third fingers). Palpate the bony zygomatic arch with the index finger. The muscles of mastication are located inferior to this bony landmark.

Interpretation: tenderness may indicate myofascial origin of pain.

Upper Extremity

Performing a thorough orthopedic exam (inspection for deformity, atrophy, and asymmetry; range of motion; provocative maneuvers; reflexes; strength; pulses) is a good start to an initial evaluation of pain in the upper extremity. One clinical pearl is to keep in mind the nervous system as a source of pain. It may be helpful to examine if the pain has a dermatomal distribution. Pathology can arise from the level of the

spinal cord, brachial plexus, to compression at the carpal tunnel. In particular, the brachial plexus (and its branches) which innervates the upper extremity is often a culprit for chronic pain in this region.

When the brachial plexus is compressed or injured (thoracic outlet syndrome, pectoralis minor syndrome), it can cause pain and paraesthesias in the upper extremity [4]. Recall that the brachial plexus travels under the scalene muscles in the neck, beneath the clavicle, and then under the pectoralis minor in the chest on its path to innervate the upper extremity. These are areas where the brachial plexus can become compressed. Tenderness at the scalene muscles and pectoralis minor can be helpful in confirming a neuromuscular etiology.

Brachial Plexus Compression Provocation Tests

The principle behind these tests is elongation of a compromised brachial plexus and its branches leading to symptoms.

Neck Rotation

1. Ask patient to turn head to left or right.
2. Wait

Interpretation: symptoms (pain, paresthesias) appear in opposite extremity (that is, turn head to left, right brachial plexus is stretched, and symptoms occur on right upper extremity).

Neck Tilt

1. Ask patient to tilt head (ear to shoulder) left or right
2. Wait

Interpretation: symptoms appear on opposite extremity if brachial plexus compression. Symptoms appear in ipsilateral extremity due to cervical spine pathology.

Upper Limb Tension Test (First Described by Elvey [5]) (Fig. 2.1)

1. Ask patient to abduct arms such that arms are parallel to floor
2. Extend wrists upwards towards ceiling
3. Tilt head (ear to shoulder)

Interpretation: in a few seconds, pain or paresthesias will confirm brachial plexus compression.

Of note there is a 90° abduction or Elevated Arm Stress Test (position patient in "hands up in the air position" as if held at gun point) which may include simultaneously opening and making a fist with the fingers and hands. If symptomatic only with opening and closing of fist, this may signify insufficient arterial supply, as in claudication.

FIGURE 2.1 Upper limb tension test. When the head is tilted (ear to shoulder) towards the limb with pain or numbness it can cause worsening of brachial plexus compression, leading to worsening of symptoms

Diagnostic muscular block (temporary chemo-denervation of muscle with short acting lidocaine) at the pectoralis minor or scalenes may help to confirm the diagnosis. Reports of botulism toxin as being diagnostic and therapeutic also exist [6, 7].

Shoulder Internal Rotation

1. Patient is seated
2. Ask patient to move arm behind back and reach up with hand as far up as possible

Interpretation: reaching the scapular spine is normal, otherwise there is a deficit in internal rotation (and adduction). Deficit may be caused by the muscle and nerve responsible for that action (teres major, latissmus dorsi), or tightness and pain in the muscle opposing the internal rotation (infraspinatus, supraspinatus).

The last clinical pearl I would like to share uses the example of examination of internal rotation for shoulder pain. Of note, the teres major and latissmus dorsi are one of the chief contributors to internal rotation at the shoulder. One can consider cervical nerve root compression, tendonopathy, etc. as a cause of pain and weakness in these muscles, thereby limiting active range of motion. However, on the other hand, one must also consider another source of the problem: tightening and shortening of the muscles *opposing* internal rotation. A tight, painful, or stiff infraspinatus is one of the chief culprits to limited internal rotation. (Occasionally, a patient will have a tight or stiff supraspinatus with similar limitation in motion.) Assess internal rotation as above. If there is shortening of the infraspinatus, (posterior shoulder stiffness) this can easily be treated and stretched to restore range of motion [8–10]. Palpation of a tender infraspinatus may also help to confirm this diagnosis. Consequently, besides considering that the muscle (or its innervation) that performs the movement is the source of the ROM deficit, one must also consider that

the muscle *opposing* the action can cause limitation in range of motion through its stiffness and pain.

Abdomen

Chronic pain in the abdomen has many etiologies, from infections (H. Pylori), inflammation (gastritis, inflammatory bowel disease, gallbladder disease), mechanical (constipation), tumors, and other visceral etiologies. However, one must consider also referred pain, nerve entrapment, and abdominal wall pain.

Carnett Test

This test is a validated and useful tool to differentiate abdominal muscle pain from abdominal visceral pain [11]. Often times when seeking an etiology for abdominal pain, multiple expensive tests, imaging, and consultations are performed only to discover that the pain is not intra-abdominal, but rather musculoskeletal in origin. This test is easily performed in the office setting.

To perform this test:

1. Patient is supine
2. Palpate point of maximal tenderness on abdomen
3. Ask patient to situp with arms folded across chest (avoid using arms in order to rely on abdominal musculature for flexion of back)
4. Interpret: if pain is stable or worse, the pain is musculoskeletal in origin. If pain is improved (given more room in abdomen from flexion) it is abdominal in origin.

Nerve entrapment is a common cause of chronic pain and can be diagnosed in part with this test and easily confirmed (and treated) with a targeted injection of local anesthetic [12].

Pelvis

The Carnett test can be adapted to differentiate between pain originating in the female reproductive system and abdominal musculature during bimanual exam [11, 13]. To perform this test:

1. Patient is in dorsal lithotomy
2. Perform bimanual exam and locate point of maximum tenderness with both vaginal and abdominal hands
3. Remove abdominal hand, keep vaginal hand in place same pressure
4. Replace abdominal hand
5. Interpret: if abdominal hand elicits the tenderness, pain is caused by abdominal musculature. Otherwise, if vaginal hand causes tenderness, pain is pelvic in origin.

Again local anesthetic injection (with or without ultrasound guidance) may be not only diagnostic but therapeutic as well.

Lower Extremity

Similar to the upper extremity evaluation, a good orthopedic evaluation is in order, starting again with inspection, range of motion, provocative maneuvers, neurological exam including strength, sensory, and reflexes, and ending with the vascular examination of pulses. Palpation of the muscles of concern is also very important along with examination for the possible dermatomal distribution of pain.

There are many common causes of lower extremity pain such as diabetic neuropathy, inflammatory conditions such as plantar fasciitis and osteoarthritis, vascular complications such as venous stasis and claudication, not to mention corns, bunions, and warts. However, given the prevalence of conditions collectively known as sciatica, some attention will be given here on physical examination of this condition.

Straight Leg Raise [14]

1. Can be performed sitting or supine
2. Lift patient's leg upwards (passive hip flexion if supine or passive knee extension if sitting)
3. Interpretation: positive if patient experiences sciatic pain at angles 30–75°. This test stretches the sciatic nerve, and if there is impingement on the nerve, will cause radicular pain.

However, not all sciatic symptoms are caused by herniated disc or other pathologies at the level of the spinal cord (epidural abscess, tumor, hematoma). The sciatic nerve courses under the piriformis muscle, which can impinge upon the nerve causing sciatic symptoms (Piriformis syndrome) [15].

Piriformis Examination

1. Patient is placed in prone position
2. Find the bony prominence of the greater trochanter of the femur (Lateral inferior hip)
3. Envision muscle arising from the greater trochanter coursing upwards and medially towards sacrum at approximately a 30° angle
4. Palpate mid muscle and its insertion at sacrum for tenderness
5. Interpretation: positive tenderness indicates piriformis pathology (inflammation, strain, trigger point, etc.)

Lastly, if patient has complaints of knee pain, an easy to perform test to help support a diagnosis of arthritis is palpation for crepitus in the knee joint.

Palpation of Crepitus

1. Patient is sitting, knees dangling.
2. Place examiner's hand firmly on the anterior knee, applying slight pressure.
3. Passively extend and flex knee with opposite hand

Interpretation: the sensation of crunching, grittiness, or grinding during joint movement confirms the presence of joint degeneration. With practice, one can appreciate mild and severe amounts of crepitus, which will enable the practitioner to predict findings prior to radiological confirmation.

Back

Back pain is one of the most common diagnosis seen in primary care. Consequently, a detailed physical exam will be described. After taking history, begin to examine the patient using a systems based framework. Keep in mind the large systems based differential: infectious, inflammatory, rheumatological, neoplastic, vascular, etc. Of note, a thorough hip examination has been included given the relationship between altered hip mechanics and arthritis and the development of low back pain and spinal disease (Hip-Spine syndrome) [16–19].

Back Examination

1. Inspect area of concern, examining for areas of redness or rash (infectious: zoster, cellulitis, abscess), masses, asymmetry, atrophy.
2. Palpate along length of entire spine for tenderness (thinking of fracture, neoplastic/infectious invasion, etc.)
3. Palpate any muscles in the region of pain, feel for taut bands of muscle fibers. Especially affected muscles include the paraspinal muscles, quadratus lumborum, gluteus medius and minimus.
4. Assess range of motion (flexion, rotation) of spine (assesses rheumatological conditions such as anklylosing spondylitis)
5. Assess neurological function: strength lower extremities one muscle group at a time, one side at a time: from hip flexion to toe dorsiflexion. Assess reflexes at patella, achil-

les tendons. Assess sensation. Assess gait and balance: tip toe walking, heel to toe walking. Assess for radiculopathy: Straight Leg Raise.

Any weakness should raise a red flag and prompt further evaluation and imaging.

6. Assess vascular system: check pulses (femoral, pedal). Weak pulses may signify vascular insufficiency which may cause claudication, local ischemia, etc.

Hip Examination

1. Inspection. Inspect gait, and observe for pelvic levelness (Trendelenberg test) relative to the floor, This may be a sign of hip pathology (neuromuscular weakness, bony pathology). A positive test may be best appreciated by observing the position of the upper body. The upper body and shoulders will lean towards affected side in order to maintain balance.

   Inspect for limb length discrepancy by measuring from the anterior superior iliac spine of the hip to the medial mediolus of the ankle. Inspect if one of the limbs is abnormally rotated compared to the other.

2. Assess range of motion: flexion, extension, adduction, abduction, internal and external rotation. Limitations in ROM can indicate intraarticular pathology, muscle tightness, etc.

3. Palpate bony structures of pelvis: the sacroiliac joint, and common tendon attachment locations such as anterior superior iliac spine, iliac crest, and ischial tuberosity. Palpate around the greater trochanter of the femur for bursitis.

4. Palpate/examine muscles: Piriformis, gluteus medius and minimus, tensor fascia lata, psoas, iliotibial band. There may be tender or strained muscles. Assess for hamstring flexibility as it can pull on the ischial tuberosity affecting pelvic positioning. This can be evaluated while patient is supine, with hip flexed at 90° and knee flexed at 90°. The

examiner lifts (passively extends) leg at the knee. If the examiner can fully extend knee, there is no hamstring tightness.

In conclusion, physical exam is crucial to narrowing down the differential diagnosis for the patient's pain. Inspection and palpation bearing in mind various systems can be helpful in diagnosing the patient's pain.

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Chapter 3
Diagnostic Evaluation for Chronic Pain

Bonnie Huang Hall

Helpful Tip

1. Order laboratory and imaging studies in order to evaluate various body systems that may cause chronic pain. Doing so may help reduce the likelihood of a missed diagnosis.

After a thorough history and physical exam, the clinician may have an idea of what may be causing the chronic pain. Although laboratory blood work or imaging are not always necessary, these studies can help support the presumptive diagnosis or eliminate other causes of pain.

Again, a systems approach to ordering blood work and radiology will be advocated in order to evaluate broad categories of diagnosis. Of course, the below (Table 3.1) is just a preliminary list, ordering tests should be refined or expanded according to patient's complaints, history, and physical.

To reiterate, the goal of having a systems based approach to diagnostic evaluation is to have an organized approach that decreases the likelihood of a missed diagnosis for the chronic pain. A colleague of mine shared that she knew of an obese patient with chronic pelvic pain who required opioid

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TABLE 3.1 Diagnostic studies listed in terms of body systems

Systems	Diagnostic studies that may be helpful
Endocrine	TSH, HbA1c (or fasting glucose)
Rheumatological	ESR, ANA, RF
Cardiovascular	Lipid panel, EKG, studies to evaluate blood flow (ABI, Doppler U/S)
Musculoskeletal	CK, plain films to start, MRI if needed for joints, spine
Neoplastic	Plain films to start for bony infiltration, CT if needed for internal organ visualization FOBT Mammography Age appropriate screening CBC
Internal organ (gastrointestinal, genitourinary, gynecological)	CT abdomen, pelvis, CMP Ultrasound, UA
Neurological	MRI spine, EMG
Infectious	UA reflex urine culture, STD evaluation

Abbreviations: *TSH* thyroid stimulating hormone, *HbA1c* glycosylated hemoglobin, *ESR* erythryocyte sedimentation rate, *ANA* antinuclear antibody, *RF* rheumatoid factor, *EKG* electrocardiogram, *ABI* ankle brachial index, *U/S* ultrasound, *CK* creatinine kinase, *MRI* magnetic resonance imaging, *CT* computed tomography, *FOBT* fecal occult blood test, *CBC* complete blood count, *CMP* comprehensive metabolic panel, *UA* urinalysis, *EMG* electromyography, *STD* sexually transmitted disease

medications for pain control. After months of suffering, plain films of the bony pelvis were eventually performed and revealed a fracture. Although not every patient with chronic pain will have such a treatable diagnosis or explanation for their pain, it is our duty to thoroughly evaluate our chronic

pain patients, and especially those on higher risk medications such as opioids. Generally, if the patient's pain is difficult to manage, this is justification for more elaborate testing and imaging. A systems based approach will enable the primary care practitioner to examine other possibilities and have a more thorough evaluation of chronic pain.

Furthermore, if a patient's pain becomes acutely worsened, a re-evaluation should be conducted. Of course, a thorough history should be first taken. This may reveal a rather innocuous cause such as weekend over-exertion, or a rather malignant etiology such as weight loss and rectal bleeding. Targeting laboratory studies to the history obtained and further imaging may indicate the reason for the recent decline in pain control. Do not be afraid of repeating laboratory studies as results may change.

Diagnostic Studies Helpful in Chronic Low Back Pain

To continue the chronic low back pain example, basic diagnostic studies that would be helpful in order to confirm the diagnosis include:

1. Laboratory studies: ESR, RF, ANA, TSH. This will help confirm or rule out rheumatological or endocrine involvement.
2. Imaging: plain films of the lumbar spine. MRI if neurological symptoms such as weakness, numbness, sciatica, or tingling exist. This will enable evaluation of tumor, infection, neurological compromise, and bony abnormalities.

Often times, ESR, RF, ANA, TSH will be negative, confirming that the chronic low back pain is not due to an autoimmune or uncontrolled endocrine process. In the average patient, imaging will often show some degenerative changes of the spine without neurological compromise. Consequently, imaging will often confirm the diagnosis of chronic low back pain, likely of muscular etiology.

Of course, this is assuming patient already had up to date health maintenance and basic laboratory studies ensuring no anemia, diabetes, and liver or kidney dysfunction. Rarely encountered will be the patient with metastases to the spine from an undiagnosed malignancy. However, this is a condition where appropriate diagnostic imaging will be invaluable, and missing the diagnosis devastatingly tragic.

Conclusions

Use diagnostic labs and imaging in order to support and specify the diagnosis primarily responsible for chronic pain. Evaluate in a systems based fashion, making sure to investigate neoplastic, autoimmune, endocrine, metabolic, infectious, musculoskeletal, neurological, vascular, and organ-based etiologies. The course of chronic pain can change. Re-evaluate as necessary.

Chapter 4
Specialist Evaluation for Chronic Pain

Bonnie Huang Hall

Helpful Tips

1. Use specialist referrals to support your diagnosis and treatment plans.
2. If patient has pain in a specific body system, make sure they see that body system's specialist at least once to confirm your diagnosis.
3. Behavioral health specialists may use cognitive behavioral therapy (CBT) to decrease pain intensity.

Introduction

The role of the specialist can be both for evaluation and/or management depending on the patient's circumstances. Recent figures indicate that only 52% of chronic pain patients in the US are managed by primary care [1], with the rest being managed by specialist care. Unfortunately, as chronic pain has grown to be a disease of epidemic proportions, specialists alone, given their smaller numbers, cannot adequately handle the volume of cases [2]. Neither, can they match the

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coordination, consistency, and cost effectiveness of care provided by the primary care physician [3]. Consequently, the role of the specialist referral will be increasingly for procedures that evaluate sources of pain, or for their input and guidance on management of chronic pain, as opposed to primary management.

Specialist Referral for the Evaluation of Chronic Pain

First and foremost, specialists generally have more in-depth training in procedures, diagnostic techniques, and management of disease in their respective body system than primary care physicians. Having acknowledged this, their role in chronic pain often is to confirm (or refute) whether the patient's chronic pain is being caused by their body system of expertise. To that regard, specialists may need to perform procedures to accurately diagnose patients. For instance, when evaluating chronic abdominal pain, one may consider referral to gastroenterologist to perform a colonoscopy or EGD. Or, when contemplating whether endometriosis is the source of chronic pain, a referral to gynecology is not only appropriate, but necessary to confirm the diagnosis with laparoscopy. Rheumatologists may confirm that a patient has fibromyalgia as their cause of pain through their specialist evaluation of the patient.

As a cautionary tale, I had inherited a complicated case of chronic abdominal pain that was supposedly caused by a ventriculoperitoneal shunt (which was properly placed). Her pain was evaluated by blood work, CT abdomen pelvis, gynecologists (she had an intrauterine device) at the local level and tertiary care center. She was managed with opioid medications alone for many years. However, the patient had never seen a gastroenterologist. When I discovered this, I referred the patient and she underwent an EGD and colonoscopy. It was found that the patient had moderate to severe gastritis that when treated alleviated most of her pain. Consequently,

the role of the specialist is to offer their advanced skills and expertise in diagnosing or confirming a specific diagnosis in their respective body system.

Specialist Referral for Management Guidance

After performing a thorough history, physical exam, and diagnostic evaluation, including a specialist confirmation of the pathology causing pain, the specialist may offer management options, treatment plans, or procedures that may help the patient manage their condition. For instance, orthopedic surgeons may offer guidance on the treatment of chronic knee pain caused by osteoarthritis. In their management plans, they may reaffirm the need for physical therapy, and describe specific indications for surgery. They may perform or advise therapeutic joint injections and reaffirm the need for weight loss. Frequently, a specialist's opinion on management of chronic pain can help to reaffirm treatment plans which often do involve weight loss, physical therapy, etc. This confirmation of the primary care physician's treatment plan may especially be helpful in reaffirming the role of the primary care physician as the primary manager of the patient's chronic pain.

In addition, specialists have experience in prescribing often high risk medications or procedures relieving pain. If there is any question that the patient's medication regimen is high risk (for instance, greater than 100 mg/day morphine equivalent, or on concurrent opioid therapy and benzodiazepines, or suicide risk and chronic opioid therapy), it may be wise to get a consultation from the pain medicine specialist. They may confirm the treatment plan of opioid reduction, discontinuation, or continuation. Furthermore, pain specialists can also offer a myriad of pain relieving procedures. See Chap. 7 for further details.

Lastly, referral to behavioral health specialist may be helpful in the management of chronic pain. It has been reported that 20–50% of chronic pain patients have co-morbid depres-

sion [4–6]. Besides the adequate treatment of psychiatric illness, the behavioral health specialist may also offer CBT (cognitive behavioral therapy). Recent studies have shown that CBT can help certain chronic pain patients with depression, mood, disability, quality of life, reduction in pain intensity, and catastrophic thinking [7, 8].

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Chapter 5
Formulating a Diagnosis for Chronic Pain

Bonnie Huang Hall

Helpful Tips
1. Treat the underlying cause
2. Identification of pain source can be the start of targeted pain management
3. Always make your own independent diagnosis and conclusions
4. Use simple questions to screen for substance use disorder and opioid use disorder

Introduction

Earlier chapters examine the various steps the primary care provider takes to begin an initial evaluation into chronic pain. The history taking process, physical examination, and diagnostic evaluation are all performed through the lens of a systems based differential. Specialists may be involved to perform advanced diagnostic procedures or evaluations that further aid in narrowing down the differential diagnosis or confirming an etiology for chronic pain. All this information will (hopefully) lead to a chief etiology/diagnosis for chronic

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pain. Why is it important to have a specific diagnosis for chronic pain? Because treatment is tailored to the diagnosis. Although chronic pain is often defined as pain persisting beyond normal tissue healing time, it does not mean that there is not a reason for it or a principle diagnosis. For example, rheumatoid arthritis and osteoarthritis are distinct causes of chronic pain with different treatments. Consequently, as in all medicine, the goal is to treat the underlying cause.

One of the most common chronic pain conditions encountered in primary care is diabetic neuropathy. Because there is an established diagnosis, accepted therapies such as gabapentin are used. In addition, if gabapentin is not enough, other medications targeted to neuropathic pain are considered. Consequently, targeting therapy to the underlying condition and etiology can allow the provider to manage chronic pain more effectively.

Types of Pain

The pathophysiology of pain is a complex matter whose review and discussion is beyond the scope of this work. Only a short description of types of pain is given with the chief goal of facilitating diagnosis and treatment. For a more detailed overview of pain physiology, refer to the first few chapters of the reference listed [1].

Pain can often be segregated based on etiology [2]:

Neuropathic – meaning nerves themselves are compromised, causing pain.

- The nervous system affected can be either the central nervous system or peripheral nerves.

Nociceptive – feeling pain due to other pathology such as:

- Inflammation
- Musculoskeletal
- Compressive
- (Temperature extremes)

With the understanding of what is causing the pain, combined with recognizing whether the etiology of the pain is primarily neuropathic or not, one can then begin prescribing appropriate pharmacological and non-pharmacological therapies. If the pain is primarily nociceptive, one can then begin by treating the underlying inflammation, musculoskeletal issues, and/or compressive etiologies. If pain is primarily neuropathic in nature, medications such as anti-epileptics and antidepressants may be more effective. Although pain is commonly grouped into these two distinct types, neuropathic and nociceptive pain conditions are not mutually exclusive, and overlap may occur. Consequently, it is important to have a basic understanding of what type of pain the patient is experiencing.

Case of Chronic Low Back Pain

Historical data has shown that the most common regions for chronic pain are (1) back pain, (2) lower extremity pain, and (3) arm pain [3]. For illustrative purposes, a case of chronic back pain will be discussed given the frequency of encountering it in primary care. This case is for teaching purposes and consequently has both not only the facts gathered during history and physical, but also the systems it addresses on the second column (Table 5.1).

No imaging performed given age and no alarm symptoms or signs. Blood work during pregnancy normal. Diagnosis: most likely back pain caused by lumbar muscle over-usage given hyperextension of back during pregnancy and weak abdominal muscles. Patient was prescribed the usual treatment of acetaminophen and abdominal core exercises and

TABLE 5.1 Example case of chronic back pain

History/Physical exam information	Systems addressed
27 yo G2P2 F comes to the office for back pain × 3 months. Patient states pain started during last month of pregnancy and has continued since. It is 5/10 and comes and goes. Worse with certain movements. It is achy, in low back, without radiation. It occurs 4–5×/week, lasts all day. Patient did not take any medication for the pain.	Descriptors ("PQRST") of pain
There is no numbness or tingling, or weakness in the lower extremities.	Associated symptoms: Nervous system
There is no bowel/urinary incontinence	Nervous system, "red flag questions"
There are no other joint stiffness, morning stiffness, no rashes	Rheumatoid/ autoimmune
Patient denies fever and chills	Infectious, also a "red flag question"
Patient denies unintentional changes in weight, heat or cold intolerance	Endocrine system
Vitals are normal	Infectious disease
Examination ROM (back) normal	Autoimmune, musculoskeletal exam
Gait and neurological exam of lower extremity normal. SLR negative	Nervous system
No other joints tender/inflamed	Rheumatoid/ autoimmune
Palpation spine normal, nontender	Skeletal system
Palpation of back musculature reveals tender tight paraspinal muscles in lumbar region. Area does not have mass. Area is not red.	Musculoskeletal system. Neoplastic, infectious disease

was symptom free at 1 month follow up. Thus, this is a case of somatic pain, caused by musculoskeletal issues. The treatment targeted the underlying cause (muscle weakness and strain) and was effective.

Chronic Back Pain with Weakness

Musculoskeletal low back pain is a clinical entity encountered almost daily in practice. Complacency may cause a failure to examine the patient properly and a consequent misdiagnosis. For example, let us alter the patient to being a 65 yo M who recently developed acute on chronic back pain after lifting garden mulch. His pain is similar but he does not mention that he has a gait abnormality. Patient attributes gait abnormality due to pain. He states, "I can't walk because of the pain." The physician does not ask about or examine the gait. Lower extremity neurological exam is not performed. The physician attributes the comment as a "normal" reaction to pain. The patient was prescribed additional opioid pain medications. His lower extremity weakness becomes troubling to his family which notice he is nearly incapable of walking without assistance from a walker, whereas previously he was able to walk without assistance. The family encourage him to return to the physician. He then communicates the fact that he is "weak." Alarmed, the physician then questions specifically about weakness and performs a gait evaluation, showing that the patient is stumbling, with one leg chiefly affected. Close neurological exam shows unilateral weakness in the lower extremity. MRI was eventually performed and patient was found to have a herniated disk. Patient received a course of NSAIDS and oral steroids and weakness and pain started to improve to baseline. Patient participated in physical therapy and full strength returned.

This second case actually highlights two points. (1) Despite back pain being an everyday complaint, one must still be vigilant and perform appropriate systems based examinations. Worsening of chronic pain can be an acute and treatable process. (2) The patient and physician had a communication barrier. The patient initially did not know how to express his complaint in a manner that will make the physician listen and examine carefully. Although the physician could have specifically asked about weakness, he did not initially do so. The patient's use of the term "weakness", an alarm symptom, allowed the physician to take his matter more seriously. Questions were then asked about weakness and a neurological examination performed. As a result of this thorough history and physical exam, a specific diagnosis was made and recovery facilitated through targeted treatment.

More Cases

The following is another case study that illustrates the thought processes, interview questions, and strategies used to evaluate and diagnose patients with chronic pain. Again, history and physical are key to making a correct diagnosis for the patient.

Case 2: Toe Pain

CC: 60 yo F with DM, HTN, HLD comes to the office stating that her "gout is flaring" on her left great toe. She states she has always been treated with indomethacin and wants a refill of that medication as she is in pain. She has had this problem on and off for a couple years.

Thought process:

1. Gout is common in diabetic persons. It is not unreasonable that she has gout. It is classically treated by indomethacin.

2. However, it is always wise to confirm the diagnosis person-
   ally and document evidence of this disease prior to giving
   treatment.

Practitioner asks questions to confirm the diagnosis of
gout: Were you ever on allopurinol? Did you eat anything
like beer, cheese, wine, or indulge in red meats? Did you ever
get a uric acid test?

Patient answers no to all questions. She actually ate salmon
and vegetables yesterday and did not drink alcohol. She
doesn't get flares that much, maybe couple times a year, so
she is not on any daily medication. She does not know what
uric acid is. She complains that her shoe has been tight and
pinching her toes lately.

Thought process:

1. Reasonable explanation. Maybe patient did not reveal that
   she indulged.
2. Let's perform a physical examination, examining for signs
   and symptoms of inflammation: swelling, heat, joint
   enlargement, tenderness at first metatarsal phalangeal
   (MTP) joint.
3. Also to be complete, a brief review of systems is
   performed.

Review of systems performed as part of routine history:
there is no fever, no chills. No other joints hurt. No other
joints affected. No skin erythema.

Thought process:

1. Alarm: no erythema? Gout usually causes an inflamed
   joint.
2. Need to examine closely.

Physical exam performed:
• Vitals mildly hypertensive 145/95 for diabetic, otherwise
  normal
• General: No acute distress. No tophi or disfiguration of
  joints.
• Gait: patient can barely put weight on affected foot

- Inspection of affected foot: there is no redness, swelling, induration, rash on left MTP, or any joint in the foot. There is no joint tenderness on palpation. There is no bony tenderness. Shoes do appear tight at toes.
- Neurological exam: there is no numbness on monofilament exam. Strength lower extremity 5/5 bilaterally.
- Pulse: 2+ pedal pulse, normal.
- ROM ankle and toes normal

Thought processes

1. This does not look like gout or diabetic neuropathy
2. Need to find out what is actually causing the pain, as gout does not seem likely.

Continued physical exam:

- Palpation of soft tissue of foot reveals the location of tenderness in muscle between the metatarsal bones of the great toe and first toe.

Diagnosis:

- Patient has muscle strain, myofascial pain.

To confirm diagnosis: Patient was advised to massage area of pain at home, take naproxen, and indeed pain improved. The patient was also advised to wear open toed slippers/loose fitting shoes. Eventually patient came in for a local trigger point injection which resolved the pain with continued home massage.

Consequently, the key lesson to remember is to always formulate an independent diagnosis through history, physical exam, and diagnostics (if needed). It is tempting to complete a 10 minute visit by simply refilling the indomethacin (or any controlled substance, for that matter) and sending the patient on their way. However, with proper assessment, the underlying cause was remedied and the patient is now pain free.

Although not every patient will have such an easily treatable cause for their chronic pain, a careful history and physical can lead to a more accurate diagnosis and thus a more success-

ful treatment. It is interesting that indomethacin previously provided did help manage the patient. However, because this patient was inaccurately diagnosed, her treatment was suboptimal and created unecessary dietary restrictions.

Substance Use Disorder and Chronic Pain

The diagnosis of concurrent substance use disorder should be considered when diagnosing and treating chronic pain, especially with controlled substances [4, 5]. Controlled substances are categorized, or "scheduled," in the US according to their potential for addiction and harm [6]. Treatment of the patient on chronic opioid therapy (Chap. 8) will detail the processes and testing required to detect a patient with an ongoing substance use disorder (and other aberrant behavior such as diversion of controlled substances). This section focuses briefly on how to recognize substance use disorder, as many clinicians have incomplete training in this matter [6]. Substance use disorder was formerly termed addiction. The American Society of Addiction Medicine states that an individual with substance use disorder will pathologically pursue reward or relief by substance use and other behaviors.

There are several defining characteristics seen in substance use disorders:

1. Craving for the drug
2. Diminished recognition of problematic behavior
3. Dysfunctional emotional response
4. Impairment of behavioral control
5. Inability to consistently abstain [6].

Some patients may not meet the criteria for substance use disorder, but still may have "risky" substance use [7]. Alcohol is the most common drug used in an unhealthy manner in the US. A single question to screen for unhealthy alcohol use is by the number of drinks consumed at one time. The criteria for unhealthy alcohol consumption can be

satisfied if 4 or more drinks are consumed at once for men (or 14 drinks per week), or 3 drinks at once for women (or 7 drinks per week). Many institutions prohibit concurrent alcohol use with chronic opioid therapy due to the risks involved.

For other drugs, any illicit drug use is deemed unhealthy. In addition, if prescription drugs are misused, it is also unhealthy. Misuse of prescription drugs includes using another person's prescription medications. This is particularly concerning with opioids, benzodiazepines, and other scheduled/addictive medications. It also includes not using the prescription drug according to the directions or purpose intended. A one line screening question for unhealthy drug use is, "How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?" where nonmedical use is defined as "for reasons or in doses other than prescribed" [7]. This same question can be applied to opioid prescriptions, "Have you ever taken opioid prescriptions in doses other than prescribed or for reasons other than pain?"

Distinguishing Opioid Use Disorder in Patients on Chronic Opioid Therapy

Diagnosing opioid use disorder in patients taking prescription opioids for chronic pain can be challenging [8]. Two tools that can be used to detect opioid use disorder in these patients include the COMM (Current Opioid Misuse Measure) and the POMI (Prescription Opioid Misuse Index) [9, 10]. POMI has fewer questions (Box 5.1) and may be more effective in the primary care setting. If unhealthy use or substance use disorder is suspected or confirmed, take this discovery as an opportunity to not only reevaluate treatment plans and diagnoses, but also to refer the patient to the appropriate behavioral health provider.

Box 5.1 Prescription Opioid Misuse Index. This tool may be used to help detect those on chronic opioid therapy for chronic pain who have concurrent opioid use disorder [9]. **Note, patients may have physical dependence in addition to misuse of opioid medications.**
1. Do you ever use MORE of your medication, that is, take a higher dosage, than is prescribed for you?
2. Do you ever use your medication MORE OFTEN, that is, shorten the time between dosages, than is prescribed for you?
3. Do you ever need early refills for your pain medication?
4. Do you ever feel high or get a buzz after using your pain medication
5. Do you ever take your pain medication because you are upset, using the medication to relieve or cope with problems other than pain?
6. Have you ever gone to multiple physicians including emergency room doctors, seeking more of your pain medication?

Conclusions

With a more accurate diagnosis, treatment can be targeted to the underlying cause and possibly be more effective than generic pain control. In addition, it is important to have a systems based approach to diagnosing the etiology of chronic pain. This chapter illustrates the thought processes involved in arriving at a diagnosis. Note that the examples rely heavily on independent history and physical exam. It is true that primary care are not experts in pain, muscles, and their innervations. Nor are primary care providers aware of all the rare diseases that may cause pain. However, the differential diag-

nosis can be narrowed down to a particular system, and from there appropriate resources can be utilized to arrive at a diagnosis. In addition, sometimes a patient arrives with a diagnosis and desires pain medication. It is wise to personally confirm the diagnosis (through history, physical, and diagnostics, referrals, or past records) prior to prescribing pain medications, whether they are controlled substances or not. Chronic pain can often co-occur with substance use disorder and opioid use disorder. There are brief screening questions to help the primary care physician detect these co-morbidities. Again, only after the correct diagnoses have been established can the appropriate treatment or referral be made.

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Chapter 6
Management of Chronic Pain: Medication

Bonnie Huang Hall

Introduction

Management of chronic pain is complex, requiring a multidisciplinary approach that includes pharmacological and non-pharmacological treatments [1]. It often times requires specialist referral for treatment and pain relieving procedures. A thorough management plan also requires addressing the psychosocial aspects of pain. There must be appropriate goal setting, expectation management, and frequent reassessment. Management also requires treatment of the underlying mechanism for chronic pain, be it metabolic, endocrine, inflammatory, neuropathic, etc. Figure 6.1 illustrates the central role the primary care physician plays in juggling the many aspects of care, while being supported by a robust healthcare system. Note that in the figure, the multidisciplinary areas overlap with the primary care providers areas, indicating that sometimes the primary care provider will manage the pharmacology, and perhaps at the same time, offer some motivational interviewing and goal setting in the psychosocial aspect. Sometimes the primary care provider can teach basic

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Healthcare system support

Pharmacology

Complementary and alternative therapy

Physical therapy

Primary care provider
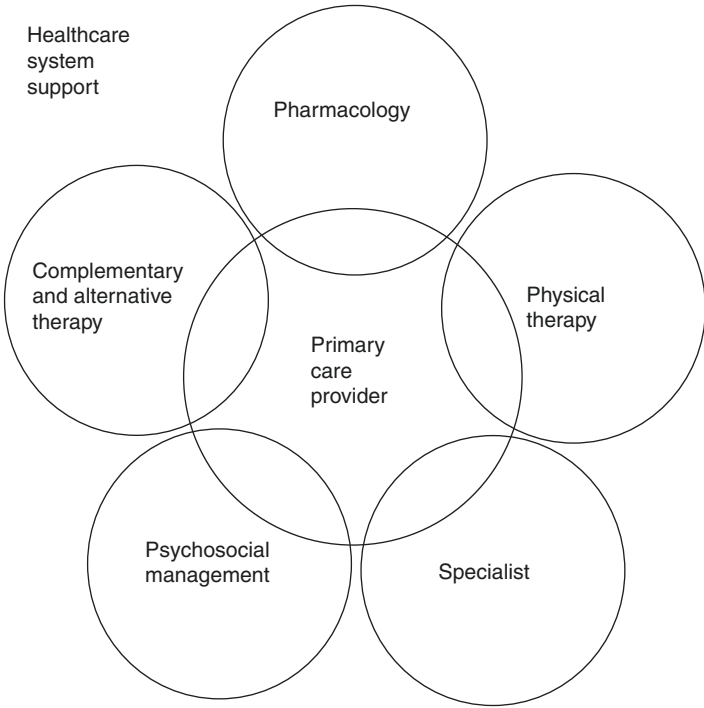
Psychosocial management

Specialist

FIGURE 6.1 At the heart of management for the chronic pain patient is the primary care provider coordinating care from multiple specialists and treatment modalities with support from the healthcare system

stretching and physical therapy techniques, such as for low back pain. Lastly, also note that in the background is "healthcare system support." This includes support from administrative policies, pharmacy, front staff, to electronic medical record reminders. These next two chapters will briefly summarize the coordinated multidisciplinary approach orchestrated by the primary care provider for chronic pain management.

Pain Medication: Introduction

Before discussing pain medication, the issue of treating the underlying mechanism for the chronic pain must be addressed. Diabetes must be controlled when managing the pain of diabetic neuropathy. Weight loss and strength training must be addressed in degenerative joint diseases. Treatment of the underlying cause (if it can be identified) must be regarded as an essential component of an effective management plan.

Consequently, chronic pain may helpfully be categorized into two main etiologies: Neuropathic or nociceptive (Fig. 6.2). That being said, all pain relief medication management begins with a step-wise escalation, starting with the safest, evidenced based medication as possible. It then progresses to including medication with increasing side effects or safety concerns, often culminating with chronic opioid therapy which has a plethora of risk, safety concerns, and efficacy concerns. Furthermore, as we will discuss in future chapters, many patients, after the exhaustion of traditional western medicine options, look to complementary and alternative therapies, which comes with its own safety and efficacy concerns.
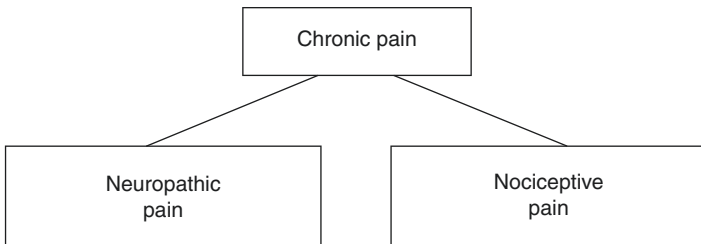

FIGURE 6.2 Pain can be separated into neuropathic or nociceptive etiologies. Neuropathic pain refers to pain originating from the nervous system. Nociceptive pain refers to the perception of pain originating from etiologies outside the nervous system. Nociceptive pain includes pain from inflammation, mechanical compression, and the musculoskeletal system

Neuropathic Pain

Neuropathic pain affects millions of patients worldwide. About 7% of the general population has chronic pain with neuropathic characteristics [2]. Experts have characterized neuropathic pain as severe and often challenging to manage [3]. Neuropathic pain can be thought of as central in origin or peripheral. Peripheral neuropathic pain is often characterized by burning or shooting sensations. It can also include abnormal sensitivity to normally painless stimuli (allodynia), or a hypersensitivity to normally painful sensations (hyperalgesia) [4]. Examples of peripheral neuropathies include diabetic and alcohol related neuropathy, radiculopathy, and post-thoractomy syndromes. Examples of central neuropathy include post-stroke, post spinal cord injury, or pain in multiple sclerosis [4].

Current recommendations from various reviews appear to have general agreement on the basic step wise approach from first line therapies to fourth line therapies for medication management for neuropathic pain with some debate over the placement of certain medications [3, 5, 6] (Table 6.1). Treating the specific diagnosis, especially in trigeminal neuralgia, seems to be a general consensus, as it has specific treatments (namely carbamazepine). That being said, most recommendations agree that first line agents include the anticonvulsants, gabapentin and pregabalin; the tricyclic antidepressants (TCAs), amitriptyline and nortriptyline; and the serotonin norephinephrine reuptake inhibitor (SNRI), duloxetine. There is currently a strong GRADE of recommendation for these agents [5]. GRADE stands for Grading of Recommendations Assessment, Development, and Evaluation. It is a standard method used to rate the level of evidence and strength of recommendations [7].

The following sections will give a few key points concerning each medication class. It is by no means an exhaustive analysis of these medications. The goal is to provide a brief overview of the class of medication in order to practically treat patients with neuropathic pain.

TABLE 6.1 Summary of recommendations on step-wise pharmacological management of neuropathic pain

	European Federation of Neurological Societies [8]	National Institute for Health and Care Excellence of the United Kingdom [9]	Canadian Pain Society [10]	Neuropathic Pain Special Interest Group [5]
First-line therapy	Specific diagnosis based.	Amitriptyline Duloxetine Gabapentin Pregabalin Capsaicin cream (localized pain for patients who declined/cannot tolerate oral treatments)	Gabapentin Pregabalin Duloxetine Venlafaxine TCA's	Gapabentin Gabapentin ER/enacarbil Pregabalin Duloxetine Venlafaxine TCAs
Second-line therapy		Try another first line therapy Tramadol for rescue therapy	Tramadol Strong opioids (Lidocaine cream or Lidocaine patches for post herpetic neuralgia)	Capsaicin patches Lidocaine patches Tramadol

(continued)

TABLE 6.1 (continued)

	European Federation of Neurological Societies [8]	National Institute for Health and Care Excellence of the United Kingdom [9]	Canadian Pain Society [10]	Neuropathic Pain Special Interest Group [5]
Third-line therapy	Strong opioids	Try another first line therapy	Cannabinoids	Botulinum toxin type A Strong opioids
Fourth-line therapy			Other opioids Lacosamide Lamotrigine Botulinum toxin Lidocaine cream Lidocaine patches	

Adapted from Cruccu [3]

Anticonvulsants

Gabapentin and pregabalin act on voltage dependent calcium ion channels in both the central nervous system and spinal cord. When the neuron is activated and there is a voltage change, calcium ion channels on the cell membrane are activated and allow for neurotransmitter release. The gabapentinoids bind to a special subunit of this voltage gated calcium ion channel, causing the channel to be internalized by the neuron. When these calcium ion channels are decreased on the cell membrane, calcium influx is limited, and therefore, neuotransmitter release is decreased [11]. By binding to these calcium ion channels, there is in essence, a reduction in pain signals.

In general, both gabapentin and pregabalin have very little drug interaction, allowing for consideration in its use in combined therapies. This is due to the fact that these anticonvulsants are excreted unchanged by the kidneys and are not metabolized by the cytochrome P450 system of the liver [11].

Gabapentin has a relatively short half life and therefore must be dosed 3× a day. The main side effects are sedation and dizziness. It is excreted by the kidneys and removed by hemodialysis, so dosing of gabapentin must occur after dialysis [12]. As gabapentin dosages are increased, less is bioavailable (given it is transport limited), and consequently higher dosages of gabapentin are not proportionately more efficacious.

Pregabalin, in comparison, is more efficacious than gabapentin, owing to its greater ability to bind to the subunit of the voltage gated calcium ion channel. Consequently, if the patient fails to gain adequate relief on maximum dosages of gabapentin, one can consider switching to pregabalin. In addition, the bioavailability of pregabalin is greater than gabapentin, due to having more than one pathway for absorption. One of the drawbacks, however, to pregabalin is that it is a schedule V drug, meaning that it is a controlled substance in the US [13]. Schedule V indicates that it is least likely of

the controlled substances to be misused, and there is very little physical or psychological dependence. Pregabalin poses the greatest threat to being misused and addictive in the opioid using population or those already struggling with substance use disorder [14].

One method of initiating gabapentin is to instruct patients to first take it at night. For instance, prior to three times a day dosing, have the patient take one tab prior to bed, and then increase to two tabs a night after a couple days. This will help them sleep given gabapentin's sedating effects. Then after a couple of days, begin taking the third dose in the day morning. Then after a couple days, transition to full three times a day dosing. This initiation of the medication at night and gradually transitioning to day time use allows the patient to adjust to the sedating effects and improves tolerance for taking the medication in the day.

Tricyclic Antidepressants

Some studies may suggest that TCA's are the most effective antidepressants for neuropathic pain in terms of number needed to treat [5]. This class includes the commonly used agents, amitriptyline and nortriptyline. Although the exact mechanisms of their analgesia is still being elucidated, the current hypothesis centers around norepinephrine. Amitriptyline increases norepinephrine and serotonin, while nortriptyline increases norepinephrine. When the reuptake of norepinephrine is inhibited by these TCA's, the increased norepiniephrine leads to inhibition of the voltage gated calcium ion channels. Voltage gated calcium ions facilitate neurotransmission. Therefore neurotransmission is inhibited as well, and pain signals are decreased [15]. TCA's may also work on other pathways as well, see Fornasari 2017 [11] for an abbreviated review. Their analgesic effects occur within a week of starting the medication, which is much sooner than their antidepressive effects. Analgesia is present even in patients without associated depression.

Side effects of TCA's include cardiotoxicity, due to their anticholinergic effects. These anticholinergic effects may lead to sedation, dizziness, dry mouth, urinary retention, constipation, orthostatic hypotension [3, 11]. Consequently, TCA's may worsen symptoms of prostatic hyperplasia, glaucoma, and cardiac conduction abnormalities. Consider obtaining an EKG prior to initiating treatment. An advantage of nortriptyline is that it has less anticholinergic effects than amitriptyline [16]. Amitriptyline is likely more effective than nortriptyline due to its ability to inhibit both norepinephrine and serotonin reuptake [17].

Serotonin Norepinephrine Reuptake Inhibitors

This class includes medications such as duloxetine, and venlafaxine. In general, these medications have less side effects than TCA's. These drugs should be tapered to avoid withdrawal symptoms with discontinuation.

Duloxetine has gained FDA approval not only in treatment of peripheral neuropathy and fibromyalgia but also in chronic musculoskeletal pain such as osteoarthritis and low back pain. Caution should be used in those with hepatic or renal insufficiency. Venlafaxine, on the other hand, has not been approved for the use in musculoskeletal pain. It has been associated with some cardiac conduction abnormalities.

A recent Cochrane review on SNRIs and fibromyalgia seem to indicate that there is low (and very low) quality evidence that duloxetine and milnacipram have a clinically significant benefit in reducing pain by 30% and creating the impression of being "much or very much improved" [18].

Tramadol

Second line agents generally include tramadol, which is a weak opioid and SNRI. A recent 2017 Cochrane Review of tramadol for chronic neuropathic pain found the evidence

supporting its benefit to be low or very low quality [19], while the latest review by the Neuropathic Pain Special Interest Group only has a weak strength of recommendation for tramadol as second line agent [5]. Perhaps in light of the evidence, the clinical guidelines of the United Kingdom's National Institute of Health and Care Excellence (NICE) states that tramadol is to be considered only as rescue therapy, or break through pain control [9]. These guidelines are aimed specifically at the non-specialist, or primary care providers, and hence, basically reiterate trying other first line therapies as "second and third-line therapy" (Table 6.1). In their view, chronic tramadol and opioid therapy are to be initiated by specialists. Tramadol is a schedule IV controlled substance in the US and requires proper counseling of patients to mitigate its risk of abuse and potentially fatal overdose due to respiratory depression. This is particularly true of the ER (extended release) forms that are NOT to be crushed, cut, broken or dissolved.

Other Agents

3rd and 4th line agents include strong opioids, botulinum toxin A, cannabinoids, and other seizure medications such as lamotrigine and lacosamide. Older reviews on the subject [6] mention other 4th line agents in the categories of SSRI's (selective serotonin reuptake inhibitors), sodium channel blockers (mexiletine), NMDA receptor antagonists (dextrometorphan and memantine). Given this book is directed at primary care, it is probably best to defer prescribing these agents to a specialist as some of these agents are controversial in that there are weak to strong GRADE recommendations **against** their usage [5].

There is also an agreement that centrally caused neuropathic pain cannot be treated with topical agents (such as Botulinum toxin, lidocaine patches/creams, or capsaicin). Topicals can be considered first line treatment for those not tolerating oral medications [9] or for the elderly [5], while

Neuropathic pain medications
Except trigeminal neuralgia: use carbamazipine first line

First line	TCAs	Anticonvulsants	SNRIs

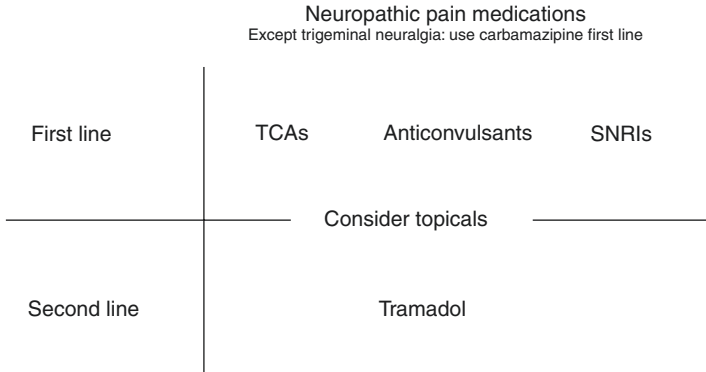Consider topicals

| Second line | | Tramadol | |

Figure 6.3 First and second line therapies for neuropathic pain. Topicals are placed on the border as they can be first or second line therapy depending on the clinical situation. TCA's include amitriptyline and nortriptyline. Anticonvulsants include gabapentin and pregabalin. SNRIs include duloxetine. Topicals include capsaicin cream, and topical lidocaine

other clinical guidelines suggest their use as second line therapy. Figure 6.3 summarizes the first two steps with topicals placed in the border between first and second line therapy to consider their use when clinically appropriate.

Finally, there are significant limitations to the current studies and their recommendations. For example, current guidelines do not indicate which first line agent to select first [5]. Consequently, as primary care physicians, we need to carefully choose agents based on side effect profiles, patient tolerance of medication, and perhaps financial considerations. Furthermore, the staples of primary care pain control, NSAIDS and acetaminophen, have not been studied for their usage in chronic neuropathic pain [5]. In addition, most of the studies have largely been in diabetic peripheral neuropathy and post-herpetic neuralgia given their common place [5, 20]. Fortunately for primary care, this allows the studies to be more applicable to our realm of practice. In addition, substantial benefit has been commonly defined to be 50% reduction in pain, and modest benefit to be 30% reduction in pain [3, 5, 6].

The overwhelming majority of clinical studies included in these reviews did not surpass 12 weeks in duration. Consequently, for many patients, optimal pain control with one agent is still wanting or may not be effective past 3 months. The benefits and risks of combination therapy, in addition to long term usage of these medications, still remains to be answered [3, 5].

Lastly, a word of caution: many of the authors writing guidelines have pharmaceutical affiliations, noted in their conflict of interest declarations. As an example, a recent Cochrane review by authors with no known conflicts of interests (dated in the same year as the NEUPSIG Lancet review) states there is little evidence to support the efficacy of nortriptyline in chronic neuropathic pain [21]. Unfortunately, it is unclear how much influence conflicts of interest may have on interpretation of results, outcomes, and development of guidelines that we as primary care base so much of our decisions upon.

Nociceptive Pain

Nociceptive pain arises outside of the nervous system, chiefly due to sensing damage to tissues [22]. Examples of nonexclusive categories of damage include inflammation, mechanical compression, and musculoskeletal conditions. It can be divided into somatic (muscle, skin, bones) and visceral (internal organ) pain [22] (Fig. 6.4). Back pain and osteoarthritis are common examples. A step-wise approach to pain control has been historically advocated. Nociceptive pain treatment guidelines for step-wise therapies have not been rigorously developed as in neuropathic pain, likely as it consists of a heterogeneous group of pathologies. Consequently, the following is a consensus for general treatment escalation. Refer to individual conditions for the best pharmacological algorithms.

Consensus seems to suggest trying nonopioid medication first, such as acetaminophen, NSAIDs, or topicals such as lidocaine patch or capsaicin. Then adjunctives such as TCAs,
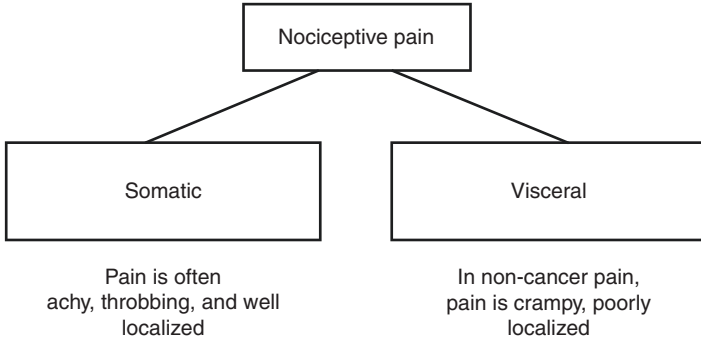
FIGURE 6.4 Nociceptive pain can be divided into somatic and visceral in origin. Note the different pain qualities depending on origin of pain

tramadol, duloxetine, and gabapentinoids are added or tried next. Finally, opioids are third line therapies (Fig. 6.5). Given the common place of acetaminophen, not much discussion in this book will be offered.

NSAIDs

A few noteworthy points about NSAIDs will be mentioned, although this is by no means an exhaustive guide to NSAID prescription. First of all, if one NSAID is not effective for pain control for a patient, consider switching to another NSAID. In addition, some studies have found that NSAIDs are in general more effective than acetaminophen [23], and that the combination has additive effects, with similar analgesia for acute pain when compared to opioid therapy [24, 25]. Given potential addiction and abuse, this information may be useful to either limit the prescription of opioids or limit the amount of opioid required in the acute pain setting.

NSAID use may cause gastropathy. Taking NSAIDs with food may mitigate its gastrointestinal (GI) side effects. Consider adding a proton pump inhibitor (PPI) for patients at high risk of GI bleeding [26]. High risk patients include

First line	Topicals, acetaminophen, Choose based on patient risk factors May combine classes if appropriate can trial different NSAIDs	NSAID "A" ↓ NSAID "B" ↓ NSAID "n"
Second line	Neuropathic pain medications TCAs, Gabapentinoids, Duloxetine Tramadol	
Third line	Opioids Use caution, may not be effective and have significant risks	

FIGURE 6.5 General step-wise medication management for chronic nociceptive pain. NSAID "A", "B", and "n" refer to the fact that different NSAIDs can be tried as one may be more effective than another for a given patient. Combinations of an NSAID and acetaminophen can be more effective than single agents alone. Topicals may be the first choice for those wishing non-oral medications, or have contraindications such as gastropathy. They include capsaicin cream, lidocaine cream or patches. Second line agents are typically TCA's (tricyclic antidepressants), gabapentinoids, and the serotonin norepinephrine reuptake inhibitor, duloxetine. Opioids are noted as third line to deemphasize their role in management of chronic nociceptive noncancer pain

those with a history of ulcers, GI bleeding, or dual antiplatelet therapy. Figure 1 in the expert consensus document on reducing the gastrointestinal risks of NSAIDs jointly authored by the American College of Cardiology Foundation, the American College of Gastroenterology (ACG), and the American Heart Association [26] contains a concise flow chart (available on pubmed via free public access) to assist with determining high risk patients.

In addition, obesity is another epidemic faced by primary care. Many patients are choosing bariatric surgery. Currently,

there is some conflicting data on NSAID usage in patients with Roux-en-Y gastric bypass and the risk of marginal ulcer disease and its complications [27–29]. Although it was not mentioned as one of the factors determined to be high risk by the ACG, some experts state to avoid their use [30], and caution (individualized risks and benefits, prescribing a low dose, short term therapy, close followup, and possibly adding PPI) should be exercised when choosing to prescribe NSAIDs to these patients.

Finally, NSAIDs (except selective COX-2 inhibitors) do inhibit platelets, but in general the duration is not as long as aspirin. Bleeding is a risk, and caution is advised during procedures.

Adjunctives

Brief points on adjunctives were discussed earlier in the neuropathic pain section.

Opioids

There is currently no evidence in treating chronic noncancer pain with opioids long term (>1 year). Opioid therapy abounds with significant risks including opioid overdose and death. In 2013 alone, millions abused opioids or became dependent on it [31]. Hundreds of thousands have already died from opioid overdose. This section will discuss the mechanisms for the risks and benefits of opioid therapy. It will also briefly discuss the pharmacology of opioids, which is key to the interpretation of urine drug tests. In addition, key evidence based facts concerning chronic opioid therapy will be discussed. How to make the clinical decision of starting chronic opioid therapy will be addressed. Management of the patient on chronic opioid therapy (COT) will be discussed in Chap. 8.

Opioids Act on Opioid Receptors

There are three types of opioid receptors, mu, delta, and kappa. Most clinically encountered opioids are a class of medication that activate mu receptors in the nervous system. Some opioids can also bind to other receptors as well, including delta or kappa. These receptors when activated, block the transmission of pain by various mechanisms, including decreasing calcium influx and reducing neurotransmitter release. These receptors are also responsible for producing the side effects such as euphoria, physical dependence, constipation, respiratory depression, itching, urinary retention, and nausea [22]. These are the "agonist" effects, when opioids activate (primarily) the mu receptor, blocking pain but also causing other unwanted effects. Familiar examples include morphine, oxycodone, hydromorphone (Dilaudid), and methadone.

In order to understand the drugs prescribed to treat some of the opioid associated problems such as respiratory depression and dependency, the concept of opioid receptor *antagonist* must be explained. Antagonist medications have the effect of binding to the opioid receptors (mu, delta, kappa) and *inactivating* the receptor, so that it cannot produce analgesia or its side effects. Common examples include naloxone (Narcan) and naltrexone, which compete for binding to all three opioid receptors and can reverse the effects of analgesia, euphoria, and most notably, respiratory depression [22].

There are also mixed agonist-antagonist opioids. These medications act as agonists on one opioid receptor, and at the same time act as antagonists on other opioid receptors. For instance, butorphanol (Stadol) blocks the mu receptor but activates the kappa receptor.

Absorption and Metabolism of Opioids

In clinical practice, morphine equivalents are emphasized as they are crucial to following prescription guidelines for

safety and efficacy. Morphine equivalents gives a rough guide to how to compare the potency of various opioids. Opioids have different morphine equivalents given various factors. Oral opioids are absorbed through the GI tract and metabolized (and therefore inactivated) by the liver. The amount of drug practically getting to the nervous system is therefore reduced due to the absorption process and liver metabolism. This is called the first pass effect. As a consequence, pathology in the GI tract and liver can then alter the bioavailability, and therefore change the potency of orally administered opioids. If there is liver dysfunction, opioids are often more potent. Similarly, intravenously administered opioids are also more potent (given the same dosage) because they are 100% bioavailable since they avoid the first past effect. Therefore route of administration and how the opioid is absorbed and metabolized affects its "morphine equivalent".

Morphine Equivalent Calculation

Handy online calculators for morphine equivalents can be found at:http://www.agencymeddirectors.wa.gov/Calculator/DoseCalculator.htm. Table 6.2 shows conversion factors in order to compute morphine equivalents by hand [32]. The Centers for Medicaid and Medicare Services (CMS) also publishes their own table as well [33]. (Note, the methadone conversion factor is much smaller in the CMS table, and not noted to be dose dependent Table 6.3.)

Conversion Warnings

The above is to calculate a patient's morphine equivalents per day. Conversion tables are to be taken as approximate conversions. As will be explained later, patients metabolize opioids differently. There are pharmacokinetic properties of opioids that can lead to overdose if patients are being switched to a different opioid [34]. Even if they are given

TABLE 6.2 Conversion factors for morphine equivalents

Opioid	Conversion factor
Morphine	1
Hydrocodone	1
Oxycodone	1
Fentanyl transdermal micrograms/hour	2.4
Hydromorphone	4
Methadone (mg/day)	Varies depending on dosage
1–20	4
21–40	8
41–60	10
≥61–80	12
Codeine	0.15

TABLE 6.3 Sample calculation: patient takes hydrocodone-acetaminophen 10–325 mg 4 tabs a day and methadone 10 mg TID. How many morphine (mg) equivalents (MME) is that per day? (Assuming methadone conversion factor is 8 at that dosage)

Steps	Example calculation
1. Add up how many milligrams total for each medication per day	Hydrocodone: 10 mg × 4 tabs/day = 40 mg/day Methadone 10 mg × 3 tabs/day = 30 mg/day
2. Multiple the total mg/day by conversion factor for that medication to get MME	Hydrocodone: 40 mg/day × 1 = 40 MME/day Methadone 30 mg/day × 8 = 240 MME/day
3. Add up all MME to get total for the day	240 + 40 = 280 MME/day

"equivalent doses" of a new opioid, there can be accidental overdose due to cross-tolerance and individual genetic variation.

Consequently, there are some warnings.

1. do not use for obtaining "dose equivalents" i.e. converting from one opioid to another.
2. new opioid must be dosed substantially *lower* in order to avoid accidental overdose
3. methadone conversion factor can vary based on dose

Methadone

Particular attention will be focused on methadone given the risks of overdose in this synthetic opioid. It is a unique opioid in that it is not only a mu and delta receptor agonist, but also an NMDA (N-methyl-D-aspartate) receptor antagonist, and inhibits serotonin and norepinephrine. Its use can be particularly advantageous compared to other opioids for certain clinical situations: allergy to morphine, renal failure because it is not significantly removed by dialysis [35], and opioid-induced hyperalgesia. However, due to its complex pharmacodynamic properties, calculating the morphine equivalents is not an exact science and research continues in this area [36, 37]. There are variations in published tables of conversion factors. Consequently, converting patients from one opioid to methadone must be done with extreme caution given the risks of overdose and deaths that may result given the long half life of methadone and individual conversion variability [38]. If required, this might best be done through specialist consultation. Methadone also may cause cardiac conduction abnormalities such as increased QTc and Torsades de Pointes. Consequently, for most primary care purposes, conversion tables for methadone should be used to calculate a rough estimate of MME for the chief purpose of determining if a

patient is on a high dose of opioids. In order to prevent accidental overdose, conversion tables should generally not be used to convert short acting medications to methadone by the average primary care provider.

Codeine Is a Prodrug

Other medications, such as codeine, are prodrugs. Prodrugs are inactive compounds. Codeine must be first metabolized by enzymes (CYP450 system) in the liver and converted into morphine before effects can occur [22]. It is also metabolized in small amounts into hydromorphone (<11%).

Opioid Metabolism May Cause Drug Interactions and Affect Urine Drug Testing Results

Opioids are metabolized by the liver by the

1. cytochrome system
2. conjugation (chiefly glucoronidation which makes them water soluble)
3. or both cytochrome system and conjugation [39].

Because many drugs may inhibit or induce the cytochrome enzymes, opioid levels can also be affected. Inhibitors may cause current levels of opioids to reach toxic levels, leading to stupor and death.

Some metabolites are active compounds and can confuse urine drug testing results. For instance, morphine is metabolized into small amounts of hydromorphone (usually less than 2.5% of the morphine concentration [40]). Hydrocodone is also metabolized to hydromorphone [39]. Chapter 8, Management of the patient on chronic opioid therapy will detail interpretation of urine drug testing in light of metabolites.

Opioids Are Excreted Renally

Lastly, opioids are also excreted renally. Caution must be taken when prescribing opioids in patients with renal dysfunction. There can be toxic accumulations of active metabolites when excretion is impaired. This is thought to occur especially with morphine, and less so with oxycodone [39].

Effectiveness of Opioid Therapy Can Vary Due to Genetics

Finally, there are many enzymes involved in metabolizing opioids. These are all coded by genes. Given genetic differences, opioids are consequently metabolized differently amongst individuals and populations. Therefore, there are varied responses to the same opioid therapy [39, 41].

Initiating Opioid Therapy: Factors to Consider

As mentioned previously, it is a harsh reality that, in most patients, chronic pain is never fully relieved. In light of uncontrolled pain, as physicians we often want to help. However, evidence has shown what many physicians have long believed about those on chronic opioid therapy- that many are indeed dependent or have opioid use disorder [42]. Therefore, extreme caution must be used when initiating and continuing chronic opioid therapy. A 2016 JAMA review summarized the CDC guidelines and evidence on prescription of opioids for chronic pain [34]. Based on the evidence from that review Box 6.1 lists key points to carefully consider when discussing or contemplating opioid therapy for patients.

Box 6.1 Key Evidence Based Points to Consider When Contemplating Opioid Therapy
- There are no studies to show effectiveness of long term opioid therapy (>1 year), most studies are for less than or equal to 6 weeks.
- Long term (2–6 months) exercise therapy and has been shown to be effective for many nociceptive noncancer chronic pains such as osteoarthritis and low back pain.
- Opioid therapy for acute pain can lead to chronic opioid therapy
- Extended release/long acting opioids have greater risk for overdose and death. Start with short acting opioids.
- The higher the morphine equivalents, the greater the risk for overdose, death, dependence, abuse.
- Evidence is inconsistent for using Opioid Risk Tool for predicting opioid misuse/abuse

These studies reveal the harsh reality of the current state of chronic opioid therapy: there will be deaths, there will be addiction, and yet, after all this, pain will still be uncontrolled. There is no dosage of opioids that does not carry risk [43]. Even at "low" MME (such as <20) there are still overdoses and deaths, just less than at greater MME (such as >50 or >100) [34, 43]. And although we have tried to develop risk stratification tools to help us to predict who will abuse opioids, current evidence is limited and their efficacy is still debatable. On the other hand, there is evidence for safer, nonpharmacological therapy such as CBT, exercise, and multimodal therapies. For noncancer nociceptive chronic pain, in my opinion, one must have a very compelling reason to initiate such a questionable therapy with so much harm.

Currently, Dowell's condensed review in JAMA of the CDC guidelines does not dictate an algorithm to follow for *deciding* to initiate chronic opioid therapy for noncancer pain. It does recommend that treatment must be individualized, and benefits must outweigh risks. The American Society of Interventional Pain Physician (ASIPP) Guidelines recommends a complete history and physical, documenting diagnosis, past interventions, social and psychiatric history prior to initiating COT [44]. The underlying presumption of requiring the full history and physical is that the information obtained will enable the primary care provider to decide whether COT is appropriate. As in much of medicine, decisions are individualized and benefits of therapy must outweigh the risks. Box 6.2 lists additional points of history that are recommended by the ASIPP and CDC to aid in deciding whether COT is appropriate.

Box 6.2 Additional History to Obtain When Contemplating Offering Chronic Opioid Therapy
- Psychiatric history: depression, suicide attempt
- Detailed substance use history
- Fall risk
- Sleep: poor sleep, sleep apnea
- Functional status: Activities of daily living, ability to work, play, socialize
- Past interventions (pharmacologic and nonpharmacologic) and outcomes
- Addiction risk screening: Opioid risk tool, etc.
- Fact checking: obtaining urine drug tests, checking prescription drug monitoring databases

Table 6.4 summarizes some factors that make chronic opioid therapy potentially more harmful. It may serve as a quick reference in order to weigh the individual risks and benefits for the patient. With more "yes" answers, the patient has more risk factors for experiencing harm from chronic opioid therapy. Obviously, some risk factors may be weighed more heavily than others.

TABLE 6.4 Checklist of clinical factors that increase the risk of chronic opioid therapy

Factors contributing to ineffective or higher risk chronic opioid therapy	Yes	No
Urine drug testing positive for illicit substances		
Prescription drug monitoring database shows multiple providers prescribing multiple opioids, or other scheduled substances		
CV system: Heart failure, cardiovascular risk factors (risk of heart attack, stroke high)		
Respiratory system: Sleep apnea, disorders of breathing		
GI system: hepatic insufficiency		
Renal system: Renal insufficiency		
MSK: frequent falls, low back pain,[a] hip or knee osteoarthritis[a]		
Endocrine: history of androgen insufficiency, erectile dysfunction, obesity (risk factor for sleep apnea)		
NEURO: fibromyalgia,[a] headache,[a] cognitive impairment		
OBGYN: pregnancy		
Psychiatric: history of suicide attempts, depression, substance abuse, history of overdose		
High scores on opioid risk assessment tools		

[a]Current evidence is limited or insufficient for improved pain or function when treating these conditions with chronic opioid therapy [45, 46]

Opioid risk assessment tools can be found online:

1. Opiod risk tool: Paper version: http://www.agencymeddi-rectors.wa.gov/files/opioidrisktool.pdf
2. Opioid risk tool Online calculator: https://www.mdcalc.com/opioid-risk-tool-ort-narcotic-abuse
3. Screener and Opioid Assessment for Patients with Pain - Revised (SOAPP-R) [47] (24 self-report questions, need license agreement.)

Again, there is limited evidence for the effectiveness of screening tools, but some reviews seem to suggest SOAPP-R has more evidence supporting its use [48].

Practical Opioid Initiation

Initiation of COT requires many steps which, when given current limitations in visit time and resources, will necessitate multiple office visits. Reasonable expectations must be set when beginning to evaluate the appropriateness of COT with patients. It does not have to be done in one visit. The primary care provider needs to form a biopsychosocial understanding of the patient and have enough evidence to support the diagnosis and treatment plan.

There are basically two purposes for initial office visits:

1. Gathering information

   • Pain and function goals
   • Support for the diagnosis
   • Find information that may make opioid treatment harmful
   • Ruling out aberrant behavior

2. Optimizing pain management

   • Assessment of goals: pain control and function
   • Medication optimization
   • Nonpharmacological optimization

If pain control or function is still not adequate in light of patient goals, then one begins to consider offering COT. This

is a crucial point. COT does NOT need to be offered. There is no need to even consider offering opioids if a patient is satisfied with their current pain treatment and function. Even if pain is not controlled and pain-related goals are not met, COT does not need to be offered if risks outweigh the benefits. This also highlights the importance of realistic goal setting.

The process of deciding whether or not to offer COT depends on history and physical, ongoing information gathered concerning the patient, and whether treatment can be optimized without opioids. This involves gathering information to support the diagnosis (labs, imaging, orthopedic consults, etc.). Recall some diagnosis may not benefit from opioids and have specific therapies. Other important facts to gather include urine drug testing results, activity found on prescription drug monitoring databases, and history about past drug use, psychiatric history, sleep history, cardiac risk factors, etc. The data gathering stage may include opioid risk factor assessments and checking if the patient has any of the conditions listed in Table 6.4. This information will help you to weigh the potential risks and benefits of COT.

Visits can also focus on optimizing current pain control and function. For instance, the medication regimen may be optimized by adding adjunctives or increasing medication dosages. The patient may have never tried physical therapy and it is warranted in their condition. Patients may benefit from orthopedic consult or a structured weight loss program.

All this time, patients goals are continually reassessed. If goals are being met (and *not* necessarily 100% pain free), then there is continued surveillance of their pain, function, and adequacy of their treatment regimen. If goals are not met, and if opioids would benefit the patient, than prescribing short term opioids may be an option. If goals are not met, and patient is not a COT candidate, then a referral to pain specialists may be required. Regardless of whether a patient is on opioids or not, continued surveillance of their pain, function, and adequacy of their treatment in light of their evolving goals is required. Figure 6.6 illustrates this process, which will likely take several office visits for a patient not currently on opioids.
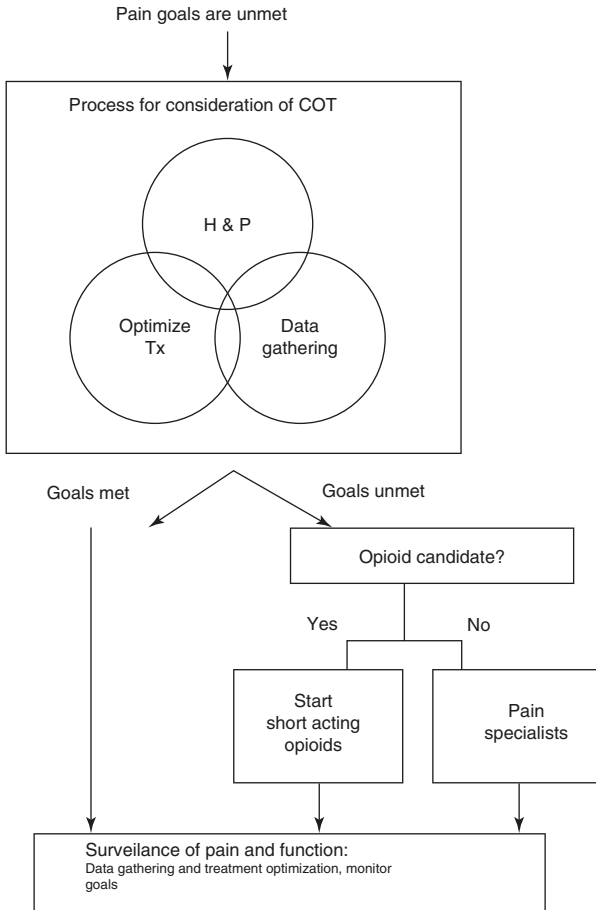
FIGURE 6.6 Deciding whether chronic opioid therapy (COT) is appropriate is a complex and time consuming process. This schematic illustrates the process by which the chronic pain patient who has unmet goals is evaluated and managed. Each circle represents the chief focus of an office visit. The circles overlap as some office visit agendas may address multiple aspects of care. Information gathering can include: diagnostics, consults, urine drug screening, accessing prescription drug monitoring sites, obtaining records, assessing opioid risk factors, and assessing patient goals. Optimizing treatment includes medication adjustment, prescribing nonpharmacological intervention, referral to psychiatry, physical therapy, and other specialists. Abbreviations: COT chronic opioid therapy, H & P history and physical, Tx treatment

Remember key evidence based facts: that chronic pain is never fully eliminated, and even with opioids, the total elimination of pain is elusive. Opioids are full of risks, from cardiovascular, respiratory depression, overdose, and death. Certain conditions offer no benefit (in terms of pain or function) versus non-opioid therapy. Many recommendations even state that nonpharmacological therapy should be first line. Providers do not need to offer chronic opioid therapy if risks outweigh the benefits. The next chapter discusses the nonpharmacological and multidisciplinary management of chronic noncancer pain.

Initiation of Short Acting Opioids Safer than Long Acting

Finally, if the provider has carefully considered and documented the risks and benefits of COT and has decided that it is appropriate for the patient, then short acting opioids are recommended over long acting [34, 44]. Low dosages are recommended. Low dose can be defined as <40 morphine mg equivalents per day [44]. Table 6.5 goes over commonly accepted definitions of low, moderate, and high dose opioid therapy [44].

Initiation often requires a full office visit to fully go over risks and benefits of therapy. Opioid treatment agreement ("pain contracts") are recommended to write down goals, define benefits of therapy, and explain risks. The treatment agreement can let the patient know expectations of behavior, frequency of urine drug testing and future appointments.

Table 6.5 Commonly accepted definitions of chronic opioid therapy strengths

Strength of opioid therapy	Morphine milligram equivalents/day
Low dose	<40
Moderate dose	40–90
High dose	>90

More on this will be discussed in Chaps. 8 and 9. Future visits assess for effectiveness, which is often defined as at least 30% reduction in pain or improvement in function. Adverse effects such as constipation and sedation should be assessed at return visits. Aberrant behavior also needs to be monitored. Routine urine drug testing and access of prescription drug monitoring databases are advised. High dose and long acting opioids should be prescribed with extreme caution and reserved for cases of intractable pain. Periodic EKG's should be considered for patients on methadone therapy. Concurrent prescription of benzodiazepines are to be avoided. And finally, reduction of opioids are appropriate if there are too many adverse effects or therapy is ineffective [34, 44]. The specifics of managing a patient on COT will be discussed Chap. 8.

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Chapter 7
Management of Chronic Pain: Nonpharmacological and Multidisciplinary Approach

Bonnie Huang Hall

Introduction

Besides prescribing medication, one of the key roles of the primary care provider is the coordination of specialists and nonpharmacological aspects of care. Management of the patient with chronic pain requires a multidisciplinary approach. Key aspects that require managing include goal setting, exercise and physical therapy, psychological and social factors, specialists and interventional pain procedures.

Goal Setting

Setting appropriate goals and expectations of treatment is included in the CDC Guideline for prescribing opioids for chronic pain [1]. Usually this centers around what is important to the patient. Many suggested goals, examples of which

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can be found at "mytopcare.org [2]," center around patient activities of daily living and function. Mytopcare.org is a free website with various resources on opioid prescribing. It was founded by Leibshutz and others at Boston Medical Center in order to facilitate safe and effective opioid prescribing in primary care.

Currently, however, there is limited evidence or instruction on how to set goals with patients with chronic pain. One study elicited outcomes important to patients with chronic pain, as if they were participating in an experimental study on a new pain medication. Most of the commonly cited endpoints were decrease pain, decrease opioid dose, decrease frequency of scheduled doses, increased ability to function, and improved sleep [3]. Another interesting study focused on soliciting two to five behavioral goals (as opposed to pain relief goals) from patients and categorizing them [4]. This study on veterans found that the more goals patients accomplished, the less they rated their pain intensity and depressive symptom severity. It suggested that perhaps if patients had more easier goals to accomplish, they would perhaps experience less pain and depression. It found the most common goal was improving the physical activity of walking. It also used a standardize script to help patients formulate their behavioral goals:

> We would like you to set some goals that you can work toward over the next few weeks. These should be goals that you can reasonably achieve over the course of therapy. Goals can be any positive behavior that you would like to increase. For example, they can be something you have done in the past but would like to do more often, something you have been meaning to do but have been putting off, or something you have never done, but would like to try. Use the goal setting form below to come up with at least 2 goals for treatment.

In this study, cognitive behavioral therapists worked with patients to ensure that their goals were:

1. a behavior within the participant's control
2. goal was measurable
3. not primarily focused on pain reduction (i.e., reduce pain totally or by a specific amount)

Consequently, a take home point is to make practical goals, which are measurable. These goals often specify an action and frequency:

• Being able to do one load of laundry once a week
• Being able to walk 10 minutes 3× a week
• Take grandkids to the park for 30 minutes once per week

However, decreased pain is still a significant goal, especially in the context of chronic opioid therapy, given the risks involved. Risks of oversedation, overdose, and death are a reality for those on chronic opioid therapy (COT). In order to determine if opioid therapy is meeting goals, goals must be specific and measurable. Many studies use pain relief of 30% (moderate pain relief) and 50% (substantial pain relief) to determine if pain therapy is effective [5–7]. Interesting to note that clinical pain relief does not entail the complete eradication of pain. Currently, complete pain relief in those with chronic pain appears to be an unrealistic goal. Proper goal setting involves the expectation that pain, unfortunately, cannot be eliminated, but rather, managed in order to accomplish patient goals. It is helpful therefore to quantitatively assess pain before and during treatment in order to determine if pain relief goals are being met. For those on any therapy including opioids, if treatment is not successfully providing pain relief, dosages should be modified or stopped. The fact that ineffective therapies (where benefits do not outweigh risks) will be tapered should also be emphasized in the goals and expectations of treatment.

That being said, lately, there has been a trend towards making behavioral or functional goals as opposed to pain intensity goals [8, 9]. This is because there is often a disconnect between pain intensity and pain pathology. At the same time, there is a correlation of patients with high pain intensity scores and feeling overwhelmed and unable to cope [8]. Returning the ability to enjoy life by restoring function, despite pain, seems to be an important outcome to these patients. It may even lead to reduction in pain intensity in the end [4].

Exercise and Physical Activity

As part of the comprehensive pain management plan, the primary care provider can also incorporate exercise suggestions. A recent Cochrane review in 2017 found evidence that exercise seems to be beneficial to adults with chronic pain with little adverse effects [10]. Indeed, exercise has recently been recommended as first line therapy (even before medication) for acute and chronic low back pain by the American College of Physicians [11]. Generally exercise has been found to improve function, disability, and sometimes decrease pain scores. Methods in which the primary care provider can encourage exercise include "behavioral control techniques." These include teaching and demonstrating exercise, promoting self monitoring techniques, and goal setting [12]. Certain conditions may benefit more from exercise or physical activity such as osteoarthritis and low back pain [13–17]. So far, no studies have conclusively shown that one method of exercise is superior to another.

The American Academy of Orthopaedic Surgeons supports the website, "https://www.orthoinfo.org/." This free website contains ready to print patient handouts on home exercises for various conditions affecting, for instance, the shoulder, hip, knee, and spine. It also contains helpful patient handouts on preventing low back pain.

There are various types of exercise therapy that may be considered in the treatment of chronic pain. Detailed discussion can be found in Chap. 16.

Diet

Currently there is not much evidence to support a certain diet for those with chronic pain. There is evidence that those with chronic pain often do not eat a healthy diet rich in fruits and vegetables [18]. Those with chronic pain often have cardiovascular risk factors which need to be modified [18, 19].

Whether or not correcting their diet will help their pain and function is still in question. Currently there is research interest in anti-inflammatory or plant based diets and their role in reducing pain and improving function [20–22]. Seaman, a supporter of anti-inflammatory diet for chronic disease and pain, makes an interesting observation that NSAIDs (nonsteroidal anti-inflammatory drugs) are often used in treatment of chronic pain, and hence infer that an anti-inflammatory diet can also be used to treat chronic pain. Again, there needs to be more evidence before diet can be regarded as an effective treatment for chronic pain.

Heat

Heat (as opposed to cold) therapy has been found to be beneficial in subacute low back pain [23, 24]. There are some small studies showing that superficial heat with or without additional modalities such as exercise and ultrasound, can show promise in improving chronic low back pain and chronic knee pain [25–28]. Heat wraps are a relatively inexpensive and easy to implement with few adverse effects when used correctly. Because patients can easily implement this therapy on their own, they may feel more self-efficacious and have less negative thought patterns (such as catastrophizing) [27].

Biopsychosocial Management

The biopsychosocial model is a framework that can be used to comprehensively treat chronic pain. It suggests that pain is not just biological or physical, but also that psychological and social factors contribute to chronic pain [29, 30]. When all three realms have been addressed, studies have shown it has been used successfully to manage many chronic pain conditions such as arthritis, fibromyalgia, chronic low back pain, sickle cell, etc. [29, 31] Often termed multidisciplinary rehabilitation, or biopsychosocial rehabilitation, it has been found

to be effective in a 2015 Cochrane review for chronic low back pain [32]. Although often requiring a team of specialists from physical therapists, psychologists, etc., the primary care provider can indeed be instrumental in beginning to address the psychological and social aspects of chronic pain [33]. Fully addressing the psychological and social aspects of chronic pain often involves cognitive behavioral therapy. Cognitive behavioral therapy (CBT), a treatment often employed by psychologists or psychiatrists, enables patients to correct negative thinking patterns and thus change behavior. A 2012 Cochrane review concluded that cognitive behavioral therapy is a useful approach to chronic pain [34]. Based on data from 35 randomized controlled trials, this review found that cognitive behavioral therapy can improve mood, weakly improve pain compared to no treatment, has small effects on pain related disability, and decrease negative thought patterns such as catastrophizing. (Studies on psychological therapies for neuropathic pain, however, were few. Consequently a 2015 Cochrane review did not find enough evidence to support use of CBT or psychotherapy for neuropathic pain [35].)

Biopsychosocial Management: Positive Affect Interventions

What can the primary care provider do? Besides educating the patient on the biological aspects of chronic pain and their specific disease, primary care providers can acknowledge the co-existence of negative mood states such as depression, anxiety, emotional distress, etc. Screen chronic pain patients for these comorbidities and treat them. Inform patients that these negative affects have been associated with more pain and disability than those with positive affects. Some studies even show that fostering a positive affect allows decrease in pain intensity and disability [36, 37]. These "positive affect interventions" are activities that primary care providers can easily direct patients to perform in a journal. Some example interventions used are seen in Table 7.1 [36].

TABLE 7.1 Positive affect interventions primary care providers can use to improve pain and disability. Adapted from Hausman [36]

Intervention name	Explanation of how to perform
Three good things	Write down three things that went well each day and why they happened
Strengths	Make a complete list of strengths Make sure to use a strength each day
Gratitude visit	Write a thank you letter to someone you know. Read it aloud to them.
Savoring	Spend time focusing on a positive experience, 2–3× a day
Active-constructive responding	When someone shares good news, practice responding positively
Life summary	Reflect and write a summary of how one desires to be remembered

Biopsychosocial Management: Correct Solicitous Relationships

Another aspect of the biopsychosocial model of pain that the primary care physician can explore is social aspects of pain. Questions to explore include [29]:

1. How has pain changed lifestyle/roles at home/employment?
2. What is the level of social support?
3. Any "solicitous" social interactions?

Solicitous interactions are social interactions in which another person potentially disables the patient by being overly concerned or anxious about the patient's pain and consequences of pain. They may say things such as, "Don't go to the party, it's too exhausting for you and will make your pain worse." Or they may spend more time helping the patient unnecessarily, "Let me get you the remote control, you can't be walking around the house in your condition."

Studies show that these relationships can cause the patient to respond by increasing disability, using more opioids [38], and experiencing more pain [39–42].

These negative interactions can be addressed by involving the spouse in the cognitive behavioral treatment plan. There is some evidence that couple interventions may be effective in reducing pain intensity [43].

Biopsychosocial Management: Minimize Catastrophizing

In addition, the primary care provider can identify catastrophizing thoughts. Catastrophizing is a cognitive and emotional response to pain consisting of three parts [30, 44]:

1. Magnification: "I keep thinking the pain will get worse"
2. Rumination: "I can't stop thinking about how much it hurts"
3. Helplessness: "I can't do anything to make it better"; "I don't think it will ever get better"

Again, catastrophizing is a type of negative thinking that significantly worsens pain and disability. Some say it is the single most important factor that impairs the effectiveness of pain relieving treatments in certain musculoskeletal conditions [45, 46]. Correction of these negative thoughts includes cognitive behavioral therapy (CBT) and acceptance and commitment therapy (a variation of CBT). In addition, physical therapy has been shown to reduce catastrophizing [47]. There is evidence to suggest that a reduction in catastrophizing precedes improved pain outcomes [44]. Catastrophizing can be measured with the Pain Catastrophizing Scale (PCS) [48]. It is a 13 item questionnaire which is available online http://sullivan-painresearch.mcgill.ca/pdf/pcs/Measures_ PCS_Adult_English.pdf.

Biopsychosocial Management: Enforce Positive Expectations and Teach Self-Efficacy

On the other hand, expectations of getting well, or being optimistic about treatment and pain, does decrease pain intensity and increase effectiveness of treatment (or placebo). If the primary care provider and patient expects there to be improvement with treatment, then the patient will more likely make progress [30]. Similarly, if patients can do more for themselves, ("self-efficacy") and feel more capable of tackling pain and achieving certain pain related goals, then they also experience improvements in pain and disability. Increasing self-efficacy can also be mediated through CBT [30]. As primary care providers, we can teach patients how to treat acute pain flareups to improve their self-efficacy [29]. This includes utilizing heat or cold packs, positional changes, massage, or exercise.

Manage Consultants

Another component of pain management is effective involvement of specialists [1]. Experts can not only provide insight on conditions causing pain, but also perform pain management therapies that require special training. For instance, urologists may offer specialized treatments such as DMSO (dimethyl sulfoxide) instillation and bladder hydrodistension for interstitial cystitis. Orthopedic surgeons can offer therapeutic joint injections or surgery.

Interventional Pain Management

Pain specialists, often neurologists, interventional radiologist, or anesthesiologists, can also provide pain relieving procedures targeted at the nervous system. Referrals to these spe-

cialists are often made after various treatments recommended by primary care physicians have failed or the patient's pain and disability is severe. The mechanisms of how these interventions work on a molecular level can be complex, but at the heart of these is that nerve function is altered. Pain is no longer perceived in the same way after these interventions. There are various techniques used to alter nerve function, also known as neuromodulation. These techniques alter the sensation of pain by affecting nerve activity through various stimuli.

There are so many methods to alter nerve function and thus change the conduction of pain signals. The primary care provider can be daunted with the complexity and diversity of these interventions. However, any intervention for pain can be thought of as a combination of three components: a stimulus that alters nerve function, a delivery method, and a nervous system target (Fig. 7.1).

The following is a brief overview of a few types of methods to deliver substances or energy to alter pain sensations. Some are more invasive and thus are surgical procedures, whereas others are noninvasive and not typically thought of as a "procedure."

One of the more common interventions for pain is injections of various compounds such as anesthetics and steroids. These include epidural injections and other spinal injections [49], intercostal nerve blockage, and other peripheral nerve injections. These injections often use anesthetics to block pain signals and steroids to reduce inflammation with reliable short term relief. Evidence for long lasting effects of pain injections for low back pain is, however, lacking [50]. In addition, literature is mixed on the efficacy of these injections on spinal stenosis, and other conditions associated with back pain [50, 51].

Other methods include sympathetic nerve blocks. This technique is typically used to treat phantom limb, complex regional pain syndrome, and pain syndromes of the head and neck [52].

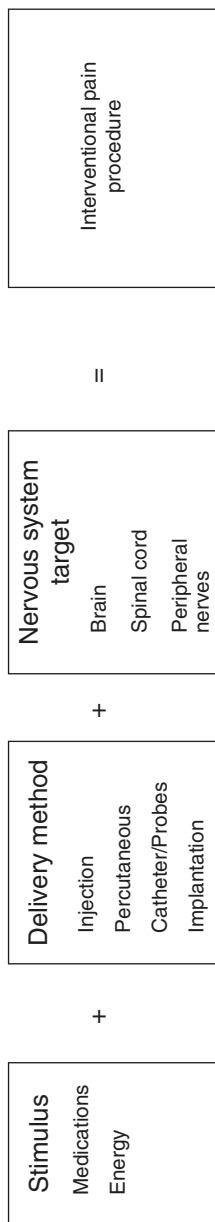| Stimulus	+	Delivery method	+	Nervous system target	=	Interventional pain procedure
Medications Energy		Injection Percutaneous Catheter/Probes Implantation		Brain Spinal cord Peripheral nerves		

FIGURE 7.1 An interventional procedure for pain is essentially a summation of three components: a stimulus, a delivery method for the stimulus, and a nervous system target. Stimuli modify nerve function. They include both medications and various forms of energy. Medications include anesthetics, toxins, steroids, and opioids. Various forms of energy include heat, cold, magnetic fields, electrical current, ultrasound, etc.

Botulinum toxin is a neurotoxin that is best known for inhibiting muscle contraction for the treatment of wrinkles. It has also been useful for the treatment of chronic migraine. A recent review discusses the myriad of pain diagnoses that may benefit from botulinum toxin [53]. Temporal mandibular joint disorders, myofascial pain, neuropathic pain, trigeminal neuralgia are just a few conditions in which botulinum toxin has been used to ameliorate chronic pain [53].

Injection of neurolytic substances have also been documented to treat chronic pain conditions. Such substances include adriamycin (a chemotherapeutic agent), alcohol, glycerol, etc.

Lastly, there is intrathecal drug delivery, so called, "pain pumps". These are surgically implanted devices that allow for the continuous delivery of morphine, baclofen, zicotinide (an analgesic acting on the calcium channel blocker) and other compounds to the spinal cord.

Radiofrequency ablation or denervation, another interventional technique used for the treatment of chronic pain, delivers thermal energy to block sensory nerves innervating the area of pain [54–56]. For instance, for knee pain, the genicular nerves are targeted. Electrical current is delivered to the tip of an insulated needle directed at the peripheral nerve. An electric field is produced at the tip of the needle which causes molecular movement and heat. At a certain temperature, the heat will cause a lesion in the nerve and is thought to be responsible for disruption of the pain signal. It has been used in conditions such as chronic low back pain, knee pain, trigeminal neuralgia, and other conditions. There is some evidence suggesting the effectiveness of these techniques in various chronic low back pain conditions and knee pain [55–57]. There are also cryoablative methods as well [58].

Invasive Neurostimlation Techniques

Invasive neuromodulating techniques include deep brain stimulation [59], spinal cord stimulation [52, 60], and periph-

eral nerve stimulation [61]. Deep brain stimulation is an invasive neurosurgical procedure where electrodes are implanted in various brain structures. Pain is replaced often by pleasant paraesthesia or warming sensation and analgesia depending on which brain structures are targeted [59]. It can be used for post-stroke syndrome. Spinal cord stimulation uses implanted electrodes to provide electrical stimulation to the spinal cord. It replaces pain with paraesthesia. It is commonly used in failed back surgery syndrome and neuropathic pain. Peripheral nerve stimulation is direct electrical stimulation of named nerves that send pain signals from the region of pain. It also requires the use of electrodes surgically implanted next to the nerve and is commonly used to treat postherpetic neuralgia, neuropathies after surgery or trauma, complex regional pain syndrome, and various migraine and headache syndromes [61].

Noninvasive Neurostimulation

Noninvasive neurostimulation techniques act on the nervous system externally. These include transcranial current or magnetic stimulation [59] for the brain, and transcutaneous electrical nerve stimulation (TENS) for the peripheral nerves. A recent Cochrane review concluded that there is very low quality evidence that transcranial magnetic stimulation and transcranial direct current stimulation may affect chronic pain and improve quality of life in the short term, but measured effects were minimal [62]. As for TENS, electrodes are applied via adhesives to the skin so that pulsed electrical stimulation can be delivered to the area of pain. Although often used as an adjunctive to the treatment of chronic pain, a recent Cochrane review was unable to find conclusive evidence that TENS is harmful or beneficial to people with chronic pain [63]. Lastly, there is ongoing research into different methods for neuromodulation including the use of ultrasound on both the brain and peripheral targets.

Conclusion

In conclusion, the primary care provider can offer so much more than prescription drugs for chronic pain. In every office visit, the primary care provider can reassess goals and expectations, encourage positive affects, and identify negative affects. They can also encourage self-efficacy and correct negative affects and social interactions via referral to a specialist trained in CBT. Teaching exercises or referral to physical therapy is another aspect of care the primary care provider can manage. In addition, the primary care provider can also coordinate care with specialists that can provide pain relieving interventions.

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Part II
The Opioid Requiring Patient

Chapter 8
The Opioid Requiring Patient: Evaluation and Management

Bonnie Huang Hall

Helpful Tips
1. Always ask when was the last dose of opioids
2. Use a template for follow ups with patients on chronic opioid therapy
3. Prescription drug monitoring databases are updated anywhere from 24 hours to 1 x per week.
4. Opioid withdrawal is generally not deadly
5. Care must be taken when prescribing clarithromycin, antidepressants, and anti-fungals with those on chronic opioid therapy. Check a drug interaction application first.
6. Sometimes there is suspected aberrant behavior or the need to taper down opioids. Difficult conversations can be made easier with rehearsal of language suggestions (see Tables 8.8 and 8.9).

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Checklist

- [ ] Documented specific pain diagnosis that requires opioid medication (i.e. osteoarthritis, fibromyalgia, postherpetic neuralgia)

  [ ] Appropriate imaging, labs, and consults done to support diagnosis

  [ ] Documentation to support opioid use: (tried and failed/allergic to other medication, tried physical therapy, been to orthopedic surgeon, optimizing non-opioid treatment)

  [ ] Urine toxicology current

  [ ] Opioid agreement current (Consisting of goals, diagnosis, treatment plan, and expectations for patient including refill frequency, visit frequency, safety measures, risks and benefits, etc.)

  [ ] Evaluate and document effectiveness of opioids every visit. Use the 4A's. Adjust dose if necessary

  1. Analgesia – Document effectiveness and pain intensity
  2. ADL's – Document effects on activities of daily living (ADL's) or goals
  3. Adverse effects – Document any side effects and treatment of side effects (docusate for constipation)
  4. Aberrant behavior: using alcohol, drugs, unexpected urine toxicology results, selling/giving opioids away, obtaining opioids from elsewhere (check prescription drug monitoring program databases)

  [ ] Assess safety of opioids: lock medications, no driving if sedated, breathing problems and contraindications, concomitant use of benzodiazepines, dosage too high. Adjust medications if necessary, refer if necessary

     [ ] calculate and document Morphine Miligram Equivalents (MME)

     [ ] Naloxone if appropriate

     [ ] Depression screen current and score appropriate

     [ ] consider opioid use disorder, refer if necessary

  [ ] Appropriate follow up interval ≤ 3 mo, sooner if adjusting/starting medication

[ ] Optimization of non-pharmacological management: Cognitive behavioral therapy (CBT) for catastrophizing, positive affect interventions, exercise, weight loss, specialist referrals, etc.

Introduction

The patient already on chronic opioid therapy (COT) requires a high degree of care and coordination for the management of their chronic pain given the risks involved with COT. Inappropriate opioid therapy can be life threatening, whereas opioid withdrawal generally is not. This chapter discusses the CDC 2016 recommendations [1] and its practical application in the outpatient visit. The focus is on the safety of the patient on COT and whether harms of treatment outweigh the benefits.

Validity of Diagnosis

In this current age of corporate medicine, we often need to treat patients on COT that we previously did not treat or are unfamiliar with. Regardless of the reason why physicians (and other providers) are treating these unfamiliar COT patients, think of your care as an opportunity to view the patient's pain condition in a new light with fresh eyes. Expect to help someone, and they might just benefit from your optimism [2].

Consequently, one of the most important things to confirm is the diagnosis of the patient. While I was in training and presenting my diagnosis to my mentor, he abruptly answered me, "I want to make my own assessments and diagnosis." Since then, I have always taken that short word of advice to heart. Make your own independent diagnosis. Do not just accept what is written in the chart. With a correct diagnosis, an appropriate (and often effective) treatment plan follows. Refer to earlier chapters which discuss thorough history tak-

ing and examination to ensure the best diagnosis. If there is not enough information that confirms the diagnosis, then obtain that information. Utilize laboratory studies, imaging, and specialists. Only after the diagnosis is confirmed can a thorough and effective treatment begin.

Therefore, when documenting the visit use the most specific diagnosis possible. Do not simply put chronic pain syndrome alone. Add in the diagnosis thought to be responsible for the patient's chronic pain. For instance, if the patient has chronic hip pain, osteoarthritis of the hip on radiography, and negative rheumatological workup, document these facts and diagnosis to support the diagnosis of osteoarthritis of the hip.

Documentation of Appropriateness and Safe Use of Chronic Opioid Therapy

Given the risks associated with COT and the unproven effectiveness in chronic noncancer pain, it is crucial to document the effectiveness of COT when choosing to continue therapy. There are various mnemonics, but the "Four A's" are a good place to start.

1. Analgesia
2. ADL's
3. Adverse effects
4. Aberrant behavior

Essentially, there ought to be adequate pain reduction. Again, many previously cited studies and Canadian guidelines define clinically significant pain reduction as at least a 30% reduction in pain intensity [3]. Improvement in function is also an important factor when assessing the effectiveness of opioid therapy. Consequently, there should be adequate documentation of improvement in activities of daily living. A quick method to track patient progress on therapy includes the Pain, Enjoyment, and General activity (PEG) scale [4]. It asks on a scale of 1–10 for this week, what was the patient's pain level, how has pain interfered with the enjoyment of life,

and how has pain interfered with general activity. It has been used successfully in various clinics to monitor opioid therapy and adjust doses appropriately [5].

In addition, the adverse effects of opioid therapy must be assessed each visit. These include adverse effects from therapy including oversedation, pruritis, nausea, hypogonadism, testosterone deficiency, mood disorders, osteoporosis, and constipation [6, 7]. The risks of opioid therapy also include opioid use disorder, overdose, and death. These risks are elevated with concurrent drug or alcohol use. In addition, there should be screening of other aberrant behaviors such as diversion and obtaining more opioids from other providers.

Periodically checking the patient's controlled substance prescriptions from the state prescription drug monitoring program is helpful, and maybe required by law. Of note, various states have different reporting requirements for pharmacies ranging from <24 hours to 1 month. California currently has a 1 week reporting time frame, while New York <24 hours. Consequently, if a patient just filled a prescription a couple days ago, it may not show up in the drug monitoring system. Verification of drug use (both prescribed and illicit) can be performed with periodic urine drug screens. Of note, it may be useful to ask when was the last dose of opioid medication in order to see if urine toxicology results are appropriate.

It is always wise to document the safety of the current opioid dosage. This first begins with calculation of the morphine milligram equivalents which can be done using online calculators [8] or apps [9]. Also refer to Chap. 6, Management of Chronic Pain: Medication, for more details. If morphine milligram equivalents (MME) are high >50, consider more frequent monitoring (every month or sooner), discuss possibility of tapering if opioid therapy is not effective, or benefits do not outweigh risks, and consider prescribing naloxone. Avoid increasing dosages above 90 MME (or concurrent use with benzodiazepines [10]) given increased risks of death [11]. If patient is already on >90 MME consider tapering, pain medicine referral, or careful documentation and justification of such a high dosage.

Also, periodically discuss other factors involved in opioid safety such as securing the medication in a lock box to avoid theft or accidental ingestion by family members or children. Safety also implies frequent visits for monitoring of therapy. CDC guidelines suggest at least every 3 months for those on COT, and sooner (days to weekly) if dosages are being titrated or started. Also, it is recommended that periodic screening for depression and other negative affects be performed. Depression can be treated in order to prevent misuse of and overdose from opioid therapy [12]. As previously discussed in Chap. 7, treating other negative affects such as catastrophizing can also help improve pain and function.

These suggestions and requirements can be systematically implemented for every chronic noncancer pain patient on COT in the clinic with an opioid treatment agreement. These agreements can have standardized components (minimum visit frequency, agreement to use only one pharmacy, random urine toxicology, minimum urine toxicology intervals, and other treatment expectations) which can be tailored to the specific patient (visit frequency 1x/months, will use this specific pharmacy, and has these individualized goals). More on this will be discussed in the next chapter.

Naloxone

Prescription of naloxone (brand name: Narcan) can potentially be life saving in the case of opioid overdose. CDC guidelines recommend considering prescription of naloxone at approximately 50 MME. Opioid overdose is characterized by apnea, miosis, and stupor, with respiratory depression being the hallmark of opioid toxicity [13]. Naloxone is the antidote for opioid overdose and is a competitive mu receptor antagonist. It will reverse apnea, miosis, and stupor. It is commonly injected or given intranasally. Oral administration is not effective (and usually impractical) given the first pass metabolism of the liver.

Administration of Naloxone

Naloxone must be given by someone other than the victim of opioid overdose. The first step is to support respiration. Respiration should be supported by bag-valve mask while the medication is being readied in a healthcare setting. Otherwise, patients (and their family and/or friends) should be instructed to call 911 and give rescue breaths. Ready to fill out prescriptions (with patient instructions) of either the injected or intranasal form can be found at http://mytopcare.org/prescribers/starting-opioids/prescribing-naloxone-2/   [14]. Figure 8.1 shows a ready to fill out naloxone prescription with accompanying (tear-off) instructions for the patient. There are also online intranasal instructions from the manufacturer of the brand name product [15]. To make things even easier, there is also a naloxone autoinjector (brand name: Evzio). Some of the pitfalls of administration is that one injection may not be enough, effects are temporary, lasting 30–90 minutes, and re-administration and prolonged patient monitoring (along with respiratory support) may be needed to ensure patient safety. The website, prescribetoprevent.org also contains useful information on how to prescribe naloxone, as well as patient education videos and materials [16]. It also has a helpful chart comparing the various naloxone products. In terms of cost, the generic vial of naloxone is the most affordable, then the intranasal formulation, and lastly the auto-injector.

Separate Chronic Pain from Other Chronic Care

Another tip that may make managing the patient with chronic pain easier is to schedule separate appointments for chronic pain if the patient has other chronic diseases. For instance, diabetes management (and chronic pain management) can be better taken care of when there is adequate time to devote to each condition. Thus, multiple visits may

FIGURE 8.1   Example naloxone (injection) prescription with accompanying patient instructions

be required to successfully manage all the patient's chronic diseases. If the patient repetitively does not show up to appointments for the management of chronic disease (or go to specialist referrals), it is necessary to remind the patient that optimal control of pain can only be accomplished if other medical issues are under control. Chronic pain should not be the most important issue to the patient, although, often times it is.

Warning patients to comply by promising to prescribe less opioids if noncomplaint may be effective for motivating patients to take care of their other chronic medical issues. Other practitioners have also used this strategy for compelling patients to go to specialist appointments, physical therapy [17], etc. However, when a patient seems to focus solely on treating chronic pain with opioids (while neglecting his/her other medical problems), this may be the first symptom of another problem. The patient may be having a poor time

coping with chronic pain, catastrophizing, or experiencing other negative cognitions. If so, the patient may benefit from a referral to a behavioral health specialist. On the other hand, the patient may also have other diagnoses such as opioid use disorder, drug abuse, or be practicing opioid diversion. Consequently, it is wise seek out the motivation behind this overly imbalanced concern.

Example Chronic Pain Documentation

Finally, the above checklist appears tedious, but often electronic medical records have ready to fill out templates that may also automatically populate critical information such as last urine drug screen, results of the most recent depression screening questionnaire, etc. An example note is written below.

- CC: follow up chronic pain   Date 3/31/2019
- HPI Pt is a 30 yo F with chronic pain from fibromyalgia. She has achy pain on upper back, lower back, lower legs and arms. She is currently taking 3 Norco 10-325 daily, and nortriptyline 25 mg QD. Pain is currently being managed by water therapy at local pool. She has been moderately fatigued and did not go to get BMP and TSH ordered last visit.

    ADLs: With the Norco's she is able to walk 15 minute/day and stand long enough to cook for herself.

    Analgesia: Her pain level is 7/10 now, and 10/10 without Norco. She has taken a dose today prior to the appointment. She is also on diazepam 5 mg TID. Last visit she was reduced to diazepam 5 mg BID, but pain was notably worse so diazepam was reinstated at TID dosing and her pain is controlled.

    Adverse effects: She denies constipation and oversedation.

    Aberrant behavior: She denies selling or giving away her medications. She denies drug and alcohol use.

Vitals 98F, 145/85, pulse 107, 160 lb, 64 inches.
GEN: NAD AAOx3
Pupils no miosis
RRR S1 S2, mild tachycardia, no mrg, lungs CTA
MSK: pt is tender at various fibromyalgia spots today

Last PHQ9 – 1/9/2019 mild depression
Last Utox – 2/9/2019
PDMP checked today 3/31/2019 and no aberrant prescriptions

A/P

Fibromyalgia: Pt has had negative rheumatological workup in 2017 (neg RF, ESR, ANA, TSH, VIT D normal. Seen rheumatologist 8/2017 who confirms diagnosis.) Pt had x-rays of cervical, thoracic and lumbar spine in 2016 and were normal. Continue nortriptyline 25 mg daily. She could not tolerate 50 mg daily due to side effects of getting rash. She has tried gabapentin and pregabalin in the past, but made her feel too sleepy and nauseated. Pt is on Norco 10-325 3 tabs daily, disp 90/month, refill 0. Currently norco helping patient perform ADL and control pain and meet goals. There is no aberrant behavior on urine toxicology, and PDMP. RTC 1 month. Pt has been to physical therapy in the past and continues water exercises at local pool which help.

Opioid Use: Pt is on 30 MME per day and also on concurrent benzodiazepines for the past 5 years. I have counseled her multiple times on the dangers of this practice and have tried weaning. She has already been reduced from diazapam 10 TID to 5 TID, last reduction 2 months ago. Last visit, she was reluctant to continue below this amount given patient has pain flares and worsening of ADL's. Consider reduction again at next visit. Pain agreement current and signed 1/10/2019. Consider discussing Narcan usage next visit.

Tachycardia: TSH ordered, patient has not yet done it yet. Reminded patient to go nonfasting to lab.

Chronic pain: RTC 1 month for reassessment

Depression: Currently no SI/HI and PHQ 9 acceptable. Continue antidepressants. Behavioral health referral pending for possible CBT.

Overweight: continue advising less carbs, whole grain, and more vegetables. Pt has lost 5 lbs since 2018.

HTN: patient is on HCTZ 25 mg QD. Follow up in 2 weeks for HTN management. Reminded patient again to get labs.

Signed John Smith MD 1645

There are a few take-home points concerning this note. Firstly, there was justification of opioid usage, namely patient failing other medications or having adverse reactions. There was also improvement of pain and function. There was also a summary of evidence supporting her diagnosis which can be copied often from a well kept problem list or previous notes if properly documented in the past. Also note that patient is on concurrent benzodiazepines and opioid therapy, which is contrary to the advice of current prescribing guidelines. However, it appears that this person was already on concurrent therapy for years previous to the guidelines. There was thus justification for the continued therapy (as weaning must be done slowly) and weaning has also been documented and attempted. Failure to wean completely was also justified as patient was unable to tolerate the worsening of pain and function. Other salient points include making close follow ups and separate visits for other medical problems (hypertension).

Opioid Weaning

For those who are on high daily MME, weaning of opioids should be considered in order to reduce the risk of opioid overdose and death. Withdrawal is unpleasant, but not deadly (although case reports exist of unusual circumstances.) Currently, there is scant evidence for the speed of taper and taper protocols [17]. However, there are many reasons that may compel different speeds of opioid tapering (Table 8.1) [1, 18, 19].

TABLE 8.1 Opioid tapering speeds and reasons

Tapering speed	Tapering reason
Immediate discontinuation	Illicit drug use
	Diversion, prescription forgery, obtaining prescriptions from multiple providers
	Overdose
	Violence toward staff/physician
Rapid tapering	Untimely requests for refills (early, off hours, etc.)
	Major adverse effects
	Opioid-induced hyperalgesia
	Other nonadherence to pain agreement
Gradual tapering	Functional goals/pain goals not met
	High MME without clear benefit
	Persistent side effects (constipation, nausea, itchiness)
	Patients on long term opioid therapy

Of course, the above are fluid suggestions. Tapering speeds and criteria must be individualized to the institution and needs of the patient. For instance, the CDC recommends a rapid tapering for overdose [1] while other practitioners support immediate discontinuation [18]. The different recommendations on overdose and tapering must be viewed in the light of the patient's current opioid dose, psychiatric state, level of pain control, social support, and comorbidities. Clinical judgment must be used to carefully weigh the risks and benefits of continued therapy in light of such a serious adverse event.

Various weaning protocols have been suggested. Barring other reasons to taper quickly, the longer a patient has been on chronic opioid therapy, the slower the taper. Of note, if a patient is found to have substance use disorder, then, it is technically no longer weaning or tapering, but rather *detoxification.* Detoxification (for instance, for those addicted to opioids) requires a special license in the United States. Various tapering protocols are listed in Table 8.2. When the regimen is used for substance use disorder, it is noted.

Table 8.2 Tapering protocols listed from fast to slow

Ultrafast	1–7 days, often an inpatient *detoxification* regimen for substance use disorder [20]
Fast	Reduce MME by 25% of the original dose every 3–7 days [18]
Fast	Reduce MME by 20–50% of the original dose per week [21]
Medium	Decrease MME by 10% of the original dose every week until 30% of *original* dose is reached. Then reduce by 10% per week of the *remaining* dose [17].
Medium	Decrease MME by 10% of the original dose every 1–4 weeks until 20% of *original* dose is reached. Then decrease by 5% of original dose weekly [18].
Slow	Decrease MME every month or two [22]

Practical Tips on Weaning Opioids [17]

- Do not need to convert to long acting opioids first in order to wean
- Often times, can taper by switching to lowest formulation of the current opioid, then increasing time between doses. (ie.hydrocodone-acetaminophen 10-325 TID to 5-325 TID. Then once patient adjusts, reduce to BID, etc.)
- It may take longer to wean from methadone
- Warn patients about brief opioid hyperanalgesia (increased pain while opioid dose is decreased), but this is short lived (few days)
- Consider treating withdrawal symptoms with an alpha 2 adrenergic agonist (commonly, clonidine), myalgias with acetaminophen, etc.
- Monitor withdrawal symptoms and slower taper if needed
- Consider an opioid tapering agreement
- Treat depression and support with CBT during tapering as patients may need to learn to cope with stressors without opioids.

Quantifying Withdrawal

Withdrawal symptoms include yawning, mydriasis, sweating, muscle and joint aches, runny nose and tearing, gastrointestinal upset, anxiety, and piloerection. There are various patient administered scales that can be used to quantify withdrawal such as Clinical Opioid Withdrawal Scale [23] or Subjective Opioid Withdrawal Scale [24].

Opioid Tapering Agreement

An opioid tapering agreement puts into writing the plan for tapering so that the patient understands what to expect. It has a few basic components [17] (Table 8.3).

TABLE 8.3 Opioid tapering agreement components

Component	Example
Reason	MME dangerous level. Current dosage is not helping. Adverse effects.

Tapering details	Start and end date. Reduction plan:
	  Week 1: oxycodone 20 mg BID
	  Week 2: oxycodone 15 mg BID
	  Week 3: oxycodone 10 mg BID etc.
	  No opioids will be prescribed after this date.

Expectations:	Withdrawal Opioid hyperalgesia Worsening depression Management plan for the above Withdrawal may occur but is not harmful. Symptoms include… You can use this scale to rate your symptoms...Please call if symptoms are unbearable. You may take clonidine and acetaminophen prescribed today for comfort. You may experience temporary worsening of pain (opioid hyperalgesia), but this is short lived (few days). Call if depression is worsening as this may be a barrier to success.
Contingency plan for taper failure	If taper is too fast (getting high withdrawal scores) please return to clinic. We can revise the schedule, refer to specialist, etc.

Other Safety Concerns

Besides the risks of overdose and aberrant behaviors, opioids carry risks to multiple organ systems. Chap. 6: Management of Chronic Pain: Medication, discussed in detail opioid pharmacotherapy. A quick list of tips (Table 8.4) may prove to be

TABLE 8.4 Clinical pearls for managing patients on COT with comorbidities

System	Helpful tips
Cardiovascular	Consider EKG for those on methadone. Use caution when prescribing other drugs that cause QT prolongation. Opioids may increase risk of coronary heart disease in females [25]. Reduce cardiac risk factors.
Pulmonary	Caution with obesity, hypoventilation disorders (sleep apnea)
Liver and gastrointestinal	Opioid effects are more potent in those with liver dysfunction; reduce dose if needed Some opioids (oxycodone, hydrocodone, codeine, tramadol) are more dependent on the cytochrome system for metabolism. Drug interactions may change effectiveness of opioids [26–28] and may lead to unexpected respiratory depression/death [29]. A drug interaction app may facilitate prescription for patients requiring polypharmacy.
Renal	Reduce dose if needed due to impairment of excretion
Endocrine	Opioids can reduce testosterone levels, causing decreased libido, hypogonadism, sexual dysfunction, erectile dysfunction, osteoporosis [30]. Treatment can include weaning, opioid rotation, or testosterone supplementation.
Immune	Opioid use may increase risk of pneumonia in elderly- possibly due to immunosuppressive effects [31]. For those prone to infection, choose opioids with possibly less immunosuppressive effects: hydrocodone, oxycodone, hydromorphone [31] or wean.

a useful reference in managing a patient with other chronic illness who also requires opioid therapy. This is not meant to be an exhaustive list.

Iatrogenic Accidental Opioid Overdose

Because as primary care physicians and providers we are treating patients not just for pain, but for multiple other conditions, it is common that we may prescribe many classes of drugs and therapies for our patients on COT. This section highlights a few common offenders that may inadvertently cause an increase in opioid bioavailability and lead to overdose, stupor, and even death. Commonly, this involves inhibition of the cytochrome system which opioid metabolism is dependent upon. Brennan 2012 summarizes case reports of various cytochrome interactions that led to opioid overdose and/or death. What makes these case reports so alarming is not only are these interactions potentially fatal, but that these fatal prescriptions could have easily been made by any primary care physician. For instance, one patient became unresponsive after taking codeine for cough while he was hospitalized on antibiotics [32]. Another adverse event occurred when an elderly patient on Fentanyl patch was treated for H. Pylori with clarithromycin [33]. A patient on methadone died when he was trying to quit smoking [34]. Tables 8.5 and 8.6 lists opioids metabolized by the cytochrome system and a few common offending agents that may lead to enzyme inhibition and opioid toxicity. Morphine, hydro-

TABLE 8.5 Opioids more susceptible to drug interactions through the cytochrome enzyme system

Opioids more susceptible to drug interactions
Codeine
Hydrocodone
Tramadol
Oxycodone
Methadone
Fentanyl

TABLE 8.6 Commonly prescribed interventions that can inhibit cytochrome enzymes

Inhibitors of cytochrome enzymes
Clarithromycin, other antibiotics
Fluoxetine, and other antidepressants
Smoking cessation
Ketoconazole and other antifungals
Grapefruit juice/extract

morphone, oxymorphone are not eliminated by the cytochrome system (but by glucuronidation) and thus have minimal interaction potential [35]. Smith 2009 gives an easy to understand summary of opioid metabolism and has extensive tables which list common inhibitors and inducers of the cytochrome enzymes [35]. Online drug interaction databases along with built-in ones in an EMR may assist in discovering adverse interactions.

Interpretation of Urine Drug Testing

Table 8.7 below adapted from Smith shows key opioids and their notable active metabolites. Given metabolites may confuse urine drug screening test results, remember to choose urine opiate screen with *confirmation* to verify the patient is on a specific opioid. Do not order screening urine drug panels for this purpose as opioid metabolites may show up as positive. Use screening tests, which are immunohistochemistry based, for assessing a panel of substances such as amphetamine, marijuana, phencyclidine (PCP), and undifferentiated opioids. Confirmatory tests utilize mass spectrometry or gas chromatography and can differentiate various opioids and offer quantitative results [36, 37]. Some urine drug screens (again, in order to assess a panel of drugs such as benzodiazepines, amphetamines, etc.) will also check for urine pH, creatinine, and specific gravity in order to assess for tampering (i.e. dilution, etc.) [38]. Minimum urine volume is often 20–30 ml and should be warm. If suspect, measure temperature and document as dilution may have occurred.

TABLE 8.7 Opioids and their notable active metabolites

Opioid	Metabolite
Morphine	Hydromorphone
Hydrocodone	Hydromorphone
Codeine	Morphine, hydromorphone
Heroin	Morphine
Oxycodone	Oxymorphone

TABLE 8.8 List of drugs and their approximate detection time frames in urine [39]

Drug	Maximum detection time in urine after last dose
Amphetamines	2 days
Benzodiazepines	
Short acting: Lorazepam	3 days
Long acting: Diazepam	30 days
Cocaine	2–4 days
Marijuana	
Single use	3 days
Heavy chronic use	>30 days
Opioids	
Codeine, heroin	2 days
Morphone	2–3 days
Hydromorphone, oxycodone	2–4 days
Methadone	3 days
Phencyclidine	8 days

If you are unsure about how to intrepret a urine drug screen that shows unexpected opioids such as hydromorphone, please check with your local laboratory for details regarding urine drug testing specifications and interpretations. They can clarify the quantity detectable by these screens and therefore help you interpret whether the unexpected opioid detected is a metabolite or not.

Interpreting results will also require understanding of how long each substance remains in the urine (Table 8.8). A careful history must be taken prior to testing to properly interpret test results. I found it extremely helpful to ask when was the last dose of opioid medication as this greatly assisted me in interpretation of results.

Agreement Violations, Unexpected Results, and Other Difficult Discussions

Unfortunately, there will be times when we must "confront" patients or (more collaboratively) discuss with them our concerns. There can be illicit drugs in urine test results, multiple visits to the ED for opioids found on PDMP reports, treatment ineffectiveness, adverse side effects, or that the patient has developed profound depression. Regardless of the concern, we as the provider must initiate a discussion to understand what has happened and discuss potential changes in opioid therapy. Undoubtedly, this can be a difficult task.

Erin Krebs at the Center for Chronic Disease Outcomes Research has developed sample scripts to help providers talk with their patients about their concerns. Table 8.9 highlights excerpts from, "Safer Management of Opioids for Chronic Pain: Principles and language suggestions for talking with patients [40]."

Why are these conversations so difficult? There is a need for change, and whatever change providers are proposing, we expect that there will be opposition to that change. Changing behavior is a difficult task, with many theories [41–43] which will be further elaborated in Chap. 10. Why do we even advocate change? Because we as providers have the facts and know it is for the benefit of the patient. We know that multidisciplinary treatment is effective and that opioids have many risks. However, patients do not know these basics, and hence, providers must formulate an empathetic relationship that empowers patients to understand the need for change. Providers can also enable patients to make changes by giving then proper expectations and the tools needed to make the change. The power of the opioid taper agreement mentioned earlier is that it gives an outline of what to do in case of withdrawal, or opioid hyperalgesia,

TABLE 8.9 Difficult clinical scenarios and example language suggestions

Scenario	Language suggestions
Unexpected results	"I called because I'm concerned about you. There was something I didn't expect in your [urine/pharmacy records], so I wanted to check in with you about how you're doing..." [Followed by silence to allow patient to talk.]
	"This pattern can sometimes be a sign that a person is at risk for opioid addiction, which is a serious disease that needs treatment." [Followed by assessment questions and offer of resource/referral.]
	"I know that medications get lost and stuff just happens. But this pattern can also look like there is a problem developing—like someone getting hold of your medicines or loss of control over how much you are using. As a doctor, I just can't prescribe if I'm not 100% sure where the medications are going and how they are being used."
	"I'm not sure what's been happening with you, but I'm concerned for your well-being."

Scenario	Language suggestions
Weaning/ reducing opioid dosages	"It's my job to weigh the potential benefits and potential harms, and to prescribe medications only when the benefits are greater than the harms. In your situation, I'm worried the risks outweigh the benefits, so I can't keep prescribing them for you." "My experience is that patients who taper opioids end up with clearer thinking and more energy to engage in positive activities that help them focus less on their pain." "For most people, the benefits wear off as the body gets used to the medications. Then they're stuck on a medicine that isn't really doing much for them. They often assume they'd be worse off without it, but it turns out that's not true. Let's talk about what you can do to live a better life, so all your eggs aren't in one basket." When tapering, after a small dose reduction, check in with the patient about any positive changes—increased energy, alertness, ability to be active, sleep. It helps to have patients focus on beneficial outcomes. It may also be helpful to note expected negative effects that did not happen: "From what you are saying, your pain seems to be about the same as before."

Table 8.9 (continued)

Scenario	Language suggestions
Discussing change in pain management	"From what you have been telling me, these medications aren't as effective as you would like. Let's think about trying something different." IF PATIENT IS DEFENSIVE: "Patients who expect drugs alone to improve their overall quality of life are usually disappointed. What are other things you do that seem to help you be more active? Let's talk about approaches that I have seen work for other patients with problems like yours." "These drugs aren't the best treatment for pain in the long term, anyway. For most people, their effects wear off over time. I'd like to try some new approaches to see if we can do better." "Patients who expect drugs to control their pain are usually disappointed. With or without chronic pain, my patients who are doing better use multiple approaches. Let's talk about what might help you become more active and do more things that you enjoy." [Consider walking, pleasant activities, relaxing activities, mindfulness meditation, avoiding thoughts that everyday pain means you are harming your body.] "I want to work with you to find a better pain management plan." "You're telling me that your pain is really terrible, and I hear you. It seems to me that what we're doing just isn't working. I know they helped you at first, but I think the effect of the medications has worn off. We should make some changes."

Scenario	Language suggestions
Responding to treatment setbacks (and focusing on problem solving)	"Remember how miserable you were on the medications? If your pain was really well controlled back then, we wouldn't be doing this at all."
	"Let's just hold on the current dose and not try to make more changes right now. How are things going with your goal to [walk every day, keep a regular sleep schedule, join the gym...]?" [Focus on ways to problem solve and help the patient reach their goals.]
	"Usually these flare-ups only last a few days. Is there anything that would help to take your mind off it in the meantime? I know you mentioned that [you do better when you're with other people; that it feels good to float in the pool...]"
	"I'm not holding out on you. If I had an easy solution for the pain today, I'd give it to you right now. I still think this is going to be worth it in the long run. [Remind the patient of their long-term goals.] How can you get back on track with [your short-term goal]?"

Adapted from Erin Krebs et al.

Table 8.10 Examples of using behavioral change constructs to formulate language suggestions when discussing changes in opioid therapy

Behavioral change construct	Interventions
Exploring patient's attitudes and beliefs, providing information concerning the severity of problem requiring change and benefits of change. This involves giving patient facts (education) on risks and benefits so that they understand the problem, what to expect, etc. Also it involves asking the patient what their opinions are.	Education for patients: "We are realizing now that there is no safe opioid dose, and higher doses are associated with more risks such as addiction and overdose." "We now know that drugs alone aren't sufficient to treat chronic pain." "You are on a very high dose of opioids, and higher doses haven't been shown to be more effective." "Withdrawal is unpleasant but not life threatening. It usually lasts only a couple days." Focus on benefits framed in terms of safety, health, patient well-being, and physician concern "For your safety..." "I'm concerned about your health" "People who have lowered their opioid dose get more energy, less constipation, clearer thinking..." Assess patient's attitudes – they may already be thinking of change or understand the problem "Have you any concerns about your medications?" "Have you ever thought of cutting back?" "Tell me what you know about the opioid epidemic." "Addiction is a known side effect that happens to a certain percentage of people on opioid therapy. It is also treatable. Do you think your body could be showing signs of opioid addiction?"

Behavioral change construct	Interventions
Comparing patients to norms, approval of others, similarity to others	"Our new policy requires everyone on opioid therapy to..." "We now know that those who have cut back on opioid therapy do better" "I wonder if you really need to be on this high a dose. In my experience, most people can cut their doses back quite a bit without any increase in pain." "People don't choose to become addicted, and there are no good ways to predict addiction. That is why everyone who is on opioid therapy needs to [explain the opioid policy in place]"
Perceived behavioral control: self efficacy, lowering barriers to change. This is basically giving patients the encouragement, confidence, and tools necessary to make the change. This involves problem solving with the patient and empathy. It may also require education (for instance, withdrawal symptoms, proper expectations, how long opioid-induced hyperalgesia will last, etc.), medication for withdrawal, a plan in case of flareups of pain, and assurance that the provider will be there to assist.	"I know decreasing your opioid dose in the past was hard for you, but we are going slower now and most people don't have any withdrawal symptoms. Regardless, let's work on a plan in case any withdrawal symptoms occur or your pain worsens." "What can we do to help you achieve your goals? What have you done so far to accomplish your goals?" "I'm here for you while your body is adjusting to the new dose. Let's make a close follow-up in a few days to see how you are doing. You're body may go through these changes [discuss changes] but they are temporary [discuss time frame]."

and provides a plan for failure/setbacks. Table 8.10 lists some main principles that guide behavioral change which are called behavioral change constructs. The approaches by Krebs et al. generally do address many of these behavioral change constructs, and hence, can be effective when used in discussing change. Consequently, with this framework, a provider can formulate his or her own way of discussing a change in opioid therapy (or any difficult situation requiring change on the part of the patient). It just requires a little thought and practice to make these language suggestions natural when using them in the clinic.

Conclusions

Management of the patient on chronic opioid therapy has many components, due to the many risks which must be addressed and documented at each visit. Use of an opioid check list, template, automatically generated, or pre-populated note may facilitate recall of important visit tasks, pertinent labs, and screenings. Opioid metabolism is complex and may utilize the cytochrome system and produce various opioid metabolites such as hydromorphone. Make sure to use a drug interaction program, especially when prescribing antibiotics, antifungals, and psychiatric medications. Ordering an opioid confirmation test and contacting the local laboratory will assist in understanding urine test results. Consider prescribing naloxone. Consider weaning when appropriate. Management of comorbidities may require separate visits. Comorbidities may affect the safety of opioid therapy and vice versa. There will be opioid use disorder, need for tapering, and adverse events which necessitate a change in opioid therapy. Difficult conversations addressing a change in opioid therapy can be made easier when using suggested language that normalizes the situation, empowers the patient to make a change, empathizes with the patient's situation, and educates the patient on the problem and what to expect.

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Chapter 9
The Opioid Requiring Patient: Office Level Management

Bonnie Huang Hall

Introduction

A systems level approach to management of the patient on chronic opioid therapy (COT) at the office or clinic level is essentially a standardized approach to this special patient population. At the heart of this is the opioid treatment agreement which spells out the expectations of treatment for both the primary care provider and the patient. As managing chronic pain may be time consuming, it may not only make the physician's life easier [1], but also is recommended by the CDC [2] and may be required by law depending on the state. The opioid treatment agreement comprises of many components. It essentially states treatment goals, risks, qualifications for obtaining prescription opioids, and explains the monitoring process.

Currently, there is no evidence that treatment agreements reduce overdose and death. In addition, there are varying physician views [1] on the usage of "pain contracts" or "pain agreements" from punitive and self-serving, to much needed

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and an improvement to chronic pain management workflow. Usage of the word "agreement" may make this treatment document more collaborative instead of punitive [2]. Explanations introducing the opioid treatment agreement can discuss the reasons that this agreement exists. Scripts can include the opioid epidemic, risks of opioid therapy, and that it is a universal policy for all patients on COT, much akin to using gloves and other forms of universal precautions (Table 9.1). Of course, the individual provider can use any combination he or she wishes or invent their own standardized script when introducing the need for the opioid treatment agreement.

Treatment agreements, and the office polices they contain, may improve provider satisfaction and confidence with opioid treatment management [3, 4]. Example office policies regarding COT [2, 5] that may be of benefit are listed in Table 9.2.

All office policies do not need to be included in the treatment agreement as they may not be pertinent to the actual

TABLE 9.1 Example scripts to use when introducing an opioid treatment agreement

Reason	Example script
Universal precautions	The opioid treatment agreement is for everyone on long-term opioid therapy, not just you. It is currently our office policy (or state law/ or recommended by the CDC).
Opioid epidemic	Currently, there is a prescription opioid abuse epidemic. Although I do not suspect you will misuse opioids, it is very common. For everyone's safety, I will need to err on the side of caution and monitor your treatment according to this treatment agreement.
Opioid risk	Currently, long-term opioid therapy has many risks and little known benefit. Consequently, this treatment agreement helps us to know if it is working well. It contains a lot of information on how we will monitor opioid therapy.

TABLE 9.2 Example office policies for the management of patients on chronic opioid therapy

Policy type	Examples
Refill	Timing of refills
	Scripts are written for a 28 day supply to prevent needing a refill on weekends when scripts are written for 30 days, etc.
	Scripts are written only from Tuesday to Thursday, and for a 28 days supply to minimize needing a refill on a holiday
	Refill requests without a visit must be given 4 business days notification
	No refill requests will be allowed after business hours, weekends, or holidays
	Who can refill
	Refills will not be made by another physician if the PCP is available.
	Conditions for refill
	There will be no refill of lost or stolen prescriptions (unless there is a police report filed)
	No walk-in refills, no early refills/or if patient "runs out"
	Must go to specialist referrals, must obtain recommended laboratories, must attend appointments for care of other chronic conditions.
	Patient must attend group visit (centered around opioid risk education, naloxone, etc.)
New patients on COT	New patients must have a urine toxicology at first appointment and bring their records or office must receive all records prior to scheduling of first appointment.
	When instituting a new pain agreement, patients are allowed a 30 minute appointment

TABLE 9.2 (continued)

Policy type	Examples
Follow up visits	Minimum intervals between office visits Must be made with PCP (if available) PCP cannot be changed for at least 6 months Requests to change PCP must be done with clinic manager (or other designated 3rd party as provider may feel it is unfair if chronic pain patients are unequally distributed)
Workflow	Designate and train person responsible for checking PDMP Designate and train person responsible for obtaining urine toxicology (or other requirement for monitoring the safety of opioid therapy) (medical assistant) and frequency (every visit?) Discuss with medical assistant/office staff ("huddle") to anticipate needs of clinic schedule and patient on COT
Pain management standards	Standards for when a referral to pain specialist or behavioral health specialist is required No initiation of opioids to treat headaches, fibromyalgia, or chronic low back pain Standardized consequences for various violations of the treatment agreement. Example: known diversion and violence towards staff leads to immediate discontinuation of opioid prescriptions. Increasing dosage without discussion with provider or using a different pharmacy is a minor violation. Violations are often categorized into "Major" and "Minor." Offices may have polices that stipulate how many major and minor violations incurred will lead to termination/weaning of opioid therapy.

chronic opioid treatment agreement whose chief purpose is to inform the patient standard requirements for refills, opioid risks, and measures to improve opioid safety. A separate chronic pain (or more specifically chronic opioid treatment) policy can address what is included in the treatment agreement along with other specifics concerning new patients on COT, frequency of checking PDMP databases and urine toxicology, standards for referrals, criteria for initiating a chronic opioid treatment agreement, definitions of and consequences for major and minor violations, etc. Of course, a clinic can simply adopt components of previously published guidelines as part of its chronic pain policy. One readily available example of a complete policy on chronic noncancer pain can be found at the University of Michigan Health System [6]. Essentially, the office policies on chronic opioid therapy will define chronic opioid therapy and dictate how a patient on chronic opioid therapy will be managed. The process of developing thorough guidelines for an entire healthcare system is beyond the scope of this book (which focuses more on the practice-based aspects of opioid management).

Lastly, there are various components crucial to constructing an opioid treatment agreement (Table 9.3). These were gleaned from readily available sample opioid treatment agreements listed in the CDC toolkit part C [2]. Main points are to discuss risks and unproven benefits of opioids, monitoring for safety, and refill requirements. Incorporating patient specific diagnosis, goals, and treatment plan will not only personalize the agreement, but help quantify treatment effectiveness (in terms of the patient's functional and pain related goals). Remember to give the patient a copy of the opioid treatment agreement. Renew annually [2] or according to current recommendations.

Table 9.3 Main components of a chronic opioid treatment agreement

Components	Example statements
Specific diagnosis and treatment plan	I, (patient's name), am being treated for (patient's pain diagnosis), with (list following medications and nonpharmacological therapies.) Treatment of chronic pain should include other classes of pain medications, behavioral health treatment, physical therapy, exercise, and specialists. Opioid therapy may be changed depending on progress or adverse effects. If there is no documented improvement, therapy may be tapered or discontinued. My goals for opioid therapy include: One of the goals of opioid therapy is to improve function and return to work I understand that pain cannot be totally eliminated but only partially relieved in order to improve my function Specifics regarding when opioids will be weaned or discontinued. Opioid withdrawal may occur, but is not life-threatening. I will not change dosage of medications without discussion with my doctor first

Table 9.3 (continued)

Components	Example statements
Risks and unproven benefits of opioid therapy	Long term opioid therapy is currently not proven for chronic non- cancer pain to provide long lasting relief or improvement in function There are substantial risks to opioid therapy including risks of addiction, overdose, death or permanent disability. Side effects may include nausea, itchiness, constipation, drowsiness, and sexual side effects. I agree not to drive or operate machinery when drowsy. Alternative therapy includes… Concurrent use of benzodiazepines (provide a list), illegal drugs, unauthorized prescription drug use, marijuana, or alcohol can lead to death, or disability. There is no minimum amount of opioids that is considered absolutely safe I understand that there is a risk of addiction with opioid therapy and I will comply with the treatment plan or referral to an addiction specialist for this condition.

TABLE 9.3 (continued)

Components	Example statements
Refill requirements	Refill at one pharmacy (patient's selected pharmacy) changes will be made only...
	Refill intervals, office visit must be made with Dr. (PCP) every (specify interval). I agree to obtain opioid therapy only from Dr. (PCP)
	Refill requests must be made 4 business days in advance
	No after hours, weekend, or holiday requests
	Lost/stolen prescriptions require a police report in order to consider re-prescribing.
	Refills require: compliance with treatment plan including referrals to specialists, laboratories, radiology, etc. I agree to attend appointments…
	No early refills. In the event I took more than prescribed or lost some pills, I understand that I will have to wait until when the next prescription is due.
	Separate visits required for chronic opioid therapy
	No walk-in refills will be made.
	If I am late to my appointment it may be rescheduled.
	Must attend one group visit/ educational seminar

TABLE 9.3 (continued)

Components	Example statements
Safety protocols and monitoring	There will be random urine collections at any time for your safety
	There may be random pill counts to ensure your safety, please bring medication bottles when asked.
	Keep opioids locked
	Naloxone prescription and instruction
	I will not take someone else's medications
	Safe disposal of opioids (Locations, or phone numbers)
	We need a valid phone number to contact you. In case you cannot be reached when we call, you must return our call in 24 hours.

Below are links to example opioid treatment agreements (Table 9.4). Some are written in layman's terms and may be more appropriate for those with lower health literacy. The FDA uses more of a discussion format instead of a "contract" format written with input from plain language experts [7]. In general, when initiating an opioid treatment agreement, I will discuss each point with the patient in order to ensure comprehension and foster a collaborative relationship.

Table 9.4 Example opioid treatment agreements available on the world wide web

Institution	Website
CDC	https://www.cdc.gov/drugoverdose/pdf/prescribing/CDC-DUIP-QualityImprovementAndCareCoordination-508.pdf
Veterans Affairs and Department of Defense	https://www.nhms.org/sites/default/files/Pdfs/OpioidTxAgreement-VA2010.pdf
Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer	http://nationalpaincentre.mcmaster.ca/documents/opioid_guideline_part_b_v5_6.pdf Appendix B-5
Utah State	http://health.utah.gov/prescription/pdf/guidelines/treatment_plan.pdf
University of Michigan Health System	http://www.med.umich.edu/1info/FHP/practiceguides/pain/pain.pdf Appendix C
Oregon State	http://www.oregonpainguidance.org/app/content/uploads/2016/05/Patient-Treatment-Agreements.pdf
New Jersey State	https://www.njconsumeraffairs.gov/prescribing-for-pain/Documents/Pain-Treatment-with-Opioid-Medications-Patient-Agreement.pdf
FDA	https://www.fda.gov/media/114694/download

Conclusions

Opioid treatment agreements and chronic pain policies currently have scant evidence (if any) concerning effectiveness in prevention of adverse events such as addiction, overdose, and death. However, it may make the management of deviant behavior (violations of the agreement), or adverse events (addiction, side effects, or overdose) a little more straightforward (and less stressful) when a protocol is already in place and the patient is aware of the protocol. Adopt and adapt various policies and work flows to make management of these complex patients a little easier.

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Chapter 10
The Opioid Requiring Patient: Systems Level Management

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Introduction

Opioid overdose is one of the most lethal effects of opioid prescription use. Unfortunately, it has become a common place. Deaths from drug poisonings are now more common than deaths from motor vehicle accidents, and fatal overdoses from prescription opioids now surpass deaths from cocaine and heroin [1]. Having a systems level approach to the opioid epidemic allows the medical community to tackle this widespread problem on a larger scale. Primary care seems a logical starting point as almost half of all opioid prescriptions are written by primary care providers [2, 3].

Guidelines from the CDC [4] serve as reminders to individuals of best practices. State legislation concerning opioid prescription serve to enforce guidelines over entire populations [5]. They also enable the creation of systems to detect aberrant behavior such as Prescription Drug Monitoring Programs (PDMP) which have been effective in reducing

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opioid related deaths [6]. (PDMP usually contain a database of patients and the controlled prescriptions they have obtained from the pharmacy.) Some states may even require treatment agreements to be started at certain times, maximum opioid prescriptions, specific requirements on when to check the PDMP database, etc., so it is wise to check with current state laws. The Arizona Department of Health Services in 2017 has compiled a list of states and their opioid prescribing laws [7].

Currently, the CDC utilizes a quality improvement (QI) approach to implementing guidelines and outlines the process step by step [8]. Some notable recommendations include forming a committee to decide what to implement, having a champion/leader responsible for the project, having adequate budget and resources for implementation, and then measuring outcomes and measures to track progress. How to perform a quality improvement project (making databases, deciding on what and how to measure) is beyond the scope of this book. *One infrequently discussed underlying premise foundational to all quality improvement project is the need for individuals to change their habits and behaviors.* However, providers do not easily change practice habits concerning opioids [9–12]. This chapter summarizes some of the main approaches published in literature on how to tackle problematic opioid prescription on a systems level.

There are some key themes in systems level management of opioid prescription and the patient on chronic opioid therapy (COT) for noncancer pain. The key components include:

- Educational Programs (for doctors and staff)
- Tracking systems (registries of patients on COT)
- Personal accountability (posting prescriber results publicly, one on one feedback with medical director about prescribing habits, comparison to department averages, etc.)
- EMR as a means to facilitate standardization of care and establish/encourage norms in prescribing (templates, alerts, lower default dosages for opioids)

- Establishing support systems (Opioid review committees, nurse coordinator/educator, pharmacy, access to expert consultation)
- Patient component (mostly education)
- Lowering barriers to guideline implementation (longer patient visits when guidelines are implemented, EMR templates)

One study also used other methods such as incentivizing compliance [13].

Education

Education has long been used on clinicians in order to influence their behavior. The classic example is attending a conference on new diabetes therapies. However, just because providers are exposed to more information, whether in person [14] or electronically [15], does not mean there will be adoption and change in clinical practice. Many studies used various forms of education to systematically implement opioid management policies. Some were more passive in nature, such as posting guidelines in resident education rooms, emailing providers, and dissemination during mandatory clinic meetings [16]. Others included lectures and online training modules with questions [17].

Academic detailing, often used by the pharmaceutical industry, is the practice of one on one discussion to educate and change provider behavior. This educational technique was used in combination with other interventions and found to be effective in facilitating system wide change [18, 19]. A recent Cochrane review also shows that academic detailing, also known as "education outreach visits," are in general effective in facilitating provider adoption of guidelines and interventions [20]. The supplementary information from Meisenberg et al. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6324493/bin/jamanetwopen-1-e182908-s001.pdf) provide specific topics that were used during their educational program. Their educational program emphasized a couple of main ideas. The first was that the opioid epidemic was initi-

ated and fueled by over prescription. The second was that provider prescription habits can influence patient outcomes such as opioid dependence. Consequently, in this instance, the program aimed to persuade the provider to change prescription habits by emphasizing the severity of the problem and linking it to individual action: lowering morphine milligram equivalents (MME) and other measures one patient at a time.

Lowering Barriers

Various studies have tried to implement guidelines by lowering the barriers to change, making the work involved in changing easier. For instance, if guidelines are complex and involving multiple recommendations (such as the CDC opioid guidelines) it is harder and less likely for physicians to adopt [14]. Many systems level management began with making EMR templates to standardize documentation and aid in following guidelines for the patient on COT [17]. These EMR templates also serve as reminders to perform urine drug screens, check PDMP databases, complete opioid treatment agreements, document physical exam and specific diagnosis, etc. Reminders, when used appropriately, have been shown to be effective in producing behavior change [21]. Some studies incorporated prompts for action in the EMR for patients on high MME or on concurrent benzodiazepines [17, 22]. New lower defaults for opioid prescriptions were also built into EMR to facilitate lowering MME per patient [18, 23]. Others made MME calculations and referrals for substance abuse and mental health easier by incorporating them into the EMR [13, 18].

One institution put a whole library of opioid prescribing resources online for providers to use [19]. Their website is mytopcare.org/prescribers and contains many useful tools such as opioid risk factor assessment, listing of each state's PDMP, information on interpreting urine drug screens, and prescribing naloxine instructions. Some systems have enlisted the aid of pharmacy by asking them to print out PDMP reports for providers or co-manage the prescription of opi-

oids. Nurse case managers and educators [24] were often used as well to facilitate guideline adherence [19]. For example, they would aid the physician in reviewing PDMP and ordering urine drug screenings. In addition, access to expert consult such as an "opioid review/oversight committee" also can be effective in lowering MME and assist in conforming to opioid prescribing guidelines [13, 18, 24].

Another common limitation is time. Longer office visits were utilized in order to implement the new COT agreement with the patient [24]. Finally, institutions held meetings to improve workflow after guidelines were disseminated [17]. It makes sense that for many people, the harder it is to do something, the less likely it will be done. Consequently, as studies have shown, utilizing methods to make the work easier will enable more compliance and thus system wide change.

Social Pressure, Professional Norms

Current studies [13, 18] have shown that using individual one on one feedback with medical directors has the potential also to conform prescriber habits to guidelines. A recent Cochrane review also confirms that, in general, managerial conducted audit and feedback to providers can be successful in implementing guidelines on a systems level [25]. Other feedback techniques include posting department statistics, averages, and comparison to individual performance publicly. These techniques involve motivating change by appealing to desires to conform to professional norms. Another example of this is various departments establishing default or standard opioid practices [18].

Patient Targeted Interventions

In applying opioid prescription guidelines, there are actually two parties that need to conform – the prescriber, and the patient. Consequently, many institutions incorporated system

wide changes that targeted patient behavior. Most of these programs have been focused on educating the patient concerning opioids. Patient training videos [17], patient pamphlets and educational materials [13, 18], and mailing out letters introducing the new opioid treatment process [24] were all examples of patient interventions. Nurse coordinators were also used to answer questions and educate patients on the new opioid guidelines [24]. Information concerning the safe disposal of opioids and realistic expectations after surgery was also provided to patients [18]. Indeed, a recent Cochrane review demonstrated that patient educational interventions in general are capable of improving clinician's adherence to guidelines [26].

Managerial Support

From what is seen in literature, many of the approaches are "top down", meaning upper management, medical directors, and senior leaders decide to implement the guidelines. That means, there must be administrative and financial support for the change as many of the changes described require time, training, and education. Finally, besides requiring time and money to implement change, fundamentally, changes in the system requires rapidly changing the behaviors of individuals in the system. The behaviors of primary care physicians, nursing, management, staff, and patients themselves need to change in order to have successful system wide management of patients on COT.

Systems Management Is Influencing Behavioral Change on a Large Scale

Many of the system wide opioid management strategies were more successful when used in combination [14, 19], likely due to the complexity of opioid management. When faced with limited resources, how does one decide which methods to implement and which are the most effective? What are the

basis for using the above techniques? I propose that we take cues from behavior change theories which have been used successfully to predict vaccination behavior of healthcare workers [27]. The above methods used to implement change on a system level can be reorganized into the following categories based on one of the most commonly accepted behavior change theory, Theory of Planned Behavior [28] and extensions of it by Godin [29]. Basically, intention to perform a given behavior (i.e. adapt opioid prescribing guidelines from management) is based on

1. Personal attitudes towards the subject
2. Subjective norms and other "norms": approval of others if change was enacted, comparing oneself to how others are complying (descriptive norms); and professional norms
3. Perceived behavioral control: similar to self efficacy, how practical/easy is the change, how difficult is it to accomplish this change?
4. Anticipated regret if change is not done
5. Moral norms: feeling obligated to change

Other theories of behavior such as health belief model [30] also consider perceived

1. Severity of the problem requiring change
2. Benefits of change
3. Cues to action (reminders)

Consequently, all the various means discussed previously to facilitating management of the patient requiring COT at the systems level were effective. Why? It may be because these interventions (and their combination) addressed the various facets crucial to behavioral change (Table 10.1).

Categorizing the systems interventions into a handful of categories crucial to behavioral change will enable us to see what areas we are not targeting, and also perhaps come up with new interventions that strike at the underlying basis for behavioral change. It will also enable us to study which combinations/types of behavioral interventions are most effective in promoting opioid prescription compliance on a systems level.

TABLE 10.1 System levels interventions and the associated behavioral change construct

Behavioral change construct	Interventions
Personal attitudes, severity of problem requiring change, benefits of change	Education for patients, physicians, and staff
Norms, approval of others, similarity to others in profession, cues to action from others	Personal accountability with medical directors, posting personal compliance with guidelines publicly, posting department statistics on guideline compliance, establishing lower opioid dosages when prescribing with EMR or department standardized dosages for opioid prescriptions
Perceived behavioral control: self efficacy, lowering barriers and facilitating the "work" of change	EMR templates with reminders and documentation prompts, easy access to MME calculators, access to opioid review committees, expert consultations, nursing to coordinate care/educate patient, prescriber education, assistance with accessing prescription drug monitoring program activity, EMR prompts, meetings to discuss workflow improvements, longer office visits
Anticipated regret for noncompliance, personal benefits of change	Personal accountability programs, financial incentive programs, education on risks of COT
Moral obligation	State laws, education on risks of COT etc., linking personal prescription habits with opioid dependence

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Chapter 11
Implementing and Following a Safe and Compassionate Opioid-Prescribing Policy

Christina Zaro

Clinicians Approach Chronic Pain/Opioid Therapy Differently

Approaches to management of chronic non-cancer pain and attitudes about opioid use disorder vary widely among clinicians [1–3]. It is clear that we do not all agree on how to treat it. In Ontario in 2011, for instance, the highest prescribers were providing opioid prescriptions 55 times more often than their lowest prescribing colleagues. Even more recently, and despite national guidelines, there still lacks a standardized approach to opioid prescribing, weaning, management of withdrawal, and opioid use disorder. Several studies [3–5] have examined reasons for this variability:

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Chronic nonmalignant pain is multifactorial with rarely only one solution. Pain is not ever just pain, as there is almost always a psychosocial component influencing its perception. Pain is caused and aggravated by a complex interaction of physical, emotional, social and cultural factors. This often makes it difficult to identify the underlying cause of pain, leading to complex multifactorial management. Different providers will develop disparate treatment plans for this reason.

Some prescribers are more able to work through the inherent tension of opioid prescribing than others. There is tension between a healer's need to acknowledge and treat a patient's pain while wanting to avoid prescribing medication that will lead to dependence and possibly addiction. There is also often uncomfortable tension arising in discussing with patients the measures to be taken to detect misuse while trying to maintain a trusting therapeutic relationship. The response to these tensions is determined by many factors, including the experience level and communication skills of the clinician, length of time of the patient-clinician relationship as well as the amount of trust within that relationship, and time available for the patient encounter.

Practice location makes a difference. Prescribers have variable access to resources for pain management depending on practice location. Although guidelines recommend a multidisciplinary approach, the reality in many communities is that resources are either unavailable or financially inaccessible. In particular, pain management consultation and physical therapy are not options for those under or uninsured. Chronic pain has been reported at significantly higher rates by rural versus urban patients [6]. And perhaps because of this and known decreased access to services in rural areas, opioid use has increased in economically disadvantaged and rural patients [7, 8].

National Guidelines Attempt to Standardize Prescribing

In response to the complexity of chronic noncancer pain (CNCP) management and increasing opioid prescribing, the US Food and Drug Administration produced the "FDA Blueprint for Prescriber Education" in 2012 [9] Updated semiannually, it addresses how to assess patients for treatment, as well as initiate, adjust dosage, and discontinue opioid therapy. It was comprehensive and much needed, but still left many questions unaddressed. Prescribers have noted that it has fallen short of offering actual specific guidance. In a qualitative analysis of prescriber responses to the blueprint, Cushman et al. [10] noted five themes of unaddressed issues:

1. what are safe alternatives to opioids,
2. how to overcome barriers to safe opioid prescribing,
3. uncertainty about government regulations,
4. the role of marijuana in opioid prescribing and
5. how to maintain a positive provider-patient relationship while implementing safe prescribing practices.

These exemplify just how difficult it is to sort through the multifaceted approach to chronic pain.

The 2016 CDC Guideline further succeeded in standardizing CNCP management and opioid prescribing, but with unexpected consequences. One of the authors of the guideline noted that some clinicians have responded with inflexible application of recommended dosage and duration thresholds [11]. Other clinicians have universally stopped prescribing opioids or been more apt to dismiss patients from their practice. Also observed is a misapplication of the recommendations to patients with cancer, surgical procedures, or acute sickle cell crises. In addition, though the guideline does not suggest discontinuation of opioids already prescribed at higher dosages, clinicians and payors have used it to justify abrupt discontinu-

ation or coverage of opioid medications. This was not the intent of the guideline, and has led to harm [12].

Knowing that CNCP treatment is complex and the guidelines are incomplete and open to misinterpretation, each practice is compelled to develop its own comprehensive policy. Policies should reflect the national guidelines, but provide instructions relevant to the patient population and community which supports that population. Policies should fill in the gaps not addressed by the guidelines, like including referral options and state-specific PDMP review requirements or clinic resources for managing difficult cases.

What Should the Policy Say?

Development of an institution wide COT (chronic opioid therapy) policy is a complex process. The main components include:

Keeping an updated problem list, changing details when plans change or at least annually

- Document the diagnosis of the chronic pain and/or source and location. Use a template to keep the corresponding overview updated with the following;
    - Brief history of CNCP course (when did it start, relevant injuries, surgeries or other inciting factors)
    - Relevant diagnostics and consultations (i.e. MRI, rheumatoid panel, pain management specialist, etc.)
    - History of treatment received/attempted (spinal injections, surgeries, PT, etc.)
    - Care plan. Includes treatment goals (pain severity and/or level of function), plan for future diagnostics and consultations
- Document opioid dependence (if applicable) as a separate problem with the following:
    - Details of opioid prescription, with allowed quantity per time period
    - Name of designated pharmacy
    - Date when medication agreement was most recently signed

– Urine drug test findings
– PDMP review: any history of inconsistent findings

Creating a medication agreement with the patient who is receiving controlled medications. This is not a legally-binding contract, but an agreement between clinician and patient documenting that the following have been discussed and understood:

• Risks and benefits of acute and chronic therapy
• Which medication(s) with doses and frequency that will be prescribed, to include specific weaning regimens if applicable
• Rules for safe use
• Pharmacy that will be used and who is allowed to pick up prescriptions
• Reasons for deactivation of agreement

The agreement should be signed by the provider and patient and scanned into the EMR. A mechanism for deactivation should be delineated.

Urine drug testing Urine should be collected at every visit, and sent for testing at least annually and more often as needed. All prescribers should know how and when to order confirmatory testing.

Process for providing refills All prescribers should have access to electronic prescribing through a dual mechanism. Paper prescriptions should be discouraged because of risk for diversion. Refills should happen during a face to face encounter and preferably only with the primary care provider. Patients need to be seen at least every 3 months, with additional month supply prescriptions sent to the pharmacy to last the length of time until the next appointment.

PDMP review Specify frequency and documentation process. Prescribers should use a template or other electronically automated process to document that the PDMP was reviewed.

Options for management of medication agreement violations or inconsistent urine drug screen results should be clearly stated:

• Minor (slow wean or increased frequency of visits or urine drug screens)
• Major (termination of prescription or rapid wean)
• Suspected use disorder (transition to medication for opioid use disorder or referral to substance use disorder treatment)

Any particular medications to be avoided Some institutions have established that carisoprodol and/or alprazolam, for instance, are not to be prescribed because of their particular risk.

How to manage "legacy patients," or patients who have been prescribed long-term opioids
Community resources available to patients with chronic pain and opioid use disorder.
Specific weaning options
Clinic resources for assistance and peer review of complex cases

Implementing the Policy

Various models have been studied for optimal implementation of opioid prescribing policies. Parchman et al. (2017) conducted 30 site visits of a variety of clinics settings. They studied how each site re-designed their approach to management of patients on chronic opioid therapy (COT). As a result, they identified a framework based on six "building blocks" [13, 14] for outpatient clinics:

• Provide leadership support. Essential to any initiative is solid buy-in from the leadership. A clinician champion and a multidisciplinary team of supporters will be needed in the clinic to help build a consensus on management of patients on COT. The best leaders are those who have a passion for the cause, i.e. a desire to address the opioid crisis or who have personal experience with an individual

who has suffered from chronic pain or opioid use disorder. Leaders provided protected time and space for the clinic staff to discuss policies. They added regular status reviews to staff and provider meetings.

- Revise and align clinic policies, use patient agreements, and define workflows for care of chronic pain patients. This is the blueprint providing guidance specific to the local practice, which completes and clarifies the less defined national guidelines. It provides tools and sets expectations for the roles of all stakeholders, including providers, support staff, and patients. Almost all of the clinics studies had policies instituted.

- Track the patient population. This building block directs us to look for best ways to identify and manage our population of patients receiving COT. Only when we can see the extent of the population can we begin to manage it. Most sites had created registries to include elements such as last time medication agreement was updated, last urine drug screen, current morphine equivalent dose being prescribed, last PHQ-9 (Patient Health Questionaire-9) score, etc.

- Implement planned, patient-centered visits. Once the policy is established and the population of chronic pain patients is defined, the clinic can prepare for the patient encounters. Clinics did this by "scrubbing charts", or chart reviews, and holding "huddles" (time spent anticipating patient needs with medical assistants) to check for needs. Some providers rehearsed difficult conversations with each other prior to their visits.

- Identify resources for complex patients. Some clinics addressed their more complex patient needs by having group visits staffed by behavioral health and physical therapy providers. Many established "opioid QI teams" to periodically review charts and offer support and specific recommendations for pain management options and weaning regimens. Particularly in rural settings, it could be useful to identify online access to chronic pain specialists and substance use hotlines.

- Measure success. This important step allows us to know what effect our policy is having on our patient population.

The clinics measured a variety of markers of success, such as PEG (pain level/enjoyment/general activity level) scores or the proportion of patients receiving high-dose COT (<90 MME).

In addition, regular educational sessions for clinic staff, clinicians, and patients about the policy is essential. For staff, discussion about the care of the patient in chronic pain and OUD (Opioid Use Disorder) helps to reduce stigma that these patients often encounter. In residency clinics, special challenges exist when preceptors guide residents using varying approaches. Discussion groups and case reviews held for residents and preceptors are helpful to address this challenge. A public health "detailing" campaign implemented in Staten Island which included patient educational posters and informal clinic visitations was shown to be successful in educating patients and clinic staff as well [15].

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Part III
Complementary and Alternative Medicine and Chronic Noncancer Pain

1.1 Introduction on Complementary and Alternative Medicine

Complementary medicine is defined as a diverse group of medical and health care practices that are not considered to be part of the conventional health care system [1]. Typically, complementary medicine is used *together* with conventional medicine, whereas alternative medicine is used *in place* of conventional medicine [2]. Nearly 40% of the U.S. population uses some form of complementary and alternative medicine (CAM) in a given year [3]. In a survey of 15 countries, up to 75% of the population (in Japan and South Korea) were using CAM [4]. Pain (especially back/truncal pain) is the most common reason why patients seek CAM [3, 5–7]. Most of these patients continue to have inadequate relief, have already seen their conventional doctors, and do not inform their doctors of their CAM usage [5, 8, 9].

So why the secrecy? Is it the attitudes of traditional western medicine towards CAM? Are patients afraid to tell doctors that their currently prescribed pain management is less than adequate? Has conventional medicine failed our patients, prompting them to seek care outside of mainstream medicine? When the best conventional pain medicines are considered "effective" by providing only 30%-50% relief, many patients are seeking relief for the remainder of their pain from CAM. Or, even more demoralizing, some may

already have given up hope of any effective treatment as they no longer take part in any medical management at all.

The conventional practice of medicine has recently begun to admit its shortcoming in adequately managing chronic pain to the satisfaction of our patients. Most notably, in 2017 the American College of Physicians (ACP) has placed acupuncture, taichi, and spinal manipulation on the list of recommended *first line* therapies for chronic low back pain, ahead of NSAIDs and other medication [10]. Around the world, medical schools are incorporating some form of CAM into their curriculum or continuing medical education [6, 11, 12]. Kaiser Permanente (a large multi-state health maintenance organization) has built an integrated center for CAM into their healthcare system [4], while government funded Medicaid of Rhode Island routinely pays for these services for select patients [13]. Undoubtedly, the prevalence (and mounting evidence for the effectiveness) of CAM is necessitating conventional medicine practitioners to at least start learning about CAM, if not incorporating it into their current management practices.

Evidence on various CAM modalities is growing and ever changing, and the best place to get current evidence is unlikely going to be a static textbook. Nor is this book meant to be an exhaustive treatise on managing chronic pain with CAM. It merely introduces concepts, frameworks, and resources to better understand CAM and how it might add to the primary care provider's management of chronic pain. Table 1 is an adaptation of the conceptual framework used to categorize CAM [6]. Actually, it can be seen as a method to categorize all medical treatments, as the table lists both CAM and their conventional counterparts.

One of the most salient points of Table 1 is that both conventional medicine and CAM can be similarly categorized. It highlights not the differences, but the inherent similarities. There is recognition by both CAM and conventional medicine that the body in pain needs to be altered and corrected. At the heart of all medical treatment is the need to restore proper function and health to the physical body, and there are just a few fundamental ways to do so.

Table 1 Main categories of Complementary and Alternative Medicine adapted from Wainapel [6]. All medical treatment, whether complementary, alternative, or conventional, seeks to alter the body by either targeting body systems or the mind

Targets methods	Brief description
Manipulative	A practitioner chiefly uses hands to manipulate/affect change onto the musculoskeletal system of a mostly passive patient. Examples include chiropractic services and cranial sacral therapy. A conventional analogy can be manually reducing a dislocated joint.
Energy/ Mechanical	Devices are used to channel various forms of energy, including mechanical onto the body/ musculoskeletal system. Examples include acupuncture and low level laser therapy, and more conventional treatments such as ultrasound, heat, cold, etc.
Exercise	Patients are active participants and are supervised/taught by the therapist. Movement encourages coordination, strength, balance, +/- mental clarity. Examples: yoga and taichi, Alexander technique. Conventional methods include traditional physical therapy.
Medicinal	Includes supplements of vitamins, herbs, foods, etc. that are topically applied, ingested, or inhaled. These substances are analagous to conventional western medicine.
Mind systems	Methods that aim to alter the physical body (or mental state) by acting chiefly on the mind. Include meditation techniques and relaxation techniques. Conventional treatments such as CBT falls into this category.

1.2 Where to Find Current Information

The NIH's National Center for Complementary and Integrative Health (NCCIH) has information concerning CAM practitioner qualifications, paying for CAM treatment, research highlights, and even continuing medical education on CAM. Newsletters such as the NCCIH Clinical Digest are monthly and provides evidence-based information on complementary and integrative health practices. A 2016 NCCIH Clinical Digest on Chronic Pain is available free online: https://nccih.nih.gov/health/providers/digest/chronic-pain and contains valuable information such as patient handouts on acupuncture, spinal manipulation, and massage therapy.

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Chapter 12
Manipulative Therapies for Chronic Pain

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Helpful Tip

1. New evidence is always emerging, keep abreast via usage of reliable internet resources.

Introduction

Manipulative techniques generally focus on affecting change on the physical body with a mostly active therapist and mostly passive patient [1]. Therapists primary use their hands to move soft tissue, muscles, tendons, and/or bones. Popular examples include chiropractic, osteopathic manipulative treatment (OMT), massage therapy, and cranial sacral therapy [2, 3]. The aim of this chapter is not to list, describe, and evaluate every type of manipulative therapy. However, a brief overview of the most commonly used techniques will be given, along with risks and contraindications, as primary care providers may be called on to give some counsel about these techniques.

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Spinal Manipulation

Spinal manipulation is the most commonly used CAM (complementary and alternative medicine) therapy used in back pain [4]. Chiropractic and osteopathic manipulative treatments are often described as hands-on treatment of the spine, including mobilization and manipulation. Mobilization utilizes low grade velocity of joints within the patient's range of motion and control. Manipulation uses a high velocity thrust applied to a joint near the end of the patient's passive range of motion. There may be an audible crack, resulting from cavitation of the joint [5]. Recent review shows that there is moderate quality evidence that spinal manipulation and mobilization is NOT better than recommended therapies for chronic low back pain both short term and at 1 year [5]. The American College of Physicians (ACP) recommends spinal manipulation as one of the therapies to consider for nonpharmacological treatment of chronic low back pain. However, they note the low quality of evidence for this recommendation, and it is listed behind other treatments of higher quality evidence [6]. A recent systematic review of non-invasive nonpharmacological therapies for pain showed that spinal manipulation does not decrease pain, but may improve function [7]. For neck pain, there is cervical and thoracic manipulation and mobilization. A Cochrane review in 2015 notes that thoracic manipulation for chronic neck pain may improve function when comparing to inactive controls (essentially no treatment) [8]. However, 80% of the studies reviewed were low to very low quality.

Osteopathic Therapy

Osteopathic manipulative therapy is defined as therapeutic application of manually guided interventions by a clinician to improve physiologic function or to support homeostasis

Table 12.1 Various Osteopathic Manipulative Therapies (OMT) and their description [1, 10]

OMT technique	Description
Counterstrain	Examiner passively shortens an affected muscle until a tender point is softened.
Muscle energy technique	Examiner applied counter force against a patient's voluntary muscle contractions. Isometric contraction is usually induced. This stretches tight muscle and fascial tissue.
Soft tissue therapy	Manual force is used to lengthen shortened fascial tissue
Spinal manipulation	Manual force is applied to spinal joint to move the joint near its end range of motion.

that has been altered by somatic dysfunction [9]. That being said, osteopathic manipulative therapy (OMT) has a wider range of techniques and applications compared to chiropractic therapy, and can even include the treatment of pneumonia and influenza [1]. Table 12.1 gives an overview of their techniques for pain [10]. Lymphatic pump techniques, also used in OMT, are not noted in Table 12.1, but aim to enhance the function of the lymphatic/immune system [11].

Massage

Therapeutic massage is defined as the manipulation of the soft tissue of whole body areas to bring about generalized improvements in health, such as relief of muscular aches and pains [12]. It is also performed to promote sleep, relaxation, and mental "stress relief". Reflexology, is therapeutic massage of foot regions believed to correspond to body organs [12]. There are various techniques used in massage [12]:

2. Effleurage: gentle stroking across length of muscle
3. Petrissage: Pressure applied across width of muscle
4. Friction: Deep massage applied in circular motions
5. Kneading: Squeezing width of muscle
6. Hacking: light slaps or "karate chops"

A recent Cochrane review for chronic low back pain showed that massage may improve pain and function in the short term compared to inactive control (i.e. no treatment) [13]. The quality of evidence was low to very low. There was no functional improvement long term. In the community, there may be a wide range of massage practitioners, from those with extensive training and certification to those with no formal training at all, as some states to do not require licensing or certification. Thus, the experience and outcome can be quite varied.

Contraindications may include massaging areas with deep vein thrombosis, burns, or tumors [12] (Table 12.2). Adverse events may include pain, muscle soreness, and stiffness [14]. More forceful techniques, such as Rolfing and deep tissue massage may be associated with rare adverse events such as thromboembolism, deep vein thrombosis, hematomas and internal bleeding, stent migrations, and nerve compression syndromes [14]. Furthermore, many practitioners also use essential oils, which may bring about its own set of risks (see later chapters for more information).

Where to Get More Information

Of course, one can actively seek the latest evidence and reviews, however, this may be time consuming and require self-motivation and financial resources. There are more passive ways of receiving current information periodically, such as subscription to an email newsletter. The NIH National Center for Complementary and Integrative

Health has a free monthly newsletter that provides evidence-based information on CAM for various conditions. For point of care information, Table 12.3 lists a few internet resources that can provide information for patients and/or providers.

TABLE 12.2 Summary of a few common manipulative therapies and their risks and/or contraindications [1, 5, 8, 10, 12, 14]

Manipulative therapy	Brief overview	Risks/contraindications
Spinal manipulation/ mobilization	Manipulation is high velocity Mobilization is slow velocity Can occur at cervical, thoracic, and lumbar spine. Often performed by chiropractor or osteopath	Spinal cord injury or stroke may be a risk in cervical manipulation. Most studies too small to detect adverse events [8]. 10–35% of cervical mobilization and manipulation respectively get adverse events such as: increased neck pain, soreness, headaches, dizziness, nausea, paresthesia, upper limb pain, fatigue, and upper back pain [8]. About 6–45% of spinal manipulative therapy had adverse events: increased pain, muscle stiffness, headache [5]. Rare adverse events of manipulative therapies include lumbar disk herniations, arterial injury, cauda equina syndrome, and death [10]

(continued)

Table 12.2 (continued)

Manipulative therapy	Brief overview	Risks/contraindications
Osteopathic manipulative therapy	Largely performed by osteopathic doctors of medicine (D.O.) Use combination of techniques including shortening muscles, lengthening muscles, isometric contractions (muscle energy), and spinal manipulation.	Contraindications include doing high velocity thrusting in patients with arthritis, osteoporosis, Down Syndrome due to risk of catastrophic spinal cord damage [1]. For spinal manipulation, refer to above. For muscle energy techniques, contraindications include recent surgery or currently in intensive care units, or anywhere where active muscle exertion can compromise healing [1].
Massage	Performed by a variety of massage therapists with varying levels of training May include deep/forceful techniques Massage of feet to benefit internal organs is "reflexology"	Contraindication include massaging sites of skin or blood vessel pathology or tumor [12]. Common adverse events are pain, muscle soreness, and muscle stiffness [14]. Rare events (usually associated with forceful techniques) include thromboembolism, deep vein thrombosis, hematomas and internal bleeding, stent migration, and neuropathies [14].

TABLE 12.3 World wide web resources on manipulative therapies

CAM	Web resource
Chiropractic	https://nccih.nih.gov/health/chiropractic https://nccih.nih.gov/health/pain/spinemanipulation.htm
Osteopathy	https://www.nhs.uk/conditions/osteopathy/ (United Kingdom)
Massage	https://nccih.nih.gov/health/massage

Conclusions

Generally, studies on spinal manipulation, OMT, and massage were done for musculoskeletal pain and headaches. Certain manipulative therapies may be of benefit to those with chronic musculoskeletal pain, mostly when compared to no treatment. Although generally safe, these therapies are not without risk and therefore appropriate patient counseling and selection is crucial. New information is always being generated. Usage of reliable internet resources and email newsletters can help with staying abreast.

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Chapter 13
Energy Based Therapies for Chronic Pain

Bonnie Huang Hall

Helpful Tips

1. Advise patients on risks and financial ramifications of undergoing acupuncture
2. Consider the risks of bleeding for anticoagulated patients undergoing acupuncture
3. LLLT may not be covered by insurance.
4. LLLT Home devices are readily available, but may not be as efficacious

Introduction

Another category of complementary and alternative medicine (CAM) are applications of energy in some form or another to bodily structures. There are different forms of energy from various wavelengths of light, thermal energy, mechanical energy, and electrical energy. The most famous example is acupuncture, where a weak electrode (the needle) is inserted percutaneously onto an acupuncture point on the body [1]. Vibratory therapy delivers mechanical

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energy, either locally or to the whole body (via standing on a vibratory platform) [2, 3]. Ultrasound delivers mechanical vibrations in frequencies we cannot hear. Low level laser therapy and other forms of light therapy delivers electromagnetic radiation. Other forms of energy that are often applied to those with chronic pain include heat, which is thermal energy.

For comparison, conventional medicine delivers energy in the form of electricity and heat to aid in tissue cutting and coagulation during surgery (electrosurgery and electrocautery). Phototherapy, delivery of electromagnetic radiation in various wavelengths, is used to treat various diseases such as psoriasis and neonatal hyperbilirubinemia. Vibrators and percussors deliver mechanical energy to assist airway clearance for those with cystic fibrosis.

In this chapter, acupuncture and low level laser therapy will be discussed given their recent recommendation as part of first line treatment from the American College of Physicians (ACP) for the treatment of chronic low back pain [4].

Acupuncture

Acupuncture is part of Traditional Chinese Medicine (TCM) with a history of over 3000 years. Original needles were made of stone and bone [5]. The traditional basis of acupuncture is that disease is caused by an imbalance of "Qi" (pronounced "chee") and acupuncture aims to restore homeostasis by allowing "Qi" (believed to be a type of energy) to flow naturally in the body. Qi flows in channels known as meridians. Single use stainless steel needles are percutaneously applied to various points on the body called acupoints. Heat, moxibusion (burning of herbs), medication or fluid, needle manipulation, and electrical stimulation can be added. Needle insertions into acupoints serve to restore the correct balance and flow of "Qi" and therefore treat disease [1, 5]. Duration of needle insertion and acupoint selection is prescribed by the acupuncturist.

The needles can serve as a weak conductor and therefore enable the flow of electrons to needle sites and between needles. Local reaction caused by mechanical needle insertion to muscle allows for the release of acetylcholine and substance P. Afferent nerves are also reported to be stimulated and block pain [1, 5]. With electroacupuncture, a continuous electrical pulse is generated between pairs of acupuncture needles [5]. There is a high degree of correlation between acupoints and myofascial trigger point locations [6]. (Myofascial trigger points are hyperirritable spots in skeletal muscle that are associated with palpable nodules in taut bands of muscle fibers and thought to cause pain, often in a referred manner.) Other acupoints are key areas of where nerves bifurcate [1].

Acupuncture Is Effective for Musculoskeletal Noncancer Chronic Pain

Regardless of whether "Qi" exists or not, acupuncture, perhaps due to the mechanisms above, has been found to be effective in treating chronic pain [7, 8]. Especially for chronic low back pain, it is effective when compared to no treatment (but not superior to other recommended treatments) [9]. Other systematic reviews conclude that acupuncture slightly decreases pain for chronic low back pain in the long term with strength of evidence rated as low [10]. Acupuncture is currently listed amongst the ACP's recommended first line therapies for chronic low back pain (with moderate quality evidence) [4]. Effects are moderate on chronic low back pain. Chronic neck pain is another realm where acupuncture has been found to be effective [11]. Other areas where there is evidence for the effectiveness of acupuncture appear to be in treating pain from osteoarthritis, shoulder pain, and headache [12]. On the other hand, recent Cochrane reviews indicate that there is insufficient evidence for the effectiveness of using acupuncture to treat neuropathic pain [13], or cancer related pain [14]. As for fibromyalgia, acupuncture effects

were difficult to interpret, with pain relief often not better than sham acupuncture or compared to traditional treatments [15]. In this same review, electroacupuncture was found to be probably better than needles alone.

Acupuncture Treatments

In 2018, Vickers et al. [12] reviewed the literature for acupuncture for chronic pain and published a meta-analysis on individual data. They found that most treatment sessions were weekly, and patients required usually around 6–15 sessions. Most sessions lasted between 15 and 30 minutes and used approximately 6–20 needles. In general, this is a large commitment on time (and perhaps financial resources), as essentially patients are going every week for 2–3 months. When counseling patients concerning acupuncture treatments, it is advisable to discuss the commitment necessary to complete treatment.

Acupuncture Risks and Adverse Effects

In addition, acupuncture is not without its risks and adverse effects. Table 13.1 is compiled from a prospective survey of more than 6300 patients who received acupuncture in the United Kingdom [16] along with Ernst's 2001 review of 9 studies of acupuncture treatments from Asia and Europe with over 250,000 total treatments [17]. Tiredness, drowsiness, and exhaustion after treatment were the most common adverse effects, whose collective incidence was 44 events per 1000 patients over 3 months [16]. As a result, patients should be counseled concerning the risks of drowsiness especially when driving. Bleeding and pain at needle insertion sites were also relatively common adverse events. This may be dependent on the "style" of acupuncture. For instance, "Chinese style" acupuncture often uses deeper muscle insertion techniques and more needle manipulation than "Japanese style". Hence, risks of pain at acupoint site may also vary by

TABLE 13.1 Adverse effects from acupuncture

Source	Adverse effect*
Insertion of needle	Severe tiredness, drowsiness, and exhaustion
	Unacceptable pain at the site of needling
	Bleeding/hematoma
	Bruising at needle sites
	Dizziness/syncope
	Nausea
	Needles being left in
	Local skin reactions to needles
	Very rare:
	Needle breaking
	Pneumothorax, or other visceral
	penetration
Moxibustion	Burns on skin
Advice from acupuncturist	Delay in diagnosis or incorrect counseling concerning medication dosages

*Effects are listed generally from common to rare

practitioner and their style of acupuncture [17]. In general, however, the adverse events are uncommon and generally well tolerated, with the overwhelming majority of patients stating they would go back again (despite the adverse event) [16]. Consequently, the overall consensus is that acupuncture is regarded as relatively safe procedure.

Acupuncture and Anticoagulation

Theoretically, anticoagulated patients should have a higher bleeding risk. However, a recent systematic review showed that the incidence of bleeding complications is still low. In this study of anticoagulated patients, there were 3974 acupuncture treatments studied with 1.4% of treatments resulting in minor bleeding, and only 1 patient (of 394) experienced serious bleeding from acupuncture [18]. Other reported bleeding events were serious, but not attributed to the acupuncture treatment itself. A small prospective study comparing those on anticoagulation/anti-platelet drugs (169 patients)

vs. not receiving either drugs (259) showed no difference in bleeding risk [19].

Acupuncture Conclusions

Acupuncture is effective generally for chronic musculoskeletal pain. Warn patients concerning the time (and perhaps, financial) commitment involved in completing treatments. In addition, counsel patients regarding adverse effects such as drowsiness, pain, and bleeding. Appropriate plans should be made to ensure the safety of patients experiencing these side effects. Assess bleeding risks for those on anticoagulation or antiplatelet therapy. In general, adverse events are rare and acupuncture is well tolerated.

Resources

- For patients and providers in the US. https://nccih.nih.gov/health/acupuncture
- For patients in the UK: https://www.nhs.uk/conditions/acupuncture/
- Acupuncture for Pain Management. Yuan-Chi Lin, Eric Shen-Zen Hsu. Springer NY, NY 2014. For history, mechanisms, and practice of acupuncture for pain. Aimed for those who may want to add acupuncture to their clinical repertoire

Low Level Laser Therapy

Light is a type of electromagnetic radiation. Low level laser therapy (LLLT) is a type of light therapy in the red or near infrared spectrum (660–905 nm). These spectrums were chosen because they can penetrate the skin, soft tissue, and hard tissue. It is also called photobiomodulation, and relies on photons to trigger biochemical changes in the cell. It is "low"

because it does not generate the energy density required to produce heat, tissue destruction, or coagulation. Proposed mechanisms of action include increasing ATP production, activation of mast cells, lymphocytes, and macrophages, and induction of transcription factors (more protein synthesis), and modulation of reactive oxygen species [20, 21].

Effectiveness

LLLT has been applied to a wide variety of clinical applications ranging from wound healing, stroke, neuropathic pain, and musculoskeletal pain. Patients may have heard of LLLT because of its commercial application in "hair growth caps" for alopecia. In the treatment of pain, LLLT can be applied to acupuncture points, myofascial trigger points, the musculoskeletal structures experiencing pain, as well as nerves and lymphatics [20, 21]. There seems to be some consensus that LLLT can be effective in treating chronic neck pain [10, 22]. The ACP's guidelines on chronic low back pain indicated that there was low quality evidence that LLLT had a small effect on pain and function [4]. A meta-analysis that was published in the same year as the ACP's guidelines studied the effects of LLLT on pain [23]. In this meta-analysis, there were 18 studies with a total of 1462 participants. The conditions studied included a diverse array of conditions that included acute back pain, a couple of studies on chronic low back pain, knee ostoarthritis, carpal tunnel, and others. They concluded that there was an overall decrease in pain found in these studies [23]. Other aspects of pain and function (immediate vs long term effects, effect on function) were not examined in this meta-analysis. Of note, 17/18 studies had less than 115 patients.

Several systematic reviews analyzed the usage of LLLT to treat knee osteoarthritis. Their findings are mixed. Earlier reviews show no significant decrease in pain and function, while later reviews show some promise [24–26]. Consequently, there is insufficient evidence to draw any firm conclusions about LLLT for knee osteoarthritis.

Certainly, LLLT has been studied in other realms (fibromyalgia, neuropathic pain, acute postoperative pain), however, there is still limited evidence supporting its use and firm conclusions cannot be made. Currently given the level of evidence, most insurance companies consider it an investigational/experimental therapy. The American Academy of Orthopaedic Surgeons has no recommendations for or against its use. The FDA has approved it for relief of muscle and joint pains [21].

Typical Treatment

From various reports [21, 27], treatment consists of applying the LLLT probe onto specific sites (about 1–15) for approximately 30s–60s per site treated. Probes are often small, 1 cm or less, and do not emit heat. Many lasers do not even emit visible light as they are in the infrared spectrum (810 nm). The therapy may also be performed with LEDs (light emitting diodes) instead of lasers. There are several sessions a week for a few weeks. There can be fast acting pain relief, and long term effects as well [21]. Currently, there is still a lot of variation in treatment sites and laser specifics (wavelengths, energy density, power, etc.), although standardization has been attempted [21, 28, 29].

Adverse Effects

Adverse effects are mainly due to the fact that lasers can damage vision. Lasers are classified into four classes based on their potential danger to the eye. Generally LLLT ranges from class I-III, while surgical lasers are class IV [21, 24]. In general, many of the reviews and studies listed no actual harms or adverse effects.

LLLT potential hazard	Adverse effect	Precautions
Lasers only	Eye damage	Do not aim in eyes Wear safety goggles

The North American Association for Laser Therapy in 2010 listed a few contraindications including:

• Pregnancy: do not aim therapy at fetus
• Cancer: do not aim therapy at sites of primary tumor or metastasis
• Epileptics: may induce seizures

Home Treatment

Treatment can also be accomplished at home, with commercially available devices using LED technology instead of lasers. LEDs do not share the laser's potential for ocular damage. Thus, LED technology increases the safety of the device. It also enables larger areas to be treated [30]. LEDs for home use, however, may not be as "powerful" as those for medical use, and thus, efficacy may also be diminished.

Conclusions

LLLT may be considered for chronic low back pain as per the ACP. In general, the evidence concerning its efficacy is still debatable. Many consider it an experimental therapy, and thus, insurance coverage may be lacking. LED technology can increase the safety of LLLT.

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Chapter 14
Medical Marijuana for Chronic Pain

Bonnie Huang Hall

Helpful Tips
1. Dispensaries sell marijuana products, usually of higher concentrations than used in most studies
2. Check local marijuana regulations by visiting trusted government websites
3. Perception and biases are common when discussing this controversial subject

Introduction

Many currently practicing physicians attended medical school when marijuana was just a commonly used street drug. It was not particularly harmful compared to other illicit street drugs (such as cocaine) and little time was devoted to its study. Marijuana's mechanisms of actions on a molecular level and its pharmacology were not taught in pharmacology courses. Now the tide has changed. The most commonly cited reason for the use of medical marijuana (i.e. medical cannabis) is for chronic pain [1, 2]. Marijuana has of late become a hot topic of debate, given preliminary evidence on its role in chronic

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pain and its complex relationship with opioids and opioid related complications. Consequently, this chapter deliberately focuses only on marijuana and its role in chronic pain.

What Is Marijuana?

Marijuana (or sometimes spelled marihuana) is a flowering plant originating from Asia that has thousands of years of history, cultivation, and medicinal usage by humans (Box 14.1) [3, 4]. Cannabis is the genus name for marijuana. In general, there are three species of marijuana:

• Cannabis Sativa
• Cannabis Indica
• Cannabis Ruderalis (uncommon)

In general, Cannabis Sativa is the most commonly used species in medical marijuana. Cannabis Sativa, of note has subspecies: it can be the commonly known plant grown for its recreational/medicinal value, or hemp which is grown for its oil, fibers to make cloth, and seeds [3, 4].

There are male and female cannabis plants. Only the female plant has medicinal/recreational value due to the substances (cannabinoids, terpenes, and other chemicals) found in high concentration in its flowers and the resin glands on the flower. The resin glands are also known as trichomes. Resin glands look like fuzzy hair like growths which can produce resin at the tips. Marijuana sometimes refers to the flower of the cannabis plant because these are the parts of the plant of medicinal/recreational value. Hashish is made from the resin glands stripped from the flower or other parts of the plant [5].

Box 14.1 A Brief History of Cannabis [3]
Early History: Chinese and Hindu pharmacology have used cannabis for thousands of years
1840 Queen Victoria may have been prescribed marijuana as pain reliever for menstrual cramps (as a tincture).

1900s Eli Lilly and Squibb were manufacturing drugs produced from marijuana

1930 Harry Aslinger, the first commissioner of the U.S. Federal Bureau of Narcotics (FBN) started making marijuana illegal in all states.

1937 Cannabis became regulated by the DEA where possession of it became a crime.

1990–1993 Cannabinoid Receptor 1 and Cannabinoid Receptor 2 discovered [6, 7]

1996 California became first state to legalize use of medical cannabis.

Cannabinoids and the Endocannabinoid System

Cannibis Sativa contains hundreds of compounds such as terpenes and cannabinoids. Two cannabinoids of significance, delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), are the two most studied components. THC is thought to be primarily the psychoactive and analgesic component [1, 8]. It acts primarily on the nervous system and immune cells through cannabinoid receptors (CB) [9]. There are two main types of cannabinoid receptors: CB1 and CB2. CB1 is found in both central and peripheral nervous system. CB2 is found on immune cells, which when activated, is inhibitory in nature. Subspecies of Cannabis Sativa are grown mainly for its recreational or medicinal value. These subspecies of Cannabis Sativa have higher amounts of THC compared to CBD.

CBD, on the other hand, does not have psychotropic effects, and may actually inhibit the psychotropic effects of THC. Generally, CBD acts weakly on CB1 and CB2 receptors. CBD works on other receptors, such as the adenosine receptor, which when activated decreases inflammation. Due to these antioxidant and anti-inflammatory properties, CBD may be exploited as a treatment for neurological diseases such

as epilepsy, multiple sclerosis, and movement disorders [10]. Pain modulation is thought to be achieved via CBD's anti-inflammatory properties [11]. The mechanisms and actions of CBD are still being investigated. The hemp subspecies of Cannabis Sativa has minimal THC and relatively more CBD.

The human body has its own endogenous cannabinoid ligands (analogous to endorphins and the opiate receptor system). With its above mentioned receptors and other signaling molecules, it forms the endocannabinoid system.

The endocannabinoid system has three main functions [9].

1. Stress modulation: acting on nervous, endocrine, and behavioral systems
2. Energy regulation: acting on intake, storage, and utilization of food
3. Immune regulation: activation during tissue injury, modulating immune and inflammatory responses

It is consequently understandable that cannabis has anxiolytic and psychotropic effects as one of the main functions is stress modulation. Due to its effect on energy regulation, it can also be an appetite stimulant.

Furthermore, it is feasible that pathology occurs when the endocannabinoid system is disturbed. It is also feasible that correction of that system can be achieved through exogenous substances such as cannabinoids [9]. Hence, there is the ongoing quest to validate this hypothesis via medical cannabis research.

What Is Medical Cannabis?

To add to the confusion of the matter, medical cannabis is not one entity. Medical cannabis is not simply smoking marijuana. Medical cannabis is divided into three main classes of substances.

There are basically three main types of medical cannabis:

1. the cannabis plant itself
2. plant derived products
3. synthesized cannabinoid compounds.

The first form of medical cannabis is the actual cannabis plant itself. The flower or resin glands (in the form of hashish) are mainly the parts of the cannabis plant of medicinal/recreational interest. The dried flowers (which many people identify as "marijuana") are readily found at cannabis retail dispensaries and are commonly sold by weight and variety [1]. Varieties are different strains of a cannabis species that can be bred for their different THC and CBD content. There are also hybrid plants as well. Varieties often have consumer oriented names such as "Cherry Cheesecake" or "Maui Haze." It is commonly smoked or vaporized. They can come pre-rolled (i.e. a "joint") and appear similar to cigarettes.

There are also plant derived products consisting of THC, CBD, other cannabinoids, and combinations thereof. Extracts, oils, and concentrates can be made from cannabis flowers and/or trichomes [12]. THC and CBD can be isolated and purified from plant material. There are also a wide range of cannabis-derived products in the form of food and snack items ("edibles"), health products, and beauty products.

THC and CBD can also be made synthetically. There are FDA approved and investigational drugs. Dronabinol and Nabilone are synthetic forms of THC which can be prescribed. These are scheduled medications. Ajulemic acid is a metabolite of THC that does not produce the adverse behavioral changes. It has mostly been explored as an anti-inflammatory agent [13]. In 2019, it was still undergoing phase 3 clinical trials. Table 14.1 lists the various methods in which marijuana and its related products have been studied in chronic pain.

Recreational vs. Medical Use

Most studies that attempt to show the efficacy of medical cannabis use cannabis and cannabis products of relatively low concentrations of THC and/or CBD compared to recreational cannabis [1, 14]. For medical use, THC has been studied in concentrations around 1–5%. Side effects often become problematic around 7–10% THC.

TABLE 14.1 Types of medical cannabis studied in chronic pain

Type	THC/CBD content or ratio	Route of Administration	US Status[*]
WHOLE PLANT			
Marijuana flowers	Varies	Varies, often inhaled via smoking/vaporizing	
PLANT DERIVED PRODUCTS			
Cannabidiol (CBD)	CBD amount varies	Oral	
delta-9 -tetrahydrocannabinol (THC)	THC amount varies	Oral	
Epidiolex[a]	>98% CBD,100 mg/ml	Oral (Oil)	FDA approved
Nabiximol	2.7 mg THC, 2.5 mg CBD	Oromucosal Spray[a]	(Available in other countries)
THC/CBD	Varies	Oral	
SYNTHETIC PRODUCTS			
Ajulemic acid	THC metabolite	Oral Capsule	FDA fast track
Dronabinol[b]	THC 2.5,5,10 mg strengths	Oral Capsule/solution	FDA approved
Nabilone[b]	THC 1 mg	Oral Capsule	FDA approved

[*]US Federal law prohibits unless otherwise noted. Some states may allow cannabis for medical use. Some states may allow for medical and recreational use. [a]Epidiolex is used in seizure disorder associated with Lennox-Gastaut syndrome or Dravet syndrome. [b]These compounds are used typically in the treatment of chemotherapy-induced nausea and anorexia from AIDS (Acquired Immune Deficiency Syndrome)

Marijuana dispensaries often carry varieties with high THC content, in the 20–30% range, likely aimed for the recreational user. These may carry more unwanted side effects without increasing analgesia. On the other hand, many patients find that inhaling cannabis plant material offers better pain relief than oral pharmaceutical preparations or extracts. The reasons for this are multifactorial [1].

Medical-Legal Issues

US marijuana dispensaries generally do not distinguish between medical or recreational use, although some countries such as Israel and Canada do [1]. State laws may limit how much a patient/user can buy. State laws may also require labeling of cannabinoid content. Currently, under US federal law, marijuana is still classified as a schedule 1 drug, meaning it has currently no accepted medical use and high potential for abuse [15]. Under US federal law, prosecution can still occur. On the other hand, synthetic cannabinoids have been FDA approved such as Nabilone and Dronabinol.

The federal and state legislation and regulations concerning cannabis is rapidly evolving. To stay abreast, these websites may be useful:

- FDA: https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-questions-and-answers#whatare
- National Conference of State Legislatures: http://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx. This website has a compendium of state marijuana laws and other web resources.

Medical Cannabis Effectiveness

Research into the risks and benefits of medical cannabis is accumulating. Due to the different dosages involved, types of medical cannabis used, and routes of administration, it has

been challenging to make sense of the current data. In 2018, a Cochrane review examined the evidence for medical cannabis in treating chronic neuropathic pain [16]. Out of the many studies initially reviewed, it based its conclusions on 16 randomized double-blinded placebo controlled trials. The trials used medical cannabis, plant-derived, or synthetic cannabis-based medications against placebo or other active treatments for chronic neuropathic pain. They found that cannabis-based medicines may increase the number of people achieving 50% or greater pain relief compared with placebo. This is based on eight studies with 1001 study participants with low quality of evidence. A secondary outcome was also analyzed based on 10 studies with over 1500 study participants. Cannabis-based medicines probably increase the number of people achieving pain relief of 30% compared to placebo (moderate quality of evidence). The number needed to treat to obtain these outcomes (NNTB) were 20 for the 50% relief, and 11 for the 30% relief. In addition, cannabis based medicines were able to benefit sleep and also psychological distress in these patients. Of note, this review cites references to the fact that current medications used to treat chronic neuropathic pain have a lower NNTB of 4–10. Lastly, similar to older reviews, there was no improvement in quality of life [14].

This Cochrane review also found adverse effects and harms. Although there was not enough information to determine if cannabis-based medicines increase the frequency of *serious* adverse events, they did determine that more study participants dropped out than placebo due to adverse events. The number needed to treat to harm an additional patient (NNTH) was 25 (moderate quality evidence). Secondary outcomes analyzed revealed that cannabis treated participants had more nervous system adverse events than placebo (61% vs 29%), with NNTH 3 (low quality of evidence). Psychiatric disorders were also an adverse event (NNTH 10).

Consequently, given the risks and frequency of adverse events, the authors of this Cochrane review concluded that

although cannabis based medications can improve chronic neuropathic pain, the risks may outweigh the benefits.

Other reviews similarly note the potential reduction in pain intensity for patients with chronic neuropathic pain [17], but also list considerable adverse effects, or caution against the unknown risks associated with long-term use [14, 18].

Cannabis Harms

Medical Cannabis Side Effects

Most commonly, the side effects reported were neurological. Sleepiness, dizziness and mental problems (confusion) are common side effects to medical cannabis treatment [16, 18]. Neurocognitive impairment was also cited in other reviews. Adverse effects include headaches, dizziness, sedation, confusion, dysphoria, poor concentration [14]. Neuropsychological functions were also impaired. Attention, learning, memory, psychomotor speed were more impaired in patients treated with 7% THC compared to 3% [19]. In addition, feelings of being "high" or "stoned" were also reported as adverse events. Generally, adverse effects associated with THC were dose-dependent [14, 19].

A summary of the mental health and cognitive harms of cannabis in the general population can be found in the review by Nugent et al. [18] and the National Academies of Sciences, Engineering, and Medicine [10]. There is agreement that cannabis contributes to worsening cognitive function and increasing the risk of certain mental health conditions such as mania, schizophrenia, and other psychoses. Currently, there is a general consensus based on limited evidence that cannabis does not increase cardiovascular ischemic disease, lung cancer, or pulmonary dysfunction (beyond an increase in cough and phlegm). Given conflicting evidence, it is unclear if there is definite proof for increasing the rates of testicular cancer. There is

strong agreement, however, that if intoxicated, there is a moderately increased risk of motor vehicle collision (which can be fatal). Some serious diseases such as tubercolosis and aspergillosis have been associated with smoking cannabis. For patients desiring pregnancy (or already pregnant) ACOG (American College of Obstetrics and Gynecology) has recommended women to refrain from cannabis use [20]. Cannabis usage has been associated with fetal harms, resulting in decreased birthweight, impaired memory function at 36 months, and altered visuospatial memory as an adult [21]. As a final word of caution, long term effects of cannabis use has not been thoroughly evaluated.

Cannabis and Substance Use Disorder

Although the primary reason why patients may seek medical cannabis is pain relief, cannabis use disorder (or other substance use disorder) may develop. In a study with chronic pain patients already on opioids, this is a small risk (2.4%). The risk of substance use disorders in this group of patients was also increased when urine toxicology was positive for marijuana [22]. In patients taking medical cannabis, the risk for cannabis use disorder was also increased [23].

Cannabis Perceptions and Other Risks

More and more, cannabis is being perceived across the US as a "safe" drug, even by wealthy, educated people [23]. At the same time, cannabinoid (mainly THC) concentrations in marijuana plants are increasing to higher and higher levels [1, 10, 23]. As previously mentioned, it has been shown that the side effects of THC are dose dependent. Consequently, it is questionable how much this perception of safety is rooted in reality. In addition, given the economic aspects and cultivation

process of cannabis, harmful contaminants may be present in cannabis such as pesticides, fungi, bacteria, and heavy metals. Lead or glass beads may be added to increase the weight. Tobacco and calamus may be added to increase the psychotropic effects of low quality cannabis. There is therefore a need to regulate labeling of medical cannabis, especially with details concerning safety and purity [24]. Lastly, like all medications, there is always the danger of accidental pediatric ingestion [24].

Conclusions

Consequently, before we give our professional opinions, we must identify our own biases, examine the evidence, and give a proper risk and benefit analysis tailored to our patients. Patients in chronic pain and their physicians are all desperately looking for a means for relief. Given that facts and perceptions are constantly changing, there seems to be few standard clinical criteria by which medical cannabis can be recommended for chronic neuropathic pain. In addition, cannabis, unlike other drugs, do not come with labels or recommendations concerning relative and absolute contraindications. As a result, counseling patients concerning medical cannabis is still a highly individualized process.

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Chapter 15
Medicinal Therapies for Chronic Pain

Bonnie Huang Hall

Introduction

What is medicine? Medicine is something that is introduced into the body (PO, IV, topically, inhaled, etc.) that aims to alter the body in order to prevent, treat, or cure disease. Drugs, as defined by Merriam-Webster, is "a substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease." The 3rd definition states a drug is a substance other than food intended to affect the structure or function of the body. This chapter addresses the various substances patients essentially use as drugs, but that are considered complementary or alternative. Common examples include easily purchased vitamins and minerals, supplements, and other nutraceuticals. Other forms of complementary or alternative medicine include Ayurvedic herbs, traditional Chinese herbal medicine, homeopathy, and aromatherapy (Table 15.1).

In order to distinguish complementary and alternative medicines (which can include other types of therapies that are not used as drugs e.g. acupuncture, chiropractic, etc.), henceforth, substances that are complementary or alternative in

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nature and used as drugs by patients will be referred to as CAD (complementary or alternative drugs). To describe in detail the many CADs consumers use to (often self treat) their chronic pain would likely require a separate multi-volume series. That is not the objective of this book. Instead, we will discuss topics that will help the primary care provider guide the patient who uses or is contemplating the use of CAD.

Table 15.1 Definitions of substances often taken in order to prevent, treat, or cure disease

Medicine type	Definition
Supplement	US Congress defined the term "dietary supplement" in the Dietary Supplement Health and Education Act (DSHEA) of 1994. A dietary supplement is a product taken by mouth that contains a "dietary ingredient" intended to supplement the diet. The Federal Food, Drug, and Cosmetic Act defines a dietary ingredient as a vitamin; mineral; herb or other botanical; amino acid; dietary substance for use by man to supplement the diet by increasing the total dietary intake; or a concentrate, metabolite, constituent, extract, or combination of the preceding substances. Unlike drugs, supplements are not intended to treat, diagnose, prevent, or cure diseases [1, 2][a]. Examples: red yeast rice, omega-3, calcium, chondroitin sulfate.
Ayurveda	Developed in India, Ayurveda literally means "life knowledge" or the "science of life". It is a system of understanding the human body and health in terms of body, mind, and consciousness. Disease is a disharmony of various components of the body such as doshas (bodily humors). Rasayana is rejuvenation of the body with three subcategories: restoration of tissues through herbs, minerals and exercises [3]. In this chapter we will refer to Ayurvedic herbs and minerals used as drugs.

TABLE 15.1 (continued)

Medicine type	Definition
Traditional Chinese Medicine (TCM)	TCM is based on balance among Yin and Yang, five basic elements, and the relationship between humans and nature. Encompassing a wide variety of techniques including acupuncture, taichi, and herbal medicines [4], TCM views pain as a result of blocked blood flow and/or "qi" stagnation [5]. In this chapter we will refer to Chinese herbs used as drugs.
Homeopathy	Developed in the nineteenth century by S. Hahnemann, this is a therapeutic method of using *dilute* medicines to treat disease. The underlying principle is "let like be treated by like" [6, 7] that is, a substance that causes symptoms in a healthy person can be used in diluted form to treat symptoms and illnesses [8]. Ingredients are listed in terms of dilution (e.g. 30C, 2X). The more dilute, supposedly, the more powerful.
Aromatherapy	Medicinal use of plant derived essential oils which are introduced to the body either topically or inhaled [9]. Common oils include lavender and peppermint. Essential oils are highly *concentrated*, and a carrier oil is used to dilute the essential oil when applied topically. Some essential oils may be ingested.

[a]Two health claims for supplements have been approved by the FDA. Calcium reduces the risk osteoporosis. Folic acid lowers the risk of neural tube defects [10]

Supplements

Given the economic impact of supplements and the high prevalence of their use, there will be a focus on supplements. In the US, natural products (nonvitamin, nonmineral supplements) were the most widely used of any CAM type [11]. For a more thorough, but brief, discussion of supplements in the US, refer to (the freely available) chapter 9 Dietary

Supplements from *Complementary and Alternative Medicine in the United States,* published by The National Academies Press [10].

Supplements: Nearly Everyone Is Using It

There are a few important points to make concerning supplements. The first is that our patients are using supplements – whether we know it or not. In 2002, the supplement industry had 18.7 billion dollars in sales [10]. Various surveys of Americans show that roughly half to two-thirds take a supplement [12]. Many are educated, older, and do not tell their physicians about their usage [10, 12]. Consequently, as primary care providers, we need to inquire concerning the supplements our patients are using, and be cognizant of the potential consequences of supplement use.

Supplements: Can We Trust What's in It?

The second point is that in the United States, supplements are not regulated as pharmaceutical drugs, but rather, more similarly to food [10]. (Albeit it is regulated in its own separate category.) One of the key differences is that pharmaceutical drugs require premarket FDA approval, risk benefit analysis prior to marketing, postmarketing reporting and surveillance (of adverse events) by industry. In short, manufacturers of the drug need to prove the drug is safe and works. On the other hand, supplement regulations do not require any of the above. The FDA, not the manufacturer, needs to show the burden of proof that a substance is unsafe in order to remove it from market. Essentially, it is waiting for serious adverse effects to accumulate before a supplement is deemed unsafe and removed from shelves.

In order to make sense of the current regulation of supplements, a simplified treatment of this subject is presented. An analogy is made with the food industry. Generally, we ingest food and it is considered safe, as long

as it is manufactured and processed accordingly to health standards. There is no pressing need for a risk benefit analysis for eating apples or canned soup. As consumers, we generally trust what is inside the soup can. No independent verification is required for food. Food is sold, and basically not removed from market, unless something happens, such as a salmonella outbreak. Then various agencies step in to remove the product. Supplements are treated similarly in the US.

However, as what is inside a supplement capsule or tablet is not as obvious as peering into a can of soup, sometimes supplements do NOT contain ingredients as labeled, contain fillers, or even other plant material which can be allergens [13, 14]. They may also contain heavy metals, fungi, or bacteria. Consequently, as primary care providers, we need to make sure our patients are taking authentic, quality products. Most commonly, this can be done by recommending brands of supplements that have been independently verified by outside laboratories (Table 15.2). For example, the "USP" verification mark can be found on some supplements after review by the United States Pharmacopeia Convention, a non-profit organization that also publishes the official US drug compendium. The label indicates the authenticity of the product, in addition to compliance with contaminant standards, bodily absorption standards, and manufacturing processes.

Safety of Supplements

However, even if the authenticity of the supplement has been verified, and it is not adulterated with harmful contaminants, there is no guarantee that the amount taken is safe for the patient's condition. There are basically three sources of safety concerns associated with supplement use [15]:

1. Adverse effects of the supplement itself
2. Drug-Supplement interactions
3. Delaying or replacing conventional treatment with a supplement of unknown efficacy.

Table 15.2 Independent laboratories or services that verify supplement authenticity, quality, and/or contaminants

Organization	Functions
USP: United States Pharmacopeia	Non-profit organization. Sets standards for drugs and supplements. Tests authenticity, contaminants, and compliance to FDA Good Manufacturing Practices. Provides a USP verification mark if meeting standards.
NSF: National Sanitation Foundation/ NSF International	For profit organization that develops public health standards for a variety of products, not just supplements. Tests products for a fee according to standards. Provides a verification mark if meeting standards.
ConsumerLab.com	For profit company. Independently tests authenticity and compares supplements. Provides supplement articles aimed at the layman. Requires fee to access information.
LabDoor.com	For profit company. Independently tests authenticity and compares supplements. Checks for heavy metal contaminants. Sells supplements. Free access to information.

Although most consumers believe that supplements are safe, supplements can be dangerous. Supplements are similar to pharmaceutical drugs in the sense that all have side effects and dose-related toxicity. Even plain water, when taken too much, can overwhelm the renal excretion system and cause severe hyponatremia. In Canada, a case of perma-

nent renal damage due to vitamin D overdose was recently published [16]. Supplements, traditional Chinese medicine, and Ayurvedic herbs alike may cause drug-induced liver injury. In addition, Ayurvedic herbs have been found to have high rates of contamination with volatile compounds, arsenic, or mercury [17]. Currently, the fraction of drug induced liver injury from supplements is growing from 12% to 21% [18]. Those who do have drug induced liver injury from CADs often have more severe clinical courses, with increased transplant rates and decreased 21 day transplant-free survival [18]. That being said, in 2013 the American Association of Poison Control Centers reports over 1600 pharmaceutical drug related deaths, and zero fatalities from supplements [19].

Consequently a few helpful tips to remember when advising patients on supplements and CADs.

1. Fat soluble vitamins can be toxic:

   - Vitamin A [20]
   - Vitamin D [21]
   - Vitamin E
   - Vitamin K

2. Supplements can cause liver injury or interact with other drugs.

   Given that there are so many supplements and herbs, primary care providers cannot be expected to know all the potential interactions, toxicities, and adverse effects associated with each supplement or herb. Consequently, it is important to have a trustworthy and informative point of care resource. Helpful websites that can be used at the point of care detail supplement doses, interactions, potential benefits, and adverse effects (Table 15.3). Bookmarking these sites on your internet browser, incorporating them into electronic medical record via templates, or typing them into other electronic medical record short cuts may facilitate timely access to supplement websites and information.

Table 15.3 Websites that may be helpful in counseling patients on supplements and herbs

Website	Information provided
NIH Office of Dietary Supplements https://ods.od.nih.gov/factsheets/list-all/	Contains fact sheets for common vitamins, minerals, amino acids, herbs, etc. Some may have fact sheets geared to professionals (stating dietary requirements and upper limits based on age, etc.)
NIH Liver Toxicity Database https://livertox.nlm.nih.gov/	Can search pharmaceutical medication along with supplements for their liver toxicity potential and/or affect on liver metabolism (cytochrome system).
NIH National Center for Complementary and Integrative Health https://nccih.nih.gov/Health/HerbListApp	HerbList App has fact sheets on more than 50 herbs. Does not require internet connection once App is installed.
Medscape Drug, supplement, Herb Interaction Checker https://reference.medscape.com/drug-interactionchecker	Allows users to input herbs, supplements, vitamins and pharmaceutical medication to check for adverse interactions. Free to use.

Specific Supplements and Chronic Pain

A recent review assessed 19 dietary ingredients for their quality, efficacy, and safety for chronic musculoskeletal pain [22]. Given insufficient evidence, it could not establish any definitive clinical guidelines. However, it did find that given minimal risks (and about equally minimal benefits), they did conditionally recommend substances such as avocado, soybean unsaponifiables, capsaicin, curcuma, ginger, glucosamine, melatonin, and vitamin D. They recommended against collagen, creatine, devil's claw, l-carnitine, methylsulfonylmethane, willow bark extract, and vitamin E.

A special mention will be made for vitamin D insufficiency and deficiency as it has been linked to those with chronic pain. A 2015 Cochrane review of 10 randomized double-blind placebo-controlled trials of vitamin D supplementation in a variety of chronic pain conditions did not show improvement of chronic pain or function [23]. Some studies did not note baseline Vitamin D status while other studies did note baseline deficiency or insufficiency. Consequently, regardless of initial vitamin D status, efficacy was not found for vitamin D supplementation in this Cochrane review. Another review published that same year similarly finds that with randomized double-blind placebo-controlled trials, the effects of vitamin D were not significant, but in other trials with designs subject to more bias, over 90% showed effectiveness [24]. A year later, a review of 19 randomized controlled trials found that there was no significant difference in mean pain scores at final follow-up in 14 trials [25]. This same meta-analysis does state there is a greater mean *change* in pain scores in the vitamin D supplementation group. Consequently, whether vitamin D supplementation is effective is still an ongoing area of research as dosages, deficiency, and pain conditions are further evaluated. Regardless, if vitamin D deficiency or insufficiency has been discovered, it should be treated to prevent adverse effects on bone density and calcium regulation. Currently, the best evidence suggests that most likely vitamin D supplementation does not have a significant effect on pain relief for those with chronic pain.

Aromatherapy

Aromatherapy is the use of essential oils as medicinal therapy. According to the United Nations Comtrade statistics, the global aromatherapy and fragrances market in 2011 was 24 billion dollars, and growing at a rate of 10% per year. A recent US survey showed that about 30% of respondents used an essential oil in the past month. (This rate of usage was similar to France.) From that survey, it was found that

over 50% of essential oil consumers used the product to treat musculoskeletal problems [26]. Currently, most of the research in aromatherapy has been on its effects on mood and stress. However, essential oils have been purported to be effective in a treatment of a wide variety of ailments, from aches and pains, bacterial infections, to warts. Essential oils are commonly inhaled, via a saturated tissue next to the patient, or vaporized. Essential oils can be applied topically if diluted properly. Some essential oils may have therapeutic uses when taken orally. A brief overview of aromatherapy is given in Aromatherapy With Essential Oils (PDQ®): Health Professional Version [27].

Currently, there is some limited evidence that essential oils may play a role in certain conditions. For example, acne vulgaris may be treated with tea tree oil [28]. Peppermint oil (often in the form of enteric coated capsules) can be used as an effective short term treatment in irritable bowel syndrome [29].

Unfortunately, essential oils used in aromatherapy are not without side effects. Essential oils are highly concentrated and can cause poisoning, especially in small children. For example, as little as 10 ml of clove oil has caused toxicity in toddlers, leading to hepatic and renal impairment [30]. Methyl salicylate is a common ingredient in lotions and creams aimed to relieve muscular aches and pains. Small quantities of wintergreen oil, which is 98% methyl salicylate, can also lead to fatal toxicity in adults and children alike [31, 32]. In addition, topical application of many citrus oils can also lead to phototoxicity, resulting in burns [33, 34]. Contact dermatitis is also a frequent side effect [35], and even airborne contact dermatitis can occur when the essential oil is vaporized [36]. In addition, the estrogenic effects of lavender and tea tree oils have been documented to cause prepubertal gynecomastia in boys [37]. For those with estrogen sensitive tumors, it may do well to err on the side of caution, and advise patients to avoid the use of these essential oils. Consequently, essential oils, if used at all, should be used with caution and stored safely out of the reach of children. Potential side effects and risks should be discussed with patients.

Homeopathy

Homeopathy is the use of very dilute substances to treat disease. In 2012, only about 2% of Americans used homeopathic remedies in the past 12 months. Respiratory and otorhinolaryngology complaints were the most common reasons for the use of homeopathy [38]. In Germany, homeopathy appears more common amongst internal medicine patients. About 35% of these patients report using homeopathy [39]. Arnica montana, a flowering plant, is one of more popular substances used in homeopathy to treat pain. Currently, the consensus is that there is limited evidence on the efficacy of homeopathy, much of the evidence is of such low quality that firm conclusions cannot be drawn, or if they were drawn, that homeopathy is not better than placebo [40–44].

Conclusions

Pharmaceutical drugs are highly regulated, with required reporting of side effects and adverse events. Efficacy must be proven in order to market these drugs. Manufacturers of supplements, homeopathy, and essential oils do not need to report side effects and adverse events. They do not need to prove these substances are effective before marketing them to consumers. Consequently, physicians and consumers do not have information on side effects and adverse events. However, this does not imply that these substances are safe or efficacious.

There is a booming economic interest behind each of these complementary or alternative drugs with minimal data to support efficacy. As physicians and primary care providers, we need to ensure the safety of our patients using supplements and at least inform them with what little information we know.

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Chapter 16
Exercise or Movement Based Therapies for Chronic Pain

Bonnie Huang Hall

Introduction

Exercise based, or movement based, therapies are another large category of CAM. This type of therapy generally involves an active participant guided by a therapist or instructor [1]. Various examples of exercise-based therapy include Tai Chi, Yoga, Alexander Technique, Pilates, and Motor Control Exercises (Table 16.1).

In general, exercise has been shown to be effective in various musculoskeletal conditions such as osteoarthritis [2, 3] and chronic low back pain [4]. A recent Cochrane review of 21 reviews that assessed a variety exercise therapies in a wide variety of chronic pain conditions (including fibromyalgia, dysmenorrhea, spinal cord injury, etc.) showed that there is low quality of evidence that exercise can improve pain severity and function [5]. Currently, it is not clear that any form of exercise is superior to another.

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Table 16.1 Various types of exercise, or movement-based therapies

Exercise-based therapy	Overview
Tai Chi/Tai Chi Quan	Originating in China, it is defined as an exercised based on slow intentional movements, often coordinated with breathing and imagery, which aims to strengthen and relax the physical body and mind, enhance the natural flow of "qi" (life energy) and improve health, personal development, and self defense. It is a multicomponent intervention, incorporating not just physical strength, coordination, and flexibility, but also mindfulness, psychosocial interactions, being in nature, and rituals [6].
Yoga	Originating in India, it is a set of poses and positions used to used to treat specific medical conditions. Asanas are postures in standing, sitting, supine, prone, or inverted positions. Yoga seeks to improve flexibility, balance, strength, and mental focus [1].
Alexander technique	Method to teach participants to recognize and self correct poor postures and release unnecessary muscle tension. Lessons are spent initially on correcting stationary positions, then to movement, then to daily activities [7].
Pilates	Invented in the 1920's by Joseph Pilates, it is series of exercises (mostly isometric contractions of core muscles) aimed to improve posture. Some of its basic principles include: centering (or tightening) trunk muscles, concentration, control of posture, and breathing. Popular method for treating low back pain [8].
Motor control / spinal stabilization exercises	Based on the theory that abnormal control of spinal muscles cause back pain, motor control aims to specifically activate and control deep trunk muscles. It is often a 1:1 intervention where participants are taught to contract specific trunk muscles, stop overcontraction of superficial muscles, and correctly use trunk muscles in static, dynamic, and functional activities of daily life [9].

Harms

From these reviews, most of the harms associated with exercise based therapies were worsening muscle pain.

Conclusions

There are various forms of exercise or movement based therapies. Exercise and movement based therapies have been found to improve chronic pain. Currently, there is no form of movement based therapy that is superior to another. Adverse events include worsening pain.

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Chapter 17
Mind-based Therapies for Chronic Pain

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Introduction

Approximately one half to two thirds of all patients diagnosed with chronic pain have some form of psychological distress, most often depression [1]. Mind-based therapies, (also known as mind-body therapies, or psychological therapies) can be used in chronic pain. In mind-based strategies, the mind is the primary effector of change on the body, as opposed to medication, exercise, or procedures [2]. These may include forms of meditation, religious practices such as prayer, psychotherapy, and traditional cognitive behavioral therapy. Almost one fifth of the US adult population currently practice some type of meditation. Some studies show that almost 60% of meditation users have some sort of pain. Most of these practiced either Tai Qi or Yoga, which traditionally have both movement-based and mind-based treatment strategies [3]. In other studies, about 60% of patients with chronic pain used prayer to cope with pain [4], while 40% state they became more spiritual or religious after onset of a painful condition [5]. Spirituality and religion can shape one's worldview and has an important role in understanding

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negative events, including illness and pain. It can also influence how one copes with these events [6]. A Gallup survey revealed that 70% of patients responded it was important or somewhat important to have a physician who was spiritually attuned to them [7]. In the addiction literature, religion and spirituality have been positively correlated with better outcomes (e.g. decreased relapse, etc.) [8]. Consequently, as primary care physicians, it is important to understand what mind-based strategies patients are using and if there are any spiritual and/or religious aspects that may be affecting their ability to cope with chronic pain.

The role that various types of complementary or alternative mind-based therapies (Table 17.1) play in chronic pain

TABLE 17.1 Mind-based therapies besides traditional cognitive behavioral therapy

Mind-based Therapies	Definitions in the context of chronic pain
Mindfulness meditation	Derived from eastern meditation practices, mindfulness meditation systematically develops and utilizes attention in order to create "insight," or a state of detached observation. It is characterized by focusing on the present moment with openness and acceptance [15, 16].
Hypnosis	Social interaction between a hypnotist and patient in which suggestions are given in order to alter pain perceptions, behavior, and/or memories [17].
Biofeedback	Biofeedback techniques involve the use of electrical sensors to monitor various physiologic processes and bring them under voluntary control, generally through relaxation [18].
Relaxation training	Any method, process, procedure, or activity that helps a person to relax; to attain a state of increased calmness; or otherwise reduce levels of pain, anxiety, stress or anger [19].
Prayer	A personal religious or spiritual act which functions as a cognitive coping mechanism, often reframing pain situations in a more positive way [6, 20].

has been studied. The evidence is generally not overwhelmingly in favor of efficacy and may be insufficient to make any conclusions due to the low quality of evidence due to the small trials of often less than 50 participants total and poor methodologies [9–14].

Mindfulness or Awareness Meditation

Eastern meditative practices differ fundamentally from Western psychologies in that the former assumes that "our usual states of consciousness are suboptimal." Eastern meditative practices assume that through "intensive mental training" it is possible to to attain states of psychological well being and insight into the nature of mental processes and reality [16]. Mindfulness/awareness meditation is based on traditions such as Buddhism and Yoga. Some of the other terms found in literature that describe this meditation include Zen, Vipassana, and Mindfulness Based Stress Reduction. It is a form of developing and training the patient to focus, or utilize attention, in order to achieve the goal of "insight". This insight into events or phenomena is achieved by cultivating "detached observation." Meditation instructions are given in order to achieve this state, enabling the patient to simply observe and focus on a specific phenomena (such as breathing, or pain) in its present moment [16]. In terms of pain control, the goal is to observe pain sensations as distinct and separate from the accompanying thoughts about pain. Examples of negative thought patterns associated with pain were discussed in earlier chapters in terms of "catastrophizing" and fears associated with chronic pain. Consequently, meditation as a treatment for chronic pain seek to identify and detach thoughts and feelings from the actual pain itself. Patients are taught to develop a nonjudgmental stance concerning their experiences, learn to pause and make deliberate responses to difficulty, instead of reacting without thinking [21].

A recent systematic review of 38 randomized controlled clinical trials showed that mindfulness meditation of various types may improve pain, depressive symptoms, and quality of

life for a wide variety of chronic pain diagnoses [15]. The evidence was rated as low quality, citing small studies of often less than 50 participants, poor quality studies with lack of intention to treat, and other factors. There was also very limited reporting of adverse events, which included worsening of anxiety and temporary strong feelings of anger toward the pain condition. Psychosis has been reported in the literature as an adverse effect of mindfulness meditation [22].

In order to find out more on mindfulness, providers can easily access information online. Several US medical school sponsored websites offer resources such as audio versions of guided mindfulness meditation, classes, and training for providers. A quick online search reveals a myriad of sites providing 12–20 minute guided meditations to help with chronic pain.

Mindfulness Resources

https://www.umassmemorialhealthcare.org/umass-memorial-center-mindfulness From the University of Massachusetts Medical School Center for Mindfulness. This has resources for physicians to practice mindfulness, be trained in mindfulness, and continuing medical education.

https://www.uclahealth.org/marc/default.cfm From the University of California, Los Angeles Mindfulness Awareness Research Center. This has free guided mindfulness meditation sessions in English and Spanish, classes, and training schedules.

Hypnosis or Hypnotherapy

Hypnosis has been difficult to define, in both clinical trials and by experts in the field. The British Medical Association in 1955 defined hypnosis as a "temporary condition of altered attention in the subject which may be induced by another person (therapist/hypnotist) and in which a variety of phenomena may appear spontaneously or in response to verbal or other stimuli. These phenomena include alterations in

conscious memory, increased susceptibility to suggestion, and the production in the subject of responses and ideas unfamiliar to him in his usual state of mind. Further phenomena such as anesthesia, paralysis and rigidity of muscles, and vasomotor changes can be produced and removed in the hypnotic state [23]." A more recent definition states that hypnosis is "a social interaction in which one person, designated the subject, responds to suggestions offered by another person, designated the hypnotist, for experiences involving alterations in perception, memory, and voluntary action [17]."

A brief history and summary of hypnosis is provided by Whorwell, in 2005 [24]. Essentially, hypnosis began in the eighteenth century as "mesmerism," which was named after an Austrian physician, Franz Anton Mesmer. He thought that entering into a trance like state was a crucial component of the healing process. The following century was marked by general disregard for the efficacy of hypnosis given the lack of research and the display of hypnosis as entertainment. By the start of the twentieth century, hypnosis was being studied in clinical trials and has become much more accepted as legitimate therapy, although, it remains outside of mainstream medicine. Part of this may be the fact that many hypnotists, or hypnotherapists, are not psychiatrists, psychologists, or medical physicians. These therapists may have little knowledge of human anatomy and disease pathology [24].

Hypnotherapy is the use of hypnosis to treat a medical condition. It relies on inducing a state of relaxation, or trance, and then making suggestions of improvement to whatever condition is being treated. In the case of pain, the suggestions could consist of experiencing a reduction in pain [25]. Patients are taught relaxation techniques (which can confuse the definition of a hypnotic intervention), ego strengthening, and coping skills. Often times initial sessions are focused on relaxation, and future sessions on the condition at hand. Home practice is essential and take home audio is an integral part of hypnotherapy [24].

Drawbacks of hypnotherapy is that is it labor intensive and costly. Most studies, if they report adverse events, state that there were no harms, albeit the sizes of most studies are very

small and may not be powered to detect adverse events. A recent review of hypnotherapy and chronic pain could only find 6 studies or reviews from the last 10 years in English [26]. The other criteria for inclusion included classification as peer reviewed clinical trial, systematic review, or meta-analysis.

Biofeedback

Biofeedback is a process in which biometric information is measured and given back to patient (and clinician) in order to gain increased awareness and control over physiological body processes [27]. Electrical sensors can measure a variety of biological metrics including muscle activity, temperature, heart rate, and skin conductance. These sensors are connected to a computer which then gives audio and/or visual feedback to the patient. The patient can then learn what behaviors, postures, or processes are beneficial, and what may cause tension, pain, etc. Patients can learn to control seemingly involuntary responses through this process [18]. Many times, patients are taught relaxation techniques in order to control these bodily processes. It is regarded as a psychological therapy because it is training the mind to be conscious of and actively control the body in order to achieve a desired response. Biofeedback is commonly used in pelvic floor and fecal incontinence rehabilitation.

A pilot study of biofeedback in 27 medication overuse headache patients by Rausa in 2016 showed that biofeedback in the short term was helpful in decreasing headache frequency and medication use. Interestingly, the authors noted a decrease in catastrophizing and an increase in active coping (which is regarded as the opposite of catastrophizing). Catastrophizing is a negative cognition associated with greater pain and disability. Examples of catastrophizing include thoughts such as, "There is nothing I can do to get better." It is discussed in greater detail in Chap. 7: Management of Chronic Pain: Nonpharmacological and Multidisciplinary approach. On the other hand, active coping examples include, "I can do something about my pain," or "I can manage my pain." In this study, there were no differences in frontalis muscle activity (the

biologic process measured) in the treatment and placebo group (active treatment). Consequently, perhaps the authors did not measure the correct biometric that would have changed due to decrease pain. Rausa hypothesizes that active coping (or other mechanisms) may have played a role in relieving pain and headache frequency. The authors state that it is still unclear the exact manner in which biofeedback is related to active coping and self-efficacy. Regardless, it is promising that this treatment modality may potentially treat chronic pain and the negative cognitions associated with it.

Biofeedback Resources

Mayo Clinic Patient Care and Health Information: https://www.mayoclinic.org/tests-procedures/biofeedback/about/pac-20384664

NIH Relaxation Techniques for Health: https://nccih.nih.gov/health/stress/relaxation.htm

Relaxation Training

Most providers may already be familiar with the basics of relaxation training. In brief, this focuses on diaphragmatic breathing, progressive muscle relaxation, and guided imagery. Indeed, a recent study exploring the teaching of these techniques in primary care, along with basic cognitive behavioral therapy was able to improve chronic pain intensity and function [28].

Prayer, Religion, and Spirituality

Prayer is a personal religious act by which the participant copes with the situation or reframes the situation. There are public religious acts that include attending church or other organized group assembly of religious devotees. Religion is often defined as participation in organized religious activities, rituals, and practice [29]. Spirituality is often defined as a per-

son's belief and search for the ultimate meaning and purpose in life. Spirituality helps shape worldview and the significance of events, and may or may not involve belief in a higher being. Interestingly, the role of religion or spirituality in coping with chronic pain can be either positive or negative [6, 8].Positive religious/spiritual coping is associated with those with a secure relationship with a benevolent God and a strong spiritual connection with others. It is also characterized by a belief in a loving God (or Higher Power) that offers support and help. There is meaning in suffering. On the other hand, negative religious/spiritual coping is associated with an insecure relationship with a higher power, belief in a punishing God, and a negative view of the world. There are feelings of abandonment by God/Higher Power. Hardships are viewed as punishment from God and that problem-solving is futile as God is in complete control [6, 8]. Those who have a positive religious/spiritual coping strategy often have higher self-esteem, growth from adversity or stress, better quality of life, and psychological adjustment, whereas those with negative coping often have depression, worse physical health, lower quality of life, and poor problem solving skills [6]. Patients with chronic pain who have positive religious or spiritual coping mechanisms do not necessarily experience less pain, but may have greater pain tolerance and functioning despite pain [20, 30].

Spirituality is most successfully leveraged in the addiction treatment realm. The 12 step programs of Alcoholics Anonymous and Narcotics Anonymous include spirituality as a core component. These programs have had much success in drug and alcohol addiction treatment. Studies have noted the correlation between participation in these programs, spiritual change, and long lasting remission from addiction [31, 32]. Some hypothesized that addiction is extremely stressful and trying, and therefore multi-component coping including spiritual and religious coping strategies need to be utilized [8].

Given that spirituality can either positively or negatively affect a person's physical and mental health, it is important that we have quick and efficient means to gather a spiritual/religious history. Wacholtz summarizes these spirituality assessment inquiries [6] (Table 17.2).

TABLE 17.2 Religious or spiritual assessment instruments

One question	Are you part of a faith community? Or Is spirituality important in the way you manage your chronic pain?
FICA [33]	**F**aith and beliefs **I**mportance of spirituality in your life **C**ommunity (spiritual) support **A**ddress: How do you wish these issues to be addressed?
SPIRIT [34]	**S**piritual belief system **P**ersonal spirituality **I**ntegration with a spiritual community **R**itualized practices and restrictions **I**mplications for medical care **T**erminal events planning

Positive re-appraisal is the process by which life events are reinterpreted in a positive light. Patients who "grow" from challenges in life, or "learn something" from stressful life events have the ability to positively re-appraise the situation. This way of thinking has been shown to be one of the factors that enable prayer and spirituality to be effective in tolerating chronic pain [20]. When we start discussing spiritual concerns, it may be beneficial to patients to help them positively reframe their situation. This may be more inline with traditional cognitive behavioral therapy. Finally, after discovering a patient's particular spiritual or religious belief, we should direct them to their appropriate spiritual leader [35].

Conclusions

Chronic pain affects the whole person, including psychological and spiritual aspects. Including mind-based therapies may be helpful in certain chronic pain patients. Many of these mind-based therapies aim to identify and eliminate negative cognitions or positively re-appraise the chronic pain situa-

tion. Many also focus on relaxation and self-efficacy. It is important to inquire about the spiritual aspects of the patient and refer them to the appropriate spiritual leader if needed.

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Part IV
Chronic Myofascial Pain

Chapter 18
Chronic Myofascial Pain, Fibromylagia, and Myofascial Trigger Points

Bonnie Huang Hall

Introduction

Chronic musculoskeletal pain has been identified as a major US national health concern [1]. Musculoskeletal pain is extremely common, affecting up to 80% of the general population. 10–20% of these suffer from chronic musculoskeletal pain [2, 3]. Musculoskeletal back pain is one of the leading cause of disability amongst workers (aged 20–64) in the United States, second only to arthritis [4]. There can be many reasons for chronic musculoskeletal pain, but one reason to consider is the presence of a trigger point. Originally defined by Travell (personal physician to President John F. Kennedy [5]) and Simmons, trigger points (also known as myofascial trigger points) are hyperirritable areas of muscle, usually located within taut bands of skeletal muscle [6]. Trigger points are unusually painful on compression and can give rise to referred pain, motor dysfunction, decreased range of motion, and autonomic phenomena [7, 8]. Trigger points are proposed to be areas of increased electri-

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cal activity of skeletal muscles caused by microtrauma from over or inappropriate use of muscle. Postural habits, skeletal asymmetry, nutritional deficiencies, and metabolic abnormalities (diabetes, hypothyroid, etc.) may contribute to the formation of trigger points [9]. They can have a characteristic twitch response when stimulated. There is some evidence that at the trigger point, there is local contraction, ischemia, edema, and inflammation [10, 11]. Trigger points are located in characteristic points along the human musculature such that, if present, are found in the essentially the same locations for every person. Trigger points can be easily treated with stretching, massage, ischemic compression, muscle energy techniques (isometric contraction), and local trigger point injections, bringing much relief to chronic pain of musculoskeletal origin [7, 8]. These treatments are collectively called "trigger point therapy."

Currently, there is still ongoing debate as to whether trigger points are valid sources of chronic pain [12–15]. However, more and more articles are being published every day supporting the claim that myofascial trigger points can play a role in relieving many chronic pain conditions from headaches and migraines, to everyday back pain, to chronic male and female pelvic pain [16–20]. During my training in internal medicine, family medicine, and obstetrics and gynecology, I had a severely limited view of myofascial pain, only giving trigger point injections on the upper back and paraspinal lumbar muscles. Other specialties such as emergency medicine also have limited training on this subject, although pain is one of the most common presenting complaints to the emergency room [9]. Many physicians, including myself, are not familiar with other trigger points in the body, their associated symptoms, and their mimicry of other diseases at presentation [9]. Truth be told, when I first read about the benefits attributed to relieving trigger points in a wide variety of chronic pain conditions, I was in disbelief. How can there be one underlying pathology for such varying pain conditions as migraines, carpal tunnel, and knee pain? But after seeing the success of using a variety of muscle based techniques to relieve trigger points, I became convinced of the existence and pathological role trigger points play as I witnessed my

patients regain function, range of motion, and freedom from chronic musculoskeletal pain. Various case reports [21] and small, low quality studies attest to its success [22]. Surely, it is not a panacea. Nor is it a treatment for neuropathic pain or fibromyalgia. However, most times in primary care we encounter primarily regional musculoskeletal conditions (such as neck pain, shoulder pain, back pain, knee pain). Furthermore, given the limited success to which chronic pain is currently treated, and the general safety of trigger point therapy, it is imperative to at least consider this diagnosis and treatment for those suffering with chronic musculoskeletal pain.

Trigger Point Characteristics and Diagnosis

Palpation of muscles is a key technique used to diagnose trigger points. Once a trigger point is palpated with appropriately firm pressure, the patient will often startle as the pain experienced is out of proportion to the amount of force applied. This is often called the "jump sign." Palpation of these tender nodules can immediately cause referred pain and reproduce the patient's symptoms. The locations of these myofascial trigger points, if present, are generally the same for every person - much akin to the locations of other anatomical landmarks. Palpation of trigger points is often characterized by prominent, more stiff/firm muscle fibers, or an actual nodule, when compared to the surrounding musculature. There can be decreased range of motion in the muscle affected, due to shortening of the muscle from the trigger point. There may be accompanying muscle twitch or spasm during palpation. The overlying subcutaneous skin may be affected, showing changes similar in appearance to "cellulite." Technically, these skin changes are called subcutaneous panniculosis, which are visible and palpable changes that are characterized by an increased granular texture [23]. There can be nerve compression from a muscle with a trigger point, causing syndromes such as thoracic outlet syndrome or carpal tunnel. Consequently, in my evaluation of chronic pain, after the appropriate traditional physical exam has been completed, I will

routinely examine for the presence of myofascial trigger points. The syndrome of having myofascial trigger points causing chronic pain is myofascial pain syndrome. In many cases, no imaging or diagnostic tests are needed to confirm the diagnosis, but only to rule out other potential causes of pain. Investigations on various modalities (such as ultrasound) to objectively detect myofascial trigger points have been conducted in the past [24], but so far, no gold standard besides physical examination has been developed [17, 25].

Myofascial Pain Syndrome Is Not Fibromyalgia

Of note, myofascial pain syndrome is not fibromyalgia. Although both cause chronic pain, there are key differences. First of all, myofascial trigger points are focal points in the muscle where there is inflammation, persistent contraction, and ischemia. Fibromyalgia does have *tender points*, but these are not associated with palpable taut bands or nodules where there is local inflammation characteristic of myofascial trigger points. Fibromyalgia has an unknown cause, whereas myofascial pain syndrome has an antecedent micro-trauma of muscular origin. Generally myofascial pain syndrome is regional, whereas fibromyalgia is widespread symmetric pain and present in both the upper and lower halves of the body. Myofascial pain syndrome does not change into fibromyalgia. There are no cognitive symptoms in myofascial pain syndrome. Treatment of trigger points is targeted at the muscle, ergonomic factors, and physical therapy, which is different from fibromyalgia [26–29].

Location of Trigger Points in Common Pain Syndromes

Of note, this book is not meant to be an exhaustive treatise on trigger points and their locations. A complete reference to trigger points can be found in Travell and Simmons [6, 30]. However, Fig. 18.1 shows the locations of some of the commonly encountered trigger points in primary care.
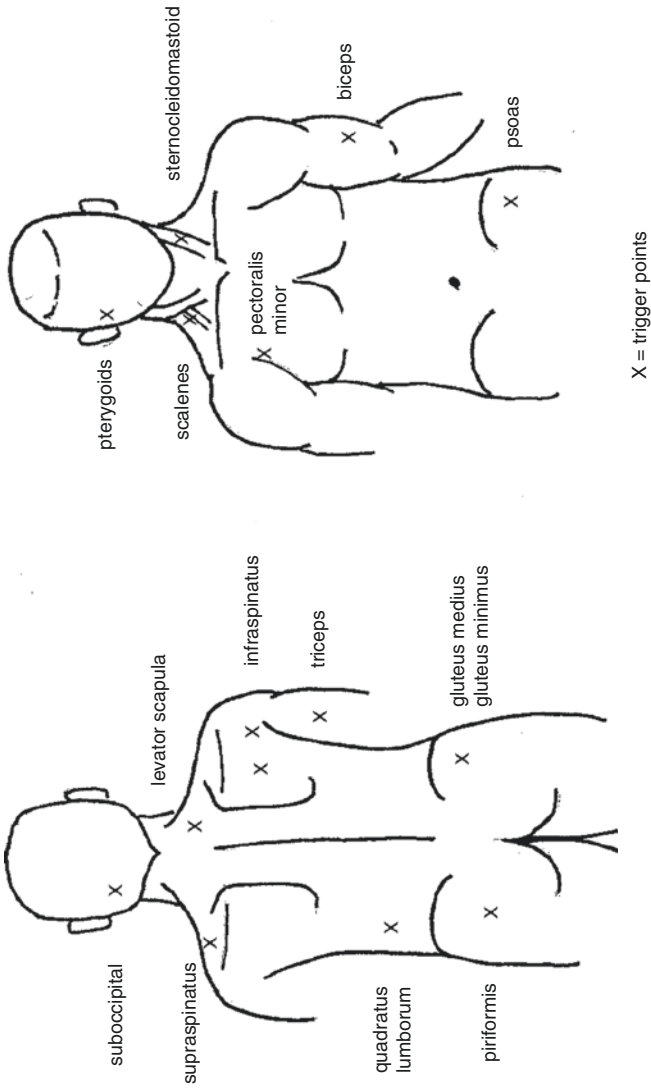
FIGURE 18.1 Outline of front and back of human body and common trigger points

Conclusions

In conclusion, myofascial trigger points are a reasonable consideration for those suffering with chronic pain. Especially for those patients who have undergone an extensive evaluation and have no reasonable cause or diagnosis for the etiology of their pain, or those whose pain has been difficult to manage under the present regimen, it is important to at least consider the possibility of a myofascial origin. Diagnosis of trigger points relies heavily on physical examination. Ancillary studies can be used to rule out other pathologies. The treatment of myofascial pain syndrome targets the musculoskeletal system. Myofascial pain syndrome is not fibromyalgia. This is important because their etiologies and treatments differ widely.

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Chapter 19
Treatment Principles of Myofascial Pain Syndrome

Bonnie Huang Hall

Introduction

Myofascial trigger points, also known simply as trigger points, are palpable hyperirritable nodules of contracted skeletal muscle, often located within taut bands of muscle fibers. They can often be the source of chronic musculoskeletal pain and are worth considering in patients with chronic pain, especially if refractory to conventional treatments. Treatment of myofascial trigger points is also known as trigger point therapy. These therapeutic tactics are chiefly targeted at the musculoskeletal system, generally easy to perform, instruct, and have the potential to bring about much sought after relief from chronic pain [1].

The general treatment principle of myofascial trigger point is to "stretch out" the "knot" in the affected muscle. The myofascial trigger point is an area of increased electrical activity and contraction, resulting in local ischemia and inflammation [2–4]. Due to the constant contraction, local blood flow cannot bring in oxygen and flush out wastes. Consequently, treatment is focused on eliminating the trigger point by

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opposing this constant muscular contraction and its perpetuating factors.

There are a multitude of ways to tackle the myofascial trigger point, as the main guiding principle is to stop the constant electrical activity and contraction. New methods are constantly being tried (for example, extracorporeal shock wave) [5]. There are, in general, three basic methods to relieve myofascial trigger points: manual therapy, trigger point procedures, and elimination or reduction of perpetuating factors. Currently, there is no conclusive evidence as to which method is the most effective.

Manual Therapy

One of the least invasive therapies targeted at myofascial trigger points is a group of therapies collectively called manual therapy. This can include massage of trigger points [6] which provides local stretch to the skeletal muscle affected. Other manual techniques include ischemic compression, which is the application of sustained constant pressure on the trigger point, often for about 1 minute. This causes local ischemia and then a resulting therapeutic hyperemia whose effects can be visible on the skin. Other techniques include isometric contraction, which can be a thought of as a form of stretching. This is achieved when the patient is asked to contract a muscle against an equal and opposing force such that there is no actual movement in the limb. Pushing against a wall or a therapist with equal force can accomplish this. Another classic way of treating myofascial trigger point is the "spray and stretch" technique. The painful muscle and the zone in which referred pain is experienced is temporarily cooled with a vapocoolant spray. Brief application of ice can work as well. During this time, the muscle is passively stretched by the provider in order to relieve the trigger point [1, 7]. Although all techniques can be tried on a patient during a single therapeutic session, some techniques may work better with other patients, depending on their comorbidities and

their level of pain. For instance, some patients may have decreased range of motion from severe arthritis and cannot flex a joint adequately in order to utilize the spray and stretch technique, consequently isometric contraction and ischemic compression may prove more useful. Finally, self-massage, using devices such as foam rollers or lacrosse balls, can be beneficial to patients as well [8]. In my experience, I have witnessed many patients improve on a home regimen of self-massage alone or in conjunction with comprehensive trigger point management plan.

Medication

There is little evidence to support the use of medications in the treatment of pain caused by myofascial trigger point. That being said, NSAIDs are often used first line. Muscle relaxants are often used, however, they cannot relieve the myofascial trigger point itself, but only the spasms reflexively produced in other muscles by a neighboring trigger point [9]. Other experts state that the traditional classes of pain medications (such as TCAs, NSAIDs, antiepileptics, and muscle relaxants) may be useful [10]. In my experience, I use medication only if the patient is in greater amounts of pain. A few days worth of muscle relaxants (cyclobenzaprine) are prescribed with or without an NSAID. Medications are prescribed to help manage the acute pain in order to enable the patient to under go either manual treatment in the office, and/or begin a home program of self-myofascial trigger point release.

Trigger Point Procedures

More invasive measures can be taken to relieve a refractory myofascial trigger point. This can include injections of various substances ranging from saline, lidocaine/bupivicaine, to botulinum toxin A [9, 11, 12]. Insertion of the needle without injected substances is referred to as "dry needling" and can

also be used to treat myofascial trigger points [1, 13–15]. There is, however, only poor quality evidence to support dry needling and it remains controversial. Insurance, as well, often does not reimburse this practice as it is considered investigational. Finally, there is a whole host of other procedures aimed at relieving or "releasing" the myofascial trigger point such as ultrasound and transcutaneous electrical stimulation [7].

Treatment of Perpetuating Factors

Treatment of perpetuating factors will help bring about resolution of the trigger point. Trigger points often may be relieved by manual therapy only to form again due to the unresolved perpetuating factors. Perpetuating factors can be metabolic and endocrine in nature, or mechanical [1, 10]. Uncontrolled diabetes, hypothyroid, and vitamin deficiencies may contribute to the perpetuation of trigger points. Once these are controlled, mechanical factors such as poor body posture, skeletal asymmetry, and ergonomics must be corrected. One example that Travell notes (and I have seen in practice) that may contribute to trigger points in the neck is turning the head unnaturally towards a night stand light while reading in bed. Correction of neck position (and light source location) enables the resolution of this trigger point [1].

Conclusions

The treatment of myofascial trigger points can be easily done by a trained primary care provider as many of the treatment techniques are manual therapies. Trigger point injections are also a reimburseable treatment modality that can easily be accomplished in the primary care office setting. Laboratory studies can help to evaluate for common contributors of myofascial pain, such as hypothyroid and diabetes. Consequently, consideration of myofascial trigger points in the differential

of chronic pain is important due to the ease at which treatment can be accomplished. The potential for pain relief with such simple and relatively inexpensive treatments is also another important reason to consider the existence of trigger points as a contributor to chronic pain.

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Chapter 20
Example Myofascial Pain Case: Quadratus Lumborum Trigger Point and Chronic Low Back Pain

Bonnie Huang Hall

Introduction

Musculoskeletal low back pain is a very common presenting complaint in primary care. Trigger points located in the quadratus lumborum muscle are often the source of chronic pain. Because the focus of the book is not on myofascial trigger points, only trigger points in the quadratus lumborum will be discussed in detail. The following is a step by step example to illustrate the evaluation and treatment of this specific trigger point. Besides performing the usual history and physical exam for back pain (ruling out neurological emergencies for instance) and ensuring a musculoskeletal origin for the pain, a trigger point examination of the quadratus lumborum is essential.

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Examining the Quadratus Lumborum

Often times the practitioner cannot adequately palpate this deeply located muscle when the patient is standing or sitting. Consequently, examining for the quadratus lumborum trigger point involves having the patient lie in the lateral decubitus position, on the unaffected side. The side with the back pain is up, facing the provider. Ask the patient to move the free, upper arm overhead, in order to further expose the muscle (Fig. 20.1). Then locate the paraspinal muscles in the region between the iliac crest and lower ribs. Just anterior to this will be the quadratus lumborum (Fig. 20.2). Deeper palpation is necessary, especially in overweight or obese individuals, in order to correctly palpate and locate trigger points in this hidden muscle. A pillow under the lower waist can further assist in exposing and locating this muscle. This position will allow the affected quadratus lumborum to arch outwards towards the practitioner. If the patient startles ("jump sign") and

FIGURE 20.1 Positioning for examination of the quadratus lumborum trigger points
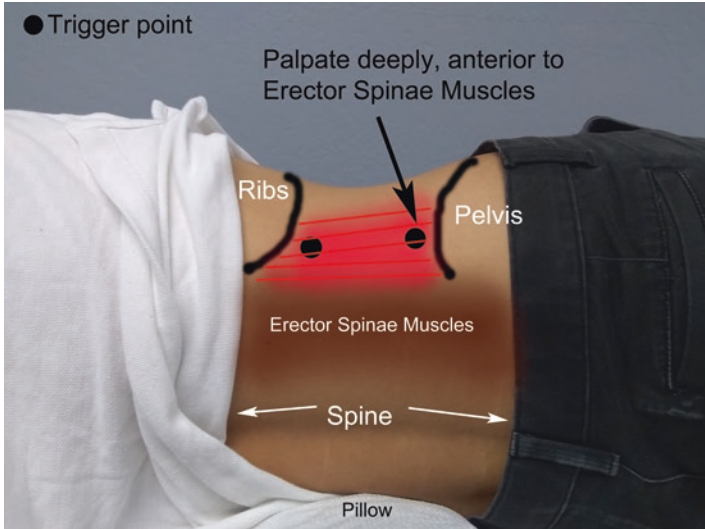
FIGURE 20.2 Locating trigger points in the quadratus lumborum

indicates that this area is quite tender, then the quadratus lumborum trigger point has been identified. Of note, both quadratus lumborum may be affected, so the examination is repeated on the opposite side.

On physical exam, the quadratus lumborum, when severely affected by a trigger point, may be shortened. An abnormal back curvature may result, causing a deviation of the spine. The patient appears to be bending sideways towards the affected muscle. This may cause the appearance of scoliosis, when in actuality there is no bony abnormality of the spine, but rather the curvature is caused by a short-ened quadratus lumborum muscle. On history, the patient may say that they "developed" scoliosis (without a history of osteoporosis) recently as adults. This may also result in the ipsilateral lower extremity to falsely appear shorter when the patient is supine. Accompanying trigger points in other muscles may also add to abnormal back posture, such as forward bending. (Examination of other muscles such as the psoas may prove beneficial as well to relieving the

patient's abnormal posture and chronic pain.) During the process of deactivation of the quadratus lumborum trigger point, these physical findings become less and less apparent, allowing for objective findings of improvement in the patient's condition.

Trigger Point Palpation Technique

Although in-depth techniques for palpation of trigger points have been thoroughly described by Travell and Simmons [1], I find that that the easiest method is an adaptation of her flat palpation method. Using the *thumb* of the provider's dominant hand, press firmly *across (perpendicular to)* a suspected taut band or trigger point (Fig. 20.3). If needed, move up and down along the direction the muscle fibers to more precisely locate the most exquisite site of tenderness which is the trigger point. The overlying subcutaneous skin slides over the affected muscle, enabling the palpation of the underlying
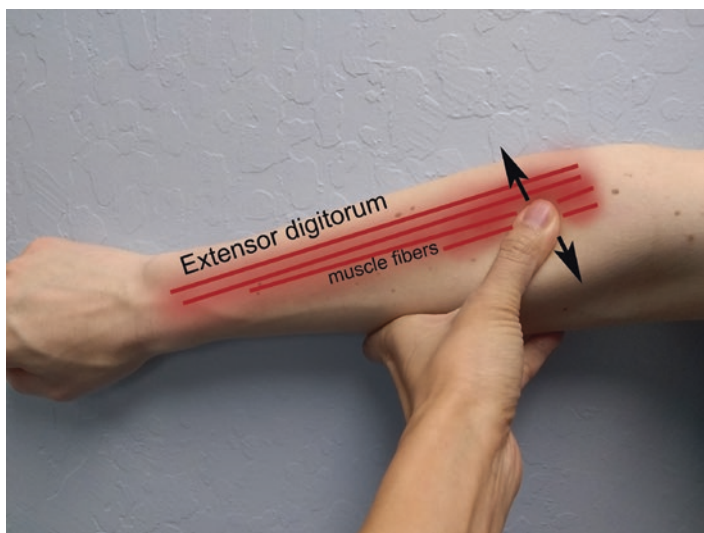
FIGURE 20.3 Palpation technique for most trigger points

skeletal muscle. With this technique, one can apply more force and detect more surface area than with an index finger. This allows for better palpation of the various muscle textures (such as nodules and tight bands) located beneath the subcutaneous skin. This technique works for most trigger points, except the internal trigger points (for instance, within the oral cavity or pelvis) which require less force and longer fingers. The quadratus lumborum, due to its deeper position, maybe best palpated with the first and second fingers.

Treatment of the Quadratus Lumborum Trigger Point

Treatment of the quadratus lumborum in a standard primary care office can be easily accomplished. Manual techniques are employed first. Generally, I spend a couple minutes massaging the trigger point as patients are familiar with this technique. This is accomplished by using the thumb (or more ergonomically, the elbow) and moving in a small circle about 1.5–2 cm in diameter, completing a circular pressing motion every second or two (Fig. 20.4). The practitioner needs to be stationed above the patient, with the hip approximately level with the patient's body. This enables the practitioner to ergonomically recruit the necessary body weight to apply therapeutic pressure onto the trigger point. If the patient is flinching due to tenderness at the trigger point, less force, slower depression of the trigger point, along with slower circles are employed. This technique allows a gradual pressing on the trigger point (due to the circular motion employed) as well as enabling fine tuning of pressure such that the patient can endure (aim for 7/10). After a few minutes of massage, the next manual technique that can be used includes spray and stretch. Given the expense of utilizing vapocoolant spray, I usually use cold packs or ice. Refrigerated cold packs are placed on the area of referred pain till skin is cooled and anesthethized. Then the quadratus lumborum is stretched. Stretching is accomplished in two methods (Fig. 20.5):
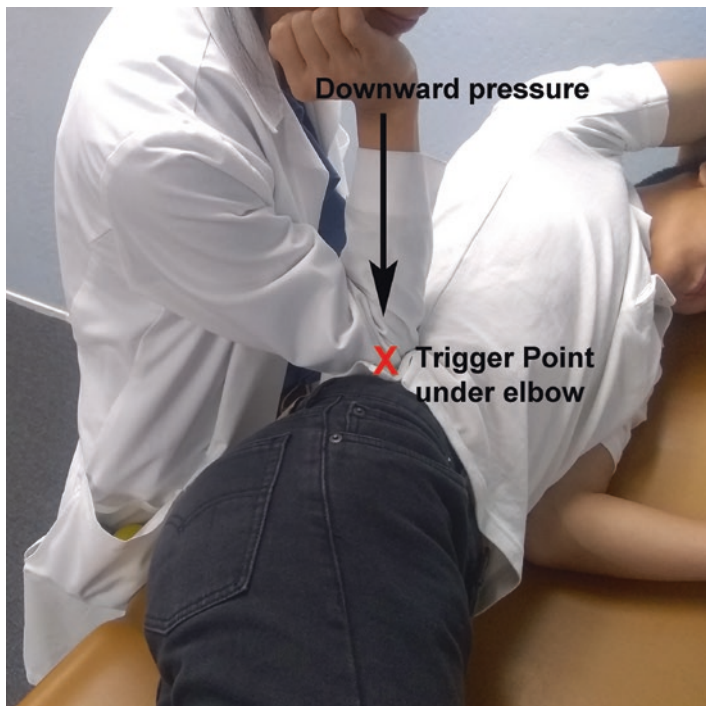
FIGURE 20.4 Cooling and passive stretching of the quadratus lumborum

1. In lateral decubitus with patient facing the provider and the affected quadratus lumborum up, move the patient's upper leg towards the provider (hip flexion), while pushing the patient's upper shoulders away in the opposite direction.
2. Repeat, but stand on the other side of the table, such that the patient is facing away from the provider. The upper leg is moved again towards the practitioner (this time in hip extension) and the shoulders away in the opposite direction.

In both cases, let gravity pull the leg towards the ground. The patient may need to scoot towards the edge of the exam table to facilitate this. In addition, this stretch is enhanced by
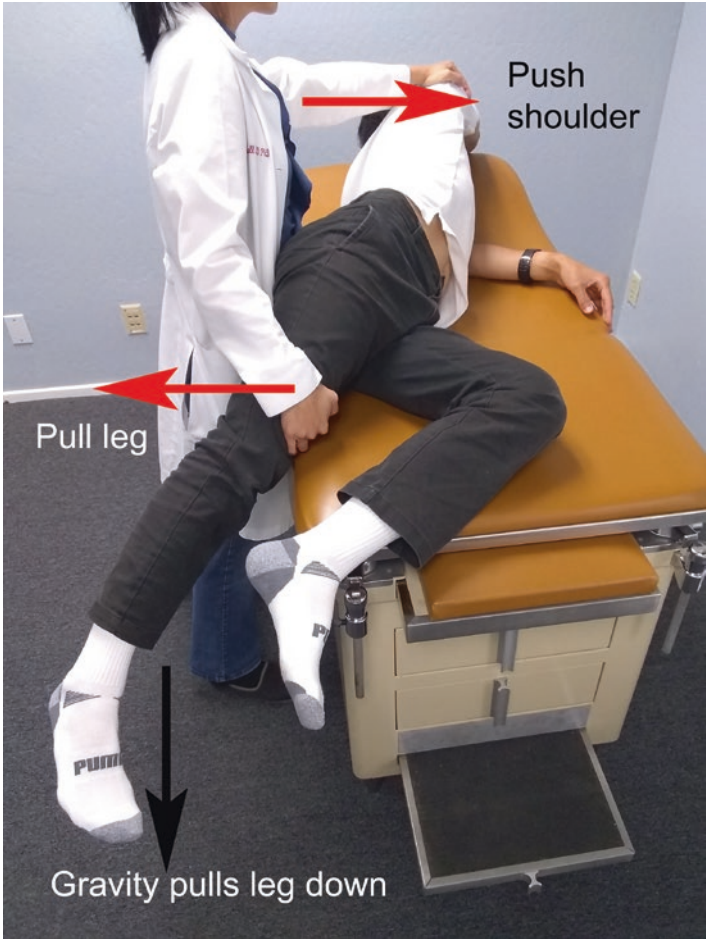
FIGURE 20.5 Stretching the quadratus lumborum after sufficient cooling. Repeat with the provider facing the patient

timing with deep breathing. The leg and shoulders are passively moved as above during inhalation, and during exhalation, release the leg from support and allow gravity to pull downwards and stretch the muscle. I repeat in sets of three. The exhalation process facilitates a reflexive relaxation in the muscles, allowing for further stretching.

While the skin is still cold, ischemic compression can be performed. This takes advantage of the pain relieving properties of the anesthetized skin as ischemic compression can be quite painful. Ischemic compression is performed with enough pressure such that when completed, the skin will have a reactive hyperemia (turn pink afterwards). The compression is held for 30–60 seconds and can be repeated with greater force until there is less tenderness in the trigger point. Ischemic compression is even more effective if the patient is in the stretch position. I repeat ischemic compression about 2–3 times in a typical manual therapy session.

Lastly, isometric contraction is then performed. While the patient is in lateral decubitus, ask the patient to externally rotate their upper leg towards the provider. At the same time, push the thigh downward with an equal force such that no movement is made. Timed breathing also facilitates this. The patient is asked to take a deep breath, and hold it. Then the patient is asked to lift the leg at the hip (external rotation) and push against the provider's hands for 10 seconds. After 10 seconds, the patient relaxes and exhales while the practitioner stops pushing. To further enhance this technique, stretch the quadratus lumborum during the exhalation/post-isometric contraction period. The muscle can stretch more easily during this time period.

Alternatively, while the patient is supine on the table, ask the patient to bend at the knee on the affected side. The patient is asked to externally rotate this flexed leg while the practitioner pushes with equal force. Timed inhalations and exhalations can also be used. Then, while the patient is exhaling and relaxing, the practitioner can push the flexed leg medially (internal rotation) and facilitate stretching during the post-isometric contraction period.

After the completion of the above manual therapies, I passively move the quadratus lumborum by rotating the thigh (internal and external rotation, flexion and extension) at the hip joint. This is called passive range of motion.

Warm packs are used to heat up the chilled muscles as needed.

Home Regimen

After this technique is employed, the patient often feels a decrease pain. A home regimen is prescribed in order to continue the progress made in the office setting. The home regimen consists of various stretches and correction of detrimental musculoskeletal habits.

Stretches

1. Supine cross leg exercise (Fig. 20.6).

Figure 20.6 Supine Cross leg exercise. This is the position for home supine stretching and isometric contraction. The arm on the affected side (ipsilateral arm) is lifted up to stretch the quadratus lumborum, while the leg on the affected side (ipsilateral leg) is turned medially. The crossed over leg is used to control the position of the leg on the affected side, pushing it medially downwards, or restoring its position. The crossed over leg also provides resistance when isometric contraction is performed. To perform isometric contraction, the crossed-over leg pushes downward while the medially turned leg attempts to move upwards and externally rotate

Have the patient lie supine and bend at the knees. Then cross the unaffected leg (i.e. contralateral leg, or leg on the side without pain) over the other leg (ipsilateral leg). Use the crossed leg to push the other leg medially. Have the patient raise the affected side's arm above the head during the stretch. To add even more therapeutic value, isometric contraction can be added. The leg that is medially turned can then externally rotate while the leg that is crossing can oppose this motion. In order to finish the exercise, uncross the unaffected leg. Then, using the unaffected leg, push up the affected leg which is internally rotated. This will help avoid strain to the affected quadratus lumborum.

2. Standing side stretch (Fig. 20.7).

Have the patient stand next to a table or counter of sufficient sturdiness to support the patient's weight. The unaffected side (that is, contralateral to the side with pain) should be next to the table. The goal is to sideways bend towards the table such that the affected quadratus lumborum is stretched. Have the patient raise the affected (ispilateral) arm above and across the head during the stretch, while the contralateral arm is planted on the table. The contralateral arm begins to bear weight as the side ways bending towards the table is increased. In order to make the stretch even more therapeutic, timed breathing should be used. The patient is to inhale deeply (and note, the body may rise upwards slightly as the quadratus lumborum reflexively contracts during inhalation). During exhalation the patient actively bends more towards the table. The process is repeated until maximally stretched. The stretch is ended when the contralateral arm leaning on the table pushes the upper body back into an upright position. This last step is crucial to prevent injury to the quadratus lumborum by eliminating unnecessary strain.
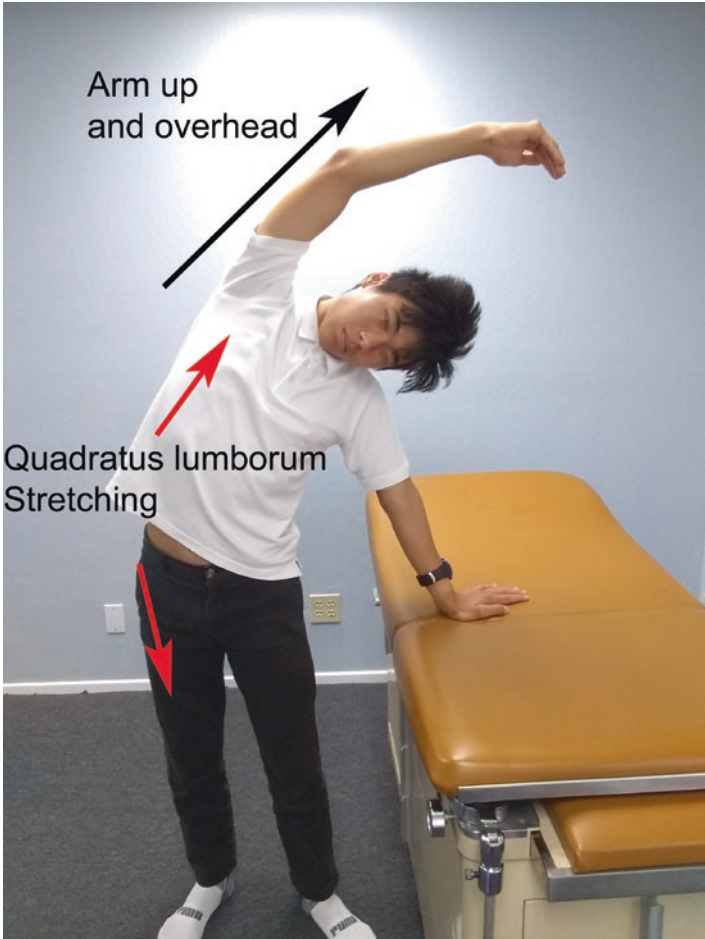
FIGURE 20.7 Quadratus lumborum stand and stretch position. The patient should be bending away from the affected side. The unaffected side's arm is leaning against a counter or sturdy table and is used to support the patient. The unaffected arm then can push the patient upright when stretching is completed. Timed breathing can make this stretch even more effective. When inhaling deeply the body naturally rises. When exhaling the body naturally relaxes, and the quadratus lumborum can stretch more, thereby bending more towards the table

Correction of Body Habits and Mechanics

While the quadratus lumborum is recovering from the trigger point, it is important to advise correct body positioning during everyday movements in order to speed healing and avoid perpetuation of the problem. One of these methods is to sit while putting on shoes or pants. This avoids any jerking movements resulting from loss of balance that can occur while standing on one leg during dressing/undressing of the lower extremities. Getting up from the chair requires a special technique. Advise the patient to get out of the chair WITHOUT bending forward. This requires scooting to the edge of the chair, and then standing up with the back straight. Sitting is similarly accomplished. With the back straight, sit down at the edge of the chair, then scoot backwards if needed.

Finally, after all trigger points have been adequately treated, it is important to examine the body for asymmetries that may contribute to shortening of the quadratus lumborum. There may be lower extremity limb-length discrepancies. One pelvis can be smaller than the other. In order to test this quickly, I usually use a thin notebook ½ inch to 1 inch or so. The patient places one foot on the book and the other on the floor. Both sides are tested. I ask if the patient feels any difference. If the patient states that the book placement does feel better, than perhaps the patient has a limb length discrepancy. One can also directly measure the limb length by measuring the distance from the anterior superior iliac spine to the medial malleolus. Correction involves orthotics. Similarly, pelvic asymmetries are tested by placing the book under one side of the pelvis (under one buttocks cheek) while the patient is sitting. Both sides are tested. Again, if the patient feels comfort on one side (and worsening discomfort on the other), the patient may have a small hemipelvis. Correction involves adequate cushioning/support on the smaller side during sitting. A word of caution – detection of limb-length discrepancy should only be embarked upon after the deactivation of the quadratus lumborum muscle.

The shortened muscle may give the false impression of an ipsilateral limb-length discrepancy.

Resolution of symptoms depends on various patient factors. I have found patients with chronic pain in smaller muscles over the span of months to be easily treatable, usually requiring only one session in the office and compliance with a home program of myofascial release and ergonomic correction. When the chronic pain has been longstanding (over a course of years), treatment usually takes months. A noticeable improvement in symptoms is usually seen in 1 month of effective therapy targeting the chiefly affected muscles.

If progress is not seen in trigger point manual therapy (usually obvious in 1 month), more aggressive techniques such as procedures (most notably trigger point injections) can be offered. Investigation of underlying metabolic and endocrine causes should be considered. This can also be done at the initial visit. In addition, trigger points in other muscles (such as the psoas, gluteus medius, gluteus minimus, and piriformis) may also contribute to chronic low back pain [2]. These, too, should be deactivated in order to bring about complete resolution of pain. Lastly, after the patient is mostly free from pain, an exercise program is started. I find that exercise often enables the patient to completely recover from their previous debility and pain.

Conclusions

Chronic low back pain is a prevalent problem in primary care. The quadratus lumborum is one of the most frequent trigger points found in chronic low back pain. This chapter provides a brief summary of techniques that can be used to treat a myofascial trigger point in the quadratus lumborum muscle. Trigger point therapy includes manual therapy and correction of body mechanics and posture. Metabolic or endocrine abnormalities may also perpetuate chronic muscle pain and should be treated. Other muscles may also harbor trigger points and contribute to chronic low back pain.

These techniques and advice can be easily incorporated into a primary care practice. Resolution of chronic symptoms may take months, and as with all chronic pain, a multidisciplinary approach may be necessary.

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