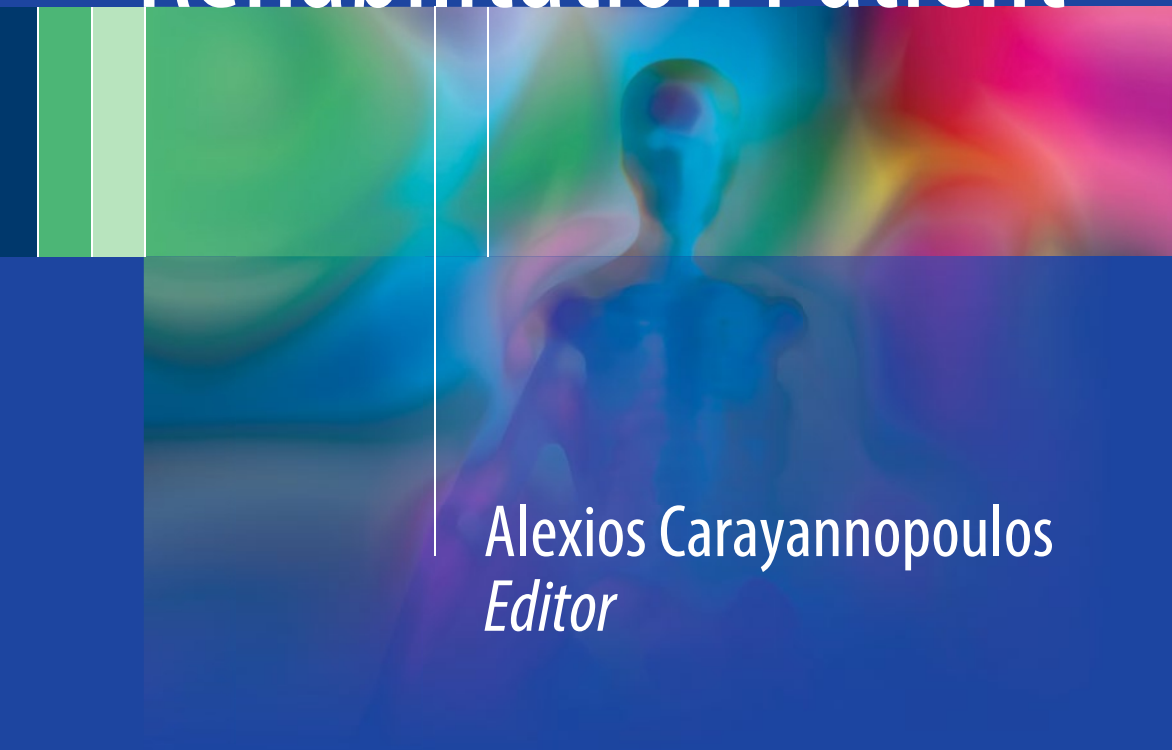
Comprehensive Pain Management in the Rehabilitation Patient



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Editor

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Preface

From the beginning, it was my idea to create a book that covers a variety of pain conditions seen by the rehabilitation specialist. I particularly wanted to include pain conditions seen in an acute or subacute rehabilitation hospital, as well as in the outpatient setting by the general physiatrist or the physiatrist subspecialized in Brain Injury Medicine, Hospice and Palliative Medicine, Neuromuscular Medicine, Pain Medicine, Spinal Cord Injury Medicine, and Sports Medicine.

This book is geared towards physiatrists in training or in early practice. It will also serve as a resource for any medical, surgical, behavioral, or allied health provider who treats pain across the rehabilitation continuum. The chapters present both biomedical and biopsychosocial perspectives, combining the multidisciplinary approach used in Pain Medicine with the interdisciplinary approach used in Physical Medicine and Rehabilitation. The book includes theory, clinical practice, and practical aspects of managing pain through rehabilitation.

Comprehensive Pain Management in the Rehabilitation Patient: A Reference Guide covers many diagnoses in a deliberately succinct and specific format. Each chapter includes a recommended reading list outside of specific references used. This is to encourage the reader to explore more about any particular topic. The book is divided into 14 parts, which cover the following topics: Introduction to pain and a review of the multidisciplinary approach; Pain in the rehabilitation patient, which covers many of the core settings of an acute or subacute rehabilitation hospital; Headache; Pain diagnostics; Medication; Injections and procedures; Behavioral management; Complementary and alternative medicine; Neuromodulation; Neuroablation; Surgical management of pain; Novel techniques; Business and legal perspectives.

I am very grateful to the hard work of my colleagues and friends who authored these chapters. They represent many different specialities and work in a variety of settings. Their generous support of my work has made this book possible.

Finally, I would like to thank my editorial team at Springer. Their assistance was invaluable in bringing this book to publication.

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Part I
Introduction to Pain

Chapter 1
Neuronal Signatures of Pain in the Rehabilitation Patient

Theresa R. Lii and Carl Y. Saab

"To have pain is to have certainty; to hear about pain is to have doubt."

—Elaine Scarry, in The Body in Pain

Pain Diagnosis Today: Pain Is What the Patient Says It Is

Pain research witnessed a paradigm shift at the turn of the century. Emerging data showed that long-lasting pain correlates with functional and structural changes that constituted putative markers of neuropathology in the brain. Accordingly, strong views were expressed in favor of labeling chronic pain as a disease entity [1]. Changes at the level of the brain-fueled speculations that chronic pain is a neurological disease with biological, or more accurately, neurophysiological underpinnings. Struggling to distinguish the homeostatic from the pathological, some cautioned against expanding this notion and creating confusion regarding "good" pain versus "bad" pain [2]. Regardless of phenomenological or epistemological arguments, we here extend this conversation with the pragmatic goal of identifying novel, objective pain diagnostics. We follow the basic premise that pain in general, and chronic pain in particular, alter neuronal function in the brain; our goal is to capture this change in neuronal activity and to use it as an objective neuronal signature of pain.

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If we accept the notion that chronic pain is a disease, it follows that chronic pain is a clinical condition that requires a unique set of therapeutic and diagnostic protocols. As other authors in this book will evidently make the case that rehabilitation patients with acute to chronic pain face limited therapeutic options, we here discuss the diagnostic part of the equation, which has received relatively little attention in the literature. The gold standard for pain diagnosis in the clinical setting remains subjective and unreliable in all patient populations, especially non-communicative patients, which are often found within the rehabilitation care continuum. Objective, cost-effective, and hassle-free measurement of pain is not only important for reaching an accurate diagnosis, but it is also critical for informing optimal treatment protocols and for maximizing function. Hence, accurate diagnosis contributes to effective pain management, reduces the risk of side-effects, and conserves tremendous resources on the part of the patient and caregiver.

Of the many challenges in managing patients with chronic pain, one of the greatest is discerning exactly how much pain the patient is experiencing, if at all. There are currently no reliable objective indicators of the presence or the severity of pain. In the 1990s, health and patient advocacy organizations urged medical professionals in the United States to recognize pain as "The Fifth Vital Sign," which led to implementation of the 0–10 numerical pain scale across nearly all medical settings [3]. Despite the ubiquity of the numerical pain scale, its routine use has not yet improved the quality of pain management outside of postoperative and emergency settings [4]. Because the numerical pain scale relies on patient self-report, its reliability can be influenced by any number of biases, such as the patient's ability to communicate or whether the patient seeks secondary gain.

Around the time when "The Fifth Vital Sign" was gaining traction, a growing body of evidence started showing that chronic pain leads to quantifiable changes in brain structure and function. Imaging studies demonstrated alterations in gray matter distribution, as well as changes in resting-state activity patterns and connectivity between the brain areas involved in the processing of nociceptive information, which will be discussed below. Furthermore, electrophysiological studies showed that pain disrupts ongoing rhythmic activity between regions of interest in the brain, mostly overlapping with those visualized via imaging techniques.

Chronic Pain Correlates with Quantifiable Changes in Brain Structure and Function

Structural Brain Imaging

Morphometric analysis can be applied to magnetic resonance imaging (MRI) of the brain to characterize changes in gray matter volume. Most frequently used in pain neuroimaging is voxel-based morphometry (VBM), in which high-resolution MRI

brain scans are spatially normalized and differences in gray matter volume are determined by comparing signal intensities between voxels [5, 6].

With regard to back pain, one of the earliest VBM studies was conducted by Apkarian and colleagues. In a 2004 study, they reported decreased gray matter volume in the thalamus and dorsolateral prefrontal cortex of patients with chronic back pain [7]. Schmidt-Wilcke and colleagues replicated findings related to reduced gray matter in the dorsolateral prefrontal cortex [8]. However, in their sample patient population, chronic back pain was also associated with *increased* gray matter in the thalamus and basal ganglia. Additionally, Schmidt-Wilcke and colleagues found that gray matter volume in the brainstem and somatosensory cortex was inversely correlated with subjective unpleasantness and pain intensity. Data incongruity can be attributed to small sample sizes and etiologic heterogeneity of chronic back pain.

Regarding migraine headache, it was also shown to be associated with gray matter reductions in the bilateral insular, motor, premotor, prefrontal, and cingulate cortices, as well as the right posterior cortex and the right orbitofrontal cortex [9]. All regions of the gray matter volume changes were negatively correlated with migraine duration and frequency, suggesting progressive gray matter reductions in relation to increasing headache duration and increasing headache frequency. Another study found that migraneurs present with decreased gray matter in the right superior temporal gyrus and inferior frontal gyrus, as well as the left precentral gyrus [10], with a correlation between the anterior cingulate cortex gray matter volume and the frequency of migraine attacks. Gray matter is also found to be decreased in patients with chronic tension type headaches [11]. In patients that develop post-whiplash injury chronic headache lasting longer than 3 months, gray matter was decreased in the anterior cingulate and the dorsolateral prefrontal cortex [12]. These changes resolved after 1 year, concomitant with headache remission. Interestingly, the patients who developed chronic headache showed increased gray matter in the thalamus and cerebellum, as well as in the brain regions thought to play an antinociceptive role.

In other pain patient groups, increased gray matter densities in the parahippocampal gyrus, hippocampus, and basal ganglia were reported in women with chronic vulvar pain [13]. In patients with complex regional pain syndrome (CRPS), gray matter atrophy was noted in the right insula, right ventromedial prefrontal cortex, and right nucleus accumbens although whole-brain gray matter and ventricular size were similar between CRPS and non-pain patients [14]. Patients with fibromyalgia were found to have less total gray matter volume, as compared to healthy controls [15]. Moreover, the degree of gray matter loss was positively correlated with the duration of the disease, with each year of fibromyalgia equivalent to 9.5 times the loss seen in normal aging. Decreases in gray matter were most notably observed in the cingulate, insula, and mediofrontal cortex. In another study, patients with fibromyalgia showed decreased gray matter in the right superior temporal gyrus and left thalamus, as well as increased gray matter volume in the left orbitofrontal cortex, left cerebellum, and bilateral striatum [16].

Functional Brain Imaging

Functional neuroimaging studies in humans have elucidated several regions of the brain that are "activated" in association with acute or chronic pain [17, 18]. Activation maps vary between studies due to the heterogeneity of pain or study design. However, there are common regions with increased blood-oxygen-level-dependent (BOLD) signal associated with experimentally induced pain, including the thalamus, primary somatosensory cortex, anterior cingulate cortex, prefrontal cortex, insula, and the cerebellum, forming the so-called pain matrix [19]. With respect to preclinical studies, some pain-related imaging data have been replicated in anesthetized animals [20].

Using positron emission tomography (PET), which uses regional cerebral blood flow (rCBF) as an index for neuronal activity, patients with ongoing painful mononeuropathy were shown to have increased activation in the bilateral anterior insula, posterior parietal, lateral inferior prefrontal, posterior cingulate, and the anterior cingulate cortices. Activation in the bilateral insula, parietal, prefrontal, and the posterior cingulate, as well as the right anterior cingulate cortex was reduced following successful regional nerve block with lidocaine, resulting in 80–100% pain reduction [21]. The cerebral activation pattern was argued to be related to the affective-motivational dimension of neuropathic pain. In patients with reflex sympathetic dystrophy syndrome (now referred to as complex regional pain syndrome), Iodine-123-labeled iodoamphetamine single-photon emission-computed tomography showed variation in thalamic perfusion contralateral to the painful limb, which was related to the temporal progression of the painful symptoms, suggesting dynamic, adaptive changes in the thalamus [22].

More advanced signal decoding methods in imaging, including multivariate voxel analysis, led to a better understanding of the mechanisms of nociceptive information processing in the brain [23, 24]. For example, acute pain increases functional connectivity between the anterior insula and orbitofrontal cortex, which significantly predicts pain [25]. Interestingly, fMRI data suggest that increased connectivity between the secondary somatosensory cortex, anterior and posterior insula, and the anterior cingulate cortex may result in analgesic effects in a phenomenon referred to as "visually induced analgesia," in which viewing one's own body reduces acute pain [26].

Limitations and Other Considerations Regarding Imaging

The goal of most imaging studies is to visualize the anatomical map (or the activity map in the case of functional imaging) of the brain during states of pain, thus gaining insight into the mechanisms of nociceptive processing in the brain. In so doing, these studies have provided valuable insight into structural and connectivity changes in the brain during pain at a high spatial resolution. However, due to limitations in temporal resolution, brain imaging provides "snapshots in time" rather than a

continuous readout of brain activity. Furthermore, imaging techniques rely on cumbersome and expensive equipment, and severely restrict movement of the studied subject for prolonged periods.

Improved experimental designs of imaging techniques (e.g., near-threshold pain/non-pain paradigm) have minimized comorbid factors associated with pain [27]. Moreover, machine learning algorithms are more efficacious at predicting a sensory experience based on spatially correlated fMRI voxels [28]. For example, thermal pain in humans can be predicted with 80% accuracy using a combination of fMRI and support vector machine learning [29].

Quantitative EEG and MEG

Compared to brain imaging, electrophysiological techniques provide ongoing, direct measurement of neuronal activity. Sampled at frequencies (~3–3000 Hz) far beyond the temporal resolution of brain imaging, local field potential (LFP) recordings reflect postsynaptic potentials and spiking activity [30]. Recordings of cortical LFP in humans subjected to cutaneous application of a moderately noxious laser stimulus showed that the primary somatosensory cortex may be the primary driver of activity in other parts of the pain matrix. Other methods for recording neuronal activity, such as electroencephalogram (EEG) and magnetoencephalggram (MEG), offer the added advantage of being primarily noninvasive. Rather than investigating the "raw" EEG or MEG traces, quantitative analysis is applied to transform the signals from the temporal domain to the frequency domain, mainly using the Fourier transform algorithm. Although earlier EEG studies focused on somatosensory evoked responses, they will not be discussed in this chapter as they are of less relevance to ongoing pain typically experienced in the clinical setting.

In patients with neurogenic pain, now referred to as neuropathic pain, EEG power is increased and dominant frequency is slowed, which is manifested by a leftward frequency shift [31, 32]. These changes are reversed following lesioning of the central lateral thalamus, which is effective in reducing pain in these patients. Slowed EEG rhythms were also observed in patients with chronic pancreatitis [33]. However, in a double-blind placebo-controlled study, patients with chronic pancreatitis, whose pain was treated with pregabalin, demonstrated *increased* EEG power in the theta (4–8 Hz) frequency range [34], which raises important questions regarding potential "contamination" of the EEG due to side-effects, such as drowsiness, which we have observed in animal studies.

Spectral analysis of MEG signals from patients with deafferentation pain syndromes reveal increased resting-state theta range activity, when compared to healthy controls, concomitant with slowing of cortical oscillatory activity [35]. Of these patients, those who derived pain relief from spinal cord stimulation showed a normalization of resting-state MEG. Patients with complex regional pain syndrome also manifest slowed cortical oscillations, as compared to healthy controls [36, 37].

Overall, chronic pain is known to be associated with significant reorganization of functional cortical networks [38, 39]. Maihöfner and colleagues used MEG to assess neuroplastic reorganization of the primary somatosensory cortex and reported that patients with complex regional pain syndrome affecting the upper limbs had smaller cortical hand representations [40, 41]. Clinical improvement was associated with restoration of cortical hand representation size. Mechanisms underlying these MEG changes have been speculated to arise from dysfunctional thalamocortical networks; however, ongoing research continues to refine the right questions to ask regarding the specific mechanisms at both the cellular and molecular levels [20, 42–46].

Can Machine Learning Reliably Classify Pain Patients?

Current evidence suggests that the experience of chronic pain recruits multiple areas in the brain and that these areas exhibit complex spatiotemporal dynamics, which are difficult to predict using univariate statistical analyses. In a univariate analysis, a single variable, such as the BOLD signal of one brain region, is analyzed under the assumption that its behavior does not interact with the behavior of other variables. In contrast, multivariate statistical analysis takes into account the behavior of multiple variables that exhibit dependent interactions on each other. Machine learning is a branch of artificial intelligence that applies multivariate analysis techniques to train its predictions on existing data and to interpret patterns from novel data sets. The primary advantage of machine learning techniques is that by using them, it is possible to interpret and to classify data from individual subjects, instead of identifying group-based differences.

Machine learning has been shown to classify fMRI scans associated with acutely painful versus non-painful thermal stimulation in healthy volunteers with an accuracy ranging between 81 and 94% [29, 47]. Moreover, Gaussian process modeling has been shown to predict subjective pain intensity [48]. Using structural MRI scans, support vector machine analysis correctly classifies chronic low back pain in 76% of subjects [49]. With regard to EEG, machine learning predicts the analgesic efficacy of opioids between individual healthy volunteers, offering a promising adjunct to the development of novel analgesic drugs [50].

Confounding Variables and Future Directions

In order for a diagnostic technology to have everyday application on a wider scale, it must be able to measure pain at an individual level and in a practical and cost-effective way. Currently, most studies mainly analyze group differences, which reduce the possibility of yielding personalized diagnostic protocols.

Moreover, dissociation of the affective from the nociceptive components of pain is key. When controlling for possible confounding variables, such as affective disorders, no significant difference in gray matter volumes is observed in patients

with fibromyalgia [51]. Physical activity associated with increased gray matter volume alone could explain the reversal in gray matter density after successful hip arthroplasty and increased exercise by the patients [52]. Other confounders include heterogenous pathologies mis-classified under one diagnostic label, which include fibromyalgia, complex regional pain syndrome, neurogenic pain, migraine headache, etc. possible misdiagnosis of cognitive disorders such as pain disorder, and lack of controlled analgesic regimens. For example, a relatively short course (1 month) of prescription opioids is enough to alter brain structure [53].

Ultimately, the ideal method for measuring pain should be noninvasive, with a high sensitivity and specificity. In general, however, clinicians will have to agree upon an acceptable classification threshold so that patients who truly have chronic pain are not unjustly denied treatment due to a false-negative result. It may also be necessary to choose a threshold that allows for an acceptable number of false positives. It is important to note that while we argue for an empirical measurement of pain, we are not proposing to replace, substitute, or to "override" the verbal report of the patient. We simply view objective pain measurement as an adjunct or supplemental diagnostic tool to aid the healthcare provider in assessing pain level and quality.

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Chapter 2
Multidisciplinary Pain Management in the Rehabilitation Patient

Tory McJunkin, Edward Swing, Kyle Walters, and Paul Lynch

Introduction

One-third of Americans, or 100 million people, suffer from chronic pain [1]. Pain affects their ability to work, engage in daily activities, and to enjoy their lives. Many of these patients get relief from conservative treatment modalities including rest, physical therapy, chiropractic care, emotional therapy, or non-opioid medications (e.g., non-steroidal anti-inflammatory drugs [NSAIDs], membrane stabilizers). Some patients do not get adequate pain relief from conservative care and may require interventional procedures (e.g., epidural steroid injections, radiofrequency ablations), opioid medications, or even surgery. Patients who do not obtain relief from these treatments may benefit from implantable devices (e.g., spinal cord stimulators, intrathecal treatments) or regenerative treatments. A growing number of medical practices provide many or all of these modalities to patients. There is evidence that this comprehensive, multidisciplinary approach to treating chronic pain is advantageous in terms of patient outcomes and costs.

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Table 2.1 Possible treatment modalities within a multidisciplinary approach to rehabilitating chronic pain

Type of treatment	Examples
Physical modalities	Physical therapy, chiropractic care, acupuncture, electroacupuncture
Emotional therapy	Biofeedback, group therapy, cognitive-behavioral therapy
Non-opioid medications	NSAIDs, membrane stabilizers, muscle relaxants
Opioid medications	Opioids, atypical opioids
Interventional procedures	Epidural steroid injections, nerve blocks, radiofrequency ablations
Implanted device therapies	Spinal cord stimulation, peripheral nerve stimulation, intrathecal pump
Regenerative therapies	Platelet-rich plasma therapy, stem cell therapies

Multidisciplinary Approach Results

The multidisciplinary approach is intended to address the individual differences in patient responses to pain treatment modalities (see Table 2.1 for a list of multidisciplinary treatment modalities). Research investigating multidisciplinary approaches to pain management, such as the "bio-psycho-social" model, have shown significant results in improving pain symptoms and functionality in patients as compared to traditional models [2]. Comprehensive pain programs that include physicians, physical therapists, CAM providers, and psychologists have consistently been found to be both efficacious and cost-effective in treating chronic pain [3]. A study that evaluated patients who were randomized to receive either a standard exercise program (control group) or a comprehensive pain program found that the comprehensive care group demonstrated long-term efficacy in terms of pain reduction and decreased disability [4].

In addition to the efficacy of multidisciplinary treatment programs, there is evidence that these approaches may reduce health care costs. A study by Blue Cross Blue Shield of Tennessee followed 85,000 patients and found that patients entering healthcare through a doctor of chiropractic (DC) cost 20% less than patients entering care with a medical doctor (MD or DO), even after patient risk adjustments [5]. Early access to conservative care in chiropractic settings provides many patients with adequate relief, without the need to progress to potentially more expensive treatments.

Multidisciplinary practices can similarly offer conservative care for patients who can potentially benefit from these treatments. Another study compared patients receiving spine surgery and patients receiving care from a comprehensive model, which included treatment from physicians, physiotherapists, and clinical psychologists [6]. While there was no significant difference in treatment effectiveness between the two groups, there was a significant difference in cost-effectiveness. At 2-year follow-up, the average cost of a patient who saw a surgeon was $14,400 compared to $8323 for patients receiving comprehensive pain treatment. Most

studies of multidisciplinary treatment of chronic pain have examined back pain. A meta-analytic review of 65 studies found that multidisciplinary treatment of back pain is superior to single discipline treatments such as medical treatment or physical therapy [7]. Not only did multidisciplinary care provide greater pain relief, but also improved mood, decreased interference with activities of daily living, and greater likelihood of returning to work than single discipline treatments. The benefits of multidisciplinary care were also more stable over time.

Other studies have extended these findings to other pain indications. For example, a randomized controlled trial assigning patients with knee osteoarthritis to either standard care or multidisciplinary care found that multidisciplinary care resulted in better outcomes for pain and functioning [8]. A study of fibromyalgia patients found that multidisciplinary treatment based on a cognitive-behavioral model enabled patients to decrease their use of opioids, NSAIDs, benzodiazepines, and muscle relaxants [9]. A multidisciplinary treatment program including physical and occupational therapy, group psychotherapy, stellate ganglion blocks, and drug therapy has demonstrated efficacy in treating patients with complex regional pain syndrome [10].

Physical Modality

The physical modality of pain treatments include a number of conservative care options, including a supervised targeted exercise plan, physical therapy, chiropractic care, acupuncture, massage, and others. Studies have shown that chiropractic manipulation, in conjunction with exercise, not only facilitates and improves recovery, but also minimize recurrence of symptomatic pain [11]. A 2004 study randomly assigned 1334 patients to receive spinal manipulation, exercise, both spinal manipulation and exercise, or best care from general practice [12]. Those assigned to complete spinal manipulation, exercise, or both experienced greater pain relief and reduced disability as compared to those who received only best care in a general practice setting at 3 and 12 months.

Physical therapy has been shown to improve function and to reduce pain for patients with chronic low back pain [13]. The most effective programs involve individualized regimens performed with supervision and include stretching and strengthening exercises. Given that benefits generally outweigh any risks, strong consideration should be given to physical therapy as an effective treatment modality for chronic pain.

Acupuncture involves the precise insertion of needles at specific points on the body with the intention to facilitate healing. Although this practice has its origins in traditional Eastern medicine, contemporary medical providers use this therapy with a sound physiological understanding. Research suggests that chemical changes in the brain occur as the result of acupuncture. These changes include increases of endomorphin-1, beta endorphin, encephalin, serotonin, and dopamine, all of which

can act to induce analgesia. In addition, because of these effects, acupuncture can be used to treat gastrointestinal problems and psychological illnesses [14].

A large number of randomized controlled trials have provided evidence that acupuncture is a valuable option in the effective treatment of chronic pain [15]. Furthermore, trials have demonstrated significant differences between true and sham acupuncture procedures, which suggests that the efficacy of acupuncture is more than a placebo effect. One study evaluated several outcomes in treating chronic low back pain with acupuncture [16]. Several thousand patients underwent treatment and were evaluated after 6 months on measures of pain intensity, pain frequency, functional ability, depression, and quality of life. Results included a significant improvement of functional ability (45.5%), decreased days per month with pain, and a 30% decrease in work absences for employed patients.

Electroacupuncture (EA) is a form of acupuncture that involves using the needles as electrodes for passing electric current. Although less common than manual acupuncture, electroacupuncture has grown in popularity since its inception roughly 50 years ago [17]. One study investigating the differences in brain activity resulting from manual acupuncture and EA found that EA produced more widespread fMRI signal increase than manual acupuncture. Furthermore, all acupuncture treatments produced more widespread responses than the placebo-like tactile control [17].

It is important to note that patient expectations can have an impact on the results of acupuncture. One study evaluated patients' attitudes towards acupuncture and expectations regarding the outcomes prior to receiving treatment [18]. The results suggested that patients with high expectations about acupuncture were about twice as likely to have good treatment outcomes compared to those with lower expectations. Results like these underscore the importance of attitudes and psychological disposition in the treatment of pain.

Emotional Therapy

The subjective experience of pain involves more than organic pathology. Psychological dispositions can influence the perception of pain, and the experience of pain itself can have a lasting effect on one's psychology. For example, patients suffering low back pain who also have major depression tend to exhibit lower success rates with many treatments, including spinal cord stimulator implantation and spinal surgery, than non-depressed patients [19]. Many pain treatments and procedures focus only on the organic factors of pain and do not address the cognitive and emotional elements. Therefore, a multidisciplinary model for the treatment of pain ought to include the option of treatments for the psychological components of pain.

Biofeedback provides one way of understanding and dealing with the physical effects of stress that result from chronic pain. This treatment strengthens the patient's ability to recognize the signs of stress arousal (e.g., shallow breath, muscle tension) and utilizes relaxation techniques to mitigate the effects of the stress [20]. Research indicates that biofeedback is effective in treating many different types of pain,

including chronic low back pain [21]. This treatment is most effective when used as one component of an interdisciplinary approach to pain management.

Group therapy is another important component in the treatment of chronic pain. By receiving therapy in a group setting, patients have support that can minimize the feelings of isolation that are commonly associated with sufferers of chronic pain. Research suggests that cognitive therapy that involves identifying and changing negative thoughts reduces self-reported pain in low back pain patients [22].

Medication Management

Several classes of drugs can be appropriate for treating chronic pain conditions. Non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, can provide effective pain relief for several pain conditions including osteoarthritis and rheumatoid arthritis [23, 24]. Neuropathic pain can often be treated successfully with antidepressant and anticonvulsant medications [25, 26]. Opioids can be effective for treating chronic pain, with previous studies finding that opioids produce an average of 28% pain relief, compared to 7% pain relief for placebo [27]. Because opioid medications present substantial risks of addiction and overdose, careful consideration should be taken in their use [28]. This includes the selection of appropriate patients, ongoing monitoring through urine drug testing (UDT), pharmacy board report reviews, and the prescription of low to moderate doses. When used appropriately, opioids can be part of an effective treatment plan for chronic pain. Atypical opioids, such as tramadol, may provide effective pain relief with significantly less risk of abuse [29].

Interventional Procedures

Patients who have not responded to conservative pain management modalities, such as those described above, may be appropriate candidates for interventional procedures. For example, epidural steroid injections (ESIs) are a widely used procedure for the treatment of chronic radiating pain. Because epidural steroid injections are used at different regions and different injection routes, and for varying patient pathology, the efficacy can be difficult to determine. However, there is general consensus among specialists that in well-selected patients, ESIs provide at least short- to moderate-term relief [30]. Also, ESIs have been shown to have a better risk-benefit ratio and be more cost-effective than other treatments such as spine surgery.

Research suggests that radiofrequency ablation (RFA) of targeted nerves, either in the spine or peripherally, can produce significant pain relief. For example, RFA of the lumbar medial branch nerves has moderate to strong evidence for pain relief [28]. In one study, lumbar medial branch nerve RFA produced a 46% reduction in mean pain and a 47% reduction in greatest pain, compared to an 8% reduction in

mean pain and 13% reduction in greatest pain for sham RFA [31]. Two-thirds of those treated with RFA experienced at least 50% reductions in pain at 8 weeks after treatment (compared to 38% of patients experiencing such relief after sham RFA).

Some chronic pain patients may be appropriate candidates for implanted devices to manage their pain. In particular, spinal cord stimulators can provide safe, effective relief of chronic pain [32]. For example, in a study evaluating the efficacy of spinal cord stimulation for treating patients with failed back surgery syndrome, patients were randomly assigned to either receive SCS or re-operation [33]. After 3 years, 47% of SCS patients received at least 50% pain relief compared to 12% of re-operation patients.

Regenerative Treatments

Many types of pain conditions, including osteoarthritis and degenerative disc disease, result from body tissues breaking down faster than the body can replace them. For these conditions, treatments with injection of biologics may have the potential to enhance the regenerative processes at the targeted area. These treatments can potentially alleviate pain, regrow damaged tissues, and/or inhibit further deterioration. For example, platelet-rich plasma (PRP) therapy is a technique to aid healing and regeneration. It begins with a small amount of blood being drawn from the patient receiving the treatment. The patient's blood is placed in a centrifuge that spins the blood, separating it into different layers. The top layer contains only plasma; red blood cells concentrate in the bottom layer. The middle layer contains a high concentration of platelets and growth factors. By concentrating these materials and injecting them at the injured site, the hope is that healing and regeneration will occur more effectively.

Early research supports this regenerative effect. A study of 91 patients receiving series of PRP injections in the knee for degenerative cartilage lesions and osteoarthritis found that PRP injections reduced pain, improved knee function, and quality of life for at least 12 months after injection [34].

Several types of tissues, found in the patient or a healthy donor, can potentially enhance regeneration through the presence of stem cells. Stem cells can be found in amniotic tissues, bone marrow, or adipose tissue. Amniotic tissues can be harvested from donors during a caesarian birth for use in the treatment of chronic pain. This tissue contains collagen, growth factors, and stem cells that are thought to induce healing. One study found injection of this fluid to accelerate healing of wounds in rats [35]. Other sources of stem cell therapies include bone marrow and adipose (fat) tissue. A study of culture expanded, bone marrow-derived stem cells found that injection of these stem cells into patients with osteoarthritic knee joints led to greater regrowth of cartilage compared to osteoarthritic joints not treated with stem cells [36]. Ongoing research is examining the potential for injections of bone marrow-derived mesenchymal stem cells (MSCs) to alleviate degenerative disc disease [37]. In an interim analyses of this randomized, placebo-controlled trial of 100

patients receiving MSC injections (high or low dose) or control injections (saline or hyaluronic acid) into degenerative discs in the lumbar spine found significantly reduced low back pain and improved function at 12-month follow-up among those treated with MSCs.

Conclusion

It has been said that when the only tool you have is a hammer, every problem looks like a nail. Patients with chronic pain conditions vary in their responsiveness to different treatments. Some patients respond well to conservative treatments. Treating these patients with invasive procedures or high risk medication can create unnecessary costs for the patient and health care system as well as increased risk of adverse side effects. For patients who do not respond to conservative treatments, there are a variety of appropriate treatments that can provide pain relief. A multidisciplinary treatment paradigm involves a comprehensive approach that includes physical modalities, emotional therapies, medication management, interventional procedures, regenerative therapies, complementary and alternative options, and surgery only when needed. The availability of all of these treatment modalities gives patients the greatest chance of pain relief to improve their functioning and quality of life.

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Part II
Pain in the Rehabilitation Patient

Chapter 3
Pain in the Spinal Cord Injury Rehabilitation Patient

Heidi Wennemer, Nadia Alwasiah, and Damon A. Gray

Introduction

Pain is a common problem for patients with spinal cord injury (SCI) and is often difficult to manage. Pain due to SCI is multifactorial and optimal treatment requires an individualized evaluation and treatment plan. The incidence of severe pain after SCI is estimated to be between 30 and 40% (Mehta S. et al, Pain Following SCI. 2014). The incidence of chronic pain after SCI is estimated to be up to 94% (Siddall 1997). Severe pain due to any source will significantly impact a patient's function, ability to perform ADLs, independence, and mood.

SCI patients with damage to the nervous system are predisposed to various types of neuropathic pain. However, one of the most common types of pain after SCI is musculoskeletal pain. Patients with paraplegia, who utilize their upper extremities for transfers, pressure relief, and other weight bearing activities, will have an increased incidence of shoulder pathology. There are also predictable musculoskeletal strain

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Table 3.1 International spinal cord injury pain classification (Bryce et al. 2012)

Tier 1: pain type	Tier 2: pain subtype	Tier 3: primary pain source and/or pathology
Nociceptive	Musculoskeletal	e.g., glenohumeral arthritis, lateral epicondylitis, comminuted femur fracture, quadratus lumborum muscle spasm
	Visceral	e.g., myocardial infarction, abdominal pain due to bowel impaction, cholecystitis
	Other nociceptive pain	e.g., autonomic dysreflexia headache, migraine
Neuropathic	Above level pain	e.g., peripheral nerve mediated; carpal tunnel syndrome; trigeminal neuralgia
	At level pain	e.g., spinal cord compression; nerve root compression; cauda equina compression
	Below level pain	e.g., spinal cord ischemia; spinal cord compression
	Other neuropathic pain	e.g., diabetic polyneuropathy; central neuropathic pain; complex regional pain syndrome

patterns caused by these activities as well as ambulation in a wheelchair several hours each day. An improperly fit wheelchair will exacerbate these problems.

SCI patients will generally have abnormal sensation below the level of injury. Altered sensation with either absent sensation, reduced sensation, or even hypersensitivity may be present. Patients with incomplete SCI may have partial sensory preservation below the level of injury. These patients may even have exaggerated pain response in some dermatomes. Complete injuries may experience hyperpathia in the zone of partial preservation.

Due to the complex nature of pain in the SCI population, evaluation requires a systematic approach. We will discuss some of the various pain models that may help clinicians analyze the multiple pain generators for each case.

Pain cannot be accurately evaluated without consideration of a patient's psychological state, as it is well known that pain is clearly influenced by behavioral components. Chronic pain predisposes individuals to depression and reducing pain has thereby been shown to have a significant effect on reducing depression (Cairns 1996).

Pain due to spinal cord injury may be separated into nociceptive pain and neuropathic pain. Nociceptive pain may be subdivided into musculoskeletal and visceral pain. Neuropathic pain may be subdivided by its location into the following: (1) above the level of injury; (2) at the level of injury; (3) below the level of SCI injury or other (Table 3.1).

Classification

Pathophysiology

Nociceptive Musculoskeletal Pain

This is the most common type of pain in SCI. It may be due to overuse or strain, arthritic changes, wear and tear of the joints, spasticity (muscle spasms), or muscle strength imbalance. A prospective study (upper extremity MSK pain during

and after rehabilitation in wheelchair using persons with SCI, 2006) found that subjects with tetraplegia showed more shoulder pain than subjects with paraplegia. Other factors that increase the risk of upper extremity or shoulder pain include the following: age, higher BMI, manual wheelchair use, or inappropriate propulsion technique.

The shoulder joint is especially at risk for overuse and muscle strain. Acute shoulder pain may develop early in the rehabilitation course, since patients with lower extremity paralysis or paresis become increasingly dependent on the use of their upper extremities for mobility. Impingement syndrome, sub-acromial bursitis, osteoarthritis, adhesive capsulitis, bicipital tendonitis, and aseptic necrosis of the humeral head should be identified as possible causes for chronic shoulder pain in SCI (spinal cord medicine principals and practice, Lin). Shoulder pain may also be due to arthritis or heterotopic ossification (HO).

The level of injury may correlate with the type of shoulder pain. Weakness of thoraco-humeral muscles contributes to shoulder pain, due to shoulder muscle imbalance. Tetraplegic patients must work harder to stabilize their joints and to keep their trunk balanced. In general, patients who have a level of injury above C6 will likely require the assistance of another person or a mechanical lift, and those with level of injury at or below C7 may be able to transfer independently.

Shoulder pain is usually experienced during daily life activities such as transfers, wheelchair propulsion, and pressure relief. It is common that more than 25% of body weight is transferred through the humerus to the thorax during these activities (upper extremity musculoskeletal pain during and after rehabilitation in wheelchair-using persons with a spinal cord injury).

Shoulder pain due to rotator cuff muscle imbalance may be prevented with strengthening of the weak muscles, which include the posterior shoulder muscles, adductors, external rotators, and posterior scapular muscles; stretching of the tight muscles, which include the internal rotators and anterior shoulder muscles. Both are done to restore muscle balance at the joint, to optimize posture, and to avoid activities that promote impingement. Activities whereby the arm is abducted and flexed more than 90° promote shoulder impingement.

Scapular pain is a common complaint. At the level of injury, neuropathic pain is often seen in mid-cervical SCI. Pain may be present over the dorsal-medial border of the scapulae, with tenderness to palpation over the rhomboids (C4-6), levator scapulae, supraspinatus, and infraspinatus muscles (C3-5). In patients with lower C-spine injury and in paraplegic patients, scapular pain may be caused by overuse of muscles supporting the shoulder girdle during transfers, as well as by the use of the upper extremities for mobility.

Facet joint pain is typically better with flexion and worse with extension. Pain due to facet joints is usually seen just above or below the surgical fusion level and is likely due to arthritic degeneration of the facet joints as a result of compensation and overuse adjacent to the facet segments. Physical therapy should be directed toward strengthening the paraspinal muscles with a slight flexion bias. Other treatments include epidural steroid spinal injections, medial branch nerve blocks with subsequent radiofrequency ablation as indicated, and trigger point injections.

Nociceptive Visceral Pain

Visceral pain may occur above, at, or below the level of injury. In a paraplegic patient, visceral pain may occur above the level of injury with myocardial infarction or pleurisy. Abdominal pathology may produce visceral pain below the level of injury. Possible causes of abdominal visceral pain include constipation, kidney stones, ulcers, appendicitis, and gallbladder stones. Visceral pain is often poorly localized and vague. It may be described as cramping, dull, or ache-like in nature.

Other Pain

Any patient with SCI who complains of headache should have their blood pressure (BP) assessed. Elevation of BP over 20 mmHg above baseline, systolic, diastolic, or both, is concerning for autonomic dysreflexia (AD). This is a potentially life-threatening condition that is unique to spinal cord injury. Any clinician treating SCI should take time to familiarize themselves with the signs, symptoms, diagnosis, and treatment of this condition.

Briefly, AD is caused by interruption of the descending inhibitory signals from the parasympathetic nervous system within the spinal cord. Damage to the spinal cord above T6 level allows the parasympathetic and sympathetic branches of the nervous system to function independently, without normal feedback inhibition. T6 is significant because the greater splanchnic nerve originates at the T5-9 levels, so injury above this nerve cuts off descending parasympathic inhibition, and allows for unopposed constriction of the splanchnic vascular bed, thereby causing severe systemic hypertension. Baroreceptors in the carotid sinus and aortic arch detect the rise in BP, therefore stimulating the parasympathetic nervous system, which acts via the vagus nerve to reduce the heart rate. This gives the classic presentation of AD, whereby there is significant hypertension (greater than 20 mmHg above baseline) with bradycardia.

Cervicogenic headaches and occipital neuralgia are also common among SCI patients. Concurrent TBI with SCI is common in traumatic SCI. Any SCI patient with new headache should be evaluated for intracranial pathology.

Muscle Spasms and Spasticity

Pain will vary with the degree of spasticity. The initial approach should include stretching and repositioning. Other treatment options include local nerve or muscle blocks, or medications.

Neuropathic Pain

After spinal cord injury, neuropathic pain may develop due to the loss of normal sensation, which is mediated by the spinothalamic pathway. This is often coupled with abnormal pain perception. Patients may experience spontaneously generated continuous pain or abnormally evoked pain. Neuronal activity is upregulated, which then leads to hyper-excitability. Although the exact mechanism is not fully elucidated, there are known neurochemical changes after SCI that contribute to the state of neuronal hyperactivity and abnormal pain perception. These include both increased excitatory glutaminergic activity involving *N*-methyl-D-aspartate (NMDA) receptor activation and intracellular cascade reaction, as well as changes in voltage-sensitive Na^+ channels, which causes nerve membrane excitability. There is simultaneous loss of endogenous inhibition from gamma-amino-butyric acid (GABA) ergic, opioid, and monoaminergic inhibitory pathways.

Neuropathic pain is often described as burning, stabbing, or tingling. However, neuropathic pain sensations vary a great deal from person to person. Some spinal cord injuries are complete and as such, lack any sensation below the level of injury. Some patients with complete injuries will have a zone of partial preservation that continues below the level of injury. Others will have incomplete injuries with some sensory preservation below the level of injury.

In either case, pain that occurs below the level of injury may be centrally mediated. Patients may also experience pain in the limbs that lack sensation, similar to phantom pain among amputees. In those patients with some sensation below the level of injury, there may be nerve pain from damaged nerves. Cauda equina syndrome, due to trauma or infection, will often cause severe pain secondary to damage of the nerve roots after they exit the conus (SCI washington.edu).

Neuropathic pain may be classified by the location of pain in relation to the level of spinal cord injury:

Above the Level of Injury

Neuropathic pain occurring above the level of injury will be similar to neuropathic pain in patients without spinal cord injury. Frequent causes include compression neuropathies and radiculopathies. The incidence of carpal tunnel syndrome is increased in paraplegic patients, as compared to the general population.

Nerve decompression surgeries should be considered very carefully in SCI patients. Although these are considered simple day surgeries, the immediate postoperative recovery for patients with paraplegia will require utilization of alternate methods for transfers and mobility. In this patient population, successful recovery and rehabilitation from a simple carpal tunnel release may necessitate an inpatient rehabilitation stay. In some cases, it may make sense to decompress

both sides simultaneously, in order to consolidate the period of dependence on others for transfers and mobility.

At the Level of Injury

Pain at the level of injury is generally segmental or radicular. Segmental pain is usually located within three levels of the spinal cord injury, in the transition zone from normal to abnormal sensation. Patients may experience a segment of hyperalgesia just proximal to the segment, where sensation is absent. For example, a patient with a T6 level of injury may have a circumferential band of allodynia at the T5 level.

Acute radicular pain is generally secondary to damage to the spinal cord itself and is most often seen at the level of injury. The onset of pain is usually within days to weeks after injury, and can be hard to distinguish from pain caused by the injury itself. Radicular pain is often caused by nerve root damage within the dermatomes of the neurological level. It is due to impingement or nerve root irritation by bone fragments, extruded disk, and inflammation. Radicular pain tends to be one-sided and is frequently described as shooting, burning, aching, or crushing. It can worsen with rest and improve with activity.

Chronic radicular pain may develop from the above mechanisms, scar tissue, or a Charcot spine. Charcot spine manifests as severe destructive bony changes due to repetitive stress in the setting of severely impaired sensation. It is most often associated with diminished or absent pain and proprioceptive sensations. Repeated subclinical injury, especially to a vertebral segment adjacent to an arthrodesis or fusion, can result in progressive joint destruction and radicular symptoms. Scar tissue may contribute to chronic nerve root impingement or irritation. Pain due to this condition is usually unilateral and described as burning or aching.

Below the Level of Injury

Pain below the level of injury is labeled central pain, which is also called dysesthetic, or diffuse pain. It is described as burning, tingling, shooting, stinging, stabbing, piercing, cutting, crushing, aching, or nagging. The pain is often diffuse and poorly localized; it is more common with gunshot wounds, advanced age, increased anxiety, and adverse psychosocial situations. This type of pain may be exacerbated by fatigue, tobacco use, stress, overexertion, bowel or bladder complications, pressure sores, spasticity, and even weather changes.

Central neuropathic pain is one of the most common types of pain in the SCI population and is usually unresponsive to standard pain treatments. Few research studies have examined this type of pain and so far none has shown any single drug to be effective for a significant number of people. Even so, many individuals with SCI have found pain relief from a combination of medications, medications in combination

with physical therapy, or other treatment modalities. Some treatments, like implanted morphine pumps, work well initially, but relief is often only temporary.

Until a widely effective treatment for central neuropathic pain is found, physicians need to work with each patient to develop an individualized treatment plan. Often, an integrated medicine approach that encompasses exercise, medication, stress reduction, and other complementary treatments such as acupuncture may be necessary to achieve adequate pain management.

The onset of central neuropathic pain is usually weeks to months after injury. It is important to note that late onset pain, or worsening pain in SCI patients, should prompt an evaluation for syringomyelia, Charcot spine, or other bony pathology. These conditions should be ruled out before a diagnosis of central neuropathic pain is made.

Other Pain

Syringomyelia

Syringomyelia is a clinical syndrome that results from an enlarging fluid filled cyst within the grey matter of the spinal cord. It develops at the site of the traumatic SCI and extends rostrally or caudally. It manifests as neurological and functional decline.

Pain due to syringomyelia is often localized to the site of injury and may radiate to the neck and upper limbs. The classic presentation includes loss of pinprick and temperature sensations in a cape-like distribution. The pain is described as aching or burning. This pain may be aggravated by sneezing, straining, postural changes, or upper extremity movement. There is associated loss of reflexes, and sensation. Pain is the most common presenting symptom. Other symptoms may include ataxia, autonomic dysreflexia, spasticity, neuropathic pain, dysesthesias, and weakness.

Post-traumatic syringomyelia is a condition that may develop months to years after a traumatic injury to the spinal cord. Syringomyela is seen in approximately 25% of patients with traumatic SCI (Post-traumatic syringomyelia review, Brodbelt and Stoodley 2003).

Complex Regional Pain

Complex regional pain syndrome is a type of generalized neuropathic pain. It is defined as hyperalgesia, not limited to a single nerve or root distribution, disproportionate to what is expected, and associated with edema, skin, and blood flow abnormalities.

There are two types of CRPS: I & II

Type I: is without nerve injury
Type II: is related to a nerve or spinal root injury

Reference: CPRS (from Indian Journal of Plastic Surgery article, Complex Regional Pain syndrome, by Sandeep J. Sebastin, 2011)

CPRS is characterized by a continuous (spontaneous and/or evoked) limb pain that is not in a specific nerve territory or dermatome, and usually has associated abnormal sensory, motor, vasomotor, and/or trophic findings. Early recognition and prompt initiation of treatment improves patient outcomes. Diagnosis of this condition is a challenge. However, the Budapest diagnostic criteria have helped clinicians to diagnose this condition more consistently:

The Budapest criteria is a clinical criteria and it consists of:

Continuous pain that is disproportionate to any inciting event in addition to…

1. At least one of symptom in three of the four following categories: sensory, vasomotor, sudomotor/edema, motor/trophic
2. At least one sign in two of the following categories: sensory, vasomotor, sudomotor/edema, motor/trophic
3. There is no other diagnosis that better explains the symptoms.

CRPS has been divided into three stages of progression. Although it is not necessary for each patient to develop all stages, recognizing the stage and the predominant complaint can help with management of patients:

Stage I (Acute Stage: 0–3 Months)

It is characterized primarily by pain/sensory abnormalities , such as hyperalgesia, allodynia, signs of vasomotor dysfunction, and prominent edema and sudomotor disturbance.

Stage II (Dystrophic Stage: 3–9 Months)

It is characterized by more marked pain/sensory dysfunction, continued evidence of vasomotor dysfunction, with the development of significant motor/trophic change.

Stage III (Atrophic Stage: 9–18 Months)

It is characterized by decreased pain/sensory disturbance, continued vasomotor disturbance, and markedly increased motor/trophic changes.

For further reference, please see dedicated chapter on Complex Regional Pain Syndrome.

Treatment

The decision for surgical treatment should be approached with caution in patients with SCI. Careful consideration must be given to the effects of surgery and hospitalization on the overall function and deconditioning of the SCI patient. Patients may lose their independence, as well as their ability to transfer and to self-propel a manual wheelchair. Therefore, prolonged hospitalizations after surgical procedures may ensue.

Non-surgical Interventions

There is a broad range of treatment modalities that may be effective in controlling and managing pain related to SCI. Some of these are effective with both nociceptive and neuropathic pain, while others are beneficial for only one. Many patients would benefit from some combination of these approaches.

One of the first strategies to consider includes activity modification. Modifications should include methods to ensure proper body mechanics, while using a manual wheelchair or during transfers, altering equipment, such as switching to a power wheelchair or a lighter weight aluminum/or titanium wheelchair, Push Rim Activated Power Assist Wheels [PAPAWS], or Magic Wheels 2 gear wheelchair wheels, and mobility and balance exercises. For patients who are obese or have suffered overuse injuries, weight loss counseling should be considered.

To restore balance, physical therapy should focus on stretching tense muscles and strengthening weak ones. Given the propensity toward shoulder dysfunction in the majority of manual wheelchair users, exercises should focus on the restoration of flexibility of the pectoral muscles, along with progressive resistance exercise for other muscles of the shoulder girdle. Exercise should be individualized given the SCI patient's motor examination and level of injury.

Studies have shown that regular exercise reduces both nociceptive and neuropathic pain in the setting of spinal cord injury (SCIRE Pain following SCI, p. 16). It has also been shown to reduce shoulder pain in a targeted SCI protocol, when secondary to overuse and muscle imbalance.

Therapeutic massage, with or without heat, is the primary treatment for musculoskeletal nociceptive pain due to muscle imbalance, muscle trauma or inflammation, muscle spasms, or secondary overuse syndromes. It may not be helpful in improving the intensity of neuropathic and musculoskeletal pain after SCI.

Acupuncture is most helpful in neuropathic pain. It was found to activate type II and III muscle afferent nerves or A delta fibers, blocking pain via the Gate Control Theory, and releases endogenous opioids, neurotransmitters, and neurohormones. It has shown equal efficacy to Trager therapy and sham acupuncture in treating nociceptive shoulder pain in SCI (SCIRE Pain following SCI p. 14). For further reference, please see dedicated chapter on acupuncture for pain control.

Transcutaneous electrical nerve stimulation (TENS) preferentially stimulates large alpha sensory nerves to reduce pain at the pre-synaptic level via the Gate Control Theory.

Furthermore, there is now strong evidence that trans-cranial electrical stimulation (TCES), in which electrodes are placed on the scalp to stimulate the cerebrum beneath, is effective in reducing neuropathic pain related to SCI. Similarly, trans-cranial magnetic stimulation (TCMS) uses pulsed magnetic fields, generated via electromagnets, which are placed over the scalp to induce neuron depolarization. There is now Level 1a evidence that this technique reduces post-SCI neuropathic pain.

Osteopathic manipulative medicine (OMM) has been shown to relieve chronic pain in individuals with osteoarthritis, but alone, it may not be effective at reducing neuropathic pain post-SCI (level 1b evidence) (SCIRE Pain following SCI, p. 10). For further reference, please see chapter on osteopathic manipulative medicine for pain.

Psychological Treatments

Patients can be taught to utilize psychological techniques to better self-manage their pain, so that pain impacts their lives less. Psychologists who have been trained in pain management can help with a variety of techniques that have been proven effective in reducing the intensity and impact of pain. For further reference, please see chapter on psychological interventions for pain.

Self-Hypnosis Training

Self-hypnosis training has proven helpful for reducing chronic pain in some SCI patients. Although individual response to treatment is variable, Level 4 evidence supports that it may reduce SCI-related musculoskeletal and neuropathic pain.

Visual Imagery

This cognitive technique is based on the cortical method of pathological pain, whereby guided imagery is used to modify behavior and the perception of discomfort. Level 1b evidence shows a positive effect on neuropathic pain (SCIRE Pain following SCI, p. 26).

Relaxation Techniques and Biofeedback

Teaching patients how to reduce muscle pain tension and "mental tension" associated with pain may be helpful in self-management. Also, training patients to attain certain EEG patterns, which have been shown to be helpful in migraine and fibromyalgia, may also reduce neuropathic and nociceptive pain in SCI.

Cognitive Behavioral Therapy

Cognitive restructuring, which can help SCI patients in pain to think differently about their pain and its effects, has been shown to lead to changes in brain activity. These changes can affect how a patient experiences their pain. Cognitive therapy works to change maladaptive beliefs and coping systems. This type of therapy is most successful within a comprehensive pain management program.

Individual Psychotherapy

This type of therapy may be used to help patients to identify desired goals and to increase pleasure and meaning in daily life. As such, it can help to reduce pain. Psychotherapy may also be helpful in managing anxiety associated with the experience of pain.

Medications

There are a number of medications that may be helpful in the management of pain for SCI patients. These medications range from non-steroidal anti-inflammatory drugs and anti-seizure medications to psychotropic drugs:

Non-steroidal Anti-inflammatory Drugs (NSAIDs)

This class includes medications such as aspirin, ibuprofen (Motrin, Advil), and naproxen, which are most commonly used to treat musculoskeletal pain in SCI patients.

Anti-epileptic Drugs (AEDs)

This class includes medication that are often used to treat neuropathic pain. One theory about their mechanism of action includes modulation of hyperactive neurons, which can potentially calm the deaferrented neurons sending neuropathic pain signals in the injured spinal cord.

Medications such as Gabapentin (Neurontin) and Pregabalin (Lyrica) are first-line agents used to treat neuropathic pain. Their proposed mechanism of action is to bind alpha 2 delta receptors on pre-synaptic neurons, thereby decreasing calcium influx, which in-turn decreases the release of excitatory neurotransmitters.

A typical pregabalin starting dose is 75 mg twice daily. This can be increased to 150 mg twice daily after 1 week, and then to a maximum of 300 mg twice daily after another 2 or 3 weeks. Maximum dosage is 600 mg per day. Gabapentin can be started at 300 mg daily per day, then 300 mg twice daily for the second day, and then 300 mg three times daily. It may then be titrated, based on tolerance and/or pain relief, up to 3600 mg per day. Both pregabalin and gabapentin should be tapered gradually upon discontinuation. The following list shows evidence related to the use of AEDs for SCI pain patients:

Gabapentin and pregabalin-

Level 1a evidence that usage reduces post-SCI neuropathic pain.

Pregabalin-

Level 1b evidence that usage with osteopathy improves post-SCI pain.

Lamotrigine-

Level 1b evidence to improve post-SCI neuropathic pain.

Levetiracetam-

Level 1b evidence showing this is not effective in reducing post-SCI neuropathic pain.

Valproic acid-

Level 2 evidence that usage does not significantly reduce post-SCI pain.

Psychotropic Medications

Antidepressants are used to treat neuropathic pain and depression. These medications include selective serotonin norepinephrine reuptake inhibitors (SSNRIs), such as duloxetine (Cymbalta) and venlafaxine (Effexor), and tricyclic antidepressants (TCAs), such as amitriptyline (Elavil) and Nortriptyline (Pamelor). Both classes are proposed to inhibit the uptake of both norepinephrine and serotonin in the CNS,

allowing the excess serotonin to inhibit painful afferents on the dorsal horn of the spinal cord. Their antidepressant function is proposed to treat the chemical link between depression and pain. Some studies show that amitriptyline (Elavil) is effective only when there is concomitant depression. Common side effects for SSNRIs are nausea, dizziness, and sweating. Common TCA side effects, which are often dose-limiting, are typically anticholinergic in nature, which include dry mouth, drowsiness, and dizziness.

Clonidine is an alpha 2 agonist thought to inhibit nociceptive input into the dorsal horn of the spinal cord. Studies have shown that it may be useful for patients who do not respond fully to opioids, and it may provide a synergistic effect with opioids in relieving pain. Clonidine has been used in combination with morphine intrathecally (SCIRE Pain following SCI, p. 54–55).

Opioids

Morphine, codeine, hydrocodone, and oxycodone are used to treat both neuropathic and musculoskeletal pain. These drugs have many side effects, including constipation and sedation, and can be habit forming. As a result, they should not be the first agents considered for chronic pain management. Opioids are most appropriately viewed as a valid second- or third-line treatment option, when other medications and interventions have not proven satisfactory. Risk factors for misuse and abuse include prior history of abuse and family history of substance abuse. When using these agents, an opioid treatment agreement between the prescriber and patient is strongly recommended.

The opioid-like medication tramadol (Ultram) has been shown to have level 1b evidence to be effective in reducing neuropathic pain post-SCI [SCIRE Pain following Spinal Cord Injury p. 52].

Muscle Relaxants and Anti-spasticity Medications

Diazepam (Valium), baclofen (Lioresal), tizanidine (Zanaflex), and botulinum toxin (Botox) are used to treat spasm-related and musculoskeletal pain. Most of these may be taken by mouth or delivered directly to the spinal cord through an implanted pump (see “Intrathecal pumps” below). Botulinum toxin is delivered through an intramuscular injection and may be useful in reducing pain related to focal spasticity. These drugs can cause sedation, confusion, and other side effects.

Baclofen is a GABA agonist. Because GABA is also involved in pain pathways, but there is limited evidence that baclofen may reduce SCI related dysesthetic pain [SCIRE Pain following Spinal Cord Injury p. 49].

Other Medications

Ketamine is a non-competitive NMDA receptor antagonist. Level 1a evidence indicates that ketamine is effective in reducing allodynia. Cannabinoids are potentially a new treatment for post-SCI pain, but in need of further study. Topical local anesthetics such as lidocaine (Lidoderm) are used to treat pain that occurs when the skin is lightly touched (called allodynia). Epidural or subarachnoid lidocaine injections may sometimes provide useful diagnostic information when considering interventional, or surgical pain treatments. Capsaicin, the spicy ingredient in hot peppers, works topically as an inhibitor of substance P.

Injections

Pain above the level of injury may be managed as it would be in patients without spinal cord injury. Interventional spine injections may be beneficial for appropriate conditions. Joint and bursa injections may be indicated for patients with joint pathology, arthritis, and bursitis. Trigger point injections may relieve pain due to myalgia. Sympathetic nerve blocks may be helpful to relieve pain due to complex regional pain syndrome.

Surgical Treatments

Dorsal column stimulation is used to treat neuropathic pain due to nerve root damage. A high frequency, low intensity nerve stimulator is percutaneously or surgically placed in the epidural space, next to the spinal cord or nerve roots. This treatment is expensive, and invasive, and is generally left to treat pain that has proven intractable to other methods. For further reference, please see chapter on spinal cord stimulation for pain.

Intrathecal pumps are used to treat neuropathic pain (using morphine or ziconatide) or muscle spasm-related pain (using baclofen). A pump containing morphine or ziconatide, baclofen, or both, is surgically placed under the skin in the abdomen. It delivers the medication directly to the intrathecal space, in an effort to directly treat the spinal cord and nerve roots in concentrations much lower than would be given orally.

Dorsal longitudinal T-myelotomy is an invasive technique restricted to non-ambulatory patients with severe painful spasticity. A dorsal approach is used to separate the anterior and posterior halves of the spinal cord, in order to disconnect the afferent and efferent nerve roots, which thereby removes the key reflex synapse responsible for spasticity.

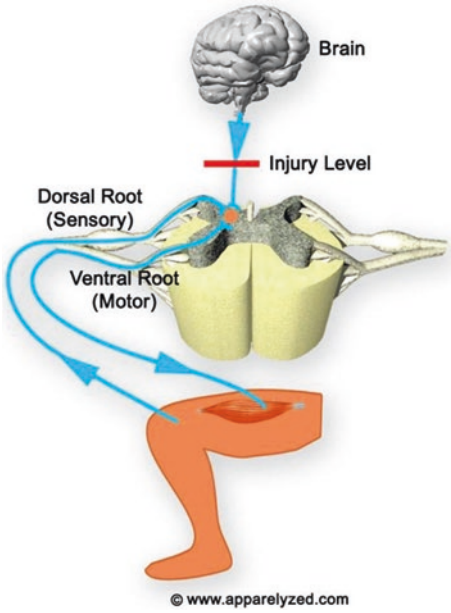

Fig. 3.1 Showing the pathways from the sensory nervous system via the reflex synapse in the spinal cord back down through the motor nervous system which invokes a reflexive spasm. Used with permission http://apparelyzed.com/spasticity.html

Dorsal rhizotomy is similar in concept to dorsal longitudinal T-myelotomy, but instead of eliminating the spasticity reflex arc within the spinal cord, this procedure divides the sensory nerve roots before they join the spinal cord, either intradurally or extradurally. The Dorsal Root Entry Zone (DREZ) variation of this procedure is supported by level 2 evidence to reduce post-SCI pain, especially when the pain is neuropathic and in a segmental (nerve root) distribution, rather than diffuse. See Fig. 3.1.

Conclusion

Patients with spinal cord injury will frequently present with multiple pain generators. Each spinal cord injury is unique and treatment plans must be individualized. Asking patients to describe pain above the level, at the level of injury, and below the level of injury is a useful first step to categorizing neuropathic pain generators. It is easy to become focused on neuropathic pain in this population, but nociceptive pain, common in patients with spinal cord injury, must also be addressed. Some musculoskeletal injuries are more common after SCI due to the daily use of their upper extremities for transfers and mobility. Providers must consider heterotopic ossification, autonomic dysreflexia, and CRPS in this population. They must also understand that patients with SCI may have very atypical presentations of pathology below the level of injury. The treatment of pain in this population requires a systematic approach

to identify each component of the pain including the musculoskeletal, neuropathic, and visceral pain. In most cases, a multifaceted approach to pain management will be more successful than a single therapy or intervention.

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Chapter 4
Pain in the Traumatic Brain Injury Rehabilitation Patient

Benjamin Seidel and Mitchell Freedman

Introduction

Traumatic brain injury (TBI) is a very common source of injury that is thought to affect 1.7 million people in the United States annually, with 3.2 million living with disability related to their TBI [1]. TBI is operationally defined as "an alteration of brain function, or other evidence of brain pathology, caused by an external force" [2]. Pain after TBI is often multifactorial, with both nociceptive and neuropathic qualities encompassing several domains, which include post-traumatic headache (PTHA), musculoskeletal trauma, and visceral pain syndromes. Headache remains the most common pain syndrome after TBI [3] and is the focus of a devoted chapter in this text (see Post-Traumatic Headache). Many of these areas overlap and are not easily remedied. Clinicians should aim to treat the source of pain, not just the symptoms.

There are many barriers to the appraisal and treatment of pain after TBI. Communication issues and cognitive deficits make evaluation of pain difficult in the rehabilitation setting, and clinicians should maintain a high index of suspicion for common causes of pain. It is imperative to take a multidisciplinary approach to both the evaluation and treatment of pain after TBI, and to incorporate a holistic and comprehensive paradigm to patient care. Clinicians may need to rely on alternative methods to explore pain after TBI such as using vital signs, caregiver attestation, or observing body language and subtle cuing to reliably diagnose such problems [4].

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Pathophysiology

Pain after TBI may arise from central and peripheral sources [5]. It is useful to distinguish intra-cranial sources of pain, such as intra-parenchymal hemorrhage and subdural hematoma from extra-cranial sources, such as fracture, visceral injury, and brachial plexopathy. Most literature supports the notion that less severe TBI results in more pain than more severe TBI, particularly in the case of post-traumatic headache [6]. Although it is unknown why this occurs, it may be related to a higher propensity for central sensitization in milder injuries, and critical disruption or malfunction of pain pathways in more severe injuries. Pain remains a real phenomenon in all types of TBI. A thorough discussion of the neuroanatomy and neurophysiology related to the appraisal of pain in humans is beyond the scope of this chapter. Please see the recommended reading list at the end of the discussion.

Many of the important structures related to the generation of pain centrally include the dorsal horn of the spinal cord, several of the ascending and descending spinal tracts, numerous brain stem structures, the diencephalon (thalamus), and many of the paralimbic, limbic, and cortical structures of the cerebral cortex [5]. Any aberrancy, disruption, or damage to these structures may result in modification of a person's appraisal of pain. It is important to note that there are very intricate interconnections between many of the cortical and subcortical structures involved in pain generation. Thereby, damage to one structure may modify output in another, which in turn may turn "up" or "down" a patient's estimate of their pain.

The major pathophysiologic distinction in TBI is between primary injury and secondary injury. Primary injury to the brain is that which causes direct disruption of the brain parenchyma from shear forces of impact. This occurs immediately and is generally not amenable to medical intervention. Secondary injury is the cascade of biochemical, cellular, and molecular events, which occurs as a result of the trauma [7]. Most research is focused on preventing or reducing secondary injury. Both primary and secondary injuries may lead to anatomic disruption of pain pathways, resulting in pain from injury.

Diffuse axonal injury, a type of primary injury, is of particular importance as it results from the immediate disruption of axons due to acceleration–deceleration and rotational forces, which cause shearing. This type of injury is important because the most common areas involved include the corpus callosum, central white matter (basal ganglia), and the midbrain, which house many of the important pain pathways in the central nervous system. Although it is conjecture, it is thought that pain may be amplified (in more mild injuries) or dampened (in more severe injuries) in this brain region.

Although the mechanism is not well elucidated, pain and sleep also appear to be very closely correlated. Alterations of the sleep-wake cycle are strongly correlated with exacerbation of pain and headache in patients that incur a mild traumatic brain injury [8]. Delayed or "post-secondary" sources of intracranial pain generation include obstructive or nonobstructive hydrocephalus, post-traumatic syringomyelia, and hemorrhagic conversion of the brain.

There are many extracranial neurologic and orthopedic injuries that can occur after TBI. Brachial plexopathy has been reported to affect slightly greater than 1% of the population after multi-traumatic injury [9], and up to 50% of patients with spinal cord injury have a concomitant traumatic brain injury [10]. In addition, orthopedic injuries (fracture, muscle tears, tendon ruptures, etc.), visceral injuries (such as liver laceration, splenic rupture) are common in polytrauma.

Chronic regional pain syndrome may occur following TBI either from peripheral nerve injury, which would result in CRPS type II, previously referred to as "causalgia," or orthopedic injuries, which would result in CRPS type I. Iatrogenic nerve transection is rare, and surgery may be the only way to restore neurologic function in some cases. Most nerve injuries are due to trauma; one study indicates that the incidence of peripheral nerve injury after TBI was as high as 34% [11]. Good prognostication with imaging/nerve conduction is paramount in determining surgical candidacy. Other complications of nerve injury may result from lack of sensation, which include falls, burns (from temperature insensitivity), and others.

Heterotopic ossification (HO) is another potential source of pain in the brain-injured patient. Among brain-injured patients, risk factors for HO include prolonged immobilization, fracture, prolonged coma, and spasticity. Autonomic factors may also play a role [11]. There is a predilection for proximal large joints of the upper and lower limbs, but HO can occur in distal joints, albeit less frequently. This is in contrast to other conditions such as SCI or burns, where joint predilection differs.

Chronically, there is a high incidence of pain after TBI. Brown et al. found that 15 years or more after injury, 79% of their patients with moderate to severe brain injury had musculoskeletal pain complaints in the 30 days preceding their interview [12]. Weakened musculoskeletal structures, neuromuscular imbalances, spasticity, poor balance, and heterotopic ossification are potential contributing factors that can cause painful chronic musculoskeletal conditions. Colantonio et al. found a higher than expected prevalence of arthritis in middle-aged patients up to 24 years after their TBI [13], and higher preponderance of chronic painful musculoskeletal conditions have been reproduced in additional longitudinal studies [14–16]. Recognition of musculoskeletal imbalance and injuries in the acute period following TBI is important to minimize long-term consequences.

Symptoms

TBI patients present with a vast array of signs and symptoms, depending on the pain generator. It is imperative to rely heavily on history and physical examination to establish a diagnosis. Patients with mild TBI may be able to express their symptoms "normally" with verbal communication, but severely injured patients may not be able to provide a medical history or describe the location, severity, or quality of their pain symptoms. Concomitant injuries from trauma often go unnoticed because of these cognitive limitations, but also because the initial focus in the acute care setting is stabilization and survival. Since patients may not be able to communicate

verbally, the clinician may need to rely on previous medical documentation, family input, caregiver observations, and physical examination, without direct input from the patient to find potential sources of pain. Patients may exhibit decreased eye contact, more frequent grimacing, or may display changes in their vital signs such as hypertension and/or tachycardia. Input from caregivers should not be overlooked, as they can be helpful in detecting subtle changes in a patient's behavior. Oftentimes, caregivers spend much more time with the patient than the physician or nurse, who may change shifts or rotate floors. A low threshold for radiographic, ultrasonographic, laboratory, or other investigations should be adopted to assess such changes in behavior.

It is frequently difficult to establish whether or not a treatment strategy has been successful. Observing for subtle changes in behavior, improvement of function during therapy sessions, family/caregiver attestation, and/or improvement in vital signs or physical exam findings are necessary to assess response to treatment. Examples include improved eye contact, decreased restlessness, or decreased resting heart rate. As cognition and communication improve, there may be improved localization and understanding of a particular pain generator and new treatment options may then ensue.

Neuropathic pain may be experienced as burning, electric, achey, or gnawing. The patient with a neurogenic source of pain may demonstrate hyperalgesia, allodynia, temperature, and vasomotor changes. Symptoms of compartment syndrome may include pain described as burning, deep, and achey, which generally worsen with passive stretching of the muscles in the compartment. Symptoms may appear disproportionate to the injury, and the patient may grimace or shout with provocative maneuvers. This must be distinguished from spasticity. Understanding tonal patterns of muscle groups in the limbs are helpful in differentiating the two. Spasticity is a common source of pain. Stretching or ranging involved body segments often provokes pain in a patient with spasticity. For those able to communicate their pain, visceral pain is often described as "vague," gnawing, deep, and generally poorly localized [17]. Visceral afferents travel back to the spinal cord along the same course used by sympathetic efferent nerves. Lower abdominal pain associated with constipation is very common seen in all stages of recovery from TBI.

Functional Limitations

TBI patients have impairments that affect their physical, cognitive, vocational, and avocational abilities. In severe injuries, patients often rely entirely on others to assist with their function. This can portend significant difficulty in the appraisal and treatment of pain in this population. Patients may not have the capacity to self-medicate and count on others to interpret their comfort level, administer medications, and/or perform a therapeutic intervention as simple as repositioning. Family and/or caregivers can misinterpret a patient's external signals and inappropriately medicate

(or not medicate). Furthermore, cultural influences can influence both the experience and the treatment of pain. In certain cultures, for example, outward demonstration of emotion is prohibited. In those patients that belong to such cultures, it may be hard for the family or caregiver to understand that reduced inhibition and emotional lability are a part of their loved one's neurologic injury and that expression of pain is a part of the natural course of the injury. They may be more likely to medicate the patient to prevent them from disruptive emotional outbursts. It may also be a cultural entity to "deal with pain," or to bear pain without any intervention, and so these patients may be less likely to receive medication. Being aware of such psychosocial influences are paramount to effectively treating pain in any population, but especially so in brain injury.

Treatments/Common Techniques

Initial

In the acute care setting, the focus is generally medical stabilization. Treatment of pain thereby relies heavily on prophylaxis for structural defects, which include fractures, hemorrhages, and contusions. Analgesia is frequently maintained with the use of intravenous, enteric, or topical medication; analgesia is important to facilitate sedation, while fractures are repaired, intracranial pressures are monitored, and the patient is stabilized.

Rehabilitation

In the rehabilitation setting, focus shifts to improving functional outcome. The rehabilitation phase of pain control requires the TBI patient's participation in self-care activities. Gentle range of motion, heating, ice, and/or physical modalities benefit the patient by maintaining range and preventing contracture, as well as for pain management, and should always be used in conjunction with pharmacologic agents. Physical modalities are often overlooked, but can be extremely helpful in pain after TBI. Adaptive equipment, therapeutic exercise, and modalities, which include application of heat, ice, and/or ultrasound are all options. These treatments are best employed within a coordinated, multidisciplinary approach using trained therapists. Complementary therapies such as energy medicine (Reiki, Tai-Chi), acupuncture, osteopathic manipulative medicine, and other manual techniques may also be helpful in managing more chronic pain issues. Mobilization and/or manipulation techniques, when used with exercise, are beneficial for treatment of persistent mechanical neck disorders with or without headache [18]. Treatment of HO includes therapy targeted at maintaining adequate range of motion.

Pain Management

Traditional treatment approaches for pain in the non-brain-injured population include using a variety of cognitive therapies, including cognitive behavior therapy (CBT) and mindfulness techniques. These cognitive therapies have proven effective for managing chronic pain in the general population [19]. Severely brain-injured patients may be unable to participate in cognitive strategies to cope with pain due to limitations in cognitive function, arousal, and/or emotional lability. Therapies to alleviate pain must therefore rely on physical modalities, exercise strategies, pharmacologic management, and interventional strategies.

Common drug classes used to treat various types of pain in the TBI population include non-steroidal anti-inflammatory agents (NSAIDs), muscle relaxants, antispasmodics (distinct from muscle relaxants), anti-depressants, opioids, and membrane stabilizers. Clinicians should be well informed of potential adverse effects of medications to avoid complications. The clinician must weigh potential medication side effects with the cognitive and functional limitations imposed by pain. Ideally, the choice of agent should minimize side effects and maximize pain reduction.

Pharmacologic agents commonly prescribed to those with chronic pain have sedative, hypnotic, psychotropic, and/or cognitive side effects, which can exacerbate the cognitive dysfunction already present in patients with TBI. [20] Additionally, pain itself has been demonstrated to depress several aspects of cognition, which include executive function and attention; in brain-injured patients, this can equate to a major impact on function. [21] Prophylactic analgesia is considered an acceptable practice in severely compromised patients, [5] especially in the setting of orthopedic injuries, open fractures, and central nervous system injury.

Opioid analgesia warrants special attention, as this drug class is currently controversial in the treatment of pain, especially in the setting of brain injury. Statistically, patients who incur TBI are male, young, and more than 50% have alcohol in their system at the inciting event. Therefore, TBI survivors may be at increased risk for substance abuse. Nevertheless, opioids can be extremely beneficial acutely, and are indicated when there is a concern for significant pain (e.g., postoperatively). The clinician needs to weigh the benefits of reduced pain with the potential risk of cognitive impairment. These impairments include, but are not limited to impaired concentration, memory, processing, and decreased psychomotor and reaction time. The long-term cognitive effects and overall efficacy of chronic opioid usage is not known. A 2010 review of the cognitive effects of chronic opioid use for chronic non-cancer pain in patients without head injury concluded that there was limited evidence of cognitive impairments. [22] Side effects include constipation, nausea/vomiting, and immunologic or hormonal influences. Tramadol, a mild opioid analgesic, has several mechanisms of action, including binding with serotonin and dopamine receptors. If used concomitantly with additional serotonergic medications (SNRIs, SSRIs, etc.), there is a risk of serotonin syndrome and a higher risk of seizures than with the medication alone.

Caregivers should be involved in the decision making and evaluation process. Medications that are given less frequently may be easier to administer and may result in greater compliance. The clinician should make every attempt to ascertain the source of pain, in order to identify and to reverse the problem as rapidly as possible.

Post-traumatic migraine and post-traumatic tension headache types generally follow similar treatment strategies when compared with their non-traumatic counterparts in non-brain-injured populations [23], and are better discussed in the devoted chapter on PTHA. Cervicogenic headaches are caused by pain generators in the C2–3 and C3–4 zygapophyseal joints (Z-joint), atlanto-occipital joint, atlanto-axial joint, or the C2–3 intervertebral disc. In cases refractory to therapy and medication, a double anesthetic block of the medial branch of the dorsal ramus is utilized to identify the pain generator with the goal of percutaneous radiofrequency ablation. Corticosteroid injection into the Z-joint is less commonly utilized [24].

Treatment of pain after extracranial neurologic injuries such as spinal cord injury, peripheral nerve injury, and/or plexopathies are more comprehensively covered in additional chapters of this text, but may cause significant neuropathic pain in patients with TBI. Treating neuropathic pain is challenging, but using a combination of membrane stabilizers, calcium channel blockers, and/or anti-depressants can be helpful in symptom reduction.

Treatment of pain from spasticity takes a pyramidal approach. Please refer to dedicated chapter in this text. Treatment of iatrogenic sources of pain consists of removal of the irritant and symptom management. Catheters, tubes, and lines are generally removed after sufficient medical recovery has occurred. Patients should be protected from grabbing or pulling on lines and tubes to prevent self-injury. Severe cognitive dysfunction predisposes patients to injure themselves.

For multiple orthopedic injuries, systemic agents are preferred. NSAIDs are generally avoided in the context of bone fracture, although this is still an area of controversy. In two review articles from 2012 and 2013, recommendations were that “clinicians should treat NSAIDs as a risk factor for bone healing impairment, and their administration should be avoided in high-risk patients” [25, 26]. Furthermore, NSAIDs increase risk of gastrointestinal bleeding and may also have cognitive effects.

For treatment of HO, NSAIDs such as indomethacin, and bisphosphonates such as Pamidronate may be utilized in a stable patient. Theoretically, these drugs prevent further bony deposition. Definitive surgical removal is reserved for functional deficits and requires bony “maturation,” which may not occur for 1 year or more after diagnosis.

Therapy for visceral injury includes medical and surgical treatments to stabilize organ damage or dysfunction. Treatment of constipation includes carefully monitoring of bowel movements, gradual reduction of opioids, ensuring adequate hydration and physical activity, and regular use of stool softeners/stimulants/osmotic agents. Better control of pain may also serve to reduce constipation.

Procedures

Orthopedically, joint aspirations with or without injections with local anesthetic and/or corticosteroids may be of benefit once the patient is medically stable. In the chronic setting, regenerative medical strategies such as platelet-rich plasma and tenotomy under ultrasound can be used to treat tendonopathies.

To help control local spasticity, there are several options. Botulinum toxin, often under ultrasound or electromyographic guidance, is injected into the motor points of specific muscles to reduce excessive tone in those muscles. Botulinum toxin injections generally retain therapeutic reduction in tone for 3 months or more. Botulinum toxin may be combined with chemical denervation using alcohol or phenol for a more permanent solution in the motor distribution of the nerve. EMG stimulation or ultrasound is used for guidance in such cases, and the results are immediate. Diagnostic blocks with lidocaine or other anesthetics are commonly used to evaluate the potential efficacy of a chemical denervation with alcohol or phenol.

Trigger point injections are commonly used in patients with post-concussive syndrome and cervicogenic headaches. Particular attention to the neck and shoulders is helpful in alleviating neck, shoulder, and headache pain. Myofascial trigger points may also be discovered in areas beyond the head and neck, and would be handled in a similar fashion. Transcutaneous electrical nerve stimulation is sometimes to assist in discovering a sensitive area, but palpation is the most common method for localization. Dry needling, prolotherapy, acupuncture, and acupressure are also utilized for myofascial pain and tight painful muscles.

Surgeries

In terms of musculoskeletal injuries, collaboration with orthopedic colleagues is required to assess weight bearing status, bone or joint stability, and the need for operative intervention. Pain management is performed in concert with orthopedic stabilization. In the case of spasticity, tendon lengthening, tendon transfer, and tendon resection may be required to achieve adequate functional outcomes. When spasticity is severe and diffuse, particularly in the lower limbs, and after an adequate trial of medication, a catheter may be inserted into the intrathecal space, which is connected to an implanted medication reservoir and battery to deliver baclofen into the cerebrospinal fluid in much lower concentrations than oral doses.

Potential Treatment Complications

Every medication which is ordered must be carefully reviewed for ongoing indication and potential complications throughout the course of treatment. Side effects from medication are common and may have a negative impact on cognition and

neural recovery, and may also have the potential for organ toxicity. Furthermore, interactions between pain medications and important stabilizing medications (e.g., anti-epileptics) must also be taken into account. For example, medications such as tramadol or baclofen can increase seizure risk in susceptible patients.

Interventionally, any injection that breaks the skin may cause infection, bleeding, or local irritation [27]. Botulinum toxin injection complications are rare, but are worth mentioning. In addition to the standard injection risks, botulinum toxin used for spasticity can inadvertently be disseminated systemically via intravascular injection, causing weakness in areas outside of the injection sites. Of particular concern are difficulties with swallowing, speaking, breathing, or keeping the neck upright [28]. Excessive weakening is a serious concern for patients, and titration of dosage should occur with each subsequent injection. Phenol and other "permanent" nerve blocks can cause severe dysesthesias, even when injected properly [29]. Theoretically, inadvertent intravascular injection can cause arrhythmias or toxicity in areas outside of the injection site. More invasive surgical interventions carry additional risks, which include infection, technical or procedural complications, and greater opioid requirements.

Evidence

Pharmacologic and non-pharmacologic outcomes in extra-cranial sources of pain in brain injury are primarily founded in non-brain-injured cohorts and extrapolated to patients with TBI [30]. Intra-cranial pain disorders (i.e., PTHA) have been researched extensively and are summarized in the headache chapter of this text. Dobscha et al. could find little evidence to help guide the clinician in pharmacologic and non-pharmacologic interventions in pain, specifically after TBI. In a systematic review of the current evidence for treatment of pain after TBI, Dobscha et al. concluded that "very little evidence is currently available to guide pain assessment and treatment approaches in patients with polytrauma" [including TBI] [31].

In terms of interventions, botulinum toxin injection has been demonstrated in numerous studies to reduce tone in patients with central nervous system disorders (including TBI) [32, 33], and to reduce pain associated with spasticity [34]. Intrathecal baclofen pump management of spasticity has also demonstrated efficacy in pain reduction associated with spasticity, mostly in the non-TBI population [35]. Myofascial pain management strategies using trigger point injections and manual medicine have been corroborated in mild TBI (concussion), but not in more severely injured patients [36, 37].

Conclusion

Patients who incur a TBI are at a particularly high risk of developing pain for a variety of different reasons. These painful sequelae from primary and/or secondary brain injury can have a lasting impact. Pain after TBI is multifactorial and can stem

from intrinsic cortical and subcortical damage, calvarial defects, or concomitant orthopedic, visceral injuries, which can lead to a combination of nociceptive and neuropathic pain states. Problems with communication and cognitive deficits complicate the work-up of pain in this population, forcing clinicians to think creatively. Evaluation and management requires a comprehensive interdisciplinary approach in both the acute and rehabilitation settings.

Treatment of pain after TBI begins in the acute care setting and continues into both the rehabilitation and community settings. Initially, maintaining adequate cerebral blood flow, keeping intracranial pressures under control, and minimizing brain damage is paramount to prevent painful sequelae such as secondary neurologic injury, spasticity, and contractures. Medical complications, such as heterotopic ossification, are difficult to predict, but earlier diagnosis and treatment improves outcomes. No matter the etiology, treatment of pain should begin with reversal of the cause. Subsequently, symptom management should ensue, which includes noninvasive methods such as positioning, modalities, range of motion, and strengthening. Medication prescription is frequently warranted, but must be monitored carefully for potential complications. Injections, intrathecal pain management, and more invasive techniques such as surgical tendon lengthening, resections, etc. should be reserved only after more conservative treatments have been unsuccessful.

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Chapter 5
Pain in the Stroke Rehabilitation Patient

Anjum Sayyad

Central Post-Stroke Pain

Introduction

Central post-stroke pain (CPSP), also known as thalamic pain syndrome, is a chronic pain condition that occurs following an ischemic or hemorrhagic stroke. Pain is associated with abnormal sensation of pain and temperature. Wallenberg first described CPSP in 1895, as a symptom of lateral medullary stroke syndrome, which is also known as Wallenberg syndrome. Dejerine and Roussy then described this condition as a lesion of the thalamus in 1906s. Cassinari and Pagni expanded the definition to included lesions along the spinothalamic pathways in 1969.

Approximately 8% of stroke patients are afflicted with CPSP, with increased risk given to increased age [1].

Pathophysiology

CPSP can occur in weeks to months after the stroke and falls under the category of neuropathic pain [2]. One hypothesized mechanism includes the result of hyper-irritable surviving cells along the spinothalamic and thalamocortical pathways [3].

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Symptoms

Onset of pain can be immediate in 20% of patients with CPSP, 50% within 1 month of acute stroke, and the remaining 30% after 1 month of acute stroke [4]. CPSP can be constant or intermittent. CPSP is associated with the following: mild hemiparesis; hemisensory deficit; hyperpathia, which is pain out of proportion to a mildy noxious stimuli; allodynia, which is perception of pain to non-noxious stimuli; hemiataxia; astereognosis, which is reduced object recognition; movement disorder, which lasts for hours on one side of the body [2]. Pain is described as burning, cold, stabbing, sharp, aching, pricking, squeezing, shooting, tingling, or heavy; it is often triggered by light touch or change in temperature [2].

Functional Limitations

Severe pain associated with CPSP can impact the performance of activities of daily living (ADLs), thereby impacting the quality of life.

Treatment/Common Techniques

Initial

First-line treatment involves oral pain medicines, which include amitriptyline, lamotrigine, and gabapentin. These medications often only provide limited relief. Other second-line medications include nortriptyline, desipramine, imipramine, doxepin, venlafaxine, maprotiline, pregabalin, carbamazepine, mexiletine, fluvoxamine, and phenytoin.

Rehabilitation

The patient should be offered supportive counseling and education on this condition. Neuropsychological strategies can be used to modulate pain perception with the use of biofeedback, self-hypnosis, and relaxation techniques. Positioning and use of resting splints are important in the prevention of contracture formation. Transcutaneous nerve stimulation (TENS) at high (70–100 Hz) and low (1–4 Hz) frequencies can be used for pain relief on either ipsilateral or contralateral sides [5].

Procedures

Acupuncture can be used though little evidence currently supports its use.

Surgery

Deep brain stimulation has been used in few recalcitrant cases of CPSP [2]. Neurosurgical ablative strategies of medial thalamotomy and mesencephalic tractomy have been used in recalcitrant CPSP associated with allodynia and hyperpathia [6]. For further reference, please see chapter on neurosurgical procedures for pain.

Potential Treatment Complications

Avoid the use of TENS in individuals with a cardiac pacemaker or defibrillator. Neurosurgical ablative interventions are often complicated by morbidity and mortality, which include onset of dysesthesias, hemiparesis, cognitive impairment, or death.

Evidence

Few treatment strategies are available to target sensory deficits associated with CPSP.

Conclusion

CPSP is a relatively common chronic pain condition that develops after stroke, which can impact the quality of life of patients. There are few treatment strategies that are evidence based, but could nevertheless potentially abbreviate symptoms if recognized early.

Post-Stroke Shoulder Pain (PSSP)

Introduction

There are many possible causes of post-stroke shoulder pain (PSSP), which include shoulder subluxation, adhesive capsulitis, impingement syndrome, complex regional pain syndrome (CRPS), brachial plexus/peripheral nerve injury, or spasticity. PSSP pain is reported in 62% of stroke survivors [7].

Pathophysiology

Risk factors associated with PSSP include motor weakness, sensory deficits, range-of-motion deficits, spasticity, and other comorbidities such as diabetes mellitus.

Shoulder subluxation is the result of excessive movement, without complete dislocation, through the glenohumeral joint. However, the presence of subluxation does not always lead to pain. The most common direction of subluxation is inferior and can be seen in up to 50% of patients following stroke [8]. Shoulder subluxation is the result of weakness of the rotator cuff muscles, which is secondary to hemiparesis.

Adhesive capsulitis, also known as frozen shoulder, is an inflammatory condition that causes fibrosis of the joint capsule that surrounds the glenohumeral joint.

Impingement syndrome is pain associated with compression of the supraspinatus muscle and/or subacromial bursa between the greater tuberosity of the humeral head and the acromion, due to hyperdynamic instability of the glenohumeral joint of the shoulder. Impingement syndrome can lead to more significant rotator cuff injury.

Complex regional pain syndrome (CRPS) following stroke falls under the category of type 1, which has previously been referred to as reflex sympathetic dystrophy (RSD) or shoulder-hand syndrome [2]. It is related to impaired regulation of the autonomic nervous system though this has yet to be proven [2]. This is reported in 12–25% of hemiparetic post-stroke patients [9].

Brachial plexus or peripheral nerve injury occurs as the result of excessive traction to the shoulder on the hemiparetic side.

Symptoms

Shoulder subluxation presents with inferior location of the humeral head relative to the acromion and can sometimes be associated with pain.

Adhesive capsulitis presents with pain associated with both passive and active range of motion, in particular with external range of motion and abduction relative to the glenohumeral joint.

Overhead activities associated with frequent shoulder abduction can cause impingement pain. Bicipital tendonitis is often involved with shoulder impingement.

CRPS is associated with edema, temperature changes, loss of range of motion, and pain with vasomotor changes [2]. Loss of range can occur over several joints, including the fingers, wrist, and shoulder, while sparing the elbow.

Functional Limitations

PSSP can impact functional use of the affected limb, but may not necessarily impact quality of life, which may be secondary to learned use of compensatory strategies by affected patients.

Both shoulder subluxation and adhesive capsulitis lead to reduced range of motion, which can impact the performance of activities of daily living.

Treatment/Common Techniques

Initial

Positioning is important for shoulder subluxation as well as in prevention of brachial plexus/peripheral nerve injury causing PSSP. While seated in a wheelchair, arm boards or arm trays should be used. Velcro can be used to secure the arm, which is prone to falling off due to poor motor control of the patient. While ambulating, arms slings can be used. Slings should be removed once in bed to prevent contracture formation. Shoulder taping, which is performed by a therapist can help to reduce shoulder subluxation. Oral medications can be initiated for pain management, such as acetaminophen or nonsteroidal anti-inflammatory drugs (e.g., ibuprofen). Oral steroids and range of motion are the initial strategies in the treatment of CRPS. Topical analgesics such as capsaicin cream or diclofenac gel may also be helpful.

Rehabilitation

Range of motion and strengthening exercises of the rotator cuff and scapular stabilizing muscles, under the guidance of a therapist, are important to address in conditions of shoulder subluxation and adhesive capsulitis. Functional electrical stimulation, directed towards the supraspinatus and posterior deltoid muscles, can be helpful in cases of pain associated with shoulder subluxation [10]. Therapeutic ultrasound can be helpful in the treatment of subacromial bursitis that contributes to shoulder impingement. Passive range of motion, massage, contrast baths, ultrasound, and desensitization strategies with active incorporation of the uninvolved side can be helpful in the treatment of CRPS [11]. Compression gloves are helpful in further controlling edema of the affected hand in CRPS.

Procedures

Acupuncture may be an option for pain management. Subacromial steroid injections can be helpful in cases of pain associated with shoulder subluxation or shoulder impingement. Glenohumeral steroid injections can be helpful in adhesive capsulitis. Cervical sympathetic stellate ganglion blocks and Bier blocks can be used in the treatment of CRPS, if oral medications fail [7]. Stellate ganglion blocks are particularly helpful in patients who have developed an ipsilateral Horner syndrome.

Surgery

Cervical sympathectomy may be an option for recalcitrant CRPS that does not respond to oral medications or the above-mentioned interventions. Surgical repair is an option for the treatment of rotator cuff tear.

Potential Treatment Complications

Excessive use of acetaminophen can cause liver damage in doses greater than 3000 mg per day. Chronic NSAID use can cause renal or gastrointestinal complications. Use of heating modalities in CRPS may contribute to worsening edema.

Evidence

FES has not been shown to be effective in the treatment of shoulder impingement. In general, the pathogenesis of PSSP has not been studied well and remains controversial.

Conclusion

PSSP is a common painful condition seen in stroke, with a prevalence of 12% at 18–30 months post stroke [12].

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Chapter 6
Pain in the Spasticity Rehabilitation Patient

Anjum Sayyad

Introduction

Spasticity is an unmasked reflex that occurs when there is a lesion in the central nervous system (CNS), a type of upper motor neuron (UMN) sign, first described by nineteenth century neurologist Hughlings Jackson [1]. Clinicians identify it as a velocity dependent increase in muscle tone when a particular muscle is stretched through its full range of motion. It can also be described as "muscle over activity." Injuries to the CNS that can lead to spasticity include stroke, brain injury, spinal cord injury (SCI), multiple sclerosis (MS), and cerebral palsy. Prevalence varies from each condition: 28–38% in stroke patients, 60–80% in SCI patients, 41–66% in MS patients, and 13% in traumatic brain injury patients [2].

Pathophysiology

Spasticity is mediated through monosynaptic and polysynaptic spinal reflexes that are unmasked after injury to the CNS. There is reduced cortical inhibition of UMN spinal reflexes, which leads to a decreased threshold for reflex firing, and subsequent emergence of spasticity [3]. Spasticity emerges in SCI patients after spinal shock resolves.

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Symptoms

There are characteristic spasticity patterns that can emerge in the upper and lower extremities. Upper extremities often will present with a flexor synergy pattern of finger flexion, wrist flexion, forearm supination or pronation, elbow flexion, and shoulder internal rotation [4]. The lower extremities often will present with an extensor synergy pattern of plantar flexion, toe flexion, knee extension, and hip extension [4]. Spasticity may also present with abnormal posturing of the trunk. Spasticity can often be made worse when the body perceives a noxious stimulus, such as bladder retention, urinary tract infection, pressure sore, ingrown toenail, constipation, occult fracture, excessively tight clothing, pulmonary embolus, or any other illness (e.g., syringomyelia).

Functional Limitations

Not all spasticity needs to be treated, and some spasticity may create a functional advantage that helps with gait mechanics, bed mobility, transfers, and general maintenance of muscle bulk. In other instances, spasticity is often associated with pain and discomfort when affected limbs are moved or stretched against the increased tone.

Many functional limitations can occur with both upper and lower extremity spasticity. Upper extremity spasticity can lead to an impaired ability to perform self-care, hygiene, grooming, feeding, and dressing. Lower extremity spasticity can impact gait, thereby increasing risk of falls and/or inability to tolerate braces.

Skin breakdown can occur in areas with joint tightness, which can limit the ability to maintain hygiene, such as cleaning the hands, genitals, or axilla. Skin breakdown can also occur with abnormal pressures across exposed joints.

Spasticity can also affect impact bladder and bowel management, as well as sexual activity.

Poor posture due to increased spasticity through the trunk can affect transfers, bed mobility, sleep, hygiene, and positioning while in the seated or supine position.

Spasticity, when sustained for an extended period of time, can lead to muscle and tendon shortening, ultimately leading to a functional state of contracture formation.

Treatment/Common Techniques

Initial

It is important to rule out other organic causes that may be exacerbating and contributing to spasticity, such as a urinary tract infection, constipation, and bladder retention. Although some clinicians opt to initiate treatment of spasticity with oral

medications, localized injection therapy with botulinum toxin is considered an appropriate first-line treatment. Oral medications include baclofen, dantrolene, diazepam, clonidine, and tizanidine. Tizanidine may have the dual ability to treat both spasticity and pain.

Rehabilitation

Physical and occupational therapy, that incorporates stretching, offers an important adjunct to both oral and injectable medication. Both can help to maintain range of motion and to determine appropriate splinting strategies for the upper and lower extremity. More than 40% of SCI-associated spasticity responds to stretching and should be performed twice daily. Stretching helps to maintain numbers of sarcomeres, reduces buildup of connective tissue, and thereby maintains muscle bulk and length [5]. Serial casting is an option for allowing sustained stretch across a muscle longer than could be offered with splinting alone [2]. Strengthening exercises can help to reduce spasticity by improving both strength and motor control.

For postural management, use of a standing frame can be helpful in allowing patients to remain in an upright position, which allows full weight bearing across extended hips, extended knee, and dorsiflexed ankles. Electrical stimulation may be used to reduce spasticity although its benefits tend to be temporary [6].

Procedures

Injection therapy is an effective way of treating localized spasticity. Phenol injections cause tissue destruction or nerve lysis, thereby reducing spasticity. Onset of action for phenol is within minutes and can last up to 6–9 months. Botulinum toxin injections prevent pre-synaptic release of acetylcholine at the neuromuscular junction, leading to temporary denervation, thereby reducing muscle contraction that contributes to spasticity. Onset of action for botulinum toxin is within 5–10 days and lasts up to 3 months.

Surgery

When spasticity is not adequately addressed in dosages that are safe with injectable or oral therapy, the spastic patient can be considered for intrathecal therapy (ITT) baclofen treatment. Intrathecal administration of baclofen is 100 times more effective than the oral dose, and therefore can be administered in microgram versus milligram amounts [7]. This reduces the risk of cognitive side effects, while allowing for easier dose titration. This does require the expertise of an interventionist or surgeon for placement of a catheter in the intrathecal space after a successful

intrathecal bolus or continuous trial, which is then connected to a pump. The pump is generally placed in the lateral lower quadrant of abdomen subcutaneously; a short inpatient hospital stay may be required.

Following implant, pumps require refill at least every 6 months depending on the dose and concentration of baclofen, which can be performed in an outpatient clinic setting. Pump batteries typically last 7 years, and require further surgical intervention for replacement. For further reference, please see chapter on intrathecal therapy (ITT).

Surgical release of contractures (tendon transfers and/or tendon/muscle-lengthening procedures) can also be considered in cases where hygiene or skin breakdown is an issue. One type of surgery is SPLATT (split anterior tendon transfer), which can help to treat a plantar flexed, inverted foot [8].

General principles for surgical release are as follows: consider surgery sooner than later, before deformities are fixed and severe; consider surgery if it can improve motor control of affected limbs; consider surgery if it reduces care giving burden or reduces the risk of skin breakdown.

Other types of surgeries performed to treat spasticity include cordectomies or myelotomies; however, these are less frequently performed mainly due to limited long-term success demonstrated [9].

Potential Treatment Complications

Oral antispasmodic medications carry sedation as a major side effect. This side effect may impact a patient's adherence to the use of these agents. Clonidine and tizanidine can cause hypotension by virtue of their alpha-2 blocking pharmacology. Dantrolene has a high risk for hepatotoxicity; it requires periodic monitoring of liver function.

Splinting or casting can cause pressure sores and should be monitored carefully by therapists and doctors.

Life-threatening complications have been noted in the literature, which include overdose or withdrawal associated with baclofen use, in either oral or intrathecal forms. Pump failures have been seen with battery failure, lack of refill, pump dislodgement/migration, or catheter block (kinking) [2]. Common adverse reactions to intrathecal baclofen include headaches, cerebrospinal fluid leak, drowsiness, vomiting, and hypotension. Patients must be screened carefully on an individual and psycho-social/family support level, to be able to follow through on appointments for regular pump refills. Additionally, patients should be screened for realistic expectations of therapy, before consideration of an ITT trial [2]. Acute baclofen withdrawal presents as high fever, confusion with hallucinations, worsening spasticity with rigidity, pruritus, seizures, or death [11]. Acute baclofen overdose include drowsiness, respiratory depression, or coma [2].

Potential adverse reactions of botulinum toxin injection therapy although reversible after 3 months, include excessive weakness, respiratory tract infections, dysphagia, fever, pain, or falls [12]. In rare cases, larger volume dilutions of botulinum

toxin therapy have been shown to spread to the contralateral limb, as proven on electromyographic studies [13]. Immuno-resistance to botulinum toxin has been seen, with loss of responsiveness to injection therapy [14]. This is likely related to an immunogenic response to the complex proteins found in the preparations of certain types of botulinum toxin injection formulations. Risk factors for the development of immuno-resistance include exposure to large and frequent doses of botulinum toxin; this has led to the gold standard practice of not injecting more frequently than every 3 months.

Potential adverse reactions of phenol injections include skin sloughing, infections, muscle necrosis, and/or pain. Sensory side effects of phenol may not be as relevant in SCI patients, who are insensate below the level of injury.

Evidence

In a Cochrane review of oral medications, limited efficacy was shown in improving functional status of patients with spasticity. Only tizanidine showed improvement of modified Ashworth score although it did not improve function. Benzodiazepines, such as diazepam, have been shown to have clinical efficacy in patients with MS and spinal cord injury. Evidence on the use of combination oral medications is also lacking in the literature. Limited evidence is seen in the literature about the efficacy of stretching on spasticity and contracture management although smaller studies have shown passive stretching to be helpful in reducing tone and increasing range of motion in patients with brain injury. Smaller studies have demonstrated the benefits of splinting for reducing spasticity of affected limbs, as it represents stretching over an extended period of time. Small trials have demonstrated the value of standing frames in spinal cord injury and MS patients. Meta analyses of randomized controlled trials demonstrated the value of strengthening exercises, while not worsening of spasticity in stroke patients. In the Cochrane review of modalities used for the treatment of spasticity, which include extracorporeal show wave therapy, repetitive transcranial magnetic stimulation, transcranial direct current stimulation, and electromagnetic therapy, only “low”-level evidence was found for transcranial magnetic stimulation. Randomized controlled trials have demonstrated a reduction of spasticity with botulinum toxin injection therapy, without improvement in function.

Conclusion

Treatment of spasticity requires careful evaluation of the patient from both a biomechanical and functional perspective. Treatment also requires careful evaluation of the risks and benefits of all medications and procedures, while employing a multidisciplinary team approach with therapists for an optimal outcome. Treatment strategies should be assessed at each visit and adjusted accordingly.

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Chapter 7
Pain in the Orthopedic Rehabilitation Patient

Joshua Minori, Edward Wieseltier, and Theresa Lie-Nemeth

Introduction

Despite continued advances in acute treatment options for the orthopedic patient, postoperative pain and its effects on the patient remain problematic. Inadequate pain control has been related to adverse events, such as coronary ischemia and infarction, impaired pulmonary function, paralytic ileus, decreased immune function, poor wound healing, urinary retention, venous thrombosis, unnecessary psychological distress, and anxiety [1]. Uncontrolled postoperative pain has also been shown to promote extended hospital stays, increased re-admissions, and higher total direct medical costs [2–4].

Arthritis is the most significant cause of disability in older Americans. It affects over 70 million people and accounts for as much as 120 billion dollars in costs annually [5]. In the United States, it is estimated that by 2030 the demand for both total knee arthroplasty (TKA) and total hip arthroplasty (THA) will increase by 673% and 174%, respectively [6, 7].

Pain following Total Joint Arthroplasties (TJAs)

Acute post-surgical pain (APSP) can often become intractable and may lead to chronic post-surgical pain (CPSP). If long-term pain persists for greater than 2 months after surgery, it has been shown to halt the recovery process, disrupt

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activities of daily living (ADL), affect quality of life, and result in physical debility leaving the patient dissatisfied with their surgical experience [8–10].

A recent prospective cohort study, which compared standardized pain scores from various surgical procedures performed in a large number of hospitals, found that major orthopedic surgery was highly associated with elevated pain scores. In fact, 22 of the 40 procedures with the highest pain scores were orthopedic surgical procedures of the extremities [11].

As for total joint arthroplasty (TJA), persistent pain and dissatisfaction at least 6 months following surgery can be as high as 20% for TKA and 8% THA. Wylde et al. [12] found that 44% of TKA patients and 27% of THA patients reported persistent pain of any severity 3–4 years after undergoing surgery. It should be noted that the majority reported mild and infrequent pain that was notably reduced from their preoperative state; however, 15% of TKA patients and 6% of THA patients reported severe-extreme persistent pain.

CPSP has a high likelihood of affecting patients undergoing shoulder replacement surgery as well. A study by Bjørnholdt et al. [13] defined persistent pain as pain experienced constantly or every day within the last month, at a level that interfered with daily activities. Although it was defined slightly differently, persistent pain was reported to be as high as 22% 1–2 years after primary shoulder replacement, and presumed neuropathic pain was 13%.

Psychosocial Predictive Factors/Concomitant Pain Problems

When working to achieve adequate pain control in the orthopedic rehabilitation patient, it is important to be aware of the psychosocial factors and predictors that put a patient at risk for developing CPSP. Persistent post-surgical pain and achievement of rehabilitation milestones are independently and notably associated with psychosocial factors, such as pre- and postoperative levels of anxiety and depression, maladaptive coping skills, social support systems, and pain catastrophizing (PC) [9, 14–16].

A wide variety of factors such as genetics, age, education, socioeconomic status, surgical duration and techniques, type of anesthesia, pain in other body areas, comorbidities, chronic opioid use, pre-operative pain, and acute postoperative pain have also been linked to an increased risk of developing CPSP [17, 18]. A recent systematic review and meta-analysis found that catastrophizing, pre-surgical mental health, preoperative knee pain, and pain at other sites are the strongest independent predictors of persistent pain following TKA [19].

Shift of Pain Burden from Acute Care Hospital to the Rehabilitation Hospital

Due to surgical advancements and subsequent shorter hospital courses of patients undergoing common orthopedic procedures such as total joint arthroplasties, the burden of early adequate pain management has recently begun to shift to inpatient rehabilitation hospitals, community-based health care providers, and the patients themselves [20].

Pathophysiology

Iatrogenic Post-Surgical Pain

Orthopedic surgery causes tissue injury and leads to the release of inflammatory mediators that may activate central and peripheral mechanisms of pain. This is termed "incisional pain" and is defined as acute pain resulting from nociceptive, ischemic, and inflammatory mechanisms, as well as nerve damage [21].

Arthritic Pain

A large number of orthopedic patients in the rehabilitation setting have a high prevalence of osteoarthritis. Overall, the pathophysiology of osteoarthritis pain remains poorly understood, and it is well known that radiographic severity does not always correlate with clinical severity [22]. However, studies are finding that sensitization, both peripheral and central, as well as hyperalgesia, are prominent mechanisms in osteoarthritis pain and may be why patients with osteoarthritis experience chronic postoperative pain after a seemingly successful total joint arthroplasty [23, 24].

Bone Pain

The pain receptors of the periosteum are supplied by a plexus made up of myelinated A-delta and myelinated C-fibers [25]. The firing frequency of noxious stimulation is high in these fibers. Also, the periosteum has the lowest pain threshold of the deep somatic structures, which is one of the reasons why bone injury is more painful than soft tissue injury [26].

Catastrophizing

Pain catastrophizing is defined as an exaggerated negative mental set or focus on pain, which is brought to bear during an actual or anticipated painful experience [27]. As previously mentioned, it is one of the strongest predictors of persistent postoperative pain. In addition, elevated PC following knee surgery in patients with osteoarthritis has been correlated with disability and increased pain levels for up to 6 months postoperatively [28–30].

Symptoms

In the orthopedic rehabilitation patient, pain can be the sequela of symptoms caused by the inciting injury or by the surgical treatment, such as effusions, edema, structural deformities, and skin abnormalities, which include surgical incisions, ecchymosis, tenting, or blistering. In patients who have undergone TJA, it is important to keep in mind that TKA tends to be more painful than THA.

Function

Pain can frequently contribute to symptoms affecting the patient's function and overall health, such as sleep disturbances, weakness, decreased range of motion, endurance, proprioception, and balance.

Psychological

Acute and chronic pain can also be accompanied by emotional distress and can make a patient more susceptible to psychosocial consequences, such as anxiety and depression.

Nociceptive

Nociceptive pain is characteristically described as sharp, aching, or throbbing in nature and is often well localized.

Arthritic Pain

Typically, symptoms of arthritis include the following: joint pain and tenderness that is worse in the morning and lessens with mild to moderate activity; difficulty walking; increased pain with prolonged or vigorous activity that is relieved by rest; stiffness or limited range of motion.

Functional Limitations

Due to Pain or Fear of Activity

Pain is a predominant limiting factor for participation in therapy and functional gains. A study by Holla et al. [31] found that the initial experience of knee pain due to osteoarthritis during physical activity leads to anticipation that further activity will cause more pain. As a result, patients may avoid activity.

Limited participation and function, secondary to pain or fear of movement, can lead to physical deconditioning and can hinder activities of daily living (ADLs) as well as mobility. It may also predispose a patient to various medical complications affecting multiple organ systems, such as the pulmonary and cardiovascular systems. Decreased active and passive range of motion following TKA can require manipulation under anesthesia to prevent contracture formation.

Due to Mechanical

Functional limitations may be due to mechanical factors associated with the injury and treatment, both surgical and non-surgical. These include, but are not limited to joint precautions, immobilization, weight-bearing restrictions, range of motion restrictions, and the use of assistive devices or durable medical equipment.

Treatment

Multimodal Analgesia

Each institution should try to incorporate a comprehensive multimodal analgesia approach to pain management, which takes advantage of the synergistic effects of different classes of analgesic agents and targets various regions of the pain pathways. The ultimate goal of any multimodal approach is to maximize the benefits of each medication, while decreasing the need for opioid use and reducing the

analgesic-related adverse effects of each medication [2]. Physicians and rehabilitation hospitals should have standardized pain control protocols, but customization is often required to some extent based on allergies and comorbidities. For example, elderly patients with preexisting cognitive decline or mild dementia are at a greater risk for postoperative delirium, and medications like opioids should be used with caution. Multimodal analgesia has not only led to a decline of postoperative pain, but has led to a decrease in rates of delirium and reduction of cognitive dysfunction [32, 33].

When ordering pain medications in the rehabilitation setting, it is important to consider scheduling them, particularly prior to therapy. If medications are scheduled, analgesia is better optimized, as serum levels are more stable [34].

Medications

Acetaminophen

Acetaminophen is best used for mild pain and in conjunction with opioids such as hydrocodone or oxycodone. Attention should be paid to the patient's hepatic function.

Topical Lidocaine

Lidocaine ointment and patches may provide a good potential adjunctive option, as there are no significant side effects. Unfortunately, a study by Khanna et al. [35] found that lidocaine patches did not provide additional relief as compared to control subjects.

NSAIDs and COX-2 Inhibitors

NSAIDs work by inhibiting the synthesis of prostaglandins in body tissues, by inhibiting at least two cyclooxygenase (COX) isoenzymes, COX-1 and COX-2. This may inhibit chemotaxis, alter lymphocyte activity, decrease pro-inflammatory cytokine activity, and inhibit neutrophil aggregation. These effects may contribute to anti-inflammatory activity. Since the traditional NSAIDs inhibit both COX-1 and COX-2, they can elicit more side effects, in particular adverse gastrointestinal events and bleeding.

In general, traditional NSAIDs are not frequently used following TJA because patients are also being prescribed some type of anticoagulation for the prevention of

thromboembolism, so the use of NSAIDs in the setting of deep vein thrombosis prophylaxis would potentially increase the risk of bleeding. However, COX-2 inhibitors, such as celecoxib, do not affect COX-1 at therapeutic concentrations, thereby decreasing formation of prostaglandin synthesis and lowering the adverse effects on gastric mucosa. COX-2 inhibitors may be used cautiously as part of a multimodal treatment regimen.

Topical NSAIDs

Topical NSAIDs include medications such as diclofenac sodium 1% gel and diclofenac sodium 1.5% in 45.5% dimethylsulfoxide solution. These have shown to be beneficial in the treatment of knee osteoarthritis. This is a potential option for adult patients who are at risk of systemic toxicity from oral NSAIDs [4].

Tramadol

This is a non-opioid derived synthetic opioid. It may act at least partially by binding to opioid mu receptors causing inhibition of ascending pain pathways. However, there are studies showing that there is no difference in pain control between placebo and tramadol groups [36].

Opioids

Opioids bind to mu, kappa, and delta in the CNS and peripheral tissues; they presynaptically lower the influx of calcium to reduce neurotransmitter release in sensory C fibers and post-synaptically increase the transport of potassium in the cell to facilitate hyper-polarization in second-order neurons. There are studies indicating that patients placed on chronic opioids prior to total knee arthroplasty may be at greater risk of poor postoperative pain management [37]. Opioids are effective at relieving severe musculoskeletal pain. Adverse reactions of CNS depression, respiratory depression, nausea and vomiting, or constipation may require adjuvant drugs, such as anti-emetics or laxatives. Opioids may also impair judgment or motor skills, resulting in changes in balance or falls [4]. Oxycodone may be the preferred agent for two reasons. First, it has higher bio-availability as compared to morphine, resulting in more stable plasma levels. Second, oxycodone is not as affected by renal dysfunction, as compared to morphine [38].

N-*Methyl-D-Aspartate (NMDA) Receptor Antagonists*

NMDA receptor antagonists potentiate the effect of opioids and prevent hyperalgesic complications from uncontrolled pain [39]. The medication ketamine is the main example. A study by Remerand et al. [40] demonstrated that patients treated postoperatively after a total hip arthroplasty with ketamine had significantly decreased morphine consumption and decreased pain. All patients were managed with a multimodal pain management regimen concurrently. Side effects include hallucinations, nausea, emesis, and vision changes. This medication is only available intravenously and intramuscularly; therefore, it is not typically used in the inpatient or outpatient rehabilitation setting.

Rehabilitation

Therapy

It is important to stress aggressive post-acute rehabilitation, with a focus on return to functional activity, in order to assure a reduction in the likelihood of uncontrolled pain [20, 41].

Modalities

Cryotherapy, or the use of ice/cold, may be beneficial to help with pain and swelling after TJA. One study by Su et al. showed that the use of a cryo-pneumatic device after TKA decreased opioid usage from hospital discharge to 2 weeks postoperatively [42]. However, a Cochrane review did not show clear evidence to support the use of cryotherapy [43].

Psychology

Most rehabilitation hospitals incorporate psychologists into the treatment program. Focus should be placed on the psychosocial factors that are known to play a key role in continued pain, such as pain catastrophizing [44].

Weight Reduction

Weight reduction is a goal that should be incorporated into the rehabilitation process due to the well-documented association with being overweight and joint symptoms [5].

Education

Information on postsurgical pain and management should be provided to orthopedic patients presenting to a rehabilitation facility. Knowing what to expect may help to alleviate anxiety associated with the rehabilitation process and the management of postoperative pain. More importantly, it can reduce the burden of acute and chronic opioid use.

A recent review showed that only 1 of 13 studies demonstrated an improvement in postoperative pain following pre-operative education, as compared to a non-educated group [45]. In contrast, there was a five-year retrospective study that looked at outpatient orthopedic surgical patients who underwent a comprehensive pre- and postoperative program with the intent of minimizing opioid use. The study revealed that 89% of the patients used less than or equal to 20 opioid tablets after undergoing common orthopedic procedures and no chronic opioid use was required [46].

Procedures

Injections

There are several forms of injections that can be performed to help with relieving pain in the orthopedic patient, prior to and after surgery, such as intra-articular corticosteroid injections of the hips, knees, and shoulders, and visco-supplementation with hyaluronic acid of the knee. Local infiltration anesthesia (LIA) with anesthetics, steroids, NSAIDS, and epinephrine has been shown to be beneficial in reducing pain following TKA [47]. Intrathecal and epidural anesthesia/analgesia, as well as peripheral nerve blocks, can be helpful in reducing pain postoperatively in total joint replacements.

Acupuncture

Although more studies need to be performed, Crespin et al. [48] found a significant decrease in moderate to severe pain after TJR with the use of acupuncture, from 41 to 15% of patients.

Surgery

Revision surgery may be required if the patient has uncontrolled pain due to a mechanical problem with prosthesis or malalignment.

Potential Treatment Complications

Modalities

Skin burns or breakdown of the incision may occur with modality use.

Medications

NSAIDS

Bleeding and renal dysfunction are the primary potential complications. There are concerns that the use of COX-2 inhibitors and NSAIDs may interfere with osseointegration and fracture healing, but there is little level I or II evidence available to support or to refute this concern.

Opioids

The risks of opioid use include addiction, allergic reaction, and the following systemic side effects:

System	Effect
Gastrointestinal	Nausea, vomiting, constipation, ileus
Respiratory	Respiratory depression, hypoxia
Integumentary	Pruritus
Neurologic	Delirium, somnolence
Genitourinary	Urinary retention

Rehabilitation

Potential complications of rehabilitation include falls and additional injuries, such as fractures, dislocation, and soft tissue damage.

Procedures and Surgeries

As with any procedure or surgery, there may be risk of infection or failure.

Conclusion

Early patient performance in therapy is closely tied to how well postoperative pain is controlled. Uncontrolled pain has a detrimental implication on the patient's ability to participate in therapy. As with any patient being admitted to a rehabilitation hospital, collaboration between the patient, family members, and interdisciplinary care team members including the surgeon, physiatrist, consulting physicians, nurses, therapists, social workers, and psychologist is critical to optimize early function and to maintain adequate pain control.

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Chapter 8
Pain in the Tendinopathy Rehabilitation Patient

Marissa L. Darling, Daniel A. Fung, and Timothy T. Davis

Introduction

Tendinopathy is broad term that encompasses all tendon disorders and is used to describe any abnormal conditions of the tendon. Tendinitis refers to acute inflammation, usually occurring over a short period of time, with evidence of incomplete tendon degeneration and inflammatory repair response. Tendinosis refers to chronic tendon injury or tendon degeneration, without the clinical or histological signs of an inflammatory response. Frequently, both the terms "tendinosis" and "tendinopathy" are used to describe chronic overload conditions of the tendon.

Despite the prevalence and rising incidence of tendinopathies, particularly in the athletic population, treatment of tendinopathies and tendon pain remains challenging and frustrating for both clinicians and patients. It is estimated that approximately 50% of sports injuries are due to overuse [1, 2]. The condition can be resistant to treatment and often recurs. Overuse injuries account for more than 7% of all physician office visits in the United States [3]. Quality of life suffers, particularly in active individuals and athletes because of chronic pain and its disruption to athletic, occupation-related activities, and even activities of daily living.

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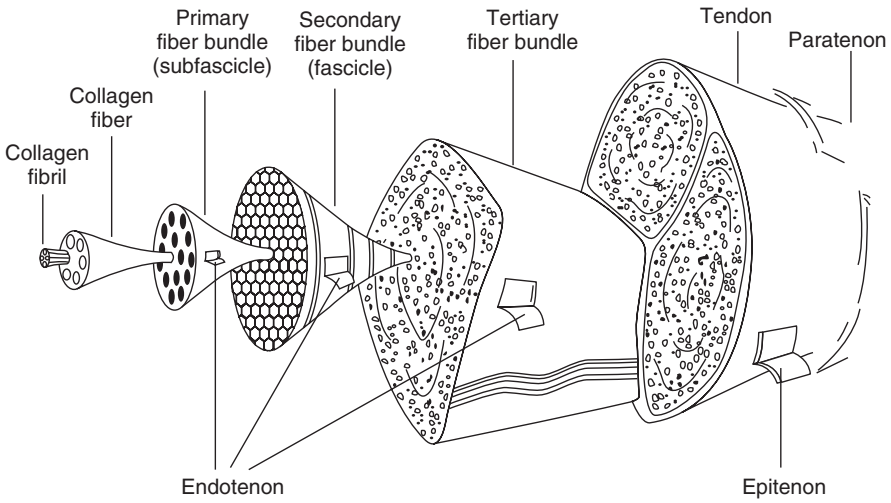

Fig. 8.1 Tendon structure (need to make our own illustration)

Pathophysiology

Tendons transmit the force of muscle contraction to bone and across joints to produce the body's movement and to provide joint stabilization. A healthy tendon comprises fibrous connective tissue, which is a complex arrangement of cells (tenocytes), collagen bundles, and ground substance rich in proteoglycans (extracellular matrix). Tenocytes are capable of proliferation and produce collagen, elastin, and proteoglycans, which maintain healthy tissue structure and function. Tenocytes are also able to resist mechanical forces and self-repair when injured. The tendon is arranged with increasing complexity from the collagen fibril, collagen fiber, the primary bundle, the secondary fiber bundle, the tertiary fiber bundle, and finally the tendon (Fig. 8.1). Each of these layers is separated by connective tissue sheaths, which also contain vascular, lymphatic, and nerve supplies, and allow for smooth movement of the tendon against surrounding tissue [4].

There is often a poor correlation between clinical symptoms of tendonopathies and objective evidence of tissue disruption. It is thought that a tendon's relatively avascular nature limits its capacity for healing. The tensile load imposed on tendons, especially in gliding zones around bony prominences, may induce transient ischemia, creating areas of tissue weakness, loss of cell viability, and even macrostructure disruption (rupture), due to poor perfusion [5]. Histological appearance of a normal tendon differs from a tendon with overuse-type tendinopathy injury/tendinosis though the exact pathological process has yet to be fully elucidated [6].

Tendinopathy seems to be the response to overuse injury resulting in a pathologic cascade of changes in the normal tendon repair process and creating a pathological cycle of degeneration and attempted failed regeneration. Microscopic examination of tissue from painful tendons reveals variable features, such as collagen disarray and fiber disorganization, increased proteoglycans and water, increased number of cells (myofibro-

blasts and fibroblasts), more chondroid appearance of tenocytes, and the presence of neovascularization [7]. However, there is an absence of inflammatory cells, indicating an insufficient repair process that leads to tendon degeneration. Macroscopic changes include tendon thickening, loss of mechanical properties, and pain [8, 9]. However, imaging studies (i.e., ultrasound, magnetic resonance imaging) reveal that these changes can exist in non-painful tendons and may be an incidental finding. Therefore, tendinopathy must require clinical symptoms and cannot be diagnosed by imaging [10].

Although overuse and overloading are commonly accepted as the cause of tendinopathy, there are a number of other intrinsic and extrinsic factors that may contribute to its development. Intrinsic factors include age, nutrition, vascular perfusion, obesity, adiposity, poor biomechanics, and anatomical variants, which include limb malalignments, bony impingement, leg length discrepancy, joint laxity, muscle weakness/imbalance, systemic disease, and possibly gender [11, 12]. Extrinsic factors include occupation, sport, physical load (repetitive or abnormal/unusual loading), training errors, such as poor technique, fast progression, high intensity, or fatigue, shoes and equipment, environmental conditions, including temperature, and running surface [13].

Common Tendinopathies

The types of overuse injury depend on several factors, including age and activity [14]. For instance, in the pediatric and adolescent population, tendons and ligaments are stronger than the epiphyseal plate, and are thus more prone to injury at the epiphyseal plate rather than the tendon or ligament. When tendon injuries do occur in children, the insertion site of the tendon at the apophyses is more likely injured than the main body of the tendon [15, 16]. In contrast, in the adult population, most tendinopathies refer to intra-tendinous condition. Older patients or adult athletes presenting to musculoskeletal clinics are usually diagnosed with traditional overuse injuries, including rotator cuff injures (18%), Achilles tendon (20%), and medial and lateral epicondylitis, which occur from sport or work-related activities [17]. Common tendinopathies in the upper extremity include rotator cuff tendinopathy, bicipital tendinopathy, and medial and lateral epicondylitis. Common tendinopathies in the lower extremity include hamstring tendinopathy, patellar tendinopathy/jumper's knee, Achilles tendinopathy, and peroneal tendinopathy [18].

Symptoms

Tendinopathy is the clinical syndrome of tendon pain and dysfunction, usually due to overuse. Symptoms include localized pain with loading, tenderness to palpation, and impaired function. Frequently, tendon pain is characterized by a transient on/off nature consistently linked to loading. Pain is preceded by excessive energy storage and release in the tendon. Therefore, the tendon is rarely painful at rest or during low-load activities. For example, a patient with patellar tendinopathy usually has

pain with jumping, but not cycling because of the different demands of the musculotendinous unit. Another characteristic pain pattern of tendinopathy is that the tendon "warms up" and becomes less painful over the course of activity, with variable times of exquisite tendon pain after exercise [19].

Functional Limitations

Chronic tendon pain itself can adversely affect quality of life because of the patient's inability to participate in exercise, athletic activities, occupation-related activities, or ADLs. However, tendinopathy is also associated with alterations in biomechanics and may affect motor control, movement variability, and strength due to disuse or guarding. Less variable motor patterns create a system that is less adaptive to changes in the environment and increases the likelihood of injury or re-injury [20].

Treatment

Optimal treatment of tendinopathy is debated, though nonoperative management is still the mainstay. Initial treatment includes avoidance of aggravating factors, relative rest, ice, stretching, and analgesic medications. Broadly, conservative management involves physical therapy including modalities, medications, and injections [21].

Conservative Treatments

Rehabilitation management includes physical therapy and physical modalities. Eccentric strengthening is one of the mainstays in the treatment of tendinopathy and involves the application of load and muscle exertion to a lengthening muscle, thought to stimulate tissue remodeling and normalization of tendon structure. Eccentric exercises should be done under the guidance of a trained physical therapist, as overloading the musculotendinous junction can lead to further injury. A systematic review by Kingma et al. found a mean pain reduction of 60% in patients with chronic Achilles tendinopathy who completed eccentric training compared to 33% in control groups (traditional concentric strengthening programs) [22]. Other studies also showed eccentric training was more effective than traditional concentric training for treating Achilles and patellar tendinopathies [23–26].

Physical modalities include sound-assisted soft tissue massage/friction massage, cryotherapy, low-level laser therapy, ultrasound therapy, ionotophoresis/phonophoresis, and extracorporeal shock-wave therapy [21]. Sound-assisted soft tissue massage (SASTM), augmented soft tissue mobilization (ASTM), or friction massage involve the application of friction-directed force onto a tendon or ligament to promote or induce physiological and structural tissue changes. This is thought to occur

through local hyperemia, massage analgesia, and reduction of adherent scar tissue [27]. Cryotherapy involves the application of cold (ice bags, ice massages, chemical cold packs, ice water immersion, ice circulating units, and vapocoolant sprays) to the injured area. This helps to reduce inflammation and swelling through vasoconstriction and decreased blood flow, as well as pain reduction through the gate control theory and by temporarily inhibiting effects to the neuromuscular system [28]. Although cryotherapy is beneficial in acute injuries, its efficacy in chronic injuries has not been as well studied [29]. Cryotherapy should be avoided in patients with cold hypersensitivity, cold intolerance, and Raynaud disease [30].

Low-level laser therapy (LLLT) uses light energy to induce ATP production, enhance cell function, increase protein synthesis, and to reduce inflammation, increase collagen synthesis, and angiogenesis. Laser sources are used at powers too low to cause measurable temperature increases, but should still not be used over cancerous areas, eyes, open wounds, pregnancy, or the epiphysis [31].

Therapeutic ultrasound is used for its nonthermal tissue healing effects and thermal effects. Low-frequency intensity ultrasound causes movement of fluids along cell membranes and formation of gas-filled bubbles, which is thought to promote tissue repair. At higher intensity, ultrasound also increases tissue temperature, reduces muscle spasm, and reduces pain. Contraindications include use over ischemic areas, deep vein thrombosis, anesthetic areas, actively infected areas, and over certain body parts such as the eyes, heart, skull, genitals, the trunk or abdomen in a pregnant woman, and over stress factors or osteoporotic areas [32].

Phonophoresis and iontophoresis use ultrasound energy and electrical pulse waves, respectively, to diffuse medication through the skin into affected areas. Commonly used medications are corticosteroids, lidocaine, salicylates, and acetic acid. Contraindications are similar to those of therapeutic ultrasound [33].

Extracorporeal shock-wave therapy (ESWT) delivers a single-impulse acoustic wave through an electromagnetic, electrohydraulic, or piezoelectric source [34]. The peak pressure of a shock wave is approximately 1000 times of an ultrasound wave. The mechanism of ESWT is not well understood. Some postulate that it stimulates production of angiogenic markers and neovascularization, while reducing calcitonin gene relayed peptide expression in dorsal root ganglions to induce tissue repair and regeneration [35].

Currently, the literature regarding the efficacy of the aforementioned physical modalities shows conflicting results and little evidence to support their use in treating tendinopathy, with the exception of ultrasound for calcific tendonitis and ESWT in calcific tendinopathy of the rotator cuff [21]. In addition, bracing/splinting is also a widely used treatment option [18].

Medication-based therapy usually includes NSAIDs, which work by inhibiting the cyclooxygenase (COX) pathway and by reducing the inflammatory response to injury [36]. Although few studies show that NSAIDS may be effective in relieving tendon pain in the short term (7–14 days), they may in fact be detrimental to the healing process by inhibiting the inflammatory response and thus normal tendon repair [21]. Pain control through NSAID use may also allow patients to ignore early symptoms, leading to further tendon damage and preventing definitive healing [37].

Furthermore, the side effects of NSAIDs are not insignificant in regard to the renal system, cardiovascular system, asthma exacerbation, and gastrointestinal bleeding, and should be used with caution in older patients with medical comorbidities. Thus, a short course of NSAIDs may be reasonable in acute tendon pain associated with inflammation (tendinitis/tenosynovitis) and perhaps early in a tendon overuse injury, but not in chronic treatment of tendinosis [7, 21, 35, 38].

Nitric oxide therapy may also be used in treating tendinopathy [39]. Nitric oxide (NO) is a soluble gas thought to be responsible for cell signaling and is synthesized by NO synthetase enzymes, which are up-regulated in tendon injury [40]. NO is postulated to enhance tendon collagen synthesis and tendon healing [41]. As such, research is ongoing regarding the efficacy of exogenous NO in the form of glyceryl trinitrate patches in treating tendinopathy, both for tendon healing, force, and pain. Three randomized, controlled, double-blind clinical studies by Paoloni and colleagues looked at whether transcutaneous administration of NO (glyceryl trinitrate patches) would enhance tendon healing in humans for treatment of lateral epicondylitis, Achilles tendinopathy, and rotator cuff tendinopathy. Treatment groups showed an improvement in pain, an increase in power, and an improvement function compared to controls [42–44]. The improvement persisted even at 3 years [45]. In 2010, Gambito et al. performed a meta-analysis on seven randomized clinical trials looking at the effects of topical nitroglycerin for tendinopathy treatment and found that it provides short-term pain relief and enhanced tendon forces in the chronic phase [46]. For now, topical glyceryl trinitrate for treatment of tendinopathy is still considered off-label by the Food and Drug Administration (FDA) and larger multicenter trials would be useful in validating this treatment modality.

Injection-based treatment includes injecting corticosteroid, platelet-rich plasma, whole autologous blood, prolotherapy, stem cells, and skin-derived tenocyte-like cells. Corticosteroid injections have remained the first-line approach to treating tendon pain through their anti-inflammatory effects [2, 47]. However, as tendinopathies frequently do not display an inflammatory state, it is not surprising that studies now show though corticosteroid injections help with pain initially [48]; they offer no intermediate or long-term benefit [3, 49–52].

A study by Newcomer et al. showed that there were no significant differences between corticosteroid injections and rehabilitation for lateral epicondylitis and that all patients had equal improvement in pain scores at 6 months [53]. A systematic review by Coombes et al. found that corticosteroids helped only with initial pain reduction in lateral epicondylitis and in rotator cuff pain [47]. Alvarez et al. found that a subacromial injection of betamethasone was no more effective than anesthetic alone in chronic rotator cuff tendinosis with regard to range of motion, quality of life, or impingement signs [48]. A systematic review by van Ark et al. found that corticosteroid injections had worse relapse pain rates when compared with physical therapy and other injection therapies at 6 months and beyond [54].

Although corticosteroids are still used as the first-line treatment of tendinopathy, they are not without risks or complications, and given the evidence in literature

at this time, it seems that corticosteroid injections remain a good treatment for short-term symptoms, but may not be very helpful for long-term management.

Platelet-rich plasma (PRP) is a concentrate of platelets obtained from patient's own blood that is centrifuged down to its various components. The PRP layer is then drawn off and re-injected into the site of injury to promote healing and regeneration by the action of growth factors and increased collagen expression, which leads to tendon cell proliferation and healing [55, 56].

So far, studies comparing the efficacy of PRP to various other treatments are still inconclusive. DeVos et al. showed that PRP injections did not improve pain or functional outcome in chronic Achilles tendinopathy compared to saline injection at 24 weeks or 1 year, nor did they change tendon structure or neovascularization based on ultrasound [57–59]. A systematic review by Paloloni et al. of human clinical trials did not find evidence that PRP injections were superior to other injections in treating tendon or ligament injuries [60]. However, a systematic review of in vivo studies by Taylor et al. showed some improvement, as well as studies by Peerbooms et al., which showed improvement in lateral epicondylitis pain compared to steroid. Gaweda et al. found improved pain and ultrasound parameters in Achilles tendinopathy [55, 61, 62]. However, Filardo et al. found no significant improvement in patients treated with PRP and physical therapy compared to physical therapy alone [63].

Similar to PRP, whole autologous blood injections are also thought to be rich in growth factors for cell proliferation and collagen regeneration [64, 65]. Although promising as a treatment option, more controlled research must first be done to determine efficacy and side effects [66–70]. Prolotherapy involves injecting proliferating agents (dextrose, phenol-glycerin-glucose, or sodium morrhuate) at painful tendon sites to induce an inflammatory response and lead to healing through tendon hypertrophy [71]. Again, given limited data, prolotherapy's true efficacy is not yet known [72–76]. Skin-derived tenocyte-like cells is a novel approach that has only been explored in clinical pilot studies. Connell et al. injected autologous skin-derived tenocyte-like cells in patients with refractory lateral epicondylitis under ultrasound guidance and found that patients reported symptom improvement at 6 weeks, 3 months, and 6 months. Furthermore, ultrasound showed statistically significant changes in the number of tears, new vessels, and tendon thickness [77]. With the exception of corticosteroid injections, more studies are needed to determine the efficacy and side effects of the aforementioned injection therapies. Other procedures in the treatment of tendinopathy include injection of sclerosing medications, such as polidocanol injections, which destroy neovasculature to provide pain relief, and future therapies involving stem cell technology in tendon grafting and repair [7].

Also included in conservative management is integrative and complementary medicine, such as homeopathy and Traditional Chinese Medicine, including acupuncture [78, 79].

Percutaneous Tenotomy (See Chap. 69)

Surgical Treatments

Surgical options are often only considered in recalcitrant cases of tendinopathy and as a treatment of last resort. Surgical procedures focus on excising areas of failed tendon healing and fibrosis, pathological nerve, and vascular ingrowth. Tissue debridement is thought to stimulate a new healing process by restoring vascularity and initiating stem cell growth and protein synthesis [7, 21]. Tenotomies can be performed open, arthroscopically, or percutaneously using ultrasound guidance [80]. The best surgical success has been seen in lateral epicondylitis and Achilles tendinopathy, with success rates in the 65% to 95% range, though these studies are generally retrospective and based on case series without adequate controls. Less evidence is available in surgical outcomes for other tendinopathies [21]. Although good results may be obtained with debridement and/or decompression, failure rates can be as high as 20–30% and involve prolonged delay to full activity of 4–12 months [3, 7, 21, 51].

Conclusion

Tendinopathies are a common and debilitating chronic condition that can be difficult to treat. They can lead to the decline in a patient's quality of life and physical fitness. Thus, it is important to understand the available treatment options and their limitations and to continue to develop novel treatment options. Still, the best initial approach is conservative management, beginning with a rehabilitation program, including physical therapy, particularly eccentric exercises. Medications, modalities, injections, and percutaneous procedures should be added to the treatment program as needed. Open surgery should be saved as a treatment of last resort for recalcitrant cases given their considerable cost and potential for morbidity, and only modest success in treating tendinopathy. Further research in the area of growth factors and stem cells is needed and may be promising in offering a treatment to reverse the degenerative process and promote the regeneration of a healthy tendon.

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Chapter 9
Pain in the Amputation Rehabilitation Patient

Edward Wieseltier, Joshua Minori, and Theresa Lie-Nemeth

Introduction

Pain can place a significant functional limitation on the lives of people with amputations. It can be difficult to treat, but with the use of a multimodal treatment paradigm, positive outcomes can be attained. This chapter will help to identify the differences between residual limb pain, phantom limb sensation, and phantom limb pain. There will be a discussion on the various treatment options, which include psychological management, physical and occupational therapy, medications, interventional procedures, and surgery.

Pathophysiology and Symptoms

Residual Limb Pain

A patient who requires an amputation of one of their limbs, or of another body part, is at risk of developing a variety of pain syndromes. One of the first postoperative complaints is residual limb pain. Residual limb pain is also known as stump pain, incisional pain, or surgical site pain. This type of pain is usually described as aching or throbbing and is localized to the residual limb. Pain typically subsides over a one to three-week time period.

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The pathophysiology of residual limb pain occurs via nociceptive nerve fibers. It has been shown that incision of deep tissue, rather than skin alone, increases the amount of nociceptive transmission through the dorsal horn neurons. [1] These nociceptive nerve fibers are carried through the fast myelinated A-delta fibers, as well as non-myelinated C-fibers.

Other causes of pain in the residual limb include ischemia, infection, neuroma formation, and pressure points from bone spurs or pathologic bone formation. Residual limb pain in a later stage could be attributed to shear forces on adherent scars, a poorly fitting prosthesis, intermittent claudication, or other medical or neurological conditions.

Phantom Limb Sensation:

Phantom limb sensation [PLS] is very common in patients with amputation. The incidence is approximately 60–80% immediately after amputation [2]. Only about 10% of patients develop PLS after 1 month. The term PLS is reserved for individuals who have an awareness of the missing portion of their limb. PLS is not painful; therefore, it is rarely a clinical problem and usually diminishes over time. A variety of sensations may be felt, such as mild numbness and tingling, itching, or a feeling as if the amputated limb is in certain postures or is undergoing particular movements. There is also a phenomenon called "telescoping," in which the distal end of the missing limb feels as if it is retracted into the proximal end. Patients feel as if they can move the phantom limb [3]. This can be used as a form of therapy in an attempt to prevent phantom limb pain.

Normally, there is an extensive array of networks in the brain that are triggered by continuous incoming modulated flow from the periphery. When this flow ceases, cortical reorganization occurs, leading to non-painful phantom sensations triggered by input from body areas adjacent to the lost limb.

Phantom Limb Pain

The International Association for the Study of Pain (IASP) defines phantom limb pain (PLP) as "pain referred to a surgically removed limb or portion thereof" [4]. Many patients will describe the pain as similar to other neuropathic pains, such as sharp, burning, stabbing, shooting, electric, squeezing, or knife-like. The pain may also feel the same as the pain that presented in the limb prior to amputation [5].

Seventy two percent of all patients with lower limb amputation report PLP [6]. Fifty percent of patients have pain within 1 week postoperatively. Pain may be delayed weeks, months, or years after the amputation [3]. Management of PLP may be challenging given that the pain is coming from a part of the body that is no longer present.

PLP is an extreme example of deafferentation. Deafferentation pain is considered to be the result of destruction of the spinothalamic tract, which transmits somatosensory information about pain, itch, and rough touch [7]. The theory behind PLP is thought to be related to neuroplasticity in the somatosensory cortex; there are plastic changes that occur just adjacent to the missing body part.

In the 1980s, Merzenich performed a series of experiments, in which he amputated the middle finger of adult monkeys and found that within 2 months, the area of cortex corresponding to this digit started to respond to touch stimuli delivered to the adjacent digits [8]. In long-term deafferentation of one upper limb, the cortical area originally corresponding to the hand is taken over by the sensory input from the face; the cells in the "hand area" now start responding to stimuli applied to the lower face region [8].

Advances in neuro-imaging and brain stimulation techniques have allowed further knowledge to be gained as to how these neuroplastic changes occur. Transcranial magnetic stimulation (TMS) is one method of noninvasive motor mapping. A coil is placed on the scalp over the primary motor cortex; a suprathreshold stimulation is applied and can then be measured by EMG. The coil can be moved up and down across the precentral gyrus (primary motor cortex) and can induce motor evoked potentials (MEP) in a somatotopic fashion.

Karl and colleagues used TMS to map motor representations in the primary motor cortex (M1) in people with amputated forearms. Their findings demonstrated that the areas on the contralateral M1 of the amputated arm had expanded representations of the body parts closest to the amputation, which included the upper arm and lip. They also discovered that the motor cortical representation of the missing limb is not completely gone. One hypothesis posits that the brain may interpret residual limb muscle contraction, and the resultant sensory information, as phantom limb movement [7].

Functional magnetic resonance imaging (fMRI) is another noninvasive brain mapping method. A study by Wrigley et al. [9] evaluated brain activity during sensory stimulation in spinal cord injury patients. The study showed that activity during sensory stimulation to the little finger was expanded into parts of the primary somatosensory cortex (S1) that would normally receive afferent information from the lower limbs.

Treatment and Potential Complications

Residual Limb Pain

Postoperative edema can contribute to residual limb pain. An immediate postoperative prosthesis (IPOP) is sometimes placed on the residual limb, in the operating room, to help prevent knee flexion contractures and to control edema. One concern with

use of an IPOP is that it can lead to hygiene problems. Other more common options for edema control include elastic wrappings or stockinettes (e.g., ACE wraps or Tubigrip), residual limb shrinkers, rigid non-removable dressings, rigid removable dressings, and prosthetic silicone or gel liners [5, 10]. Problems with non-removable rigid dressings and IPOP include difficulty with inspection and desensitization. Other forms of compression, if applied incorrectly, could contribute to skin breakdown or a tourniquet effect.

As with any major surgery, postoperative pain may be significant. A stepwise approach to pain management should be utilized to treat residual limb pain in the rehabilitation setting. If the pain is mild, the patient's pain may be controlled with acetaminophen. More likely, patients will have moderate to severe pain requiring opioids with or without acetaminophen. Opioids bind to mu, kappa, and delta in the central nervous system and peripheral tissues. They pre-synaptically lower the influx of calcium to reduce neurotransmitter release in sensory C fibers and post-synaptically increase the transport of potassium in the cell to facilitate hyperpolarization in second-order neurons.

Commonly used opioids include hydrocodone and oxycodone. Hydrocodone/acetaminophen combinations come in 5, 7.5, and 10 mg strengths of hydrocodone and patients may be prescribed one to two tablets, every 4–6 h, as needed for pain. The prescriber should be aware of the amount of daily acetaminophen consumption. Oxycodone/acetaminophen can be substituted, if hydrocodone is insufficient. The dosing is one to two tablets of oxycodone/acetaminophen, 5/325 mg, every 4–6 h, as needed for pain. Oxycodone, without acetaminophen, may also be used for breakthrough pain, if the patient is consuming higher amounts of acetaminophen or has liver dysfunction. Oxycodone immediate release may be dosed 10–20 mg, every 4–6 h, as needed for pain. [11].

Sustained-release opioid formulations are also available and may be used in combination with an immediate release opioid for optimal pain relief. In addition, it may be advantageous to schedule pain medications prior to therapy so that the patient can obtain the most benefit during their sessions [5]. The more commonly used sustained release opioids include sustained release morphine sulfate, dosed at 15 mg increments, every 12 h, and sustained release oxycodone, dosed at 10 mg increments, every 12 h. Potential side effects of opioids include nausea, vomiting, constipation, drowsiness, dizziness, and respiratory depression.

If patients cannot tolerate opioids, tramadol may be tried. Tramadol is a non-opioid derived synthetic opioid. It acts by binding to opioid mu receptors, in addition to inhibiting norepinephrine and serotonin reuptake. This medication carries some similar side effects to opioids, except that tramadol can lower the seizure threshold and potentiate the serotonin syndrome in combination with certain other medications, such as SNRIs and SSRIs. Tramadol carries a risk of abuse potential, but much lower than opioid analgesics. For tramadol dosing, start with 50 mg once daily or twice daily. Increase by 50–100 mg daily in divided doses, every 3–7 days, as tolerated until pain relief. Total daily dose should not exceed 400 mg daily, and in patients over 75 years old, 300 mg daily.

Tapentadol is a newer opioid analgesic which has two mechanisms of action: a mu-opioid receptor agonist as well as a norepinephrine reuptake inhibitor, similar

to tramadol, but more potent. It is available in immediate and extended release formulations. The immediate release formula comes in 50, 75, and 100 mg strengths taken every 4–6 h, while the extended release is available in 50, 100, 150, 200, and 250 mg strengths, taken every 12 h. Use of tapentadol is not recommended for patients with severe renal or hepatic impairment and is contraindicated in patients with risk of seizures.

Phantom Limb Sensation

Patients should be educated and reassured that phantom limb sensation is normal. Recognizing PLS early on can help to prevent progression to phantom limb pain. Simple techniques such as light massage or tapping of the residual limb, vibration, and transcutaneous electrical nerve stimulation (TENS) can help to avoid this progression. For phantom itch, patients may try scratching the contralateral intact limb in the same location of the itching [5].

Phantom Limb Pain

Psychological Management

Working with a rehabilitation psychologist in the acute inpatient rehabilitation setting can be beneficial. The psychologist can help the patient to cope with their new self-image. Biofeedback and cognitive behavioral therapy can also be used to reduce pain. Biofeedback therapy can incorporate techniques such as progressive muscle relaxation or guided imagery, together with electromyographic (EMG) biofeedback or skin temperature feedback. Muscle relaxation techniques help to reduce muscle tension and to increase blood flow and may be efficacious in treating PLP [12]. Thermal biofeedback training is thought to help in PLP by mediating net regional sympathetic arousal. It allows an individual to monitor peripheral temperature and to thereby indirectly monitor and modify sympathetic activity. In a small study, Harden and associates demonstrated that by using thermal biofeedback, a patient can have reduction in PLP over a 4–6 -week course [12].

Rehabilitation Management: Physical and Occupational Therapies

Desensitization of the residual limb is important in the postoperative phase of rehabilitation. Limitations to desensitization might include non-removable postoperative casts or IPOP. Rubbing or massaging the residual limb is recommended for desensitization. Therapists may also apply different textures to the residual limb. Soft tissue and scar mobilization can also be performed. These techniques are initially performed by the therapist and then taught to the patient.

Physical modalities such as acupuncture, TENS, vibration, and ultrasound are thought to relieve pain through the gate control mechanism. If the non-nociceptive A-beta fibers are activated through these modalities, transmission of the nociceptive A-delta and C-fibers will be inhibited [13].

Mirror therapy has been shown to be very beneficial in helping to treat PLP. In mirror therapy, the patient looks at the reflection of their intact limb in a mirror box. This can induce sensations of movement in the phantom limb. Physiological studies have shown that both the mirror-box therapy and the motor imagery resulted in increased excitability of the corticospinal spinal pathways [14]. This partially depends on the so-called mirror neuron system, which includes neurons that are active not only during the execution of the task itself, but also during the observation of the task [15]. A controlled neuroimaging study of motor imagery in PLP resulted in a significant decrease of intensity and unpleasantness of pain, which correlated with reduction (improvement) of cortical reorganization [16].

Medication Management

Pharmacologic therapy is the mainstay for patients experiencing phantom limb pain. The following will provide a breakdown of the different classifications of medications and dosing considerations:

Topicals

Lidocaine acts by stabilizing the neuronal membrane through inhibiting the ionic fluxes required for initiation and conduction of impulses, thereby affecting local anesthetic action. Options include application of lidocaine 5% transdermal patch or ointment. There are very few side effects. At most, the patient may experience local erythema or a rash. Patches should be applied at a maximum of three daily for 12 h [17]. Lidocaine ointment might be a preferred choice, as applying ointment allows the patient to perform desensitization techniques concurrently.

Capsaicin, a highly selective agonist for transient receptor potential vanilloid 1 (TRPV1), expressed in nociceptive fibers, can be helpful for PLP, though the evidence for its efficacy is mixed [18, 19]. The cream or patch is applied to the affected area, three to four times daily. The main side effect is a burning sensation that decreases with continued use.

GABAergic Drugs

Gabapentin is a very common medication used to treat neuropathic pain and is less expensive than other formulations of neuropathic pain medications available. Gabapentin interacts with the alpha 2 delta subunit of L-type calcium channels. The

mechanism of action is not well understood, but is thought to involve a decrease in calcium currents. Common side effects include sedation, dizziness, and peripheral edema. As with many of the neuropathic agents, patients who are more sensitive to medications should "start low and go slow."

The following are some dosing considerations for gabapentin. Start with 100–300 mg at bedtime, or 100–300 mg, three times daily. Increase by 100–300 mg, three times daily, every 1–7 days, as tolerated until pain relief. The maximum daily dose is 3600 mg in patients with normal renal function [17]. Given that some patients with amputation may also have renal impairment, it is important to adjust the dose based off of creatinine clearance (CrCl). If CrCl is 30–60, the dose should be between 200 and 700 mg every 12 h. If CrCl is 15–29, patients should receive between 200– and 700 mg daily. If CrCl is less than 15, then the dose should be between 100– and 300 mg daily.

Pregabalin also interacts with the alpha 2 delta subunit of L-type calcium channels. Pregabalin requires less frequent dosing than gabapentin. The drawback is that it is more expensive than gabapentin. Common side effects include sedation, dizziness, and peripheral edema. It is usually better tolerated than gabapentin [17]. Pregabalin may be started 50 mg three times daily, or 75 mg twice daily. The dose can be increased to a total of 300 mg daily, after 3–7 days, then increased again to 150 mg/day, every 3–7 days, as tolerated until pain relief. Maximum daily dose is 600 mg [17]. Pregabalin dose should also be adjusted depending on CrCl. Any patient with a CrCl of 30–60 should decrease their dose of pregabalin by 50%, divided BID or TID. For CrCl 15–30: if patient requires 150 mg/day with normal renal function, then decrease dose to 25–50 mg/day and administer daily or divided BID. If patient requires 300 mg/day with normal renal function, then decrease dose to 75 mg/day and administer daily or divided BID.

Other anticonvulsants used in the treatment of PLP include carbamazepine, oxcarbazepine, topiramate, and levetiracetam. These anticonvulsants may be used in combination with each other, or with antidepressants [5].

Tricyclic Antidepressants

Tricyclic antidepressants (TCAs) act by inhibiting the reuptake of norepinephrine (NE) and serotonin (5HT). Anti-neuralgic properties of TCAs are independent from their antidepressant effects. Tertiary TCAs such as amitriptyline and imipramine have a larger side effect profile when compared to secondary TCAs, but tertiary TCAs tend to be more effective than secondary TCAs for painful peripheral neuropathies [20]. O'Connor et al. [17] stated that TCAs appear to have equivalent analgesic benefits in both depressed and nondepressed patients with neuropathic pain. Of the TCAs, secondary amine TCAs, including nortriptyline and desipramine, are recommended because they provide pain relief that is comparable to amitriptyline and other tertiary amine TCAs while causing fewer side effects. Some potential side effects include sedation, postural hypotension, arrhythmias in patients with cardiac disease, seizures in patients with epilepsy, and weight gain.

The following are some dosing considerations for secondary amine TCAs (nortriptyline and desipramine). Start with 25 mg at bedtime; increase by 25 mg daily every 3–7 days as tolerated until pain relief; the maximum daily dose should not exceed 150 mg [17].

Serotonin Norepinephrine Reuptake Inhibitors (SNRI)

Consider this class of medication if the patient is experiencing depression or anxiety, associated with pain. Medications in this class include venlafaxine and duloxetine. These medications inhibit the reuptake of serotonin and norepinephrine as well. Duloxetine is the only FDA approved medication with both pain and psychiatric indications (diabetic neuropathic pain, fibromyalgia, generalized anxiety, and major depression). For duloxetine, start with 30 mg once daily. Increase to 60 mg once daily after 1 week. Do not exceed maximum daily dose of 60 mg twice daily [17]. It is important to understand that the nor-epinephrine effect occurs between 60– and 90 mg, and higher doses are more serotonergic and used for primary mood disorders. For venlafaxine, start with 37.5 mg once or twice daily. Increase by 75 mg each week as tolerated until pain relief. Do not exceed maximum daily dose of 225 mg daily [17]. Again, it is important to understand that the dose for targeting neuropathic pain is generally 75 mg daily.

Tetracyclic Antidepressant (TeCA)

Mirtazepine is helpful for sleep, anxiety, depression, and neuropathic pain. This medication may be started at 15 mg nightly, or 7.5 mg in patients who are more sensitive to medication. The dose can be increased, up to a maximum of 45 mg. Weight gain is a potential side effect.

Opioids

Opioids have been shown to be helpful in PLP, in particular, IV morphine in the perioperative phase and oral morphine for intermediate and long-term treatment [18]. Ideally, opioid use should be used in the acute phase, while other medications are being titrated. Long-term use should only be considered if other treatments are ineffective. The lowest effective dose should be given, while monitoring for signs of misuse. Equi-analgesic dosages should be used for other opioid analgesics. With morphine, start with 10–15 mg, every 4 h, or as needed. After 1 to 2 weeks, convert the total daily dosage to a long-acting opioid analgesic and continue short-acting medication, as needed. If a patient reaches a total daily dose of 120–180 mg of morphine, then they should be evaluated by a pain specialist.

NMDA (*N*-methyl-*D*-aspartate) Receptor Antagonists

Medications such as ketamine produce dissociative anesthesia by blocking NMDA receptors. Interventional pain clinics often administer this medication via IV infusion. Potential side effects include hallucinations, panic attacks, and increased cardiac output. Other NMDA receptor antagonists include oral memantine and dextromethorphan [18].

Calcitonin

There use of calcitonin for neuropathic pain, including phantom limb pain, is off-label. In particular, the IV formulation has been shown to be beneficial [18]. The mechanism of action for its anti-nociceptive effect is not entirely understood, but it may be centrally acting by exerting action on serotonin. Increases in serum beta-endorphin levels caused by calcitonin may also contribute to analgesia, presumably because of an association with opiate receptor uptake [21]. Most common side effects are nausea, vomiting, and flushing.

Interventional Procedures and Surgery

Residual Limb Pain from Neuromas

For neuromas in the residual limb, injections with steroid and local anesthetics may be considered. If neuroma pain is persistent, neuroma ablation can be performed using phenol, alcohol, or cryoablation. Radiofrequency ablation has also been attempted. If these techniques do not resolve the pain caused by neuromas, surgical excision can be performed with an 80% success rate [5].

Phantom Limb Pain

Preoperative, intraoperative, and postoperative epidural anesthesia should be utilized if possible, in particular for patients who suffer with painful limbs prior to amputation. In a study by Karanikolas et al. [22], optimized perioperative analgesia starting 48 h preoperatively and lasting 48 h postoperatively markedly decreased phantom limb pain at 6 months postoperatively.

Spinal cord stimulation (SCS) involves placement of electrodes in the epidural space, over the dorsal columns. An electric current is then applied to achieve

sympatholytic and other neuromodulatory effects. Phase 1 of the treatment involves a percutaneous or paddle SCS trial, which includes temporary placement of an electrical stimulator with an externalized generator. Only those patients with positive outcomes are considered for permanent implantation, which includes an internal electrode array and implanted pulse generator (IPG). Clinical results indicate beneficial effects of SCS in PLP patients on immediate as well as long-term outcomes although the percentage of patients maintaining optimal pain control declined with time [23].

Deep brain stimulation (DBS) involves placement of implantable leads in subcortical areas, such as the thalamus, basal ganglia, and the peri-aqueductal gray, through which electrical stimulation is performed. DBS has been used to treat several areas of chronic pain [24]. The use of DBS for PLP is controversial. However, some patients benefit from DBS, experiencing long-term pain relief and improved quality of life [25]. For further review, please see dedicated chapter on DBS for pain.

Dorsal root ganglion (DRG) stimulation has a similar approach to dorsal column stimulation. In a retrospective case series of patients, who were suffering from PLP with or without residual limb pain and underwent DRG stimulation implant, the results showed improved ratings of quality of life and functional capacity. Furthermore, some patients were able to reduce or to eliminate pain medications [26]. Using an epidural approach under fluoroscopic guidance, the stimulating contacts were placed near relevant DRGs based on individual pain distributions. Successful trial was considered when patients achieved 50% or greater pain relief in their primary area over several days. Pain reduction on average was 52% at last follow up in the study.

Conclusion

Patients with amputation can experience residual limb pain, phantom limb sensation, and phantom limb pain. Pain may be difficult to treat, but many options exist to reduce discomfort. The physician, therapy team, psychologist, and nursing staff need to work in an interdisciplinary fashion to evaluate and to control pain. It is also very important to make sure the patient and their families and/or caregivers are well educated about the potential complications, such as PLP, prior to the amputation, as well as treatment options and care postoperatively. Rehabilitation is very important for the patients to reach their maximum functional capacity.

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Chapter 10
Pain in the Cancer Rehabilitation Patient

Ryan Murphy and Jonas Sokolof

Introduction

Pain related to cancer and its accompanying treatments includes a variety of syndromes, within multiple subtypes of oncologic disease. Optimal pain management requires patience on behalf of both the patient and provider, as many treatments fail before some degree of benefit is achieved. Evaluation and management of cancer-related dysfunction, including pain, is becoming more prevalent. In part, this is secondary to more patients surviving longer, which is subsequent to advancements in treatments and improvements in outcomes. There are now dedicated fellowship-trained sub-specialists in cancer rehabilitation within the specialty of Physical Medicine and Rehabilitation. The cancer rehabilitation specialist's role is often to evaluate and to manage neurologic and musculoskeletal dysfunction in the oncologic setting. Currently, there are multiple resources to direct care of this patient population.

Many disorders cause pain in patients with cancer, including graft-versus host disease, radiation-induced myopathy/plexopathy, radiation fibrosis syndrome, complex regional pain syndrome, adhesive capsulitis, aromatase inhibitor-induced arthralgias, mucositis, deep vein thrombosis, pathologic fractures, spasticity, dystonia, avascular necrosis, bone pain, pelvic pain, post-surgical pain syndromes, and lymphedema. This chapter will focus on two disorders, which are most commonly seen in the cancer rehabilitation setting. Both disorders may affect the function, level of pain, and/or quality of life of the patient with cancer.

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Chemotherapy-Induced Peripheral Neuropathy (CIPN)

Natural History

Incidence of this syndrome varies widely within patients and by type of chemotherapy. Typically, symptoms will initially present in the distal portion of the toes or fingers. Symptoms then gradually migrate proximally over time, in a symmetric "stocking and glove" distribution. This type of neuropathy is usually a dose-dependent process, which occurs during chemotherapy treatment. There may be a "coasting effect", whereby symptoms progress for 2–6 months after cessation of treatment. Platinum agents are the most common source for CIPN, with reports of 50–100% incidence from the use of such agents. Taxane-induced CIPN may occur in a range of 15% to greater than 60%. Vinca-alkaloid agents have been shown to vary widely; Vincristine is similar to Cisplatin, with almost 100% incidence. Other Vinka-alkaloids may have less than 10% incidence [1]. More recent systematic reviews from 2014 suggest that the estimated prevalence of CIPN within the first month of chemotherapy may be as high as 68% [2].

There is considerable variation in the prevalence reported within the literature, depending on whether the data was patient- or clinician-reported; patient-reported outcomes were typically significantly higher [3]. Predisposing factors include treatment with multiple chemotherapy agents simultaneously or sequentially. Other factors include premorbid acquired or hereditary neuropathy, which may have been previously undiagnosed. Symptoms of CIPN typically improve within the first 3–6 months after cessation of treatment; however, recovery is often incomplete (20–35%). Rapid improvement of symptoms after chemotherapy cessation may be predictive of the overall prognosis for recovery of sensation and pain [1, 4]. However, permanent CIPN has been reported more than a decade after ending chemotherapy, often presenting with sensory symptoms in the lower extremities [5].

As for possible prevention, many of the treatments studied, which are described in later sections, have had disappointing results. A recent report in 2014, published by the American Society of Clinical Oncology (ASCO), included Clinical Practice Guidelines, which reviewed the available literature and concluded that no agents were recommended for the prevention of CIPN [6].

Pathophysiology

Mechanisms for CIPN: Platinum agents initially bind to DNA and then induce apoptosis of neurons within the dorsal root ganglion (DRG) of sensory nerves. A "coasting effect" may occur due to the accumulation of platinum within the cell body, which generally results in symptoms long after treatment has been completed. Taxanes inhibit proper microtubule function within the mitotic spindle, thus interfering with axonal transport in a length-dependent manner. This occurs in both

motor and sensory nerves and in a symmetrical distribution. Vinca-alkaloids also inhibit proper microtubule function, which interferes with axonal transport in both motor and sensory nerves in a symmetrical length-dependent pattern [1].

Signs/Symptoms

Signs: changes in gait pattern, falls, impaired pinprick sensation or proprioception, allodynia, myalgias, tremors, hyperpathia, orthostatic blood pressure.

Symptoms: numbness, tingling, burning, dysesthesias, paresthesias, cramping, autonomic symptoms including constipation, diarrhea, abnormal sweating, and dizziness have all been reported [7].

In current clinical practice, CIPN is often assessed using one of several common toxicity scales; however, these scales are limited as they rely predominantly on subjective patient reporting rather than objective quantitative testing [8].

Functional Limitations

Impairment of fine motor movements, dexterity, and coordination during tasks such as working, using a telephone, writing, ambulating, which may result in balance difficulty, gait dysfunction, impaired proprioception, self- care, mobility, and other routine daily activities or tasks.

Treatments

Options include trialing an alternative chemotherapy agent with a lower neuropathy side effect profile, lowering the dose, or discontinuing the offending chemotherapy agent. A significant number of the treatment options are based on expert collective opinions, case reports, anecdotal evidence, and randomized clinical trials. Otherwise, they are extrapolated from known treatments for diabetic neuropathy, herpetic neuralgia, or other types of pain.

Medications [4, 9–14]

Non-steroidal antiinflammatory drugs

Ibuprofen, naproxen, meloxicam, celecoxib

Opioids

Tramadol, tapentadol, codeine, hydrocodone, oxycodone, oxycontin, methadone

Antiepileptics

Gabapentin, pregabalin, venlafaxine, duloxetine, amitriptyline

Antispasmodics

Cyclobenzaprine, metaxalone, baclofen, tizanidine

Supplements

Glutamine, *N*-acetylcysteine, alpha lipoic acid, curcumin, metanx, vitamin E, magnesium, and glutathione.

Topical

Diclofenac, lidocaine, compounded creams

Rehabilitation

Exercise, PT, and OT with modalities such as aquatic therapy, paraffin wax baths, desensitization techniques, manual massage, myofascial release techniques, ice, superficial heat, TENS unit, biofeedback, cryotherapy, stretching, general exercise, and trigger avoidance [4, 9, 10, 15, 16].

Procedures

Peripheral nerve block, ganglion block; secondary myofascial trigger point injection.

Surgery

None.

Other

Adaptive equipment, compression gloves, stockings, sleeves; adequate glucose control and monitoring of HgA1c levels; assessment of serum folate level, vitamin B12 level [17], and thyroid function for deficiency and need for supplementation;

evaluation for undiagnosed chronic neuropathies such as Charcot Marie Tooth (CMT), idiopathic forms, ETOH or toxin induced; evaluation of other comorbidities that cause or exacerbate neuropathy [10].

Evidence-Based Treatment

This type of neuropathy has proven difficult to manage and to treat. Many drugs have been tested, which include anticonvulsants, antidepressants, and compounded creams. Most randomized controlled trials testing a wide variety of drugs, with different mechanisms of action, have not proven to be efficacious [10]. Gabapentin was not effective in treating oxaliplatin-induced CIPN in a Phase 3 randomized, double blind placebo-controlled crossover trial in 2007 [18]. However, there is growing evidence that serotonin and norepinephrine dual reuptake inhibitors (SNRIs) may be effective in treating neuropathic pain [19]. First-line treatments for some clinicians include amitriptyline, duloxetine, and pregabalin with some basis stemming from trials or consensus statements [20–22].

Trials by Goldstein et al. (2005) and Wernicke et al. (2006) have demonstrated that duloxetine is an effective form of treatment for painful diabetic neuropathy. However, the best evidence for the use of duloxetine for CIPN came more recently through a phase 3 randomized placebo-controlled trial of 231 patients by Smith et al. in 2013 [23]. This study demonstrated that patients with painful CIPN, who used duloxetine as compared to placebo for 5 weeks, resulted in a greater reduction in pain (59% versus 38%). Additionally, their results suggested that patients who received platinum-based drugs experienced more benefit from duloxetine than those who were treated with taxane-based drugs.

This data led to the development of the American Society of Clinical Oncology Guidelines in 2014, which gave a moderate recommendation for the treatment of CIPN with duloxetine. However, the guidelines also recommended clinicians to provide education and to inform patients of the limited scientific evidence for the treatment of CIPN, potential side effects, and cost of the use of medications, such as tricyclic antidepressants, gabapentin, and pregabalin [6].

Just as other areas of medicine, genetic susceptibility has been explored for CIPN to attempt more individualized treatment based on genetic status. This may aid clinicians in prescribing more effective treatment in the future [24, 25].

Post-reconstruction/Post-mastectomy Syndrome

Natural History

Significant morbidity after surgical treatment for breast cancer has been well-documented. Some figures in the literature report that up to 68% of women will experience some level of impairment, which can involve shoulder pain, rib pain, decreased

range of motion, lymphedema, and neuropathy [26]. The incidence of post-mastectomy pain syndrome (PMPS) has been reported to range from 30 to 70% [8, 27–30]. According to the International Association of Study for Pain (IASP), post-mastectomy pain syndrome (PMPS) is pain of neuropathic origin, which is likely caused by peripheral neuropathy, often involving the intercostobrachial nerve [31, 32]. The lateral cutaneous branch of the second intercostal nerve is often resected during mastectomy and this nerve is reported to be injured in 80–100% of cases with axillary dissection. Tumor involvement or radiation fibrosis in the brachial plexus may also result in or contribute to PMPS [33]. Some evidence suggests that post-operative pain may also influence the development of chronic post-mastectomy pain [34]. This syndrome occurs following procedures performed to treat breast cancer, such as breast conserving surgery, breast reconstruction, or tumor enucleation [27, 29, 35]. However, this syndrome has also been reported in patients with only sentinel node biopsies, with sparing of the intercostobrachial nerve [8, 35, 36].

Recently, a cohort study by Couceiro et al. in 2014 examined the prevalence and associated risk factors of 250 women treated surgically for breast cancer. The results demonstrated a strong association of post-mastectomy pain syndrome (PMPS) in patients undergoing quadrantectomy with axillary lymphadenectomy, in patients with a prior history of headache, and in patients less than 50 years of age [37].

Pathophysiology

Pain, scar tissue formation, altered joint motion, venous/lymphatic congestion, neuropathy, plexopathy, and tendonosis are all possible etiologies, which may lead to rotator cuff impingement, adhesive capsulitis, complex regional pain syndrome, lymphedema, axillary web syndrome, contracture, and many other disorders.

Signs/Symptoms

Signs: scapular dyskinesia, glenohumeral restriction, loss or restricted range of motion, impingement syndrome, rotator cuff tendonosis

Symptoms: arthralgias, chest wall pain, shoulder pain, scapular pain, cervicalgia, intercostal brachalgia, axillary or arm swelling

Functional Limitations

Impairment in activities of daily living (ADLs, instrumental ADLs), ambulation, posture; restriction with spine or joint range of motion and/or flexibility; difficulty with self-care, driving, dressing, working, exercise; symptoms including arm fatigue, pain at rest, pain with wearing clothing, and sensitivity to temperatures.

Treatments

A significant proportion of treatment options are based on expert collective opinions, meta-analyses, case reports, anecdotal experience, small randomized clinical trials, or extrapolated from evidence of treatments for diabetic neuropathy, chemotherapy-induced neuropathy, herpetic neuralgia, or other types of pain.

Medications [11, 12, 20, 38–41]

Non-steroidal anti-inflammatory drugs

Ibuprofen, naproxen, meloxicam, celecoxib

Opioids

Tramadol, tapentadol, codeine, hydrocodone, oxycodone, oxycontin, methadone

Anticonvulsants

Gabapentin, pregabalin, venlafaxine, duloxetine, amitriptyline

Antispasmodics

Cyclobenzaprine, metaxalone, baclofen, tizanidine

Supplements

Glutamine, *N*-acetylcysteine, alpha lipoic acid, curcumin, metanx

Topical

Diclofenac, lidocaine, compounded creams

Rehabilitation

PT and OT with modalities; aquatic therapy; desensitization techniques; manual massage; myofascial release techniques; ice; heat; paraffin wax baths; cryotherapy; biofeedback; TENS unit; lymphedema therapy, if indicated; bracing; splinting; orthotics; compression garments; osteopathic manual medicine; exercise. Deep heat such as ultrasound or phonophoresis is generally contraindicated [15].

Procedures

Breast implant removal; breast tissue expander removal; chemo-port removal; neuroma resection; contracture release; peripheral or ganglion nerve block; spinal cord stimulator; intrathecal pain pump; cortisone injection; botulinum toxin injection; plastic or general surgery for scar tissue/adhesion resection; myofascial trigger point injection; pulsed high intensity laser therapy [42, 43].

Surgery

Pre-procedure rehabilitation; autologous fat grafting for scar adhesion release and tissue regeneration [44].

Other

Yoga; meditation; acupuncture; walking; rubbing or applying pressure to areas of pain; support groups with other survivors or community members [45].

Potential Treatment Complications

Deep vein thrombosis; bleeding; pulmonary embolism due to bone marrow dysfunction and impaired ability to form and break down clots inherent with cancer and related treatments in the setting of deconditioning or prolonged hospitalization; cellulitis; infection; worsening of lymphedema or edema; other side effects from medications listed above, which can include worsening fatigue, somnolence, dizziness, lightheadedness, insomnia, vertigo, serotonin syndrome from the interaction of multiple medications such as an antidepressant with another SNRI/TCA added for neuropathic pain; fragility fracture from osteoporosis or impending fracture from metastatic bone lesions.

The potential risks and benefits of pursuing any course of therapy must be carefully weighed. Physical or mental impairment can arise at any point in the disease or treatment process. Preventive counseling with education, prior to treatment or surgery, on understanding and recognizing potential symptoms will lead to the best outcomes.

Evidence-Based Treatment

Clinical studies yielding evidence-based recommendations remain scant. A few small studies with varying treatment are notable. In 2011, Caviggioli et al. treated patients with fat grafting surgery for PMPS with reduction in VAS pain scores in all 72 treatment arm patients at 1 year follow-up [44].

Shin et al. in 2014 completed a small non-controlled prospective pilot study of 19 patients with PMPS by treating myofascial trigger points in the subscapularis and pectoralis muscles with ultrasound-guided injections using lidocaine. They reported 74% of study patients rated their pain significantly lower on the VAS along with improved range of motion in both external rotation and abduction both post-injection and at 3 month follow-up [42].

In 2015, Ebid et al. reported on the long-term efficacy of pulsed high-intensity laser therapy (HILT) for PMPS. This study, which was double-blinded, placebo-controlled, and randomized, assessed 61 patients, for 4 weeks of HILT, undergoing three treatments per week. In addition, both the active and sham HILT groups were also enrolled in a routine physical therapy program. After completing HILT, and at the 12 week follow-up visit, they reported the active HILT group demonstrated a statistically significant improvement in shoulder range of motion, decreased pain, and increased quality of life compared to the sham HILT group [43].

Conclusion

Data from the available literature does support the use of medications and modalities for the treatment of neuropathic pain in the cancer rehabilitation setting. However, providers must balance the side effects and potential complications given the vulnerability of the oncologic patient population, which may be on active treatment. It remains widely believed that impaired sleep may worsen overall pain perception. Sleep disturbance can occur after starting new medications used to treat disorders discussed in this chapter. Otherwise, side effects may be mild and temporary. Benefits may outweigh common side effects of procedures and medications discussed in this chapter, which warrant discussion with the patient before discontinuing treatment.

Functional disorders responsible for pain and neurologic sequelae can limit quality of life long after completion of cancer treatments. Physiatry is an ideal specialty to continue the enhancement in cancer survivor treatment given its success with the treatment of disorders limiting function in all patient populations. Many patients require lifelong evaluation and treatment. There is a potential for complications along the continuum of care due to recurrence of cancer or related treatments. Moreover, there are now physiatrists sub-specializing in cancer rehabilitation, who will continue to establish new use of the physiatric skill-set and knowledge aimed at restoring or optimizing function to maximize quality of life in cancer survivors.

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Chapter 11
Pain in the Spine Rehabilitation Patient

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Introduction

Pain in the spine rehabilitation patient may occur from a single source or may be multifactorial in origin. The area of pain may involve the cranio-spinal junction, cervical spine, thoracic spine, lumbar spine, or sacrococcygeal region. Adjacent structures may also cause pain including atlanto-occipital joints, atlanto-axial joints, uncovertebral joints, zygapophyseal joints, costochondral joints, sternochondral joints, and ligamentum flavum. Pain originating in the spine and adjacent structures as a result of the degenerative cascade is one of the most common complaints in medicine today. Back pain, specifically low back pain, is the leading cause of disability throughout the world [1]. It is also the number one reason for missed work days [2]. An estimated 80% of adults will experience some form of back pain during their lives.

Psychosocial Factors

There are many psychosocial variables in the degenerative spine pain population. As back pain is the leading cause of disability in the world, the morbidity it creates places great stress not only on individual patients, but also on their families, as well as on the system as a whole. A report published by the Council for Disability

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Awareness demonstrates approximately 30% of greater than $130 billion in disability benefits was related to musculoskeletal disorders, including back pain. Of patients receiving these claims, over 75% received under $2000 per month in benefits. This places a majority of these patients at or below the national poverty level for a family of four [3]. Persons living in poverty are twice as likely to develop depression. This, coupled with the high prevalence of depression and chronic back pain, is significant. Since opiate medications remain one of the most powerful and common analgesic options, the risk of opiate abuse is significantly increased [4, 5].

Anxiety disorders manifest with many salient characteristics and have significant implications in spinal pain. These features include doubt, inability to cope, and increased body awareness, which can lead to increased anxiety about their condition, subsequently leading to pain catastrophizing [5]. Even if the patient does not meet diagnostic criterion for a type of anxiety disorder, they may still exhibit many of these characteristics to some degree [6].

It is important that the treatment and management of degenerative spine pain patients be multifactorial in its approach, especially with respect to the aforementioned psychological components. Treatment of the psychological implications and consideration of the associated social issues must be integrated in the treatment of the physiological conditions.

Pathophysiology

The spinal column is a complex anatomical structure. It is comprised of bone, ligaments, muscles, tendons, discs, and cartilage. Degenerative conditions may affect one or all of these components. In the initial stages of an injury, patients may present with a narrower range of affected structures. As a patient's condition ages, degeneration increases and may manifest with several of the conditions below.

Spondylosis

Spondylosis is a general term for degenerative osteoarthritis of the vertebrae. It may occur at the facet joints, neural foramen, lateral recesses, central canal, or at the vertebral endplates. It results from a change in the normal anatomical weight distribution on the spine. It may result from poor posture, repetitive movements, or any injury to the spine or muscles, which support the spine. The change in weight distribution causes excess bone growth. Degenerative changes occur over many years. Poor posture, muscle weakness, or injury to a spinal muscle results in a change in the normal spinal curvature, which can lead to either increased or decreased kyphosis or lordosis. The constant abnormal pressure on the facet joints and discs results in excess bone growth.

Injured discs frequently result in spondylosis. A disc which loses its elastic properties from disc displacement places significant stress on the facet joints, as well as the vertebral endplates. Excess bone growth occurs at both affected endplates to

support the damaged disc. This also occurs at the superior and inferior articulating processes to support the stressed facet joints. The resultant bone is abnormal and forms at the regions of most stress.

Spondylosis will continue to occur, as long as abnormalities exist in the normal anatomic weight distribution of the spine. As the degeneration progresses, excess bone growth may impede vital components of the vertebrae. Resultant arthritis of the facet joints limits range of motion, alters weight distribution, and causes axial pain. As arthritis occurs around the disc at the endplates, neural compromise becomes a concern. The neural foramina may become infiltrated, or the lateral recesses and central may become stenotic.

Spondylolisthesis

Spondylolisthesis is the displacement of a vertebral body. Listhesis occurs after a fracture of the pars interacticularis (spondylolysis); most commonly, L5 displaces anteriorly over the sacrum. Another common form is Hangman's Fracture, a traumatic spondylolisthesis occurring at C2–C3, as the result of severe subluxation from hanging, car crash, or trauma from a sports injury. These events result in fracture of the pedicles and pars interarticularis of the C2 vertebrae and anterior displacement respective to C3. Anterior displacement causes encroachment on the central canal, stretching of the interspinous ligaments, including the ligamentum flavum; thereby resulting in further instability, pain, and radicular symptoms.

Spondylolysis

Spondylolysis is an injury over the area in the vertebral arch between the superior and inferior articulating processes, the pars interarticularis. The injury most commonly results from strenuous sport or exercise, whereby the spine is hyperextended and rotated repeatedly. This repeated motion can lead to development of a stress fracture in the pars interacticularis, contralateral to the active side. It most commonly occurs in younger, extremely active populations [7]. Participants in certain sports are also more at risk. Repeated vigorous unilateral rotational motion, such as in tennis or football, and repeated hyperextension in gymnastics and cheerleading commonly result in the development of spondylolysis [8]. The injury most commonly occurs in the lower lumbar spine at the L5 vertebrae where the lumbar lordosis transitions to sacral kyphosis, whereby the sacrum is also immovable placing a great deal of stress upon the L5-S1 facet joints [9].

Although many instances of spondylolysis are asymptomatic, which therefore may go untreated unless found through focused examination or imaging, a consequence of the fracture includes weakening of the facet joint, which in turn decreases the spine's ability to maintain alignment. Untreated or severe cases may progress to

spondylolisthesis [10]. When listhesis occurs, further symptoms develop. Facet injury, disc injury, and central canal impingement may occur.

Most instances of spondylolysis are treatable by conservative means, such as activity restriction, bracing, core strengthening, and in the most severe cases, surgery. Most commonly, treatment involves a multi-modal approach, including activity restriction, bracing, and physical therapy regimens focused on strengthening the core. It is vital to avoid any activity which puts undue stress on the spine, such as bending, twisting, heavy lifting, or the activity which caused the injury itself. An anti-lordotic brace worn for short periods each day may relieve symptoms by reducing load on the injured site, placing the spine in slight flexion. The brace is tightly fitted and very rigid, which also limits range of motion. Recovery can be 6–12 weeks depending on severity [10]. Since this injury most commonly occurs in younger highly active individuals, the duration of restriction is vital in the overall rehabilitation process.

Zygopophyseal (Facet) Arthropathy

Zygapophyseal (facet) arthropathy is any disease of the facet joints. It may be from inflammation, arthritis, or complete joint degeneration. Zygapophyseal arthropathy usually manifests as pain localized over the particular facet joint. It is frequently defined as axial, or non-radiating back pain, which is made worse by extension and rotation. As arthropathy progresses, bone spurs may develop from osteoarthritis, which increase pain, inflammation, and decrease range of motion. The formation of bone spurs is known as facet hypertrophy. These spurs may develop on the anterior portion of the joint and can result in encroachment on the spinal canal, resulting in lateral recess and foraminal spinal stenosis. Absence of identified arthropathy on common imaging techniques, such as radiography and MRI, does not rule out the zygapophyseal joint as a potential pain generator. Pain is usually localized over the affected joints; however, pain across the neck, shoulders, and posterior head is commonly associated with cervical facet arthropathy [11]. Pain referred across the shoulders, posterior ribs, and flanks is common from thoracic facet arthropathy [12]. Lumbar facet arthropathy may present with referral pain across the low back, into the buttock, and posterior legs above the knee [13].

Third Occipital Nerve (TON)

The third occipital nerve is the superficial medial branch of the C3 dorsal ramus. It provides sensory enervation to the posterior neck as well as cutaneous tissue of the sub-occipital region, which is a common region of headaches. This nerve also enervates the C2–C3 zygapophyseal joint. Arthroparthy of this joint from osteoarthritis, or from whiplash injury, may result in irritation of the TON, causing referred pain in the sub-occipital region.

Cervicalgia/Cervicogenic Headache

The atlanto-occipital (AO) joint and atlanto-axial (AA) joint are common sources of occipital headaches; however, these syndromes are frequently undiagnosed due to the absence of any non-invasive testing to confirm pain generation. The only diagnostic test is infiltration of a local anesthetic into the joints, in order to assess reduction of pain in the region. These joints are small articular joints, different in structure to the zygapophyseal joints; however, similar pathologies may afflict these joints. AO and AA pain may result from osteoarthritis, inflammation, or injury. Whiplash is a common mechanism for AO and AA pain. Headaches are the most common complaint associated with AO and AA arthropathy. The AO joint is innervated by the C1 ventral rami. The AA joint is innervated by the C2 ventral ramus. Both nerves branch from the trigeminocervical nucleus, which receives afferent input from the upper spine and head. For this reason, referred pain patterns across the upper cervical, suboccipital, mastoid, and even temporal regions may result from AO and AA joint arthropathy [14].

Pathology of the AO and AA joints, as well as the upper cervical facet joints innervated by branches from the trigeminocervical nucleus, may cause cervicogenic headaches. It is hypothesized and repeatedly concluded that the overlap of continued grey matter from the upper spinal dorsal horn and the afferent fibers of the trigeminal nerve in the pars caudalis may be involved [15]. The nociceptive input from the upper cervical nerves causes a misinterpretation at higher brain centers, resulting in pain not only in the watershed of the cervical nerve, but also the trigeminal nerve [16].

Lateral Recess Spinal Stenosis

The medial aspect of the neural foramen is the lateral recess. The pedicles form the posterior aspect of the neural foramen, the vertebral body, and the anterior aspect of the disc. In the middle of the posterior aspect of the foramen are the facet (zygapophyseal) joints. Stenosis of the lateral recess is caused by bone spur encroachment. Facet arthropathy can lead to bone spur formation. Disc pathologies may also lead to the formation of bone spurs at the endplates. These bone spurs narrow the doorway for the nerve to exit the spinal column, leading to radicular symptoms in the dermatome of the exiting nerve root, or may impinge upon a descending nerve root, leading to radicular symptoms in the corresponding dermatome. Because the facet joints, vertebral bodies, and discs form the entire neural foramen, bone spurs are not limited to formation at the lateral recess. Lateral recess stenosis is usually accompanied by foraminal stenosis, and in some cases, central canal stenosis.

Foraminal Spinal Stenosis

The pedicles form the posterior aspect of the neural foramen, the vertebral body, and the anterior aspect of the disc. In the middle of the posterior aspect of the foramen are the facet (zygapophyseal) joints. Foraminal stenosis is caused by bone spur formation in any or all of these structures, which encroach on the lateral aspect of the neural foramen. It is commonly accompanied by lateral recess stenosis, and likely present if there is central canal stenosis. Foraminal stenosis, like lateral recess stenosis, causes radicular symptoms in the dermatome of the exiting nerve root.

Central Spinal Stenosis

The central canal is formed by the lamina and vertebral bodies, discs, and ligamentum flavum. Damaged or bulging discs may result in the formation of bone spurs on the posterior aspect of the vertebral endplate. These bone spurs may encroach upon the central canal, causing stenosis of the anterior portion. Furthermore, with age, the ligamentum flavum loses elasticity and becomes hypertrophic. This hypertrophy encroaches on the posterior central canal. Radicular symptoms result from canal encroachment. Stenosis may occur in the posterior canal, anterior canal, or along the lateral canal in the vicinity of the medial aspects of the lateral recess. Resultant radicular symptoms may be unilateral or bilateral and may affect the dermatome corresponding to the stenotic canal level.

Dorsal Root Ganglion

The dorsal root ganglion (DRG) is located within the foramen of each nerve root. It is the collection of nerve soma from the root dermatome. The DRG receives afferent signal from the distal nerve and transfers these signals to the spinal cord. As a collection of nerve bodies, it is slightly larger in diameter than the rest of the nerve root. Since it lies in the foramen and is slightly larger, the DRG is especially vulnerable to stenosis. Bone spurs from the facet joints, vertebral endplates, or encroachment from the discs may compress or damage the DRG. Dermatomal pain, weakness, and numbness are common symptoms.

Scoliosis

Through congenital defect, injury, neuromuscular condition, or degeneration of idiopathic origin, the spine may deform in the sagittal plane or coronal plane. A sagittal deformity is scoliosis, where the spine develops curvature laterally, rather

than the normal anterior-posterior S shape. Coronal deformity is either called kyphosis, whereby the normal thoracic kyphosis is increased, or decreased lordosis, whereby the lordosis of the cervical and lumbar spines decreases.

Congenital scoliosis results from abnormal segmentation of the vertebrae during the first trimester in utero. Vertebral bodies may not form completely, may not segment, or may not segment completely, all of which can result in vertebral segments fused bilaterally or unilaterally, or in partial and complete malformations of one or several vertebral bodies. The abnormal structure causes a lateral curvature of varying severity [17]. The progression of congenital scoliosis depends on many factors, which include the type and significance of abnormal segmentation.

Neuromuscular scoliosis is caused by numerous conditions, which affect the brain, spine, and musculature of the spine. Upper or lower motor neuron disorders, which include cerebral palsy, poliomyelitis, and myopathic conditions, which include thoracic myelodysplasia, have exceptionally high instances of neuromuscular scoliosis. Neurological injury from trauma, especially if resulting in paralysis of the spinal musculature, progresses to scoliosis in every instance over 10 years [18]. A condition that affects the muscle tone of the spinal musculature, particularly of the thoracic spine, may hasten the onset of neuromuscular scoliosis. Neuromuscular scoliosis is the most rapidly progressing form of scoliosis and frequently needs surgical correction.

Idiopathic scoliosis accounts for the majority of cases. In these cases, there is no causative injury, congenital condition, or comorbidity. Idiopathic scoliosis is most commonly diagnosed during puberty as adolescent idiopathic scoliosis (AIS).

Minor curvatures typically do not manifest with pain, neuropathy, or organ impingement, thereby such curvatures are usually diagnosed following adolescent school screening, as an incidental finding on a physical exam, or from radiography. Patients with more severe curvature may develop pain and eventual difficulty with breathing. Curvature is measured by a Cobb angle, which is the angle of the intersection of the line of the superior endplate of the cephalad end of the curvature and the line of the inferior endplate of the caudad end of the curvature. Most cases manifest less than a 20-degree Cobb angle and are only observed for progression. As the curvature progresses past 20°–25°, a brace and therapy is warranted. Individuals with higher risk of curve progression are in greater need of therapy and bracing. Therapy and bracing is focused on offloading the curvature, while training the patient to feel comfortable in performing activities of daily living with the curve off loaded and the angle slightly reduced [17]. When the Cobb angle progresses to 40° or greater, surgery may be indicated [19].

Scoliosis may also manifest in adults secondary to comorbidities, which include degenerative disc disease, facet hypertrophy, and spondylosis. Since the lumbar spine is most commonly affected by these disorders, adult degenerative scoliosis manifests most commonly in the lumbar spine [19]. As the discs, ligaments, and zygapophyseal joints lose stability and integrity, the musculature of the back causes a curvature. This curvature increases as the degeneration increases [17]. Other forms of scoliosis are not frequently associated with severe pain. Degenerative scoliosis, accompanying any number of degenerative spine conditions, frequently results in both axial and radicular symptoms, which may or may not be more severe on one side versus the other.

Vertebral Compression Fractures

Vertebral compression fractures are frequently the result of bony pathologies causing decreased density, as can occur in post-menopausal women. The cause may be a minor trauma, such as a short fall. Otherwise, fractures may develop over time, with anterior or lateral flexion, due to significant loss in bone density. The vertebral body lacks the strength to support the load of the spine above it, resulting in compression and loss of vertebral height in the anterior column. The compression results in a wedge shape, sloping posterior to anterior, whereby the posterior column is usually unaffected. If the posterior column is affected, neurological symptoms such as radiating pain in the corresponding dermatome may ensue.

Typically, pain is localized to the region surrounding the affected vertebral bodies. Compression fractures are usually managed with conservative measures first. Many patients live with the condition without surgical intervention. Pain usually diminishes over time as the bone heals in the compressed state. Immobilization with rigid LSO or TLSO bracing is used in conjunction with pain medications and physical therapy, which is focused on strengthening and supporting the core musculature. Therapy also includes supplements to address decreased bone density, with the goal of prevention of worsening fracture or development of new fractures.

If pain is not relieved by conservative means, surgical intervention is appropriate before the condition reaches the chronic stage. Minimally invasive surgical procedures, such as vertebroplasty or kyphoplasty, are performed. In the vertebroplasty procedure, a catheter is used to inject cement directly into the affected vertebral body to stabilize the fracture and to relieve pain. There is no restoration of vertebral height with this procedure [20]. With kyphoplasty, a balloon is inserted into the vertebral body and inflated to restore the vertebral body to its natural height. The cavity is then filled with cement to stabilize the fracture and to relieve pain [21]. For further reference, please see dedicated chapter on vertebral augmentation.

Retropulsion of fragments, as a result of the fracture, may cause neural compromise. Depending upon the size and degree of retropulsion, neurosurgical intervention may be required in lieu of the minimally invasive approaches listed above.

Vertebral Burst Fracture (Traumatic)

When the spine undergoes a sudden and severe axial load, such as from a fall landing on the feet or the head, causing a compression force greater than the vertebral bodies are able to support, burst fracture occurs. Significant axial load causes compression of the vertebral body, impacting the anterior, middle, or posterior vertebral columns. Most fractures also involve the destruction of one endplate; in some cases, both vertebral endplates are involved [22].

Burst fractures vary in severity, which depends on the mechanism of injury, the number of vertebrae and vertebral columns involved, and the degree of neural compromise. There are various classification systems available to predict spinal

instability from burst fractures. There are differing indications for surgical versus non-surgical intervention. Due to the forces needed to cause a burst fracture, hospitalization is required with concomitant imaging to facilitate appropriate classification. AP and lateral plain films are typically the first line imaging obtained. CT scan can accurately diagnose the impact of fracture on the spinal canal and can identify fragmentation. Magnetic resonance imaging may also be used to diagnose associated soft tissue injuries [23].

If the risk of spinal instability is minimal, non-surgical interventions may be used, which include body casts, TLSO bracing, and long-term bed rest. Wood et al. (2003) found no significant difference in the long-term outcomes of patients with stable burst fractures using surgical versus non-surgical intervention; however, there was a significantly reduced cost with non-surgical interventions [24]. Unstable fractures, and those with neural compromise, require surgical intervention to preserve the integrity of the canal and to stabilize the spinal column.

Spinal Disc Injuries

The spinal discs are a common and significant pain generator of the spine. The disc is made of a strong, fibrous shell, called the annulus fibrosus, which contains a gel-like central material called the nucleus pulposus. The annulus is comprised of several laminae of strong fibrocartilage, which contain the nucleus to provide a strong yet flexible shock absorber to counteract compressive loads on the spine. Spinal discs, also known as intervertebral discs, function to separate each vertebral body, distributing weight evenly across the entire vertebral body and disc. Uneven pressure as the result of poor posture, severe compressive load such as lifting a heavy object, or other significant axial loading injury may cause damage to the intervertebral discs.

The disc may bulge, whereby the outer annulus is not compromised, but the nucleus disseminates into the interior laminae, which results in abnormal shape, change in weight distribution, and resultant progression to disc protrusion. This protrusion may compromise neural roots, the central canal, or may have no neural affect. Similarly, if there is force significant enough to rupture the disc, or if degeneration is severe enough, the lamellae of the annular tear, resulting in the leaking of the nucleus pulposus, which is called a disc herniation [25]. Degeneration due to aging also results in damage to spinal discs. Degenerative disc disease is the natural dehydration of the nucleus pulposus, which causes weakening of the annulus due to age, with the greatest incidence in people over the age of 40 [26].

If the herniation or bulge does not impinge a nerve root or leak nuclear material near neural tissue, there may be little to no pain from injured discs. Schmorl's nodes occur when the disc bulges into the adjacent vertebral body, potentially through to the marrow of the vertebrae. These nodes may either be asymptomatic or cause significant inflammation and axial back pain [27]. However, if the bulge impinges on the central canal or nerve roots, there may be significant tissue irritation and radicular symptoms similar to spinal stenosis. If the nucleus pulposus herniates into

the central canal or surrounding neural tissue, chemical radiculitis may ensue whereby cytokines (phospholipase A_2) present within the nucleus encourage inflammation in surrounding tissue, including nerve root sheaths, resulting in symptoms of radicular pain, paresthesias, and weakness [28].

Sacroiliac Joint Pain

The sacroiliac joint (SI) is a diarthrodial joint between the sacrum and the ilium, bilaterally. These two joints are responsible for supporting the entire weight of the torso. A normally functioning SI joint is joined by many strong ligaments, superficially, and deep within the joint, both anterior and posterior to the sacrum. These ligaments maintain joint stability from all angles. A number of factors may influence SI joint compromise. Acute injuries to the pelvis may stretch the ligaments, resulting in hypermobility. Uneven musculature of the low back or changes in normal spinal curvature, such as decreased lumbar lordosis, alters the normal weight distribution throughout the SI joint, also resulting in hypermobility. Disorders of the SI joint may also develop as the result of altered weight distribution from lumbar and lumbosacral fusions [29]. Women may experience pain in the sacroiliac joint after or during pregnancy due to hormonal changes, or during the vaginal birth of a large baby [30].

Patients may present with pain in the SI joint without radiological findings as the result of inflammation. When the condition becomes chronic, long standing arthritis may develop with associated radiological findings. In severe degenerative cases, the joints may ankylose. The SI joint is also affected in cases of ankylosing spondylitis. Rest, ice, and NSAIDs are the typical first-line treatment of SI joint pain in the acute stage, especially if a specific injury can be identified. If pain continues for extended periods, SI joint belts may be worn to provide support and to prevent further ligamentous deterioration. Physical therapy exercises, focused on strengthening and balancing the surrounding musculature, may relieve SI joint pain and prevent reoccurrence. Chiropractic and osteopathic manipulation of the SI joint are also common treatments. Steroid and anesthetic injections into the SI joint and the surrounding ligamentous tissue temporarily relieve symptoms and inflammation. Pain diminishing after administration of anesthetic also acts as a diagnostic tool, confirming the SI joint as a pain generator. In some cases, where there is significant joint instability, or when pain is refractory to injections and other modalities, an SI joint fusion is performed. Different combinations of metal hardware and bone grafts are used to fuse the joint, stabilizing and eliminating motion. Some patients still experience long-term pain after SI joint fusion, at times requiring re-operation or leading to chronic pain [31]. For further details, please refer to the dedicated chapter on SI joint dysfunction.

Other Pain Considerations in the Degenerative Spine Patient

Cluneal Nerve Pain

The cluneal nerves innervate the low back and buttocks region. The superior cluneal nerves are most commonly associated with low back pain. These are the terminal branches of the lateral dorsal rami of L1-L3. These nerves wrap posteriorly over the posterior iliac crest, passing through the thoracolumbar fascia. At this junction, nerve entrapment may occur, causing pain in the region of the distal branches of the nerve, along the low back and upper buttocks [32]. This pain is often misdiagnosed as being spinal in origin. Anesthetic blocks of these nerves confirm the diagnosis, and steroid injections along the iliac crest may reduce entrapment caused by inflammation. Surgical neurolysis of the cluneal nerves, after anesthetic confirmation of pain relief, may also be performed as permanent treatment of cluneal nerve pain [33].

Rib Pain

The costovertebral joints may be affected by osteoarthritis, as with any other joint. The ribs join the vertebrae in two locations: at the body of the thoracic vertebrae and along the transverse process, except the eleventh and twelfth ribs, which are only joined at the body. These joints allow for gliding of the ribs back and forth to account for expansion during breathing. These joints are innervated by the intercostal nerves. Dysfunction of this joint can lead to pain along the entire affected course of the intercostal nerve to the anterior chest wall.

Costovertebral joint dysfunction should be considered in cases of atypical chest pain, as referred pain from the joint and intercostal nerves may present similarly to visceral pain throughout the chest. A condition known as costochondritis may develop, which can lead to unnecessary and expensive cardiac and pulmonary work ups. Costovertebral joint dysfunction may result from massive intra-thoracic forces created by coughing or sneezing, as seen with respiratory infection [34]. Costovertebral joints and intercostal nerve damage should be considered as a source of pain in patients who undergo thoracotomy, resulting in a condition called post-thoracotomy pain syndrome [35]. The sternocostal joint may also be affected by thoracotomy procedures, chest trauma, repeated coughing, sneezing, or vomiting in a similar manner to the costovertebral joints. In rare cases, some patients may also develop inflammation of the cartilage in these joints, resulting in pain. It may be of viral origin or from any of the aforementioned causes. This inflammation is distinct from costochondritis and is known as Tietze syndrome [36].

Coccydynia

After a fall, childbirth, or prolonged pressure on the coccyx, from prolonged sitting, pain may develop in the coccygeal region. A sudden fall and childbirth may cause partial or full dislocation of the saccrococcygeal joint, which results in stretching of the ligaments and abnormal movement of the coccyx. This abnormal movement causes inflammation of the tissues and resultant localized pain. This pain usually increases when sitting or lying in a supine, fowlers, or semi-fowlers position [37]. The incidence of coccydynia is higher in obese individuals [38].

Treatment

There are numerous treatment considerations in degenerative spine pain patients. Throughout the entire treatment algorithm, psychosocial factors should be considered. The first line of pain treatment is usually medication. There are many therapeutic options; however, whatever approach is taken should be multimodal. Goals should be set with patients to include increased activity, decreased pain, and decreased symptom duration. Setting goals with the expectation of no pain leads to patient disappointment, anxiety, and increased requirement of medication. In most cases, treatment should progress from the least invasive to the most invasive option. This course is obviously altered if significant neural compromise should develop, as seen with some cases of burst fracture or spodylolysis, which may require immediate surgical intervention. Even after surgery, patients are still at risk of developing a number of the aforementioned conditions and a similar algorithm should be followed.

Medications

Topical

Topical medications, applied directly overlying the area of pain, are frequently used; however, consideration to the patient's individual insurance plan should be made due to the potential high cost and limited coverage of these medications for use with back pain. Topical medications, which are usually a combination of compounded or non-compounded single or combination oral medications, often have fewer systemic effects than their oral counterparts. Topical medications such as the anesthetic Lidocaine and non-steroidal anti-inflammatory drug Diclofenac are some of the most common. Side effects from these medications are limited to the application site, and there are little to no systemic effects [39]. There are also a number of pharmacy-compounded topical creams containing combinations of muscle relaxers,

anesthetic, and neuropathic agents. These are similarly applied to affected regions, providing similar or better relief than single medication creams such as Diclofenac [40]. Specific attention should be paid to concentrations of each component; however, while systemic symptoms are significantly reduced, toxicity is still a concern if topically applied in high enough concentrations [41].

NSAIDs, COX-2 Inhibitors, and Other Anti-Inflammatory Agents

Non-steroidal anti-inflammatory drugs, NSAIDs, such as Ibuprofen and Naproxen, are typically over-the-counter medications and frequently the first medication taken by patients in pain. These are also referred to as non-selective cyclooxygenase (COX) inhibitors. They target both COX-1 and COX-2 enzymes, which are responsible for the production of prostaglandin and thromboxane, both associated with inflammation. COX-2 is mostly associated with inflammation causing pain, while COX-1 is associated with mucus production, specifically gastric mucus. Peptic ulcer formation and gastrointestinal bleeding are risk factors for long-term NSAID use. Meloxicam, while still considered non-selective, has less effect on mucus production than other NSAIDs [42]. COX-2 inhibitors have minimal effect on gastric mucus production; thus, gastrointestinal side-effects are limited. The increase of vascular side-effects, such as myocardial infarction and stroke as the result of COX-2 inhibitors, must be considered [43]. Acetaminophen is also considered, although it is most frequently combined with other drugs such as opiates. Hepatic function should be considered in patients on long-term acetaminophen.

Opiates and Synthetic Opiates

As back pain is so prevalent, it is one of the highest reasons for use of opiates. Many opiates are available with a similar mechanism of action, binding to mu, kappa, and delta receptors in the central nervous system causing analgesia. However, each patient metabolizes these and other medications differently.

Pharmaco-genomic testing should be considered for patients who complain of inadequate analgesia or analgesia not lasting appropriately. This allows the prescriber to identify which opiates would be metabolized most appropriately by the patient, providing the most predictable analgesia. This genetic test need only be performed once in a patient's lifetime, which tests multiple enzymes present within the patient's liver. Other options should be considered before initiating an individual on long-term opiate therapy for a number of reasons, which are widely published. In certain cases, degenerative spine patients do require long-term opiate medications to live comfortably and maintain function. Due to the likelihood of comorbid

psychological factors in this patient population, these patients should be carefully monitored. Stress should be made on the fact that due to the condition of the patient's spine, they may not be completely pain free.

Therapy

Back health is extremely important in being able to participate in activities of daily living (ADLs). Degenerative spine pain patients may feel severely limited due to pain. In certain cases, range of motion may be physically limited from the severely degenerated spine. Many targeted therapies have already been mentioned, with respect to a specific pathophysiology. In general, physical therapy, aqua therapy, and occupational therapy should focus on exercises that strengthen and support the affected degenerative regions. This muscular support will in turn reduce stress on the spinal column. Therapies should also focus on managing ADLs, either by educating the patient how to alter his or her ADLs due to the condition, or by redeveloping musculature and realigning posture to perform ADLs with less pain. Please see dedicated chapters on physical and occupational therapy.

Minimally Invasive Therapy

By and large, the most frequently performed treatments of the degenerative spine include minimally invasive therapies, such as epidural injections, radiofrequency lesioning, and nerve blockades. These therapies are generally performed before surgery is recommended, for both diagnostic purposes and therapeutic purposes to manage symptoms related to degeneration of the spine.

Epidural Steroid Injections

The epidural steroid injection is a very common procedure, whereby a corticosteroid is injected into the epidural space, outside the thecal sac. Placing steroid directly over the affected tissue, or as close as possible to it has many effects. These effects include controlling localized inflammation and improving microcirculation, which in turn reduces edema, blocks neurotoxic phospholipase A_2, and stabilizes the neural membrane blocking the conduction of c-fiber nociception [44]. These injections are used for patients with radicular symptoms, such as chemical radiculitis, painful radiculopathy, and complex regional pain syndrome. There is limited research to support the use of epidural steroid injections for axial pain; however, due to the close proximity of the facet joints and epidural space, there may be some therapeutic benefit [45].

There are many approaches to the epidural steroid injection. Generally broken into three categories, interlaminar, transforaminal, and caudal, these correspond to the location they are injected. Interlaminar epidural injections are placed between the lamina delivering the steroid solution directly around the central canal. The medication flows cephalad and caudad from the location of injection in the epidural space, which covers multiple sites of pathology. Medication commonly spreads several levels in the central canal, into the lateral recesses and in some cases to the neural foramina [45]. Fluoroscopic guidance and contrast should be used, providing an epidurogram to evaluate success or failure of the injection. The needle may be redirected if contrast is unilateral or not sufficiently spreading. In the degenerative spine patient, spondylosis may disrupt the needle entry site. The ligamentum flavum may also be abnormally dense or flaccid, making needle entry difficult [45, 46]. Injections may be done at any level in the lumbar and thoracic spine; however, due to the extremely minimal posterior epidural space of the cervical spine, interlaminar injections are seldom performed above the C7-T1 interspace [46].

If pain relief from interlaminar epidural injections is inadequate, or if the pain and associated diagnostic findings are localized to a few nerve roots, a transforaminal approach may be indicated. Cervical transforaminal injections may be performed as cephalad as the C2–C3 foramen [46]. In this case, a needle is passed into the tissue surrounding the nerve root where it exits the neural foramen. Fluoroscopy and contrast is used to ensure proper placement and medication uptake into the epidural space. Digital subtraction angiography may also be employed to ensure no vascular uptake. A radiculogram should show contrast along the exiting nerve root, through the neural foramen, the lateral recess, and in many cases into the central canal spreading more than one vertebral level. Despite this spread, the treatment effect is generally limited to where the medication is able to reach a high enough concentration. If pathology exists across many levels or bilaterally, the patient may require multiple injections. Patients often experience mild concordant pain during this injection, as the medication is delivered directly around the irritated nerve root. A transforaminal approach may also be used for diagnostic purposes as a selective nerve root block (SNRB). A SNRB administers a local anesthetic around the desired nerve root. If the patient's pain is replaced with numbness, the injection is diagnostic for specific nerve root involvement.

The caudal approach is performed at one location, through the sacral hiatus. With this approach, there is minimal risk of dural or vascular puncture. In patients presenting with low back and radicular symptoms status post-spinal surgery, the caudal approach may be preferred due to the alteration in the ligamentum flavum, which may occur from surgery [46, 47]. The caudal approach treats multilevel lumbosacral radicular symptoms, but has little effect on sacroiliac or lumbar facetogenic pain. Fluoroscopic guidance and contrast is recommended for this injection, although there is a viable blind technique [47]. The epidurogram should show contrast spreading bilaterally over several levels of the sacrum and into the lumbar epidural space.

Zygapophyseal (Facet) Treatments

There are a number of minimally invasive therapies for zygapophyseal joint pain. Both therapeutic and diagnostic injections may be performed for facetogenic pain. The zygapophyseal joints, innervated by the medial branches, are responsible for axial, non-radiating pain. One of the most common procedures for the treatment of axial pain is radiofrequency ablation, which is also referred to as RF rhyzotomy or neurotomy. Destruction of the medial branch is done by application of radiofrequency energy through a cannula overlying the nerve. Prior to lesioning, stimulation ensures capture of the multifidi muscles and absence of motor spinal nerve root stimulation to ensure that only the medial branch is targeted. This procedure provides long-term denervation to the targeted facet joint. Although RF ablation is very common, it is not typically the first line of treatment. Prior to RF treatment, the medial branches should be blocked diagnostically with local anesthetic to ensure the correct pain generators are targeted [48]. Medial branch blocks and associated radiofrequency ablation may also be performed at the third occipital nerve for the treatment of headaches.

Similar to orthopedic joint injections, corticosteroids and/or local anesthetics may be delivered directly into the zygapophyseal joints. These injections may be done at any level throughout the cervical, thoracic, or lumbar spine, providing relief of axial pain at the affected levels. Although the joints are of differing structure, the concept is similar for atlanto-axial and atlanto-occipital joints in the treatment of cervicogenic headaches.

Sacroiliac Treatments

The sacroiliac joint is innervated by lateral branches of the sacral dorsal rami. Lateral branch blocks may be performed with local anesthetic as a diagnostic tool for SI joint pain. If these injections are therapeutic, but pain returns, the lateral branches may undergo radiofrequency lesioning [48]. The SI joint may also be directly injected with a combination of corticosteroid and local anesthetic.

Neuromodulation (Neurostimulation)

Neuromodulation, spinal cord stimulation, and peripheral nerve stimulation are the latest therapies available to the degenerative spine patient. The exact mechanisms of action are unknown; however, it is generally understood that the nociceptive pain signals are interrupted due to nerve depolarization caused by electrical stimulation. Therefore, the patient feels pleasurable paresthesia in place of neuropathic pain [49]. As many degenerative spine pain patients suffer from chronic pain, neurostimulation has many applications in the treatment of such conditions.

Stimulation is carried out by leads connected to a pulse generator, similar to a pacemaker. These leads have a variety of contact patterns, ranging from 4 to 16 on each lead. The leads may be wire-shaped for minimally invasive percutaneous insertion or paddle-shaped for surgical implantation. The leads are placed in the posterior epidural space overlying the origin of the targeted nerve roots. Leads may be placed at any level of the cervical, thoracic, lumbar, and sacral spine in the epidural space, depending upon the targeted pain regions. Epidural spinal cord stimulation is most commonly used for treatment of neuropathic pain, such as radiculopathy and complex regional pain syndrome. Mechanical pain, such as facetogenic and sacroiliac pain, is difficult to treat with epidural spinal cord stimulation. More recently, high frequency non-paresthetic stimulation and dorsal root ganglion stimulation have been introduced for the treatment of spinal and radicular pain.

Peripheral nerve stimulation may be performed for the treatment of such conditions, in which the stimulation leads are implanted in the fascial layers directly overlying the dorsal rami leading to the facet joints or the sacroiliac joint. Nociception is interrupted due to depolarization of the afferent nerve fibers innervating the joints, resulting in a paresthesia rather than pain.

Other minimally Invasive Therapies

With patients on chronic opiate therapy, or with patients requiring analgesia without the systemic effects of opiates, certain medications may be injected via an intrathecal pump. These pumps have a reservoir, which is filled with medications directly administered into the thecal sac to affect the central nervous system directly. FDA-approved medications include Morphine, Ziconotide, and Baclofen; among other non-FDA-approved medications, Bupivacaine and Fentanyl are delivered at very controlled rates through a catheter into the thecal sac.

Epidural adhesiolysis is usually performed in post-surgical patients who develop adhesions and epidural fibrosis. As many degenerative spine patients may undergo one or many surgeries, post-surgical scarring can increase some degenerative spine symptoms. Adhesiolysis eliminates the fibrotic tissue with administration of a hypertonic solution directly injected over the area. Contrast flow noted in Radiculograms and epidurograms may improve after this procedure, complimenting therapy of epidural steroid injections.

Surgical Options

In certain cases, the degenerative spine pain patient may need to undergo surgery, usually performed by orthopedic spine or neurosurgeons. Typically, surgery is indicated if function is severely limited and there is potential for neural compromise. Depending upon the condition, the goals of the surgical procedure are usually

decompression and stabilization. In the event of significant neural compromise and compression, decompressive procedures, such as discectomy and laminectomy, are performed. In cases of diminished spinal stability or severe deformity, as presents with spondylolisthesis or severe scoliosis, spinal fusions are performed. There are a number of surgical options. Please see dedicated chapters on neurosurgical and orthopedic procedures for pain.

Conclusion

The degenerative spine pain patient may present with multiple degenerative conditions, as well as comorbidities, which make treatment and management challenging. For this reason, the treatment regimen must be multifactorial, focused on reducing pain, increasing function, and returning to activity. Treatment options are vast. It is therefore important to understand that the degenerative spine pain patient may not be pain free from therapy and that treatment goals should be individualized for optimal outcomes.

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Chapter 12
Pain in the Pelvic Rehabilitation Patient

Anjum Sayyad

Introduction

Pelvic Floor physical therapy is a relatively new discipline, starting nearly 40 years ago. It is estimated that nearly 10–20% of women experience chronic pelvic pain, and nearly one-half of all women will experience pelvic floor pain and/or dysfunction within their lifetimes [1]. There are no specific demographics by race, ethnicity, education, or socio-economic status that predispose women to be at greater risk, except that they tend to be of reproductive age. Chronic pelvic pain is defined as a noncyclic pain of 6 months or longer duration, which localizes to the pelvis, anterior abdominal wall below the umbilicus, lumbosacral back or buttocks and leads to functional disability [2]. Common causes of pelvic pain are gynecologic, gastrointestinal, urologic, or musculoskeletal in nature.

History taking can be limited by the patient, in light of their cultural perceptions of what is appropriate for open discussion, even with a healthcare provider. The provider must exercise great sensitivity and must cultivate trust, in order to ensure eliciting the most accurate history. It is important to elicit alleviating and exacerbating factors, levels of pain, prolonged postural or positional issues, impact on functional and/or sexual status, bladder and bowel involvement, past testing, and treatment strategies. Also important is to determine what brought that patient to seek healthcare attention, as well as their goals for treatment.

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Assessment of the pelvic floor involves an internal pelvic exam, in addition to the usual physical examination of the lumbosacral and lower extremity musculoskeletal and neurologic systems. A practitioner will assess for impairments involving sensory deficits, weakness, pain, range of motion, and coordination of muscles.

The observation portion of the exam involves assessing for asymmetry and skin abnormalities. The palpation portion of the exam involves assessing for sensory deficits, tender points, and trigger points. The internal exam involves assessing strength, endurance, coordination of pelvic floor muscles for volitional activation, and relaxation.

Anal Pain

Pathophysiology

Anal pain encompasses coccydynia, levator ani syndrome, and proctalgia fugax. The levator ani muscles (pubococcygeus, puborectalis, and iliococcygeus muscles) and coccygeus muscles form the base of the pelvic floor.

The term coccydynia was first introduced in 1859 [3]. Coccydynia indicates pain located around the coccyx itself. The most common cause of coccydynia is external trauma, such as a direct fall unto the coccyx, leading to a bruised, dislocated, or fractured coccyx [4]. Less frequently, coccydynia can be caused from prolonged sitting on narrow, hard, or uncomfortable surfaces. Other causes include repetitive minor trauma, such as bicycle riding or vaginal childbirth. Risk factors include obesity and female gender; women are five times more likely to develop coccydynia as men [5]. Additionally, adults and adolescents are more likely to be diagnosed with this condition than children [6]. It can also be associated with psychological disorders [7].

The pathophysiology of levator ani syndrome includes the levator ani muscles itself, whereby excessive tension is thought to occur, leading to myalgia [8].

The pathophysiology of proctalgia fugax includes smooth muscle dysfunction in the anus [8].

In general, it has been proposed for all these conditions that muscle fiber trauma leads to peripheral and then central sensitization, via a pathway of continued stimulus on local nociceptors. In turn, this causes amplification of the perception of pain from changes in the dorsal spinal cord.

Symptoms

Coccydnia is worsened when changing from a sit to stand position and is localized to the coccyx (tailbone). It may also present with sexual intercourse or with bowel movements.

Levator ani syndrome consists of dull ache or pressure pain located deep within the rectum, with referred pain to the thigh and buttocks, which can last for 20 min or longer, in the absence of any other finding [8]. Patients describe the sensation as that of “sitting

on a ball" [8]. Prolonged sitting or defecation, lasting for 20 or more minutes, can bring on the pain [8]. This syndrome is often seen in women under the age of 45 [8].

Recurrent pain lasting from seconds to minutes is seen with proctalgia fugax [8]. The pain is often severe, sharp, and can awaken individuals during the evening. It can occur in both men and women, starting in young adult life and usually stopping by middle age [8].

Functional Limitations

Coccydynia and proctalgia fugax affect the patient's ability to sustain prolonged sitting and standing; pain generally occurs during defecation and sexual intercourse.

Levator ani syndrome affects sexual intercourse and can also lead to urinary frequency and/or urgency.

Treatment/Common Techniques

Initial

Coccydynia is often thought to be secondary to pelvic floor dysfunction. Coccydynia generally resolves in weeks to months and should be initially treated conservatively. Early treatment may involve the use of a donut or wedge pillow, also known as a coccygeal cushion, which are available over the counter [5]. In levator ani syndrome, intra-vaginal finger exam may reveal a tender muscle band located within the levator muscle. Physical examination is normal in proctalgia fugax. Workup may involve endoscopy and/or imaging studies, which can include CT or MRI, to rule out other serious diagnoses, such as cancer [8]. Most common medications prescribed for pain relief include the non-steroidal anti-inflammatory drugs (NSAIDs). Other medications can treat anal pain, by inhibiting smooth muscle contraction: Inhalers (salbutamol), oral medications (diltiazem and clonidine), and topical medications (nitroglycerin) [8].

Rehabilitation

Modalities with heat or cold can be helpful. Perineal strengthening exercises can be helpful. Patients can be trained to adopt proper sitting posture. Pelvic floor therapists can employ multiple strategies, including trans-anal digital massage, which can reposition a dislocated sacro-coccygeal joint, transcutaneous electrical stimulation (TENS) with either an external or intra-pelvic probe, and electromyographic (EMG)-based biofeedback [8]. Visual biofeedback involves the use of internal and external sensors of muscle activity, which are displayed on a screen for patients to view as they activate and/or relax muscles. Referral to a comprehensive pain management program may be necessary if there is a possibility of psychological overlay in symptoms.

Procedures

A series of coccygeal injections with local anesthetics, with or without steroids, can be used to treat intractable coccydynia [9]. Electrogalvanic stimulation can be effective in treating levator ani syndrome. It uses high voltage, low frequency oscillating electric current via a probe placed in the rectum, which causes fatigue of levator ani muscles [8].

Surgery

Coccygectomy is a surgical procedure of last resort, which involves surgical amputation of the coccyx [10].

Potential Treatment Complications

High complication rates with failure to relieve pain are often seen with surgical coccygectomies [5].

Evidence

Little evidence exists to support the use of interventional procedures in the treatment of chronic coccydynia. Similarly, little evidence is present to support the use of coccygectomy as a way of treating chronic coccydynia.

Conclusion

Anal pain can be a self-limiting condition, which can respond readily to conservative treatment. A smaller subset of patients develop more chronic pain and can be more challenging to treat, and for whom limited evidence is present to effectively treat them.

Interstitial Cystitis: Painful Bladder Syndrome

Pathophysiology

Interstitial cystitis (IC) is characterized as a painful bladder syndrome with associated frequency, urgency, and nocturia, which is seen predominantly in women [11]. Pathophysiology for this condition is not clear, though there are many theories including: occult infection, mucosal/epithelial dysfunction, allergic hypersensitivity, neurogenic inflammation, autoimmune dysfunction, and urine toxicity [12]. No single theory fully explains this condition, but one theory proposes that IC is related

to altered integrity of the glycosaminoglycan layer within the bladder, which can lead to an increased permeability to solutes, in particular to potassium [13]. The theory goes on further to suggest that continued exposure of the bladder wall to potassium causes mast cell degranulation, which can lead to an inflammatory response, sensory nerve depolarization, and subsequent pain [13].

Symptoms

IC is characterized by exacerbating and remitting episodes of pain, which can be triggered by emotional and physical stress. Common symptoms include urgency, nocturia, frequency, pelvic pain, pelvic pressure, bladder spasm, dyspareunia, dysuria, and pain after intercourse. Pain is often worse with a full bladder and is felt in the low abdomen, perineum, vulva, vagina, low back, and/or medial thighs [12]. Pain is often relieved with voiding [12]. On average, patients with IC will void 16 times per day, with normal volume of voids [12]. IC is often associated with pelvic floor dysfunction and with pelvic floor muscle spasms. Symptom severity can wax and wane on a daily basis. This condition can coexist with other pain conditions, such as irritable bowel syndrome or fibromyalgia.

Functional Limitations

Patients with this condition will have poor quality of life, as IC generally negatively impacts sexual activity and bladder function.

Treatment/Common Techniques

Initial

Dietary modification towards a milder diet with fewer irritants may be the first step in treatment. A food diary may be kept to monitor symptoms as foods are eliminated and then re-introduced into the diet, which helps to identify the culprit food item [12]. Fluid restriction is not recommended [12]. Oral medications may be prescribed to target allergic response (hydroxyzine), neural inflammation (amitriptyline, gabapentin), pain symptoms (opioids), general inflammation (NSAIDs) to reduce urgency (anticholinergics) and dysuria (pyridine) [12]. Smoking cessation should be encouraged. Behavior modification should be implemented with timed voiding and bladder retraining [12].

Rehabilitation

Psychology can work with the patient to learn and to implement biofeedback, meditation, self-hypnosis, psychotherapy, and relaxation techniques.

Procedures

Acupuncture can be trialed for pain relief. Workup may involve the use of cystoscopy and urodynamics. Intra-vesical therapy may be employed to create a high concentration of drugs within the bladder, while minimizing systemic side effects. Drugs that may be employed include dimethylsulfoxide, heparin sulfate, local anesthetics (bupivacaine and lidocaine), caustic agents (silver nitrate and clorpactin), Bacillus Calmette-Guerin (BCG), hyaluronic acid, and capsacin [14].

Surgery

Bladder biopsy may be necessary to rule out other diagnoses.
Hydro-distention may be performed as a diagnostic and therapeutic tool; 30–50% of patients can experience relief with this procedure [12].
Percutaneous implantation of a sacral nerve stimulator can be used for pain rel. ief, acting as a neuromodulator [15]. Laser surgical resection can be employed in cases of gross inflammatory lesions of the bladder wall, also known as Hunner's patches [16] Cystectomy is reserved for patients who do not obtain relief by less radical treatment strategies [12].

Potential Treatment Complications

Surgery has the risk for infection or bleeding. Many patients still have significant pain complaints even after more aggressive procedures are employed and are therefore not often used.

Conclusion

IC is chronic bladder condition in which the etiology is not clear. Diagnosis is often delayed as is treatment. Women with this condition may do well with early recognition and treatment.

Painful Sexual Intercourse: Dyspareunia, Vulvodynia, and Vaginismus

Pathophysiology

Vulvodynia may be caused by sensitivity to chemicals, leading to irritation and eczematous changes in the introitus.

Vaginismus occurs with involuntary spasm of the bulbocavernosus (introital) muscles of the vagina.

Symptoms

Dyspareunic pain is located in the genital region and is associated with vaginal sexual intercourse. It is seen more commonly in females than in males. It is also seen commonly in post-partum women. The pain usually occurs during intercourse, but can also occur after intercourse. The pain is highly associated with comorbid depression and anxiety.

Vulvodynia and vaginismus both include pain that occurs with penetration, often burning in nature. Vaginismus has the additional finding of involuntary spasm with vaginal penetration. Vaginismus may have comorbid psychological issues.

Functional Limitations

Women with dyspareunia tend to have reduced frequency of intercourse, lower levels of desire, and decreased likelihood to achieve orgasm.

Treatment/Common Techniques

Initial

Care should be taken during the vaginal examination, as this particular patient population reports greater sensitivity, even with the use of tampons. Physical examination is unremarkable in patients with dyspareunia. Physical examination in patients with vulvodynia may reveal erythema, with or without ulcerations and nodules [17]. Physical examination in patients with vaginismus reveals difficulty in the insertion of a digit or speculum. Patients may benefit from a trial of conservative strategies with lubricants. Topical medications can be prescribed, which include lidocaine, amitriptyline, baclofen, or estrogen ointments. Oral medications can include the use of antidepressants, (tricyclic antidepressants such as nortriptyline, amitriptyline, or desipramine or serotonin norepinephrine reuptake inhibitors such as venlafaxine) or anticonvulants (gabapentin, pregabalin, or carbamazepine) [18].

Rehabilitation

Patients may benefit from a combination of pelvic floor physical therapy and cognitive behavioral therapy [19]. The goal of pelvic floor therapy is to improve proprioception and control of the pelvic floor muscles, to reduce tone, increase

elasticity of vaginal tissues, and to desensitize. Pelvic floor therapy will involve manual therapy, EMG biofeedback, and electrical stimulation [20]. Vaginal dilators can be employed to supplement manual techniques [21]. Electrical stimulation directed at specific pelvic floor muscles can help to build strength and improve coordination. Discharge instructions should include a home exercise program as well.

Procedures

Colposcopy and biopsy may be necessary to visualize lesions [22]. Some patients may benefit from trigger point steroid injections and bupivacaine injections.

Surgery

Vestibulectomy is the surgical treatment option when all other measures fail [23]. Surgical release of an entrapped pudendal nerve can also be performed.

Potential Treatment Complications

Care should be taken in the use of oral antidepressants in individuals who may have comorbid cardiac arrhythmias. Electrical stimulation is contraindicated in patients with concurrent pregnancy, urinary retention, or cancer diagnoses. Surgical complications can include acute blood loss anemia, wound infection, scar tissue formation, lubrication reduction, and persistence of pain.

Conclusion

Most women with this condition often suffer in silence. Conservative pelvic floor rehabilitation treatments can prove to be very helpful in most cases. In more refractory cases, physicians can help with improving tolerance to these therapies by prescribing oral medications for anticipatory pain relief.

Pelvic Girdle Pain: Sacroiliac Joint Dysfunction and Pubic Symphysitis

Pathophysiology

Pathophysiology of pelvic girdle pain is due to biomechanical dysfunction of the ligaments and muscles, leading to increased motion of the joints in and around the pelvic girdle.

This pain is often seen in pregnancy, where some natural widening occurs in the face of the ligament-relaxing hormone relaxin, as well as an anterior shift of the center of gravity, which occurs from biomechanical stressors associated with a gravid uterus; both factors lead to an increased lumbar lordosis [24]. Approximately 45% of pregnant and 25% of post-partum women suffer from pelvic girdle pain [25]. Separation of the pubic symphysis is considered pathologic if greater than 10 mm, which can be seen in traumatic labor and delivery [26].

Myofascial pelvic pain syndrome results from abnormal biomechanics of the pelvic floor muscles, such as from overuse injuries, trauma, pelvic asymmetry, and/or visceral pathology, leading to the presence of trigger points.

Sacroliac joint (SIJ) dysfunction is associated with excessive movement through the SIJs, leading to misalignment.

Psychological and/or social factors may also contribute to the pathogenesis of these conditions.

Symptoms

Pelvic girdle pain is specifically felt between the iliac crest and gluteal fold, often in the area of the SIJs, specifically through the pelvis, vagina, vulva, rectum, and bladder. This pain can radiate to the upper thighs, buttocks, or lower abdomen. Pain is often described as aching, diffuse, and persistent.

SIJ pain is often reported in the posterior aspect of the pelvis, below the belt line, causing numbness, popping, or clicking. It is thought to be the cause of chronic low back pain in 15% of cases [27]. It is commonly seen following trauma, pregnancy, or sports activity. There are no associated sensory or motor changes, which help to differentiate it from lumbar radiculopathy.

Pubic symphysitis pain is located in the anterior pelvis, with tenderness over the pubic symphysis. If pain transforms from an acute inflammatory process to a chronic condition, it is referred to as osteitis pubis [28].

Persistent pelvic floor pain can lead to involuntary pelvic floor spasms, causing urinary frequency, dysuria, constipation, or dyspareunia.

Pain is made worse with activity and may not necessarily improve with rest.

Functional Limitations

This is the most common cause of disability in patients under the age of 45 and reportedly affects 2% of workers in the United States every year [24]. Standing, walking, climbing stairs, bed mobility, and sitting endurance may be greatly limited.

Treatment/Common Techniques

Initial

Initial evaluation involves a thorough history and physical examination. In general, no specific physical exam maneuvers are diagnostic for the condition, although multiple provocative maneuvers exist, which include Gaenslen's test, sacral thrust, and Yeoman's test [24]. Imaging studies are usually not helpful. Conservative treatment involves icing for acute pain and heating for chronic pain. Patients may also benefit from use of a SI joint belt to provide stability and to facilitate motor control of core muscles, especially during gait; however, SIJ belt should only be applied for short periods [29]. Activity modification is directed towards minimizing asymmetrical forces on the trunk and pelvis, which often includes correction of a leg length discrepancy through appropriately applied heel lifts [24]. Acetaminophen is not thought to be effective, but is the only safe option for pregnant patients. NSAIDs may be used in non-pregnant patients.

Rehabilitation

For treatment, physical therapists can employ manual joint mobilization, muscle energy techniques, and therapeutic exercise. Manual techniques include myofascial release, osteopathic manipulative medicine (OMM), soft tissue mobilization, and trigger point release. Orthotics can be used for correction of leg length discrepancies. Exercises that involve single-leg weight bearing or excessive abduction should be avoided [29]. Exercises are directed towards strengthening and activating core muscles, such as the abdominal and pelvic floor muscles, to help increase stabilization across the pelvic girdle [30].

Procedures

Acupuncture may be a safe adjunctive intervention. Trigger point injections can be performed whence trigger points are clearly identified in the pelvic floor for symptoms of myofascial pain [18]. Fluoroscopically guided intra-articular steroid injections can be diagnostic and/or therapeutic for this condition [24]. Radiofrequency neurotomy (pulsed or continuous) can be used to treat zygapophysial joint pain, as well as SIJ pain [24]. Prolotherapy using phenol or glucose, or platelet-rich plasma injections, can help with ligamentous pain [24].

Surgery

Arthrodesis is considered a treatment of last resort for sacroiliac joint dysfunction [31].

Potential Treatment Complications

Arthrodesis has the highest risk for complications, including infection and chronic post-surgical instability of the pelvis.

Evidence

Evidence behind the various treatment strategies is limited, as many studies often do not distinguish pelvic girdle pain from low back pain [32]. However, there is moderate evidence to support the use of exercise therapy for treating pain, disability, and/or sick leave for pelvic girdle pain of pregnancy. In 2013, a Cochrane review showed that a SIJ belt can improve pain but not necessarily function. Acupuncture has been found to be significantly better than sham therapy for evening pain and function, but not as much for average pain. OMM significantly improved pain and function. The combination of manual therapy, exercise, and education also improved pain and function.

Conclusion

The etiology and onset of pelvic girdle pain is not entirely clear, nor is there a guarantee for full relief of pain symptoms. Treatment is effective when symptoms are identified early, which can help to avoid exacerbating activities that could lead to mal-adaptive behaviors. Coordination across multiple disciplines such as physiatry and physical therapy is necessary for optimal treatment.

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Chapter 13
Pain in the Burn Rehabilitation Patient

Peter I-Kung Wu, Andrew Joyce, and Jeffrey C. Schneider

Introduction

Burn injury can be one of the most painful and disabling forms of trauma. Pain from the burn injury itself, subsequent graft donor sites, and daily wound treatments is a significant complication of rehabilitation, compounded by the psychological trauma of burn. Aside from major injuries associated with the burn incident (e.g., fractures, perforations, hemorrhaging, etc.), burn can be associated with painful complications [1], including scars and contractures, osteophytes, heterotopic ossification (HO), infection, compartment syndrome (CS), amputation, and neuropathies. Preventing and treating these complications are critical for optimizing recovery and minimizing pain.

Pain management, which involves a multimodal approach, forms an integral part of care, from the acute burn center, through inpatient rehabilitation, and as an outpatient. Poorly managed pain can impact sleep, affect mental health, increase the risk of suicidality, decrease compliance, reduce confidence in the burn team, prolong hospitalization, and hinder rehabilitation. Effective pain management can significantly influence the burn survivor's overall recovery [2].

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Anatomy

The skin is composed of the epidermis and dermis [3]. The epidermis, composed of keratinocytes, serves as the outermost tissue barrier that protects against fluid loss, microbiologic invasion, and chemical penetration [4]. The underlying dermis is a vascularized fibro-connective tissue that provides elasticity and durability, houses dermal appendages like hair follicles and sweat glands, and supports thermoregulation, metabolism, and growth factors for repair. Various structures within the dermis transmit sensory information, including free nerve endings (pain, temperature, and crude touch) whose fibers travel in myelinated Aδ fibers (fast pain) or unmyelinated C fibers (slow pain) to the central nervous system, along with Meissner's corpuscles (light discriminatory touch) and Pacinian corpuscles (pressure) that transmit through Aβ fibers [5].

Pathophysiology

The extent of tissue damage from thermal injury relates to the location, duration, and intensity of heat exposure [6]. After burn injury, the skin can lose its ability to act as a protective barrier and homeostatic regulator, and there is an associated cascade of physiologic processes. A rapid inflammatory reaction occurs within minutes of injury, mediated by serotonin, histamine, bradykinin, leukotrienes, and prostaglandins, resulting in edema. Further injury ensues as neutrophils release oxygen radicals. Damage leads to microvascular permeability, vasodilation, extravascular osmotic activity, and opening of endothelial intercellular junctions, which can ultimately result in fluid loss, impaired thermoregulation, and susceptibility to infection [7].

Nociceptive Pain: Nociceptive burn pain is related to the total body surface area (TBSA) [2], depth, and location of the burn. Instant pain following thermal injury is mediated by thermoreceptors and mechanoreceptors that transmit through Aδ and C fibers. Full-thickness burns result in sensory impairment as destroyed nerve fibers do not transmit pain. With more superficial burns, undamaged and exposed nerve endings will generate pain from the moment of injury and throughout the course of treatment that may last for years and may also result in altered sensations causing neuropathic pain. With nociceptive pain, primary and secondary hyperalgesia may emerge immediately following injury [1]. In primary hyperalgesia, local nociceptors at the site of injury and adjacent skin become sensitized by the burn-induced inflammatory response. In secondary hyperalgesia, dorsal horn excitability is increased through the *N*-methyl-D-aspartate receptor as a consequence of repeated and continuous stimulation of nociceptive afferent fibers, leading to increased sensitivity in the surrounding unburned areas [8]. This central sensitization may become irreversible and result in chronic pain [2].

During rehabilitation, patients may experience constant, dull, background pain from the burn injury itself, which can be none to moderate intensity and easily under-appreciated. They may have expected postoperative pain following surgeries like skin grafting or contracture release, or they may experience unpredictable

breakthrough pain. However, pain from recurring dressing changes, wound cleaning, debridement, and joint ranging physical therapies (PT), called procedural pain, is the greatest source of pain. Procedural pain can be of short to medium duration but severe in intensity and lead to progressive anxiety and anticipatory stress [9].

Neuropathic Pain: Regenerating nerves may give rise to complex pain syndromes, thought to stem from dysfunction in the peripheral or central nervous system. Intense tingling and itching may accompany tissue regeneration [2]. Following healing of open wounds, neuropathic pain, felt as burning, tingling, cold, cramping, stabbing, shooting, pins and needles, and electric shock, can affect 15–37% of patients [6]. There may be hyperalgesia and allodynia. Neuropathic pain typically begins at 4.3 months after injury, improves at 7 months, and resolves by 13 months, but may also persist for years. Patients with hypertrophic scars, pruritus, increased skin grafts, and psychiatric diagnoses have increased risk [10].

Pruritus is linked to both the chronic inflammatory state and altered pain pathways of burns. While some investigators consider it is related to axonal sprouting in the dermis and thus a neurologic complication, histamine, which is found in abundance in burn wounds, is implicated as a primary mediator [11]. Pruritus can affect as many as 76% of burn patients [12] and persist for years, causing daily discomfort in approximately 50% between 2 and 7 years after injury [13].

Complications of Burn

Scars and Contractures: Hypertrophic scarring results from excessive collagen formation during wound repair [14] and can affect 32–67% of those severely burned, being more prevalent among darker pigmented individuals [11]. Hypertrophic scars can cause neuropathic pain via small nerve fiber damage, rendering cold and heat hyperalgesia and thermal allodynia [15]. A subset of hypertrophic scars may even contain nerves with neuroactive peptides that are able to worsen pain [16].

Contraction of scar tissue, especially in scars that cross a joint, decreases range of motion (ROM) and scar stability. Contractures most commonly occur at the shoulders, elbows, and knees and can be affected by length of stay, inhalation injury, and extent of burn. In severe cases, scar contracture can result in painful subluxations and dislocations, commonly from hyperextension of the metacarpophalangeal and metatarsophalangeal joints in dorsal burns [11].

Osteophytes: Osteophytes are the most frequently observed skeletal alteration in adult burn patients, frequently affecting the elbow, occurring along the articular margins of the olecranon or coronoid process, believed to be caused by superimposed minor trauma to affected areas. Pain, nerve impingement, and restricted ROM progressing even to joint ankylosis can occur [17].

Heterotopic Ossification: HO, the abnormal formation of bone in soft tissue, has an incidence of 0.15–4% depending on burn severity, affects the elbow in over 90% of cases [6], and can begin 1–3 months after injury [18]. Patients may have joint pain, swelling, erythema, ROM limitations [19], and peripheral nerve injury (e.g., ulnar neuropathy) from entrapment by heterotopic bone. Risk factors for HO

development include greater than 30% TBSA burn, arm burns and grafts, prolonged ventilation, multiple surgeries, prolonged immobilization, sepsis, and inhalation injury [20].

Infection: Avascular necrotic tissue (eschar) is a protein-rich environment favorable to microbial colonization [21], with *Staphylococcus aureus* being a common early cause and *Pseudomonas aeruginosa* being the most common cause of infection [22]. Increased surface bacterial load and impaired immune defenses further increase the risk of peripheral intravenous- and central line-related infections [23]. Locally tender, hot, erythematous, and swollen tissues may indicate invasive infection. Septic arthritis can also result, typically from penetrating burns into a joint or hematogenous seeding of bacteria, with symptoms of joint pain, swelling, and color change that may be masked by the overlying burn or graft. The hands, hips, knees, and wrists are most frequently affected. Septic arthritis may cause gross dislocation due to capsular laxity or cartilage and bone destruction or result in severe loss of ROM [6].

Compartment Syndrome: Deep muscle injury and necrosis resulting from deep burn injuries, high-tension electrical injuries, burn-associated crush trauma, high-volume resuscitation with circumferential burns, pressure from tightly applied splints, and patient malpositioning can lead to edema, increased compartmental pressure, and CS [24]. Untreated CS can result in limb ischemia, nerve dysfunction and paralysis, and severe pain that is deep, throbbing, and unrelenting [8].

A rare complication in burns with anterior trunk circumferential eschar is abdominal CS, in which volume overload with resuscitation, capillary leak, and third-spacing lead to splanchnic edema and increased intra-abdominal pressure that can lead to organ ischemia and failure [25]. Mortality rates for abdominal CS remain high despite intervention [26].

Amputation: Significant extremity myonecrosis secondary to electrical burns, usually at the sites of entry and exit of the electrical current, or vascular compromise due to circumferential full-thickness burns exacerbated by fluid resuscitation may require amputation [27]. Low-voltage (<1000 V) injuries commonly result in amputation of digits. High-voltage injuries frequently (10–50%) result in major amputation [11]. Refer to the chapter 9 on Pain in the Amputation Rehabilitation Patient for management of amputations.

Neuropathies: Risk factors for developing mononeuropathies include electrical injury, intensive care, and alcohol abuse. Nerve compression from osteophytes, heterotopic bone, scarring, CS, tissue swelling at the carpal or cubital tunnel, bulky dressings, and improper positioning can result in pain, dysesthesias, weakness, and muscle atrophy [28]. Neural injury from electrical burns results from the preferential transmission of current, which favors the path of least resistance, through nerves, resulting in cerebral syndromes (e.g., loss of consciousness, hemiplegia), plexopathies, and painful peripheral neuropathies that may have delayed onset [29]. Mononeuropathy multiplex and peripheral polyneuropathy may be due to a combination of direct thermal injury to nerves and the body's systemic response [11]. Polyneuropathy is common in those with greater than 20% TBSA burn and electrical injury, emerging within 1 week as distal extremity paresthesias and weakness [6].

Pharmacologic Treatments/Early Measures

Nociceptive Pain: Opioids are the first-line analgesics [1]; however, efficacy to alleviate procedural pain and anxiety has been limited [9]. Using long-acting opioids (e.g., extended-release morphine, oxycodone, and hydromorphone; methadone; etc.) for background pain along with short-acting opioids (e.g., oxycodone, hydromorphone, morphine, fentanyl, codeine) for procedural pain and breakthrough pain is standard of care. Frequent pain and anxiety reassessment is essential to titrate dosing as pharmacokinetics may be altered after burn due to altered perfusion, metabolism, and plasma protein levels [30]. A multimodal approach with adjunctive agents is recommended.

Nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen may be useful alone for small or mild burns. Both can be used adjunctively with opioids for moderate to severe background pain. Tramadol is useful as an intermediately potent analgesic if NSAIDs are contraindicated.

Benzodiazepines (e.g., diazepam, lorazepam, midazolam) are commonly used to manage anxiety and reduce the perception of pain. Conscious or deep sedation using midazolam and an opioid have been employed for procedural pain [2]. Various combinations of propofol, ketamine, and dexmedetomidine have also been used for procedural pain and anxiety [31, 32].

Regional anesthesia and peripheral nerve blockade, such as lateral femoral cutaneous nerve block or fascia iliaca compartment block, have been used successfully to control graft donor site pain [33, 34]; however, they are less commonly used due to infection risk with indwelling catheters.

Local analgesia using both topical and subcutaneous infiltration of anesthetics (e.g., lidocaine, bupivacaine, eutectic mixture of local anesthetics—EMLA) controls skin grafting pain while avoiding the risks of general and regional anesthesia [8, 35, 36]; however, usage has been controversial due to reports of local anesthetic-induced seizures from enhanced absorption at the open wound [37].

Neuropathic Pain: Although treatment of burn-related neuropathic pain is not well-studied, pharmacologic management includes anticonvulsants (gabapentin, pregabalin) [38], tricyclic antidepressants (amitriptyline, nortriptyline), and serotonin-norepinephrine reuptake inhibitors (duloxetine, venlafaxine) given their efficacy in other populations and with some able to stabilize mood to address the psychological contribution to pain [31]. Gabapentin has been suggested as first-line therapy for neuropathic and persistent pain, but it may not provide benefit in the acute setting [2, 39].

Pruritus management has relied on antihistamines. H1 receptor antagonists (e.g., cetirizine, diphenhydramine, hydroxyzine) are most commonly used but only effective in 20% of patients as sole therapy. H2 receptor antagonists (e.g., cimetidine) have been used with some success. Topical antihistamines, doxepin [40], EMLA, and corticosteroids (e.g., hydrocortisone) can be applied over healed

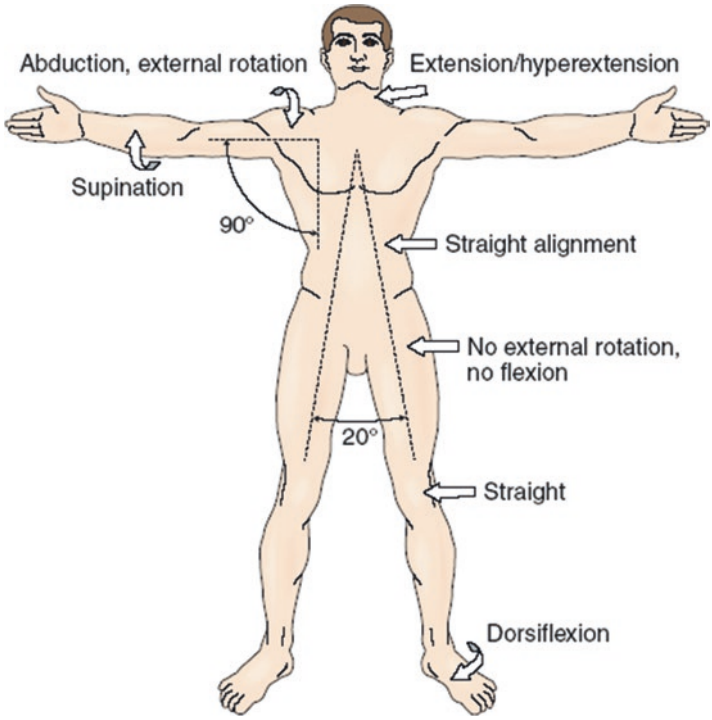

Fig. 13.1 Optimal positioning to prevent burn contractures

wounds. Newer approaches for pruritus include gabapentin [41], pregabalin [42], and ondansetron [43].

Scars and Contractures: Measures to prevent hypertrophic scarring include compression garments (e.g., plastic elastic, cotton elastic, or adhesive elastic bandages; custom-made) and silicone gel sheeting [44, 45]. Pressure garments, which decrease scar formation through a pressure effect on capillaries and soft tissue to create relative tissue hypoxia (25 mmHg is needed) [46], should be worn up to 23 h daily for 6 months to a year [47]. Positioning and splinting, typically to maintain tissues in an elongated state (i.e., extension and abduction), should be paired with early active and passive motion therapy to prevent contracture development or reformation after release surgery. See Fig. 13.1.

Heterotopic Ossification: Treatment of HO begins with conservative measures. NSAIDs, bisphosphonates, and radiation therapy have proven efficacy for HO prophylaxis in patients with major hip surgery [48–50] and spinal cord injury [51, 52] but have not been commonly reported for burn patients [53]. Provision of perioperative radiation therapy, however, has been recommended to decrease HO recurrence in burn patients [54].

Infection: Early eschar excision, wound debridement, and wound closure can decrease the incidence of invasive wound infections [55]. Performing bedside sterile

wound care and implementing preemptive barrier precautions prevent nosocomial microbial transmission [56]. For preventing infection, using topical antibiotics (mupirocin, neomycin, bacitracin, mafenide acetate) on a rotating basis substantially reduces microbial load and antibiotic resistance. Topical silver sulfadiazine, the most widely used silver-based agent for burns, has broad-spectrum antibacterial coverage (including *Pseudomonas aeruginosa*), while silver ion eluting dressings may provide additional coverage of methicillin-resistant *Staphylococcus aureus* [44] and require less frequent dressing changes, which improves comfort [21, 57]. Topical application of honey, a natural antimicrobial, may accelerate wound healing [44]. Proper nutrition along with anabolic agent supplementation (e.g., oxandrolone, insulin, insulin-like growth factor 1) for a hypermetabolic state assist with wound healing and immune competence [58]. Infectious Disease consultation should be requested and appropriate antibiotic therapy started for known infection.

Compartment Syndrome: Prevention and early detection by monitoring compartment pressures can avoid CS. Monitoring intra-abdominal pressure has been recommended for patients with greater than 30% TBSA burn who require significant volume resuscitation [26]. Preventative measures include relieving external pressure, elevating the injured extremity to heart level, and providing appropriately calculated fluid resuscitation, including use of hypertonic or colloid solutions to limit volume [59].

Rehabilitation

Nociceptive Pain: Given the strong psychological influences of the pain experience, with pharmacologic approaches alone being unable to completely manage procedural pain and anxiety in up to 75% of burn patients [60], incorporating nonpharmacologic and psychological adjunctive therapies is recommended for optimal pain and anxiety control.

Cognitive interventions include distraction, guided imagery, and reappraisal techniques [61]. Music therapy can be applied according to specific protocols [62, 63], including listening to, singing, or creating music; responding to musical cues; vibroacoustic therapy; imagery [60]; or entraining vital rhythms [64] to manage pain and anxiety of mild intensity [65] and strengthen coping skills [66]. Sensory focusing, which directs attention away from emotional unpleasantness, can provide greater analgesia compared to music therapy and reduce remembered pain [67]. Virtual reality distraction can reduce procedural pain [68, 69], be effective for greater pain intensities [70], and remain effective with repeated use [71].

Behavioral interventions are based on respondent (e.g., relaxation training) and operant conditioning (e.g., rewarding patients after completing PT). Having patients apply relaxation techniques, including jaw relaxation [72], relaxation breathing [73], biofeedback [74], progressive muscle relaxation [75], and stress inoculation [76], or simply having them participate in wound care can reduce perceived pain and anxiety and empower patients with a sense of control over their pain experience [77].

Hypnosis and rapid induction anesthesia [78] are considered effective adjunctive interventions to reduce anxiety and opioid and anxiolytic requirements; however, trained staff, time, and patient cognitive effort are required, and results may vary by patient [79–82].

Complementary therapies, including massage therapy, thought to increase vagal and serotonergic activity [83]; transcutaneous electrical nerve stimulation (TENS), which stimulates nerve fibers [84]; auricular acupuncture, thought to release endogenous opiates [85, 86]; and therapeutic touch, which balances body energy through non-contact manual manipulation [87], have been shown to decrease procedural pain and anxiety [88].

Neuropathic Pain: A cornerstone of pruritus management are emollients, which include simple moisturizers, *aloe vera*, lanolin, liquid paraffin, coconut oil, and various vegetable oils to improve skin quality. Scar massage, as well as the therapeutic effect of emollient application, decreases pain and itching [89]. Compression garments and extremity elevation appear to be effective for neuropathic pain [10]. Somatosensory rehabilitation may also be effective for neuropathic burn pain [90]. Topical adjuncts like cold compresses, colloidal oatmeal, pulsed dye laser, silicone gel, and TENS also have positive effects [43].

Scars and Contractures: Rehabilitative measures include functional orthoses, splinting, bracing, and serial casting [91] for anti-deformity positioning; avoidance of direct sunlight; scar massage [92]; and supervised ROM exercises [93]. Burns across joints and exposed tendons should receive empirical splinting, such as dorsal hand splinting or surgical high-top shoes with a metatarsal bar to prevent metacarpophalangeal and metatarsophalangeal joint hyperextension subluxation, respectively [6]. ROM exercises may begin within 1 week of skin grafting. PT and aerobic and resistance training lead to improvement in contractures and fewer release surgeries [94]. Intralesional steroid injections [95] and light- and laser-based therapies have also been used with some clinical improvement [96].

Heterotopic Ossification: During the acute inflammatory phase, the involved joint should be rested in a functional position and receive periodic, gentle, passive ROM to avoid both aggravation of inflammation and prolonged immobilization, both thought to contribute to HO development. After inflammation subsides, positioning and gentle PT that includes pain-free passive, active-assisted, and active ROM exercises that do not exceed the point of resistance should be applied to prevent worsening of joint motion [97].

Neuropathies: Proper positioning to avoid excessive stretch of nerves (e.g., lying supine with shoulder in 90° of abduction and 30° of horizontal adduction to avoid excessive stretch of the brachial plexus, or limiting the frog-leg position to avoid peroneal nerve injury) [28], avoiding prolonged immobilization, using splints, monitoring wound care, preventing contractures, and properly applying casts and bulky dressings to avoid compression of superficial peripheral nerves can mitigate neurologic complications. Effective splints avoid pressure over bony prominences and are compatible with grafts.

Behavioral Management

Pain is significantly influenced by psychological factors [98]. Burn patients often have complicated psychiatric needs, spanning preexisting psychosocial risks, such as substance abuse, psychiatric disorders, and domestic abuse; to anxiety, depression, and post-traumatic stress disorder from the burn trauma; to sleep disturbance, delirium, and distress caused by pain and medications. These can worsen the pain experience, adversely affect long-term outcomes, and increase the risk of suicide. Almost all burn patients require Psychology or Psychiatry evaluation to diagnose, prevent, and treat psychological sequelae and psychosocial inciting risk factors ("yellow flags") that influence pain [84].

Interventions/Surgery

Scars and Contractures: Acute management of deep burns includes resurfacing with skin grafts or substitutes to hasten wound healing and prevent contractures [99]. Secondary procedures are delayed until scars have matured, which may take approximately 1 year. Release of formed contractures through scar excision, soft tissue rearrangement, and skin grafting seeks to improve joint ROM. Various reconstructive techniques, including grafts, flaps based on random vascularization, tissue expansion, and newer techniques involving flaps based on defined vascularization, and dermal substitutes that avoid the need for donor grafts have been reported to improve ROM, scar quality, and cosmesis [100]. Risks include lack of graft take, necrosis, and flap loss.

Osteophytes: Osteophyte excision is indicated when there is severely limited ROM or nerve entrapment. Removing bony growth from the olecranon and coronoid process along with breaking down adhesions can restore ROM. Surgery should be postponed until there is no granulating surface or active scar tissue and should be followed by postoperative PT [17].

Heterotopic Ossification: Excision of elbow HO significantly improves functional ROM, independent of TBSA burned [101]. Surgery is traditionally reserved, except in cases of nerve compromise, until after radiographic evidence of HO maturation, which is usually 12–18 months [97]; however, studies also show good results from early HO excision [102]. Ulnar nerve release and transposition can be performed along with HO excision [54]. Surgical complications include infection, nerve injury, HO recurrence, vascular injury, wound problems like synovial cutaneous fistulas, and delayed healing [101].

Infection: Excision of the wound and infected tissue, or incision and drainage may be needed for invasive infections.

Compartment Syndrome: Early decompressive escharotomy of deep circumferential limb burns along with fasciotomy for CS can prevent amputation [103]. Decompression, nerve release [104], and debridement of myonecrotic tissue for limb CS associated with electrical or crush injuries have provided good return

of function [105]. Split-thickness skin grafts, regional composite grafts, or skin-stretching devices to facilitate primary re-approximation of wound edges are used for closure [106]. Decompressive escharotomy of the anterior trunk, percutaneous peritoneal drainage, and even laparotomy may be needed to relieve abdominal pressures greater than 25 mmHg in established abdominal CS [107].

Neuropathies: Nerve compression from edema or eschar requires immediate decompressive fasciotomy or escharotomy, while surgical intervention for compression from hypertrophic scarring is often delayed [108]. Surgical decompression and nerve release are commonly performed for peripheral neuropathies [108], such as HO resection and ulnar nerve transposition for ulnar neuropathy [54]; median, ulnar, radial, posterior tibial, and peroneal nerve release in electrical burns [104, 109]; and anterior interosseous nerve neurolysis and repair for burn scar compression [110], with improvements in pain and function. Nerve release always carries the risk of rapid nerve injury or transection, wound dehiscence, and infection [111].

Potential Treatment Complications

Sedation is the most common adverse effect of opioids, opioid-like pain medications, and antihistamines and can limit participation in PT. For other adverse effects of medications, refer to the Medication Management chapter 28 on Adjuvant Medications for Pain.

Regional nerve blocks are associated with risks of muscular weakness, overdose, and infection via the catheter. Systemic absorption of lidocaine carries the risk of cardiac arrhythmias and seizures.

Silicone gel sheets for hypertrophic scarring may result in skin maceration or contact dermatitis.

Poorly applied splints and casts for contractures may cause loss of skin grafts, skin abrasions, pressure sores, and compression neuropathies, commonly seen in the peroneal nerve.

There is a small but potential carcinogenic risk of radiotherapy for preventing HO recurrence [112].

Current Developments

Fat grafting, or lipotransfer, is currently being investigated for treating neuropathic burn scar pain, hypothesized to provide benefit through regenerative characteristics to improve scar quality and reduce inflammation [113]. CO_2 fractional photothermolysis may be efficacious to reduce neuropathic pain, scar tightness, and pruritus [114]. Nabilone, a synthetic cannabinoid receptor 1 agonist, has also been studied for controlling neuropathic pain [115]. Use of intravenous lidocaine for procedural pain is under investigation [116], as is botulinum toxin injection for pruritus [117].

Investigations have been made in topical antimicrobials, including antibiotics like firmocidin, fusidic acid, and nubiotics; other agents like drug potentiators; biofilm disrupting agents; antimicrobial peptides and compounds; photodynamic therapy; metal- and halogen-based antimicrobials; and antimicrobial organisms (e.g., bacteriophages) [118].

Investigations continue to evaluate novel dressings to facilitate wound healing and pain reduction for superficial and partial-thickness burns, including hydrocolloids, polyurethane films, silicon-coated nylon, biosynthetic dermal substitutes, calcium alginate fiber, and biocompatible protein [119]. Further investigations have evaluated "artificial skin" products [44], acellular hydrogels [120], and cultured epithelial autografts for epidermal regeneration [121].

Work continues to develop virtual reality systems capable of greater immersion and interactivity for distraction therapy [122].

Conclusions

Management of burn pain is most effective through a multimodal approach that must be individualized for the patient and requires regular reassessment of efficacy of treatments.

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Chapter 14
Pain in the Neuromuscular Disease Rehabilitation Patient

David Haustein and Steven Papuchis

Introduction

Neuromuscular diseases refer to a group of disorders affecting one or more of the components of the peripheral nervous system, ranging from the proximal cell body, the nerve root, the peripheral nerve, the neuromuscular junction, and the target muscle. These disorders frequently will result in neuropathic or musculoskeletal pain or both, and proper diagnosis of the pain source will help guide a multidisciplinary treatment plan.

Motor Neuron Diseases

1. Introduction

   Motor neuron disease (MND) is a collection of progressive neurodegenerative diseases that affect nerve cells in the brain and the spinal cord. This section will focus on amyotrophic lateral sclerosis (ALS), the most common motor neuron disease in adults. Patients with ALS have an average survival of 3–5 years after symptom onset [1–3].

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2. Pathophysiology

   The pathophysiology underlying ALS and other motor neuron diseases is unknown. The etiology of pain in patients with ALS is frequently multifactorial and progresses along with the disease [1–3].

3. Functional limitations

   Patients experience difficulty with mobility and ADLs due to the progressive nature of the disease.

4. Symptoms

   Patients can experience a wide variety of pain symptoms . The most common causes of pain are related to cramps, spasticity, and immobility, but muscular atrophy, joint stiffness, and contractures may produce pain as well [1–3].

5. Treatment

6. Initial

   - Cramps
   - Unfortunately, medications for cramps in patients with ALS have limited evidence to support their use. Vitamin E, magnesium, carbamazepine, phenytoin, verapamil, and gabapentin are occasionally trialed; while quinine is used in Europe, it is not FDA-approved for the treatment of cramps [1, 2].
   - Spasticity
   - Oral baclofen is the preferred initial agent. Tizanidine, diazepam, and dantrolene are used occasionally, but diazepam is associated with respiratory depression and dantrolene may cause generalized muscle weakness and thus is avoided in MND patients [1, 2].
   - Immobility
   - Reduced mobility can result in pain from adhesive capsulitis, mechanical back pain, and pressure areas on the skin. NSAIDs, with or without the addition of acetaminophen, may be appropriate for mild to moderate pain. Opioids may be required for severe or refractory pain. Patient-controlled analgesia (PCA) devices are seldom used due to patient's difficulty in controlling the device.[1, 2,]

7. Rehabilitation

   - Physical and occupational therapy can assist with stretching activities to preserve joint range of motion and to help manage spasticity, including modalities. PT and OT can also assist with mobility and transfer training, durable medical equipment for eating and bathing, and home safety evaluations.
   - An assistive technology professional (ATP) may assist with optimizing comfort in a wheelchair with adequate support and cushioning.
   - Orthotics such as an ankle foot orthosis (AFO) to treat foot drop may assist with ambulation and transfers early in the disease. A resting hand splint may help preserve range of motion in the hand [1, 2].

8. Procedures

   An intrathecal baclofen pump may be helpful in patients with severe spasticity unrelieved with oral medications or in patients who cannot tolerate the side effects of oral anti-spasmodics [1–3].

9. Surgeries

   Tendon lengthening procedures are possible for patients with severe spasticity and contractures. However, patients with ALS are very high-risk surgical candidates, especially late in the disease course [4].

10. Potential Treatment Complications

    Although higher than manufacturer-recommended doses of oral baclofen have been used, caution should be exercised given the possible side effects of weakness, fatigue, and sedation. Narcotics can cause respiratory depression [1, 2].

11. Evidence

    Per a 2013 Cochrane review, there are no randomized controlled trials regarding pain management in ALS; most management techniques come from case series or case reports [3].

12. Conclusion

    Pain is a common complaint for patients with ALS and other motor neuron diseases. Focus should be on symptom management, with close follow-up, to reduce pain and to improve quality of life for these patients.

Radiculopathies

1. Introduction

   Radiculopathies involve a pathologic process affecting one or more spinal nerve roots leading to both axial and referred pain, often including paresthesias and weakness. The most common cervical level involved is C7, while the most common lumbar level is L5 [1, 2].

2. Pathophysiology

   Common etiologies include herniated discs, spondylosis, and facet arthropathy; less frequent causes include tumors and infection. Pressure against a nerve root or inflammation is theorized to lead to a hyperexcitable state, producing pain and radicular features [5].

3. Functional Limitations

   Patients can have weakness, impaired sensation, and pain that limits ADLs or mobility.

4. Symptoms

   Axial and radicular pain, dermatomal paresthesias and/or sensory disturbances, and muscle weakness in a myotomal pattern can be seen.

5. Treatment

   (a) Initial

   Conservative management consists of oral analgesics such as NSAIDs or acetaminophen and rehabilitation. Adjunctive medications may include antispasmodics such as cyclobenzaprine. Tricyclic antidepressants and antiepileptics like gabapentin may help treat neuropathic pain [6–8].

(b) Rehabilitation

Posture and good body mechanics may help to reduce pressure on the nerve root(s); patients are frequently told to avoid repetitive and heavy lifting during the acute phase. Patients with cervical symptoms should avoid neck extension and may consider cervical traction with physical therapy. Heat and cold modalities can help temporarily, as well as use of a TENS unit [1, 2, 9].

(c) Procedures

Epidural steroid injections may be helpful for alleviating radicular symptoms. While the transforaminal approach is associated with higher efficacy than the interlaminar or caudal approaches, it also carries an elevated risk of adverse events [10].

(d) Surgery

Indications for more invasive surgical procedures such as a discectomy or laminectomy include intractable pain, not responsive to conservative measures, severe and progressive neurologic deficits, or progression to myelopathy [1, 2].

6. Potential Treatment Complications

(a) Symptoms suggestive of cauda equina syndrome require emergent surgical referral.

(b) Avoid deep heating methods as these can worsen inflammation.

(c) Transforaminal epidural steroid injections performed with particulate steroids may lead to a CVA or SCI due to infarction [5, 10].

7. Evidence

Short-term and intermediate-term use of opioids has been effective in controlling neuropathic pain symptoms. However, there are no long-term randomized controlled trials that look at the long-term efficacy and safety of opioids in treating neuropathic pain [11].

8. Conclusion

Acute radiculopathies are often initially treated conservatively with a combination of NSAIDs, neuropathic pain medication, and physical therapy. Progressing to interventional injections or surgery may be appropriate when conservative measures have failed to produce pain relief.

Plexopathies

1. Introduction

The brachial plexus is a confluence of nerves that begins as the nerve roots exit the middle cervical to upper thoracic spinal canal and combine to produce individual peripheral nerves that innervate the upper limbs. Similarly, the lumbar and lumbosacral plexus exit the lumbar and sacral spine and innervate the lower limbs [1, 2]. Common causes of plexopathies include traumatic injury, compres-

sion such as in thoracic outlet syndrome, invasion via cancer, infection, idiopathic or associated with a metabolic syndrome as in diabetic amyotrophy [1, 2]. This chapter will focus on acute brachial neuritis, neurogenic thoracic outlet syndrome and neoplasm, or radiation-induced plexopathy.

2. Pathophysiology

   (a) Acute brachial neuritis (aka neuralgic amyotrophy or Parsonage Turner syndrome)

   A disorder that typically presents with severe shoulder and upper arm pain followed by marked weakness and/or paresthesia in the involved limb. There is some evidence to suggest the disorder may be immunologically mediated. The patient's severe pain preceding the weakness is important in establishing a prompt diagnosis and in differentiating acute brachial plexus neuritis from cervical radiculopathy [1, 2].

   (b) Thoracic Outlet Syndrome (TOS)

   Neurogenic TOS is caused by compression of the brachial plexus as it passes between the scalenes, between the first rib and the clavicle, or between the pectoralis minor muscle and its insertion at the coracoid process. The lower trunk is most commonly affected, causing weakness, numbness, and possibly atrophy of the hand [1, 2].

   (c) Neoplastic and Radiation-Induced Plexopathy

   A neoplasm can invade the brachial or lumbosacral plexus directly, causing pain, paresthesias, and weakness. Sometimes the radiation beam treating a nearby cancer inadvertently damages a portion of the plexus, although this is now less frequent due to improved targeting of radiation [1, 2].

3. Functional Limitations

   Depending on the severity of the injury, patients can experience anything from transient symptoms to permanent disability affecting all of their ADLs and mobility.

4. Symptoms

   Frequently, patients with a plexopathy will experience neuropathic pain. There may also be weakness and paresthesia in the distribution of the involved nerve segments [1, 2, 12].

5. Treatment

   (a) Initial

   Neuropathic pain medications and NSAIDs may help to alleviate acute pain. To treat the severe pain associated with acute brachial neuritis, opioids may be appropriate, and oral corticosteroids may help, but do not alter disease progression.

   (b) Rehabilitation

   - Physical and occupational therapy can assist with range of motion exercises and gentle strengthening of both affected and supporting musculature. Education regarding posture may alleviate pressure and strain on the plexus in TOS. If ADLs have been affected, OT may prescribe adaptive equipment to assist with feeding or dressing.

- Physical therapy may assist with lymphedema management [1, 2].
- Orthotics may be necessary to accommodate for weakness.

(c) Procedures

- TOS: Botulinum toxin injection to the scalenes, subclavius, and/or pectoralis minor may be possible, but more evidence is needed [1, 2].
- Neoplastic plexopathy: Radiation treatment to shrink the tumor burden may provide relief, but there is risk for radiation-induced plexopathy as well. Regional blocks may prove to be helpful in alleviating the patient's pain [1, 2].

(d) Surgery

- TOS: In severe cases, scalenectomy or possibly first rib resectionmay be required [1, 2].
- Sympathectomy, rhizotomy, or occasionally nerve transfers or reconstruction have been utilized in select patients with radiation plexopathy [1, 2].

6. Conclusion

The brachial and lumbosacral plexi are susceptible to a wide variety of pathologic processes, but their treatment frequently involves pain control and rehabilitation, restoring range of motion and strengthening of both the denervated muscles and the surrounding musculature.

Mononeuropathies and Peripheral Neuropathies

1. Introduction

Mononeuropathies are lesions isolated to a specific nerve, whereas peripheral neuropathies will involve a process causing dysfunction of multiple nerves.

2. Pathophysiology

Entrapment of a nerve causes pressure leading to a hyper-excitable state, producing symptoms of pain, paresthesias, and weakness. Systemic disease states such as diabetes, thyroid disorders, certain vitamin deficiencies, alcoholism, chemotherapy, infections, and vascular disease can produce characteristic patterns of damage to axons, myelin, or to both [1, 2, 5].

3. Functional limitations

Patients can have focal or generalized weakness, impaired sensation/proprioception, and pain that interferes with ADLs and mobility.

4. Symptoms

Patients frequently complain of paresthesias and/or impaired sensation and muscle weakness in the distribution of the affected nerve or nerves. Common descriptors of neuropathic pain include burning, aching, tingling, pins and needles, shooting, and/or lightning pain [12, 13].

5. Treatment

   (a) Initial

   First-line medications for peripheral neuropathy include pregabalin and gabapentin. These medications can be used alone or in combination with SNRI antidepressants, such as duloxetine and venlafaxine. Tricyclic antidepressants are also used, but have a higher side effect profile compared to other medications. Topical lidocaine patches are well-tolerated and useful in well-localized pain. Adjunctive medications include tramadol, topical capsaicin, and other antiepileptic medications [6–8, 14].

   (b) Rehabilitation

   - Physical therapy referral for a TENS unit trial may be helpful in the treatment of neuropathic pain. Superficial heat such as whirlpools and fluidotherapy may also be helpful to some patients. Low-level laser may be helpful, but more research is needed.
   - Occupational therapy referral for neural mobilization or "nerve gliding" is proposed to have a positive therapeutic benefit in entrapment neuropathies, but the evidence is limited.
   - Wrist splints for patients with carpal tunnel syndrome (CTS) occasionally provide relief. [1, 2, 9, 15]

   (c) Procedures

   For carpal tunnel syndrome, therapeutic injections with steroid into the entrapment site may reduce inflammation, pain, and paresthesias [1, 2].

   (d) Surgery

   In CTS, carpal tunnel release effectively reduces pressure on the median nerve, diminishing pain and paresthesias [1, 2].

6. Potential Treatment Complications

   Deep heat (i.e. ultrasound, short wave diathermy) is not recommended as this typically worsens neuropathic pain [9].

7. Evidence

   (a) Opioid analgesics can be used to treat neuropathic pain, but there are concerns over long-term use and side effects [11].

   (b) Most TENS unit studies looked at short-term outcomes only; more data is needed on long-term outcomes [9].

8. Conclusion

   Treatment of pain associated with entrapment neuropathies typically begins with avoidance of aggravating activities and orthotics as needed, progressing to surgery if symptoms are significantly interfering with function. Neuropathic pain due to an underlying peripheral neuropathy is typically controlled with oral medications, but diagnosing and treating the underlying cause is important to prevent progression of the disease.

Neuromuscular Junction Disorders

1. Introduction

   Disorders affecting the neuromuscular junction include diseases such as myasthenia gravis (MG), Lambert Eaton myasthenic syndrome (LEMS), and botulism, as well as the congenital myasthenic syndromes. While these disorders only affect the neuromuscular transmission and not the sensory fibers associated with pain, the resulting muscular imbalances and weakness can cause strain and fatigue.
2. Pathophysiology

   Antibodies against the pre- or post-synaptic neuromuscular junction membranes cause LEMS or MG, respectively. The exotoxin of *Clostridium botulinum* irreversibly blocks the release of acetylcholine at the neuromuscular junction [16].
3. Functional limitations

   Ptosis/diploplia can cause difficulty with ADLs, mobility, and driving. Chewing and eating may become difficult. If weakness involves the patient's arms or legs, a patient's ADLs and mobility may be significantly compromised.
4. Symptoms

   These disorders can cause weakness of the extraocular, bulbar, and proximal muscles, causing diplopia, ptosis, and difficulty with chewing and swallowing. LEMS can cause leg weakness. Botulism can cause a rapidly progressive descending weakness [16].
5. Treatment

   (a) Initial

   Pain with these disorders is usually musculoskeletal in origin and can be managed through acetaminophen or NSAIDs. Treating the underlying disorder will be useful to limit the musculoskeletal and functional impairments and may include:

   - MG: Anticholinesterase medications and immunosuppressive agents
   - LEMS: Treat underlying disease, possibly immunosuppressive agents
   - Botulism: Supportive care; antitoxin can be considered.

   (b) Rehabilitation

   Gentle strengthening and stretching activities will prevent pain, disuse atrophy, and preserve range of motion, while the underlying etiology is being treated. Disciplines involved may include speech and language pathology for bulbar symptoms, physical therapy for muscular strengthening, and range of motion exercises, and occupational therapy to assist with rehabilitation of ADLs.

   (c) Procedures

   For MG and LEMS, intravenous immune globulin (IVIg) and plasmapharesis may be considered to treat the underlying disease.

(d) Surgery

MG: Thymectomy is occasionally considered.

6. Potential Treatment Complications

There are case reports of gabapentin causing exacerbations of myasthenia gravis. IVIg treatment is associated with adverse effects including headache and thromboembolic events.

7. Evidence

There is a lack of evidence to support any particular intervention for the treatment of pain in patients with neuromuscular junction disorders.

8. Conclusion

While neuromuscular junction disorders are typically pure motor syndromes, pain due to muscular fatigue, strain, and restricted range of motion can be typically treated conservatively through rehabilitation and oral analgesics as needed for episodic pain.

Myopathies

1. Introduction

Similar to the disorders of neuromuscular transmission, myopathies will cause weakness without the paresthesias or neuropathic pain, which are common to other neuromuscular disorders. Disorders of the muscle will frequently affect the proximal musculature symmetrically [16].

2. Pathophysiology

Muscle disorders can be caused by abnormal dystrophin (i.e. Duchenne and Becker muscular dystrophies), inflammation (inclusion body myositis, polymyositis, dermatomyositis), endocrine abnormalities (thyroid or adrenal disorders), drug-induced or toxic, metabolic, congenital, or related to periodic paralysis [16].

3. Functional limitations

Proximal weakness will cause difficulty with arising from a chair, ascending stairs, and overhead activities. Progressive disorders (i.e. muscular dystrophy) will cause gradual loss of independence in ADLs and ambulation.

4. Symptoms

Depending upon the etiology, a child or teenager may plateau in functional gains with the dystrophinopathies or an adult may complain of slowly progressive proximal weakness with one of the inflammatory myopathies. Pain is usually associated with the lack of mobility; typical sites include the back, legs, shoulders, and neck [17].

5. Treatment

(a) Initial

Initial treatment of pain should include rehabilitation and modalities, accompanied by oral analgesics if required (acetaminophen, NSAIDs).

(b) Rehabilitation

- Physical and occupational therapy can help to strengthen weak muscles, teach compensatory techniques, and to ensure that range of motion is maintained. Bracing may be appropriate to limit contractures and to provide comfort. Modalities may be helpful in pain relief.
- Working closely with an orthotist to manage cervical orthoses or ankle foot orthoses may be helpful.
- An assistive technology professional may be able to optimize wheelchair seating and trunk, arm, or head support to alleviate pain.

(c) Procedures

For musculoskeletal pain, an intra or periarticular steroid injection may be indicated to help alleviate pain.

(d) Surgery

Surgical consultation may be required for painful or function-limiting contractures.

(e) Potential Treatment Complications

Exacerbation of pain may occur with both conservative and surgical treatments.

6. Evidence

Randomized controlled trials for the treatment of pain in patients with myopathy are lacking.

7. Conclusion

The treatment of pain in the patient with a myopathic process is largely conservative and involves the multidisciplinary rehabilitation team. Occasionally, oral analgesics including acetaminophen or NSAIDs are required.

Conclusion

A multidisciplinary approach in the treatment of pain for patients with neuromuscular disorders can help to address both the neuropathic and musculoskeletal features that are encountered across this disease spectrum. Incorporating analgesics, rehabilitation therapies, modalities, and interventions or surgeries as necessary will help to improve the pain control and quality of life for patients with these unique disorders.

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Chapter 15
Pain in the Complex Regional Pain Syndrome Rehabilitation Patient

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Introduction

Complex Regional Pain Syndrome (CRPS) is a rare form of chronic pain that usually occurs after trauma to an extremity. It has an incidence rate from 5.46 to 26.2 per 100,000 persons [1]. The frequency of CRPS is three times higher for women than for men [2]. The most frequent triggering events include fractures, sprains, and elective surgeries [3]. It is characterized by unremitting pain or burning sensation in the affected area that can be exacerbated by painful or non-painful stimuli. The syndrome may progress, causing signs and symptoms to spread to other sites. It is typical for the pain to be disproportionate to the extent of the initial injury, and autonomic, sensory, skin, bone, and motor abnormalities often manifest [2, 4–7]. CRPS occurs as a result of central and peripheral nervous system dysfunction.

The mechanisms involved in CRPS are still not fully understood. It remains unclear which treatment options for CRPS are most appropriate. The severe pain associated with the syndrome, and its resistance to conventional therapies, often causes significant disturbances in the personal and social lives of patients, ultimately resulting in substantial debilitation and loss of quality of life. The negative outcomes of the disorder often cause psychological distress and neuropsychological deficits, prompting caretakers, friends, and family members of CRPS patients to support them through their journey to recovery.

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Brief History

Complex regional pain syndrome has been labeled many names, reflecting the evolution of the medical understanding of this condition over the past 150 years. It was first documented in the American Civil War following battlefield injuries [2]. In 1994, the International Association for the Study of Pain (IASP) assembled a group of pain medicine experts who came to a consensus about the diagnostic criteria for reflex sympathetic dystrophy (RSD) and causalgia, which were renamed complex regional pain syndrome (CRPS) types I and II, respectively [1, 7]. The disorder has also been called 'Sudeck's atrophy', 'algodystrophy', 'osteodystrophy', 'shoulder-hand syndrome', and neurodystrophy'; however, the new term was adopted with the hope of portraying the complexity of its pathophysiology and diagnosis that were previously not recognized [1]. The difference between the two designations is based on the inciting event. CRPS type I always arises from an initiating noxious event, such as a fracture, or by immobilization of a limb due to a cast. CRPS type II is diagnosed by a defined nerve injury; however, both types are characterized by the same clinical symptoms.

It was not long after the adoption of the IASP criteria that it was proven to be extremely sensitive, rarely missing cases of CRPS, although contributing to its over diagnosis [2, 7]. In 2003, a meeting was held in Budapest, Hungary, to resolve the issue of low specificity with recommended improvements to the IASP criteria. Once the results were published, the Budapest criteria were found to have a specificity of 0.69, which was nearly double the specificity of the IASP criteria of 0.36 [8]. The increased specificity of the new criteria was adopted with the idea that easier identification of CRPS would improve research into the pathophysiology and treatment of the disorder, without unnecessarily reducing or harmfully altering the clinical diagnosis. To date, there is very little high-quality research on the treatment of CRPS and very few proposed mechanisms of the disorder have substantial evidence confirming their validity [6].

Pathophysiology

CRPS patients often present with symptoms after an initial tissue injury of minor to moderate severity; however, spontaneous onset occurs in <10% of patients [3]. Less than 4 months after injury to the limb, typical signs of inflammation occur including pain, redness, swelling, and warmth [9]. As the healing process progresses, sensory loss and noxious sensations present. In the beginning stages, allodynia, whereby non-painful stimuli evoke intense pain, hyperalgesia, whereby painful stimuli evoke intensified pain, unusual hair and nail growth, sweating, and muscle fatigue first present [3, 9]. Whereas a typical injury would subside, this disorder persists and can spread, which typically only disperses proximally or on the originally affected limb.

The Gardener Diamond Syndrome is also common in CRPS patients, whereby spontaneous bruising occurs months after the initial trauma in uninjured areas [9]. Abnormal motor activity, such as tremors and spasmodic movements may occur, greatly intensifying the debilitating effect of the disorder due to a reduction in cortical thickness in the dorsolateral prefrontal cortex and ventromedial prefrontal cortex of the brain [10].

Chronic cases of the disorder can also present with urological complications, gastrointestinal disturbances, neuropsychological deficits, and temporary loss of consciousness [9]. In addition, it is not uncommon for chronic CRPS patients to feel coldness in the affected limb, which has been attributed to hypersensitive sympathetic activity [4]. In approximately 50% of chronic Type 1 CRPS cases, the patient also develops a reduced sense of touch and a reaction to painful stimuli either on the entire half of the body affected by the disorder or in the upper quadrant of the affected limb [11].

The mechanisms behind CRPS are not fully understood; however, there are multiple proposed mechanisms that may cause disturbances in the central and peripheral nervous system leading to CRPS symptoms. Based on experimental evidence, *N*-methyl-D-Aspartate (NMDA) receptors on neurons in the spinal cord dorsal horn become hypersensitive and trigger the amplification of pain signals, causing the characteristic central sensitization seen in CRPS [4, 12]. Due to the significance of NMDA receptors in the pain associated with CRPS, NMDA antagonists such as ketamine have been of special interest in drug therapy. There are also theories that suggest that the pain receptors in the affected limb become overly responsive to catecholamines [3, 4].

Basic Principles (Diagnostics, Treatment)

According to the Budapest clinical diagnostic criteria, there are four criteria to be met in diagnosing CRPS [8]:

1. Continuing pain, which is disproportionate to any inciting event
2. Must report at least one symptom in three of the four following categories:

   Sensory: reports of hyperaesthesia and/or allodynia
   Vasomotor: reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry
   Sudomotor/Edema: reports of edema and/or sweating changes and/or sweating asymmetry
   Motor/Trophic: reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nails, skin)

3. Must display at least one sign, at time of evaluation, in two or more of the following categories:

Sensory: evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or deep somatic pressure and/or joint movement)
Vasomotor: evidence of temperature asymmetry and/or skin color changes and/or asymmetry
Sudomotor/Edema: evidence of edema and/or sweating changes and/or sweating asymmetry
Motor/Trophic: evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nails, skin)

4. There is no other diagnosis that better explains the signs and symptoms

There are many modes of therapy for CRPS, including the following: pharmacological therapies, which include both oral medications and intravenous infusions; physical modalities, such as physical and occupational therapy; psychological interventions, such as biofeedback; injection therapies, such as sympathetic nerve blocks; implanted device therapies, such as spinal cord stimulation (SCS). A multi-disciplinary approach incorporating treatments from modalities has been recommended as the most effective treatment strategy [7]. A typical treatment algorithm might begin with physical modalities, minimally invasive injection therapies, and psychological interventions and would then progress, as necessary, to include more invasive therapies, such as spinal cord stimulation.

Common Techniques (Multi-modal Treatment Options)

Pharmacological Treatment

Cation channel blockers, such as gabapentin (Neurontin) and pregabalin (Lyrica), are widely used for neuropathic pain, including the treatment of CRPS. Evidence for their efficacy in treating CRPS is mostly anecdotal, though some case reports and case series support their efficacy [13–15]. Though there is evidence that opioids can be effective for neuropathic pain in general, there have not been high-quality studies demonstrating their efficacy specifically in CRPS [16–19]. Consequently, some authors recommend using them only as a second- or third-line treatment for CRPS [7]. Opioid dosage should not be repeatedly increased in response to inadequate pain relief.

NMDA antagonists, such as ketamine, have held significant interest due to their role in central sensitization. In a non-randomized study of 33 patients with CRPS, 54% of patients were pain-free 3 months after their first sub-anesthetic ketamine infusion, and 31% were pain-free for 6 months [12]. After a second ketamine infusion, 58% of patients were pain-free at 1 year and 33% were pain-free for more than 3 years. The results of the study suggest that a stepwise approach to treatment may be more successful than administering a single dose. In another study, 20 patients received ketamine infusions for CRPS [20]. All patients reported remission, with 16 of the 20 patients continuing to report cessation of pain at 6 months.

There is some evidence that the efficacy of ketamine infusions is affected by pain duration. A case series of seven patients with CRPS types I and II found that

ketamine produced effective pain relief for patients whose pain durations were 4–8 months, but not effective in patients whose pain durations were 10 months, 3 years, or 15 years [21]. One patient with a pain duration of 5 years received partial relief. However, in another non-randomized study of 20 patients with CRPS (with durations ranging from 6 to 84 months, and a mean of 49.4 months), ketamine infusions produced complete pain relief at 6 months in over 50% of patients [22]. Although there is promising research on ketamine therapies, the evidence is not strong enough to consider it a first-line treatment. However, due to limited therapeutic options, it will continue to be studied and used when other treatments prove to be ineffective.

Bisphosphonates, a class of drugs that prevent the loss of bone mass, have been examined as a treatment option for CRPS patients due to the majority of CRPS patients suffering from bone and joint pain [9]. By inhibiting bone resorption, bone is preserved despite disuse or immobility, and pain relief is exhibited by select patients [7]. Three high-quality studies of bisphosphonates specifically evaluated the effectiveness of clodronate, alendronate, and neridronate for the treatment of CRPS and similarly reported substantial improvement in pain [23–25].

Physical Modalities

Physical and occupational therapy play an important role in functional restoration. Physical therapy primarily focuses on physical activity, desensitization of the limb, and normalization of movement through a progressive routine of activity that begins with mild exercises [26]. Other physiotherapy interventions include graded motor imagery, which focuses on training the brain to reduce painful sensations from the affected limb by repairing sensory mismatches in the brain [27, 28]. Two high-quality studies found that graded motor imagery significantly decreased pain in complex regional pain syndrome. Mirror therapy, which was traditionally used to alleviate pain in phantom limbs, is also employed as part of graded motor imagery to decrease pain in CRPS patients.

Injection Therapies

Stellate ganglion blocks or lumbar sympathetic blocks are often used both in diagnosing and treating CRPS, the selection of which depends on whether the CRPS is in an upper or lower extremity, respectively [29, 30]. The success of a sympathetic nerve blocks indicates sympathetic mediated pain, whereas a lack of response would indicate sympathetically independent pain. Sympathetic nerve blocks also have therapeutic value, in that they may produce pain relief in CRPS, long outlasting the anesthetic effect. Inadequate or partial response to sympathetic blocks in CRPS patients should indicate the need to progress to more invasive therapies, such as neurostimulation or intrathecal drug infusion (e.g., baclofen) [31].

Implanted Device Therapies

A spinal cord stimulator may be implanted, after a successful trial, to relieve pain in a CRPS patient through the use of electrical pulses delivered to the dorsal column of the spinal cord [32–34]. Spinal cord stimulation (SCS) has demonstrated an impressive ability to reduce pain and to improve the quality of life of patients for up to 2 years after implantation; however, SCS does not improve motor function and should therefore be used in tandem with physical and occupational therapy [32]. Some studies have also used peripheral nerve stimulation for CRPS, instead of or in addition to SCS, with success [35]. One recent randomized trial of 152 subjects with lower limb CRPS, compared traditional spinal cord stimulation (SCS) targeting the dorsal column to stimulation with stimulation involving leads placed along the dorsal root ganglion (DRG) [36]. Compared with traditional SCS, DRG stimulation was better at confining sensation to the primary area of pain, without recruiting non-painful neurons. DRG stimulation produced superior pain relief for 12 months. Implanted intrathecal pumps may be effective for some CRPS patients. A double-blind study of seven patients with dystonic CRPS found support for the use of intrathecal pumps for delivering baclofen, with patients achieving good outcomes for analgesia and functional restoration [37]. Intrathecal infusion for CRPS without a dystonic component is not supported by the literature.

Psychological Treatments

Though psychological treatments have the potential to benefit many types of chronic pain patients, there are reasons to believe that they are especially important for CRPS patients. Adrenergic mechanisms may be involved in the onset and maintenance of CRPS [38]. Dysphoric emotional states, such as anxiety, anger, and depression, can lead to an increase in the release of catecholamines, which are implicated in the development of CRPS [39–43]. Psychological factors, such as stress and catastrophic thinking, can also influence inflammatory mediators [44, 45].

Very few RCTs have been conducted on psychological interventions for CRPS. One study randomized 18 patients with CRPS to complete PT, either with or without autogenic relaxation therapy. The addition of autogenic relaxation therapy improved patients' limb temperature [46]. Other non-randomized studies, which include case series and case reports, provide some support for the use of biofeedback, such as providing feedback about the temperature of the affected limb, in conjunction with relaxation training, psychotherapy, such as cognitive behavioral therapy, and intensive graded exposure for treating CRPS [47–51]. The appropriateness of psychological interventions will depend on the patient. The clinician, patient, and their family should understand the importance of psychological function in recovery from CRPS and should pursue psychological treatment when appropriate, such as when the clinician identifies a possible anxiety disorder.

Specific Applications to Patients in Rehabilitation Settings

The acute stage of CRPS lasts 1–3 months after onset; it is considered the best stage to put the disorder into remission. In addition to the treatments described above, many of which can be applied in a rehabilitation setting, some additional treatment options may be applicable for the treatment of CRPS, specifically in a rehabilitation setting. Because the earliest stage of CRPS is mostly exacerbated by the inflammatory process, corticosteroids are successful at managing pain and swelling [11]. There is strong evidence that oral corticosteroids can be effective at improving CRPS symptoms [52]. This is likely to be true early in the course of the condition in cases with prominent inflammation. Longer courses of corticosteroids have serious contraindications and have not been studied.

In addition, free radical scavengers, such as vitamin C, are suspected of reducing the high levels of reactive oxygen species involved in the inflammatory mechanisms associated with early stages of CRPS type 1 [53]. A high-quality study found that vitamin C can inhibit the occurrence of complex regional pain syndrome following a wrist fracture. It is unclear whether vitamin C can be used as a treatment in later stages of CRPS.

Evidence

Though there is evidence supporting a number of treatments for CRPS, the majority of these therapies lack high-quality studies supporting their use (see Table 15.1 for a summary). More research, particularly placebo-controlled RCTs, is needed on various treatments for CRPS. Generally, there is some supportive non-randomized evidence for conservative treatment modalities, such as physical therapy, injection therapies, such as sympathetic nerve blocks, psychological treatments, such as biofeedback, pharmacological treatments, such as ketamine, bisphosphonates, and neurostimulation, such as spinal cord stimulation. Effective treatment of CRPS is likely to be most effective in a multi-modal, interdisciplinary approach.

Conclusion

Complex regional pain syndrome is a rare but severe chronic pain condition. Though many questions remain both about the processes involved in the development of CRPS and the effective treatments, the available evidence supports a number of treatment modalities at different stages of treatment. Several forms of physical treatment, including physical and occupational therapy, have received research support, particularly in restoring function to the affected limb. A number of pharmacological treatments are utilized in treating CRPS and have varying levels of support. Opioids

Table 15.1 The level of supporting evidence for various treatments of complex regional pain syndrome

Treatment	Level of evidence
Physical treatments	
Physical therapy [54–56]	2
Occupational therapy [55, 56]	2
Graded motor imagery [27, 28]	2
Mirror therapy [57, 58]	2
Sensorimotor retuning [59, 60]	3
Injection therapies	
Stellate ganglion block [61]	3
Lumbar sympathetic block [61]	3
Brachial plexus block [62]	4
Epidural analgesic infusion [63, 64]	3
Psychological treatments	
Autogenic relaxation [46]	2
Biofeedback [47]	4
Psychotherapy [48–50]	3
Intensive graded exposure therapy [51]	3
Pharmacological treatments	
Bisphosphonates [23–25]	1
Cation channel blockers [13–15]	4
Oral corticosteroids [50]	1
Ketamine [12, 20, 21]	3
Opioids [16–19]	4
Vitamin C [53]	1
Implanted device therapies	
Spinal cord stimulation [32–35]	2
Peripheral nerve stimulation [35]	3
Dorsal root ganglion stimulation [36]	2
Intrathecal drug infusion [7]	3

and cation channel blockers are widely used for CRPS, based on their efficacy in treating neuropathic pain more generally, though specific support in treating CRPS is primarily anecdotal. The use of vitamin C and oral corticosteroids, particularly early in the progress of CRPS, is supported by RCTs. Infusions of drugs such as ketamine and bisphosphonates appear to have the potential to provide lasting relief to some CRPS patients.

Anesthetic blocks, often of the sympathetic nerve pathways, are widely used in diagnosing and treating CRPS, with some supportive evidence. Additionally, given the suspected role of behaviors and psychological processes in at least some cases of CRPS, psychological interventions are often considered. These therapies may address stress, anxiety, and other dysphoric states that interact with physiological processes involved in the development of CRPS, and can therefore provide some CRPS patients with relief. For CRPS patients whose condition is refractory to other

therapies, the use of implanted devices, particularly SCS, is supported. Many of these treatments can be delivered in a rehabilitation medical practice or coordinated with appropriate specialists.

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Chapter 16
Pain in the Addiction Rehabilitation Patient

Frank R. Sparadeo

Introduction

The death rate from drug overdose in the United States more than doubled during the period from 1999 to 2013. It is estimated that the death rate was 6.0 per 100,000 population in 1999, and has risen to 13.8 per 100,000 by 2013 [1]. These overdoses are attributable mainly to the misuse of prescription controlled substances, especially opioid analgesics, anxiolytics, and sedative hypnotics [2, 3]. A corresponding increase in morbidity, as measured by visits to the Emergency Department (ED), has also occurred because of the use/abuse of prescription drugs, which has increased 153% for opioid analgesics and 124% for anxiolytics and sedative hypnotics [4, 5].

In view of these alarming statistics, many states have developed initiatives to reduce prescriptions of opioid analgesics in general, and in particular to people experiencing chronic pain. Numerous individuals who have developed tolerance are unable to get an increase in their opioid analgesic medication dose, or they are being slowly titrated down. These public health policy changes are creating problems for the population of chronic pain patients who have relied on opiate analgesic medications for many years. It is not uncommon to see a patient with a history of chronic pain to be on the same dose of medication for 1 or 2 years. These patients describe a "subclinical" withdrawal state, which is characterized by general feelings of malaise, excessive irritability, generally feeling "sick", but never in full withdrawal. These patients are often seen by their family, and sometimes their physician, as complaining, depressed, or catastrophizing. A subgroup of patients supplement their prescriptions with illicit opiate analgesics and sometimes even heroin.

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Definitions

It is important when treating patients with chronic pain and addiction to define these conditions, as follows:

Pain

Pain is defined by the International Association for the Study of Pain (IASP) as a "psychological state" characterized by "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [6].

Addiction

Addiction is defined by the American Society of Addiction Medicine (ASAM) as a primary, chronic disease of brain reward, motivation, memory, and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social, and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors [7].

It is interesting how both definitions infer significant brain-based perspectives, which implies a need to understand the individual with either affliction from a neurobehavioral perspective. The influence of genetics is an integral part of various aspects of both conditions. Gene expression is influenced by the presence or absence of polymorphisms, which alter the brain's neurotransmitter system. Reward-deficiency syndrome is a good example of the presence of excessive polymorphisms in the expression of dopaminergic genes [8, 9]. An individual with altered gene expression in the dopaminergic system is highly vulnerable to the development of opioid addiction. That individual may also have an altered perception of the severity of pain and its implications (reduced joyfulness). Such an individual is likely to be prescribed an analgesic opioid, which will then initiate the rapid formation of addiction to opiates.

The Pain and Addiction Paradigm

Assessment of Addiction in the Chronic Pain Patient

The most common drug of addiction in the chronic pain patient is obviously opioids followed by benzodiazepines. It is often the case that clinicians treating chronic pain patients conceptualize the addiction disorder as either a "pseudo addict" or an

addict. The distinction is made on the basis of the presence of drug-seeking behavior. Addicts typically present with obvious drug-seeking behavior, often fail toxicology screens, and frequently run out of their medications. Pseudo addicts with chronic pain are troubled by their prescription dependence and engage in more subtle drug-seeking behavior, which disappears with adequate dosing. These patients are often irritable and demanding and often feel that they are not being treated properly by their healthcare team.

There is a natural progression through characteristic phases of pseudo addiction, which include the following:

1. There is an inadequate prescription of analgesics to relieve or to reduce pain in the patient.
2. There is escalation of analgesic demands by the patient, associated with behavioral changes to convince others of the pain severity.
3. There is a crisis of mistrust between the patient and the healthcare team in providing appropriate and timely analgesics to control the patient's level of pain [10].

The distinction between the pseudo addict and the addict is sometimes difficult to make, but an adequate diagnostic assessment will be helpful to determine the proper diagnosis. It is often the case that a pseudo addict is so frustrated that they may engage in increasingly bizarre drug-seeking behavior in an attempt to convince the physician or other clinician for the need of additional pain medication. The physician is likely to view this behavior as an indication that the patient is an "addict" and then try to avoid the patient. Eventually, the physician will refer the patient to a mental health professional for the treatment of addiction. Once this occurs, it is not likely that this patient, who is now labeled as an addict, will have any chance of receiving sufficient analgesia; thereby, the patient will be expected to continue to suffer in pain, with pain flare-ups likely.

A psychologist, with a specialty in pain management, should be able to provide an adequate assessment of the drug use component of the patient's presentation. The use of standardized psychological tests, as well as the administration of a comprehensive history that includes corroboration from family members is necessary. This author has had great success in treating patients who were pseudo addicts through the use of Suboxone.

Treating Pseudo Addiction and Chronic Pain

The treatment of non-malignant chronic pain with opioid analgesics has resulted in massive increases in the amount, duration, and expense of pharmacotherapy. Opioid availability has increased substantially and prescription drug dependence is the fastest growing epidemic in this century. The number of opioid overdose deaths has now exceeded all accidental deaths, including alcohol fatalities. Many of these patients became addicted to opioids because of painful conditions, such as back problems, failed surgery, arthritis, headaches, fibromyalgia, and neuropathies.

When buprenorphine/Suboxone was first being prescribed for office-based opioid treatment, two categories of patients emerged: (1) those who were prescribed opioids for pain and had difficulty reducing their dosage; (2) those who, when exposed to opioids, became addicted and started using more than prescribed. Buprenorphine resulted in rapid withdrawal suppression and excellent pain relief, such that many of the patient's symptoms stabilized and they were able to taper down dosage without return of pain. Others got acceptable pain relief initially, until during dose reduction, the pain complaints returned and persisted.

The treatment needs of these populations are distinct, as most patients with chronic pain, who have never abused medications, do not perceive themselves as an addict. Having these patients engage in traditional substance abuse treatment requires a pain management approach focusing upon the emotional and behavioral consequences of pain, suffering, and functional disability, as well as a clear understanding of the implications of their addiction.

After initial stabilization of withdrawal symptoms, and titration of medications for pain control, it is useful to engage the patient in a pain group as a long-term weekly group therapy service. The format can be a combination of process and education group, which this author has found to be helpful, but not sufficient to meet the more comprehensive needs of this population. Ultimately, a comprehensive program that addresses medication issues, addiction, and pain management is necessary to treat these complicated patients successfully.

Referral Sources and Initial Patient Evaluation

Patients who have become physically dependent upon opioids for pain are referred from their primary care physician, surgeon, or other pain specialists for evaluation. Self-referrals should be encouraged, with the expectation that ongoing treatment involvement with their prescribing physician is required for participation. Most patients have already been on opioids for years and have failed multiple medical and surgical interventions. Referring physicians are concerned about the dosage and duration of opioids complicating evaluation and management, often secondary to concurrent but occult physical dependence symptoms. Many patients have already been tried on long-acting opioids or have attempted opioid tapering or substitution without benefit.

Treatment begins after the first contact with the pain and addiction specialist. Upon the initial telephone call or first visit, a clinical screening procedure, focusing upon the nature, urgency, type of problem, reason for referral, and requested services, is undertaken. A brief substance use and medical history is obtained, along with appropriate insurance coverage information, and an appointment is set up for a formal intake. It is useful if the intake process is a three-stage assessment, involving a substance abuse counselor, addiction medicine specialist, and a clinical psychologist.

Patients entering into a Pain and Addiction Program should complete the standard addiction assessment procedure prior to acceptance into the program. The assessment procedure should include the use of standardized questionnaires that assess common emotional and behavioral problems associated with addiction and chronic pain. Use of these instruments allows for quantitative measurement of problem severity, based upon evidenced-based research and clinical practice guidelines and protocols.

We know from years of clinical experience that the clinical conditions associated with substance abuse and dependence are inter-related and share common neuronal pathways. Most patients presenting for substance abuse treatment have co-occurring brain-based conditions and complications. For example, greater than 50% of patients with a substance use disorder also have emotional problems with anxiety, depression, and post-traumatic stress disorder. However, the substances themselves can cause the same biochemical alterations that mimic these diagnoses, and are described as "substance induced". Making the proper diagnosis is important, as substance-induced disorders improve with abstinence and without medications, whereas truly co-occurring disorders may not. If a physician is not careful, premature treatment may add more medications to someone who is not stable from a substance abuse perspective and may result in worsening of the addiction and an increased risk for metabolic interactions, as well as risks for adverse outcomes, which include overdose and death.

The clinical challenge is to assess the pain symptoms and functional coping strategies to determine the relative contributions of opioid-induced hyperalgesia, tolerance, physical dependence, withdrawal-mediated symptom relief, and the concurrent emotional and behavioral conditions associated with chronic pain and disability. Every patient entering treatment should complete a series of standardized instruments assessing anxiety, depression, opioid misuse, and addiction risk. After completion of clinical evaluations by addiction medicine and treatment specialists, the assessment should be reviewed by a multidisciplinary team, including the clinical psychologist pain specialist, to determine if further in-depth evaluation or more intensive chronic pain treatment is required.

Chronic Pain Program Assessment Procedure

Once the initial evaluation has been completed and the multidisciplinary team review has occurred, the relative contribution of addiction and chronic pain to treatment need is established. Patients with more problems from loss of control and opioid abuse will be referred into a more traditional substance abuse treatment program. Patients with chronic pain, physical dependence, and pseudo addiction will be referred into a Chronic Pain and Addiction Program. For those who are eligible and who accept the recommendation to enter a Chronic Pain and Addiction Program, a more focused assessment of pain relief in relationship to drug dosage, pharmacokinetics, and the onset of withdrawal symptoms should be completed.

Clinical protocol instruments measure opioid effects and withdrawal severity in relationship to the extent of pain relief. Measurement allows for an estimation of the extent of tolerance and physical dependence and whether pain is due to changes in sensitivity from exposure to opioids (hyperalgesia) or secondary to the underlying painful condition. During the development of this clinical protocol, it should be recognized that pain complaints require more extensive evaluation than a simple visual scale, measuring pain severity from 1 to 10. Quantifying pain severity, and its interference in daily functioning, is necessary to develop a comprehensive pain management plan.

Once it is determined that a patient can benefit from a Chronic Pain and Addiction Program, they are offered admission. At that point, more extensive, objective, evidenced-based assessment instruments are utilized to determine the extent of suffering and impact of pain on daily activities. These instruments assess cognition, sickness impact, expectancies, personality structure, co-occurring affective and traumatic disorders, as well as family and occupational functioning. These assessments can be extremely successful in the management of chronic pain and the choice of pharmacotherapy, as well as presurgical evaluations for implantable medication pumps or electronic devices. These evaluations have saved insurers thousands of dollars in unnecessary and ineffective treatments. They have proven medical necessity and benefits, especially in improving functional outcomes and in reducing long-term pharmaceutical and surgical costs.

The following is a list of the formal testing that often occurs in patients admitted to the pain and addiction program:

CNS Vital Signs (Cognitive Screening)
Substance Abuse Expectancies Questionnaire
Sickness Impact Profile
West Haven-Yale Multidimensional Pain Inventory
McGill Pain Questionnaire
Survey of Pain Attitudes
Chronic Pain Coping Inventory
Pain Intensity Chart
Pain Drawing
Personality Assessment Inventory
Beck Depression Inventory
Back Anxiety Inventory
Substance Abuse Subtle Screening Inventory

Additional testing should be available when necessary. In view of the frequency of PTSD among chronic pain patients, the Detailed Assessment of Posttraumatic Stress is utilized. A comprehensive assessment of neuropsychological status should be utilized in those patients who fail the CNS Vital Signs and who have not had neuropsychological assessment in the past. The results of the testing will be summarized in a written report that will also contain conclusions and recommendations.

Medication Management

The role of opioid medications in treating chronic pain is complex and frequently controversial. Increased opioid prescribing has resulted in the induction of opioid withdrawal and opioid dependence. Many patients are unable to get long-term opioid management by a physician, as evidenced by the fact that over 50% of patients in methadone maintenance programs have chronic pain as their chief complaint. The benefits are now being re-evaluated as long-term use of opioid medications may do little to relieve chronic pain and in fact, may cause debilitating side effects that limit one's function and mobility even greater.

Elimination of opioid medication has been found to be a successful component of most pain management programs. A recent study of patients attending the Pain Rehabilitation Program at Mayo clinic found that at discharge, 3.7% of patients were taking opioid medication, a significant decrease from admission data indicating that 45% of patients were using daily opioids [11]. Immediately following completion of the Mayo program, it was found that patients with severe and disabling pain at admission experienced significant improvement in physical and emotional functioning with decreased pain severity, despite tapering these medications. It was also found that patients who tapered these medications experienced the same improvement in function as those patients who completed rehabilitation but did not take opioid analgesic medications [11].

When buprenorphine became available for office-based opioid treatment, it was recognized that the withdrawal suppression and analgesic effects could be utilized to accomplish these inter-related chronic pain and addiction problems. Buprenorphine products have significant efficacy in suppressing withdrawal symptoms, allowing the patient to break the association of the appearance of withdrawal symptoms from breakthrough pain. Once withdrawal symptoms have been stabilized, the dose of buprenorphine is titrated for pain control. After the patient has attained relief from both the withdrawal and pain complaints, a determination is made to taper medications and to provide behavioral treatment for restoration of function.

Determining the Best Approach

The clinical challenge is to determine the best setting and intensity of treatment, as most pain programs were designed for tertiary care, inpatient, specialty rehabilitation, were often not covered by insurance, and required treatment outside of the patient's own community. Furthermore, many pain programs had little experience with substance abuse, such that many were ineffective and did not address the long-term addiction potential and risks when transferred back to their home. As a result, it was recognized that a higher intensity of services than traditional outpatient and office-based medical services were often necessary for successful attainment of pain and withdrawal treatment goals.

Many patients have struggled with the balance between pain control, improvement in functioning, and the development of withdrawal symptoms. Pain relief becomes associated with pharmacokinetic and pharmacodynamic factors that intensify the relationship between dose and relief. Many have difficulty getting adequate pain relief because of acquired tolerance; thereby, they confuse the development of withdrawal symptoms with breakthrough pain. Patients often resist the idea that they have become physically dependent and minimize the impact of physiological neurologic adaptation on their pain complaint and functional status. Few have received instruction on management of withdrawal symptoms, or on the development of addictive behaviors. If we are considering changes in pharmacotherapy, the patients' lack of knowledge and skills for both pain and the addiction require frequent treatment attendance and monitoring for functional improvement. Because of this constellation of patient characteristics and drug-related neurologic adaptation, most patients meet the criteria for treatment in an ASAM level 2 intensive outpatient treatment program (IOP).

Over the last 10 years, this author and his team have been increasing the focus, within general IOP programs, on pain management and withdrawal symptom relief. Through alteration of content, and focus upon the similarities in recovery from addictive illness and chronic pain, most patients were able to benefit. By treating both conditions at the same time, we recognized that those with more intensive pain management needs did better with more pain-related content, as well as the opportunity to interact with other patients with similar problems. We gradually recognized that there is a growing need to expand the pain treatment track into a formal IOP level of care; hence, this lead to the development of the program for integrated behavioral and pain management treatment.

Referral sources have requested consultation for possible addiction and for recommendations on pharmacotherapy issues. Our comprehensive evaluation procedure addresses these issues and provides an integrated report back to the referral source. It is expected that the referring physician will continue in a collaborative care arrangement through the/addiction pain treatment. An attempt to enrich the physician's understanding and medication management skills, by providing ongoing concurrent treatment services rather than simply taking over pharmacotherapy from every referral source, should occur.

A Working Program

This author spearheaded the development of a pain/addiction treatment program 10 years ago, which now involves a medical director and various clinical staff. This program has had a conservative approach to the management of opioid medications. The program team works with each patient and their referring physician to review past medication strategies and to make recommendations for improved relief and functional status. Our goal is to eliminate the use of pain medications, when appropriate. The choice of medication and dose tapering is individualized and supervised by our staff. Factors such as medication efficacy, safety, drug interactions, and practical issues such as costs are taken into consideration when making medication

adjustments. Through education and therapy sessions on an individual and group basis, patients are provided with practical recommendations as to the benefits and risks associated with the various classes of medications used in chronic pain conditions. Special attention is made to select the least reinforcing and non-addicting options, and to make informed decisions on evidence-based medication use for both prescription products and dietary and herbal remedies.

Intensive Outpatient Treatment Program (IOP) for Pain and Addiction

The design of the pain and addiction program provides intensive treatment, 3–4 times per week, for 3 h of participation at each IOP session. Total weekly participation ranges between 9 and 12 h per week. Topics include four general areas pertinent to chronic pain and addiction:

- Prescription medications and hidden addictions.
- Medical aspects of tolerance and physical dependence.
- Alternative and complementary medicine and chronic pain.
- Pharmacologic management and pain/addiction recovery skills.

Group therapy is an integral part of the program. When chronic pain intrudes in a patient's life, many find themselves overwhelmed by intense, often negative, emotions including panic, fear, grief, and anger. Like the originating pain, these emotions affect the body, sapping energy, and intensifying pain. As a result, more time may be spent alone and less time with friends and family.

The type of group therapy offered does not focus on the "why" of pain, but instead focuses on the "how" of pain, in an effort to get the patient back to a normal life. Group therapy sessions are designed to help patients to recognize and to deal with negative changes and emotions, to improve relationships, and to become more effective at managing their pain. Group therapy is a combination of informal discussions about how lives have been affected by chronic pain and formal lectures on how to effectively deal with pain. Many people find that talking with others, whose lives and family have been negatively affected by chronic pain, can be helpful. This is particularly true when they also support making positive changes to lead a new life.

Conclusion

The dual problem of chronic pain and addiction challenges even the best of clinicians and clinical teams. Patient's seeking treatment need expert assessment of past drug use, current medications, potential for escalated drug seeking, understanding of the complex relationship of the various medications to each other, as well as on the patient. This should always take into account co-morbidities, past medical issues, genetic predisposition, and the pain experience itself. The pain and addiction

clinician must be aware of substance abuse counseling techniques, the dynamics of chronic pain, and the beliefs and coping strategies of the patient, in relation to their perception of their pain, the impact of their pain on their life function, and the relationship of their pain to the medications being taken. Simply dismissing a patient as a "drug addict" is not helpful and is in fact harmful to the patient. It is incumbent upon the care giver to learn about the complex relationship of analgesic medication effects, chronic pain, genetics, and behavior. The knowledge of the most successful approaches to managing the problem of chronic pain and addiction is available, but the treatment course is long and complex, which should be anticipated once a patient has been identified.

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Part III
Headache

Chapter 17
Primary Headaches in the Rehabilitation Patient

Jeremy Goodwin

Introduction

In the general medical outpatient setting, the most common year-round reason for medical consultation is pain, including headache. Unfortunately, the level of training in the diagnosis and management of such problems has yet to be optimally addressed by most clinical programs, at least to a reasonable degree considering the shortage of specialists in the area and the frequency of such problems. This is particularly true for headache. As a result, many clinicians on the "front lines" fall short of being able to provide adequate care to many patients whose headaches are not as clear-cut as teaching sources commonly suggest. For example, about 40% of migraine headaches are misdiagnosed by family practitioners and only half of those who might benefit from preventative therapy are provided it [1]. This problem can extend to the rehabilitation setting, where significant cross-training is required to care for injured or disease-compromised patients, a number of whom have pre-existing conditions including primary headaches.

As is the case within general medical clinics and inpatient wards, co-morbidity in the rehabilitation setting can be viewed as complicating the focus of care, or it can be seen as part of the overall clinical picture and treated as such. Consultation with another service is an option when co-morbid headaches are difficult to manage; however, the rehabilitation clinician should be able to construct a reasonable differential diagnosis of headache and should be able to attempt several approaches to care before seeking help from others. It can be a serious mistake to discount an exacerbation of pre-existing headache or, even worse, new occurrence of headache when the picture is less clear and the risk of making an incorrect diagnosis potentially

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dangerous. Secondary headaches must be ruled in or out. When the situation is under control, with or without the help of other professionals, the clinical focus can then shift back to the prescribed rehabilitation program.

This chapter will focus on often thinly covered, but extremely important, concepts that should make the treatment of the primary headaches easier. *The focus is philosophical yet practical*. It should equip the clinician-in-training with the cognitive tools to help ameliorate the pain and its interference with the rehabilitation program, while empowering the patient to more effectively advocate for him or herself by actively participating in the treatment decision-making process. The emphasis is on the diagnosis and separation of individual and mixed primary headaches with a nod toward secondary headaches that may mimic them. The full treatment plans would likely be ongoing and include post-discharge plans from the rehabilitation setting; however, these are beyond the scope of this book. The recommended reading section at the end should help compensate for those who wish to take headache medicine further. The outcome ultimately depends on the overall clinical scenario, the type of confounding headache, the patient's age, personality and psychological profile, cultural and financial resources, as well as the attitude and knowledge of the clinicians involved.

The primary headaches include the following: tension-type headache; migraine with and without aura; migraine variants; cluster headaches and other trigeminal autonomic cephalalgias; primary or idiopathic stabbing headache; cough, exertional, and sexual activity-related headaches; primary thunderclap headache; nummular; new persistent daily headache.

Psychological Concepts Useful in the Management of Headache

Philosophically speaking, there are essentially two forms of headache, two types of patients, and two types of treating clinicians. These will be discussed over the next few paragraphs. **Whether primary or secondary in designation, the two main types of headache are those that are easily treatable versus others that are relatively intractable.** Approximately 80–90% of headaches are primary [2]. They are the result of a confluence of predisposing genetic, environmental, psychosocial, and sensory mis-processing factors. Primary headaches are not secondary to another condition. They are essentially idiopathic and the pain is generally recurrent-acute, but may be chronic in nature. **Secondary headaches** are by contrast symptomatic of injury or other clinical disorders. They are covered elsewhere in this book.

While easily treatable, headaches of any type are inconvenient if painful, and they are generally not life affecting. However, the relatively refractory headaches require considerable resources to manage them. The skills and costs often lie beyond the patient's geographical location or financial resources. It is this type that frustrates patients, families, and clinicians alike.

At some point, out-of-control headaches of any type can change a relatively highly functioning patient, which is **the first of the two kinds of patients**, to the **second kind**, whose family, vocational, and psychosocial lives have been severely disrupted by pain and suffering. Such suffering can render them psychosocially dysfunctional, which is a significant therapeutic problem in and of itself that can complicate the picture. *Note that this dysfunction is usually created by refractory headaches and the frustration involved and not the other way around*. This is so in the majority of cases. To determine otherwise mandates the involvement of a highly trained mental health professional to assess more thoroughly a potential co-morbid psychiatric disorder. It must be a professional who is knowledgeable about the evaluation and management of chronic pain and suffering; otherwise, such an evaluation and intervention is likely to prove less accurate and potentially damaging.

An interdisciplinary and/or multimodal approach to care is best advised *before* such complications develop. Prevention of escalation should be at the front of every clinician's assessment. Too often, early signs of co-morbidity are ignored or go unnoticed and at some point, it may be too late to do much about it. Fortunately, a single clinician well versed in a number of approaches to the diagnosis and management of headache can achieve much. Not every problem needs to be solved immediately yet early clarification can help others to provide effective management after the patient is discharged from the rehabilitation program.

A common problem is poor communication or misunderstanding between clinician and patient. Their goals may differ. Clinicians tend to focus on what they feel are the key medical or surgical issues ("at least we can cut it out or block the pain with medication"), whereas patients worry more about how they might be affected as a person or how their condition might interfere with their role as a family member or provider ("what if I can't work again or properly take care of my newborn child, while experiencing recurrent pain like this?"). Communication is of utmost importance to minimize anxiety yet, in order to communicate effectively, there must be an interpersonal *connection*. If the clinician is both a healer and an empathetic human being, such qualities are likely to foster connection with the patient. Caring is *always* possible, whereas cure is not. This is akin to the difference between the biopsychosocial versus the biomedical approach to the treatment of pain.

Contrary to a popular saying, pain *does* kill. Suicide is not uncommon, especially by those who feel alone in their suffering. This is a perception that is derived from feeling that their pain is neither sufficiently validated nor appropriately managed. Suicide is also more likely to occur when hopelessness and helplessness result in what psychologists refer to as a change in the ***locus of control*** [3]. This factor can be ascertained on interview. Essentially, it describes a patient's attitude regarding his or her ability to self-modulate pain when given the tools to do so. This is the best-case scenario; the worst-case scenario occurs when there is no locus of control, constituting a loss of hope or a medical surrender. The middle ground, or third type, is when patients feel reliant upon the "magical" powers of others to cure them. *Mental health specialists trained in pain management can be very helpful here*. They can empower patients to help themselves. *They should be introduced as pain specialists with a psychological background, the goal of their involvement being to*

enable patients to cope more effectively. Even a single consultation or a few clinical sessions in either a group or individual setting can be useful. **It is *vital* that the patient not mistake the message or referral to mean that "the pain is all in your mind". That is every bit as important to them as knowing that there is no tumor present responsible for the pain.** Pain is always real when experienced. The cause is relevant only in terms of how it is best handled and that cause may at times be hard to determine.

Very broadly speaking, **clinicians themselves may also be of two types.** Many are disease or medically focused, whereby interventions are largely predicated upon an understanding of the disease process per se. Essentially, if unwittingly so, treating the patient becomes somewhat incidental. Their **biomedical** perspective to care is predominantly pharmaceutical, interventional, or surgically based. Other, more empathetic and "people-oriented" practitioners with a **biopsychosocial** perspective see patients as persons afflicted with life-affecting conditions, providing them with an opportunity to try different approaches and to devise a plan of care based upon a patient's personality, their family dynamics, socioeconomic and cultural influences, as well as their medical condition. In either case, treatments might include those lying outside allopathic or "western" medicine; although, it is increasingly common to find practitioners combining them in an integrative or collaborative manner. Not all approaches need be tried within the rehabilitation setting; however, a few are easily initiated there.

Clinicians and nursing staff can provide patients with contact information for post rehabilitation care. It is always a good idea to ***foster realistic expectations***, an example of which is that in the long run, most primary headaches are generally managed rather than cured; hopefully, this will diminish the problem by 50–75% and ongoing care will likely be required after discharge. At some point, patients may even "grow out of them". In a tiny minority, some headaches have an onset well into the seventh decade [4].

Medical Factors Important in the Management of Primary Headaches

It may be helpful to think of the primary headaches, especially migraine, as aberrantly amplified and prolonged normal physiological processes that result in head pain. Pain is the most focused-upon symptom, but it is not always present or even necessary for the diagnosis; "acephalgic migraine" and migraine variants are the best examples of this. The notion of sensory hypersensitivity is not very different from the basic concepts used to explain neuropathic pain or the hypersensitivity to stimuli seen in fibromyalgia, all being aberrant responses to *normal* stimuli caused by dysfunctional central nervous system processing, which might involve wind-up and centralization of pain [5]. This may explain the therapeutic overlap of certain agents commonly employed in pain and headache management. The treatments may help to re-set the nervous system's processing of sensory input.

Unfortunately, where headaches are concerned and especially the primary headaches, pain generators are still imperfectly understood. Such missing information is not merely academic given the fact that treatment strategies vary considerably depending on the headache subtype, pathophysiology involved, and the clinical presentation. They all help to more accurately define the type of headache. However, detailed assessment in making the most accurate diagnosis as possible is not always easy. Clinical acumen and experience, along with a broad knowledge of diagnostic and therapeutic interventions are invaluable given the lack of evidence-based methods and objective testing that might otherwise be applied. Headache medicine, for all its advances in pathophysiology over the past half-century, is still not unlike the field of psychiatry. To a great extent, the diagnosis is determined via a signs and symptoms approach, sometimes necessitating a diagnosis of exclusion, a case in point being that of migraine.

Despite the significant overlap between the fields of pain and headache medicine, the details of management may differ in important ways. For example, **medication overuse can lead to chronicity of headache**, with different time periods of overuse being needed for different classes of medication [6]. This is not really a concept thought to affect other forms of pain; although, there are emerging percepts that contradict such a position. Some workers believe that pain medication can, over time, negatively affect a patient's perception of pain and/or decrease their pain thresholds.

Importantly, *many of the compounds used to abort, prevent, or to minimize the frequency or recurrence of several primary headaches cannot be used to make the diagnosis, even when successful*. This is so because such compounds might work well on several disorders, not all of which need be headache. Epilepsy, hypertension, facial pain, stroke, anxiety, insomnia and depression, and others might all respond to a narrow range of medication. Such conditions can also result in the emergence of a new headache disorder or exacerbation of an already present one. Furthermore, several types of headache may respond to the same treatment. Triptans, for example, may alleviate headache associated with stroke, but leave the patient dangerously untreated for a life-threatening condition if a full workup is deferred. Triptans may also alleviate tension-type *appearing* background headache present between acute exacerbations of migraine, something seen in both chronic-from-the-start migraine, as well as the etiologically different form of migraine transformed from episodic to chronic by overuse of *any* abortive medication, the latter being a condition that can usually be reversed by detoxification and carefully implemented prophylaxis. *However, triptans will fail to alleviate tension-type headache when migraine is not present*. This brings up the point that the lesser pain experienced between peaks of migraine intensity appears similar to, but not quite the same, as tension-type headache. While there has been much debate about these two similar types of headache lying in a continuum, at this point in time, most workers in the field believe that they are disparate; although, there may be a subset of people for whom such a continuum exists. Therefore, the art of thorough history taking is crucial as is the physical examination. Both help to define the initial or presumptive

differential diagnosis so that appropriate imaging studies and tests might be most efficiently obtained. A good history does not preclude the physical examination or testing, but rather *directs* them. The diagnosis is usually reached via a combination of all three.

The Importance of Differentiation of Selected Primary Headaches

The primary headaches are predominantly migraine and its variants, tension-type headache, cluster, and other so-called trigeminal autonomic cephalalgias, which include a number of others, such as exertional and cough headaches, most of which have several subtypes. Some of these are extremely uncommon. They will be mentioned only briefly here, but can be read about in more detail in the "recommended reading" section at the end of this chapter. They can also be looked up on-line.

Primary headaches tend to begin most often as recurrent-acute head pain with associated signs and symptoms. Some types involve the autonomic nervous system; whereas, others are chronic from the start. New Persistent Daily Headache is the classic example of this. Autonomic nervous system-related signs and symptoms are nearly always present in the trigeminal autonomic cephalalgias and, to a far lesser degree, migraine. While many primary headaches are episodic in origin, most can become chronic over time and most commonly via overuse of abortive medication; although, chronicity can manifest from the start or can be created by other mechanisms, such as stress-induced vacillation between more than one form of headache [7]. Once again, a case in point is chronic migraine. Determining how and when it became chronic can drastically alter the treatment plan. *Importantly, chronic migraine cannot be diagnosed in the presence of medication overuse* [7]. Chronic migraine, which includes headache for more than 15 days a month, may be very similar in presentation to transformed migraine; the latter being an older term most commonly associated with medication overuse, but potentially inclusive of other mechanisms. Other mechanisms include frequent triggers by one or more co-existing headache disorders.

Despite their similarity in presentation, the approach to treatment of certain headaches that have become chronic is different. Medication over-use headache, which was previously known as rebound headache, is an umbrella term covering many forms of once-episodic headaches that include, but are not restricted to, migraine. It is not difficult to treat if one understands what likely caused the persistence or intractability. Additionally, good clinical skills and an encouraging bedside manner help substantially. This is described further in its own subsection.

Regardless of the cause of chronicity, headache subtypes can occur alone or together. The importance is that the differentiation between co-existent headaches helps the clinician to elucidate potential endpoints, treatment goals, or the best

timing and sequencing of them. The only way to obtain this information is through a very detailed history, which includes asking questions from several angles since many patients experience headache as a continuous uni-dimensional type of pain, until they are taught to separate signs and symptoms. This is not unlike learning to listen to an orchestra perform. With up to 106 musicians performing on the stage alone or together, it becomes far more interesting to the listener when individual instruments, melodies, and musical counterpoints, etc., can be discerned, whilst never losing track of the whole score. This requires education beyond medical school and residency training. A similar analogy can be made using team sports, whereby an understanding of the role various players have on and off the ball enhances understanding of the game. If multiple headaches are diagnosed, given that several treatments may cover several forms of headache, fewer compounds might then be needed as a component of care.

The reason for near black and white classification of headaches by the International Headache Society (IHS) is mostly to improve the sensitivity and specificity of research protocols. This is to assure that the same form of headache is more likely to be consistently diagnosed, which makes it easier to judge the efficacy of treatments for them, whether new or in comparison to one another.

In non-research clinics, headaches are often of a mixed type of etiology, and the pathophysiology remains even more controversial. There is also far greater overlap and mixing of terminology in the clinical, as compared to the research setting. An example would be "cluster-migraine", for which there is no IHS diagnosis. However, the two separate types of headache, cluster headache and migraine, can co-exist. Interestingly, *when this happens, a treatment often helpful for one, but not the other, may work well for both*. Oxygen, via a non-re-breathable face mask, may thereby alleviate a migraine headache, just as preventative medications that are typically useful for only one might help with the other. In other words, it is important not to get too caught up in the research setting's "rules"; it is important to maintain the flexibility of mind that facilitates creativity, as well as a healthy level of skepticism, whereby mechanisms of action or causation are concerned. Rarely do the data for such things remain static, and to achieve this flexibility of mind, keeping up on the literature is important.

For the most part, while there are few specific bedside neurological examination techniques or "high-tech" tests available outside of the research setting to diagnose primary headaches, **some procedures can help to clarify the differential diagnosis and/or prognosis**. Tests are necessary at times to rule in or out other possibilities that might mimic certain headaches and facial pain. They can also help to predict a successful treatment of an already confirmed diagnosis or can help to justify a different, longer lasting, if sometimes more expensive approach to alleviation of pain, such as by **neuromodulation** (i.e., peripheral nerve stimulation). Three successive and successful diagnostic and therapeutic greater occipital nerve injections, if only of temporary help, might justify the use of a peripheral nerve stimulator, a modality that has the potential for effectively aborting cervicogenic as well as cluster headaches. For further details, please see chapter on peripheral nerve stimulation.

Other interventional techniques may also be of value. Diagnostic and/or therapeutic applications of anesthetic agents placed into the intra-nasal region (lidocaine, procaine, or rarely cocaine), or peri-cranial muscle injections of Botox A, etc., are commonly used to alleviate specific pains in the short or the long term, respectively. Some injections are purely diagnostic, some therapeutic, and others both.

Imaging studies may also be useful. For example, tumors may "mimic" migraine, as can seizures. Tumors can cause epilepsy as well as stroke, both of which can lead to intense headache. Therefore, objective tests may be required to narrow the differential diagnosis. Trigeminal neuralgia must be differentiated from painful trigeminal neuropathy, the latter of which includes *negative* symptoms, such as loss of facial sensation, with *positive* symptoms of trigeminal neuralgia, such as spontaneous lancinating, stabbing, and aching facial pain. These symptoms are sometimes the result of a tumor in the cavernous sinus.

Facial pain alone is often due to irritation of the root of the fifth cranial nerve by an abutting pulsating artery that injures the nerve, while that same pain, which is sometimes experienced bilaterally, can be produced by a multiple sclerotic plaques adjacent to the nerve root. A head MRI and MRA with contrast can help to rule in or to rule out a mass-producing headache. In the second case, pressure-induced peripheral cranial nerve pain should be considered. Because radiologic technology and diagnostic protocols undergo such rapid change, it is *best to check with a neuroradiologist for the most appropriate imaging study* based upon the signs and symptoms and differential diagnosis. An **EEG** might also prove useful if post-ictal seizure-related headaches are suspected. For the most part, at least where the primary headaches are concerned, the neurological examination is generally normal and head MR imaging is unrevealing.

Clinical Relevance of the Language and Nosology of Headaches

Knowledge of pathophysiologic terminology can be important for authorization of procedures, depending on the health insurance companies' policies. Additionally, this will facilitate a means of communication between clinicians from different generations. While occipital neuralgia is a more recent and accurate term for what was once referred to as "occipital neuritis", even today there are cases where only one or the other term will qualify for a peripheral nerve stimulator, despite them being the same disorder. For example, it was not long ago that "sick headache" was still accepted by Medicare as a pseudonym for migraine. Outdated terminology is abundant in clinical medicine, mostly outside of the research setting; yet; such terminology is still important to know.

It is also important to understand that the language used in most respected textbooks and papers can rapidly become accepted as "gospel" by the medical community. Through time, and by convention, this language becomes the dominant

descriptors or hypothesized causes of pain for a given diagnosis. These then become recognized as "fact", even when at a later time the information is known by many to be incorrect. Misnomers and misinformation can persist for years and can even appear in the latest revisions of a textbook. For example, as will be mentioned below, "vascular headache" is an inaccurate and well-outdated term [8], which was replaced in recent years by the concept of neurovascular pain; yet, it is still commonly used. Failure to stay abreast of such things can be clinically limiting, contributing to misdiagnosis as well as mismanagement given that optimum therapy depends upon accurate understanding of the mechanisms of dysfunction.

Even simple pain descriptors can be problematic. For example, **"stabbing" pain does not equate with cluster headache,** as might be taught in medical school. It is seen in other trigeminal autonomic cephalalgias as well. That group of headaches now includes **paroxysmal hemicrania**, and the stabbing symptom is a defining pain in another primary headache disorder, **idiopathic stabbing headache**. Even **migraine** may include stabbing pain and **autonomic dysfunction**; yet, it is in a category of its own. Boundaries between syndromes are not always sharp. **Throbbing, pulsating pain** may be a frequent manifestation of migraine, but are also prominent features of caffeine withdrawal headache and acute sinusitis. *Even the **unilaterality of migraine** is merely a most common scenario*. In fact, just as lateralized partial seizures can secondarily spread, so too can migraine phenomena, as often as 40% of the time [9]. It may typically begin on one side and then become bilateral, especially during sleep. It may then awaken one with pain on both sides, even if generally felt as most intense on the side of origin. **Nausea and vomiting** are prominent features of most migraine attacks, 80–95% and 50% respectively; yet, in a very small minority (perhaps 3–5%), they are both absent. Clinically, they may not be a necessary feature of migraine, even though they are considered so for research purposes. There is room for greater flexibility in the clinic. While **cervicogenic headaches** are typically described as unilateral, Nicolai Bogduk has stated wryly that on occasion they **can be "bilaterally unilateral"**. As can be seen by these examples, nosology is not always clear-cut, so it is best to minimize rigidity of thinking regarding diagnostic criteria by being as open as possible to frequent changes within the classification systems.

Exacerbation of Headache

Primary headaches can be induced or exacerbated *directly or indirectly* by ongoing medical or surgical issues that may or may not be painful, which include internally disrupted cervical disks from C4-C5 and up, cervical facetogenic pain, reactive myofascial pain, restless legs syndrome (RLS), periodic limb movements of sleep (PLMS), as well as obstructive sleep apnea. Injury or pain from other conditions, the treatments for those problems, exercise or lack thereof, dietary factors, sexual activity or exertion, and irregular sleep patterns can all make headache worse in terms of frequency and intensity. *If sleep apnea is present, headaches, anxiety, or*

depression may be extremely difficult to control. Additionally, with non-restorative sleep due to other interferences with sleep architecture, including alcohol, or movement disorders such as RLS, PLMS, or alpha-wave intrusion of sleep as seen in fibromyalgia, headaches may become very hard to manage. Even a number of commonly used antidepressants such as TCAs, SSRIs (but usually not SNRIs) might exacerbate the movement disorder, even though they may be appropriately prescribed for other signs and symptoms. If a TCA causes sedation but exacerbates RLS/PLMS, then it is of no help. Each patient is different. It is always important to keep the bigger picture in mind. Conversely, dopaminergic compounds used to treat sleep-disrupting disorders, such as RLS and PLMS, may result in hallucinations or compulsions. These often manifest in psychosocially disruptive behavior and the emergence of addictions, the ramifications of which can be serious both legally and socially, and can negatively affect headache frequency clinically. *Knowledge of pharmacology and drug–drug or drug–disease interactions is of paramount importance whenever clinical outcomes are concerned*.

Stress is most commonly cited as a trigger for headaches, but that is itself a complex topic. Stress can be both a cause and a result of headache. A migraine headache may *follow* stress, such as after completion of a demanding project. Stress can negatively affect eating schedules and the type of food consumed, can increase alcohol consumption, can decrease time and energy available for exercise, and can disrupt sleep patterns. All of these can, even without stress as a factor, trigger certain headaches. All can induce migraine. In the laboratory setting, nitrates, such as in nitroglycerin paste, are more reliable in inducing headache, at least in migraineurs, than are the more commonly cited triggers of alcohol, stress, chocolate, or nuts. *However, stress plays a minimal role in the onset of cluster headache, and relaxation training is fairly worthless in its prevention. Alcohol, in contrast, is a clear and avoidable trigger*. As aforementioned, one type of headache can trigger another, bouncing back and forth. Hence, failure to recognize a person's different headache subtypes, triggers, and the lifestyle factors that impact them can lead to relatively ineffectual results in terms of management.

Where migraine is concerned, during an attack, oral medication absorption is diminished in some patients and the head pain can rapidly escalate to a point where it becomes very difficult to alleviate. This phenomenon mandates **early treatment**, usually within the first 20 min. However, if done so too frequently, it **can lead to medication overuse headache**. Thus premature or excessive treatment can prove counter-productive. Treatment recommendations require thoughtful and careful observation, as well as patient and family education. It is important to remember that each individual is different. **A really helpful question is, "when you develop the migraine pain on one side or the other, do you lay your head down on a soft pillow, gently applying pressure to that side, or does that make it worse?"** If the answer is "worse", then such rapidly escalating one-sided allodynia, which is defined as pain from a non-painful stimulus, requires aggressive and early abolition. Otherwise, it may last miserably for 72 h and may prove relatively refractory to treatment. If the person lies down with the painful side touching a pillow with gentle pressure providing some relief, then there is a more leeway in trying distraction,

relaxation, or other methods to avert a full-blown, long-lasting migraine headache. Even a visit to the Emergency Department (ED) with bright lights, loss of rest, forced movement, noise can be highly stressful and can significantly worsen a migraine attack. After all, most migraineurs wish only to lie down in a quiet, dark place in order to sleep it off.

Sometimes, **distraction** can avert a migraine headache or a tension-type headache, the latter of which can sometimes turn into a migraine if co-existent. Again, care in advising patients based upon their own profile, history of pain, alleviation, plus back-up strategies are necessary for optimal results. **If medication overuse has turned episodic headaches into the chronic type,** ***preventative medication will usually fail until detoxification has been in place for 1–3 months*** [10]. Because of this little known fact, previously tried and failed preventatives might thus be reconsidered at a later date, post detoxification. *Patients should have at least a couple of safe abortive medication options to use at home or at work in case one fails*. Conversely, failure to bring some headaches quickly under control can negatively impact the time needed for headache relief. Subsequently, this can perpetuate suffering or can require an otherwise preventable visit to the ED. Too many such episodes while in the rehabilitation setting will impede therapeutic success, will increase the cost of care, and will prolong the time needed for healing and recuperation. It becomes a balancing act, as medicine so often does. The trick is to avoid it becoming a circus.

A Word on the Use of Medication

One of the most common reasons for failure to help those with chronic pain and intractable headache is misuse of medication by clinicians, let alone patients. As a headache and pain specialist for both adults and children, it is not unusual to receive a referral for care that contains a list of up to 30 medications that have been tried and "failed". Generally, failure is due to a lack of understanding about how to apply pharmacologic knowledge differently than might be the case in other areas of medicine, with the exception of general pain management and epilepsy. It simply is not taught in medical school or in most residency programs, and those gaining such experience in fellowships or by trial and error are small in number. The following are some general principles to keep in mind with patients suffering primary headaches, either episodic or chronic in presentation:

1. The "scientific" approach of trying one medication at a time may fail because medications often work best when prescribed using a multimodal/interdisciplinary approach and also when **lower doses of more than one medication are combined with others. These include herbs and complementary systems of care, rather than higher doses of a single medication alone.** Trying one agent per month may fail to reap rewards, even within a year. The torture endured by patients from such practice cannot be justified. While there may be

small differences in efficacy or "numbers needed to treat" (NNT) to gain a good result between classes of medication for certain disorders, or specific agents within a family of a class that is a drug of choice (i.e., indomethacin), **it is wise to ask about previous use, success vs. failure, history of adverse effects, and sensitivity to dosage and tolerance to any medication being considered with reference to close relatives, even if they were used for different disorders (such as depression instead of headache).** Genetics do play a role in the efficacy and side effect profiles of medication; therefore, a good family history of medication use can be very informative and can even be predictive of success or failure. *It is important to always ask if a patient is sensitive to medication in general*. If so, start with doses lower than usual, increase more slowly than usual, and monitor very closely.

2. **If medication overuse is deemed to be a factor in headache chronicity, a toxic clean out is required** before or during introduction of a preventative medication, whether utilized for the first time or if being re-tried. It will not work until detoxification is complete. **Abortive medication needs to be restricted to a frequency of no greater than 2 days per week**, with an occasional extra day for an important commitment, but extra days should be infrequent. Multiple safe doses on each of those 2 days would be an acceptable practice. Fourteen doses spread over two, 24 h periods per week will not induce rebound headache; yet, two doses daily each week, also totaling 14 doses per week, may in fact induce rebound headache over a period of time. Patient education is essential for teaching patients to pick their headache battles by using medication with care and utilizing other approaches when possible. This generally takes 4–12 weeks. ***Using different abortive medications on different coupled days each week will NOT diminish medication over-use***. In other words, 2 days of frequent Excedrin Migraine use (caffeine, aspirin, and acetaminophen), followed by 2 days of hydrocodone, and two more days of naproxen sodium (Aleve) will only reinforce the chronicity of headache. The only way to make detoxification work is to see the patient frequently enough to be able to better control, or to at least involve a pain specializing mental health professional for continued support in coping with and engaging in relaxation and stress management techniques for pain. Additionally, Chinese medicine could be added, if applicable, in conjunction with medical and behavioral psychoeducation. There is no singular recipe for success.

Importantly, the weaning schedule employed by many for detoxification often makes little sense pharmacologically and psychologically. ***Anxiety created by a poorly executed weaning schedule, in addition to a quick return of pain discourages patients from compliance***. When a patient presents initially on three to five abortive medications, sometimes taken at levels dangerous to the liver and kidneys, without effectively alleviating the pain, then blood tests are in order to gauge any potential damage to the organs of concern. Immediate cessation of one or two of the over-used medications, or a rapid wean over 10 days may be necessary. It is important to take it slower with those medications that may result in physical withdrawal or for which greater degrees of temporary

efficacy are suspected. *Failure to explain these principles to the patient will increase anxiety and/or non-restorative sleep, which can thereby lead to serious exacerbations of pain and non-compliance*. This author uses an analogy to explain to the patient that: **"In order for one to define the types of stones and rocks on a river bed, it is necessary to allow the mud in the water, created by walking in the stream, to settle or run off…".** Most understand this picture quite well.

A common clinical error made in weaning overuse of around the clock (RTC) and over-the-counter (OTC) medications, regardless of the potential for physical withdrawal, is to simply drop the number by a set amount over a specified period of time, too quickly, such as 8 tablets a day dropped to 7, 6, 5, 4, 2, 1, and 0, respectively, over 10 days. If the half-life is long, then that approach might be satisfactory. Drugs with a longer half-life wean themselves down slowly. However, if the pharmacologic half-life, which is the time needed to remove half of the medication from the body, is short, then such a mere few hours, then once eight tablets have been rapidly dropped to four per day, pain is likely to rebound furiously and withdrawal might kick in. *It is of value then to break the pills in half, or to prescribe a half-strength tablet, and to then repeat the same process starting with eight lower strength tablets per day and timing the wean similarly until completely off*. This affords time for the body and the brain to re-set itself; although, it will generally take 4–12 weeks, during which time preventatives can be started and increased in dose, alone or in combination.

If in-house, a **"blind cocktail"** can be utilized where the offending agent is dissolved in fruit syrup and incrementally decreased by a set percentage every few days until off. At some point, the weaned-off medication becomes a placebo. ***Ethically speaking, permission should be granted with full disclosure of the process and the reasons for it, and the patient specifically informed that he or she would not be told exactly when the medication has been eliminated***. It is best to give the inactive juice for at least 3 days beyond the point of drug elimination because that will prove more convincing to the headache sufferer once they realize that the medication was not needed to prevent headache recurrence. *Informed consent will prevent a feeling of having been duped by the clinician*. This can be used with any medication over individually determined periods of time. It works very well for opioids too.

It may not be possible to wean off all medication, at least for a while, but very low doses might not interfere with clinical improvement. Anecdotally, I once reduced a patient's 120 mg dose of daily oral methadone, which was divided into q 8 h intervals, without difficulty, by about 10 mg every 2 weeks. The patient was fearful given that he had been on that dose for 13 years, until he got down to 5–10 mg a day, at which point he could not let go. His anxiety would flare, as would his intense migraine headaches. So, he was given more control and weekly meetings with stress management mental health workers, through which he further reduced the dose to 2.5 mg and then off. He just needed more time.

Everyone is different. I had always been truthful and respectful of this particular patient; because of that trust, he agreed to this schedule. He knew that it was a crutch, but he was afraid. Being brave, he participated and actually wanted off, once he understood the medical and hormonal ramifications of daily opioids and how it was not working anyway. He ended up returning to full time work after 8 years of being unable to function even on high dose methadone prescribed by another clinician 13 years prior. He was provided help with **hormonal replacement** medication, given that opioids, pain, and stress all diminish release of luteinizing hormone (LH) from the posterior pituitary gland and, as a result, testosterone. Even the estrogen, from which it is converted in fatty tissue, significantly decreases. Both are involved in hundreds of chemical reactions around the body and the negative effects of low blood levels are considerable. *DHEA will NOT serve to replace the testosterone*. **Some require an antidepressant for a while**; bupropion HCL being a good choice given its dopamine and nor-epinephrine elevating activity that can boost energy, as well as libido. It can also elevate anxiety in some, especially at the higher dose. Nonetheless, he rediscovered his interest in women and within a year he was remarried. There was little to be gained by forcing a quicker reduction. With others, that might not be the case.

3. Starting multiple medications, or going through a trial of several classes over time should be started as a "cluster" and not simultaneously. It is important to start low and to climb in dose of each medication slowly. Each additional preventative should be added and separated by 2–3 weeks rather than replacing one medication with another every 4–8 weeks as is the more common practice. This is critical to be able to monitor side effects. This is only necessary in hard to manage cases. **It might achieve results earlier than the traditional way and then one can slowly back off one medication at a time, until the fewest number of preventatives remain; hopefully, with few adverse effects and lower dosing of each one.** On occasion, success gained with one weaned off medication may not recur, even when ramped up again. There is no good explanation for this.
4. In general, and for the purpose of illustration, **for migraine and** sometimes for severe tension-type headaches, I usually start with **magnesium** 150–250 mg once or twice daily for its headache relieving effect, which includes relaxing muscles and improving sleep patterns, while shutting down certain calcium channels. One should watch out for too much stool softening. It should be started with a single dose daily, 1–2 h before bedtime, which can always be increased by adding another dose to breakfast after a couple of weeks if necessary. **Vitamin B2** (riboflavin) at 400–500 mg/day can be started at the same time (for migraine). Adding the herb **Butterbur standardized extract**, 50–75 mg twice daily, at a later date, considering CoEQ10, 50 mg p.o. t.i.d. as well, before prescribing allopathic medication, often works, and all four medications are OTC. *This is especially a good idea in children where cognitive performance in school is of concern as parents generally prefer to avoid giving*

their children prescription medication whenever possible. **Prescription medications**, too, can be started a couple of weeks apart in those who are sensitive, in order to better determine or to separate the cause, if any, of adverse side effects. These can be seen in the individual headache summaries below for more detail. It may take a couple of months or more to notice an inarguable change in headache frequency. The higher or more consistent the frequency, the easier it is to judge the effects early, especially when a brief headache journal is kept. One should avoid *over*-focusing on the headaches though. ***All prescription and OTC medications and herbs can be slowly tapered off after a reasonable level of control has been reached and maintained for 6–9 months***. *They can be restarted or increased again if the clinical picture worsens*. Changes in lifestyle and avoidance of triggers should be maintained.

5. Choosing an effective prophylactic or even an abortive medication for migraine and other headaches can be difficult. If the headache is easily aborted without many adverse effects, or if the headaches do not last more than a day and occur with a frequency fewer than three a month, prophylactic medication may be unnecessary. Alternatively, it might be wise to stay with the "natural" preventatives. A patient's previous experience with one or more such agents must be always considered, just as co-morbidities like epilepsy, cardiovascular disease, neuropathic pain, other headaches, hypertension, diabetes should as well. Additionally, the experiences of a closely related family member with the same agents or classes should be factored in to prescription decision making. Furthermore, different medications from the same class may be tried following failure of one, given that every individual has a unique response to each medication or combination of medications. For example, if gabapentin (Neurontin) fails or is poorly tolerated, try pregabalin (Lyrica) before giving up on that class, or vice versa. If seizures and difficulty with absorption are issues, then Lyrica is a better first choice of the two. Gabapentin is absorbed in a complex manner that can lead to saturation of intestinal transport mechanisms, which can lead to unpredictable blood levels, especially at doses approaching 1800 mg or more, two to three times daily. Pregabalin (Lyrica) is always 90% absorbed and is dosed up to a maximum of 200 mg 2–3× a day. I generally find twice daily dosing to work well with each. Gabapentin has poor anti-seizure capability, as compared with its pharmacological cousin pregabalin. This may be important in cases where seizures lead to headache. **Whether it be an antidepressant, an antiepileptic medication, a NSAID, beta-blocker, triptan, opioid, or ergotamine derivative, the manufacturing company and health insurance's claims of superiority or equivalency apply only to large groups and not necessarily to individuals.** It is important to be critical of such claims and to try other medications in the same or a different class. Otherwise, it is important to consider creative combinations as necessary.
6. Many medication classes are sub-grouped into families, the most well known of which is the NSAID family. It is the same with seizure medications, antidepressants, antihypertension medications, and opioids. **Where success is achieved**

in terms of headache relief, but complicated by adverse affects or lack of health care coverage, changing to a similar medication within the same family still within that class may prove beneficial. Inefficacy may be improved by a change to a medication still within that class but sub-categorized into another family. *There are apps for smartphones that will provide such information on, as well as the best prices, for medications should the insurance company refuse coverage or if the patient is paying by cash.* **"Good RX"** is one that can be downloaded without charge to a smartphone or computer for the best prices in any geographical area.

7. Ergotamine and DHE, as well as methysergide medication protocols for migraine can be found on-line and in most headache textbooks and manuals. To a significant degree, the Triptans have become the abortive class of choice for both migraine and, with some preparations, cluster headache using subcutaneous and intra-nasal delivery. Insurance coverage can be problematic given the false assumption that the medications within a class are equivalent. That dictum applies only to large groups, not to individuals. Only the least expensive ones are usually covered. The data of efficacy reveals little between them; although, there can be differences in the rate of absorption, half-life, and cost, which is based upon the preparation and delivery system. As with opioids and NSAIDS, the variation of response between individuals can be impressive even if, overall, one brand may be roughly equivalent to another where population statistics are concerned. Prior to using expensive Triptans, it may be worth a trial of an oral combination of high-dose aspirin or a NSAID, in addition to 10 mg Reglan or to 25 mg Compazine and a strong cup of caffeinated tea or coffee. The first dose only of anti-inflammatory should be 1.5× the maximum usual single dose.
8. **It is important to at least briefly discuss the controversy surrounding use of opioid medication for the relief of headache and facial pain versus pain management in general.** It is a topic that has generated heated discussion for decades, especially with respect to general pain management. If anything, it has become an even more controversial subject today, especially in light of the fact that in 2016, various medical societies, government health agencies, individual health insurance plans, hospital systems, and clinics recently put into force prescription altering guidelines, rules, and regulations. These occasionally come with a disclaimer that they are but "suggestions" to control a so-called epidemic of addiction. Millions of patients have had their opioid medications severely cut back or stopped altogether by clinicians who are now either too afraid to prescribe them for fear of government recrimination or who are feeling empowered to refuse such treatment now that the tide has turned against the pain medicine establishment that had long supported properly prescribed opioid use for otherwise intractable pain. The resultant debate has literally ricocheted around the media with tempers flaring on both sides. In turn, this has made the situation more of an emotionally driven political disagreement than a medical or scientific one. **The question is, "Is there a role for opioids in headache management similar to that of pain management?"** The answer is "yes" and "no" as elaborated below.

The increased availability of opioids for intractable pain was originally promoted by pain specialists for good reason and *as part of a multi-modal and interdisciplinary plan of care, when other agents failed to satisfactorily quell moderate to intense pain, but only in carefully selected and monitored patients*. That was the intent. Many clinicians without deep interest in this area of medicine did not follow the guidelines and problems evolved rapidly with the industry-made medication finding its way to the street, briefly displacing heroin and other agents in their wake. As a result, opioids became a "gateway" medication to other abused drugs; although, the use of statistics has been skewed for political reasons more so than scientific ones. Only 13% of the deaths each year were by patients prescribed opioids for chronic pain. These few were not separated from the nearly 90% who more likely have a chemical dependency disorder, for whom that branch of medicine falls short in terms of options, efficacy, and philosophy.

The application of opioids for intractable daily headache, or for intermittently severe headaches unresponsive to other medications, has been less enthusiastically promoted. Data are lacking but Saper et al. in 2000 published a 5 year long prospective study whereby sustained release opioids used in over 300 patients carefully selected for intractability of near daily headache, plus absence of factors predictive of addiction, fared less than spectacularly well. One hundred and sixty completed the study, but only 23% could be said to have shown improvement; 40% showed some evidence of self-adjustment of dosage but without an impressive gain in function. Hence, compared with general chronic pain, the use of opioids in the amelioration of headache and facial pain is less common except, perhaps in departments of emergency medicine [11]. **That left room for various populations such as pregnant women to utilize opioids, especially given the potential teratogenicity of many other abortives. Generally, this was only after reasonable alternatives had been tried and failed, and if the patients had passed a variety of psychological profile assessments.**

The main issues are multilayered and difficult to sort. This is due to a lack of well accrued data, failure to separate important sub-groups of users who have died or nearly died by accidental or otherwise overdose from those who are suffering intractable pain but who are compliant, and also from those who use opioids recreationally or as an escape from life's stress, or both. Whether or not the recently recorded increase in overdose-related deaths that have suddenly come to public attention is a true epidemic or something considered by many to be a matter of importance due to the relative increase in numbers of Caucasians who have died, as compared to the historical trend of it being a mostly African American or Hispanic problem. Some feel that it is a new focus on an old problem given that the opioids involved on the street have increasingly been found to be industry-made, as against the traditional drug cartel-imported merchandise, which so-called "junkies" commonly used for decades and over which few seemed to really care. Is it really a new problem and if so, is it a failure of the field of pain medicine, addiction medicine, or something else? There is room to touch on only a few of these points herein.

It is not incorrect to state that the majority of clinicians only have a passing interest in chronic non-cancer pain or headache care and that many are glad to see the relative liberalization of opioid use championed by pain specialists these past 30 years, currently being reigned in. But is this a just move? Is it creating an even worse problem now that drug cartel-manufactured opioids are dangerous combinations of compounds such as fentanyl and heroin, made into faux tablets sold as oxycodone? This is in addition to their quickly rising value, which is coincident with genuine prescription medication restriction, despite the fact that only recently did heroin drop in value considerably. The statistics quoted about this and the more human side rarely try to separate the various user sub-groups; therefore, conclusions drawn by either side are merely conjecture. As a result, many in chronic pain are now suffering unnecessarily, even if it is but a subset of them who used opioids primarily for intractable headache management, which is the focus of this chapter.

The system of care and distribution that put the increased availability of such medication in the hands of many clinicians and patients, without adequate education and training, is really a system fault on multiple levels for the problems that resulted. It is important to realize that the 16,000–17,000 or so overdose-related deaths in the USA in 2013 and 2014 were matched by overdoses from NSAIDS, such as ibuprofen. The latter, however, created no uproar. Furthermore, the number of accidental or deliberate deaths by gunshot wounds was at least double that number and has remained so for years, again without significant reaction by individual states or the federal government. **Contrary to the statements made by irresponsible clinicians in the media of late claiming otherwise, no one ever stated that addiction to opioids was impossible, only that the likelihood was far lower than previously assumed, as long as the patients were carefully selected and monitored in an interdisciplinary program run by knowledgeable clinicians.** The figures quoted for addiction risk varied, but were most credibly in the order of 5–20%. Most commonly, 10% was chosen as a round number and very careful selection of patients was strongly encouraged. If there is no family history or patient history of addiction behavior by a patient in their early to mid-thirties, the risk of addiction is extremely small; although, physical tolerance and dependence will occur. Neither of which, alone or together constitute addiction or even need to be present for a chemical dependence disorder to exist. Unfortunately, that last admonition for careful selection and monitoring was not followed well by many prescribers, the majority of whom had little training in the use of opioids, which was often by choice. Internists, family medicine clinicians, and orthopedic surgeons accounted for the vast majority of prescriptions.

Industry-made medication inevitably found its way onto the black market in part due to the problem mentioned above, not to mention there being no national data base for detailed prescription tracking. This made “doctor shopping” easier for addicts, or even addicts with genuine pain, many of whom who were turned down for care of their pain without being offered appropriate alternatives. Thus, mis-prescribing and poor monitoring resulted in a number of problems culminating in the present “crisis”.

The recommendations first made by top pain specialists, such as Russel Portnoy et al., have now been refashioned in a distorted format with a few improvements and some drawbacks by relatively non-expert panels, and pushed as "guidelines" creating pandemonium. At present, many clinicians are applying "recipe" medicine formats in trying to comply with the guidelines, many of which are considered unreasonable, yet are being adhered to as if law. As a result of suddenly being cut off from their clinician-prescribed medication, some patients have gone to the black market or have "doctor-shopped" to bolster their supply. It is likely a small minority; although, media-fanned publicity suggests otherwise. Most patients have clearly stayed within the limits of their pain medicine agreements; yet, now they have deteriorated as a result of sometimes too extreme and too rapid a reduction in dose, without other forms of pain management being put in the place of the withheld opioids.

Where heroin had previously dropped in value on the street, the current scarcity of the industry-made pharmaceuticals has created a new market for drug cartel-made medication but it is still unclear who is buying what. Heroin mixed with fentanyl is now produced as faux oxycodone tablets by drug cartels, and it has escalated in value and the deaths continue. It is a complicated mess.

On the positive side, if costly and inconvenient, the new guidelines do have some merit, especially where more frequent and highly accurate drug screening is now utilized. This includes more consistent use of pain agreements, incorrectly referred to as pain "contracts", while chart reviewing and computerized data base information checking is now more regularly employed in a "trust but verify" approach, helping to bring the situation under control. Interview and risk assessment tools are also now being more routinely used; although, they cut into the limited time available to care for patients adequately in other ways.

Adding in another controversial topic, **there are clinicians who refuse to prescribe opioids alone or in combination with state-legal medical marijuana or who will only prescribe one or the other.** Newer formulations of medical marijuana are being created in order to maximize the pain alleviating affect of cannabinoids (CBD), while minimizing the THC-driven hallucinogenic and other negative affects that lead to being "stoned", which may create damage to the brain [12].

Medical marijuana has evidence for and against its use in pain and headache management, as it does for management of agitation from dementia, glaucoma eye pressure, PTSD, and seizures, the other conditions for which it is used [13]. **It can prove opioid sparing, can be helpful with some forms of intractable pain and headache, and it does not slow respirations**. But the results are inconsistent. At this point the evidence for or against its use, with or without opioids, remains highly controversial. Even benzodiazepines have been used for years together with opioids quite safely. Many patients have benefited, but only when appropriate education and safety guidelines have been firmly put in place. Today, clinicians are wary of prescribing these too. As previously stated, time is needed for better research to more accurately address these unanswered questions.

This author has used opioids (as well as medical marijuana) sparingly with headaches and facial pain, an example or two being provided here. There are no formulae. Each patient is different. There are a number of ways by which opioids can be given in the short term or intermittently to effect significant relief of pain, when other means fail. *In carefully selected patients*: IV, IM, SC, intra-nasal, trans-buccal, and oral methods can all work. For example, while oral steroids coupled with verapamil for 3 weeks may be the best or first approach to getting cluster headaches, also known as "suicide headaches", under control, opioids in fairly strong doses can be used initially for immediate affect for a couple of weeks, while the other medications begin to take effect. **This short course must be agreed to before starting it, which is necessary in only a minority of cases.** The same applies to the pain of trigeminal neuralgia or to extremely severe migraine headaches, which are unresponsive to more traditional approaches taken at home and/or which might take time to work. This includes episodic or chronic headaches or severe facial pain unresponsive to two or more already tried approaches, including a DHE protocol, oral steroids, or something similar. This assumes that all of the above safeguards are in place. *Furthermore, several different opioids might need to be tried due to differences in individual response, which can be up to 40 times the dose between individuals with what appears to be a similar level of pain This difference in dose is caused by pharmacologic tolerance, genetic variance of opioid receptor response to different opioids, and alterations in metabolic pathways by other medications taken*. **It must be agreed upon with the patient that opioids are to be used ONLY as directed and for a relatively short time. There should be zero tolerance for any deviation from the prescription without medically re-consulting. This means that clinicians need to be accessible outside of normal hours. Clear boundaries must be set and always enforced**.

Careful documentation of the reasoning involved behind such prescriptions, with adequate screening and monitoring, is vital in today's contentious milieu. One unfortunate example within my own clinic was unforeseeable. A 6′6″ male with Post-Traumatic Stress Disorder (PTSD) and a history of domestic abuse, the latter coinciding with frustration and anger at his migraine pain that, in turn, exacerbated his anxiety and PTSD, was calmer on marijuana and his headaches less frequent. He was therefore safer around the two children and their 5′4″ tall, 120 lb mother, his wife. I prescribed state-legal medical marijuana without realizing that he lived in federally funded low-income housing during the Bush Sr. administration. When his apartment manager found out and reported him, the family was evicted given the federal government's then position on the subject. That would not likely happen today, yet *sometimes a social worker's advice or evaluation might prove as helpful as anyone's in making such a prescription determination*. The aroma associated with smoking marijuana can increase the likelihood of burglary such that other methods of ingestion might be advisable, as long as it is accompanied by appropriate education. The affects differ in intensity and duration. **There are many other less controversial compounds that should be tried first, while data are accruing.**

9. If stress management, OT/PT, acupuncture, and other avenues of care do not start for 2–6 weeks, which is more likely to be a problem outside of a rehabilitation setting than within it, a "failed" medicine, opioid or not, may have had an insufficient opportunity to work, especially if it was more likely to do so in conjunction with the other modalities and over time. It can be re-tried. Such incoordination occurs commonly in the outpatient setting. *Clinic staff and the clinician in charge must keep on top of referrals in order to effectively coordinate an interdisciplinary and multi-modal approach to care*. When the timing is off, efficacy drops precipitously.
10. Last, while stated all the time, patients do NOT fail treatments; treatments fail patients. This is a form of blaming the patient, which rarely proves constructive. It is akin to saying that "pain never killed anyone" or that "the pain is all in your head". There is nothing to be gained from such comments and much to lose. In other words, it is not just the pathophysiology, pharmacology, and pharmacodynamics that are important but the psychological milieu in which care provided that is important. **CURE should never be sought at the expense of CARE.**

A Brief Outline of the Primary Headaches: Description, Relevant Pathophysiology, Differential Diagnosis and Treatment

Tension-Type Headache

This is the most common of the primary headaches and the most nebulous and confusing from an etiologic perspective. There is a slight predominance in females. The pathophysiology is as yet still unclear. It may be that a number of its subtypes have different etiologies, which makes it difficult to tailor treatment if it is indeed bad enough to warrant something beyond OTC medication. The approaches generally used are "trial and error" treatments, the choices being strongly influenced by one's training and orientation given the conflicting data over presentation, cause, and treatment. Manual manipulation, relaxation techniques, pharmacology, acupuncture, and lifestyle changes are all used to fairly similar degrees of efficacy. There is no overwhelming evidence that any one approach is much better than another. The caveat is that over-use of abortive medication for any type of headache can and often does lead to chronicity of pain, which renders all preventatives relatively useless until resolved through a clean-out process known as detoxification. Detoxification should be carried out over 1–3 months, as outlined above.

Tension-type headaches can trigger other headaches, migraine being the most common. Contrary to that implied by its name, the pathophysiology of tension-type headache is less clear than one might think. Countless EMG studies have been attempted to evaluate the role of muscular tension and spasm in the genesis of pain, with differing results. There is no robust correlation between tension in the muscles

of the head, shoulders, and neck with the onset of such headaches; although, many patients would argue that point, as would some clinicians [14].

Tender points and trigger points appear to correlate with severe tension-type headaches, as well as cervicogenic headaches in mechanisms of pain induction. This is highly variable. Botox A, used quite successfully in a number of headache studies as a prophylactic medication for migraine, for which it is FDA-approved, is felt by some to exert its effects on such headaches by mechanisms other than pericranial muscle relaxation alone. It is thought to play a less consistent role in ameliorating tension-type headaches, even if it does relax and weaken muscles into which it is strategically injected [15]. Others disagree, and use it off-label for tension-type headaches with claims of considerable, if not largely anecdotal, success [14]. It likely has both central and peripheral affects, at least where migraines are concerned, and those mechanisms of action are still being debated [15]. There may be a preponderance of evidence in rigorously conducted studies supporting the use of Botox-A in the treatment of chronic migraine as compared to episodic migraine. This too is debatable. However, in cases where abnormally persistent muscular tension creates noticeable muscular hypertrophy, such as around the neck and shoulders, Botox A can be used, along with relaxation training and stretching exercises, to bring those muscles down in mass and level of tension or tone. Thereby, this increases flexibility and diminishes potential pressure on pain-sensitive structures.

Most patients do not tend to seek professional treatment for tension-type headaches alone, but they will do so if it leads to other more debilitating headaches, even if they do not recognize such a relationship before consultation. Conversely, eliminating other headache disorders and triggers as a cause of the recurrent-acute head pain associated with tension-type headache is important. Other headache and cervicogenic pain disorders have more clear-cut options for treatment. For this reason, tension-type headache will not be discussed in much more detail here, except where they worsen other subtypes of headache by co-existing with them. Many of the over-the-counter medications, mineral supplements, such as magnesium, and even prescription medications used for other primary headaches and medical disorders sometimes work on tension-type headaches as well. The medications most often prescribed are low-dose tricyclic antidepressants because of their pain-relieving qualities. From that class, nortriptyline is the safest from a cardiac standpoint, as it is least likely to induce arrhythmias. It is the main metabolite of its pharmacologically "dirtier" parent compound, amitriptyline.

Migraine Headaches

Migraine headache is very common, affecting about 6% of males and 18% of females after puberty, totaling almost a billion people worldwide, which includes approximately 12% of adults. These headaches are more likely to be under-reported and research in this area is also grossly underfunded. It is one of the single highest

causes of lost productivity in the workplace due to sick leave, disability, or impairment. Amazingly, it is still under-diagnosed, especially when chronic. It is often confused with entities that rarely, if ever, occur. Chronic sinus headache is the most common error, because such headaches occur only *acutely* and with documented acute sinus infection or impaction. Migraine prevalence changes with age and geographic location, but it is always more common in females after puberty, prior to which there is a slight predominance in males. About 10% of children suffer from migraine or its variants; pre-pubertal rates being almost equal between boys and girls, perhaps at that age being weighted slightly more toward males. It can be diagnosed in babies and toddlers too, but always as a diagnosis of exclusion. It is exceeded in prevalence during childhood only by tension-type headache. There are racial and geographic differences too, probably because it is multifactorial in terms of causation.

Unlike tension-type headache, migraine is usually **activity inhibiting**; therefore, it is responsible for a significant negative economic impact in the workplace and well as poor function at home. While migraine may share some features with severe tension-type headache, especially where mild and persistent background pain exists between acute exacerbations in the chronic form of migraine, most workers do not consider migraine to be on a continuum with tension-type headache. However, this may eventually prove to be the case in a small subset of patients. The importance of this is not merely academic. Treatments are myriad and quite effective with migraine, but far less effective with tension-type headache, unless the latter are co-existent with migraine or other headaches. For example, triptans may work on both types of headache, migraine and tension-type, but only when a person has both disorders. It is not effective when tension-type headache stands alone.

Migrainewithout aura is far more common than migraine with aura. There is a slightly greater risk of stroke in the latter group, in addition to the potential presence of a migraine "mimicker", such as a brain tumor. A spread of neuronal slowing across the cortex inducing a change in cortical blood flow correlates with the manifestation of an aura, the type determined by the area of cortex involved. **Auras are more varied than commonly assumed, which take the form of visual, sensory, motor and language dysfunction.** There are subtypes of each category; although, visual is the most common and well known. It is important to ask about other forms too. They usually occur over a period of about 5 min but can last up to an hour under normal circumstances. Aura usually occurs just prior to or during the headache, **even in the absence of pain** (acephalgic migraine). Treating the aura early will not reliably prevent the onset of pain and nausea. It may simply delay them a little. If the pain that follows is usually hard to control, then treating the aura is worth a try. Care plans need to be individualized.

Auras may manifest with both negative and positive symptoms such as scotomata, which is defined as the absence or "greying out" of parts of the visual field, or flashes of light and scintillating visual distortions in a field of vision, which include fortification spectra. Other examples are numbness, weakness, tingling of a limb, inability to find correct words during speech, or dysarthria. There are about five types of visual auras; although, most experience only two at any one time. Auras can

be experienced in both visual fields but sensory-motor auras are usually unilateral. In neurology, the further back toward the occipital visual processing centers one goes, the more equally visual neurologic phenomena are experienced in both visual fields.

Retinal migraine, on the other hand, is experienced in only one eye, which is different than an aura affecting the visual field in both eyes, because the eye is as far anteriorly as one can go. The retina is really brain tissue and the optic nerve is a bundle of central nervous system neurons historically misnamed as a peripheral cranial nerve but retained as such as a matter of convention. **Retinal migraine must be differentiated from embolic stroke** in the areas supplied by its tiny blood vessels. One can consult with an ophthalmologist, neuro-ophthalmologist, or a neurologist on this matter.

Sensory-motor and language centers are more anterior, which may explain their greater tendency toward unilaterality where auras are concerned. The feeling of "déjà vu" is also a common aura and this can progress along a continuum of **changes in awareness** to an almost trance-like decrease in consciousness. **Such events can be hard to distinguish from a seizure, especially when there is no pain or when a seizure is followed by headache.**

Those diagnosed with migraine *with* aura (approximately 20%) also tend to experience migraine *without* aura, and both are preceded by **premonitory symptoms, otherwise known as the prodrome**, about 60% of the time. The latter are not auras but herald the onset of a migraine and are less well described. They include food cravings, changes in energy level, and alterations in mood such as euphoria or irritability. They generally appear hours before an aura and/or the headache.

It is worth noting here that ***migraine variants*** can occur in adults, if less commonly so than in children and young teenagers. Interestingly, variants may not include headache. Instead, they may consist of elaborate auras and changes in level of consciousness, which are often misunderstood by observers to be the effects of illicitly used mind-altering drugs or complex partial seizure activity. The **Alice in Wonderland syndrome** is one of the most well known of these if beyond the scope of this chapter and book. *Migraine is therefore a diagnosis of exclusion sometimes following an extensive work-up for epilepsy amongst other things.*

The pain of migraine, if present, is usually moderate to intensely severe **unilaterally or bilaterally** and worsened by movement or sensory stimulation. The pain can be extremely intense, coming in waves. Stabbing pains may be superimposed over a sickening ache. Migraine can also be triggered by tension-type or other headaches, or even by generalized pain syndromes, such as fibromyalgia, or very localized problems, such as cervicogenic neck pain. Most patients with migraine wish to lie still in a quiet and dark room and try to sleep it off.

Migraine can occur at any time but is most common on arising in the morning or after a period of severe stress. It can wake a person up but this occurs with low frequency when compared to cluster headaches. The pain can build quickly or over a few hours and generally lasts 4–72 h. In children, it may last only 2–48 h, sometimes without any pain and sometimes in the form of non-painful migraine variants. Beyond that, it is referred to as **status migrainosus**, which is a problem requiring a

visit to the hospital Emergency Medicine Department, whereby a variety of IV approaches can be implemented to alleviate symptoms and a battery of appropriate diagnostic scans can be safely undertaken.

The pain of migraine is most commonly unilateral at onset, but it can spread. It is bilateral 40% of the time and usually centered around or above the eye. Migraine pain is usually throbbing or pulsating, and may be described as an unbearably intense ache over which stabbing pains are superimposed. Autonomic signs are *generally* not present.

Sometimes, migraine is holocephalic from the start and it can follow a tension-type headache. It should not be side-locked. That is a red flag for other pathology. Even if 90% of attacks are on one side, the few recalled on the other side are a good sign. One needs to pursue this question aggressively given that side-locked headaches require imaging studies to rule in or out a tumor or other pain-inducing mass.

The timing of the pain and its quality must also be assessed as thoroughly as possible. Does it occur with sudden cessation in caffeine consumption? How many ounces of what are consumed each day? Does it inhibit activity? Is it related to a particular point in the menstrual cycle? **Importantly, does the sufferer experience hyperpathia or hyperalgesia on the painful side of the head?** If he or she can lie down and find some comfort with pressure of the pillow on that side of the head, then it is not as vital to alleviate the pain within the first 30 min or so because the level of central pain is less and absorption from the gut is still likely to be functional for a while. If they cannot even gently touch that side of the head, then urgent medication delivery is needed and may need to be given via injection subcutaneously, intravenously, intramuscularly, or sniffed intranasally to bypass a quickly "locked-up" GI system that cannot absorb oral medication. Early use of Reglan may slow this "GI shut-down" and minimize nausea and vomiting, allowing for oral medication to be better absorbed. Without quick treatment, the headache may last for 2 or 3 days. Of much importance is that the *Triptan wafers that dissolve on the tongue (for those who have trouble swallowing tablets and capsules) are absorbed from the gut when swallowed with saliva or fluid. They are NOT absorbed sublingually or transbucally*. This is not commonly appreciated. It will therefore relieve pain no faster than regular oral preparations.

In those who experience the pain 15 or more days per month, the condition is considered chronic, but it is necessary to define chronic headache(s) carefully in order to design the most effective treatment plan. **Chronic migraine can be diagnosed only when medication overuse is ruled out**. There is often a co-existent headache that has, to the patient, become merged into one terrible pain. Pain need *not* be present to make the diagnosis; yet, it is to the patient, that which most clearly defines migraine. The co-existent headaches may be treated differently if they can be separated by detailing the patterns of signs, symptoms and triggers, as well as by defining the conditions and timing under which episodic headaches eventually became chronic. As mentioned earlier, "…to see the stones on the riverbed it is necessary to allow running water to clear itself of mud". In the case of migraine, this may entail a gradual withdrawing of analgesics, as any and all can create chronicity. This should be followed until the once episodic headache subtypes become clear.

Preventative or prophylactic medication can be given early on, but there may be little efficacy until detoxification is complete. It may take 1–6 months for a re-set, but most commonly the time to detoxification is 2–3 months, at which point the patient's headache may have become episodic again. **Success of treatment is not defined by cure but by a significant reduction in frequency and intensity.**

Migraine is often referred to as one of the "vascular headaches", despite the fact that over the past few decades its pathophysiology has become better understood and this concept has been deemed to be invalid [8]. **"Neurovascular"** is a more appropriate term, given that the headache generators appear to reside within the brainstem, midbrain, and possibly the hypothalamus, along with involvement of intracranial vessels and meningeal arteries innervated by trigeminal nerve endings. Together, these structures are known as the **trigeminal complex**. In affect, there appears to be a dysregulation of pain signaling or even merely the *perception* of pain, which is akin to hearing a song without an external source such as a radio nearby, that initiates an inflammatory response at nerve endings that is then *followed* by changes in vascular dilatation and increased blood flow.

Vascular changes were once felt to be the initiator of pain by stretching nerve ending-innervated arterial walls. This has long been discounted. Changes in regional blood flow within the brain during a migraine attack have been shown by transcranial Doppler studies to persist for up to 3 days even after the systemic manifestations of migraine are alleviated by triptans or other compounds. In the research setting, a "new" migraine occurring within 24 h of an alleviated one is considered to be recurrence of the same one. If recurrence occurs after 24 h, it is counted as a second attack. This is well to bear in mind when attempting to keep track of the number of migraines experienced each month.

There is considerable overlap in the signs and symptomatology of migraine with epilepsy, transient ischemic attacks, and stroke, as well as the potential affects of cerebral tumors, severe tension-type, and caffeine rebound headaches such that certain questions and tests are necessary to narrow the differential diagnosis. However, the diagnosis can accurately be made without Doppler studies and MR imaging; although, the latter may still be necessary to rule in or out pathology that presents in a similar clinical manner as a "migraine mimicker". The neurological examination should be normal in the absence of other pathology. Of course, one must never take a change in type or frequency of such headaches for granted simply because migraine was diagnosed in the past. Other pathology is always possible later on, or may have been missed previously; thereby, it may require a full work-up.

Chronic Daily Headache and New Persistent Daily Headache

In the setting of a rehabilitation program, chronic daily headache is a condition likely well documented prior to admission; yet, it deserves its own section. Given the often mixed types of headaches involved, including new ones due to head injury, all headache subtypes need to be clarified and managed over time by first

eliminating abortive medication over-use, which is the most common culprit of chronicity. **Eighty percent of patients with chronic daily headache seen in headache clinics are determined to have medication overuse as the cause of their chronicity, regardless of the underlying and once episodic headache subtype** [16]. Migraine and tension-type headaches are most commonly involved. *As one author noted, "Chronic daily headache is but an umbrella term or parking lot where the vehicle may be parked until it is properly identified".*

Headaches *other* than migraine and tension-type need to be ruled in or out as well. Medical and psychiatric co-morbidities are also of great importance since they can seriously affect the approach to treatment. The literature is mixed with respect to psychological predisposition to chronic daily headache, as it is to the psychological predisposition to pain chronicity in general. Examples of **co-morbidities** that commonly affect the success or failure of general headache care include obstructive sleep apnea and other reasons for non-restorative sleep. Non-restorative sleep makes the treatment of headache and co-morbidities much harder to manage. Poor quality of sleep negatively affects many medical disorders, psychosocial stressors, and other conditions. A **thorough sleep history** is important here.

Medications chosen by the rehabilitation specialist for any condition can be problematic. Should an antidepressant be chosen for its pain-relieving or pain-preventative properties (or for insomnia, etc.), then certain classes of antidepressants can worsen RLS and PLMS, or throw a patient with bipolar disorder into a manic phase. Like tension-type headache, chronic daily headache can be a fairly nebulous constellation of signs and symptoms, the pattern of origin often requiring an outpatient and occasionally an inpatient headache specialist, as well as other specialists' consultation and care.

There is still debate as to whether or not there exists a pathophysiologic continuum running from migraine to tension-type headaches, or whether they are entirely separate entities. Of note is that migraine-relieving medication may effectively eliminate the tension-type component of pain experienced between migrainous episodes, but only when the two conditions co-exist as separate entities. The pain between acute exacerbations of properly diagnosed chronic migraine may appear to be tension-type, but generally it does not respond in the same way. Therefore, it may be different in nature.

Clarification of migraine as the predominant type of headache may prove difficult when other features of migraine such as nausea, phonophobia, or photophobia are absent. Even the basic pathophysiology is unclear with respect to episodic versus chronic migraine. Some evidence points to dominance of peripheral pain generating mechanisms where episodic tension type headache is concerned, with centrally mediated mechanisms dominant in the chronic variety. Despite the fact that muscle tenderness upon palpation of pericranial muscles has proven to be a useful criteria for research selection of patients with chronic tension-type headache, this needs to be separated from the more commonly seen pain-radiating **trigger points.** These sources of discomfort are often elucidated when reactive muscle spasm to an underlying pain generator is present, such as myofascial pain overlying a **cervical facet arthropathy**, whereby trigger points are the soft tissue hallmark. Other examples of

confusing findings on physical examination include the non-radiating but painful **tender points,** which are characteristic of **fibromyalgia**, a central generalized neurological sensory misprocessing disorder that *feels* to the patient as if it is a widespread painful joint or peripheral muscular disorder. It requires a rheumatologic work-up to rule in or out **polymyalgia rheumatica**, **systemic lupus erythematosis** (SLE), **Lyme disease, rheumatoid arthritis,** and other disorders that can present similarly.

Some workers separate chronic headaches into those with a duration averaging more or less than 4 h in duration. If shorter in length, then the differential diagnosis includes cluster headache, other trigeminal-autonomic cephalalgias, hypnic headache, or idiopathic stabbing headache, etc., all of which can be transformed from episodic to chronic in nature. If the headaches last longer than 4 h on average, chronic migraine and its variants (MOH being excluded), as well as hemicrania continua, chronic tension-type headache, and New Persistent Daily Headache are then the focus.

To manage chronic daily headache properly where the "rebound" phenomenon (MOH) is concerned, overused abortive medication needs to be weaned down and restricted on average to a maximum of 2 days per week. This must be done wisely for pharmacologic, psychological, and pathophysiologic reasons. Two doses a day for a prolonged period of time is far more likely to induce chronicity and a refractory response to analgesics and preventatives than the same number of doses taken over a mere 2 days a week for the same period of time. For example, six doses of one abortive medication taken each of 2 days is less likely to induce medication over-use headache than the same total of 12 doses spread over a whole week, week in and week out. Even though ineffective, patients will continue to take abortive medication daily. This is out of desperation because it may very temporarily "take the edge off" daily recurrent pain. **Such patients usually keep bottles of the offending analgesics at home, a frequently visited friend's home, at work, in the car, and/or in their purses.**

It is important to make changes gently, with reassurance, and to add lifestyle changes and other types of therapy as might seem reasonable when possible. Removing or weaning medication too quickly merely increases anxiety, which thereby proves to be counter productive by increasing the frequency or intensity of headache. Sometimes, patients are on 2–5 abortive medications. These medications can be stopped at different rates but something still needs to be offered for pain relief, with strict boundaries. Integrative approaches using allopathic and complementary approaches to care can prove highly effective. The pain is real. There is a reason that they were driven to use so many medications. It was a matter of being poorly managed. Once the underlying episodic headaches have been well defined, it is much easier to incorporate specific allopathic medication, herbal, or complementary therapeutic techniques to effect change.

New Persistent Daily Headache is another hard to manage chronically painful condition. It was first described in the mid-1980s and it can be extremely refractory to treatment. It can occur in both sexes and in children as well as in adults, but

importantly, other than for occasional history of infrequent headaches, it is a stand-alone **disorder of sudden onset often following a viral illness or specific event,** ***for which the date can be accurately recalled***. It may involve symptoms suggestive of migraine and/or tension-type headache, but its onset is extremely abrupt and chronic from the start. It is usually unresponsive to medication, injections, or manual manipulation. The pain of new persistent daily headache is usually bilateral and of moderate intensity, but it does not inhibit movement. It changes little with specific activity, but can vary from day to day. One can have a concomitant medication overuse disorder that does not invalidate the diagnosis, as long as a clear separation in time can be determined. Neurological, imaging, and CSF pressure studies are generally unremarkable as is the psychology work-up, except where persistent pain brings about psychosocial disruption. To make this headache diagnosis safely, a **cerebrospinal fluid leak must be ruled out**, the positional relationship to exacerbation of pain often becoming less marked with time to the point where a patient might have forgotten having ever experienced it. **Cerebral venous sinus thrombosis** is another serious problem causing similar pain. A magnetic resonance venogram (MRV), MRI, MRA, as well as assessment for a CSF leak or build-up can all be useful here to clarify the diagnosis.

The usual range of medications for pain and headache are tried but rarely does anything work. This can be terribly discouraging to the patient such that emotionally supportive measures and education of coping skills is vital. About a third prove self-limiting within 3 months and 75–85% are alleviated within 2 years. Rest may prove unrelenting and all one can try are the usual approaches to chronic pain, using opioids as a last resort. If the latter proves useful, it must be measured in terms of functionality and not simply in terms of the level of pain. The safeguards mentioned earlier must be applied along with informed consent of the risks involved.

Trigeminal Autonomic Cephalalgias (TACs)

In medical school it is common to focus upon severe stabbing pain as being the sine quo non of cluster headaches; yet, this is rarely so. At least it might be held in reserve pending other information given that migraine can produce stabbing pain as can a number of other headaches and facial pain conditions such as trigeminal neuralgia and trigeminal neuropathy, the causes of which can differ within and between themselves. While **"cluster-migraine"** is an oft-used clinical term, along with "mixed vascular headache disorder", neither are recognized headache entities by the IHS. ***Nonetheless, cluster and migraine headaches can co-exist, the importance of which is that treatments that may typically work with one and not the other may actually "cross over" and be worth a try, which thereby potentially minimizes the need for multiple treatments***. An example would be migraine that is surprisingly alleviated with 100% oxygen at a high flow rate of 7–12 L per minute utilizing a non-re-breathable facemask.

The involvement of the autonomic nervous system in some of the signs and symptoms induced by this group of headaches is reflected in the group name. They are referred to separately as cluster headache, paroxysmal hemicrania, and short-lasting unilateral neuralgiform pain with conjunctival injection and tearing (SUNCT). More recently, the latter's name has been changed to the more accurate and less confining term, Short-lasting Unilateral Neuralgiform attacks of headache with cranial Autonomic features (SUNA). **Basically, the longer the name, the shorter the duration of stabbing pains that occur more frequently over a 24 h period. The importance of such differentiation lies in the difference in responsiveness to treatment.**

Cluster Headache

Cluster headaches have been referred to as "suicide headaches", given that some patients will actually smash their heads against a wall in hope that pain will override the intense, unbearable stabbing. Some have even taken their lives. *Compared with migraine, these headaches are more likely to wake one up from sleep and they are not activity inhibiting*. Nausea is inconsistent. Patients cannot keep still or find a comfortable position to minimize the pain; as such, they tend to pace with much anxiety. There is a predominance of cluster headaches in females, but the prevalence is much lower than migraine, being about 1 in 250 to 1 in 100 people. The numbers are in flux as our ability to define and to refine them changes. These changes in ratios and prevalence are due to how data are ascertained.

The pain is almost strictly unilateral, as opposed to migraine, but it can shift sides during or between cluster periods, as defined below. It centers around the eye, supra orbital or temporal areas, all of which are innervated by the first branch of cranial nerve 5, aka V1, as compared to trigeminal neuralgia-caused pain, which tends to involve branches V2 and V3. Many rate cluster headache attacks as more painful than childbirth.

A **cluster attack** or headache is a horrendously painful immediate onset of lightning bolt-type, periorbital, stabbing pains that may average 15–180 min in duration, with an average of 45–90 min, which may repeat up to eight times a day, daily or every other day. A **cluster period** or "bout" denotes the weeks or months over which these attacks tend to occur each year, usually a similar pattern in a particular person; although, there is much variation between individuals. Periods usually last at least a week, but may continue for months. If the **period of remission,** or time between attacks, is less than a month over the course of a year, it is classified as **chronic.** In general, 10–20% of cases are chronic. About 80–90% are **episodic.** Episodic cluster headaches becoming chronic occur in about 10% of cases, while 30% of chronic cluster headache disorders become episodic. Within an individual, the pattern may remain quite constant, even if there is much variance between individuals. **Triggers** include alcohol, which usually occurs only during a cluster period, stress, and exertion. Hormonal changes, allergies, stress, and specific foods do not

seem to be triggers. To varying degrees, a**utonomic features** on the side of pain include the following: nasal lacrimation; conjunctival injection and tearing; Horner's syndrome; ptosis. Some are short lived, whereas a partial Horner's syndrome may persist in some.

A common treatment approach is to provide **subcutaneous sumatriptan**, **intranasal zolmitriptan,** or **home oxygen via a non-rebreathable face mask** for acute attacks, while starting a preventative program of high-dose **oral steroids** tapered over 3 weeks giving moderate to high-dose daily **SR verapamil** a chance to "kick in" and to replace the steroid. **Opioids** can be used as well if the above proves unsatisfactory, but that should be a back up plan preferably with a headache medicine consultation if available. **Occipital nerve blocks and peripheral nerve stimulation of the greater occipital nerves** might prove to be medication sparing.

Paroxysmal Hemicrania and Hemicrania Continua

Paroxysmal hemicrania occurs far less often than do cluster headaches, and hemicrania continua even less often than that. The latter will be mentioned here only briefly. Paroxysmal hemicrania is similar to cluster headache, except that attacks are shorter, usually lasting 2–45 min, which may recur several or more times a day, averaging 11. The distribution of severe pain is very similar to that of cluster headache; although, tearing is usually absent. The episodic and chronic forms are defined the same way as in cluster headache. Many sufferers of paroxysmal hemicrania report at least one feature of migraine such as nausea, vomiting, photo or phonophobia; yet, it does not respond to agents commonly useful in managing migraine. The agitation and restlessness of paroxysmal hemicrania resembles that seen with cluster headache. While the attacks are short, they occur often frequently enough to require the use of indomethacin. **Topiramate** may also work if the patient develops gastric irritation using indomethacin. As with cluster headaches, **greater occipital nerve blocks and peripheral nerve stimulation** may prove effective.

The pain of episodic hemicrania continua, especially between attacks, is said to be more intense than any of the other trigeminal autonomic cephalalgias. **Both disorders, PH as well as HC, are indomethacin responsive; whereas, cluster headaches are not. This is one of the rare cases where a diagnosis can be made on the basis of response to a medication.** Indomethacin is a NSAID that might affect receptors in the CNS differently than other NSAIDS, or it may affect spikes of increased CSF pressure differently. It may also have unique affects amongst NSAIDs on nitric oxide production or inhibition. The data are unclear. **Neither chronic migraine nor new persistent daily headache will respond to indomethacin.** This helps to separate hemicrania continua from other causes of unremitting headache.

Hemicrania continua is not merely chronic paroxysmal hemicrania and it is a rare disorder. This author, a specialist in both headache and pain management in adults and children, has only seen two cases in over 20 years. With signs and symptoms in common with migraine, it is *often misdiagnosed as chronic migraine*. However, if the

autonomic signs and symptoms are focused upon, it may be *misdiagnosed as chronic cluster headaches*. **An absolute response to indomethacin is the best way to eliminate the other two primary headaches as the cause of the pain.**

Short-Lasting Unilateral Neuralgiform Headache with Conjunctival Injection and Tearing (SUNCT), More Recently Changed to Short-Lasting Unilateral Neuralgiform Headache Attacks with Cranial Autonomic Symptoms (SUNA)

Also rare, this headache disorder, which occurs with or without tearing, is not well understood in terms of its pathophysiology. However, like other headaches in this class, pituitary imaging for secondary causes is important. The moderately intense, but very short lasting if many stabbing pains, which are usually triggered cutaneously by chewing or by the feel of wind on skin, are in the same V1 distribution as the other trigeminal autonomic cephalalgias. However, more recent reports describe a wider distribution of unilateral pain [17]. It is NOT indomethacin or Triptan responsive and neither does it respond to oxygen applied at a high rate via a non re-breathable face-mask. Lamotragine and topiramate appear to be the most successful pharmacologic approaches used to date, but the data are scarce. **As with all but cluster headaches in this class, steroids have limited efficacy** and are typically not employed unless nothing else known to sometimes work fails. Because the attacks may be as few as three or four, or as many as 30–100 a day with each attack lasting 5 s to 5 min, it is more commonly confused with trigeminal neuralgia than it is with cluster headache. This is despite involvement of the V1 over V2 or V3 branches of CN5.

Idiopathic Stabbing Headache

This is another rare disorder that may be unilateral or bilateral in distribution, with stabbing pains lasting 1–10 s. Because migraine and trigeminal autonomic cephalalgias also include stabbing headache, this entity is not well understood. Only the V1 innervated region is affected. Autonomic phenomena are generally absent. It may be responsive prophylactically to indomethacin in some cases, just as it might respond to gabapentin.

Exertional, Cough, and Sexually Related Headaches

There are lumpers and splitters and some classify all of these headaches as variants of exertional headaches, while others prefer to separate them. There do appear to be significant differences between them, so they will be presented here separately. The

history gives rise to differing nosology. C**ough headaches** last a mere second to 30 min in duration, sometimes with a dull ache persisting for several hours, and can be triggered by abdominal straining or the valsalva maneuver. Their onset is rapid. They can be experienced bilaterally, unilaterally, in the vertex, frontal, temporal, or occipital regions.

Exertional headaches, which may be pulsatile as well as sharp or "splitting", are brought about by activities such as running or weight lifting and may last anywhere from a few minutes to a day or two. Many features of migraine may be present. The onset may be delayed until after the period of exertion and may build rapidly or slowly.

Sexually related headaches are classified as **"pre-orgasmic" and "orgasmic"**, the latter accounting for about 75% of cases. The type of sexual activity is irrelevant. The former are dull and either holocephalic or occipital, and cervical in distribution; tension slowly builds as sexual excitement increases. Relaxation maneuvers can head them off. Some benefit may be obtained with refraining from sexual activity for a few days, but for most the onset is unpredictable and need not occur with immediate resumption of sexual activity.

Orgasmic headaches are far more intense, to the point of being explosive, usually lasting 1–3 h. They have a similar distribution and about half of those who experience them are migraineurs. Relaxation techniques are rarely effective.

NOTE: In evaluating patients with headaches such as these, it is important to be aware that traction on the cerebellar tonsils due to posterior fossa abnormalities is a common secondary cause. There are a significant percentage of these patients with Arnold-Chiari malformations, especially type 1. A neurosurgical evaluation is reasonable, given that skull base surgery is sometimes warranted to open up an otherwise too small posterior fossa and because the list of potential secondary causes is very long.

In all of the above, **indomethacin** can be used acutely, an hour or so before expected activity or over time, titrating the dose, using the SR tablets with food, or even the immediate acting version as needed. **Topiramate** may help as a preventative if daily indomethacin causes gastric distress. **Beta blockers** can be useful too; although, the less cardiac function affecting ones are best, especially with exertional headaches brought on by physical training. This is due to the need to avoid becoming "winded". Beta-blockers can interfere with sexual function as well.

Hypnic and Nummular Headaches

Hypnic headaches are also uncommon. They are a sleep-related, dull headache, sometimes with a stabbing component that has an age-related onset, which ranges from 30 to 80 years old. The average age at onset is 50 years old or older. It always begins during sleep and at roughly the same time each night. Early hours of the morning are most common. The pain is holocephalic, throbbing, and devoid of autonomic signs and symptoms. It usually resolves within 15–60 min, but can last

several hours. About two-thirds experience these headaches 4 days a week, whereas others experience them on a nightly basis. Pathophysiologic dysfunction of the suprachiasmatic nuclei important in the regulation of biological clocks or rhythms, melatonin dysregulation, and subsequent dysregulation of serotonin during REM sleep have all been postulated to cause the problem; however, nothing is proven as of yet.

Nummular headaches are also uncommon; although, the incidence appears to increase once clinicians are aware of this disorder. Generally speaking, this oddly and variously described itching, throbbing, sharp, stabbing, burning, or pressure-like discomfort, which occurs in a highly circumscribed area "like a coin" region of the scalp, is usually felt only on one side. This most often affects the parietal region, but it can occur in the occiput and frontal regions as well. It is usually chronic, present on 15 or more days a month, may be continuous, or may last many hours each day. The episodic variety of nummular headaches lasts from 30 min to as long as 5 or 6 days at a time, but no more than 14 days a month. The cause is unclear and many localized and pharmacotherapeutic approaches have been tried with mixed results. Whether or not an irritable branch of small nerves from the soft tissue layers is involved is as yet unclear, but injections of steroid mixed with lidocaine have been unimpressive.

Conclusion

Evidence-based medicine is important to accrue. However, the more specific the conditions under which variables and data are analyzed, the less generalizable the conclusions. Therefore, expert opinion holds a valuable place in deciding upon applied principles given that real-life patients are often quite unlike the carefully selected populations under study. This makes both approaches to data accumulation valuable. In this chapter, I have attempted to meld the two and to emphasize the "grey areas" as much as the more clear-cut area, given that so many patients fall into that "less than definitive" realm.

The details of treatment protocols are ubiquitous but the thinking processes behind their application are not. It is my hope that in reading this chapter a greater appreciation for the need of creative thinking, along with the importance of current guidelines and "facts" will lead to superior care. Although much of the above may go beyond that seen and dealt with in the rehabilitation setting, the same principles can be used by clinicians who work in other settings. Above all, it is important to know that all guidelines change over time. For the astute clinician, it is critical to keep up with an ever-evolving data base such that we can best help our patients.

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Chapter 18
Secondary Headaches in the Rehabilitation Patient

Jeremy Goodwin and Zahid Bajwa

Introduction

The vast majority of headaches are of the tension, migraine, and cluster types, which are classified as *primary* headaches and are discussed in the previous chapter. Unfortunately, many patients develop refractory headaches, which usually consist of one or more primary headache disorders complicated by analgesic medication overuse, poor coping patterns, or failure to identify triggers. In such cases, an interdisciplinary management approach is needed.

Of particular concern to patients and clinicians are the *secondary* headaches, also known as organic headaches, accounting for fewer than 10% of all recorded headaches [1]. By definition, they are symptomatic of underlying disease, structural pathology, or pain-inducing processes different from those traditionally ascribed to the primary headaches. Organic headaches may be secondary to elevated cerebrospinal fluid (CSF) pressure, known as benign intracranial hypertension or pseudotumor cerebri; to bleeding from congenital aneurysms or arteriovenous malformations (AVMs); to ischemic or hemorrhagic stroke; as well as to pain caused by mass lesions or mass effect, such as tumors, hematomas, AVMs, and trauma, or infectious

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processes such as meningitis, encephalitis, and cerebral abscesses. The clinical importance of organic headaches despite their relatively low prevalence compared with primary headaches illustrates important principles of diagnosis and treatment useful to the clinician prior to obtaining specialist consultation.

The topic is complex, with potentially far-reaching consequences if errors in the workup are made. The important point for the evaluating clinician is to know *when and what to look for* when suspecting an underlying cause of headache, *and how to evaluate it within the financial limits of today's medical environment or within the constraints of the patient's medical condition.* This requires knowledge of headache presentation, the limits of clinical dogma, awareness of new or less commonly used tests, and a familiarity with imaging and other diagnostic studies, not to mention a compassionate bedside manner.

This chapter focuses on the clinical signs, symptoms, and diagnostic workup of selected categories of secondary headaches. Cerebral tumors, stroke, subarachnoid hemorrhage, vascular anomalies, spinal headache (i.e., spontaneous CSF leaks or those caused by lumbar puncture or epidural misplacement), and infection with the human immunodeficiency virus (HIV) are some of the vehicles used to discuss common clinical scenarios and approaches to decision making. The information that follows is based on both the published literature and our clinical experience as neurologists and headache and pain specialists.

Special emphasis is placed on the importance of maintaining patient comfort, dignity, and self-esteem. This approach is crucial to the success of therapy, even if success is not always defined as "cure", and is especially important in cases of terminal disease or those in which the primary diagnosis or headache symptom is disrupting patient and family dynamics.

Diagnosing Headaches as Primary or Secondary

Differentiating secondary from primary headaches can be difficult. The quality of pain may be indistinguishable from that of migraine, tension-type, or other primary headaches. In such cases, the Inter National Headache Society (IHS) states that the *temporal* relationship between the headache and underlying pathology should be the deciding factor [2]. Preexisting headaches *aggravated* by an organic process are still considered primary. If the onset of headache occurs in close proximity to the underlying structural problem, it is considered secondary. Sometimes the question is merely academic or impossible to answer. For example, how does one classify long-standing, stereotypic, but side-locked migraines when a magnetic resonance imaging (MRI) scan of the head, obtained to evaluate the cause of new-onset seizures, reveals the presence of an AVM ipsilateral to the headache, and in a position to cause pain? Are the headaches then primary or secondary? Perhaps the more important question concerns the risk of hemorrhage and neurologic deficits if the malformed blood vessels are left alone, removed, or otherwise treated.

The Psychology and Ethics of Headache Evaluation

Patients (and parents) often seek consultation for their headaches in hope of reassurance that they (or their children) do not have an underlying disease of which pain is but one symptom. They also want to understand *why* they are experiencing headaches. This need to understand is of fundamental importance to many patients and their families, a point often missed by clinicians. In our experience, also supported by literature, patients' need to understand their disease may surpass their need for reassurance that pain medicine will be made available or even that the pain can be relieved [3]. This point is surprising only if one assumes that most patients do not think much about the details of their condition or care. Failure to appreciate this concept may lead to poor communication, mutual loss of respect, and frustration on both sides, which can certainly wind up the level of pain or the frequency of headaches, unnecessarily increasing the patient's suffering.

Pain and headache may either impact or be impacted by patient coping skills, expectation of outcome, or feelings of helplessness and hopelessness [4]. Clinicians need to incorporate the psychology of health and disease in their approach and not merely focus on the more tangible medical signs and symptoms. Patients are people, not diseases; and their fear of brain tumors, for example, often goes unstated. It is beneficial to broach the subject regardless of whether or not the pattern of headache raises a concern in the clinician's mind. It is surprising how frequently patients breathe a sigh of relief when they find out *why* their headache is likely to be caused by a tumor. Even when a tumor *is* diagnosed, the patients' anxiety and fear of the unknown can be lowered when they are given an understanding of the mechanism of pain appropriate to their level of interest, as well as knowledge of what to expect over time. This approach minimizes the likelihood of depression caused by the feeling of hopelessness and helplessness that accompanies escalating and misunderstood refractory or frequently recurrent pain.

Diagnostic headache evaluations can be a double-edged sword, especially with regard to ethical considerations. Treatment of structural pathology may prove preventative of serious problems such as stroke, seizures, or even death, and may minimize or eliminate the headaches. However, many identifiable structural anomalies may or may not be amenable to, *or* even appropriately subjected to, invasive intervention. *Importantly, there may be no relationship between the pain and the anomaly found.* Risk versus benefit must therefore be carefully considered before embarking on the "latest and the greatest" diagnostics. Tests alone may carry physical, emotional, and financial risk, leading to significant ramifications for the patient as well as for the family. Contrary to the opinion of many clinicians, *patient refusal to consider invasive treatment is not,* per se*, reason for psychiatric consultation.* Such refusal certainly merits a gentle, affirming, and understanding discussion though, perhaps over several sessions, in order for the patient to process the information at his or her own speed. Informed consent or refusal is not always accomplished by a 5-min distillation of the medical "facts" and the dual signing of a piece of paper.

Arteriovenous Malformation and Headache

Occasionally, stereotypic-sounding migraine headaches with aura, especially if side-locked (always starting on the same side or in the same place), may turn out to be secondary to underlying structural pathology, sometimes with an associated risk of bleeding and stroke. A good example is an AVM, in which veins connect directly to arteries without the usual intervening arterioles [5, 6]. Finding an AVM in a family member with migraine may prompt evaluations in relatives known to experience similar headaches, but who have not yet undergone a formal workup. Should all related family members with headache be similarly evaluated? What about those without headache? Whether or not such evaluations are warranted is a matter of controversy and depends on the pathology in question, the philosophy of the clinician, and the individual patient's resources and wishes. In general, focal seizures, vascular bruits, equivocal computed tomographic (CT) scans, and episodes of hemorrhage increase the likelihood that studies will reveal a clinically important headache-related lesion.

Do AVMs cause headache? Some researchers consider them more likely than aneurysms to cause migraine-type symptoms. Even here, some investigators postulate AVMs and migraine to be but co-morbid conditions, with the main contribution of the AVM being that of potential cerebral ischemia or severely diminished blood flow leading to temporary or permanent neurologic sequelae. This process may affect the *nature* of the aura but is unlikely to be *causative* of pain, the aura being an independent process added to by the embarrassment of blood flow caused by the AVM. In animal models, and to some extent in humans, a slowly spreading electrical depression of cortical neuronal function appears to correlate with the migraine aura more so than simple blood flow changes. Although a brief leading wave of small vessel hyperperfusion followed by a more prolonged state of hypo-perfusion or oligemia may be associated with cortical neuronal depression, actual ischemia (more severe) is not usually observed during the aura [7]. The pathophysiology of migraine remains controversial and is discussed in more detail in the previous chapter.

Finding an abnormality such as an AVM may have unexpected social and behavioral ramifications. For example, it may place a "red flag" in the person's medical record that could interfere with his or her ability to procure a change in, or an upgrade of, a health insurance plan. Furthermore, it could lead to patient hypervigilance over somatic sensations, causing anxiety and, therefore, more frequent headaches. The situation is analogous to MRI-discovered disk bulges in those with spinal pain. Such findings are common but may bear no causal relationship to the back pain. Patients may have trouble understanding the logic of the clinician's recommendation that no invasive treatment is advised, so careful explanation is usually necessary. This takes the time that many clinicians feel they do not have. However, not taking the time to fully educate the patient may lead to more clinic phone calls and worsening of headaches due to stress. The patient may eventually find someone willing to operate. Paradoxically, for the "worried-well" patients, ordering a head scan, even if likely to be unremarkable, may actually

prove cost-effective because of the value of reassurance. But the clinician should be aware that an unrelated anomaly might be found, avoiding the problematic cascade of events mentioned earlier. What, then, is the appropriate course of action when a structural lesion is found? Weighing the relative pros and cons of neurosurgical intervention in a headache-prone, but otherwise asymptomatic individual with, for example, a scan-discovered cavernous angioma, requires expert advice and involves a number of variables. If the anomaly has not bled, surgical advice might be to operate only if the headaches become worse or if positive or negative neurologic signs develop, such as seizures or paresis, respectively [8]. An AVM may or may not mandate a more aggressive approach than a cavernous angioma. Much of this decision is made between the consultant specialist (in such cases, a neurosurgeon) and the patient. The primary care clinicians and/or physiatrists should remain involved, however, because they usually get to know the particular patients better, and can help the specialist and patient to communicate, adding their own perspective, as appropriate.

Sometimes, the motivation for further workup is to protect the clinician's legal coverage, such as when clinician and patient expectations do not coincide. It is important to be honest about this consideration, but separating social from purely medical decision making may prove difficult. We suggest integrating these points into an informed-consent approach so that the decision to undergo certain tests is a mutual agreement between patient and clinician with careful and detailed documentation. Where appropriate, evaluation by a psychologist specializing in chronic pain can prove extremely helpful in trying to decide between options.

Ramifications of Being Diagnosed with a Terminal Illness

Many patients, when diagnosed with headaches caused by an inoperable brain tumor, complications from acquired immunodeficiency syndrome (AIDS), or metastatic cancer, feel as concerned for those whom they will leave behind as they do for themselves. Spouses and partners diagnosed with terminal diseases may feel that they are abandoning their loved ones in the same way that parents' worry about not being around for their children when they will be needed most. The person *not* diagnosed with the problem may feel guilty about his or her relative health. These fears often go unexpressed and may need to be addressed by caregivers to help patients, friends and family come to terms with these issues. Discussion, clarification, and resolution might also facilitate financial planning, a common concern of dying patients [9]. Some patients fear severe pain worse than death. Anxiety, depression, and suicidal ideation are common when pain is poorly controlled [10]. However, impending death in those diagnosed with a terminal disease may evoke angst and fear for reasons other than pain and may bring to consciousness spiritual concerns (not necessarily religious) that can interfere with mood and sleep. These feelings and concerns may indirectly worsen pain and suffering and increase the severity and frequency of coincident *primary* headaches.

When Should a Head Scan Be Obtained?

In general, a head scan is obtained to rule in or out organic pathology that might account for the headache disorder. There are times when MRI, magnetic resonance angiography (MRA), magnetic resonance venography (MRV), or CT scanning is clearly the method of choice. As an introduction to the topic, some general principles might prove useful. They are discussed in greater detail elsewhere [11, 12].

CT scanning is less expensive than MRI, is usually more readily available, and takes about one-third of the time to perform. This is useful in trauma patients and in those who are delirious or have a hard time lying still. It may also be the imaging modality of choice (with thin cuts and bone windows) when calvarial tumors or skull-base pathology is suspected [13]. Except for the superiority of CT in early imaging of hemorrhage, and the clarity with which it reveals bone fractures (MRI being better for bone *marrow* changes), the resolution of MRI is much higher overall. MRI is not affected by the bone-reflection X-ray artifact that interferes with CT resolution at the bone–soft tissue interface; therefore, it visualizes the brain-stem and posterior fossa much better. Furthermore, MRI reveals subdural hematomas better than CT when blood is in the isodense phase with bone. MRI shows meningeal inflammation well, whereas CT scanning does not. This distinction is helpful when the patient refuses lumbar puncture, putting the patient at risk for a herniation through the foramen magnum in the skull base. It must be noted, however, that lumbar punctures have been reported to cause meningeal enhancement. *A gadolinium-enhanced MRI best precedes the lumbar puncture in these cases and also replaces the need for pre-lumbar puncture CT scanning.*

If the headaches are non-progressive, and stereotypic, without any sign of raised intracranial pressure or progressive neurologic dysfunction, and the neurologic examination is normal, then imaging is likely to be normal and probably not indicated. *A "non-focal" neurologic examination, however, cannot rule out a midline lesion for which there may be no lateralizing signs.* Examples include medulloblastomas, cerebellar astrocytomas, craniopharyngiomas, ependymomas, and tumors or cysts of the pineal region.

MRI can visualize AVMs, internal carotid dissection, sinusitis (without having to order special CT views through the sinuses), venous sinus thrombosis, and some aneurysms (although MRA or MRV may do so even better). MRA to a large degree obviates the need for more invasive cerebral angiography and can also be used to investigate the neck vessels in cases where stroke or transient ischemic attacks are of concern. MRA reliably detects aneurysms 5 mm in size or larger. It may even resolve them to 3 mm, but not as reliably as angiography. MRV is particularly useful for ruling in or out thrombosis of the venous sinuses. This is important in the differential workup of benign intracranial hypertension, especially in a potentially hypercoagulable patient who has cancer or is pregnant.

When it is necessary to see aneurysms that are smaller than 5 mm, or when the tendency of MRA to overestimate vessel stenosis influences treatment decision

making, traditional *cerebral angiography is still the gold standard.* The latter may also more accurately depict the feeding vessels of AVMs. The risks of modern cerebral angiography are really quite low in appropriately selected patients.

MRI is particularly useful for localizing obstruction of CSF pathways and for evaluating Arnold-Chiari malformations and lesions of the skull base. It also depicts white matter lesions associated with multiple sclerosis and small vessel disease, the differentiation between which may depend on age, presence or absence of small vessel disease, and the experience of the radiologist and clinician. Adding iodine contrast to CT, or gadolinium to MRI, markedly enhances the sensitivity of these scans to a variety of lesions. *There is no cross-allergenicity between these agents, and gadolinium is safer than CT contrast in patients with compromised kidney function.*

Pregnancy, the presence of metallic implants, and the types of lesions under investigation (and their expected location) affects the choice of scanning. It ·is probably best to clarify for the radiologist what is in need of being ruled in or out so that the most appropriate technology can be employed (the radiologist usually being the most up to date on evolving technology).

Situations that raise concerns about organic pathology of headache:

- Progressive headaches over days or weeks, and increasing in intensity
- New-onset headaches
- New-onset headaches with exertion, coughing, lifting, or orgasm
- Changes in level of consciousness, stiff neck, or papilledema
- Unexplained fever
- Radical increase or change in previously established headache pattern
- New-onset headaches in an immunocompromised patient or one diagnosed with cancers known to metastasize to the brain
- Reasons to obtain head scans in adults with headache:
- Progressive headaches over days or weeks, and increasing in intensity
- New-onset headaches
- New-onset headaches with exertion, coughing, lifting, or orgasm
- Changes in level of consciousness, stiff neck, or papilledema
- Unexplained fever
- Radical increase or change in previously established headache pattern
  - Persistence of headache-associated neurologic deficits
  - Neurologic deficits found on examination and referenced to the brain
  - Electroencephalographic (EEG) evidence of a focal brain lesion
  - A partial or generalized seizure history
  - Orbital bruits, especially with eye(s) that protrude, are painful, or reddened
  - Side-locked headaches or headaches of unvarying location, or new-onset migraine with aura
  - Patient anxiety regarding the potential presence of a structural lesion (if not already ruled out by a scan)

- In cancer patients, depression, personality change, or unusual sensitivity to opioids, with or without headache, should prompt the clinician to order a head scan even if patients have already had one
- Presence of ventriculoperitoneal shunt
- Nocturnal or early AM emesis or headaches that are worse after lying down for hours

Reasons to obtain head scans in children with headache [14]:

When the headache history is less than 6 months or the child is under the age of 7 years, imaging should be done routinely.

Reasons stated above for adult headaches (substituting the anxious "patient" for "parents")

- Behavioral changes are noted
- Motor or learning skills fail to advance or begin to deteriorate
- Head circumference is considerably out of proportion to height
- Physical growth is not maintained
- Pain is not relieved by simple analgesics
- Diagnosis of neurocutaneous syndromes (neurofibromatosis or tuberous sclerosis)

Headache Associated with Brain Tumors

The percentage of tumors that cause headache is now estimated to be lower than previously thought. This is because brain imaging for various complaints has become more common, and so-called silent tumors are increasingly being found. But, it is important to be aware that tumor-related symptoms and signs are not limited to headache and seizures. For example, sudden loss of, consciousness associated with positional changes, stroke, drop attacks, early morning nausea and vomiting with intense headache, or headache exacerbation with the Valsalva maneuver (abdominal straining) may be caused by a third ventricle colloid cyst or a pedunculated tumor blocking CSF flow. This should be evident on imaging studies. Personality changes may also be the first sign of a metastatic or primary tumor.

Headache is overestimated as a symptom of brain tumors, the location and type of which do not correlate well with location or type of tumor. Headache is a common symptom of tumors, but tumors are a rare cause of headache. Less than 1% of patients presenting to headache clinics have a brain tumor [15]. The incidence is approximately ten times less when only *chronic* headache is concerned. This is true at least in those who undergo head imaging despite a normal neurologic examination [16]. However, as previously noted, concern over the *potential* presence of a tumor may be the patient's primary motivation for clinical evaluation. Headache as the lone symptom of a brain tumor occurs about 8% of the time [17]. The overall percentage of patients with a tumor-caused headache in neurosurgery clinics may be higher because of referral bias (the mass having often been diagnosed previously and elsewhere by brain scan).

What factors are predictive of pain? The site and rate of tumor growth may be more predictive of pain than size alone. Infratentorial and posterior fossa tumors tend to present as headache more often than supratentoria tumors [16], especially if CSF obstruction is involved. Sixty percent of childhood brain tumors are infratentorial as compared with 5–20% of adult masses. This may explain why children are more likely to present with tumor-associated headaches than are adults. Migraine with aura, even when successfully controlled with anti-migraine medication, may be tumorous in origin [18]. Furthermore, slow-growing tumors are far more likely to present with seizures than with headache [19, 20]. According to autopsy studies of patients with cancer metastases or primary intracranial tumors, leptomeningeal involvement occurs only 1–8% of the time, yet 33–76% of such patients experience headache. Other regions within the brain or cranium that are less sensitive to pain are unlikely to result in pain, unless expansion raises intracranial pressure or causes a midline shift.

Whether a tumor is primary or secondary may affect the clinical presentation. Although some literature suggests that metastatic tumors are more likely to cause headaches than are primary ones [21], other studies have found the incidence to be roughly equal [22]. Multiple sites simply make the pain less localized. Thirty percent of the time, metastatic brain tumors are the first sign of cancer anywhere in the body, but only about half of them are traced back to the primary site before death (most commonly the lung) [22]. In general, breast, lung, and melanoma cancers are most likely to invade the brain, whereas prostate cancer metastasizes to the skull, pelvis, and vertebrae.

Tumors compressing brain tissue from outside tend to induce seizures and neurologic deficits before they cause headache. Whatever the tissue type of origin, when headache occurs, metastatic or primary tumors present as tension-type headache far more often than migraine (77% vs. 9%; with 14% mixed) [23]. Migraine-like symptoms occur quite often as the result of intraventricular tumors [24]. Anti-migraine medications may occasionally alleviate the pain. This is a reason to not rely too much on the description of headache alone or response to medication as a means of reassuring patients that they do not need an MRI scan to rule out a structural cause of pain. Although most tumor-caused headaches are bilateral, there is some correlation between the most painful side and the site of the tumor. However, in cases involving considerable swelling and mass effect, false localizing signs and symptoms are common. Interestingly, raised intracranial pressure, long assumed to be a pain generator, does not seem to be the cause of pain per se [25]. It is more likely caused by displacement of, or traction on, pain sensitive structures within the cranium [2].

Treatment

Most of the following medications are prescribed in the usual adult and pediatric doses. Aspirin and simple analgesics may help with mild pain. Aspirin, as well as most non-steroidal anti-inflammatory drugs (NSAIDs) should be halted if surgical

intervention is likely. Aspirin irreversibly inhibits platelet function and increases the likelihood of bleeding. NSAIDs reversibly inhibit platelet function, but can still increase bleeding time. Using non-platelet affecting modified aspirin analgesics, such as trilisate or salsalate, or the new cyclooxygenase-2 (COX-2) selective NSAIDs, seems a reasonable alternative, but there are few data available to support this approach.

When edema is present, dexamethasone, 4 mg PO BID to QID, can be helpful for pain, seizures, or neurologic deficits, but this drug can also interfere with the diagnosis of lymphoma because it is a component of lymphoma chemotherapy. Use of the drug can cause the mass to temporarily disappear, which can result in a falsely negative scan. If lymphoma is suspected, steroids should generally be discontinued until the diagnosis is clear. Steroids can also mask a serious anticonvulsant allergy, and patients with terminal diseases at some point may not benefit from continued usage [26]. Although clinicians in neurosurgical practice typically use dexamethasone on a QID schedule, others feel that a BID dose is just as effective. To titrate, some advise doubling the dose each time, because improvement in symptoms is dose dependent in some patients.

Opioids, surgery, and radiation may all help to attenuate pain, but other avenues might be tried early on. Tricyclic antidepressants (TCAs) may also decrease the pain, but tend to lower the seizure threshold. The same goes for tramadol and bupropion. Selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine, paroxetine, sertraline, or citalopram tend to cause seizures less frequently, but may also be less effective in terms of pain or headache control. Although poly-pharmacy has a definitive role in pain management, often out-performing high doses of single agents, tramadol mixed with TCAs, SSRIs, and opioids can lower the seizure threshold, even at relatively moderate doses, and can cause seizures, even in those who are not predisposed [27]. One must mix agents with caution.

Anti-epilepsy medications, such as phenytoin, carbamazepine, divalproex/VPA, gabapentin, oxcarbazepine, and topiramate, used sometimes in combination with phenobarbital, may prove useful at moderate to high doses for tumor-caused headaches using the usual doses for seizures, or exceeding them if clinically well tolerated and demonstrably more efficacious. Of these, only gabapentin and topiramate require no blood work or blood-level assessment. Gabapentin especially interacts well with most medications and can safely be used in excess of the Food and Drug Administration (FDA)-recommended maximum dose of 1200 mg PO TID. If needed and tolerated, up to 2000 mg PO TID can be used with safety [28]. We tend to use gabapentin BID for symptoms of pain and headache alone, using a TID schedule if seizures are present or if more than 4000 mg/day is needed (failure of absorption occurs at single doses above 2000 mg). For topiramate, starting at 25 mg PO QD to BID, increasing by this amount weekly, soon accelerating with 50 mg weekly incremental jumps (if tolerated), until reaching 150–200 mg PO BID, is worth trying as there is increasing evidence of its efficacy for the prophylactic treatment of headaches.

Clonazepam is a benzodiazepine that may help to diminish the chronic tension-type headache associated with some tumors. It is also an anti-epileptic, anxiolytic,

and hypnotic that may shorten sleep latency, diminish nocturnal myoclonus (periodic leg movements of sleep), and attenuate restless leg syndrome. It may also reduce myoclonus associated with high-dose opioid use. Whether or not it interferes with deep stages of sleep is controversial. A common dose would be 0.5–2 mg PO QHS or BID. Because clonazepam has a long half-life, it need not be given more frequently than BID, but it is often best given 2 h before HS.

Tumor-caused headaches that are migrainous in quality occasionally respond to anti-migraine medications. The importance of this response is that migraine as a diagnosis is not ruled *in* by a therapeutic response to anti-migraine medications; conversely, the presence of a tumor is not ruled *out.* Several causes of headache may respond to anti-migraine medications, including cluster headache, analgesic rebound headache, and so-called spinal head aches. *In cases of severe anxiety, especially resulting from fear of terminal disease ("dread" in psychiatric parlance), low-dose perphenazine, prescribed at 2–4 mg PO BID, may prove more useful than high dose benzodiazepines in bringing about a sense of calm.* This is about 1/10 to 1/20th the dose used in the management of psychosis. The classes of medications mentioned earlier can be safely used together if the clinician is skilled and experienced in rational poly-pharmacy.

What about postoperative pain? NSAIDs are very helpful and can be opioid sparing. The two classes act synergistically to relieve pain. One published regimen for pharmacotherapy following surgery consists of mixing methadone, NSAIDs with or without acetaminophen, hydroxyzine, and a tricyclic antidepressant [29]. Many variations on this theme are possible and reasonable, which should be tailored to the patient's reliability, financial means, age, and general health.

Behavioral Intervention and Acupuncture in Secondary Headaches

Other headache treatments used alone or in combination with medication play an important role in patient care. It should be borne in mind that relaxation exercises are helpful in terms of coping with mild to moderate pain and bringing it under control. Suffering from pain and headache varies less between individuals than the wide variety of pain mechanisms might suggest. Support groups and cognitive-behavioral and psycho-educational classes are useful for those suffering from long-standing, life-disrupting pain, recently defined terminal illness, no matter the diagnosis. This is important when selecting individuals for group therapy.

Mental imagery, deep and slow (diaphragmatic) breathing, meditation, and biofeedback are all useful adjuncts to pain control and are most effective when suited to the patient's personality. Acupuncture is helpful in the management of primary headaches [30], but we do not have enough experience with its use in the management of secondary headaches to comment on its efficacy in the latter case. There is some evidence to suggest that it helps in the management of anxiety. However, the range

of skills, experience, and depth of training of the acupuncturist have a significant impact on efficacy. It is important to remember that the same must be said regarding allopathic medicine and surgery. There are many who have "certification" but lack in-depth training, making it difficult for the non-practitioner of acupuncture to evaluate their skills. Unfortunately, when the pain becomes increasingly intense and persistent, adjunctive measures and medications of all types may prove ineffective irrespective of the level of skill of the practitioner, allopathic or otherwise. Only very high doses of opioids, radiation treatment, surgery, or combination of all three are likely to help; however, this often comes at great cost. Sometimes, the only relief from pain seems to come with loss of consciousness.

Headaches Associated with Stroke

The IHS suggests that headaches be considered secondary to a stroke if the pain begins within 48 h of the development of central nervous system signs and symptoms. The mechanism of headache in such cases is unclear. Data on pain associated with vascular pathologies vary greatly. In general, headache is most likely to occur in the case of large vessel occlusive stroke, least likely as a result of lacunar infarcts, and intermediate in the case of embolism [31]. Hemorrhage may be painful, otherwise symptomatic, or silent. Here, as with tumor-associated headache, the value of lateralization, intensity, and quality of pain is of dubious value and the literature is conflicting. Study results depend on methods of patient sampling, type of questionnaire used, and subtype of stroke studied. Not all data are intuitively obvious.

In cases of headache associated with *unilateral* stroke of the internal carotid artery territory, about two-thirds of patients experience *bilateral* head or neck pain. Regardless of the side(s) affected, the headache often radiates frontally, even if the stroke involves the posterior circulation (vertebrobasilar system). Bleeding into the occipital lobe may refer pain to the ipsilateral eye; whereas, temporal lobe pain is often referred anteriorly to the ipsilateral ear. Pain in the temples may refer from hemorrhage into the parietal lobes, and frontal pain is most likely to originate in the frontal lobe [32]. As stated earlier, there are no clearly useful stereotypic patterns of stroke-caused headache; but, it is worth noting that *there exist documented cases of intracerebral hemorrhage associated with migraine symptoms, remarkable only for an unusually protracted and prolonged course.* As with tumor headaches that sound migrainous, *the danger of misdiagnosis is lessened with the use of appropriate imaging studies.*

Subarachnoid Hemorrhage-Induced Headache

In subarachnoid hemorrhage (SAH), where bleeding occurs within the cerebrospinal fluid, blood pressure and intracranial pressure must be controlled to minimize further blood vessel leakage. Sometimes, lowering the blood pressure eases the

headache, but this result is more likely to occur with headaches caused primarily by the elevated blood pressure itself. In SAH, much of the pain comes from meningeal irritation. Several causes for SAH are reported but discussion of these is beyond the scope of this chapter. SAH occurs most commonly as the result of head injury, followed by spontaneous rupture of an aneurysm or AVM; it is less caused by hemorrhagic cavernous angiomas and tumors. Surgical excision of cavernous angiomas (a common fortuitous finding on head scan) is recommended only if bleeding has occurred, or if their placement is likely to irritate pain-sensitive structures, which thereby explains the headaches. *Hemosiderin staining of surrounding brain tissue, denoting an old site of bleeding, can be discerned by MRI, but not by CT; whereas fresh blood is best assessed by CT.*

Interestingly, the risk of bleeding depends on the type of vascular anomaly. According to some studies, it also depends on race. An aneurysm is 5–25 times more likely to bleed than is a cavernous angioma, but this may not be true in the Asian population for reasons that are unclear [33]. Because of the high prevalence of cerebral aneurysms in persons diagnosed with hypertension, some investigators consider hypertension to be a risk factor for aneurysm formation [34]. The risk of aneurysms bleeding as the result of hypertension is less clear [35]. Approximately one-quarter of patients found to have an aneurysm have at least two or three of them [36]. The relationship of this finding to the likelihood of bleeding probably depends on a number of anatomical and physiologic factors. AVMs also have a higher lifetime likelihood of bleeding than do cavernous angiomas, and surgical removal of an AVM, or other type of intervention, should be considered if the patient is young and if the AVM is accessible. The chance of hemorrhage is approximately 3% per year.

Are there any warning signs or symptoms of the pending hemorrhage of an aneurysm? Sentinel (“thunderclap”) headaches may precede SAH by several months; although, the association is somewhat controversial. In a recent prospective study of about 100 patients presenting with severe sudden-onset headache, almost two-thirds were found to have SAH, two-thirds of which were caused by aneurysms [37]. The issue of sentinel headaches, their typical workup, and when to proceed to angiography, even if the CT scan and CSF studies are normal, is discussed by Raskin [38], based on his own extensive experience and that of others [38–43]. Unfortunately, many patients are misdiagnosed or inadequately evaluated and die as a result. In such cases, warning headaches were often dismissed as sinusitis, or tension-type or migraine headaches [37, 44]. Exertion factors may also prove to be important in up to one-third of cases. If hemorrhage occurs, the initially unilateral headache, associated with hemorrhage, rapidly generalizes and often spreads to the occiput and neck. The neck may become stiff through irritation of the meninges (meningismus). Photophobia, sonophobia, loss of consciousness, seizures, or a combination of these findings, may occur. Such headaches are usually different than any other previously experienced headache, and are classically described by the patient as “the worst headache ever.” *If lumbosacral roots are irritated by blood in the CSF, the patient may even report symptoms of sciatica.*

SAH is a medical emergency requiring both neurologic and neurosurgical consultation. If SAH is strongly suspected and a CT scan is negative, lumbar puncture

reduces the false-negative rate of CT scanning from 5 to 10% to under 1%. Xanthochromia, which is yellowing of the CSF as the result of hemolyzed blood, appears within 4–12 h and lasts up to 12–40 days [45]. Treatment and assessment techniques of SAH and other vascular disorders are discussed elsewhere [45], but with regard to pain management, oral or intravenous opioid pain medication may be necessary to decrease the pain, with some clinicians choosing codeine and other stronger opioids. The need for careful attention to changes in mental status in the acute stage may make the latter approach a bit risky, unless the clinician is skilled in the dosage of opioids, conduction of the neurologic examination, and pain assessment. The very calm, darkened, and quiet environment of an intensive care unit will help to minimize dangerous reactive fluctuations in blood pressure. Some sedation, using phenobarbital or midazolam, both of which prevent or minimize the likelihood of seizures, is often advised. Frequent neurologic assessment is also necessary. If the workup remains negative, the treatment is usually bedrest for 4–6 weeks, with slow or gradual resumption of normal activities. Some clinicians use intravenous calcium channel blockers, followed by oral dosing, in the hope of minimizing the risk of delayed vasospasm; but, there is reason to doubt that the mechanism of action of calcium channel blockers in the periphery is mirrored in the central nervous system [46]. Pain modulation, for example, may occur via the effects of calcium channel blockers on the serotonin system.

Ischemic Stroke and Headache

Reports on headache patterns in stroke and transient ischemic attacks vary widely in their conclusions. This has much to do with populations and types of pathology studied, as well as variation in study design. It is important to ask about headache; however, it loosely correlates with the type of circulation involved (anterior versus posterior), and may precede a cerebral vascular accident by days or weeks, serving as a warning of impending problems [47]. One multicenter prospective study of more than 3000 patients with a variety of stroke presentations could conclude only generally that deep, small vessel hypertension and anterior circulation-related infarcts were less likely to cause headaches than were posterior circulation and cortically based infarcts. Patients with headache were statistically more likely to have ischemic heart disease, but the duration of pain or ischemic symptoms and gender were unrelated factors [48]. Other researchers have found headache more likely to occur in females [49] or in males [50].

In ischemic stroke without bleeding, the reflex, which leads to a rise in blood pressure, is necessary to maintain or to restore cerebral perfusion through areas of swelling; although, sometimes reperfusion precipitates bleeding. Most neurologists try to maintain systemic systolic blood pressure between 115 and 180 mm Hg. Careful judgment is needed. *For stroke, short-acting nitro-paste is a better choice of antihypertensive medication than the longer acting calcium channel blockers.*

Dramatic worsening of stroke can be seen with the use of nifedipine, presumably from loss of cerebral perfusion as the result of a profound drop in systemic blood pressure. Nitro-paste can instantly be removed and very quickly metabolized should a drop in blood pressure correlate with re-occurrence or progression of symptoms.

Besides the antihypertensive class of medication, other agents used to diminish pain, such as the "strong" opioids, may also decrease blood pressure, extending the area of ischemia and infarction. Furthermore, in opioid-naive patients, even moderate doses of such analgesics may suppress the rate of respiration if mentation is already depressed. On the other hand, pain stimulates respiratory drive. Again, skill in assessment and medication titration is required to treat pain safely in this setting. In general, weaker oral opioids, such as hydrocodone, or lower doses of intravenous opioids might be used more safely. Previous use (tolerance) of opioids may affect the dose needed to gain an effect. High doses or stronger opioids may be required in patients with a high degree of pharmacologic tolerance. Vasoconstrictors for headache relief in ischemic stroke are obviously contraindicated. The potential complication of analgesic rebound headaches must always be kept in mind if analgesics are used for an excessive period of time. It is advisable to reassess the patient periodically to determine the continuing need for scheduled medication, preventative or abortive.

Intracerebral Hemorrhage, Subdural Hematomas, and Epidural Hematomas

The data regarding intracerebral hemorrhage, which involves bleeding into the brain tissue itself, is likewise contradictory. Taking stroke as a whole, data range from little to no correlation [49], to fairly well defined criteria [51]. The latter study found that vomiting, younger age, and the presence of headache are of value in looking for SAH; whereas, the absence of headache, older age, and lower systolic pressures were indicative of probable ischemic stroke. *Higher systolic blood pressure, in conjunction with headache, was somewhat predictive of an intracerebral hemorrhage or hemangioma.* Headache is commonly known to follow or to occur in conjunction with a stroke; but, it can also precede the event by days or weeks, depending, in part, on the mechanism or type of stroke [47].

In the case of *subdural* hemorrhage, where the headache is unilateral, it is usually ipsilateral to the pathology. The hematoma may require surgical intervention. The frequency of headache ranges from 11% to 53%, to 81%, depending on whether it is an acute, subacute, or a chronic condition [52]. When the cause of pain is an *epidural* hemorrhage, focal neurologic signs may accompany the pain, as might changes in the level of consciousness, with or without the overemphasized "lucid interval". Therefore, powerful and centrally active analgesics should be used only when frequent neurologic evaluations are possible. Otherwise, simple non-platelet affecting analgesics are used to minimize pain.

Treating Acute Headache with Opioids and Managing Complications

Fortunately, most cases of stroke-related headache are self-limited. Furthermore, neurologic deficits or changes in mental status often rapidly supersede the headache. Of course, where intracerebral hemorrhage or SAH is concerned, surgical intervention may prove necessary to preserve normal function or to minimize the chance of recurrence.

The type of stroke dictates the direction of treatment, which is the major reason that a CT scan of the head is obtained as early as possible. Early CT differentiates hemorrhagic from ischemic stroke. Unless very large, an ischemic stroke may not appear on CT for up to 24 h; however, hemorrhage is visible immediately. The amount and location of blood within brain parenchyma, or within the subarachnoid space, affects the differential diagnosis, prognosis, and direction of evaluation and treatment. Whether anticoagulation is advised in the face of progressive signs and symptoms, as well as which analgesics should be used for severe headache control, depends on the presence or absence of hemorrhage, its location, symptoms, signs, and the amount of bleeding. Consultation with a neurologist is advised.

As yet, few data are available on the use of COX-2-selective inhibitor (COX-I sparing) NSAIDs for headache management; but, these drugs do *not* increase bleeding times, and their use seems reasonable if the pain is not self-limited and if other analgesics are contraindicated. If the pain is intense, as long as the clinician keeps a close eye on the patient's mentation, it is likely safe to carefully titrate short-acting, low-dose opioids for acute pain relief, as long as naloxone is on hand. *However, if sudden deterioration occurs, it may be difficult to separate drug-induced sedation from event progression; for this reason, many clinicians advise against use of sedating agents.* If used, especially in the patient who has been taking opioids long-term and is physically dependent on them, naloxone can induce a stressful withdrawal syndrome, which can lead to tachycardia, arrhythmias, non-cardiogenic edema, as well as a rapid increase in blood pressure. In cases of SAH or intracerebral bleeding, the latter may prove devastating.

To minimize complications in using naloxone, we recommend the following approach:

- Dilute a 0.4-mg vial of naloxone in a 10 mL syringe of normal saline, and give it intravenously, at a rate of 1–2 mL every 1–2 min, to reverse narcotization without loss of analgesia or induction of withdrawal.
- In patients who have been using opioids for some time (daily for more than 1–3 weeks, depending on the route, frequency, and dose), the half-life of naloxone may be shorter than the opioid used such that repeat doses may be needed every 30–45 min, until the situation is stabilized.
- If blood oxygen saturation or the respiratory rate drops ominously, the entire 0.4 mg (or more) dose is rapidly given as a single intravenous bolus.

Headaches Caused by Low Cerebrospinal Fluid Pressure

It is not only *elevated* CSF pressure that is associated with headache. Headache may also result from *low* CSF pressure, presumably from traction on pain-sensitive meningeal and intracranial structures. In cases where radioisotope studies show no leak, with the radioactive isotope passing directly into the bladder, and the CSF pressure remains below 60 mm H_2O, the condition is said to be *spontaneous.* If a leak is found following an invasive procedure, or if a disease process is considered causative, the condition is said to be *symptomatic.* Although headache-related low CSF pressures may occur above 60 mm H_2O, to as high as 90 mm H_2O, manometric studies usually reveal pressure readings between 0 and 40 mm H_2O [53].

Leakage or decreased production of CSF is associated with a number of conditions, which include torn dural sleeves around nerve roots, spinal arachnoid cyst rupture, bony erosion by tumors, complications from choice of pressure valves in ventricular shunting, procedure-induced dural tears, trauma to the head and neck, as well as sudden physical or even sexual exertion. Systemic illnesses such as uremia, meningoencephalitis, diabetic ketoacidosis, and severe dehydration can also cause low CSF pressures.

Spinal Headaches

Diagnosis

Spinal headaches are not difficult to diagnose. The IHS criteria use 7 days as the window of time following a procedure, during which time one may attribute a causal relationship. Spinal headaches usually follow an invasive procedure and become intense and generalized within 15 min of assuming the upright position. They significantly diminish or resolve within 30 min of lying down; but, some patients experience an onset and offset within 20–30 s. Non-specific associated symptoms of nausea, tinnitus, or lightheadedness may occur. The postural component may become less pronounced if the condition becomes chronic. Cranial nerve VI, being the longest such nerve, is the most likely to be affected by processes causing cranial nerve neuropathy, which manifest as palsy and the inability to move the eye laterally) [54].

If the duration exceeds 14 days, then the clinician should consider CSF fistula headache, which is a similar problem that occurs secondary to trauma, neurosurgical procedure, or erosive lesions. As far as diagnostic tests are concerned, manometric assessment by lumbar puncture, radio-nucleotide CSF flow studies, and pledgets in nasal passages to catch leakage from the cribriform plate and paranasal sinuses can be useful. CT scan with myelogram may help to visualize dural tears that would otherwise be missed. MRI of the brain may reveal dural enhancement secondary to vascular engorgement. The latter finding may also occur with infection or inflammation

of the meninges; therefore, it is non-diagnostic. More sophisticated uses of MRI are coming into vogue. These include specially timed and T2-weighted proton-density studies of the spinal canal or skull base. It is advisable to order the tests with which the radiologists performing the diagnostic testing are most familiar.

Most clinicians focus on postural symptoms as the hallmark of low CSF pressure. However, *postural or exertion factors may be noted in conditions other than that of low CSF pressure.* Obstructions to ventricular CSF flow, Arnold-Chiari malformation type 1, subdural hematomas, cerebral venous thrombosis, and sinus disease can all lead to positional and postural headache. Reactive brain edema, which can cause slit ventricles, may displace brain tissue downward, accounting for Arnold-Chiari type I findings.

Spinal headaches occur most commonly following dural puncture via spinal tap (10–30% of the time), and less often following misplaced epidural catheter placement or epidural steroid injections into the intrathecal space. Females and younger patients are most likely to develop headaches following lumbar puncture [55]; although, prepubertal children rarely, if ever, get them [56]. Larger gauge needles, the angle of the needle-tip bevel, which should be parallel to the length of the body or spine so that it does not cut dural fibers, the type of bevel itself, and the number of punctures seem to correlate most clearly with this problem. Although these associated factors seem reasonable, their link with spinal headache has not been rigorously proven. However, it has become widely accepted that *positioning of the patient after the procedure has no bearing on the outcome, nor does the length of time of such positioning. S*ome clinicians even advocate early mobilization [57, 58].

Treatment

Caffeine sodium benzoate, 500 mg IV TID may ameliorate the headache; oral caffeine preparations are less effective. The addition of 500 mg of caffeine to IV lactated Ringer's solution or to normal saline can be helpful, while being mindful of palpitations and insomnia. Simply increasing the fluid intake alone rarely helps, unless the patient is severely volume depleted or dehydrated. Even theophylline 282 mg PO TID has been used. However, none of these approaches are as effective as an epidural blood patch. Blood patches can be very effective and should probably be used earlier and more often than current practice. Injection of 10–20 mL of autologous blood, just below the original puncture site is the quickest and dost effective way to alleviate the problem, but occasionally the pain worsens. The injection can be repeated, if necessary. Fever, coagulopathies, local infection, and the presence of an intrathecal or epidural catheter or stimulator electrode is a relative contraindication to this procedure.

The mechanism of pain relief by blood patch is unknown and controversial. It may involve compression of the dural sac or the formation of a gelatinous tamponade

among other mechanisms. Simple analgesics, abdominal binders, and support hose have been used, adjunctively, to hasten relief of headache. Because most spinal headaches spontaneously resolve within 4–7 days (53% versus 72% respectively), some clinicians feel it is worth trying rest and caffeine first. However, many patients are either too uncomfortable or do not want to wait for this less invasive approach. Blood patches should be considered if no improvement is seen with conservative measures after 48 h. If all the preceding treatments are unsuccessful, then radioisotope studies are used to locate the leak before more invasive intervention is considered.

Headache in the HIV-positive Patient

Many HIV-positive patients have relatively benign primary headaches. In outpatients with AIDS, the cause for non-emergent headaches is found only 50% of the time [59]. Primary pathology has been detected in even fewer cases, about 17% [60]. Headache as a presenting symptom of AIDS occurs in 55% of patients studied in a University of California AIDS clinic [61], but other have found the number to vary between 12.5 and 27.9% [62]. Among hospitalized patients, serious pathology may be found more than 80% of the time [62, 63]. Migraine and tension-type headaches are common. Analgesic rebound phenomenon is a frequent cause of chronic daily headache, and this population in particular is prone to overuse prescribed and over-the-counter medications for the pain and anxiety with which they are often faced. Patients may use pain medication primarily to ameliorate anxiety-exacerbated pain, with little insight into this use by the provider or the patient. Psychologic assessment by a mental health profession who specialized in pain may prove to be enlightening and constructive. Psychosocial stressors must be addressed to avoid the scenario of inadvertent misuse of pain medications to effect better pain control. Behavioral training as a means to education and mind-body awareness is crucial to the success of pain and headache management. Periodic refresher courses may be necessary to reinforce any gains made.

Etiology

Frequently, headaches may be explained by cause other than primary headaches, stress, or overuse of pain medication. Headache resulting from aseptic meningitis, possibly a function of HIV infection itself, is not uncommon. CSF studies may prove of limited value in these cases because the pleocytosis found is non-specific and seen in asymptomatic HIV infection. Substance abuse should also be considered in the differential diagnosis of frequent headaches. Caffeine and other drug withdrawal syndromes may include headache as a symptom. Amphetamine, crack, and cocaine use can cause vasculitis, vasospasm, headache, and stroke. Opioids may release histamine, causing head pain. Anti-HIV medications can also cause headaches.

Secondary headaches occur quite often in the HIV-positive population, regardless of the presence or absence of a previous headache disorder. Referral bias skews the reported incidence, but the percentage of headaches considered secondary to serious and potentially fatal complications, such as cryptococcal meningitis may be quite high. Cryptococcal meningitis is the most common cause of secondary headache in adults with AIDS, although far less so in children as is true with other opportunistic diseases [62–64]. In patients with AIDS, several disease processes may be occurring simultaneously. Metabolic, nutritional, psychiatric, and neurocognitive facts may alone, or together influence the clinical presentation, which makes the diagnosis and management a challenge.

The likelihood of headaches being secondary in type depends on the stage of HIV infection. The differential diagnosis also varies according to the CD4 count. The CD4 count that is less than 500 dramatically raises the risk of opportunistic infection or meningitis. These etiologies should be considered if mentation is altered, the patients has a stiff neck (meningismus), or there are localizing neurologic signs, such as cranial neuropathy.

Among patients with cryptococcal meningitis and who are HIV-positive, 45% have no prior history of a previous AIDS defining illness. The headaches may be frontotemporal and accompanied by papilledema, nausea, vomiting, and meningismus. Neuroimaging results are frequently negative; although, gadolinium-enhanced MRI may reveal infected and inflamed meninges as with any meningitis, and Virchow-Robin spaces around blood vessels may appear dilated on MRI. The serum antigen test is a reasonable screen for patients not wishing to undergo a lumbar puncture when suspicion is low, or in those for whom lumbar puncture is contraindicated.

Tuberculosis and lymphomas can also affect the meninges, producing headache and neurologic deficits. In such cases, MRI and lumbar puncture are standard elements of the workup. Microbiologic blood studies and polymerase chain reaction (PCR) studies for tuberculin and cryptococcal antigens should be performed routinely, as mentioned in the discussion that follows.

Pain by Anatomic Location

Intracerebral infections can also cause headache. Headache associated with toxoplasmosis may be unilateral, bilateral, or holocephalic. It is often accompanied by hemiparesis, language dysfunction, or personality change. The presence of a choreiform movement disorder makes the likelihood of toxoplasmosis very high. Lymphomas may be meningeal or intracerebral. Clinical presentation depends on the location. Differentiation between lymphomas and toxoplasmosis depends on one or more of the following: imaging findings, response to treatment, and/or brain biopsy.

Typically, serial scans are used to monitor response to medical treatment for up to 14 days before biopsies are performed. It is important to follow the lesions to resolution, because more than one type of mass may be present. Use of steroids

should be minimized, unless there is sufficient swelling to cause brain herniation. As mentioned earlier, steroid-affected lymphomas may diminish on scans, only to reappear later. Furthermore, immunosuppression by steroids, in addition to the suppression caused by HIV alone, may put the patient at higher risk for superinfection or may interfere with the success of antibiotic and antiviral therapy.

Diagnosing Brain and Meningeal Pathology Associated with HIV Infection

Obtaining a gadolinium-enhanced MRI scan may prove useful, even if the results are negative, because of the likelihood that an other scan will be needed later in the course of treatment. Having a baseline scan with which to compare any new scans may significantly clarify equivocal findings. Lumbar puncture, when needed, should include routine microbiologic studies of the *CSF,* including the PCR test for *Mycobacterium tuberculosis.* Both blood and CSF should be evaluated for cryptococcal infection.

A thorough history and physical examination, including but not limited to a detailed neurologic examination, is usually necessary. On occasion, an EEG may prove to be helpful in differentiating migraine from epilepsy and moderate to severe dementia from depression (pseudodementia). Moderate to severe dementia should show up on an EEG as generalized or regional slowing. The EEG of a depressed person with severe psychomotor slowing and a paucity of verbal output, which mimics some forms of dementia, should be normal, unless a concurrent problem exists. Three normal sleep-deprived EEGs have much greater reliability, in terms of ruling out a seizure disorder, than does a single sleep-deprived or non-sleep-deprived test. Sleep deprivation helps to reveal a seizure disorder by making the brain tired and irritable, which increases the chances of the patient falling asleep. Sharp waves and other signs of epileptiform activity occur most often during the transition from wakefulness to sleep and vice versa. MRI may further evaluate areas of general or focal slowing and other types of abnormal EEG activity. In this way, physiologic and anatomic findings can be correlated.

Treating AIDS pathology-related headaches is a matter of managing the underlying condition and using analgesics judiciously, with attention to alteration in mental status. An excellent and practical overview of this topic, and related ones involving neurologic manifestations of AIDS, is available elsewhere [65].

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Chapter 19
Posttraumatic Headache in the Rehabilitation Patient

Brian D. Greenwald, Sagar S. Parikh, Julie Ferris, and Michael Ra

Introduction

Posttraumatic headaches (PTH) may develop in up to 90% of patients with TBI [1–7]. Although the amount of disability created by PTH varies, headaches (HA) are clearly a significant source of morbidity [8, 9]. PTH can exacerbate other common disorders seen after TBI including insomnia, affective disorders, behavioral disorders, and cognitive impairments [10]. PTH therefore has a significant direct and indirect effect on social and vocational functioning.

Sources of Head Pain

Potential sources of head pain that should be considered in the patient presenting with PTH include intracranial, cranial, and cervical structures. A careful history combined with a comprehensive exam of both the head and neck is the key component of localizing the source of pain and optimizing treatment. When using standard classification criteria, patients with PTH may have overlapping headache types. Defining a precise headache category may not be clinically valuable, as there may be more than one generator of pain in PTH [11]. The mechanism of injury may provide clues to distinguish types of PTH.

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Table 19.1 Acronym "COLDER" for symptom evaluation of PTH [12]

*C*haracter: dull, throbbing, lancinating, sharp, etc
*O*nset: any precipitants, relationship to menses, time of day, temporal relationship to injury, etc
*L*ocation: unilateral, bilateral, occipital, vertex, radiating
*D*uration and frequency: length of time the headache has been present, onset relationship to trauma, frequency during the week
*E*xacerbation: physical activity, stooping, valsalva, bending, touch (allodynia), stress, poor sleep, menses, weather changes, etc
*R*elief: medications that work, how frequently they are taken, response to rest, dark or quiet

The patient should also be asked about severity-associated symptoms (nausea, vomiting, photophobia, visual changes, phonophobia), presence of aura, and the degree of functional disability associated with HA episodes, including vocational impact (e.g., how many days of work missed per month). Other relevant historical information should include previous history of head injury or premorbid history of HA, history of psychiatric illness, and other symptoms related to postconcussion syndrome or impairments from a more severe TBI [11]. On history, the acronym "COLDER" (see Table 19.1) may assist with asking high impact questions to help with evaluation and treatment [12].

The physical examination should include observation, neurological examination, cervical range of motion, palpation of cervical and cranial musculature, palpation for "clicking" in the temporomandibular joint (TMJ), palpation of the greater and lesser occipital nerve, ocular examination, and auscultation for bruits. Myofascial pain is very common in the sternocleidomastoids, trapezius, and other cervical musculature after whiplash or inertial injury, as discussed below. It is interesting to note that the zone of referred pain for the sternocleidomastoid extends to both the retroorbital and periorbital areas; associated "autonomic" symptoms include vertigo, tinnitus, and a sense of fullness in the ear, as well as ear pain (commonly confused for otitis externa). The cervical musculature is also a major source of afferents to the vestibular systems integrating eye, head, and neck movement, thereby making dizziness a common complaint in this patient population (so-called cervical vertigo) [11].

Posttraumatic Migraine

Introduction

The rate of posttraumatic migraine has been reported to be as high as 49% in the first year following mild TBI, and the rate of tension-type headaches has been reported as to be high as 40% (Lucas et al. 2014). Correlation between injury severity and the development of PTH has not been identified; disabling headaches may occur in even the mildest of injuries [13].

Pathophysiology

There are multiple theories regarding the etiology of PTM, including damage to meningeal blood vessels, meningeal irritation, injury-induced neuronal hyperexcitability, alterations in the trigeminal vascular system, and cortical hyperexcitability [14].

Symptoms

Migraine headaches are typically unilateral in location, throbbing, moderate in intensity, and aggravated by physical activity. They are often associated with nausea, phonophobia, and photophobia and may be associated with an aura. Females and those with a prior history of HA seem to be especially at risk [15]. PTM may occur alone or as part of a constellation of symptoms referred to a post-concussive or posttraumatic syndrome. Symptoms may include poor concentration, confusion, amnesia, fatigue, irritability, depressed mood, and anxiety [15, 16].

Functional Limitations

PTM can be challenging to treat and may pose significant difficulty for individuals attempting to re-enter the workforce or continue educational endeavors.

Treatment

Initial

Avoidance of migraine triggers, proper sleep, and regular exercise are all beneficial for migraine prevention. Additionally, the use of a headache diary may aid in the identification of specific headache triggers and may be a beneficial part of the overall treatment plan [17, 18].

Medication

Individuals with PTH may have one or more headache types, including migraine or tension. Watanabe et al. performed a systematic review for treatment of PTH and found insufficient evidence to support a specific treatment modality. The authors suggest categorization of primary headache typology, consideration for trial of acetaminophen or nonsteroidal anti-inflammatories, and limited use of opioids. For those meeting criteria for migraine or probable migraine, a trial of triptans is recommended [18]. Treatment for migraine headaches can be summarized in Table 19.2 and can be divided by abortive, prophylactic, and other therapies.

Procedures

Botulinum toxin injections are an effective prophylactic treatment of migraine headaches.

Table 19.2 Pharmacologic treatment of migraine headaches

Prophylactic	Abortive	Other agents
Beta-blockers (propranolol, metoprolol)	Acetaminophen	Fiorinal
Anticonvulsants (topiramate, valproate)	NSAIDs	Corticosteroids
Antidepressants (tricyclics and SSRI)	Ergot derivatives	Oxygen therapy
Calcium channel blockers (verapamil, nifedipine)	Triptans	
Botulinum toxin	Opioids	

Note: *NSAID* nonsteroidal anti-inflammatory drug, *SSRI* selective serotonin reuptake inhibitor

Evidence

A recent prospective analysis of 254 patients with chronic migraine found a reduced number of headache days and improvement in the quality of life with the use of Onabotulinum toxin A [19]. Although the use of botulinum toxin for the treatment of migraine headaches has grown in recent years, there is limited data regarding the use of such intervention following TBI. A cohort study of 64 military members with chronic PTH following TBI reported improvement in headache in 64% of those receiving Onabotulinum toxin injections [20]. Although promising, further research is needed in the PTM population.

Tension Type Headache

Introduction

Tension-type headache (TTH) is historically the dominant classification type of PTH [21].

Pathophysiology

The pathophysiology of TTH is controversial and it likely represents a spectrum of disorders with several etiologies. Depending on the location, myofascial trigger points have been linked in literature to various categories of headaches including TTH.

Symptoms

A typical presentation of tension-type headache is bilateral head pain of pressing or vice-like quality of mild to moderate intensity. It generally occurs later in the day, and generally, movement does not worsen the headache. TTH are generally not

associated with nausea or vomiting, photophobia, or phonophobia. Pericranial tenderness also appears characteristic of TTH. Differentiating TTH from other headache types is challenging. Medication overuse headaches described below also need to be considered. Typically, TTH is diagnosed by the absence of other symptoms that are characteristic of other primary headaches.

Functional Limitations

TTH can pose significant difficulty for individuals attempting to re-enter the workforce or attempting to continue educational endeavors.

Treatment

Standard TTH treatment overlaps with migraine HA treatment [12]. See Table 19.2.

Cervicogenic Headaches

Introduction

Diagnosing a PTH due to cervical musculoskeletal causes (cervicogenic headaches) can be complex given that the primary causes of these headaches can share patterns of referred pain. Derangements of cervical joint surfaces, inflammation of nervous structures, or strain of the neck musculature can often mimic each other, which thereby mandates proper diagnosis. The prevalence lies between 0.4 and 2.5% in the general population, but can be as high as 53% for patient who sustained whiplash injuries. [22]. Cervicogenic headaches include, but are not limited to, headaches from cervical facet joints. Depending on the location, myofascial trigger points also cause cervicogenic headache. See Table 19.3 for diagnostic criteria.

Pathophysiology

The mechanism with which facetogenic headaches refer pain is similar in concept to most causes of cervicogenic headaches. Cervical spinal afferent nerves (primarily A-delta and C fibers), traveling from cervical spine structures, converge on second-order neurons within the central nervous system, which also receive ascending afferents from other cervical and even trigeminal inputs, before ascending towards the thalamic pain centers [23]. In addition, sensory fibers from upper cervical roots interact with trigeminal nerve fibers near the trigeminocervical nucleus in the upper cervical spinal cord [24]. Thus, due to convergence, cervical spine pain stimuli can be referred to the occipital, auricular, frontoparietal, and orbital regions of the head. In cervical facetogenic pain, the most common joints affected are the C2/C3 and

Table 19.3 Cervicogenic headache diagnostic criteria as proposed by the International Headache Society [31]

A. Pain, referred from a source in the neck and perceived in one or more regions of the head and/or face, fulfilling criteria C and D
B. Clinical, laboratory, and/or imaging evidence of a disorder or lesion within the cervical spine or soft tissues of the neck known to be, or generally accepted as, a valid cause of headache
C. Evidence that the pain can be attributed to the neck disorder or lesion based on at least one of the following:
1. Demonstration of clinical signs that implicate a source of pain in the neck
2. Abolition of headache following diagnostic blockade of a cervical structure
D. Pain resolves within 3 months after successful treatment of the causative disorder or lesion

C3/C4 levels, and thus the spinal nerves involved are most commonly C2, C3, and C4. In the atlantoaxial region, the most common joint affected is the C1/2 joint.

Symptoms

For cervical joint-related cervicogenic pain, typically the pain is unilateral and starts in the neck, radiating cephalad to the oculo-frontal-temporal areas. Pain is usually described as a dull headache, non-throbbing in nature; however, it is often accompanied by sharp pain on cervical extension. Pain may be triggered by certain neck postures or movements and may also be elicited by external pressure and palpation to the upper neck region bilaterally over the palpable facet joints. Though there is pain on range of motion, it is questionable whether this represents actual range of motion limitations.

Functional Limitations

Cervicogenic headaches can pose significant difficulty for individuals attempting to re-enter the workforce or continue educational endeavors.

Treatment

Initial

Conservatively, treatment for most types of cervicogenic headache include physical therapy, manual massage, modalities such as heat and transcutaneous electrical nerve stimulation (TENS), as well as medications such as anti-inflammatory agents.

Generally, these conservative measures are initiated prior to more targeted interventional treatments.

Rehabilitation

Myofascial pain is usually a secondary diagnosis from a primary source, whether it be poor posture, repeated manual stress, or even facet joint arthritis. Typically, postural training and myofascial release can be initiated in physical therapy; however, there has not been strong evidence to support either.

Procedures

Diagnostic medial branch blocks for the corresponding zygapophyseal joint-related pain (i.e. C2–3 and C3–4 Zygapophyseal joints), which are blocked via the C2 and C4 medial branches and C3 and C4 medial branches respectively, can be conducted. Once a successful block is obtained (characterized by a significant decrease in pain relief over the course of the half life of the anesthetic used), one can continue further and perform radiofrequency ablation (RFA) of these particular medial branches.

Evidence

Conservative treatments are not strongly supported in the literature, apart from manual massage therapy, which does show promise [23]. Current literature supports the use of diagnostic medial branch blocks for the corresponding zygapophyseal joint-related, as opposed to intra-articular zygapophyseal joint injections. A prospective controlled study looking at the efficacy of dry needling in 52 subjects with MPS found that the reduction in pain, which included a significant reduction found after dry needling, was positively correlated from the transition of an active trigger point to one that was latent or absent [25]. There was also a positive correlation with improvements in range of motion. Another study, this one randomized controlled, looking at 72 subjects pre- and post-dry needling also endorsed significant decreases in pain levels measured by the visual analogue scale and pain-pressure threshold [26].

Neuromas/Neuralgias

Introduction

Injuries to subcutaneous tissue and nerves are common following TBI, either as a direct result of traumatic injury or secondary to neurosurgical intervention. These injuries are an important cause of PTH and must be distinguished from other PTH etiologies. Neuroma formation may result following nerve trauma and can develop many years following craniotomy [27]. See Table 19.4 regarding the diagnosis of ON.

Table 19.4 Diagnosis of Occipital Neuralgia. The International Headache Society has listed their diagnostic criteria as below [31]

1. Paroxysmal stabbing pain, with or without persistent aching between paroxysms, in the distribution(s) of the greater, lesser, and/or third occipital nerves
2. Tenderness over the affected nerve
3. Pain is eased temporarily by local anesthetic block of the nerve

Pathophysiology

Direct trauma to any of the nerves that innervate the scalp can lead to neuropathic pain. With regard to occipital neuralgia, the greater occipital nerve provides sensation to the posterior scalp. It originates from the medial branches of the C2 dorsal ramus, with some contribution from C3. The lesser occipital nerve provides sensation to the posterolateral scalp. It originates from the C2 and C3 branches in the cervical plexus. The third occipital nerve provides sensation to the upper neck and lower posterior scalp and originates from the C3 nerve.

Symptoms

Headaches are generally associated with tenderness of the scalp, typically along an incision or area of scar. Palpation of the area may cause nerve-type pain, with reproduction of headache symptoms. Generally, patients with occipital neuralgia present with persistent, stabbing, shock-like pain, emanating from the superior neck, travelling to the posterior or posterolateral scalp. It is noted to present as unilateral pain in 85% of cases [28]. Patients may have tenderness to palpation in the occipital region.

Functional Limitations

Neuralgia and neuromas can pose significant difficulty for individuals attempting to re-enter the workforce or continue educational endeavors.

Treatment

Initial

Treatment options include icing of the area, topical agents, and other medications typically used for treatment of peripheral neuropathic pain, such as NSAIDs, tricyclics, and antiepileptic drugs.

Rehabilitation

Modalities, massage and focused physical therapy directed at alleviating muscle tension and aligning posture may be beneficial.

Procedures

Greater occipital nerve block has been studied and proven to be highly efficacious.

Evidence

Greater occipital nerve blocks have not only been shown to be efficacious in occipital neuralgia, but in various other headache syndromes as well, including migraines [29].

Temporomandibular Disorders

Introduction

Temporomandibular disorders (TMD) are a type of craniomandibular pain syndrome that can include the muscles of mastication of the temporomandibular joint (TMJ) itself. TMD is often seen in conjunction with direct trauma to the craniomandibular complex. Along with involvement of the TMJ, TMD may also involve the muscles of mastication, craniomandibular osseous structures, and surrounding soft tissue. In one study by Goncalves et al., headaches occurred in 85.5% of those with TMD, with the most common headache type as migraines and the next common as tension type headaches [30].

Pathophysiology

TMJ pain most commonly arises from joint mal-alignment or improper biomechanics. As would happen with any joint, dynamic alterations in joint movement can lead to stress and inflammatory changes, which can thereby lead to an abundance of inflammatory cytokines and joint degeneration.

Symptoms

Most commonly, pain from TMJ disorders are focused ipsilaterally around the muscles of mastication or the joint itself, with referred pain up to the temporal region of the head. The pain may be associated with auricular pain, as well as ear stuffiness

Table 19.5 Diagnostic criteria for TMD [31]

A. Recurrent pain in one or more regions of the head and/or face fulfilling criteria C and D
B. MRI and/or scintigraphy demonstrate TMJ disorder
C. Evidence that pain can be attributed to the TMD disorder, based on at least one of the following:
1. Pain is precipitated by jaw movements and/or chewing of hard or tough food
2. Reduced range of or irregular jaw opening
3. Noise from one or both joint capsule(s) of one or both TMJs
4. Tenderness of the joint capsule(s) of one or both TMJs
D. Headache resolves within 3 months and does not recur, after successful treatment of the TMJ disorder

and tinnitus. Bilateral and facial pain most often involve the muscles of mastication and is characterized as dull aching pain, while pain emanating from the TMJ may be sharp in presentation and focused posterior to the zygomatic arch. Temporal headaches that occur in the morning may be related to grinding of the jaw overnight. Other symptoms of TMD may include decreased mandibular ROM, crepitus, and myofascial pain [32]. TMD is a subtype of secondary headache disorders by the International Headache Society (HIS) in the International Classification of Headache disorders [31]. See Table 19.5.

Functional Limitations

TMD can pose significant difficulty for individuals attempting to re-enter the workforce or continue educational endeavors.

Treatment

Initial

Pharmacotherapy can also be used from NSAIDs and Tylenol, to anxiolytics, and tricyclic antidepressants.

Rehabilitation

Conservative measures include patient education, elimination of maladaptive oral habits, behavioral therapy, physical therapy with modalities, and intra-oral appliances to provide optimal mandibular alignment [32].

Procedures

Minimally invasive injections to the TMJ space, in cases of joint dysfunction, can be an option.

Surgery

More invasive surgeries may involve arthrocentesis, arthroscopy, arthroplasty, or total joint replacement depending on the joint pathology and patient's clinical presentation [32].

PTH Due to Altered Intracranial Pressure (ICP)

Introduction

Raised ICP, also known as intracranial hypertension, is defined as ICP greater than 20 mmHg [33, 34]. Elevated ICP may occur acutely following traumatic event, such as with an epidural hematoma, or gradually as is often the case in hydrocephalus. Low ICP, although less frequently discussed, is an important cause of headache following TBI. Common causes of low intracranial pressure in the TBI population include CSF leak, overshunting from VPS or EVD, and lumbar puncture. Syndrome of trephined (ST), also known as "syndrome of the skinning flap", is a controversial complication following decompressive craniectomy. The syndrome, although difficult to characterize, consists of a decline in cognitive status or a plateau in functional gains following craniectomy, which is usually reversible with cranioplasty. The majority of information known about this syndrome has been obtained from review of case reports, as large scale research regarding this topic has yet to be performed.

Pathophysiology

Elevated intracranial pressure leads to traction of the meninges. ST is thought to be secondary to compression of the brain due to atmospheric pressure with secondary alterations in cerebrovascular flow and cerebrospinal fluid flow.

Symptoms

Symptoms of elevated intracranial pressure vary depending on severity and can include headache, papilledema, cranial nerve palsies, motor dysfunction, nausea, vomiting, somnolence, and coma. In severe cases, elevated ICP may result in life-threatening brainstem compression due to uncal or tonsillar herniation. Headaches due to low ICP are usually orthostatic in nature; they are worse when the patient is

upright and improve when the patient is lying down. The pain is often bilateral, although diffuse head pain is common. Additional symptoms may include nausea, vomiting, neck stiffness, and diplopia. Anorexia, photophobia, vertigo, dizziness, tinnitus, and ataxia may also occur. With regard to ST, multiple symptoms of this syndrome may be seen, including a variety of cognitive changes, alterations in motor function such as hemiparesis or gait disturbance, impaired arousal, seizures, visual impairment, and headaches. In the majority of cases, there was partial to complete recovery of all symptoms following bone flap replacement [35].

Functional Limitations

ST should be considered in all craniectomized patients with arrest of functional gains. The deficits from ST may compound impairments seen after brain injury requiring craniotomy.

Treatment

Impairments caused by ST should be reversible with cranioplasty. Cranioplasty should be considered after craniectomy, as soon as medically appropriate.

Medication Overuse Headaches

Introduction

Medication overuse headaches (MOH) may be seen from overuse of a variety of analgesic and/or abortive headache agents, including ergotamines, opiates, caffeine, triptans, NSAIDS, and/or barbiturates. Stopping the drug generally results in worsening of headache; this is particularly noted when medication is stopped suddenly, as opposed to slowly weaned with concurrent alternative headache management options prescribed.

Pathophysiology

The precise mechanisms that lead to MOH are still uncertain. However, multiple factors seem to play a role, including genetic predisposition, central sensitization, and biobehavioral factors. Clinical and preclinical studies have consistently demonstrated increased excitability of neurons in the cerebral cortex and trigeminal system [36].

Symptoms

Patients with MOH generally present with the criteria of chronic TTH and simple analgesic use for more than 15 days/month, for more than 3 months of ergotamine, opioid, triptan, or any combination of medications for more than 10 days/month for more than 3 months. MOH is more commonly seen in conjunction with overuse of short-acting analgesics rather than longer acting medications. Medications that include caffeine could cause rebound headache when discontinued. Caution must be exercised in patients with headaches when analgesics are used to treat non-headache symptoms, because this practice may precipitate MOH.

Functional Limitations

MOH may also make headaches refractory to prophylactic headache medication.

Treatment

Treatment of MOH relies on the gradual weaning of the patient from the offending agent. This process could obviously result in a worsening of the headache. Although a washout period may take 3–10 weeks, some patients require hospitalization for this process. Consideration should also be given to replacing short-acting analgesics with long-acting substitutes during the weaning process [12].

Other Trauma-Related Headaches

A variety of dysautonomic headaches have been reported after trauma. They are generally unilateral and are associated with hyperactive sympathetic signs. Carotid cavernous fistulas may occur with head trauma. This is caused by a communication between the cavernous sinus and the carotid arterial system. Patients often present with decreased vision, external ophthalmoplegia, and proptosis. Radiology is helpful in confirming the diagnosis, and timely intervention is required to prevent morbidity and mortality. Cavernous sinus thrombosis may also occur after head trauma. This should be considered in a patient who presents with headache and cranial nerve findings. Carotid artery dissection may occur in association with head and neck trauma. Neck and facial pain, headache, unilateral pulsatile tinnitus, and visual complaints may be seen in isolation or in combination. Early diagnosis and treatment are important to decrease morbidity and mortality. Posttraumatic seizures may manifest as headache. Ictal headaches can occur before or after seizure activity. Posttraumatic sinus headaches can be seen in patients with a history of sinus or facial fractures.

Conclusion

The differential diagnosis in PTH is broad. Performing a comprehensive history and physical history is critical for correctly diagnosing the responsible pain generators for PTH in a given patient. More than one pain generator may be present. Treatment should be multimodal. The clinical subtype of PTH should dictate pharmacological intervention. Long-acting medications are less likely to contribute to MOH. Physical therapy/manual medicine to the upper cervical spine and associated musculature may be a useful treatment modality for most types of PTH. Consideration should be given to nerve blocks. Acupuncture, massage, biofeedback, and cognitive behavioral therapy all may assist in the treatment of PTH.

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Part IV
Multi Modal Approach: Pain Diagnostics

Chapter 20
Diagnostic Radiology and Pain in the Rehabilitation Patient

Aaron L. Harman and Van T. Nguyen

Abbreviations

CT	Computed tomography
MRI	Magnetic resonance imaging
US	Ultrasound

Introduction

Since the discovery of x-rays by Wilhelm Röntgen in 1895, imaging has been employed in a vast number of diagnostic applications. For hundreds of years, the only way to peer inside a patient was to make an incision; however, with the advent of diagnostic imaging, this could suddenly be done non-invasively. It is therefore not surprising that an editorial in the New England Journal of Medicine listed medical imaging as one of the top 11 most important developments in the past 1000 years of medicine [1].

Recently, there has been increasing public awareness and concern regarding radiation exposure to patients undergoing diagnostic imaging. From 1980 to 2006, radiation exposure related to medical imaging increased from 0.54 millisieverts (mSv) per person to 3.0, nearly a sixfold rise [2]. While radiologists and radiation physicists are charged with having true expertise in the field of radiation biology, non-radiologists should be prepared to answer questions from patients about potential health risks when ordering imaging tests.

Ionizing radiation, as opposed to non-ionizing radiation, can cause biologic damage to cells and has been linked to an increased risk of developing malignancies in a cumulative, dose-dependent fashion. There are three imaging modalities commonly used in the evaluation of pain, which employ ionizing radiation: radiography,

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computed tomography (CT), and fluoroscopy. In contrast, there is no ionizing radiation exposure from MRI or US, and therefore no increased risk for malignancy.

The potential diagnostic benefits from medical imaging must always be weighed with the risk of cancer induction. To gain perspective on the relative risks, the average American is exposed to 3.1 mSv per year of "background" radiation, which is a combination of terrestrial and cosmic sources [2]. By comparison, the doses of antero-posterior (AP) and lateral views of the lumbar spine are approximately 0.7 and 0.3 mSv, respectively [3]. CT uses a higher dose of radiation than conventional radiography. A CT of the lumbar spine is approximately 6 mSv. The risk of developing fatal cancer has been estimated to increase by 5.5% for each 1 Sv (1000 mSv) received; thus, a CT of the lumbar spine would theoretically increase one's risk of cancer by approximately 0.03%. This is a gross estimate and it is important to understand that children are more at risk of cancer induction from radiation exposure, whereas the elderly are less at risk. Of note, the baseline risk of developing fatal cancer in the U.S. population is approximately 20% [4].

In the current climate of healthcare economics, cost-effectiveness is extremely important to keep in mind when ordering expensive diagnostic studies. While imaging has the potential to easily demonstrate pathologic findings, it would be prohibitively expensive to indiscriminately order imaging studies without stratifying patients based on risk and need.

Since 1993, the American College of Radiology (ACR) has published evidence-based guidelines called "Appropriateness Criteria" for a variety of clinical presentations and conditions, which are free to the public online. Imaging modalities are rated from 1 to 9, which is based on their appropriateness in the evaluation of each clinical situation. Additionally, each modality is designated as one of six relative radiation levels, which give non-radiologists insight into the risk conferred to patients.

Modalities

Essentially, radiography and CT are both performed by placing a patient between a radiation source and a detector, sending a concentrated beam of ionizing radiation into the patient and creating an image based on the distribution and intensity of radiation which passes through the patient and hits the detector. Radiographs are two-dimensional images, while CTs are three-dimensional volume sets.

While radiography is able to evaluate the bones, it does not have the ability to evaluate the soft tissues or to provide cross-sectional imaging. For example, chronic discitis/osteomyelitis could cause destruction of the vertebral endplates, which would be visible on radiograph; however, acute infections are radiographically occult. Similarly, degenerative disk disease may cause narrowing of the intervertebral distance and endplate changes; however, radiographs cannot reveal the extent of spinal cord or nerve root impingement. CT is able to evaluate soft tissues, but is often inadequate for spinal pathology.

Magnetic resonance imaging (MRI) is performed by placing the patient in an extremely strong magnetic field, sending multiple radiofrequency pulses into the patient, detecting subtle differences in the time it takes for hydrogen atoms in the body to realign themselves, and plotting this information as shades of gray in space in order to make pictures that can be interpreted for diagnosis. Contrast is not needed for diagnosing many causes of pain, such as spondylosis or fractures. However, contrast is indicated in cases of suspected infection or malignancy. As MRI utilizes an extremely strong magnet, patients with ferromagnetic implantable devices, which include cardiac pacemakers, cannot undergo this study.

Nuclear medicine encompasses a group of modalities, which are less commonly used in the field of pain management than the tests listed above; however, nuclear medicine is extremely useful in certain situations.

The following sections discuss the imaging workup of common entities, which are managed by pain specialists.

Headache

Headaches are extremely common, affecting up to 60% of the population [5]. In the majority of cases, clinical history and physical examination can be used to accurately make the diagnosis. Only patients with the following "red flag" clinical features should be further evaluated with medical imaging, which can be easily remembered with the mnemonic "**SNOOP**" [6]:

1. **S**ystemic symptoms or illness (e.g. fever, vomiting, stiff neck, pregnancy, malignancy, immunocompromised state, anti-coagulated)
2. **N**eurologic signs or symptoms (e.g. altered mental status, focal neurologic signs or symptoms, seizures, or papilledema)
3. **O**nset is new or sudden
4. **O**ther associated conditions (e.g. following trauma, awakens patient from sleep, or is worsened by Valsalva maneuver)
5. **P**rior headache history is different from current (e.g. in pattern, severity, or frequency)

In addition, imaging should be considered if the patient does not respond to conventional therapy. Even in patients with symptoms that are concerning enough to warrant imaging, a significant finding is made in only 0.4% of examinations [7]. CT and MRI are the two imaging modalities used to evaluate headaches. MRI is more sensitive than CT for all disease processes, but is also more expensive.

In patients who present with an atraumatic thunderclap headache, or the "worst headache ever", it is necessary to evaluate the patient for a subarachnoid hemorrhage, which may be due to underlying cerebral aneurysm or arteriovenous malformation. CT is an extremely useful modality in the detection of subarachnoid blood. A study of 3132 patients who visited the emergency department with this presentation found the sensitivity and specificity of CT for the detection of subarachnoid

hemorrhage was 92.9 and 100%, respectively, which improved to 100 and 100%, respectively, within 6 hours of headache onset [8]. Acute subarachnoid blood appears denser (brighter) than surrounding CSF on CT and decreases in density with time.

Once subarachnoid blood is detected, either by CT or lumbar puncture, there is some debate as to the next step in management. CT angiography (CTA) and MR angiography (MRA) are both respected as useful diagnostic tools, with high sensitivities for cerebral aneurysms [9, 10]. Although these sensitivities may be good enough in other realms of diagnostic imaging, the prognosis of ruptured cerebral aneurysms is so poor and the consequences of missing the diagnosis are so severe that their negative predictive values are often not felt to be sufficiently high enough to send the patient home without further workup. For this reason, catheter-based angiography is usually performed for further evaluation, regardless of whether or not the CTA or MRA is positive. This has led some to argue for skipping the CTA or MRA, which could potentially save both time and money.

If there is clinical concern for a brain tumor, MRI of the brain, with and without a gadolinium-based contrast agent, is the examination of choice. CT can often demonstrate large masses and associated vasogenic edema; however, small masses are often completely invisible by CT.

The diagnosis of meningitis is made clinically and by CSF analysis. Although leptomeningeal enhancement may be seen on MRI, the role of imaging is primarily to evaluate for complications such as subdural empyema, ventriculitis, and hydrocephalus.

Elbow Pain

Many causes of elbow pain can be diagnosed clinically and managed conservatively, with diagnostic imaging available for refractory cases. For example, tennis elbow (aka lateral epicondylitis) can be diagnosed clinically by eliciting reproducible tenderness to palpation of the lateral epicondyle with pain upon wrist extension; however, imaging may be employed if there is clinical concern for a radial collateral ligament injury.

Radiographs are the best initial test for the evaluation of elbow pain. In patients with acute elbow pain, radiographs can make the diagnosis of fracture, dislocation, joint effusion, lipo-hemarthrosis, and soft tissue swelling. In patients with chronic elbow pain, radiographs can make the diagnosis in cases of osteochondral unit injuries, intra-articular loose bodies, osteoarthritis, or calcium pyrophosphate deposition disease. Anteroposterior (AP), lateral, and oblique views are considered standard [11]. A variety of stress positions can also be utilized to elicit dynamic instability caused by underlying ligamentous injuries. If radiographs are negative, the next best step is MRI, which can characterize abnormalities of the cartilage, ligaments, muscles, and subcutaneous tissues.

If there is specific clinical concern for intra-articular loose bodies or synovial abnormality, such as clicking, locking, or limited range of motion, and if the radiographs are

negative, CT or CT arthrography may be performed; however, MR and MR arthrography are widely preferred. MR arthrography involves the intra-articular injection of a diluted gadolinium-based contrast agent or normal saline.

Ultrasound examination of the elbow and other joints is a less expensive alternative to MRI for evaluation of ligaments and tendons. However, musculoskeletal ultrasound is highly operator-dependent, and a statement put forth by the Musculoskeletal Ultrasound Task Force of the American Medical Society of Sports Medicine has indicated that an operator should perform at least 50 ultrasound examinations of a joint or other anatomic structure, before achieving proficiency [12]. Also, US cannot evaluate the bone marrow.

Nuclear bone scan is usually performed to evaluate for malignancy, but can also be used for the detection of stress fractures, healing fractures, and infection.

Hand/Wrist Pain

Evaluation of hand and/or wrist pain should begin with a history and physical examination, with imaging available if necessary. As with other areas of the appendicular skeleton, the first imaging test should be radiography. The standard views are anteroposterior (AP), lateral, and an oblique. The lateral view is useful for evaluating for soft tissue swelling. Specific views for the parts of the anatomy, such as the scaphoid and Norgaard views, can be performed to address specific clinical questions. Dynamic views such as power grip and radial or ulnar deviation can be useful to evaluate for instability, which may be indicative of ligamentous injury [13]. In patients with arthritis, plain films are extremely useful in evaluating the extent and distribution of disease.

MRI is important in the workup of wrist pain given its ability to evaluate the soft tissues. Its utility is evidenced by the finding in one study that the diagnosis and treatment was changed in 50% of cases after the MRI was performed and interpreted [14]. MR arthrography can be performed to enhance the diagnostic yield when evaluating internal structures (ligaments, cartilage, and the TFCC).

The main advantage of CT over MRI is its superior spatial resolution. In patients with a known fracture presenting with wrist pain, CT is preferred for its ability to evaluate cortical and trabecular alignment. When there is a suspected fracture, but radiographs are negative, either MRI or CT are appropriate choices [15]. The main disadvantages of CT versus MRI are the use of ionizing radiation and the less sensitive depiction of soft tissues.

Ultrasound has the advantage of being able to observe functional anatomy. For example, stenosing tenosynovitis involving the flexor digitorum tendons, or intersection syndrome involving the first and second extensor compartments may be diagnosed by observing in real time with ultrasound. Ultrasound is also useful in the evaluation of the extra-articular soft tissues and can diagnose ganglion cysts. Again, limitations are that it is highly operator-dependent and cannot evaluate the marrow.

Nuclear bone scan is sometimes used to rule out occult fractures. However, given its low specificity and inability to evaluate the soft tissues, bone scintigraphy is not performed as commonly as MRI. In patients with suspected reflex sympathetic dystrophy, a three-phase bone scan may be performed, which has characteristic findings.

Low Back Pain

Low back pain (LBP) is one of the most common health problems in the United States, affecting up to 84% of adults at some point in their lives [16]. Although most low back pain is a self-limited process, it is a common reason for physician visits [17] and carries a significant cost to the healthcare system [18]. Utilization of diagnostic imaging is a significant contributor to this cost, both directly and indirectly, from downstream effects, which include surgery. For this reason, it is important for the clinician to understand the appropriate indications for ordering imaging examinations.

The role of diagnostic imaging in the management of low back pain has been a source of confusion to referrers. One notable reason for this is that lumbar disc abnormalities have been commonly found in asymptomatic patients on myelography, CT, and MRI [19–22]. For patients with uncomplicated back pain, the American College of Physicians, American Pain Society, and American College of Radiology unanimously agree that no imaging is indicated [23, 24]. Even the majority of patients with back pain and radiculopathy will recover within 8 weeks. This is supported in a meta-analysis by Chou et al. in 2009, which demonstrated no significant difference between patients who received immediate lumbar imaging, versus usual care [25]. However, imaging should be considered in cases of severe or progressive neurologic deficits, or when history or physical examination raises the suspicion for serious underlying disease. The following are considered “red flags”, which suggest a more serious problem:

1. Trauma, cumulative trauma.
2. Unexplained weight loss, insidious onset.
3. Age >50 years, especially women, and males with osteoporosis or compression fracture.
4. Unexplained fever, history of urinary or other infection.
5. Immunosuppression, diabetes mellitus.
6. History of cancer.
7. Intravenous drug use.
8. Prolonged use of corticosteroids, osteoporosis.
9. Age >70 years.
10. Focal neurologic deficit(s) with progressive or disabling symptoms, caudal equina syndrome.
11. Duration longer than 6 weeks.
12. Prior surgery.

Fractures

Radiography is used when a spinal fracture is suspected. The standard protocol for lumbar spine radiographs is an anteroposterior (AP) and lateral view. CT has a greater sensitivity for fractures, but exposes patients to more radiation. In one study of 26 blunt trauma patients, plain film of the spine had a sensitivity of 73%, specificity of 100%, and negative predictive value of 92%, while CT had a sensitivity of 100%, specificity of 97%, and negative predictive value of 100% [26].

In treatment planning for painful vertebral compression fractures, MRI plays an important role. Only acute fractures should be treated with vertebroplasty or kyphoplasty, and MRI can beautifully show bone marrow edema, which is indicative of an acute fracture. MRI can also be helpful in the workup of suspected tumors, which can be biopsied at the time of vertebroplasty.

In patients who have a contraindication to MRI, a nuclear medicine study called bone scintigraphy can be utilized. This involves the intravenous injection of a radionuclide-tagged chemical, which is taken up by actively turning over bones. Acute fractures will avidly take up the radiotracer, while chronic fractures may only have faint or no uptake.

Spondylosis

Degenerative disk disease and facet joint hypertrophy can be diagnosed on plain film, CT, or MRI. The major advantage of MRI over the other modalities is its ability to beautifully depict pathology of soft tissues, such as the intervertebral disk, spinal cord, and nerve roots. While plain film and CT can demonstrate productive vertebral endplate osteophytes and facet joint hypertrophy, they cannot show nerve root or spinal cord compression by the disk.

As mentioned earlier, asymptomatic people have been found to have degenerative changes in the spine, and the degree of abnormality found on imaging often does not correlate with the severity of symptoms. Therefore, imaging is reserved for patients with duration of pain longer than 6 weeks with conservative management.

Post-Procedural Evaluation

Failed back surgery syndrome (FBSS) refers to chronic back pain following back surgery, which typically includes a laminectomy. MRI is the mainstay in evaluating FBSS. When soft tissue is seen extending beyond the vertebral body interspace, MRI can distinguish between disk material and scar, each of which are treated differently.

Hip Pain

Chronic Pain

Clinical history is essential for selecting the appropriate imaging workup in patients with hip pain. Range of motion, gait disturbances, duration of symptoms, and pain patterns, which include exacerbating vs. relieving factors, are important clinical details. Radiographic evaluation is recommended for initial evaluation and can characterize common disorders, such as osteoarthritis.

MRI is both sensitive and specific for detecting many abnormalities involving the hip or surrounding soft tissues and should generally be the imaging technique used following radiographs [27]. Osteonecrosis is a very common cause of chronic hip pain, for which MRI is routinely used [28]. MRI is also helpful in detecting occult fractures, soft-tissue injuries, infection, inflammatory processes, and neoplasms.

Diagnostic and therapeutic joint injections are useful for confirming the location of pain and for short-term pain control. Joint aspiration is also useful in diagnosing the presence of infection or crystal arthropathies.

In the presence of normal radiographs, and in the absence of access to MRI, a nuclear medicine bone scan may be a useful technique. Radionuclide bone scans are effective for detecting or excluding subtle osseous abnormalities [29].

Prior Arthroplasty

The number of primary total hip arthroplasties performed in the United States was 220,000 in 2003 and this number is expected to rise to 572,000 by 2030 [30]. Patients with loosening or infection usually present with pain, whereas those with particle disease and resulting osteolysis can be asymptomatic. Complications can be difficult to identify clinically, so understanding the use of imaging is of particular importance. All symptomatic patients should undergo radiography. Comparison of prior imaging to current studies facilitates the diagnosis of subtle changes that can occur in hardware loosening, particle disease, or infection.

Radiography is the standard first examination for evaluating total hip arthroplasties and is useful to evaluate component position and wear [31]. Radiographic features of loosening can be present, even if symptoms are absent.

Arthrogram performed with contrast instilled into the joint can detect sinus tracts, fistulae, and collections that connect to the joint and can help to evaluate component loosening. Fluid sampling can be done at the time of arthrography [32].

Computed tomography can aid in the assessment of bone, cement, and soft tissues surrounding the metal components. Osteolysis, implant position, hardware

integrity, wear, fractures, heterotopic ossification, hematomas, and fluid collections can be assessed [32].

Magnetic resonance imaging (MRI) techniques have enabled useful information to be obtained, even around total hip replacements. Structures such as the joint capsule, intra-articular content, muscles, nerves, vessels, and tendons can be evaluated [32].

Nuclear bone scans are sensitive indicators of a failed arthroplasty, but are not able to reliably indicate the cause of failure [33]. Thus, the absence of increased uptake on the bone scan is thought to be strong evidence against a prosthetic complication, such as loosening or infection.

Vascular-Associated Pain

Claudication

Peripheral arterial disease (PAD) affects nearly eight million patients in the United States and up to 20% of patients in the primary care setting. Increased prevalence among older patients, diabetics, and those with end-stage renal disease is well established. This disease progresses from an asymptomatic process to claudication and then to critical limb ischemia [34].

In combination with the history and physical examination of patients, noninvasive hemodynamic studies have become an important tool for evaluating peripheral vascular disease [35]. The presence of a normal ABI, both at rest and following exercise, in a patient with compressible vessels effectively excludes atherosclerotic occlusive disease as a cause of leg claudication and obviates the need for additional arterial imaging [36].

Catheter angiography is considered the gold standard for evaluating and characterizing arterial lesions. This is an invasive procedure, though an intervention can be performed at the time of the study.

Magnetic resonance angiography (MRA) techniques continue to evolve, including the use of non-contrast imaging sequences in patients with renal insufficiency. Some technical problems limit the utility of MRA for imaging peripheral vascular disease. Challenges include image quality related to low signal/noise ratio, motion artifacts, long acquisition times, the exclusion of patients with pacemakers or other metallic implants, and loss of signal in arterial segments within metal stents or adjacent to prosthetic joints.

Compared to MRI, computed tomography angiography (CTA) has the advantages of rapid acquisition, compatibility in patients with pacemakers/defibrillators, and generally less metallic artifact. Claustrophobia is also less of an issue. Although calcified vessel walls can limit the ability to interpret CT images, studies have demonstrated the accuracy of CTA for evaluating PAD and have shown strong con-

cordance between CTA and catheter angiography for establishing an accurate treatment plan [37].

Deep Venous Thrombosis

Lower-extremity deep venous thrombosis (DVT) has an estimated annual incidence of approximately 5 per 10,000 in the general population, with the incidence increasing with advancing age [38]. Classically, a patient with symptomatic lower-extremity deep venous thrombosis (DVT) presents with localized pain and tenderness or with edema and swelling of the lower extremity.

Ultrasound (US) is widely recognized as the most cost-effective and preferred imaging modality for diagnosing proximal DVT [39]. Real-time duplex US is noninvasive, can be performed at bedside, and is reliable for serial evaluation. It can be limited in its evaluation above the inguinal canal and below the knee. US evaluation for DVT is often combined with real-time Doppler imaging, such as duplex, continuous-wave, and color-flow Doppler imaging. Color-flow Doppler imaging can assist in characterizing a clot as obstructive or partially obstructive [40].

First-line therapy for DVT is systemic anticoagulation to reduce the risk for DVT extension and pulmonary embolism and to reduce the likelihood of recurrent DVT and post-thrombotic syndrome. It is generally accepted that the benefits of anticoagulation therapy in patients with proximal DVT outweigh its risks. Because below-the-knee (distal) DVT rarely results in pulmonary embolism, the role of anticoagulation therapy in the setting of distal DVT is controversial. However, up to one-sixth of patients with distal DVT will have thrombus propagate above the knee, and therefore, follow-up ultrasound is recommended in 1 week if anticoagulation therapy was not initiated at presentation [41].

MRV and CTV are alternative imaging options, especially in patients who are unable to undergo US (e.g. overlying dressing/casting material, inability to tolerate ultrasound compression), or if there is high suspicion of pelvic or IVC thrombosis. MRV and CTV can be used to evaluate extravascular anatomy, which can be useful for diagnosing external sources of venous compression or alternative pathologies.

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Chapter 21
Electrodiagnostic Studies for Pain in the Rehabilitation Patient

John R. Parziale

Introduction

Electrodiagnostic testing is an extension of the physical examination and is a procedure that has been used for decades to evaluate patients with suspected neuromuscular diseases. Most neuromuscular specialists would agree that these studies are essential in revealing the nature of underlying disorders, often beyond what is possible on physical examination alone. However, these tests have associated healthcare costs, may be uncomfortable, and the results of such testing may be dependent upon the experience, skill, and expertise of the person(s) performing these studies.

Electrodiagnostic testing (EDX) includes analysis via electromyography (EMG) and nerve conduction studies (NCS). The electromyographic examination is a study of muscle via a needle electrode examination; nerve conduction studies are performed by providing an electrical stimulus along segments of a peripheral nerve toward a receiving electrode, and both sensory and motor nerve fibers may be tested.

There are two types of nerve injury that are generally detected; axonal degeneration (or axon loss) and segmental demyelination, a focal conduction deficit along an intact axonal. Causes of axonal degeneration include compression or traumatic injury of the nerve, nerve ischemia, and inflammation; these changes are generally identified on the electromyographic examination. Demyelination may be caused by an area of focal compression of the peripheral nerve and/or an autoimmune disorder such as Guillain-Barré syndrome and is evident on nerve conduction studies. More refined nerve conduction studies such as repetitive stimulation may be performed for disorders such as myasthenia gravis. Dynamic electromyography may be helpful

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in evaluating muscle function in patients with spasticity [1]. Somatosensory-evoked potential (SSEP) testing may be used diagnostically for upper motor neuron injuries or for monitoring spinal cord function during spinal surgery procedures.

Study Parameters and Applications

Electrodiagnostic testing is generally performed by a physician with specialized training in the procedure. Neurologists and physiatrists must complete rigorous training in order to complete the requirements of their specialties and/or successfully pass board certification examinations.

Temporal Considerations

The ability of electrodiagnostic testing to identify neurologic changes depends, in part, on the duration of the patient's symptoms. Motor nerve conduction studies may show a reduction in the size or shape of the action potential as soon as 3 days after injury, and sensory nerve conduction studies may show changes as soon as 10 days after injury. The EMG examination may not show mild changes for at least 21 days after injury, and more substantive changes may take 5 weeks or more to become apparent [2]. It is therefore common for electrodiagnostic testing to be performed after symptoms have been present for 21 days or more in order to increase diagnostic sensitivity and specificity.

There are exceptions to this guideline. Early nerve conduction studies may help locate a lesion along the path of a nerve that will become impossible to localize once Wallerian degeneration has occurred or to differentiate between axon loss and demyelinating lesions for prognostic purposes. In these cases, nerve conduction studies may be done early, but should be repeated along with a needle electrode examination 21 days later [3].

Electromyographic testing can be used as an indicator of the severity of a neurologic injury, and early axonal regeneration may be seen by 6 months post-injury.

Contraindications

Electrodiagnostic testing is generally considered a safe procedure. While transient discomfort may occur during the procedure, there are few potential complications. Patients and/or referring physicians may raise concerns regarding the safety of electromyography in anti-coagulated patients, but few (if any) cases of intramuscular hemorrhage are reported as long as simple procedures such as applying pressure to the EMG needle insertion site are utilized.

Another frequent concern is whether nerve conduction studies are safe in patients with implanted cardiac devices such as a pacemaker or implanted cardiac defibrilla-

tor (ICD). In a study of ten patients with implanted pacemakers and five patients with ICDs, none of the electrical impulses generated during routine nerve conduction studies of the left peroneal and/or median nerves in nine patients were seen on the surface ECG or detected by the pacemaker or ICD. In none of the patients was a pacemaker or ICD function affected by nerve conduction studies at any of the stimulation sites, including Erb's point [4].

Lymphedema in a limb has been cited as placing the patent at increased risk for infection following needle puncture for phlebotomy, intravenous line placement, and other procedures. However, lymphedema is not a contraindication for performance of electrodiagnostic testing and there is no increased infection rate in lymhedema patients who have electromyographic procedures [5].

Diagnostic Value

Electrodiagnostic studies can lead to a change in diagnosis or additional diagnoses.

Electrodiagnostic examinations are not only informative, but can confirm, refute, alter, or give additional details to an initial clinical diagnosis. In one study, electrodiagnostic testing substantially altered 42% of diagnoses, confirmed 37%, and did not clarify the diagnosis in 21% [6]. Other studies have shown that over 50% of cases and/or provide a new or unsuspected diagnosis in 31–43% of cases [7]. In a group of 98 hospitalized patients, electrodiagnostic studies confirmed a clinical diagnosis in 53% of cases and provided a new, relevant diagnosis in 12.6% of patients where the vast majority (94%) of these cases were referrals from the neurology service, implying that subspecialty evaluation had occurred at the time of referral. These findings frequently led to further testing or new treatments [8].

Prognostic Value

The following are examples of conditions that have been studied relative to the prognostic value of electrodiagnostic testing.

Cervical Radiculopathy

Cervical radiculopathy results from a pathologic process that affects a nerve root of the cervical spine. There is a large differential diagnosis for neck, upper limb, and shoulder symptoms, and there can be a complex electromyographic pattern; in 50 cases of surgically proven cervical root lesions, a range of needle EMG patterns was found with EMG demonstrating less specificity for the C6 nerve root and greater specificity for C7 and C8 radiculopathies. The surgical group in this study was more severely affected than patients who did not require surgical intervention and suggests

a limitation of precise localization of root lesions by EMG [9]. Physical examination findings, in conjunction with EMG results, can be important; in one study, if a reflex was lost or weakness was noted, the likelihood of a cervical radiculopathy being confirmed by EMG was significantly greater. The combination of weakness plus sensory loss or reflex changes on physical examination resulted in a ninefold greater likelihood of cervical radiculopathy [10]. Somatosensory-evoked potentials and related tests may be useful, but are not recommended for the vast majority of patients who are referred for evaluation of possible cervical radiculopathy [11].

Carpal Tunnel Syndrome

Carpal tunnel syndrome is a median neuropathy at the wrist as the nerve passes, along with nine flexor tendons of the hand and fingers, through a narrow bony canal with a ligamentous roof. Various grading systems are used to estimate the severity of nerve dysfunction in this disorder. Many electromyographers have traditionally used a severity modifier such as "mild, moderate or severe" when giving a clinical impression of a diagnosis of carpal tunnel syndrome, but the validity of this approach has been debated [12]. Robinson states that it is unclear that the "severity" of the carpal tunnel syndrome should be used to guide treatment and has questioned whether it is truly best to defer surgery for someone with severe symptoms or functional impairment because the EDX results were "mild CTS", or conversely, whether a patient with severe EDX findings should have surgical treatment if there is minimal functional impact from the disease [13].

Lumbar Radiculopathy

Electromyography may be helpful in predicting the likelihood of improvement after lumbar epidural steroid injections. A retrospective review of 39 subjects demonstrated that patients with EMGs who were considered positive for radiculopathy were significantly more likely to have functional improvement using the Oswestry Disability Index after an epidural steroid injection than patients with a negative or normal electromyographic examination, and that analog pain scores in these individuals were not predictive in the decision making of treatment options for patients with lumbar radiculopathy [14]. A study of 170 patients who had EMG examinations prior to transforaminal ESI were questioned at 30 days following the procedure; 37.7% of the patients with an EDX that demonstrated radiculopathy noted improvement following the procedure, while only 17.8% of patients with a "negative" EDX reported improvement in their pain level. The difference between these groups was statistically significant. The authors acknowledged that the improvement rate in both groups was low and speculated that this was because the patient population studied had either an atypical clinical presentation or equivocal imaging studies [15].

Piriformis Syndrome

Piriformis syndrome is characterized by buttock pain with radiation to the leg and/or foot and has been described as a cause of up to 5% of cases of sciatica. Sciatic nerve irritation may be caused by compression due to piriformis muscle spasm in the pelvic floor. Electromyography can detect myopathic and neuropathic changes and a delay in the H reflex with the affected leg in an adducted, internally rotated, and flexed position for 2 min, as compared with the H reflex in the anatomic position, suggests entrapment of the sciatic nerve at or near the hip abductor external rotator group under which it passes, including the piriformis muscle. This "FAIR test" of muscle activity during hip Flexion, Adduction, and Internal Rotation has both sensitivity and specificity greater than 80% and has diagnostic and prognostic value. Patients with a positive test were likely to improve clinically following botulinum toxin injection to the piriformis muscle and physical therapy, whereas patients with a negative test were unlikely to show clinical improvement following injection [16, 17].

Spasticity

Dynamic electromyography involves the analysis of activity of specific muscles and/or muscle groups in patients with upper motor neuron conditions. Isolation of muscles that are in constant spasm and/or muscles that contract inappropriately, i.e. during activation of antagonist muscle groups, can be a useful strategy to target specific muscles for surgery or neuromuscular blockade [1]. The FDA has recently approved the use of botulinum toxin as an indication for treatment of adult patients with upper extremity spasticity, and this has expanded the therapeutic options for patients with spasticity caused by brain injury, stroke, multiple sclerosis, or traumatic spinal cord injury.

Diabetic Peripheral Neuropathy

Nerve conduction studies and EMG have a low sensitivity in the diagnosis of early diabetic peripheral neuropathy (DPN), but can be helpful in the later course of the disease. The sensory nerve action potential (SNAP) of the sural nerve correlates with functional mobility as measured by the 6-min walk test, and peroneal motor nerve conduction velocity correlates with several quality of life (QOL) measures. Treatment options for painful neuropathy include lifestyle management (diet, increased exercise, etc.) and medications such as gabapentin, pre-gabalin, and duloxetine. Improved control of hemoglobin A1C can prevent DPN in patients with Type 1 diabetes and can be useful in managing nephropathy and/or retinopathy in Type 2 diabetics, but there is insufficient evidence that controlling HbA1C improves or prevents the progression of DPN in patients with diabetes mellitus type 2.

Neuromuscular Diseases

Electromyographic testing is helpful in diagnosing neuromuscular diseases including amyotrophic lateral sclerosis (ALS) and/or various types of muscular dystrophy. However, the role of testing in the direction of treatment has been less clear. In part, this may be because these diagnoses have been described as causing "painless weakness" since sensory nerve fibers are not thought to be affected with diseases of the anterior horn cell, muscle, or the neuromuscular junction. In fact, pain is a very common component of these conditions; over 70% of patients with these conditions have complaints of pain, often related to depression, bursitis, and/or joint contractions. Identifying muscle spasm via electromyographic testing may permit the treating physician to determine whether interventions such as a muscle relaxant or trigger point injection can be of benefit [18].

Complex Regional Pain Syndrome

A diagnosis of Complex Regional Pain Syndrome (CRPS) may demonstrate a normal result on EDX (CRPS-I) or can be associated with an elecrodiagnostic abnormality (CRPS-II). The quantitative sudomotor axon reflex test, or QSART, is thought to evaluate sympathetic fibers by assessing how sweat glands respond to electrical stimulation. A small electrical current passes through electrodes placed on the forearm, foot, and leg, while a computer analyzes the response of nerves and sweat glands. A positive QSART is highly predictive of a positive clinical response to sympathetic blockade ($p < 0.001$) [19]. QSART measures the postganglionic sudomotor response and will be unable to detect preganglionic lesions. Unfortunately, QSART is time-consuming, requires special equipment including a room that is both temperature- and humidity-controlled, and is not widely available [20].

Post-Traumatic Injury

Following severe trauma, as with a brachial plexopathy, the examining physician is often asked to answer two questions: (a) is the injury pre-ganglionic, i.e. a potential nerve root avulsion, or a post-ganglionic injury with greater potential for recovery, and (b) is the injury "complete" without visible recruitment activity or are there intact axonal tracts? Pre-ganglionic nerve root avulsions often exhibit a normal or nearly normal SNAP, since the sensory nerve cell nucleus is located within the dorsal root ganglion; with post-ganglionic peripheral nerve injuries, the SNAP is significantly reduced or absent. A complete peripheral nerve injury will not enable the muscle to contract under voluntary control, but an incomplete nerve injury shows evidence of visible recruitment within a muscle or muscle group.

In incomplete nerve injuries, the recruitment pattern on EMG examination is a predictor of which muscles may be considered "good donors" for muscle transfer following severe trauma. The EDX can assess recovery of function following severe trauma by 6 months post-injury via measurement of (a) an increased motor unit action potential (MUAP) as compared with a study performed 4–6 weeks post-injury, and (b) the presence of nascent polyphasic waves, indicative of peripheral nerve sprouting. If either or both of these are present, the examining physician may predict with greater confidence that the muscles and nerves tested show signs of physiologic recovery [21]. The presence of abnormal EMG potentials in the paraspinal muscles suggests a root avulsion or an injury proximal to the division of the posterior primary ramus from the spinal nerve root [22]. SSEPs may also be helpful; and proximal plexus injuries, or point potentials are absent while per point potentials are absent with nerve root avulsions [23].

Surgical muscle transfer to gain function may be determined as appropriate at approximately 6 months post-injury, depending on the length of the nerve to be regenerated. Repeat studies performed at intervals of 8–10 weeks may be helpful in monitoring the recovery of patients with traumatic neurologic injuries.

Summary

The electrodiagnostic examination provides ample and important diagnostic and prognostic information to the clinician treating patients with many types of painful conditions. These tests provide the clinician with a more accurate and comprehensive diagnosis and can guide treatment, i.e. determining which nerve root is involved in a radiculopathy, identify whether a spastic muscle or muscle group is amenable to treatment with a blocking agent such as phenol or a neurotoxin, or by assisting a surgeon to know whether a post-traumatic nerve injury is likely to recover or, if not, which muscles are good candidates for transfer.

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Recommended Reading

For a comprehensive and detailed discussion of electrodiagnosis:
Campbell WW. Essentials of electrodiagnostic medicine. 2nd ed. New York: Demos; 2013.
Dumitru D, editor. Electrodiagnostic Medicine. Philadelphia: Mosby; 2001.
For a brief yet concise overview:
Chemali KR, Tsao B. Electrodiagnostic testing of nerves and muscles: when, why and how to order. Cleve Clin J Med. 2005;72:37–48.

Part V
Multi Modal Approach: Rehabilitation

Chapter 22
Physical Therapy and Pain in the Rehabilitation Patient

Hubert van Griensven

Introduction

Pain rehabilitation can sometimes be straightforward, but is often multi-faceted and potentially complex. Aspects of rehabilitation such as manual therapy and exercise prescription have traditionally been applied to aid tissue healing and recovery of function. However, pain can occur without injury and injury-related pain may or may not be proportionate to the inciting event [1]. Psychological factors, changes in the way the sensory nervous system functions, and social circumstances can all influence the perception and consequences of pain. In patients for whom pain becomes a prominent problem in its own right, approaches to rehabilitation may have to be practiced in a psychologically informed manner [2]. Moreover, explanations of the way persistent pain behaves cannot reasonably be limited to a tissue injury model, but must include functional changes in pain physiology [3].

This chapter aims to put the rehabilitation approaches available for pain patients into an overarching context. For didactic purposes, issues pertinent to assessment, treatment, and management are discussed in relation to acute, subacute, or chronic pain. Awareness of these issues can help the clinician to formulate a therapeutic strategy that takes into account the physiological, psychological, social, and physical factors relevant for the individual's pain problem. This strategy must be formulated in collaboration with the patient and should include patient empowerment and pain education [4, 5].

For the purpose of this chapter, pain associated with an immediate injury is defined as *acute pain* [6]. As healing takes place and the body recovers, we can speak of *subacute pain*. Some authors categorize pain as *chronic* or *persistent* when

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it has been present for more than 3–6 months, but it may be more appropriate to define chronic pain as pain which is present even though restoration of normal physiological function may be expected. For example, fracture of a bone is typically associated with acute pain. Within a few weeks in a cast, this pain can be expected to subside and we speak of subacute pain. However, if pain continues to be present several months after healing is expected to be complete, the pain is referred to as chronic.

Acute Pain

When pain is of recent onset, it is referred to as *acute* [6]. It is typically associated with injury, the development of pathology, or surgery. In neurophysiological terms, the pain perception is a direct consequence of the stimulation of free nerve endings and *nociceptors* at the peripheral terminals of sensory neurons of types C and Aδ. Nociceptors are high threshold receptors which normally respond only to tissue damage and excessive levels of stimulation. The nociceptive system plays an important role in protecting the body by providing a warning system of impending or actual damage. Pain resulting from nociceptive stimulation can thus be seen as *adaptive*: it stimulates behaviors that aid recovery, while inhibiting those that are likely to maintain or to aggravate the injury. Acute pain is therefore often classified as *nociceptive*.

Acute pain tends to show a relatively predictable and consistent response to mechanical testing. In line with selective tissue tensioning principles developed by Cyriax, the pain can be expected to be aggravated by tests, postures, and movements which put pressure or tension on the affected tissues [7]. Conversely, offloading the tissues can be expected to reduce the pain. Analgesic medication acting in the periphery including NSAIDs also relieves acute pain, as does any other intervention which reduces inflammation and nociceptive stimulation such as cold compresses or rest. As a consequence, the relationships between tissue injury, inflammation, nociception, and acute pain are relatively clear. Pain-relieving strategies at this stage are therefore more or less identical with strategies to reduce inflammation and to promote tissue healing. Clinicians can use pain levels to guide the selection, dosing, and progression of treatment.

Although acute pain perception is relatively predictable, it is important to remember that pain at any stage can be influenced positively or negatively by psychological mechanisms such as placebo or nocebo [8]. For example, there are documented cases of acute pain as a consequence of imagined injury [9] and acute injury without pain [10].

Subacute Pain

Once the inflammatory process transitions into tissue healing, pain is typically classed as *subacute*. This pain can still be viewed as nociceptive and adaptive, and its management is typically consistent with control of inflammation, promotion of

tissue healing, and early recovery of function. The focus of rehabilitation gradually shifts from injury management to recovery. A gradual progression towards full recovery is generally expected, unless the injury is of a permanent nature.

In addition to dealing with the physical aspects of recovery, therapists are advised to monitor for factors that are predictive of chronicity and to act on them if present. Research investigating persistence of pain or pain-related disability suggests that many of these factors are of a psychological or social nature, rather than physical [11]. In back pain, these were first described as *yellow flags* [12]. They include high levels of pain, nerve root pain, and specific spinal pathology, but also beliefs about the work-related nature of pain, psychological distress, and compensation issues [13]. A systematic review found high level evidence of psychological risk factors for persistence in neck and back pain, specifically passive coping, pain cognitions such as catastrophizing, beliefs that pain had to be avoided, poor self-perceived health, as well as distress, anxiety, and depression [11]. Psychological distress and depression were also identified as risk factors for chronicity of low back pain in another review [14]. For musculoskeletal pain in general, pain duration and severity, history of previous pain, and higher number of pain sites have been shown to be predictive of poor outcome [15]. Other factors include anxiety, depression, higher disability levels, and poor coping strategies (ibid).

Recommendations for patients at risk of developing persistent pain include creating a positive expectation of recovery, focusing on functional gain rather than pain reduction, teaching active coping strategies, and regular monitoring [12]. Any beliefs regarding the nature of the pain which are likely to engender counterproductive coping strategies (for example that a disc has literally slipped out from the spine) should be corrected and replaced with more helpful models of understanding [16]. Where occupational factors are identified, liaison with the employer may be advisable [12, 17]. Research strongly suggests that early occupational intervention is important [18]; for principles of workplace rehabilitation, refer to Gibson and Strong 2013 [19].

Patients may think that only diagnostic imaging techniques such as x-ray radiography or magnetic resonance imaging (MRI) can diagnose their pain. However, spinal MRI scans performed on asymptomatic healthy participants show a high rate of false positives [20]. Moreover, the contribution of diagnostic tests to patient reassurance has been shown to be either insignificant or transient [21] and may even lead to iatrogenesis when done in the acute or subacute phases [22, 23]. In back pain, MRI scans are likely to influence outcomes only when there is clinical evidence of a serious underlying condition [24]. Clear explanations and watchful waiting may be more beneficial to patients than arranging investigations routinely [21].

Chronic Pain

Pain which either outlasts the expected healing time or is present for more than 6 months is regarded as *chronic* or *persistent* [6]. In terms of musculoskeletal structures, it may be a feature of incomplete healing, ongoing dysfunction, or a

systemic condition such as fibromyalgia syndrome or rheumatoid arthritis. When pain is chronic, it no longer fulfills its protective function and becomes *maladaptive*: the presence and variation of the pain does not correspond well with what is happening in the tissues. As a consequence, acting on chronic pain does not help the physical problem in the same way that acting on acute or sub-acute pain may. Doing so is in fact likely to be counterproductive: long-term protection, withdrawal, and rest can lead to deconditioning of the body, with consequences of the ability to take part in work and social activities [25]. The emphasis of therapeutic strategies therefore shifts from treating physical injury to dealing with the pain as an entity in its own right. This includes addressing central sensitization; dealing with the patient's perception of pain, dysfunction, and recovery; contribution of significant others, work and other social factors; and overall function, health, and well-being. This shift must be shared and agreed by the patient, so that mutual expectations are aligned and realistic [5].

Neurophysiologically, persistent pain may be associated with enhanced pain processing in the central nervous system or *central sensitization*, i.e. the "increased responsiveness of nociceptive neurons in the central nervous system to their normal or sub-threshold afferent input" [26], or long-term potentiation of synaptic transmission strength [27]. In addition to barrages of nociceptive stimulation from the periphery, central sensitization may be driven or maintained by a reduction in descending inhibition, enhanced descending facilitation, and activation of astrocytes and glial cells in the dorsal horn [28–32].

Central sensitization has been implicated in several conditions associated with persistent pain, including arthritis (both rheumatoid and osteo), chronic fatigue syndrome, and fibromyalgia [33–35]. It may have a genetic component, so clinicians are advised to ask about the prevalence of pain problems in close relatives [30, 35]. The presence of other pain problems, both in the patient and in close relatives, may also hint at the presence of central sensitization [36, 37]. Events such as stressful circumstances or injuries may play a role in the expression of genetic predispositions; phenotypic makeup does not provide an excuse not to engage with the patient. Further confirmation of possible central sensitization can be obtained by objective testing of sensitivity to a variety of stimuli, both locally and at a distance to the main pain site [37, 38]. Severe increases in pain in response to gentle manual therapy approaches and exercises may also be suggestive [37]. Patients suspected of having a central component to their pain problem may benefit from adjuvant medications such as gabapentin, pregabalin, or tricyclic antidepressants [39].

The way the patient assesses their pain has consequences for their perception and management of that pain; so pain rehabilitation must include education to provide the patient with a helpful understanding of pain physiology [40, 41]. Central sensitization alters the relationship between stimulus and pain, sometimes in unpredictable ways. Pain physiology education can help patients to understand how their pain behaves, thus reducing its threat value. It supports the argument that pain does not necessarily require avoidance of activity [42]. Pain physiology education on its own has shown only small clinical effects [43–45], so it has to be combined with other approaches [46]. The type of education may be guided by the presence of

maladaptive or confusing pain cognitions and central sensitization [47]. When it is explained well, patients have the capacity to understand the neurophysiology of pain, a capacity which may be underestimated by clinicians [48]. However, for patients to accept the explanation, it is important that it addresses specific concerns that they may have [49].

Important aims of a rehabilitation program include reducing fear of activity, safe and graded increases in activity, and return to meaningful activity [16]. Combined with pain education, this has the potential to reduce the threat value that the pain has for the patient [50]. Strategies may include setting goals and 'pacing' of activities in order to interrupt cycles of overactivity and under-activity by making activity less dependent on pain levels [25]. From the point of view of chronic pain physiology, rehabilitation aims to reduce drivers of central sensitization while maximizing descending inhibition.

For the evaluation of progress, the additional use of validated performance tests of tasks such as the ability to walk, stand up from sitting, stair climbing, and reaching is recommended [51]. A number of validated self-report questionnaires is available to assess pain-related psychological issues such as fear-avoidance, catastrophizing, and pain beliefs [52]. Rehabilitation can incorporate, or be practiced in conjunction with, psychological approaches [25, 53]. Psychologically informed rehabilitation is particularly relevant if the pain has led to disability, anxiety, depression, or social isolation [54, 55]. The following section gives an overview of the most common psychological approaches in current use.

Cognitive-behavioral therapy (CBT) has been used in the management of chronic pain since the 1980s [56]. There is a wide variety of cognitive-behavioral approaches, but all aim to act on thoughts in order to influence emotions and behaviors [57]. With regard to pain, CBT is predicated on the idea that one's cognitions influence pain-related feelings and behaviors [58]. For example, a patient's interpretation of the origin of the pain, as well as their ability to accept the pain and to cope with it, has consequences for their emotional well-being and choice of coping strategies. CBT has been shown to be beneficial for pain-related mood, catastrophic thinking, and disability [59].

The last 20 years have seen a gradual rise of the use of approaches based on *mindfulness*, a technique that has its roots in Buddhist meditation, but which does not require that context [60]. At the heart of mindfulness practice is paying attention to, and accepting, what can be perceived in the present moment (ibid). In this context, the term *acceptance* does not refer to 'giving up' or undergoing everything passively, but rather to giving up the struggle against things that cannot be changed such as persistent pain [56]. Thoughts about issues in the past, present, or future are acknowledged but not adhered to, as are any feelings of attachment or aversion to whatever is being perceived [60, 61]. This can help to uncouple pain from associated suffering, to diminish the drive to attempt to escape from the pain and to reduce blame and resentment regarding the origin of the pain. Although mindfulness practiced as an intervention in its own right has shown limited clinical benefit [62–64], it has become a common element of pain management programs [65].

Acceptance and commitment therapy (*ACT*, pronounced as 'act') is strongly linked with mindfulness. At the centre of ACT is the concept of psychological flexibility, such as one's ability to change behavior according to one's personal values and goals in life [65]. In the management of persistent pain, this includes evaluating whether the struggle against pain may be moving one away from one's values and goals and investigating strategies which may be more helpful in this regard [66]. ACT has been shown to be a viable alternative to CBT [67], although there is disagreement over as to the extent of it being a separate approach [68, 69].

Conclusion

This chapter has provided a model for the assessment, treatment, and management of the pain patient. This model incorporates numerous factors including the physical, psychological, and social. It also draws on the way the sensory nervous system may change its function in response to pain and highlights the importance of patient involvement and pain education. Subsequent chapters will provide more detail about individual approaches.

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Resources

Ronald Melzack and Patrick Wall were instrumental in developing pain into a field in its own right. Their two classic texts remain among some of the most accessible introductions to the field:

Melzack R, Wall P. The challenge of pain. London: Penguin Books; 1996.

Wall P. Pain—the science of suffering. London: Phoenix; 1999.

The May 2011 issue of the journal Physical Therapy, vol. 9, issue 5, *was dedicated to psychologically informed rehabilitation of back pain and has contributions by experts from around the world*.

Every two years, the International Association for the Study of Pain (IASP) publishes the refresher course transcripts from its world conference. These provide a review of current research and practice in the pain field. The latest edition is Raja S, Sommer C, editors. Pain 2014. Washington: IASP Press, 2014.

van Griensven H, Strong J, Unruh A, editors. Pain. A textbook for healthcare practitioners. Edinburgh: Churchill Livingstone, 2013. Brings together chapters by experts from around the globe, covering the many facets of pain and its rehabilitation.

Chapter 23
Manual Therapy and Pain in the Rehabilitation Patient

Alison E. Mulcahy

Introduction to Manual Therapy

Manual therapy techniques are skilled hand movements intended to improve tissue extensibility, increase range of motion, induce relaxation, mobilize or manipulate soft tissue and joints, modulate pain, and reduce soft tissue swelling, inflammation, or restriction. Manual therapy began as manipulative therapy and has evolved through the years with the influence of many professionals. Manual therapy that PTs use now is a combination of techniques designed to affect muscles, ligaments, tendons, and connective tissue, in order to improve the impairment and functional limitations of the patient. These techniques include the following:

- massage
- gentle joint mobilizations
- thrust manipulation
- soft tissue mobilization
- passive range of motion
- stretching [1, 2]

Manipulative therapy can be dated back to Hippocrates, with reference to spinal manipulation, and likely even before that time. Spinal manipulation by bone setters was popular among the general population and went in and out of favor with the medical profession, depending on current medical concepts of the time. In the 1800s, physicians and newly organized professional chiropractors practiced and taught the notion that one needs to maintain a normal musculoskeletal system to maintain health. They believed that vertebral alignment or mal-alignment related to function or dysfunction.

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Chiropractic care became popular with the end of WWII, and then years later in 1958, physical therapy grew, and this growth threatened chiropractors.

Physical therapy began in the early twentieth century, with therapists labeled as "reconstruction aides" during World War I. This term later evolved into professionalized "physical therapists", with significant help from Mary McMillan. By the 1950s, PTs from around the world were becoming more prominent in their teachings. Physicians and PTs continued to promote manual and manipulative therapy, with major influences from many professionals, including the following:

- James Cyriax: He focused on the differential diagnosis of pathology with selective tissue tension testing. He believed that when the painful tissue is taut, it recreates the patient's pain; when the tissue is relaxed or on slack, the symptom decreases [2].
- Freddy Kaltenborn: He believed that joint restrictions and soft tissue changes should be evaluated and that treatment should include glide and traction mobilizations.
- Robin McKenzie: He believed in directional preference to treat lumbar pain and discussed contraindications to lumbar manipulative therapy.
- Geoff Maitland: He felt that assessment and treatment of joints should include oscillatory movements, instead of only manipulation.
- Brian Mulligan: He believed that mobilization with movement facilitates joint mobility and function.
- Stanley Paris: He helped to disseminate information about manipulative therapy and taught Orthopedic Manual Therapy (OMT); he felt that if joint mobility impairments are corrected, pain will thereby decrease [3].

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- Manual techniques may include passive stretching, soft tissue mobilization, joint mobilization, or manipulation.
  - Passive stretching must be sustained for a period of time, in order to allow the muscle to restructure itself and to settle into the lengthened position, which is its new resting position.
  - Soft tissue mobilization improves tissue mobility by decreasing adhesions. It may include cross friction massage to scar tissue, in order to increase mobility. Trigger point release to a muscle trigger point and myofascial release can also be employed [4].
  - Joint mobilization, in low-grade oscillatory motions, is used for immediate pain relief, whereas sustained mobilization, with larger amplitude oscillations, may be used for joint restriction that causes pain.
  - Thrust manipulation can be used to improve joint mobility when mobilization is not effective and when no contraindications to manipulation exist [3].

- Manual therapy techniques aim for tissue deformation in an effort to elongate connective tissue. In order for plastic deformation to occur, which is a permanent change, micro-failure must occur first. Micro-failure occurs when fibers and/or fiber bundles break due to sufficient tensile load placed on the fiber, causing it to break. When the load is removed, the fibers recoil and a new connective tissue length is established [5]. When microfailure does not occur, but new length occurs, this is called creep, which is a temporary increase in fiber length.
- Pain management via manual therapy may occur due to a new connective tissue resting length, or theoretically due to pain inhibitory mechanisms that become activated during mobilizations or manipulation [3, 5].

Manual Therapy Recommendations

1. Mobilization with movement is recommended for a patient with painful shoulder elevation and shoulder impingement syndrome [6].
2. Manual therapy, in addition to exercise therapy, is recommended for a patient with mechanical neck disorder, not manual therapy alone [7].

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Chapter 24
Modalities and Pain in the Rehabilitation Patient

Alison E. Mulcahy

Introduction to Modalities: Therapeutic Electrophysical Agents

Modalities, including therapeutic electrophysical agents (EPAs), are a group of agents used to supply forms of energy to the body. EPAs may be used in combination with other techniques, including manual therapy and exercise, to treat patients with impairments related to soft tissue pathology. This section will discuss a variety of EPAs used in the physical therapy clinic. It is beyond the scope of this text to discuss all types of EPA used, and therefore, focus will be on more commonly used agents for pain management. It should be noted that there are indications and contraindications to the EPAs that are not discussed in this section and are beyond the scope of this text. It is recommended that the clinician research specific contraindications prior to initiating any treatment with therapeutic electrophysical agents [1].

Iontophoresis

Iontophoresis is a type of modality, in which electrical energy transfers a medication through the skin, to an affected painful area [1].

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- Iontophoresis works by placing a therapeutic substance, which is under an electrode with similar polarity such that electrical energy pushes the substance through the skin.
- Medication or other non-medication substances are used. Some examples of medications for analgesic or anti-inflammatory effect include the local anesthetic lidocaine and the corticosteroid dexamethasone.
- This technique assists with pain management in acute inflammatory processes of superficial structures. Iontophoresis allows the medication to be directed at the desired site without systemic side effects [1].

Transcutaneous Electrical Nerve Stimulation

Transcutaneous electrical nerve stimulation (TENS) is used for pain modulation, in which electrodes are placed on the skin and an electrical current is then sent through the skin to the afferent nerves, which then override the painful sensation [1].

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- TENS can be used at sensory, motor, or noxious levels and is named based on which nerve fibers are stimulated.
  - Sensory level TENS: Stimulates A-β nerve fibers. The patient reports feeling "pins and needles" sensation, with no muscle contraction.
  - Motor level TENS: Stimulates A-β nerve fibers and motor fibers due to an increase in amplitude and duration. The patient reports feeling "pins and needles" and can feel, palpate, and even see a concomitant muscle contraction.
  - Noxious level TENS: Stimulates A-β, motor, A-δ, and C fibers. The patient reports feeling the stimulation, which occurs just below the patient's level of pain tolerance threshold, and a muscle contraction is visible [1].
- TENS works to control pain via the gate control theory and release of endogenous opiates.
  - The electrical current from the TENS unit stimulates sensory peripheral nerves A-β, which enter at the same nerve root level as the nociceptor A-δ and C fibers. The evoked activity of the A-β fibers inhibits the transmission of the pain at the spinal cord level, reaching the subcortical and cortical levels. Therefore, the pain message reaching the cortex is decreased and the patient feels less pain.

  - Pain is also modulated by endogenous opiate release; the stimulation of the A-β nerve fibers opens the spinal gate, which triggers a release of endogenous opiates, endorphins. With a negative feedback loop, it closes the gate by releasing more endorphins [1].

Ultrasound

Ultrasound (US) is acoustic or mechanical energy that travels through a medium of frequencies, above the threshold of human hearing. There are three types of US therapy: conventional US, low-intensity pulsed US (LIPUS), and MIST therapy. LIPUS is used for bone healing; MIST therapy is used for wound cleaning and debridement of wounds; therefore, these two therapies are not to be discussed in this section [1].

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- Conventional US is used for soft tissue pathologies and has both thermal and mechanical (non-thermal) effects.
  - Thermal effects for tissue healing occur when the acoustic energy is absorbed in the soft tissue, creating vibration via a cycle of compression and rarefaction. The more forceful the vibration, the more heat that is generated.
  - Mechanical effects occur due to acoustic cavitation, the phenomenon of micro-bubbles forming in the fluids and surrounding soft tissue when the acoustic energy from ultrasound is absorbed. The micro-bubbles will oscillate when the acoustic energy is sustained. US creates stable cavitation, which triggers micro-streaming, a flow of fluid in the area of micro-bubbles; this allows ions in the tissue to flow in and out in order to promote healing [1].
- To address pain, thermal effects can increase temperature in tissue </=5 cm deep, and mechanical effects may promote an anti-inflammatory effect by moving fluid [1, 2].

Cryotherapy

Cryotherapy is the use of cold application to treat an injury. Cryotherapy is used during acute or sub-acute phases of injury, to regulate the healing process [1].

Pathophysiology, Techniques, and Pain Management

- Cold therapy works by superficial application of the cold item, which then draws the heat from the skin. Cold is not transferred to the skin, because heat is always transferred from high heat to low heat.
- The amount of subcutaneous tissue involved has an effect on heat and cold transfer; the more subcutaneous the tissue, the more heat is retained.
- Cryotherapy assists pain relief through decreasing subcutaneous and intramuscular temperatures by 17 and 7 °C, respectively [3]. By decreasing the local tissue temperature, an analgesic and anti-inflammatory effect occurs, which helps to regulate the normal healing process [1].

Dry Needling

Dry needling, which is often referred to as "trigger point dry needling", is a type of treatment performed by PTs in many US States. PTs can perform dry needling after he/she completes continuing education courses to become certified. Solid, fusiform needles penetrate the skin to affect a muscle trigger point in order to reduce pain.

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- Dry needling helps to regulate the chemical response within the muscle caused by injury to the muscle. Regulating the chemical response of tissue allows the tissue to normalize and pain decreases.
- A PT examines and evaluates a patient for trigger point referral pain. A solid needle is inserted into the muscle; it may be left in the muscle for a period of time (e.g. 30 min), or it may be moved (pistoned) in and out of the muscle to stimulate the fibers. After the procedure, the patient may perform exercises and/or stretches immediately after treatment and frequently that day. He/she may then perform manual therapy.
- Dry needling helps to alleviate pain by increasing blood flow to the local area, decreasing the amount of built-up toxins that make up the trigger point [4].

Spinal Traction

Spinal traction is a technique used to increase the intervertebral spaces in the cervical or lumbar spine in order to alleviate pain [1].

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- Traction includes manual or mechanical traction. Common ways to perform mechanical traction utilize pneumatic, weighted, or motorized devices.
  - Pneumatic devices and weight devices are common for cervical spine treatment.

– Pneumatic device: An air cushion is inflated to increase intervertebral disc space, and deflated again at the end of treatment.
– Weighted device: A unit is suspended over a door with a counter weight, usually water, on one end and the patient's head is in a sling on the other end
  – A motorized device can be used for lumbar or cervical traction.

– Lumbar spine: The patient's lower half of the body is secured on a specific treatment table using a harness and cable connected to the machine.
– Cervical spine: The patient's head is secured in a unit using Velcro straps and a cable is connected to the machine.

The machine is programmed to pull for a specific amount of time, as intermittent or sustained, and pulls at a specific weight, which is dependent upon body weight and type of traction [1].

- The proposed benefits of using spinal traction for pain relief include elongating the spine to decompress the joints and intervertebral discs, which in return will result in widening of the foramina, decompressing nerve roots, and decreasing joint adhesions.

Moist Heat

Moist heat is a type of superficial thermotherapy. A hot pack is used for symptom relief by warming up the soft tissues.

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- Heat is transferred via conduction between the hot pack and the skin. Skin temperatures can increase to 114.4 °F at 6 min of application time [5].
- A hot pack is stored at 70–76 °C (158–168 °F) in a hydrocollator. For use, it is wrapped in layers of cloth to act as a protective barrier between the patient's skin and the hot pack [1].
- Moist heat increases local skin and soft tissue temperature, causing vasodilation of blood vessels to bring blood flow to the area, which facilitates wound healing and stimulates thermoreceptors, which encourage a thermal sensation and lessens pain [1, 6].

Modalities: Recommendations

1. Iontophoresis with Dexamethasone is recommended for plantar fasciitis pain [7].
2. Cryotherapy is recommended for pain relief [8].
3. Dry needling is recommended for plantar heel pain [9].
4. Moist heat after exercise is recommended to reduce delayed onset muscle soreness [10].
5. TENS is not recommended for chronic low back pain [11].
6. Therapeutic ultrasound is not recommended for chronic low back pain [12].
7. Lumbar traction is not recommended for chronic low back pain [13, 14].
8. Cervical traction is not recommended for cervical radiculopathy [15].

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Chapter 25
Occupational Therapy and Pain in the Rehabilitation Patient

Janet L. Rivard Michaud and Jill Kauders Levine

Abbreviations

OT	Occupational therapy
OTs	Occupational therapists
OTAs	Occupational Therapy Assistants
ADLs	Activities of daily living
HPI	History of present illness
PMH	Past medical history
PSH	Past surgical history
ROM	Range of motion
MMT	Manual muscle test
VAS	Visual Analog Scale
UEs	Upper extremities
LEs	Lower extremities
IADLs	Instrumental (higher level) activities of daily living
AROM	Active range of motion
AAROM	Active assistive range of motion
PROM	Passive range of motion
A/AA/PROM	active, active assistive and passive range of motion
PREs	Progressive resistive exercises
RSD	Reflex sympathetic dystrophy, now known as complex regional pain syndrome
HEP	Home Exercise Program
TENS	Transcutaneous electrical nerve stimulation

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MLD	Manual lymphatic drainage
CTS	Carpal Tunnel syndrome
TOS	Thoracic outlet syndrome
CRPS	Complex regional pain syndrome

What Is Occupational Therapy? (OT)

Occupational therapy is the art and science of daily living. Occupational therapists assist people of all ages to be as independent as possible in the things they need or want to do every day. This may mean developing new skills, remediating/rehabilitating past skills, adapting with the use of alternative techniques or equipment, or in some cases transitioning to new levels of assistance or activity choices. Prevention and wellness are also important aspects of occupational therapy. A satisfying quality of life and sense of empowerment are always components of how occupational therapists define independence in daily function [1, 2].

Who Provides Occupational Therapy Services?

Occupational therapy may be provided by occupational therapists (OTs) or occupational therapy assistants (OTAs). Occupational therapy students may also provide direct care under supervision during their fieldwork training.

Occupational therapists function independently and perform all elements of the OT evaluation and treatment. They are responsible for supervision of all care delivered by OT assistants. Occupational therapy assistants deliver services based on the assessment completed by the occupational therapist, under their supervision, and always in collaboration.

Occupational therapy is provided to individuals, groups, and populations in a wide variety of settings including hospitals (inpatient, acute, rehabilitation, and psychiatric), nursing homes, assisted living, group homes, day programs, schools, home-care, hospices, community mental health centers, work programs, industry, and wellness centers as well as private offices, clinics, and research centers [2].

Occupational Therapy's Approach to Pain

Many individuals receiving occupational therapy services have complaints of pain. For some, this is acute and short-lived, responding quickly to therapy. For others, it is of greater duration often with an exacerbation-reduction quality. In both

situations, pain can limit therapeutic outcomes, disrupt daily functioning, and decrease general wellness. Since it permeates one's life, avoidance of pain can become the primary life goal and area of focus.

Pain is a subjective and highly individualized experience. Individuals develop varying degrees of tolerance based on their unique physiology, functional demands, life experiences, coping abilities, and support networks. The subjectivity of pain is due also to its highly complex, protective nature, which remains relatively poorly understood. Two implications of pain are clear. First, the presence of pain is a protective warning signal to the person that "something is wrong", although current medical knowledge and technology may not be able to identify a problem source. Because of this, all pain complaints must be respected and validated for their meaning and impact on the individual person. Second, pain has both components and significant effects that are physical, psychosocial, and functional. For best results, each of these factors must be evaluated and addressed.

Assisting people with pain presents both a challenge and an opportunity to occupational therapists. The usual challenge of finding the best, most effective combination of therapeutic techniques often feels more imperative when pain is present. The pervasive effect of pain on an individual's overall life demands a comprehensive and holistic approach that incorporates both physical and psychosocial interventions. As such, pain complaints and those people with them require special consideration.

General guidelines and areas to consider are offered in the following outline. Philosophically, these considerations are holistic and systems-oriented, incorporating the following theoretical bases: Rehabilitation Model, Model of Human Occupation [3], Biomechanical Model, Bio-psychosocial Theory, Behavioral Medicine techniques, Learning Theory, Osteopathic Medical traditions, Self-Management approaches, and Relational Theory [4].

Acute and chronic pain can be caused by both organic and non-organic forces, which are often not completely understood by the medical community. Pain is experienced differently by each individual and therefore requires an individualized approach to treatment planning and intervention. Whenever possible, a multidisciplinary team approach is recommended to address this complex syndrome.

The purpose of an occupational therapy program for pain is to ameliorate the effects of pain by teaching self-management techniques and by providing direct therapies. This approach is unique. Unlike many pain programs that primarily focus on pain management, with the expectation that pain will be a lifelong concern, this approach also provides for direct treatment for pain reduction. The overall goal of this combined focus is functional independence and an improved quality of life.

Functional outcomes are determinants of successful therapy. General goals include independence or modified independence in activities of daily living (ADLs), home care, work/school, leisure, socialization, stress management, and self-management. It is expected that pain will be eliminated or reduced to a level that can be self-managed and does not interfere substantially with function.

Evaluation Areas [2, 6]

Occupational therapy intervention begins with a comprehensive, individualized evaluation in collaboration with each client. Establishing a strong therapeutic relationship and setting the stage for working as a team are critical parts of the evaluation and subsequent therapy process. The specific combination and extent of areas evaluated are at the discretion of the primary therapist per individual needs and referral data. These may include, but are not limited to the following:

- History of present illness (HPI)
- Past medical history (PMH)/past surgical history(PSH)/allergies
- Posture/alignment
- Range of motion (ROM)
- Strength: pain level may limit the extent of formal manual muscle test (MMT)
- Special tests/provocative maneuvers as needed
- Soft tissue assessment including a neuro-musculoskeletal and fascial approach
- Integumentary system including scars, skin grafts, incisions, wounds, edema, etc.
- Sensation
- Coordination
- Functional mobility
- Balance
- Pain assessment and history

    1. Specific pain locations throughout the body
    2. Quality of pain
    3. Intensity of pain 0–10 scale, visual analog scale (VAS), Wong/Baker Face Scale [7], FLACC Scale [8]
    4. Duration of pain complaints
    5. Frequency of pain complaints
    6. What triggers pain?
    7. What increases pain?
    8. What decreases pain?

- Cognition/perception as needed
- Psychosocial skills and status with emphasis on coping skills, social supports, communication of needs, life roles (i.e. parent, student, worker, friend), and use of time (many clients have lost the structure of work due to pain and have no leisure pursuits)
- Functional skills/ADLs: occupational therapists typically assess the following areas of daily living:

    1. Self-care (bathing, dressing, hygiene, oral care, hair care, medication management)
    2. Home care (cooking, cleaning, laundry, safety procedures, financial management, phone use, etc.)

3. Child care, elder care, pet care
4. Community access (transportation, accessibility needs, use of community resources, communication with agencies/providers)
5. Work/school
6. Leisure
7. Socialization
8. Time management
9. Sleep/work-rest balance in daily routines
10. Some considerations:

- Consider activities that require static or moving but unsupported upper extremities (UEs), repetitive movements, awkward, or prolonged postures.
- Consider that an individual may continue to pursue all basic ADLs and higher level tasks (IADLs), but with difficulty such as pain, increased effort, increased time, or compensatory patterns that promote dysfunction in another area.
- Vocational skills, worksite assessments, and task analysis or simulation of specific activities, which cause pain, may allow for better assessment of pain related to responsibilities at work.

Potential Treatment Modalities [1, 2, 6]

This is not a comprehensive list. The combination and extent of these and other treatment techniques are at the discretion of the primary therapist per individual needs. Please note that not all occupational therapy practitioners will utilize all of the treatment options below. These may differ based on philosophical approaches or types of advanced training.

Functional Activities [1, 2, 6, 9]

The hallmark of occupational therapy is the use of *occupations* (purposeful daily activities that have value and meaning) as both treatment methods and outcomes. Therapy often consists of actual self-care, home, school, work, leisure, or social activities that are chosen relative to each individual's values, goals, and life-roles. These occupations are used to improve performance, to learn new skills, or to develop adaptive approaches. Adaptive equipment may also be used for better levels of success in these important daily tasks.

Most people don't seek therapy purely because of pain, but because their symptoms have begun to interfere with their lives. Clients typically define the interference with their lives by the activities they are unable to do, unable to do well, or only able to do with pain or other symptoms.

Occupational Therapists use task analysis to determine what limits occupational performance and then choose functional activities, as well as any of the other treatment methods listed to promote what is known as the "just right challenge" in therapy, combining both the stretch of challenge and the opportunity for success. Using purposeful activities that hold meaning and value for an individual is a powerful motivator in therapy. It is an ideal way to help all people and especially people with pain to see what they can do and how this may improve over time.

Manual Therapy Techniques [2, 6, 18]

These are hands-on therapy techniques that address specific systems of the body, individually or in combination, to reduce pain and to restore optimal mobility in each system:

Joint mobilization
Muscle energy techniques [10]
Trigger point release [11, 12]
Stretching, passive range of motion (PROM)
Soft tissue mobilization, massage
Strain-counterstrain techniques [13, 14]
Nerve gliding
Fascial mobilization
CranioSacral therapy [15]
Visceral manipulation [16].
Manual lymphatic drainage/lymphatic drainage therapy [17]

Therapeutic Exercise/Neuromuscular Re-education

The natural state of the body is to be in motion. Occupational therapy uses therapeutic exercise and movement in a graded manner, as the individual's condition allows, to promote optimal healthy movement in the body and to prevent tissue shortening, which may add to pain. Special attention is given to promoting normalized movement patterns whenever possible. Some intervention examples include the following:

active/active assistive/passive range of motion (A/AA/PROM)
Stretching
Strengthening

- Isometrics
- Progressive resistance exercises (PREs) as tolerated-weights, theraband, etc.
- Work simulation

Plyometrics
Desensitization
Mirror therapy [19]

RSD (reflex sympathetic dystrophy) Stress Loading Protocol [20]
Aquatic therapy
Home exercise program (HEP)

Modalities [21]

Occupational therapy practitioners may use a variety of modalities, such as those listed below to help prepare the body for functional activity by decreasing pain, edema, and muscle spasms, and by normalizing tissue mobility:

Heat
Cold
Ice massage
Ultrasound
Electrical stimulation
Iontophoresis
Biofeedback
Cold laser
Fluidotherapy
Paraffin
Contrast baths
TENS
Kinesio Tape [22]

Wound Care/Scar Management [23]

This may include cleansing, debridement, appropriate dressing changes, monitoring of wound closure, and patient education regarding home management of the wound. Scar management may include scar massage, desensitization, fascial mobilization, and monitoring for raising or keloid formation. If the latter two are present, they may also be managed with silicone scar pads and fitting for compression garments as needed.

Orthotics/Positioning

Orthotics can be used for a variety of reasons with a person who is experiencing pain. In general, an orthotic is used to rest a joint or muscle, to provide support or protection to healing tissue, or to serve as a reminder to avoid positions of strain/stress. Orthotics can be used during functional activities, at night while sleeping, or a combination of the two. OT providers are trained to fabricate custom-made orthotics as needed, in addition to issuing commercially made items.

Education about positioning can help a person who is experiencing pain. Teaching about neutral postures and proper ergonomics during functional tasks both at work and at home, as well as during sleep, may be very helpful in decreasing pain or preventing exacerbations.

Self-Management

Occupational therapy's primary goal is to promote independence in everyday function. Direct therapies to reduce or to eliminate pain are one piece of this process, but both may require substantial time for success. The second and concurrent method is to develop self-help skills to manage pain in the interim. Occupational therapy practitioners work with each client to develop an individualized plan to manage pain and to assume a primary role in their health and wellness. Examples of self-management techniques, which may be incorporated into OT treatment, include the following:

Pain scale (i.e. 0–10 max)
Informal coping skills rating scale 9 (i.e. 0–10 best)
Stress management/coping skills
Relaxation techniques
Communication skills, such as expression of needs and limit setting
Goal-setting
Problem-solving and planning
Time management
Leisure skills
Work/school/volunteer skills
Compensatory skills in the areas above

- Work amplification
- Worksite adaptation
- Energy conservation
- Postural re-education
- Body mechanics
- Ergonomics
- Cognitive/perceptual retraining
- Pain behavior modification
- Training in the use of adaptive equipment

Case Study: Acute Wrist Injury

Jeff was a 45 year old male with a PMH consisting of hypertension and cardiomyopathy, as well as PSH of a double bypass with valve replacement. He tripped and fell onto his left hand causing significant wrist pain and immediate edema. He went

to the emergency room. An x-ray did not reveal any fracture; however, as he reported his pain to be a 9/10, and there was significant edema noted over his radial wrist, he was placed in a thumb-spica cast. He followed up one week later with the hand surgeon. A repeat X-ray continued to be negative for fracture; therefore, he was sent to occupational therapy for evaluation. After evaluation, it was noted that Jeff presented with continued pain complaints at his radial and dorsal wrist, decreased ROM, and poor functional strength of his wrist and hand. In addition, his wrist extensor muscles were tight and he presented with significant bruising and edema over his dorsal and radial wrist. He was instructed in gentle active and active assistive ROM exercises. Then, a tubigrip compression sleeve was applied to help control the edema. A volar wrist splint was fabricated for use as a support to help rest his wrist between ROM exercises.

He was evaluated for OT treatment twice weekly. Treatment consisted of soft tissue mobilization, including MLD (manual lymphatic drainage) and fascial mobilization to his forearm, gentle P/AA/AROM, functional grasping of corn particles and rice, and translation of marbles and coins into and out of his hand.

After 2 weeks, his thumb pain continued without improvement. After discussion with the hand surgeon, another X-ray was taken. Once again, no fracture was noted, despite significant pain at his scaphoid. Therefore, a new thumb-spica splint was fabricated to help better support the scaphoid and to rest his thumb abductors/extensors and wrist extensors. Jeff's pain improved slightly over the following 2 weeks, but continued to be significant, especially with active use of his wrist and thumb. Iontophoresis with dexamethasone was initiated at his first dorsal compartment with only minimal improvement.

Then, a CT scan of his wrist and scaphoid was ordered and, once again, no fracture was found. The results of the CT scan were reviewed with the patient, and after further evaluation of his tendons, crepitus was noted at the intersection of his thumb abductors and wrist extensors, which was indicative of intersection syndrome. A cortisone injection was given by his hand surgeon and pain finally began to slowly improve. OT treatment was slowly transitioned to include functional strengthening including wrist exercises, hand strengthening with theraputty, clothes pins of different resistances, lifting of different sized pots and pans, pouring from a pitcher into cups, and simulating lifting and diapering a baby as he had a 5-month old son at home. Jeff was eventually able to transition away from the splint and was discharged from OT treatment after 6 weeks. He was advised to continue with his HEP until his left upper extremity strength normalized.

Case Study: Low Back Pain and Carpal Tunnel Syndrome in Pregnancy

Kathy was a 34 year old woman who presented to occupational therapy pregnant with her second child and in her 26th week of gestation. Her first pregnancy was complicated by back pain and sciatica, which was significant enough at times to

require her to crawl instead of walk. She also had back labor during delivery. Normally very active and physically fit, she worked as a dog groomer, typically lifting up to 100 lb. and repetitively using her upper extremities (UEs) throughout her work day. This was in addition to interacting with her animal clients and their human families. Her baseline was a very high pain tolerance and minimization of symptoms, with a functional style of pushing herself through all necessary tasks. She was fully independent with basic self-care and all life roles until her pregnancy progressed.

In her second pregnancy, she rated the intensity of her back pain at 6/10 on the Visual Analog Scale (VAS). She also had symptoms of carpal tunnel syndrome (CTS) in her left dominant hand, as well as some lower extremity (LE) swelling from being on her feet all day at work. Spider vein varicosities were present and painful at times. Scissoring, brushing, and washing of dogs all increased her CTS symptoms of pain and numbness, especially in her left hand, though bilaterally at times. Lifting exacerbated her back pain and sciatica. She was also responsible for providing all before and after school care for her 8 year-old daughter. Her husband commuted long hours to work, leaving before 7 a.m. and returning after 7 p.m. in the evening, which limited his ability to help with home and child care tasks. Occupational Therapy consisted of the following:

- Education regarding joint protection, ergonomics, and adaptive methods to perform her job and home care responsibilities with the least amount of strain.
- Splinting for CTS at night and rest during the day when able; kinesio tape was applied to her wrist for support and to encourage lymphatic flow when unable to use the splint.
- Recommendation was made for support stockings to be worn during the day to promote optimal LE circulation and to prevent edema.
- Baby hugger abdominal support was introduced as an option for later in pregnancy, but ultimately was not needed.
- A scissor style with easier grip and action was recommended. She was encouraged to use either a scissor or comb in her hand at one time, instead of using both, whenever possible. Unfortunately, while this lessened hand strain it also decreased her usual efficiency.
- Lifting continued, but was performed at reduced levels. The use of dog ramps and assistance to lifting was included as pregnancy progressed, in an effort to decrease back strain.
- Back pain was directly addressed by manual therapy, including application of muscle energy techniques to her pelvis and sacrum; strain-counterstrain technique was employed for strain of her bilateral piriformis, adductor, hamstring, gluteal and quadriceps muscles; CranioSacral therapy techniques were employed to address neuro-fascial restriction patterns. These methods were used to improve alignment of her pelvis and sacrum, as well as to reduce muscle shortening to eliminate sciatica. Pregnancy-related ligamentous laxity did mandate recurrent treatment, while self-help techniques were taught for use between OT sessions.

- Nerve gliding, unwinding, ROM, and soft tissue mobilization were applied to her bilateral forearms, hands, and wrists to minimize CTS symptoms. Cold water plunges were also used to reduce inflammation.
- A home program was developed including self-help techniques, gentle functional lumbar stabilization exercises in supine position (and quadruped when possible to reduce pressure from fetal position and size), stretching to LEs and UEs, as well as cat and camel stretching when able. Stretches to facilitate delivery position were included. Whenever possible, meditation and daily time for herself were incorporated to promote a better work/rest balance.
- Education regarding her diagnoses, ergonomics, self-help strategies, work-life balance, and adaptive methods were ongoing throughout OT.

Response to OT Intervention

Kathy was able to walk throughout her pregnancy and was able to continue with her business actively. She hired assistants only at the end of her pregnancy, to help with heavier tasks of washing and lifting dogs. She continued to do the actual grooming herself. Her pain levels decreased to 0–3/10 on the VAS and she used self-help techniques to manage these symptoms. CTS symptoms decreased to a manageable level and resolved shortly after delivery, as did LE swelling. She continued her HEP after delivery and throughout the time she was nursing. The duration of therapy was from weeks 26 to 40 of her pregnancy, and one follow-up visit 3 weeks after delivery to facilitate post-partum optimal alignment and to upgrade her HEP.

Case Study: Thoracic Outlet Syndrome (TOS) Progressing to Complex Regional Pain Syndrome (CRPS)

Melanie was a 38 year old right-handed woman. She was married, the mother of two young sons, and worked as an event manager. She presented to occupational therapy with a complicated medical history, which culminated with a diagnosis of complex regional pain syndrome (CRPS) affecting her right upper extremity.

Her earliest symptom began during her senior year of high school with right shoulder pain limiting her role as an outstanding varsity shortstop. She managed her pain with over-the-counter mentholated rubs and she continued to play, but lost her Allstate berth. Her symptoms resolved fully over the summer in recreational play. She proceeded to participate in varsity softball during college, with minimal difficulty until her junior year, during which time she injured herself in an effort at a poorly designed swinging drill. Her symptoms were primarily in the area of coordination, such as throwing a ball 20 feet over the first baseman's head. She described feeling as though her arm would fly off when this occurred. She experienced frustra-

tion with her lack of accuracy in power throwing. The need to switch her position to first base led her to seek evaluation at a local hospital's orthopedic clinic.

As a college athlete with overall excellent fitness, little was detected on initial consult, despite higher level complaints of lessened strength and coordination. Over a period of 1 and1/2 years, she was finally diagnosed with an impingement syndrome. No therapy was ordered and she continued with her usual participation in both college and softball, but with a shared starting position. She experienced mild exertion-related pain of 3/10 or less on the VAS. After graduation, she underwent a partial excision of her right coraco-acromial ligament. Pain fully resolved, but she still complained of altered coordination, diminished accuracy with throwing, and she developed a compensatory carpal tunnel syndrome while scooping ice cream during a summer job. Post-college work was as a manager in the entertainment field and she progressed well, but with decreasing pursuit of her valued athletic role due to frustration by her changed performance.

At the age of 32, she sustained a new injury while shoveling snow rapidly and tossing the heavy snow upward and to her right side. After many repetitions, sudden pain began in her right arm and upper chest and increased to 10/10, which necessitated emergency room intervention. She tried numerous medications, including analgesics and muscle relaxants; however, to little effect. Her pain remained high enough to induce vomiting. She then experienced changes in sensation with parasthesias present throughout her hand. Additionally, her hand got very cold.

She was seen by a hand surgeon who then followed her. Over time, her right thumb became less functional. She participated in intermittent occupational therapy to address her hand symptoms. Treatment included fluidotherapy, edema management using coban wrap, splinting, manual therapy, and a graded exercise program. She was consistent with all components of her home program. Eventually, it was noticed that atrophy was occurring in her hand in the interossei and both thenar and hypothenar eminences. It became difficult for her to avoid cradling her arm as pain remained at severely high levels of 9/10 on the VAS. Her right hand was also observed to turn blue when transitioning from supine to sit.

Eventually, she required fusion of her right thumb due to the level of atrophy. OT intervention brought her to a level of movement in her right hand that allowed for pursuit of self-care and moderate home care tasks. Her hand pain resolved, though her hand remained less functional due to the atrophy and fusion. She continued to be unable to work. The remainder of her right UE and thoracic inlet area remained at high levels of pain and pressure and the blueness of her hand persisted. Then, a diagnosis of primarily vascular thoracic outlet syndrome (TOS) was made.

Occupational therapy intervention proceeded. Eventually, the decision was made for surgical intervention and her right first rib was subsequently removed. During surgery, significant subclavian artery compression from thoracic outlet syndrome (TOS) was noted, with little resolution after rib removal. Her TOS was actively addressed in OT, with a combination of the following: manual therapy was used to decrease anterior-posterior muscle imbalance throughout the thoracic inlet area; posterior scapular strengthening was used to improve posture and limit recurrence of compression on the neuro-vascular bundle; graded exercise under 90° of shoulder

flexion was used to improve shoulder and UE strength bilaterally; training was given to enable transition to a left-handed thrower, as she wished to return to softball but would no longer be able to throw well with her right hand due to thumb fusion; adaptive throwing with her right and catching left was taught to allow the greatest options in sports performance.

Rehabilitation was protracted and required approximately 2 years in total, but resulted in pain resolution and return to work as a manager in the event industry, albeit in a different capacity. She moved to self-employment and limited her schedule to running several events per year. Distributing her work over time allowed her to continue in her vocational pursuit. She did return to recreational softball for a while.

In this case, pregnancy increased all TOS symptoms and limited performance in all life areas. Symptoms of right thoracic inlet and UE pressure, pain, numbness, cold, and cyanosis recurred, and forearm atrophy further increased. Breast feeding added to pressure and pain, as did simple breast-size enlargement with pregnancy, exacerbating an already protracted shoulder girdle posture. This occurred despite an ongoing HEP, which she followed consistently. Her second pregnancy was spontaneous and exacerbated all symptoms, which had become manageable; it also added hypoglycemic responses to her presentation. The severity of muscle tetany in the region of her stomach, which was as an extension of her thoracic inlet pain and pressure, limited oral intake. Vomiting secondary to pain was common.

During her pregnancies, Melanie continued with her HEP as able and returned to occupational therapy focusing primarily on manual therapy. CranioSacral therapy, other fascial release methods, lymphatic drainage, and postural re-education were the primary treatment modalities used. Tai Chi loosening motions and meditation were also incorporated. After several years, she was eventually diagnosed with RSD/CRPS. With limited hand motion from fusion and severity of pain, the RSD stress loading protocol was no longer a viable intervention. ROM, manual therapies, and functional activities were thus the mainstay of OT. Desensitization was also used in the context of both manual therapy and her ADLs, to encourage touch to the affected side. As pain and pain-related vomiting limited oral intake, it was necessary to keep quick sugar and protein snacks available during sessions to treat drops in blood sugar. Positioning was used to optimize posture, and support of her distal UE was used to prevent a traction effect from her protracted shoulder girdle when lying supine. An ongoing HEP was used throughout, and ergonomics for all daily activities were reviewed and emphasized.

To date, Melanie receives intermittent occupational therapy to manage her ongoing symptoms which increase with weather changes, extended physical demands, and with fatigue. She actively uses pain and stress management techniques. The focus of OT intervention is on decreasing hyper-responsivity of the sympathetic nervous system by incorporating many of the treatment methods previously described. She has had periods of improved function, which have allowed a return to running in short road races at slower speeds. Also, she continues to be able to work, but frequently has to adapt all of her activity demands and must hire additional assistants for support. Her goal is to return to a more active, though adapted,

lifestyle with occasional road races with her two sons. In retrospect, it is clear that Melanie might have benefitted a great deal from earlier OT intervention, at the point when she was primarily dealing with an impingement syndrome. Her case is an excellent argument for early onset therapy as a way to possibly prevent the extremes of a CRPS diagnosis.

Conclusion

Occupational therapy is an integral part of the care plan for individuals of all ages with diagnoses leading to pain. Promoting independence in daily function, developing self-management skills, and actively working to decrease pain by addressing its causes are all part of the OT experience. Early intervention is strongly encouraged to prevent limitations in function and promote empowerment in addressing the potentially debilitating effects of both acute and chronic pain. However, later onset of therapy can still be very helpful, as can intermittent or ongoing treatment in more chronic care situations.

In considering inclusion of occupational therapy for an individual client, consider the following questions:

1. Has pain limited the pursuit of daily activities?
2. Has pain limited performance of daily activities which are still pursued? For instance, are tasks performed with pain, increased effort, increased time, decreased frequency, with fatigue, with assistance or avoided?
3. Has the client altered performance of usual activities in a manner that may cause additional injury or negative compensatory patterns?
4. Does the client feel satisfied with the quality of performance in the tasks he/she needs or wants to do every day?
5. Does the client feel empowered in managing symptoms and getting through a daily routine?

If the answers to these questions note any concerns, occupational therapy can help.

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Chapter 26
Aquatic Therapy and Pain in the Rehabilitation Patient

David McIntyre

Introduction/History

Aquatic physical therapy is a scientific therapeutic approach that uses the unique properties of water to enhance interventions for patients living with pain [1]. The use of water as a medical application for treatment of disease gained a foothold in Europe in the 1600–1700s. At that time, it was referred to as hydrotherapy [2]. During that time, physicians began to experiment with the physical properties of water at varying temperatures, its effects on the human body, and its ability to treat illness and disease. Up to this point, water was largely a passive modality for soaking, friction baths, wet compresses, or for drinking. It was not until the late 1890s that the idea of using water's buoyancy to assist exercise began to emerge. The term "hydrogymnastics" was introduced and entailed underwater active exercise to replace passive treatments [3].

Specifically, techniques such as Bad Ragaz focused on trunk control exercises in linear planes, whereas the Hallwick method helped disabled patients to enjoy independent movement in water, not otherwise possible on land [3]. During this time, European settlers noticed Native Americans using hot spring spas for many of the same purposes. It was not long thereafter that hydrotherapy was brought to the New World by physicians trained in Europe [3]. Subsequently, therapeutic exercise in water became an acceptable treatment modality after physicians noticed successful treatment of patients suffering from polio as well as patients with orthopedic injuries sustained from both world wars.

However, as patients treated with this modality recovered and needed less intervention, aquatic therapy began to decline. As technology advanced, Americans experimented with more technological treatments for disease. Intricate insurance

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reimbursement procedures and a paucity of adequate training of professionals also played a significant role. It was not until the 1970s–1980s, when a new emphasis on exercise and healthy living arose, that aquatics gained new favor [2]. A resurgence of research in aquatics for the treatment of diseases, such as arthritis, helped to expand the popularity of aquatics as a viable treatment modality [3]. By the 1990s, most new treatment facilities being built incorporated a pool, whereby water therapy could be offered as a treatment modality in one form or another [3]. However, despite renewed interest, subsequent reimbursement issues continued to prove problematic. This was possibly due to a lack of high-quality efficacy studies and a continued neglect of aquatics as a staple in a professional training curriculum [3].

The properties of water lead to beneficial physiological responses, which make it an excellent medium for rehabilitation. At 4 °C, the specific gravity of water is 1, while the average body is slightly less dense, with a specific gravity equal to 0.974 [4, 5]. Thus, the average body will float when the lungs are filled with air. Individuals with more lean muscle mass have a higher density of about 1.1 and tend to sink, while individuals with higher amounts of adipose tissue are less dense than water and tend to float [4, 5].

According to Archimedes' principle, when a body is completely or partially immersed in a fluid at rest, it experiences an upward thrust equal to the weight of the fluid displaced. For the most part, submerged bodies in water displace an amount of water that weighs more than itself, with a resultant opposite and upward force known as buoyancy [4, 5]. As more of the body is immersed, more water is displaced, which exerts a larger force opposite to the direction of gravity. A body in waist-deep water is approximately 50% weight bearing, whereas a body submerged to the neck experiences only the compressive force of the head [4, 5].

The principle of buoyancy is particularly useful when patients have fractures, joint pain, or weight-bearing precautions, because the force of gravity is essentially negated; therefore, patients experience decreased compressive forces, impact, and loading [3]. Buoyancy can also be used to support, assist, or resist movement, depending on the direction of movement. Buoyancy assists upward movement of the limbs, resists downward movement, and supports horizontal movement through the water. In addition, the property of buoyancy allows patients to participate in activities that would otherwise be too painful on land. For example, closed chain functional activities such as squatting, stair climbing, lunging, and walking are often impaired on land because of pain. However, at the right depth in water, these essential movements can be corrected and practiced because of the reduction of gravitational forces mentioned.

Hydrostatic pressure increases with depth; at 4 ft, it exerts a force slightly greater than normal diastolic blood pressure [4, 5]. This pressure is exerted evenly over the patient's entire surface area and helps to decrease edema [4, 5]. This pressure experienced over the total surface area of the skin may lead to sensory overload as well as a reduction in the perception of pain [6]. It also assists with venous return in a cephalic direction, increases both central blood and cardiac volume, and causes increased stroke volume, with lower heart rates [4, 5]. Blood flow increases to muscle and kidneys, aids in excretion of metabolic wastes, and strengthens respiratory

muscles, which are forced to move the chest wall against pressure created by the water [4, 5].

The viscosity of water offers natural resistance to an object moving through it in any direction. When a body moves through water, it experiences a drag force due to viscosity, which can be used for resistance training [4, 5]. This resistance can be increased by increasing the surface area of the limb with additional equipment, such as paddles. Also, water offers more resistance as a body moves through it with more force; therefore, water requires more power output from the patient. This resistance drops instantly when the patient stops the movement.

Recommended therapeutic water temperatures vary depending on the pathology being treated. Warmer temperatures may be more effective for rehabilitation purposes, with typical therapy pools kept between 33 and 36 °C [7]. Warm water transfers heat almost immediately upon immersion, aids in muscle relaxation, and decreases pain perception [5]. Warmer water temperatures and buoyancy may influence spinal segmental mechanisms and block nociception by stimulating mechanoreceptors and thermal receptors [8].

Indications

When deciding if aquatic therapy is indicated, it is useful to consider whether or not the properties of water are best suited to address the patient's needs and personalized goals and whether or not water will enhance the therapist's interventions. Pain, stiffness, movement dysfunction, cardiovascular endurance dysfunction, gait, and balance deficits are just some of the impairments that can be addressed in water. Persistent low back pain leads to avoidance of daily activities and also contributes to further exercise intolerance, with subsequent further loss of functional capacity [9]. At the same time, evidence has shown that exercise can decrease pain, disability, time off work, and can increase quality of life in patients with chronic low back pain [10]. Devising a suitable rehabilitation program that addresses deficits can prove to be problematic.

When pain limits a patient's ability to move or to exercise, water provides a comfortable and safe alternative environment. Thermal effects, hydrostatic pressure, and buoyancy provide joint unloading and proprioceptive input that can reduce pain. These properties also improve blood flow to tissue, which enables greater ease of movement and reduce stiffness in patients with restricted range of motion. Furthermore, buoyancy and hydrostatic pressure support upright postures and reduce gravitational forces, allowing patients to practice normal gait and movement patterns that are too painful on land. As noted earlier, hydrostatic pressure improves cardiovascular efficiency, whereas buoyancy allows patients to participate in endurance activities, such as deep water running.

A graded rehabilitation program can be devised in which patients, who are otherwise unable to tolerate land-based interventions, begin their rehabilitation in the water. As patient's symptoms improve, they can move to more shallow waters,

slowly introducing gravity, and culminating in a return to land-based rehabilitation. Aquatic therapy can also be used to help motivate patients who are poorly compliant to treatment, or who have failed to respond favorably to other rehabilitation programs [11].

Finally, when deciding if water is a viable treatment option, it is important to consider a patient's comfort level within a pool environment. Some patients have a fear of water and are unable to tolerate being submerged, getting their face wet, or floating either prone or supine. Other patients may be uncomfortable donning a swimsuit and getting into a pool used by the public. Fear and anxiety can create an unsafe environment for both patient and therapist. Patients who enjoy water are much more likely to take advantage of a community pool in order to continue independently with an exercise program.

Functional Limitations

In order to identify a patient's functional limitations, a physical therapy examination is performed on land. Examination begins with a thorough history, which includes the mechanism of injury, subjective identification of exacerbating and alleviating factors, and difficulties with ADLs, work, and leisure activities. Physical examination includes ROM assessment and strength assessment, and may include functional movements such as gait, squatting, stair climbing, lunging, balance, transfers, and bed mobility. The therapist notes painful movements and locations as well as compensatory strategies. Active and passive motion of the limbs and peripheral joints may also be assessed to determine if they play a role in functional limitations. Patient's self-report of pain and disability may be assessed using patient reported outcome measures, such as the Oswestry Disability Index (ODI).

Treatment/Common Techniques

Aquatic interventions and exercises are chosen based on their ability to alleviate symptoms and to strengthen and stabilize the core. The patient is taught how to achieve and to maintain a neutral spine. Exercises are given to strengthen core muscles, which include the transverse abdominis, obliques, and lumbar multifidi. Patients with back pain may find it easier to perform trunk muscle exercises in an aquatic environment, before transitioning to land [12]. Furthermore, exercises that strengthen muscles of the trunk will allow arm and leg movements to be performed with more force and accuracy [13].

During the early phase, the therapist may initially engage the patient by having the patient float in different positions. This is in an effort to alleviate symptoms and to allow better access, which can provide tactile cues while the patient learns to achieve neutral posture [14]. Once the patient understands how to maintain neutral

spine in different positions, he or she can begin to practice full active range of motion of the extremities. Then, the patient can incorporate functional movement patterns. These activities begin in deep water to take advantage of water's therapeutic properties in an effort to reduce axial loading and painful stimuli.

During the intermediate phase, the patient can practice gait patterns through water walking, squat mechanics, lunges, and stair climbing. During this time, the therapist evaluates form, patient tolerance, and pain levels. These interventions are performed at a depth to allow for both comfort and closed chain activities.

As the patient progresses to the late phase, he or she can move to shallower water to slowly introduce gravity and to progress toward more dynamic control of posture. For clients with chronic pain, a pool may be the primary environment to maintain function, fitness, and conditioning, given water's ability to unload painful joints and soft tissues. Although the patient is monitored constantly during aquatic treatments for a positive or negative treatment response, formal reevaluation should be performed on land to accurately assess patient progression. The therapist notes improvements in both active and passive range of motion of the spine and the extremities. Monitoring occurs in both open and closed chain exercises and assesses movement patterns during functional tasks, which include gait, squats, lunges, stair climbing, transfers, and bed mobility. The same assessment tool is readministered to evaluate the patient's perceived improvement in function and quality of life. These results are used as a guide for current and future treatment plans including if and when to initiate land-based interventions.

Currently, no standard guidelines exist for the use of aquatic exercises in treatment of chronic low back pain, particularly regarding the required number of sessions, duration, and frequency [7]. Several studies recommend 2–5 treatments per week for at least 8 weeks, which includes a warm-up phase, followed by resistance training, aerobic conditioning phases, and ending with a cool-down phase [10, 15]. Recovery can be divided into an early phase, intermediate phase, and a late phase [14]. Theses phases are marked by increasing resistance, whereby workload can be defined by individual patient characteristics and treatment response.

Initial treatment during the early phase of recovery focuses on a reduction of symptoms and correction of abnormal posture, which can be achieved by simply immersing the patient in deep water with the use of floatation devices to reduce axial compression [14]. While suspended in deep water, the therapist can provide verbal and tactile cues to teach the patient pelvic tilts and abdominal bracing. Once the patient can independently achieve and maintain normal posture, they can begin graded, general deep water exercise, which starts with low resistance, assisted motions including hip flexion-extension, hip abduction-adduction, and upper extremity horizontal abduction-adduction. It has been shown that this type of exercise may improve both pain and disability, and may maintain quality of life in patients with chronic low back pain [10]. Deep-water running is a common type of assisted, aerobic exercise that affects mobility, strength, and endurance, while concurrently reducing pain and physical disability [15]. As the patient progresses to the intermediate phase, resistance can be increased by adding repetitions, increasing velocity of movement, and increasing water turbulence. Certain devices such as

noodles, buoyancy cuffs, and paddles can be added to the limbs to further increase resistance.

In the late phase of recovery, resistance is increased by having the patient transition into shallower water to participate in closed chain functional movements. By changing the depth of exercise, the therapist can slowly introduce gravitational force and axial load. Activities such as walking, squatting, lunging, and stair climbing can be practiced with less buoyancy acting on the patient. The end goal is to return to land therapy in order to achieve maximum function. Again, resistance is increased in the late phase by adding repetitions, increasing velocity and turbulence, or incorporating devices that take advantage of buoyancy and viscosity. Treatments should be closely supervised by trained and licensed therapists, who can monitor patient response and can determine when a patient is ready for added resistance and exercise intensity. Many patients with chronic pain suffer from a number of comorbidities affecting the cardiovascular, pulmonary, neurological, and/or musculoskeletal systems. It is imperative that the therapist understands how exercise and the properties of water can impact a patient's preexisting condition. Recording parameters such as vital signs, subjective exertion, and pallor are very helpful in determining if and when to increase exercise intensity. General exercise intensity can also be monitored using the Borg Scale, as it has shown adequate reliability in quantifying training loads during aquatic exercise [16].

Potential Treatment Complications

Aquatic exercise for people in pain must be undertaken with caution, because reduced pain perception during aquatic exercise may make it easier to over-exercise. This can occur because the perceived workload is less than that perceived during land-based exercise [17]. Both animal and human studies suggest that sensory overflow may be the mechanism by which pain is less well perceived when the affected body part is immersed in water. Pain modulation is consequently affected with a rise in pain threshold, which increases with temperature and water turbulence [18]. Even though patients may leave the pool at the end of the treatment session with lower pain levels than when they began, they may return for follow-up appointments complaining that they experienced higher pain levels later in the day. Clinical experience can be instrumental in identifying patients who may be at risk of over-exercise.

The comprehensive examination performed prior to beginning aquatic treatment can also help to identify patients with poor activity tolerance and high irritability, as well as other comorbidities. Cardiovascular disease, for example, can be influenced by water immersion and aquatic exercise. For patients with left ventricular dysfunction and/or congestive heart failure, immersion up to the neck could produce temporarily abnormal hemodynamic responses [19]. Identifying comorbidities is also important from a thermoregulation standpoint. In warm water, heat loss is limited. Therefore, a systemic rise in temperature occurs, which could lead to overheating. This is especially important to consider with bariatric patients, prenatal women,

patients with multiple sclerosis, cardiac issues, and children. Because chronic pain can impair functional mobility, balance and gait safety precautions should be in place to prevent injury in and around the pool. Patients may be at a higher risk of slipping on the pool deck or falling while entering or exiting the pool.

Evidence

Several studies over the last two decades have demonstrated that therapeutic aquatic exercise can be a safe and effective treatment modality for patients with chronic low back pain [11, 16, 20]. This is especially true for patients who may have difficulties with the weight-bearing components of land-based interventions [21]. Joint off-loading, which occurs in an aquatic environment, may also provide the optimal environment for patients to exercise aerobically and at higher intensities than would be possible on land [7]. In particular, the addition of a deep-water running program, which was conducted at an individual workload of the aerobic threshold, to a multimodal physical therapy program, produced significant improvements in nonspecific chronic low back pain [22]. However, despite evidence to suggest that therapeutic aquatic exercise is beneficial to patients with nonspecific low back pain, when compared to land-based interventions, these effects are open to interpretation.

Therefore, it cannot be concluded that aquatic therapy is the superior treatment modality [20, 22]. Furthermore, due to the heterogeneity of study interventions, no standard guidelines exist for aquatic treatment of chronic low back pain, particularly with regard to the number of sessions, duration, and frequency [7, 10]. Although standard treatment frequency has yet to be determined, a dose-response effect was observed in some parameters, with greater benefits obtained when exercising 3 days per week compared to 2 days [7, 13]. Adherence to aquatic exercise appears to be high and results were similar to other interventions [21]. This may be due to the fact that aquatic exercise is safe, enjoyable, and well tolerated; furthermore, aquatic exercise can serve as the initial treatment for patients who have become disillusioned after failed land-based interventions.

Conclusion

Water has historically been used to treat a variety of ailments. Enthusiasm for its regenerative properties spread from Europe to the North America, as early as the 1600s and 1700s. The properties of water provide a suitable and tolerable environment for patients with chronic pain, enabling them to engage in movement and exercise. Exercise is geared toward improving functional movements as well as overall health. As with other physical therapy modalities, aquatic therapy should be provided by a skilled and licensed physical therapist or by a physical therapist assistant trained to identify and to monitor unique treatment responses of patients suffering from

chronic pain. While there is sufficient evidence to suggest that therapeutic aquatic exercise is beneficial to patients with chronic low back pain, more quality research studies are needed to further substantiate it as a viable treatment option.

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Chapter 27
The Burdenko Method and Pain in the Rehabilitation Patient

Igor N. Burdenko, Joseph P. Carroll, and Paul J. Salvi

Pain is a language. Pain is similar to an emergency call. Pain is complex, it can be physical, it can be psychological, it can be emotional, it can be all of those things together, and it can definitely be confusing.

If present for too long, pain can be devastating to the human body. Everyone experiences pain at some point in their life for some reason. Because of our individual differences, we all have different tolerances to pain as well as individual pain thresholds. It is how we deal with pain that allows us to remain active, healthy, and independent. In this chapter, we share our experience and discuss The Burdenko Method's principles, philosophy, and main characteristics using water and land as its primary modalities of treatment in pain management.

Why do we use the water? The answer is simple: we were born of water. The gestation of our bodies took place in an aquatic environment where we were able to float and to develop in comfort and safety. There was freedom for our bodies to grow and to expand without the compression of gravity, which allowed us to feel the soothing support given to us by the natural state of buoyancy. Historically, water has a long record of helping people and animals to overcome injuries and disease as well as promoting health and relaxation. In this chapter, we document how it can be used to treat and to manage pain.

Igor Burdenko's interest in using the water came from his early experiences in the days after World War II ended. His father had returned home from fighting and

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had suffered five wounds during his military service. After the war, the country and town where he lived were ruined. There were limited or no medical facilities, and few doctors, nurses, or healthcare workers were available for him to enhance full recovery. The one thing that was still there was his family and the natural environment around him.

Before the war, Igor's father had been a swimmer and believed that movement in the water would help him get stronger, having been so weakened and in pain from his injuries. Every day, Igor's father would ask him to bring him down to a small pond in their neighborhood so that he could begin his recovery. Igor watched how his father experienced pain relief once he got into the pond. He could see how the pain would subside and how a relaxed state would subsequently take over, while he began to move his body and restore his health.

This early experience stayed with Igor throughout his education and became a topic and training tool for himself and his athletic development during college and graduate school. He earned an M.S. in Sports Medicine from the University of Riga, a Ph.D. from the Moscow Pedagogical University, and a rehabilitation specialist degree from the First Moscow State Medical University [1]. Igor continued his work and was later promoted to the Ministry of Sport and Education to conduct research in his method of using water and land exercises to improve the performance of the human body.

He continued this work into the 1980s in the Soviet Union and eventually emigrated to the United Stated in 1981 with his family. In his new found home, he was able to slowly build up his connections with people who were familiar with his programs to make gains in the medical and athletic communities. People of all ages and ability levels were amazed at the success his method gave them to improve themselves both in athletics and in every day capacities. That success continues through today.

The Burdenko Method is founded on a philosophy combining WATER and LAND exercises to educate its students in how to move their bodies safely, efficiently, and gracefully from rehabilitation, into conditioning, and progressing all the way up to training, based on the principles of Fitness Intelligence. It has eight main characteristics that separate it from traditional rehabilitation and training programs, which can be summarized as follows:

Combination of two modalities, water and land
Six essential qualities
Deep water in vertical position
Different starting positions
Exercises with different speeds
Exercises in multiple directions
Attention to body alignment
Keeping the patient involved in recovery.

It all starts in the water. Water supports, assists, and resists. The threefold power of water gives us the freedom to train our bodies to move again.

The first major thing one encounters in the water is the supportive force of buoyancy. This is the upward force of the density of a fluid acting on an immersed object.

Table 27.1 Effects of compression of water

Increased centralization of blood volume	Decreased heart rate
Increased work of breathing	Increased cardiac output
Increased sodium and potassium excretion	Increased intramuscular blood flow
Increased plasma levels of dopamine	Decreased joint pressure
Increased lymphatic return	Relaxation
Increased range of motion	Decreased pain
Changes in muscle tone	Provides traction

Put simply, when an object is immersed in a fluid, there is the antigravity force that holds the object up. The denser the fluid, the more the object is held up. When one enters the water, pressure helps to counteract the downward force of gravity on the human body. It relieves the body of compression, and frequently relieves pain. The deeper a person goes into the water, the less pressure there is from gravity.

Starting at the knees, this force is reduced to approximately 70% of body weight; at the waist, it is reduced to approximately 50%; at the neck, it is reduced by about 90%! [4]. Each person has a unique body type and body mass, so these values are variable; however, the one factor that is consistent across all body types is a reduction in compression.

The water has amazing abilities to heal the human body. The physiology of immersion alone lends itself to the healing process. Immersion forces derive from the forces of hydrostatic pressure and its ability to assist the patient, especially in human physiology.

Hydrostatic pressure is the force on the immersed body by the surrounding fluid. This compression of water helps to create physiological effects on the human body that can be simplified in the following Table 27.1: [2–7]

Understanding the physiological effects of water will allow the practitioner to guide the rehabilitation process with a better understanding of the potential outcome of the patient undergoing treatment, as well as a better understanding of how the potential outcome will differ from those obtained by traditional land-based therapies. There are some limitations and precautions unique to each case, which should be considered when creating a treatment plan. The most obvious of these is the patient's acceptance of being immersed in water. Not everybody has had the ability to grow up with access to safe and clean recreational water activities and may have misgivings about entering into a water and land based rehabilitation program. In these cases, gradual explanation and progression of the program should be undertaken in order to ensure a solid level of trust between the patient and the practitioner. Using proper buoyancy devices and appropriate guidance makes water therapy accessible to everyone, regardless of their ability to swim.

The third power of water is its ability to offer resistance. The density of water allows individual grading of resistance levels and progression of muscles as hard or as gentle as needed in order to complete the rehabilitation process. Hidden in the ability to resist is the turbulence and turbidity of water on limbs as a patient moves through water. The tactile compression of water surrounding limbs and the turbulence

of the water as it flows around the immersed patient create a gentle massage effect that can reduce pain, which is similar to how a water jet from a hot tub massages the muscles and reduces their tension at rest. The most obvious difference is that people move their own limbs and relearn how to use their bodies and how to create balance of the Six Essential Qualities of human performance (Fig. 27.1).

These qualities are the cornerstone of The Burdenko Method and are displayed in a basic pyramid hierarchy [1]. Within each quality, there are specific exercises that allow the practitioner to address the needs of the patient, while developing the particular quality to that level. After each level description, there are examples of both pool and land exercises to help illustrate how The Burdenko Method is utilized in practice.

The first quality, which is at the base of this pyramid, is **balance** (Fig. 27.2). Without balance, nothing can last. This is not just the balance of the human body to remain upright, such as in a standing posture, but also in the balance of the entire body and all of its systems. When the body functions, it needs to have the right amount of balance in order to maintain homeostasis, to tolerate everyday changes, and to endure the stressors of our activities. Balance helps the body to remain resilient to disease and to injury. Laying the foundation of balance in the pool sets the basic parameters and helps the patient to understand the physical requirements that all other exercises in The Burdenko Method will require.

The second quality is **coordination** (Fig. 27.3a, b). The controlled contraction and relaxation of muscles in the human body help to create movement. The more control over movement that can be obtained, the better quality of movement that will ensue. Some aspects of coordination are complex, whereas others are simpler. All successful motion must use a coordinated pattern of movements.Discoordination of movement often creates stiffness and injury. In The Burdenko Method, specific exercises are taught, which use the principle of progressing from simple to complex instruction. This helps to ensure that the patient is able to understand and to digest how each body part functions individually, as part of a group, and then eventually as part of a whole. Repeating these patterns creates plasticity in the brain by challenging it just to aid in regaining control over painful body parts.

The third quality is **flexibility** (Fig. 27.4a–c). Each muscle needs to have the right amount of flexibility in order to function. In traditional rehabilitation, flexibility is often the first quality that is addressed, even though it is often not the best first step. Achieving good, lasting flexibility is best done through active movements, which cannot take place without a good foundation of coordination and balance.

The quality of endurance ability to produce for an extended time or to last performs best when all the qualities before it are built solid. We often see biomechanical breakdowns and injuries when fatigue settles into the systems, as a result of too much energy spent trying to maintain balance, or from being forced to perform coordinated movements poorly. Additionally, it can also be the result of muscles being asked to pull through large ranges of motion and/or by being forced to spend energy trying to stabilize their ends under load.

Speed and quickness (Fig. 27.5a, b) are often used interchangeably and involve the ability of the body and its parts to change direction and velocity. Mastering these

Fig. 27.1 Six essential qualities

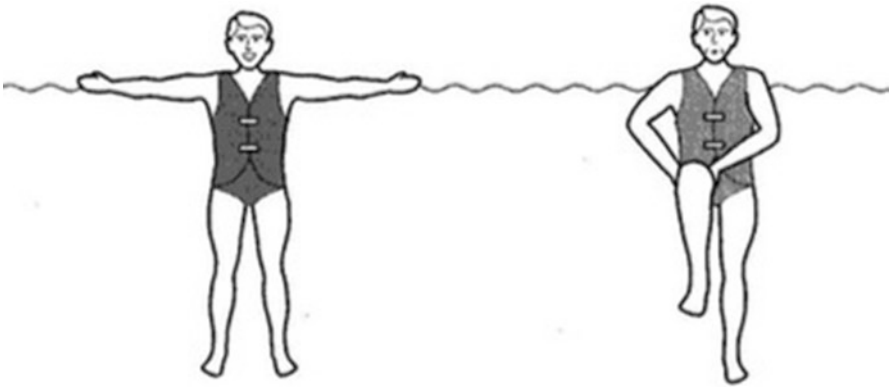

Fig. 27.2 Balance

qualities allows the patient to perform all tasks at a greater confidence level and with better resiliency. It also allows the patient to challenge his/her physiology and to properly stress his/her cardiovascular systems to yield the maximum benefit.

The last quality is **strength** (Fig. 27.6a–d). This term is used more to define the ability to resist pressure, and less by its relationship to power production. There are many different examples of strength. Some strength is physical whereas some is emotional, but both are necessary for us to overcome injury and to get back to enjoying life. We train strength in The Burdenko Method by increasing pelvic awareness, by controlling our center of gravity on land, and by controlling our center of buoyancy in water. Once these factors are controlled, patients can safely progress through various loads on the human body and return to a higher level of function.

Understanding how to utilize mass and buoyancy help us the patient to understand how the human body is affected by forces around it. These forces can be seen in Figs. 27.7 and 27.8.

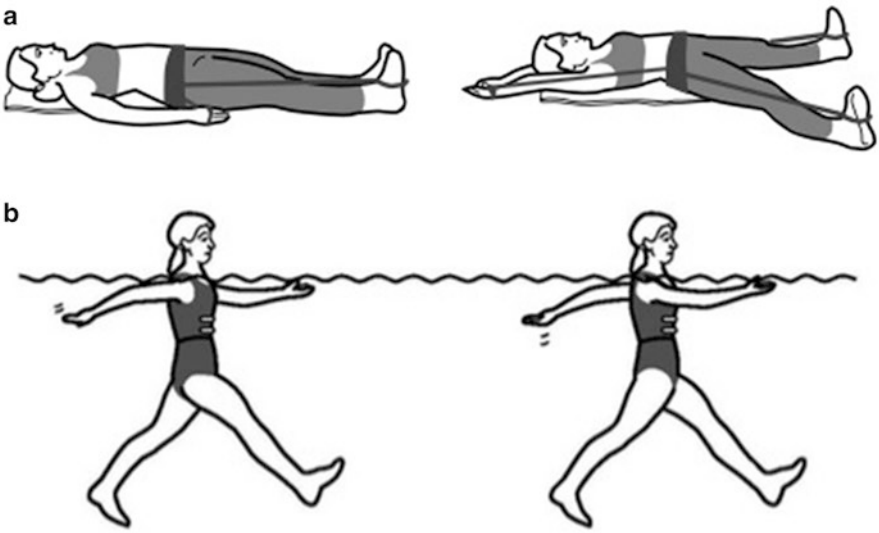

Fig. 27.3 (**a**, **b**) Coordination

Using these concepts also helps to formalize a relationship between gravity and buoyancy, which can be important once a patient is progressed from water exercise to land exercise. Patients cannot live in the water, so therapy must evolve gradually into the world of gravity and resistance, using the same principles and similar, familiar exercises that were taught in earlier levels (Fig. 27.1).

When patients move in the water, they have to expend conscious effort to facilitate correct movement. The extra resistance of water forces the patient to recruit more of muscle fibers and motor units to perform tasks and to create coordinated actions. The extra benefit of this added stress is the ability for these new motor skills to translate onto land and ultimately into regular performance.

Vertical Position is Functional Position

Human beings are land creatures, whereby a bipedal design is used to hold the body upright and to propel the body with maximum efficiency and stability. However, in the presence of pain, this design changes, often leading to poor posture, deviation of gait, and a decrease in mobility. When a patient is started in a pool program, the goal is to return the body to its most natural state. This is accomplished by beginning the program in the deep water in the **vertical position**, which promotes the natural alignment of the body in its best position. In order to achieve the vertical position, an appropriate level of buoyancy should be added to the patient to maintain the head out of the water and to encourage relaxation of the body, which will reduce the anxiety of immersion that some people may have and maintain safety as a priority.

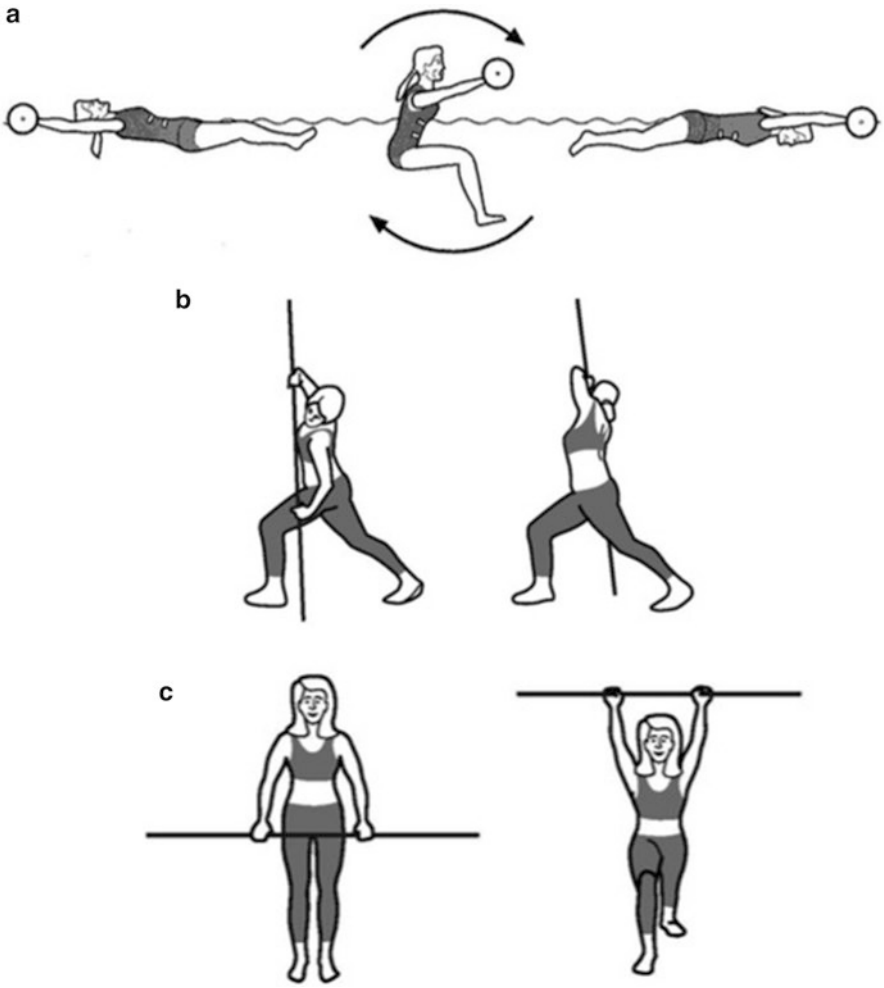

Fig. 27.4 (**a**–**c**) Flexibility

Choosing the right buoyancy device allows the patient and therapist to achieve all of these factors. First, the device must have a good distribution of buoyancy forces, such as buoyancy vests and cervical collars, which will help the patient to achieve the right mobility in the water with better alignment, less pain, and improved ability to perform exercises without having to fight the device and maintain vertical position. Uniform buoyancy creates an all over support structure and helps to maintain proper alignment by keeping the upward forces of the vest well balanced on the human body. Choosing the proper buoyancy device will also help to provide traction for the spine and all joints in the body. Using the wrong buoyancy device tends to promote an asymmetrical support structure, which increases the displacement of the

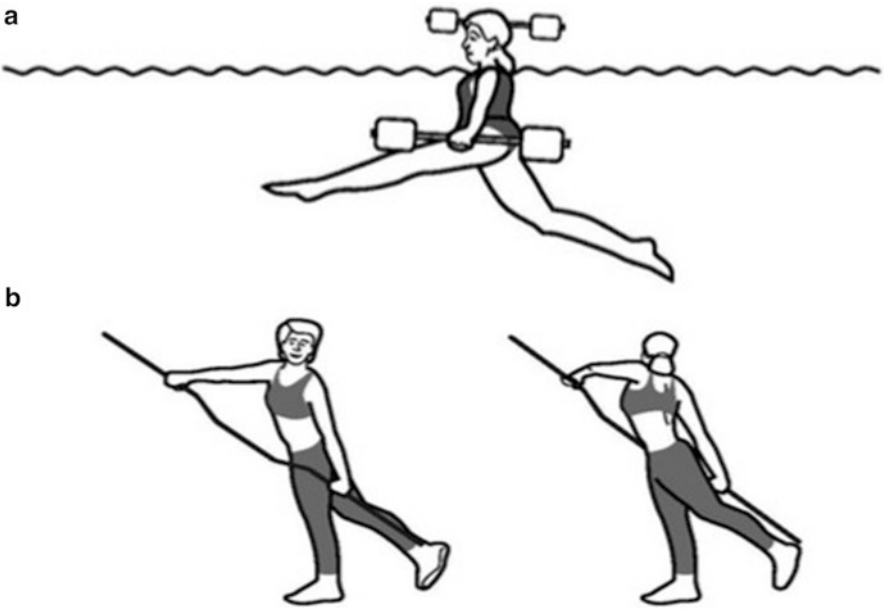

Fig. 27.5 (**a**, **b**) Speed and quickness

wearer, taking them out of alignment, upsetting the center of buoyancy, and subsequently increasing pain.

These are important factors to consider in how much and what kind of device to choose for each treatment and each individual. The more lean body mass the patient has, the more buoyancy that will be needed. Conversely, the more adipose tissue the patient has, the less buoyancy that will be needed. Using the right equipment for the right exercise will always yield the best results. Wasting time to attempt excessive adaptations will delay healing and can discourage progress in the program.

Application of buoyancy devices below the center of buoyancy can increase the rotational forces by lowering the center of buoyancy (COB) and decreasing stability and alignment of the patient. There are times when the therapist may want to apply this as a challenge, but in most cases, it is wise to use the most stable support available.

After the patient is comfortable controlling him/herself in the vertical position, the therapist will start to challenge them by changing starting positions for each exercise, including supine, prone, side lying, and a dynamic combination thereof. In changing planes, the therapist can address multidirectional stability as well as dynamic postural control, by challenging the patient's body with variable orientations to gravity. Then, progression can be made to exercising in multiple directions; which includes forwards, backwards, sideways, and turning, while increasing or decreasing vertical heights to make sure that patients are progressing, developing the six essential qualities, and ensuring balance throughout the whole body. It is

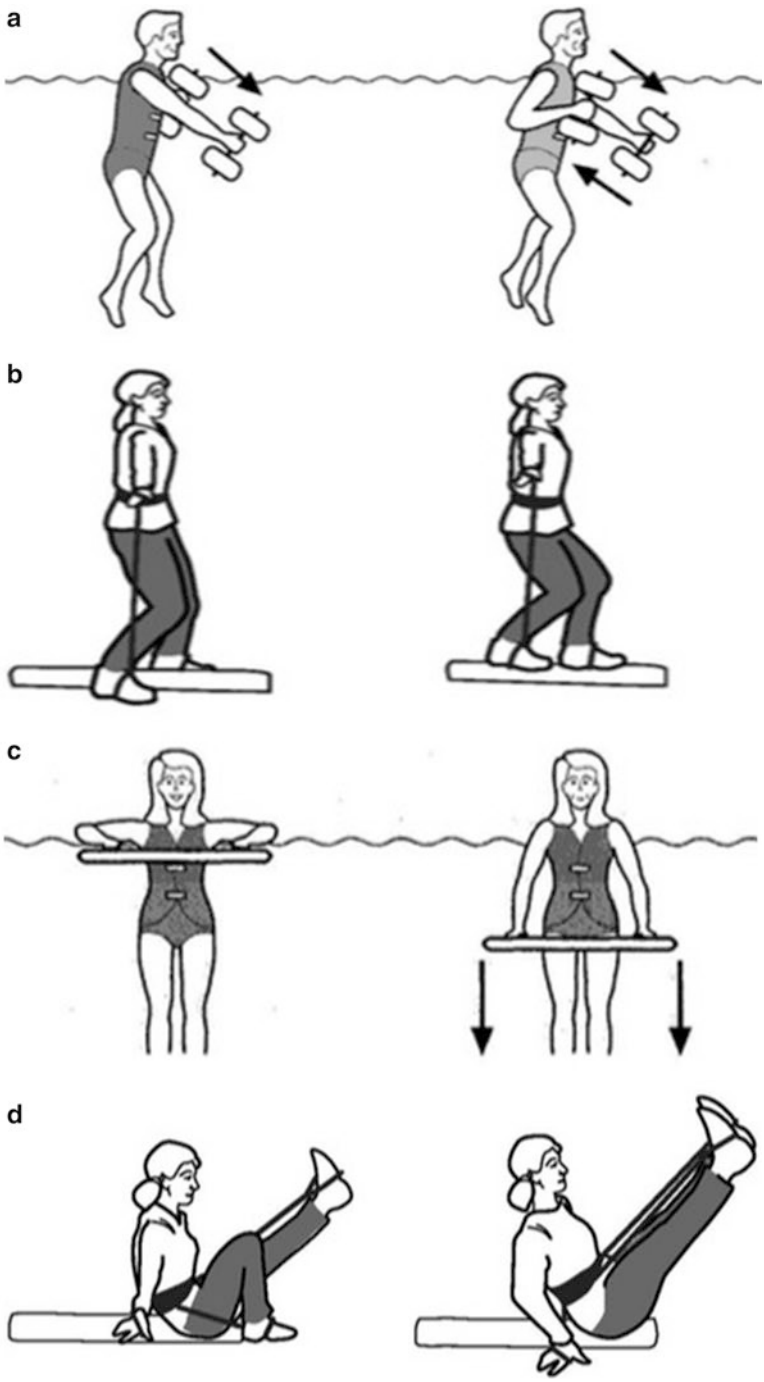

Fig. 27.6 (**a**–**d**) Strength

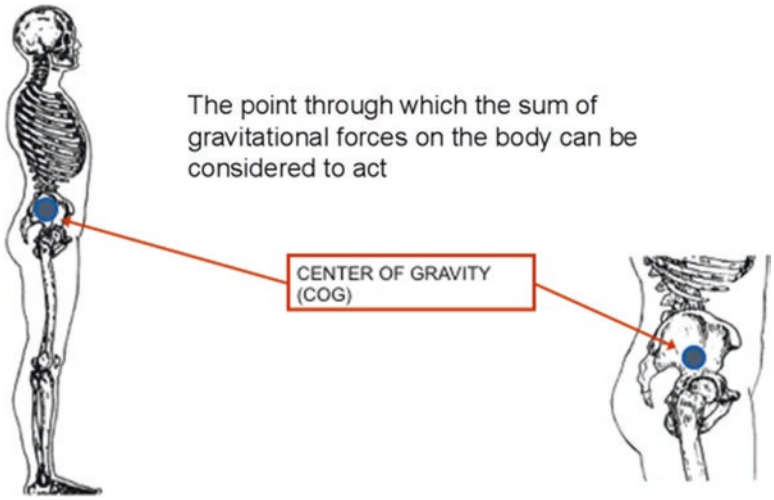

Fig. 27.7 Center of gravity

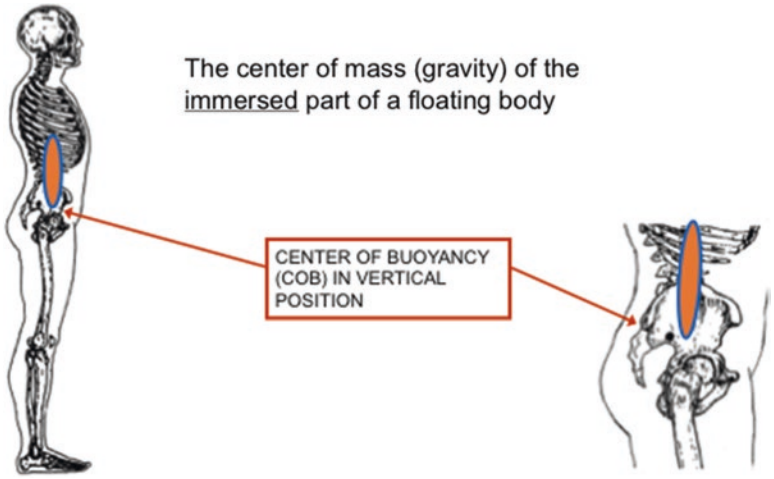

Fig. 27.8 Center of buoyancy

important to ensure a good balance between opposing muscle groups, in addition to building up and supporting the joints from every angle possible.

Exercising with different speeds challenges the ability of the body to control changes in force intensity and to maintain its posture. It also prevents adaptation of the human body to the exercise and lends to the creation of more complex movement patterns as well as increased muscular coordination.

All of these principles hinge on the performance of each exercise with proper alignment. This correlates to maximizing the ability of each person to do each

exercise correctly and safely, while increasing control over each joint and position to stimulate proper healing. Too often, you can see people doing exercises for exercise sake, which risks injury and pain by not being aware of proper movement and discouragement by a resultant lack of progress.

Conclusion

The most important part of The Burdenko Method is keeping the participant actively involved in the water during the rehabilitation process. This creates a healthy environment and working synergy between practitioner and patient.

Using The Burdenko Method in conjunction with traditional approaches in rehabilitation gives the patient and the practitioner the greatest range and best opportunity to reduce pain and return to function. At the fundamental level, it teaches the active approach to recovery and empowers the patient along the course of their rehabilitation and ultimately over their condition.

Implementation and Case Study in Rehabilitation Using The Burdenko Method

A patient with musculoskeletal pain is often referred to a physical therapist. A physical therapist trained in The Burdenko Method will begin by performing a clinical evaluation. The initial evaluation takes place on land and consists of a thorough history including vital signs, blood pressure, outcome assessment, standing and dynamic posture, weight-bearing tendencies, coordination during gait, range of motion, balance, and strength. Pain will be evaluated for location, severity, radiation, frequency, and duration, as well as length of time present and origin of pain.

Regardless of the type of injury, the therapist should spend time on assessing the patient's activities of daily living (ADLs) and to review and instruct the patient in often overlooked but simple techniques for pain reduction. For example, most people get dressed in a standing position, but once injured, this simple daily task might require flexibility and balance that the patient does not have. Teaching them how to dress from the sitting position will help them conserve energy and to avoid pain.

Posture and gait are two areas that are often affected and may factor into development of pain. Therapists should spend time to work on postural alignment in standing, sitting, and while walking. Restoring normal arm swing during ambulation will help to relax tight muscles in the neck and thoracic spine. It is important to align the head over the shoulders and the shoulders over the pelvis; bringing the patient from a forward flexed posture to a vertical posture will allow the lower back and gluteal muscles to relax.

Many patients in pain, especially spine related, have difficulty rolling from side to side and getting in and out of bed. Simple instructions on abdominal bracing, log rolling, and how to move from standing to sitting to lying should be covered. Proper positioning in bed can allow better relaxation, can take stress off of joints, and can even aid in edema reduction. It is also very important to teach patients how to get to the floor and rise to standing. Another functional activity to address is ascending and descending stairs.

The first session after the evaluation initiates the active phase of rehabilitation. In The Burdenko Method, this session will take place in the pool. Preference is to begin the rehabilitation process in the deep end of a warm water pool. The patient will wear a buoyancy device, which will assist them to achieve a vertical position with their head out of the water in the deep end. In this position, which emphasizes postural alignment, the patient will escape from the forces of gravity, allowing his/her joints to decompress, to receive traction, and to obtain pain relief.

Depending on the severity of the injury, and the patient's ability to control their movements, the therapist will select 3–4 exercises to be done at a slow pace of movement from the first level, **balance**. Patients who cannot tolerate weight bearing on land, or who have their movements limited by pain, are generally able to move through the water freely and without pain. The Burdenko Method uses total body movements as opposed to isolated movements of the injured area. Moving the entire body, including extremities that are not injured, will provide a means to allow the injured area to relax and to achieve pain relief, while addressing the six essential qualities and promoting whole body health.

Most patients will benefit from a program attending two sessions per week under the guidance of the therapist, which includes daily practice of the previously instructed home exercise program. Initial instructions to the patient will include discussion of their diet, hydration, deep breathing techniques, and activity modification. Many patients will benefit from massage as well as use of homeopathic topical pain relieving creams in the early stages of rehab.

The progression of The Burdenko Method will include continuation of deep water exercises, emphasizing pain-free range of motion. Then, there will be addition of more challenging exercises by adding speed and change of direction to movement patterns while maintaining postural alignment. Within 2–4 sessions, most patients are able to have partial weight bearing introduced by beginning to exercise in the shallow end of the pool, in addition to deep water exercise. Weight bearing will be 20–30% at chest-depth and 50% at waist-depth water.

Case study: An 80 year-old male is referred for The Burdenko Method, after failing traditional land therapy. This patient presents with severe osteoarthritis of his right hip. He deferred surgery because he had a high risk of potential complications from hip replacement surgery due to medical comorbidities, including advanced cardiac and renal diseases. He was treated by a physical therapist using ultrasound and passive range of motion exercises. After six sessions of therapy, the patient refused to continue due to increased pain after each session. He was thereby referred for a trial of aquatic therapy using The Burdenko Method. Upon evaluation, he ambulates with a rolling walker with partial weight bearing on the right side; both active and passive ranges of motion were painful on land.

The patient was very deconditioned, requiring the physical therapist to enter the pool with him. His body was so weak that he could not find a balance between his center of buoyancy and his center of gravity. This caused his legs to float to the surface in either front or behind him unless the therapist helped to correct his alignment. Movement in the water was pain free and the patient was encouraged to have finally achieve pain relief. He successfully completed six sessions in the pool, initially in the deep end, then began to touch down at neck depth, and then at chest depth. After ten sessions, he was walking 50% without any assistance and navigating stairs in and out of the pool without requiring the chair lift. He was reporting carryover with 50% pain relief on a daily basis, including easier transfers, and he was negotiating a flight of stairs at home daily.

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Part VI
Multi Modal Approach: Medication Management

Chapter 28
Adjuvant Medications for Pain in the Rehabilitation Patient

Alexios Carayannopoulos

Introduction

Pain management is of paramount importance, not only to inpatient rehabilitation patients in pain after trauma or surgery, but also to outpatient rehabilitation patients who present to their physiatrist, primary care physician, or Emergency Department in pain [1]. Additionally, cancer pain remains a major burden both for patients and their families, especially in light of longer life expectancy of cancer sufferers undergoing rehabilitation [2]. Finally, chronic pain hasdramatic effects not only on quality of life measures, but also on healthcare costs and societal costs from absenteeism and early retirement [3].

Historically, opioid mediations were the mainstay of treatment for acute and chronic pain conditions. However, because multiple studies have been published outlining the adverse effects of chronic opioid therapy for non-malignant pain, renewed interest has arisen in non-opioid medication options [4]. Many medications not originally designed to treat pain are now used within the framework of multimodal analgesia or are used to treat specific pain indications [5].

Pain can be broadly categorized into two major subtypes, which include nociceptive and neuropathic pain. Nociceptive pain is subsequent to normal activity in neural pathways, as the result of actual or potential tissue damage, which can be seen in postoperative pain states, osteoarthritis, and mechanical low back pain [6]. Neuropathic pain results from a lesion or damage to the somatosensory system, and may be generated by either the peripheral or central nervous system, or both, which can be seen in painful diabetic peripheral neuropathy, central poststroke pain, and postherpetic neuralgia [7, 8].

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Pain management is greatly relevant across multiple medical specialties, which includes physical medicine and rehabilitation and requires a multidisciplinary approach to recognition, diagnosis, treatment, and education. Moreover, a thorough and holistic approach is important to explore the myriad factors that affect patients experiencing pain in the rehabilitation continuum, whether acute, chronic, or both [5]. Multiple options for pharmacological therapy are available and the goal of this chapter is to provide a foundation of adjuvant medications traditionally used for pain, while highlighting available literature, newer drugs, newer methods of administration, as well as an update on recent guidelines and newer indications for the use of classic analgesic drugs.

Topical Agents

Reason to Use

Peripheral mechanisms are thought to be appropriate targets and these mechanisms are relevant in many chronic pain diagnoses, which include musculoskeletal, rheumatologic, and neuropathic pain states. These agents mostly act at the local level in the peripheral tissues, which include soft tissue and nerves, without raising serum drug levels. Therefore, these agentshave a reduced risk of drug–drug interactions and systemic side effects, which is helpful in patients who are otherwise receiving systemic medications.

There are three categories of treatments, which include the following: *Topical Local Anesthetics* (heated lidocaine/tetracaine topical patch, lidocaine/tetracaine cream 7%, lidocaine patch 5%, eutectic mixture of lidocaine 2.5% and prilocaine 2.5%; *Topical Non-Steroidal Anti-Inflammatory drugs (NSAIDs)* (Diclofenac topical solution 1.5%, Diclofenac sodium gel 1%, Diclofenac epolamine patch 1.3%); *Topical Capsaicin* (Capsaicin cream or lotion, Capsaicin patch 8%).

Mechanism of Action

Heated lidocaine/tetracaine releases lidocaine and tetracaine to provide local analgesia to skin using a novel heating element to enhance drug penetration. Lidocaine and tetracaine amide and ester-types of local anesthetics, respectively, which block sodium ion channels needed to initiate and conduct nerve impulses, resulting in local anesthesia. Tetracine is also the strongest NMDA channel blocker of the class. With inflammatory conditions, animal studies have shown abnormal sodium channels, which when blocked, reduce spontaneous nociception.

Lidocaine patch 5% blocks abnormal activity in sodium channels, which have been shown to be abnormally active in neuropathic and inflammatory conditions.

Lidocaine has also been shown to block expression of nitric oxide as well as pro-inflammatory cytokines, providing another mechanism for pain relief, as well as providing a protective barrier from cutaneous stimulation in patients with allodynia.

Topical NSAIDs have a mechanism similar to other non-steroidal anti-inflammatory drugs, by inhibiting the cyclooxygenase enzyme, resulting in reduced formation of prostaglandins, thromoboxanes, and prostacyclin. They were developed to achieve localized anti-inflammatory effects of these medications while trying to avoid the systemic side effects [9].

Topical Capsaicin (8-methyl-*N*-vanillyl-6 nonenamide), the pungent ingredient of chili peppers is an agonist of the transient receptor potential vanillin 1 receptor (TRPV-1), an ion channel receptor complex that is expressed on nerve fibers in the skin for nociception. It is also responsive to heat, acidity, and endogenous metabolites of polyunsaturated fatty acids [10]. Administration topically leads to enhanced stimulation of TRPV-1 initially, followed by a reduction in stimulation, which corresponds to initial increase in pain, followed by pain relief.

Efficacy

Clinical trials have shown heated lidocaine/tetracaine topical patch to be very effective for the following: local dermal analgesia for superficial venous access, local dermal analgesia for superficial dermatologic procedures, shoulder impingement syndrome, myofascial trigger point pain, patellar tendonopathy, and carpal tunnel syndrome.

The development of a patch for topical administration of lidocaine has resulted in a new first-line treatment of localized neuropathic pain, with very limited adverse systemic side effects [11]. The lidocaine patch was the first FDA-approved drug for postherpetic neuralgia, and significantly reduces pain in patients with postherpetic neuralgia and allodynia [12, 13]. It can also be effective for allodynia, as seen in a variety of neuropathic pain conditions such as stump neuroma pain, intercostal neuralgia, diabetic polyneuropathy, meralgia paresthetica, post-thoracotomy pain, complex regional pain syndrome, radiculopathy, and post-mastectomy pain. Other applications in the literature include idiopathic sensory polyneuropathy, HIV-associated neuropathy, carpal tunnel syndrome, erythromelalgia, low back pain, myofascial pain, osteoarthritis, and postoperative pain [11]. The patch is placed directly over the painful area with intact skin for 12 h on and 12 h off, with pharmacokinetic studies revealing on 3% of the lidocaine systemically absorbed, accounting for its low rate of adverse effects [14]. There are conflicting results in the literature, as recent trials of lidocaine patch 5% or cream did not show any benefit in patients with postsurgical peripheral nerve pain [15] or in mixed neuropathic pain [16].

Topical NSAIDs have been shown to be efficacious for osteoarthritis of the knee, and a 2012 Cochrane Collaboration showed that the particular formulation, not just

the active medication was essential in terms of efficacy. Topical NSAID patches have been studied in acute ankle sprain, acute minor soft tissue injury, and acute back strain, with statistically significant reductions in pain as compared to placebo. They are recommended for short-term relief of soft-tissue injuries and chronic joint-related pain [17].

Clinical trials of capsaicin patch include those for postherpetic neuralgia, HIV polyneuropathy, and painful peripheral neuropathy, which have had mixed results. Capsaicin in low concentrations (<1%) with repeated administration has been used to treat neuropathic pain, but data are poor and a meta-analysis found that the effect is unlikely different than placebo [18]. However, a more recent higher concentration (8%) formulation has shown efficacy over control with 0.04% capsaicin in postherpetic neuralgia and HIV-related polyneuropathy with a low adverse event profile [19].

Side Effects

Clinical studies show the most common local reactions were erythema, skin discoloration, edema, application site burning, dermatitis, pruritus, and rash, all of which were mild and resolved spontaneously after treatment. The biggest advantage of all topical medications is their lack of clinically significant systemic activity. In terms of topical NSAIDs, no serious adverse effects were reported during the short-term placebo-controlled studies, which included application site reactions. Adverse effects of lidocaine patch include skin irritation at the site of application. Adverse effects of capsaicin patch include application site erythema, pain, pruritus, and transient increase in pain, all of which where transient and self-limited.

Dosage

The amount of lidocaine/tetracaine to be dispensed is dependent on the size to be treated, but in general should be applied thinly and evenly using a flat dispenser.

The current FDA-approved labeling recommends up to three lidocaine patches over the skin for 12 h of a 24 h time period, although up to four patches have been studied and found to be well tolerated. The patch should be used with caution in severe hepatic disease, or in those taking anti-arrhythmic or local anesthetic drugs.

For topical NSAIDs, the appropriate amount should be measured using a dosing card supplied in the drug carton, 2 g for the elbow, wrist, hand, and 4 g for the knee, ankle, and foot, not to exceed 32 g/day, over all affected joints.

For topical Capsaicin, the recommended dose is a single 60 min application of up to four patches, which is repeated every 3–4 months as needed for maintenance pain control. Pre-treatment with a topical anesthetic can be performed to reduce initial increase in pain from application of the patch.

Acetaminophen

Mechanism of Action

Acetaminophen is a synthetic analgesic derived for *p*-aminophenol, which has a short action centrally, through the spinal cord and cerebral cortex, with weak central inhibition of prostaglandin synthetase, but also activation of the endocannabinoid system and spinal serotonergic pathways [20]. Additionally, it raises the pain threshold through inhibition of nitric oxide, which is mediated by neurotransmitters including NMDA and substance P. Acetaminophen is also antipyretic.

Efficacy

Acetaminophen is likely the most commonly used medicine for analgesia and is considered first-line therapy for treating the pain of osteoarthritis. It is used in combination with opioid drugs, which include codeine, dihydrocodeine, hydrocodone, oxycodone, and pentazocine, as well as with tramadol. Because acetaminophen is an effective antipyretic, it is used in preparations to treat any clinical state in which fever may be present, including upper respiratory and urologic infections. It is also used in combination products for insomnia, cold, flu, menstrual cramps, and sinus congestion.

Side Effects

Concerns over hepatotoxicity with potential for overdose, which is unintentional in 50% of cases, have led the FDA to enforce a reduced dose per tablet; hepatoxicity is unlikely in doses below 4 g/day [21, 22]. Acetaminophen has been linked to elevation in INR with warfarin treatment [23]. Associations between acetaminophen and renal cancer [24], childhood asthma [25], and changes in blood pressure [26] have been postulated but not substantiated.

Dosage

For analgesia, the conventional dose is 325–650 mg PO every 4–6 h until pain or fever is relieved, with a 4000 mg PO daily considered to be the maximum safe dose in adults and 3000 mg PO daily in the elderly, and a limit of 2000 mg/day PO with hepatic disease. Parental usage of acetaminophen is not widely used in the US, but can be especially helpful in postsurgical pain for its opioid sparing effects [27]. Preoperative administration reduces postoperative nausea and vomiting if given prophylactically at induction of anesthesia [28].

NSAIDS

Aspirin

Mechanism of Action

Also called acetylsalicylic acid, aspirin is a broad-spectrum inhibitor of prostaglandins, which have a variety of effects including sensitization of nociceptors. It is ten times more potent as a COX inhibitor than its metabolite salicylic acid. When a single dose is given, COX-1 activity is blocked irreversibly as is the body's thromboxane synthesis for several days.

Efficacy

Because it is rapid acting, it is very effective for short-term pain complaints, which include headache. Aspirin is comparable to acetaminophen for being the most ubiquitous and widely used over-the-counter pain reliever. Aspirin is also used for prophylaxis of myocardial infarction and cerebrovascular accident.

Side Effects

In a subset of patients with asthma, nasal polyps, and/or urticaria, which is also known as Franklin's triad, exposure to aspirin can lead to anaphylaxis, causing contraction of the bronchioles, laryngeal edema, hypotension, and even death. Aspirin binds irreversibly to platelets, which can effect bleeding time for up to 3 weeks. The most common adverse effect is GI upset. Serious side effects include the following: ringing in the ears; loss of hearing; hives or rash; swelling of the eyes, face, lips, tongue, or throat; wheezing or breathing difficulties; hoarseness; fast heartbeat or fast breathing; cold, clammy skin; bloody vomit or vomit that looks like coffee grounds; bright red blood in stools or black or tarry stools. Because of the high risk of bleeding, use of aspirin for analgesia has largely been abandoned.

Dosage

Aspirin is typically taken every 4–6 h to treat fever and pain. It is usually taken once a day to lower the risk of a heart attack or stroke. Typical dosages range from 50 to 6000 mg, QD.

Non-Asprin NSAIDS

Mechanism of Action

Non-aspirin NSAIDs act directly on spinal nociceptive processing to inhibit cyclo-oxygenase (COX) activity, of which there are two isoforms, COX-1 and COX-2. Various NSAIDs inhibit the isoforms differently with an overall goal of inhibiting COX-2, while preserving COX-1 as GI upset is reduced by homeostasis of the COX-1 system. There are two relatively selective COX-2 inhibitors on the market, which include celecoxib and meloxicam. Previous selective COX-2 inhibitors valdecoxib and rofecoxib were voluntarily removed from the market in 2004 and 2005, respectively, related to cardiovascular complications. Additional central mechanisms for their action have also been demonstrated.

Efficacy

The efficacy of NSAIDs in both acute and chronic pain is well established. There is no difference in analgesic efficacy between non-selective (nNSAIDs) and selective (Coxibs). In addition to their adjuvant effects with other analgesics, NSAIDs also have an opioid sparing effect up to 35%; however, a 2011 Cochrane review on the efficacy of using NSAIDs with opioids for the treatment of cancer pain concluded that there was not a significant clinical difference between using either medication alone or combining them in the short term [29, 30]. There have not been enough studies to determine combined efficacy for long-term use. NSAIDS have been found to be effective in the treatment of chronic low back pain and chronic osteoarthritis pain [31, 32]. There is some evidence that NSAIDS are effective in lumbar radiculopathy but generally not found to be effective in neuropathic pain [33]. Parenteral forms have been used to manage postoperative pain. Rapidly dissolving formulations are useful for acute pain, but not for arthritis. Unless contraindicated, NSAIDs should be used as standard therapy for both pain and fever reduction.

Side Effects

Like aspirin, the most common side effect is GI upset. Under recognized kidney dysfunction is not uncommon. NSAIDS used in combination with acetaminophen has been associated with both liver dysfunction as well as acute and chronic kidney failure. Because of concerns over its effect on the cardiovascular system, the American Pain Society's updated guidelines in 2008 recommended that Celecoxib be used rarely and only in highly selected patients. Despite good data, confusion still exists over the safety of nNSAIDs and Coxibs.

Dosage

The starting doses are individualized based on the formulation and elimination half lives and range from once daily to three times daily. New preparations of old compounds include ketorolac nasal spray, recently approved by the FDA [34]. Other developments include preparations to mitigate the risks of NSAIDS, including nano formulations of diclofenac [35] and indomethacin [36], as well as injectable diclofenac sodium solubilized with hydroxypropyl-beta-cyclodextrin, with proven efficacy at significantly reduced doses [37].

Anticonvulsant Drugs

Mechanism of Action

Anticonvulsant drugs inhibit neuronal hyperactivity along pain pathways with several mechanisms of action, which include GABAergic and glutamatergic neurotransmission, alteration of voltage-gated ion channels, and alteration of intracellular signaling pathways. These drugs provide pain relief by modulation of neuronal sensitization to primarily treat neuropathic pain, but have also been used for other disorders characterized by sensitization of the central nervous system, including fibromyalgia and migraine headache.

Efficacy

Randomized controlled trials have demonstrated the efficacy of carbamazepine and gabapentin for neuropathic pain, pregabalin for neuropathic pain and fibromyalgia, and topiramate for migraine headaches. Initially, gabapentin and pregabalin were indicated for neuropathic pain of various origins [38], but there are now good data that these drugs are effective in postherpetic neuralgia [39], diabetic polyneuropathy [40], and central pain after spinal cord injury [41]. Through the concept of central sensitization, fibromyalgia is also an indication in some countries [42]. Furthermore, with their effect on neuropathic pain and reduction in central sensitization, these drugs have also been used more in acute pain indications [43, 44], as well as in burn-related pain [45].

Carbamazepine

Carbamazepine blocks ion conductance of frequency-dependent neuronal activity, but does affect normal nerve conduction. It suppresses A-delta and C-fiber to decrease pain. It was the first anticonvulsant to be used to treat trigeminal neuralgia (TN) [46], not seizure treatment, and is now considered first-line therapy for the

treatment of pain from TN. It is also considered useful for glossopharyngeal neuralgia [47]. Common adverse events include gait disturbance/ataxia, sedation, dizziness, and possible hematopoietic effects and hyponatremia, which generally necessitate monitoring and make it difficult to administer at times.

Gabapentin

Gabapentin acts thorough modulation of the alpha-2-delta subunit of N-type calcium channels and works on the supraspinal level at the locus coeruleus. It is effective for the treatment of painful diabetic neuropathy and is FDA-approved to treat postherpetic neuralgia. It is considered the first choice for most neuropathic pain conditions due to ease of use, tolerability, safety profile, and lack of interaction with most other medications. Common adverse events include sedation, ataxia, dizziness, and peripheral edema. Effective doses range from 300 to 3600 mg/day in divided doses.

Pregabalin

Pregabalin is a calcium channel-modulating drugs that reduces neurotransmitter release by binding to the alpha-2-delta subunit of N-type calcium channels, like gabapentin. It is FDA-approved for the treatment of painful diabetic peripheral neuropathy, neuropathic pain secondary to spinal cord injury, postherpetic neuralgia, and fibromyalgia. Common adverse events include sedation, dizziness, peripheral edema, and weight gain. Effective doses range from 150 to 600 mg/day in divided doses.

Topiramate

Topiramate blocks voltage-dependent sodium channels, increases GABA-A, blocks AMPA/kainite glutamate receptors, and inhibits carbonic anhydrase. It is FDA approved for migraine prophylaxis. Common adverse events include anorexia, weight loss, paresthesias, dizziness, sedation, nervousness, and memory changes. Effective doses range from 100 to 400 mg/day in divided doses.

Others

Lamotrigine has been studied in a variety of populations, with mixed results. Positive trials were reported with HIV-related neuropathy, trigeminal neuralgia, and central poststroke pain, however studies were not ideal [48]. Lacosamide is an anticonvulsant with sodium channel antagonism studied in multiple RCTs in painful diabetic neuropathy with limited efficacy [49]. Topirimate (above) and valproic acid have had mixed results with neuropathic pain [50].

Botulinum Toxin

Mechanism of Action

Botulinum toxin, which includes a family of neurotoxins with seven serotypes (A to G) and produced by the bacteria Clostridia botulinum, acts presynaptically at the neuromuscular junction to prevent release of acetylcholine by binding irreversibly to the presynaptic membranes of the acetylcholine. It is thought that inhibition of glutamate, substance P, and calcitonin-related peptide, which results in decreased afferent nociceptive transmission is also involved and that this is independent of acetylcholine release inhibition [51]. Only types A and B are available for clinical use.

Efficacy

In the US, four botulinum toxins are approved by the FDA for clinical use. There are three types of A toxins, which include Botox, Xeomin, and Dysport. There is one type B toxin, which includes Myobloc. Numerous publications and evidence-based reviews have demonstrated both the efficacy and safety of the botulinum type A toxins for the management of spasticity. As of 2013, only Botox is approved for the treatment of upper extremity spasticity. Botulinum toxin type A is approved for the treatment of blepharospasm, strabismus, torticollis, and hemifacial spasm. Additionally, botulinum toxin type A has FDA approval for chronic migraine headache, for which a reduction in the number and severity of headaches has been shown, with mixed results in tension-type, cluster, and chronic daily headaches [52]. Botulinum toxin type B has approval for cervical dystonia. Recent studies reveal insufficient evidence to support use in either myofascial or musculoskeletal pain [53, 54].

Side Effects

Adverse effects include weakness, cramping, hematoma, bruising, swelling, flu-lied syndrome, dysphagia, nerve trauma, and pain. The FDA has issued a black box warning on all botulinum toxins with respect to the risk of toxin spread beyond injection site. Use with an aminoglycoside or spectinomycin antibiotic should be pursued with caution. Using botulinum toxin with pre-existing neuromuscular disease, myasthenia gravis, Lambert Eaton Syndrome, peripheral neuropathic disease predisposes patients to severe reaction, which can include dysphagia or respiratory depression. Corneal exposure or laceration can occur when used to treat blepharospasm.

Dosage

Units of the botulinum toxins are not interchangeable and the dosing for each is unique. There is no direct formula for conversion of doses between the different toxins. With Botox, 1–12 units/keg are used, depending on the size of the muscle with 50 units per site, with an initial safe dose of 400 units in total. The onset of action occurs within 24–72 h, and the peak effect occurs within 4–6 weeks. Injections should be performed no more frequently than every 3 months, which can subsequently decrease antibody formation.

Sodium Channel Antagonists

Mechanism of Action

Blockade of the sodium channel prevents upstroke of the axonal action potential, which can result in pain relief if blockade occurs at pain-sensitive sensory neurons. There are seven or more sodium channels in the human body, which are classified by their sensitivity to tetrodotoxin (TTX), all with different sensitivities to sodium channel antagonists.

Efficacy

Systemic sodium channel blockers have been shown to decrease postoperative pain and analgesic requirements in a few studies, with conflicting results for use with neuropathic pain.

Lidocaine

Lidocaine has been studied in experimental, postoperative, and neuropathic pain. At maximal tolerable doses (3 μg/mL), lidocaine reduces postoperative and neuropathic pain, but has little effect on human experimental pain, with sub-anesthetic doses of systemic lidocaine providing relief in diabetic nerve pain, neuropathic pain states, and cancer. Lidocaine dose is 2 mg/kg administered over 20 min, followed by 1–3 mg/kg/h, which is titrated to effect.

Mexiletine

Mexiletine is a bioavailable analog of lidocaine, given orally. Early reports found it to be effective in neuropathic pain, including painful diabetic neuropathy, alcoholic neuropathy, peripheral neuropathy/nerve injury, and central thalamic pain; however, later reports dispute its efficacy with neuropathic pain, and as such, are rarely used. The maximal tolerable dose is 900 mg/day, but it is questionable if this dose results in analgesic plasma levels, and dose-limiting side effects occur at lower plasma concentration than analgesia.

Lamotrigine

Lamotrigine is a sodium channel blocker that also has activity at glutaminergic sites, giving it an anticonvulsant effect. It has been shown to decrease acute pain and reduces analgesic requirements of postoperative pain. Efficacy is based on dose, and doses in the range of 200–400 mg/day have been efficacious in neuropathic pain. Side effects are minimal.

Procaine

Procaine was one of the first local anesthetics to be used systemically for pain and was initially used to supplement general anesthesia and to treat musculoskeletal pain. There is limited evidence for its use in postherpetic neuralgia and one study that shows efficacy in postoperative pain using 4–6.5 mg/kg. Procaine has very little toxicity when delivered systemically, but has a very short half-life.

Flecainide

This rarely used drug has been shown to suppress ectopic nerve discharge in neuropathic rats, with mixed clinical utility. Efficacy was shown in postherpetic neuralgia but not in a pilot study on cancer pain.

Calcium Channel Antagonists

Mechanism of Action

Calcium channel antagonists block the N-type calcium channel in the superficial dorsal horn to modulate membrane excitability and inhibit neurotransmitter release, which results in pain relief. There are six calcium channel subtypes throughout the nervous system, including the following: L, N, P, Q, R, and T.

Efficacy

The N-type calcium channel blockers have the greatest analgesic efficacy; L-type have moderate analgesic efficacy; P and Q types have minimal analgesic efficacy. Only the N-type has efficacy on painful and non-painful acute thermal and mechanical thresholds, which suggests a greater analgesic potency than sodium channel antagonists.

Ziconatide

Ziconatide is a 25-amino acid peptide, a synthetic version of a peptide found in the venom of the marine snail, Conus Magus, which specifically and selectively binds presynaptically to the N-type voltage-sensitive calcium channels, resulting in decreased neurotransmitter release. Phase III trials have shown a decrease in postoperative pain when delivered epidurally or intrathecally, and have been shown to be effective in the treatment of neuropathic pain intrathecally. Two studies, including one for cancer-related pain and one for non-cancer-related pain, showed a significant reduction in pain [55, 56]. Adverse effects include dizziness, nausea, gait ataxia, confusion, nystagmus, constipation, which are dose-related and quickly reversible by decreasing or discontinuing the drug. The drug has a narrow therapeutic window, in the range of 1–3 μg/day. It can be used with other intrathecal drugs, has no lethal dose, and has no withdrawal syndrome upon abrupt cessation.

Nimodipine/Verapamil

Nimodipine is a L-type calcium channel antagonist that has been shown to decrease postoperative opioid requirements, decrease morphine requirements in cancer patients who require morphine dose escalation, and to prevent and treat migraine as well as chronic daily headache.

Tramadol

Mechanism of Action

Tramadol is a synthetic 4-phenyl-piperidine analog of codeine. Although its action is not completely understood, it is thought to work in the CNS and differs from opioids in that analgesia is only partially blocked by the antagonist naloxone, suggesting an additional non-opioid component. Tramadol binds weakly to the mu-opioid receptor and inhibits reuptake of both norepinephrine and serotonin [57]. It has an affinity for the mu-opioid receptor 1/6000 that of morphine and 1/10 that of codeine.

Efficacy

The WHO recommends tramadol as a second step agent used for malignant pain, osteoarthritic pain, low back pain, painful diabetic neuropathy, fibromyalgia, restless legs syndrome, postherpetic neuralgia, postsurgical or dental pain, and in conjunction with NSAIDs for breakthrough pain. Tramadol has shown benefit in three RCTs investigating diabetic peripheral neuropathy and mixed neuropathic pain, with less constipation than other weak opioid analgesics [50].

Side Effects

Adverse side effects can be intolerable in up to 30% of patients, which include nausea, vomiting, constipation, dizziness, and lethargy. The two most significant side effects include seizure and potentiation of the serotonin syndrome. Seizure risk is increased when tramadol is taken with other psychoactive drugs or in patients with a history of seizures/epilepsy, head trauma, alcohol, or drug withdrawal. Seizures can be treated with benzodiazepines or barbiturates. Serotonin syndrome can develop when tramadol is given with SSRI, SNRI, or MAOI drugs, all of which can increase serotonin levels, especially in the elderly [58].

Dosage

For the average healthy adult, dosages range from 50 to 100 mg every 6 h, not to exceed 400 mg/day depending on the chronicity and severity of pain. Dosage adjustment is recommended for the elderly, not to exceed 300 mg/day. Advanced liver disease prolongs the drug's half-life, and dose should not exceed 100 mg/day. For immediate release tablets, in adults, start with 50–100 mg every 4–6 h as needed. For extended-release tablets, in adults, start with 100 mg once a day, usually not more than 300 mg/day.

Tapentadol

Mechanism of Action

Tapentadol is a newer centrally acting analgesia with a dual mechanism of action, which includes mu opioid reuptake inhibition and norepinephrine reuptake inhibition [30, 59]. It is a unique class of analgesic drug, registered for use in moderate to severe pain unresponsive to conventional non-opioid medication. It has a much lower affinity to the mu receptor than morphine, but analgesia only one-third less than

morphine, which is in part due to its inhibitory effect on norepinephrine reuptake and subsequent augmentation of descending inhibitory pathways of pain control [59].

Efficacy

A review of 42 trials comparing tapentadol with oxycodone and other opioids shows comparable efficacy in moderate to severe pain and reduced GI upset, as compared to fentanyl, hydromorphone, morphine, ocymorphone, and oxycodone [60]. A meta-analysis shows better outcomes for tapentadol as compared to oxycodone [61].

Dosage

For immediate release tablets, the initial dose should be 50, 75, or 100 mg PO, Q 4–6 h depending on pain intensity. The maximum dose should be 600 mg/day. For extended-release tablets, the initial dose should be 50 mg PO BID, with a maximum dose of 500 mg/day.

Local Anesthetics

Mechanism of Action

Local anesthetics (LA) block the propagation of action potentials at the sodium channel in a reversible fashion, in peripheral, central, spinal (intradural and extradural), or epidural nerves. They are divided into **amide** (lidocaine, mepivacaine, prilocaine, bupivacaine, ropivacaine, and levo-bupivacaine) and **ester** (procaine, chloroprocaine, tetracaine) LA. In neuraxial administration, blockade of both sodium and potassium channels in the dural horn inhibits propagation of nociception and also inhibits release of substance P by presynaptic inhibition. An in-depth understanding of the neuroanatomy in electrophysiology and physical chemistry of LA is critical before using local anesthetics, but is beyond the scope of this chapter. A detailed discussion of each specific amide or ester local anesthetic can be found in any standard textbook of anesthesiology [62, 63].

Efficacy

The efficacy of LA is dependent on multiple factors, including the minimum blocking concentration, which is the dose of LA that effectively stops nerve impulse propagation, as well as additives to LA, and others. An in-depth discussion is also out of the scope of this chapter.

Side Effects

CNS toxicity is dose-dependent and is thought to be secondary to injury to Schwann cells, inhibition of fast axonal transport, and disruption of the blood–brain barrier. Toxicity can present as circumoral numbness, facial tingling, slurred speech, restlessness, and tonic–clonic seizures, all of which can increase in medical conditions including acidosis, arterial hypoxemia, increased cerebral perfusion, or decreased protein binding. Because local anesthetics are CNS depressants, depression of cortical inhibitory neurons may lead to seizure activity.

The cardiovascular system (CVS) is affected less often than the CNS because the CVS can better tolerate the effects. Lidocaine toxicity is manifest by hypertension, bradycardia, and hypoxia. Bupivacaine toxicity is manifest by sudden cardiovascular collapse and ventricular dysrhythmias. Cardiac toxicity is a reflection of blockade of sodium channels, which can impair cardiac conduction and automaticity and is seen on electrocardiogram by widening of the QRS complex and prolongation of the PR interval. Because bupivacaine has a stronger affinity for resting and inactive sodium channels, it dissociates slowly from sodium channels. Administration of 20% intravenous lipid can be used for sudden cardiac collapse [64].

Dosage

Local anesthetics with different potency use are commonly used in regional anesthesia and pain medicine. Dosages are dependent on the different LA used in its specific application, and are beyond the scope of this chapter. However, the maximum recommended dose of common anesthetics is as follows: Bupivacaine (without Epinephrine) 2.5 mg/kg, not to exceed 175 mg; Lidocaine (without Epinephrine) 4.5 mg/kg, not to exceed 300 mg; Ropivacaine 5 mg/kg, not to exceed 200 mg; Procaine 7 mg/kg, not to exceed 350–600 mg [64].

Monoclonal Antibodies

Although no agents are specifically approved for pain, several agents are approved for rheumatoid arthritis (RA), with a secondary effect of pain reduction. These agents include anti-TNF agents and one anti-IL6 antibody. Please see section on “DMARDS”.

Alpha-2 Agonists

Mechanism of Action

Alpha-2-adrenergic activation represents an inherent pain control system of the central nervous system, with alpha-2-adrenergic receptors found in the substantia gelatinosa of the dorsal horn and the brain. The dorsal horn is the apparent site where these medications work to inhibit somatic pain.

Efficacy

Alpha-2 agonists are mostly used for acute pain, with the exception of tizanidine [65].

Clonidine

Applications routes of Clonidine include intravenous, intrathecal, epidural, oral, transcutaneous, and perineural. Systemic administration reduces opioid requirements postoperatively. Intrathecal administration works synergistically with morphine. Perineural administration can increase the duration of local anesthetics.

Dexmedetomidine

Dexmedetomidine has been used for sedation during surgery and in the postoperative period, with better selectivity than clonidine. Although not widely studied for pain, there is evidence to suggest an opioid-sparing effect in postoperative pain, with limited evidence for reducing intensity of pain.

Tizanidine

Tizanidine reduces spasticity by increasing presynaptic inhibition of spinal cord motor neurons, which has intrinsic analgesic activity as well. Please see section below on “Muscle Relaxants”.

Side Effects

Alpha-2 agonists have opioid sparing effects with significant sedation but without respiratory depression. They also exhibit bradycardia and hypotension, which can be limiting [65].

Dosage

For intravenous sedation and analgesia, clonidine can be given with a bolus dose of 3 μg/kg, followed by a continuous infusion of 0.3 μg/kg/h. For reduction in the need for both intra-operative and postoperative analgesics in adults, intravenous Dexmedetomidine can be given with a bolus dose of 0.5–1 μg/kg, with or without continuous infusion of 0.5–2 μg/kg/h.

Calcitonin

Mechanism of Action

Calcitonin is a polypeptide hormone, which is produced naturally but the parafollicular cells of the thyroid gland [66].

Efficacy

Efficacy has been shown in chronic pain states in older studies, which have been confirmed by more recent studies, including short-term course of calcitonin in later stages of CRPS [67], chronic phantom limb pain after amputation [67, 68], and acute pain from osteoporotic vertebral compression fractures [69].

Side Effects

Common side effects of Calcitonin may include rhinorrhea, epistaxis, nasal irritation, dry nose with crusting, headache, dizziness, nausea, vomiting, anorexia, stomach pain, flushing of the face (warmth, redness, itching, or tingly feeling under your skin), skin rash or itching, and increased urination.

Dosage

Calcitonin in a dose of 50–100 IU daily, which can be given either subcutaneously or intra-nasally, should be considered in all patients with serious pain secondary to acute vertebral fractures for both symptom relief and facilitation of mobility.

Cannabinoids

Mechanism of Action

Cannabinoids act on two receptors: CB1, which are located in the brain, spinal cord, and on primary sensory nerve terminals, and CB2, which are located on microglia, macrophages, monocytes, B lymphocytes, and T lymphocytes. Activation of CB1 receptors decreases transmission of pain. Activation of CB2 receptors decreases sensitization of afferent terminals, plasma extravasation, and inflammatory cell mediator release. Derivatives of the cannabis plant have been used anecdotally for anorexia, insomnia, pain, nausea, and others for more than 5000 years [70]. The primary component is delta-9-tetrahydrocannabinol, but there are at least 85 different cannabinoids exhibiting a variety of effects, the two most relevant of which include cannabidiol (CBD) and cannabinol (CBN) [70].

Efficacy

Peripheral cannabinoid anti-nociceptive mechanisms may prove to be effective as anti-hyperalgesic and anti-allodynic effects of locally delivered drug have been seen at doses that are otherwise not effective systemically. Clinical trials studying the effects of inhaled cannabis have shown efficacy in receiving chronic pain. Specifically, there is increasing evidence of efficacy in central neuropathic pain states [50]. There have been at least seven high-quality studies investigating neuropathic pain, and all but one were positive [71]. Trials have been performed on two cannabis-based extracts, Cannador and Sativex, which is an oral capsule and sublingual spray, respectively. Two synthetic cannabinoid compounds are available commercially, which include dronabinol and nabilone. Both have had mixed results in treating chronic pain.

Side Effects

The main psychoactive compound in cannabis is delta-9-tetrahydrocannabinol, which is responsible for its psychoactive side effects.

Dosage

This is highly variable and dependent on patient and disease state. Because it is a drug of abuse, chronic opioid therapy can be applied to use of cannabinoids. Clinicians should be responsible to educate patients on marijuana safety and efficacy, and to counsel patients on the responsibilities, with appropriate follow-up to assess efficacy and side effect. Not allowing concomitant administration with an opioid should be strongly considered [72].

Disease-Modifying Anti-Rheumatic Drugs (DMARDS)

Mechanism of Action

DMARDS are the mainstay of pharmacotherapy for rheumatoid arthritis (RA) and include biological and non-biological types. *Non-biologic DMARDS* include the following agents: Hydroxychloroquine, Sulfasalazine, Methotrexate, Leflunomide, Cyclosporine, Gold (IM/PO), and Azthioprine. *Biologic DMARDS* include the following: *Anti-tumor necrosis factor (TNF) agents* (etanercept, infliximab, adalimumab); *Co-stimulation modulators* (abatacept); *Anti-B-cell antibodies* (rituximab); *Interleukin (IL)-1 receptor antagonists* (anakinra); *Interleukin (IL)-6 antagonists* (tocilizumab); *Protein kinase inhibitors* (tofacitinib) [73, 74].

Efficacy

The drugs are typically added early on with rheumatoid arthritis and are frequently used in combination with other DMARDS. The use of DMARDS for RA, psoriatic arthritis (PsA), and ankylosing spondylitis (AS) has led to improvement in pain, with most studies showing improvement in pain with initiation of non-biologic DMARDS for RA and PsA [73]. Sulfasalazine is the only agent to decrease pain in AS.

Side Effects

The safest non-biologic agents are Hydroxychloroquine and Sulfasalazine, which can cause retinopathy or hyperpigmentation, and myelosuppression or GI disturbances, respectively. The other agents have a more toxic profile, which includes myelosuppression, hepatotoxicity, pulmonary involvement, renal dysfunction, and more.

The biologic DMARDS have the following adverse effects: TNF agents (infection, demyelinating disease, autoimmunity, malignancy, exacerbation of CHF); Co-stimulation modulators (infection, exacerbation of COPD); Anti-B-cell antibodies (infection, death, progressive multifocal leukoencephalopathy); IL-1 antagonists (injection site reaction, infection); IL-6 antagonists (transaminitis, leucopenia, thrombocytopenia, hyperlipidemia, infection, bowel perforation); Protein kinase inhibitors (leucopenia, anemia, transaminitis, hyperlipidemia, bowel perforation, infection) [73, 74].

Dosage

Dosages are highly variable based upon the agent and severity of disease.

CNS Stimulants

Mechanism of Action

All stimulants work by increasing dopamine levels in the brain. Dopamine is a neurotransmitter that is associated with pleasure, movement, and attention. The therapeutic effect of stimulants is achieved by slow and steady increases of dopamine, which are similar to the way dopamine is naturally produced in the brain. *Amphetamines* stimulate the release of catecholamines in the CNS that may result in analgesia. *Caffeine* has an additive analgesic effect when used with aspirin and acetaminophen, and is used in several pain syndromes, which include headache, postoperative pain, and cancer [75].

Efficacy

Amphetamines are co-administered with opioids to treat opioid-related sedation and to enhance the opioid analgesic effect and are sometimes used to treat depression [76].

Side Effects

Effects of stimulant use include increased alertness, wakefulness and endurance, with subsequent increase in productivity, motivation, and arousal. Stimulants can lead to increased heart rate, blood pressure, and body temperature; nausea; visual disturbance with blurred vision; and muscle spasms. Stimulant overdoses can result in heart problems, strokes, convulsions and, if not treated immediately, death. The long-term effects of stimulant use can include addiction paranoia, aggression, problems thinking, anorexia, visual and auditory hallucinations, delusions, and severe dental problems.

Dosage

Stimulants generally follow dose–response curve and are not effective until the dosage reaches a specific level for a patient's specific need. For safety, it is always best to start with a low dosage and then slowly and carefully titrate upward over 4–8 weeks until a therapeutic effect is reached. Stimulants can be given on their own set schedule, such as BID or TID, or they can be simultaneously given with an opioid dosage.

Corticosteroids

Mechanism of Action

Corticosteroids directly inhibit C-fiber neuronal membrane excitation and induce synthesis of a phospholipase-2 inhibitor, which prevents release of substrate for prostaglandin synthesis. They provide pain relief through direct analgesia, reduction in inflammation, and modulation of pain transmission pathways. Long-term pain reduction may be secondary to changes in gene expression [77].

Efficacy

Corticosteroids reduce pain from inflammatory conditions, arthritis, and complex regional pain syndrome. There is no evidence to support their use in radiculopathy [78].

Side Effects

Adverse effects are seen more commonly with systemic administration, as compared to topical or injectable formulas, which include insomnia, increased appetite, hypertension, hyperglycemia, osteoporosis, immune suppression, myopathy, and Cushing's syndrome. Dexamethasone, methylprednisolone, triamcinolone, and betamethasone have scant mineralocorticoid activity. The enhanced glucocorticoid activity of betamethasone and dexamethasone lead to more hyperglycemia, as compared to the others.

Dosage

Dosages are variable depending on steroid used and mode of administration. The relative potency and equivalent dose of steroid preparations available for commercial use is as follows: Betamethasone 25–30 mg potency, 0.6 mg equivalent dose; Methylprednisolone 5 mg potency, 4 mg equivalent dose; Triamcinolone acetonide 5 mg potency, 4 mg equivalent dose; Dexamethasone sodium phosphate 25–40 mg potency, 0.75 equivalent dose.

Muscle Relaxants

Mechanism of Action

Muscle relaxants can be classified as either *antispasmodic* or *antispasticity* agents. These agents act at several different sites, which include the following: (1) direct effect on skeletal muscle fibers (dantrolene); (2) polysynaptic reflexes (benzodiazepines, baclofen, tizanidine); (3) descending facilitatory systems (benzodiazepines). Currently, only four oral medications are approved by the FDA to treat spasticity from a CNS disorder: baclofen, tizanidine, dantrolene, and diazepam [79–81].

Efficacy

The use of these agents is limited to the treatment of acute muscular problems. Placebo-controlled trials reveal short-term efficacy in the treatment of low back pain. The use of these agents chronically is controversial given the lack of data and potential for abuse and dependency. Systemic medications provide the greatest benefit in mild–moderate, generalized spasticity. They reduce tone and pain, but do not directly improve function.

Baclofen

Baclofen acts as a GABA agonist at GABA-B receptors on the spinal cord to inhibit evoked release of excitatory amino acids. It may also reduce substance P in the spinal cord, contributing to decreased pain. It is indicated for the treatment of spasticity secondary to spinal cord injury and multiple sclerosis, with a greater effect on lower extremity tone than upper extremity tone. Adverse effects are mild and include sedation, weakness, lowered seizure threshold, GI upset, tremor, insomnia, and confusion. Doses range from 15 to 80 mg/day in divided doses [82].

Tizanidine

Tizanidine is a centrally acting alpha-2-agonist, similar to clonidine, which reduces spasticity by increasing presynaptic inhibition of motor neurons in the spinal cord. It may reduce pain secondary to an alpha-2 adrenergic agonist effect. It is indicated for the treatment of spasticity from spinal cord injury, multiple sclerosis, and acquired brain injury. Clinical trials have found tizanidine to be as effective as oral baclofen or diazepam but with a better tolerability. Adverse effects are mild and include sedation, hypotension, dry mouth, bradycardia, dizziness, and potential for hepatotoxicity. Doses range from 2 to 4 mg QHS to 36 mg/day in divided doses [82].

Dantrolene

Dantrolene is the only antispasticity agent with a peripheral site of action, which acts at the level of the muscle, by blocking the release of calcium from the sarcoplasmic reticulum to reduce extrafusal muscle fiver strength and muscle spindle contraction. Dantrolene is the preferred agent for spasticity of cerebral origins including CVA, CP, and TBI as its use in SCI and MS is potentially limited by weakness. Adverse effects include hepatotoxicity, sedation, weakness, fatigue, GI disturbance, and paresthesias. Doses range from 50 to 400 mg/day in divided doses [82].

Diazepam

Diazepam has its antispasmodic effect by neuronal inhibition secondary to postsynaptic GABA-A activity at the spinal cord level, but acts diffusely throughout the neuraxis to increase presynaptic inhibition and to reduce mono- and poly-synaptic reflexes. Diazepam has demonstrated benefit in spasticity from SCI and MS. Adverse effects include sedation, memory impairment, and decreased REM sleep. This drug should not be used in TBI because of its adverse effects on attention and memory. Doses range from 2 mg BID to 60 mg/daily in divided doses [82].

Other Agents

Centrally acting muscle relaxants include metaxalone, methocarbamol, orphenadrine, cyclobenzaprine, carisoprodal, and chlorzoxazone, which have mechanisms of action poorly understood, but may work by inhibition of interneuronal activity in the descending reticular formation and spinal cord. No evidence suggests that one agent is superior to the other. Cyclobenzaprine has a structure which is analogous to the TCAs. Carisoprodal is metabolized to meprobamate, which is a scheduled potential drug of abuse [80–82].

NMDA Receptor Antagonists

Mechanism of Action

These agents block glutamate action at NMDA receptors, which are calcium channels for which glutamate is the natural ligand. This channel has been associated with central sensitization, which has been associated with the development and maintenance of chronic pain [83]. The dissociative anesthetics ketamine and phenylcyclidine provide analgesia at sub-anesthetic doses. Ketamine reduces the level of sensitization by modulating the "wind up" process, with other sites of action including nicotinic, muscarinic, opioid, AMPA, and Kainite receptors, with inhibition of serotonin, dopamine, and down regulation of certain ion channels [5]. Amantadine has the same mechanism of action as ketamine.

Efficacy

Ketamine was originally introduced in 1963 as a dissociative anesthetic, the use of which has been gaining favor in the setting of pain management, as well as acute and chronic pain states [84]. Use of Ketamine for chronic pain has been limited by parenteral administration, but Ketamine has proven benefit for terminal cancer pain, especially in an opioid tolerant patient. It is also used in postoperative pain for its opioid sparing effect and decrease in postoperative nausea. It has also shown benefit in complex regional pain syndrome [85]. Amantadine, which is better known for its antiviral, dopaminergic, mildly anticholinergic, and glutamate receptor blocking effect, has been shown to decrease neuropathic pain in cancer patients.

Side Effects

Use has been limited due to the parenteral route of administration (ketamine and phenylcyclidine) and narrow therapeutic window with significant psychomimetic side effects.

Dosage

Dosages are variable per drug. For ketamine, an initial infusion of 10 μg/kg/min after a bolus of 0.5 mg/kg has been shown to decrease postoperative morphine requirements.

Conclusions

Pharmacological management of pain should be multimodal, but one of many options used in multidisciplinary management of pain. Medications should be introduced in a stepwise fashion, with careful attention to available research, when applicable. With an increasing understanding of the individual differences in perception of pain and an appreciation of the multifactorial nature of pain, the future is bright in terms of individualized pharmacologic control of pain.

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Chapter 29
Basic Psychopharmacology for the Treatment of Pain in the Rehabilitation Patient

Timothy J. Bunton, Peter Breslin, and Zia Uddin

Chronic pain and depression are multifaceted diseases in which patients suffer from both emotional and physical symptoms. Many patients who suffer from chronic pain also struggle with depression and/or anxiety as well. These mood disorders can in turn increase both the sensitivity to and perception of pain, further exacerbating the chronic pain issues. Psychotropic medications can serve multiple roles in treatment as they can simultaneously alleviate pain and treat underlying mood disorders, thereby increasing patients' abilities to tolerate any residual pain.

Tricyclic Antidepressants

Studies have clearly demonstrated that TCAs have analgesic properties separate from their benefit on anxiety and depression, which are commonly found comorbidly. The analgesic mechanism of action of TCAs has been seen through its effect on serotonin, norepinephrine, opioid, NMDA, and adenosine receptors. TCAs with the greatest effect on serotonin have been shown to have the strongest analgesic effect, as has been shown in numerous studies involving amitriptyline. In general, the therapeutic effects of TCAs on pain are seen more rapidly, at lower serum blood levels, and at lower therapeutic doses as compared to when treating for depression or anxiety.

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Table 29.1 Tricyclic and tetracyclic antidepressants

Medication	Dose range (mg)	Anticholinergic	QTc prolongation	Weight gain
Amitriptyline	10–300	++++	+++	++++
Amoxapine	50–400	++	ND	++
Clomipramine	25–300	++++	++	++++
Desipramine	10–300	+	+++	+
Doxepin	10–300	+++	+++	++++
Imipramine	10–300	+++	+++	++++
Nortriptyline	10–200	++	+++	+
Protriptyline	10–60	++	NA	+

Scale: 0 is none and ++++ is high; ND is no data available

Dosing and Safety

With the exception of clomipramine (25 mg initial dose) and amoxapine (50 mg initial dose), doses of TCAs begin at 10 mg and can be increased by 10–25 mg/week until an adequate therapeutic dose is met. Lower doses are effective in targeting pain symptoms, while minimizing the side effect burden as well. The most common side effects can be categorized under anticholinergic (dry mouth, constipation, urinary retention, and blurred vision), gastrointestinal (nausea, vomiting, dyspepsia, and anorexia), cardiovascular (tachycardia, palpitations, arrhythmias, hypertension, hypotension, and heart block), and neurologic (ataxia, tremors, paresthesias, and sedation). The sedation secondary to TCA usage can be beneficial when administered at bedtime. Constipation caused by opiates can be worsened with concomitant TCA use. TCAs are relatively contraindicated in patients with severe heart disease and an EKG should be obtained prior to initiating care if risk factors are present. See Table 29.1.

SNRIs

The first serotonin–norepinephrine reuptake inhibitor (SNRI), venlafaxine (Effexor), was introduced in 1994. Since then multiple other medications including duloxetine (Cymbalta) have been introduced. They all share the same mechanism of action as they selectively block the reuptake of serotonin and norepinephrine. They are used for a variety of ailments including depression, anxiety, obsessive–compulsive disorder, and fibromyalgia. The descending pathways in the spinal cord are moderated by serotonin and norepinephrine and inhibit the sense of pain. SNRI medications increase serotonin and norepinephrine and thus decrease the experience of pain.

There is extensive research in using duloxetine for analgesia. It currently has FDA approval for diabetic neuropathy, fibromyalgia, osteoarthritis, and musculoskeletal back pain. Dosing for duloxetine ranges from 30 to 120 mg daily. Evidence shows analgesic response at doses of 60–120 mg daily. Duloxetine is generally well tolerated, with nausea being a common side effect which is usually self-limited or

can be alleviated by lowering the dose. Although the half-life of duloxetine is 12 h, it is often used as a once daily medication.

Venlafaxine does not currently have FDA approval for any pain indications, but there is substantial evidence for its efficacy for analgesia. Doses greater than 150 mg are necessary for analgesia as venlafaxine acts as a SSRI below 150 mg. Venlafaxine is available in an XR and IR formulation. The XR formulation is more readily prescribed as it is dosed once daily and less likely to cause hypertension compared to the IR formulation. The XR is usually started at 37.5 mg and slowly titrated up to 450 mg. It is typically prescribed in the morning as it is activating and will otherwise cause insomnia. Abrupt discontinuation of venlafaxine is associated with withdrawal (flu-like symptoms, nausea, anxiety, dizziness) and thus a slow taper is required upon discontinuation.

After first-pass metabolism, venlafaxine is metabolized into its active metabolite desvenlafaxine (Pristiq), which is currently used to treat depression and menopause. Currently there is limited evidence available for its use in analgesia, however as it is a metabolite of venlafaxine, evidence is anticipated to be forthcoming in the near future supporting its use in pain.

Milnacipran (Savella) was the first drug approved by the FDA for fibromyalgia. It is currently not FDA approved for depression. The starting dose of milnacipran is 12.5 mg which is then titrated up to 50 mg twice a day. Dose can eventually be titrated up to 100 mg twice daily.

SSRIs

The first selective serotonin reuptake inhibitor fluoxetine (Prozac) was introduced in 1987, and since then several medications in this class have been released and have become the mainstay in treatment for depression. Since 1987, SSRIs have had FDA approval for treatment of anxiety disorders, obsessive–compulsive disorder, and bulimia nervosa. They are also commonly used in treating post-traumatic stress disorder, premature ejaculation, premenstrual dysphoric disorder, irritable bowel syndrome, migraines, and attention-deficit hyperactivity disorder. Compared to TCAs, SSRIs are better tolerated and much safer in the event of an overdose scenario and have thus become first line in treating mood disorders. There have been a number of studies which have demonstrated SSRIs to provide clinically significant analgesia, although their effect is not as pronounced as the relief provided by TCAs.

Antipsychotics

Chlorpromazine (Thorazine) was initially introduced as an anesthetic and was found to have use in patients with mental illness, as it provided a calming effect in the 1950s. Antipsychotics (also known as neuroleptics) have greatly advanced and are

now used to treat a myriad of conditions. They are commonly used to treat psychiatric disorders such as schizophrenia, bipolar disorder, and depression. They are also used in patients with obsessive–compulsive disorder, nausea, dementia, autism, and PTSD. It is interesting to note that haloperidol (Haldol) has molecular structural similarities to both morphine and meperidine. Although antipsychotics are not commonly used in pain, there are data to suggest that neuroleptics such as haloperidol and fluphenazine can be useful in treating neuropathic pain, as well as when significant emotional distress and suffering accompanies symptoms of pain. Chlorpromazine and prochlorperazine have also been used with some success in treating migraine headaches. Neuroleptics also play an integral role in treating delirium. Post-operative and cancer patients frequently suffer from delirium or encephalopathy and in these contexts, it is difficult to appropriately assess pain. It is imperative to monitor encephalopathic patients for signs of pain as it is commonly missed in the hospital setting. When using neuroleptics, it is important to monitor QTc intervals, lipids, complete blood count, and basic metabolic panels.

Benzodiazepines

Chlordiazepoxide (Librium) was introduced in 1955 followed by diazepam (Valium) in 1963. These medications work as agonists at the GABA receptors. Benzodiazepines are used as anxiolytics, antispasmodics, anticonvulsants, and for treatment of insomnia, catatonia, and alcohol withdrawal. They also carry the benefit of being able to be administered orally, intravenously, intramuscularly, and rectally. It is crucial to understand that many patients with chronic pain also suffer from comorbid anxiety disorders, which may also need treatment. Benzodiazepines do carry the potential for addiction, and must be carefully used when opioids are used concurrently. They also have the risk for respiratory depression and sedative effects. Of the benzodiazepines, diazepam is the most commonly used to treat pain associated with muscle spasms. When used as a skeletal muscle relaxant, the dose range is from 2 to 10 mg PO three to fours times daily. When used to treat spasticity in the acute setting, it is given in the IV or IM formulation, with a starting dose of 5–10 mg; it can then be used as needed every 3–4 h.

Monoamine Oxidase Inhibitors

Due to the potentially serious side effects, multiple drug interactions, requirement for restricted tyramine diet (with the exception of the selegeline patch), and minimal benefit in pain management, MAOIs are rarely used in this setting. Of this class, phenelzine has demonstrated adjuvant analgesic properties in patients with atypical facial pain, migraines, and chronic fatigue syndrome.

Mood Stabilizers

Lithium and many of the antiepileptics (with the exception of gabapentin and pregabalin) are mainstay treatments in psychiatry for bipolar disorder, depression augmentation, and impulse control disorders. They have been used in many pain disorders with anecdotal success, but they lack consistent studies demonstrating their efficacy in pain. Thus, mood stabilizers are generally considered second-line therapy and utilization is best when there is a bipolar disorder component. This is particularly important since many treatments for pain management can precipitate a manic episode (opioids, steroids, antidepressants).

Lithium

Lithium has frequently been used off-label to treat migraines and cluster headaches. Its mechanism of action in pain management is thought to involve action on nerve and muscle cells by altering cation transport across cell membranes, increasing glutamate clearance, and influencing reuptake of serotonin. Lithium has a narrow therapeutic index (dose range 900–2400 mg/day) and side effects make it a medication that requires relatively close monitoring. Baseline labs include basic metabolic panel (BMP), complete blood count (CBC), beta-HCG (females not known to be sterile), TSH, and an EKG. Lithium level (target 0.5–1.2 mEq/L) should be obtained 4–5 days after the medication is initiated and then monitored after any changes. Side effects include and are not limited to what is seen in lithium toxicity: nausea, vomiting, diarrhea, arrhythmia/palpitations, sluggishness, ataxia, confusion, tremors/fasciculations, and in severe cases seizures or encephalopathy.

Antiepileptics

Antiepileptics (including gabapentin and pregabalin) share a similar mechanism of action through various forms of neuronal membrane stabilization. Gabapentin and pregabalin (discussed further below) are generally considered first line in neuropathic pain and act through calcium channel modulation. Valproic acid, phenytoin, carbamazepine, oxcarbazepine, lamotrigine (Lamictal), and topiramate (Topamax) exert their therapeutic effect though sodium channel blockade. Valproic acid acts on neuronal sodium channels; however, its effect in pain is theorized to be due to increased GABA availability via inhibition of its degradation and increased release from synapses. Baseline labs including liver function tests, complete blood count, and blood levels must be checked when starting valproic acid (obtained 3–4 days after initiation, target range of 50–100 μg/mL, daily dose typically ranges from 500 to 1200 mg). Valproic acid carries a black box warning for hepatotoxicity and pancreatitis.

Phenytoin (daily dose 300–600 mg) acts on sodium channels by inhibiting the release of excitatory glutamate preventing ectopic discharges. Due to its inducing action on CYP3A4 and CYP2C19, medications such as methadone, tramadol, fentanyl, lamotrigine, and carbamazepine must be monitored and adjusted accordingly. Carbamazepine (daily dose of 400–800 mg) has a chemical structure similar to TCAs and is the first-line treatment in trigeminal neuralgia as well as having efficacy in other neuropathic pain disorders. Oxcarbazepine (daily dose of 900–1800 mg) is the keto-analog of carbamazepine. Its benefits are its usage in patients unable to tolerate the side effects of carbamazepine and it does not require as close monitoring of blood levels or laboratory abnormalities, though hyponatremia may be seen. Lamotrigine (daily dose of 100–200 mg) blocks sodium channels in actively firing neurons as well as prevents release of glutamate which is involved in pain propagation. Rashes must be monitored with a watchful eye for any signs of Stevens-Johnson syndrome. Topiramate (daily dose of 100–200 mg) has multiple mechanisms of action. It blocks neuronal voltage-gated sodium channels, enhances GABA activity by binding to GABA(A) receptors, and inhibits carbonic anhydrase (causing increased risk of kidney stones). Topiramate can also be used to aid in weight loss and alcohol abstinence when in appropriate patients with these comorbidities.

Gabapentin and Pregabalin

Gabapentin (Neurontin) and pregabalin (Lyrica) are generally first-line treatments, particularly in the setting of painful diabetic neuropathy, post-herpetic neuralgia, complex regional pain syndrome, and other neuropathic pain types. In the psychiatric world, gabapentin is often used as an adjuvant to treat anxiety, which is commonly comorbid in chronic pain patients. Gabapentin and pregabalin are structurally similar to GABA, but have little to no influence on the GABA system. The therapeutic effect on neuropathic pain is through action on the alpha2delta1 subunit of L-type voltage-gated calcium channels. The downstream effect of this is decreased release of glutamate, norepinephrine, and substance P.

Dosing and Safety

Gabapentin is initiated at 300 mg on day 1, then 300 mg BID on day 2, then 300 mg TID on day 3. Each subsequent week, the dose can be increased by 300 mg to be titrated until pain relief is achieved or a maximum of 3600 mg/day is met (dose range between 900 and 3600 mg/day). For neuropathic pain, pregabalin (daily dose of 300–600 mg) is initiated at 50 mg TID for 1 week, then can be increased to 100 mg TID. Studies have demonstrated that doses of 600 mg daily or more do not have any added benefit on pain symptoms and produced greater side effects. Both gabapentin and pregabalin have a similar side effect profile, which are mainly

CNS-based in nature. Dizziness, drowsiness, ataxia, and fatigue are commonly noted and these symptoms are reduced by slower titration and lower target dose. There have also been cases in which pregabalin produced symptoms of euphoria, which should be monitored for in bipolar disorder and abuse potential (pregabalin is a Schedule V controlled substance).

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Chapter 30
Opioids for the Treatment of Pain in the Rehabilitation Patient

Christina Lamar and Anjum Bux

Introduction

Opiates are naturally occurring analgesic alkaloid compounds originating from the opium poppy plant *Papaver somniferum* [1]. The psychoactive compounds found in the opium plant include morphine and codeine. The term opioids is the broader term including opiates; semi-synthetic compounds derived from morphine, which include heroin, hydromorphone, hydrocodone, oxycodone, and oxymorphone; as well as synthetic compounds not derived from morphine, which include fentanyl, buprenorphine, and methadone. Opioids act on the nervous system to provide analgesia and euphoria.

The use of the opium plant dates back to 3400 B.C. with the Sumerians who cultivated the opium poppy in lower Mesopotamia and referred to it as the "joy plant" for its euphoric effects [2]. This was later passed on to the Egyptians in 1300 B.C., who again recognized the opium poppy for its euphoric effects. It was Hippocrates in 460 B.C., who first recognized the analgesic effects of opium. Throughout the periods of Alexander the Great, and time periods leading up to the nineteenth century, opium continued to be used for analgesia and sedation by those involved in medicine to treat pain associated with certain disease states. It was also commonly used by those enamored by its psychogenic and euphoric effects, such as the literary greats, John Keats and Elizabeth Browning.

In the early nineteenth century, a German Chemist, Friedrich Serturner isolated morphine from opium [2]. After this development, morphine soon became the mainstay for the treatment of pain, anxiety, respiratory problems, and "women's ailments". During the Civil War, morphine was commonly used as a pain killer for injured soldiers. These soldiers soon became addicted to morphine with their

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increased use of the drug during battle. Soon thereafter, heroin was synthesized as a derivative of morphine and thought to be an alternative "non-addictive" morphine substitute for medical use.

In the early 1900s, Congress began to enact limitations on the distribution and use of morphine and heroin due to their hazardous use and dependence. Shortly after, oxycodone was synthesized by German scientists as a drug that was thought to retain the analgesic effects of morphine, with less dependence. Oxycodone was approved by the FDA in 1950 as Percodan and became widely available for medical use [3].

Throughout the latter part of the 1900s to present day, the landscape of pain continued to change with the development of new synthetic "morphine-like compounds", which expanded the treatment of pain. Unfortunately, with the increase in availability of alternative pain medications, abuse and misuse of these medications were also on the rise. In 2012, there were 259 million prescriptions written for opioids in the United States [4]. Of the 21.5 million Americans who had a substance use disorder in 2014, 1.9 million had a substance use disorder involving prescription pain relievers and 586,000 had a substance use disorder involving heroin [5]. The treatment admissions and overdose death rates have increased in the recent years leading to 18,893 overdose deaths related to prescription pain relievers in 2014 and 10,574 overdose deaths related to heroin in 2014 [6].

Initiation of Chronic Opioid Therapy

There is no direct evidence to support the use of one opioid over the other, aside from comorbid risk factors, including renal or hepatic impairment. There is also no recommended specific starting dose or specific method of titration. A rational approach to prescribing can be aided by a careful review of the patient's medical history. A patient with moderate to severe acute and/or chronic pain, who has not improved with non-opioid therapies, is a potential candidate for opioid analgesics. When the decision is made to start a patient on opioids, the prescriber should determine which opioid to use and with what dose to start. Also, the prescriber should be mindful to assess for the risk of opioid abuse.

Whether or not a patient is opioid naive can help to determine starting formula of medication. Patients with minimal to no recent opioid exposure should be started at the lowest possible dose of a short acting opioid and titrated upward, based on pain scores and functional outcomes. If the patient continues to have breakthrough pain, which is not relieved with short acting opioids, then one may consider a sustained release opioid or a long acting opioid, in addition to the short acting opioid regimen. Caution is required, as sustained release opioids and long acting opioids may accumulate in fixed doses. Typically, continuous opioid therapy for chronic pain aims to avoid the "rollercoaster" effect of brief periods of pain relief followed by breakthrough pain. Continuous therapy produces stable analgesia that is targeted less at total abolition of pain and more toward augmentation of the patient's function at a tolerable level of pain.

In assessing the patient's risk for opioid abuse, the provider should understand a patient's risk factors before initiating treatment, to enable appropriate monitoring. A patient's probability of opioid abuse is linked to risk factors influenced by the patient's genetics and environment [7]. Patients need to be appropriately screened for risk factors with screening tools such as the Drug Abuse Screening Test (DAST), the Prescription Drug Use Questionnaire (PDUQ), the Opioid Risk Tool (ORT), or the Screener and Opioid Assessment for Patients with Pain (SOAPP). Once opioid treatment is initiated, the prescriber needs to continually monitor adherence to treatment with the use of random Urine Drug Screening (UDS), the Prescription Monitoring Program (PMP), and random pill counts, if deemed necessary. In addition, treatment benefit needs to be monitored with pain score and functionality assessments.

Opioids bind to receptors primarily in the brain and the spinal cord, producing relief from pain by inhibiting the transmission of pain conveyed by the nerve cells. There are three principle classes of opioid receptors: mu, kappa, and delta. In addition, there have been up to 17 additional receptors reported, including Epsilon, Iota, Lambda, and Zeta. Furthermore, more specific to the primary mu receptor, there are three sub-types of the mu receptor: mu1, mu2, and mu3. The pharmacodynamic response to a particular opioid depends on its affinity for a particular receptor and whether the opioid is an agonist or antagonist. For example, morphine is an agonist, which exerts a supra-spinal analgesic effect at the mu1 receptor, respiratory depression, and physical dependence at the mu2 receptor, and sedation and spinal analgesia at the kappa receptor.

Selected Opioids

Morphine

Morphine is the prototypical mu opioid receptor agonist, against which all other opioids are compared for equi-analgesic potency. It is available in short acting and sustained released formulations. Its dosing frequency is every 8–24 h.

Morphine has an oral bioavailability of 35–75%, is relatively hydrophilic, and has less than ideal analgesia due to the delay in transport across the blood brain barrier. Additionally, it has a slower onset of action compared to other opioids; therefore, it has a delayed onset of action. Morphine's efficacy and toxicity are mitigated or perpetuated by two of its major metabolites: morphine 3 glucoronide (M3G) and morphine 6 glucoronide (M6G). M3G lacks any mu receptor activity and has been shown in animals to cause generalized hyperanalgesia and tolerance. M6G has intrinsic opioid agonism and sustained analgesia, with side effects such as sedation, respiratory depression, and nausea. Chronic use of oral morphine ultimately results in higher circulating concentrations of the glucoronides than the parent compound. Patients who experience side effects attributable to these compounds may be candidates for an opioid rotation.

The elimination or morphine is dependent on hepatic mechanisms; therefore, it should be used with caution in cirrhotic patients. Morphine metabolites are excreted through the kidneys; therefore, dose should be adjusted in those with renal impairment. Ultimately, morphine's analgesic effects and side effects are likely related to complex interactions between the parent compound and its glucoronide metabolites. Exactly how specific diseases, polypharmacy, and patient age influence ratios of individual glucoronide metabolites to morphine remains unclear.

Oxycodone

Oxycodone is a semi-synthetic congener of morphine that has been used for over 80 years. Sustained release oxycodone possesses many of the characteristics of an ideal opioid, including no ceiling dose, minimal side effects, absence or minimal active metabolite, easy titration, rapid onset, short half-life, long duration of action, and predictable pharmacokinetics (Tables 30.1 and 30.2). Milligram to milligram, oxycodone is more potent than morphine and has a shorter onset of analgesia with less plasma variation (Fig. 30.1). Accordingly oxycodone is associated with fewer side effects than morphine.

Oxycodone is predominantly a pro-drug and undergoes hepatic metabolism via cytochrome P450 2D6 enzyme, where it is converted to oxymorphone, an active metabolite with mu opioid agonist properties, and noroxycodone, an inactive metabolite. The kidneys excrete oxycodone; therefore, the dose should be adjusted in renal dysfunction.

Table 30.1 Strength, dosages, and onset of commonly used opioid analgesics

Drug	Strength relative to morphine	Usual starting oral dose (mg)	Dosing interval (h)	Onset (min)
Morphine	1	10–30	IR: 3–4	30–45
			ER: 12	
Hydromorphone	5	2–4	4–6	30
Oxycodone	1.5–2	5–15	4–6	30–60
Methadone	7.5	2.5–10	8–12	60–90
Oxymorphone	7	5	12	30–60

Table 30.2 Bioavailability, half-life, and duration of commonly used opioid analgesics

Drug	Bioavailability-oral (%)	Half-life (h)	Duration (h)
Morphine	30–40	2–4	3–4
Hydromorphone	25	2–3	2–3
Oxycodone	60–80	3–4	4–6
Methadone	80	22	6–12
Oxymorphone	10	6–8	3–4

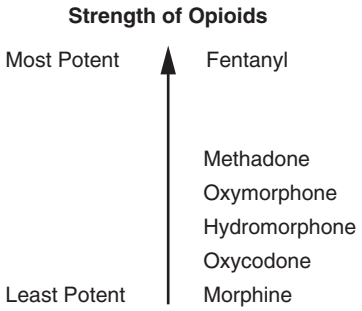

Fig. 30.1 Strength of opioids

Oxymorphone

Oxymorphone is a semi-synthetic opioid that has been available as an oral formulation since 2006. Oxymorphone is primarily a mu opioid receptor agonist that has more affinity for the mu opioid receptor than morphine and is ten times as potent as morphine when given IV. Oxymorphone has greater affinity for the delta receptor, with agonism decreasing tolerance, and less affinity for the kappa opioid receptor unlike oxycodone. Like fentanyl, oxymorphone has less histamine release from mast cells than morphine and is more lipid soluble than morphine and oxycodone. The increase in lipophilicity leads to maximum plasma concentrations in 30 min as compared to morphine IR in 1.2 h.

Oxymorphone's bioavailability is only 10%, due to extensive first-pass hepatic metabolism; however, greater lipid solubility facilitates its ability to cross the blood brain barrier (BBB) and may account for its rapid onset of analgesia. For immediate release (IR) formulations, onset of analgesia is 30–60 min, with predictable dosing. For extended or sustained release (ER/SR) formulations, steady state occurs in 3 days with every 12 h dosing.

Oxymorphone is hepatically metabolized and renally excreted. Dosing adjustment is required for hepatic and renal impairment. Oxymorphone is contraindicated in those with moderate to severe hepatic impairment. Caution, with dose reduction, is recommended in those with renal impairment. The main metabolite is oxymorphone-3-glucoronide, which has unknown activity. There appears to be minimal interaction with the cytochrome P450 enzyme systems, which can lead to less inter-patient variability and fewer drug–drug interactions. In turn, this gives oxymorphone a significant advantage over other opioids. Compared to other strong opioids, oxymorphone has similar efficacy in the treatment of acute, chronic, and cancer pain, with a similar side effect profile. Taking this medication with food greatly increases the maximum plasma concentration; therefore, it is advisable to avoid eating 1 h prior to or 2 h after taking this medication. Alcohol should be avoided, as it can produce an almost 300% increase in plasma concentration.

Hydromorphone

Hydromorphone is a hydrogenated ketone analogue of morphine, which can be formed by *n*-demethylation of hydrocodone. It can be given oral, IV, epidural, or intrathecal. As an oral medication, it is available in both an IR and an SR formulation.

Hydromorphone is hydrophilic and possesses strong mu opioid receptor agonist activity, with a similar duration of analgesic effect as morphine (3–4 h). Side effects such as pruritus, sedation, nausea, and vomiting occur less frequently with hydromorphone. Hydromorphone's milligram-to-milligram potency is estimated to be 5–7 times that of morphine. Onset of analgesia is 30 min when administered orally.

Hydromorphone undergoes hepatic biotransformation into its primary metabolite hydromorphone-3-glucoronide (H3G), which is renally excreted. H3G lacks analgesic efficacy, but possesses potent neuro-excitatory properties, which are ten times stronger than the parent compound; however, because H3G is produced in such small quantities, its effects are negligible, except in cases of renal insufficiency, when it may accumulate.

Methadone

Methadone is structurally unique and unrelated to other opium-derived alkaloids. It is lipophilic, is basic, and exists as a racemic mixture. The D-isomer antagonizes the NMDA receptor and inhibits both serotonin and norepinephrine re-uptake, while the R-isomer possesses the opioid receptor agonist properties. Methadone has a lower affinity for the mu opioid receptor; conversely, it has a greater affinity for the delta opioid receptor. Interestingly, methadone's delta receptor affinity is felt to lead to desensitization, and likely account for methadone's ability to counteract opioid-induced tolerance and dependence. Also, it is the action at the NMDA receptor that may be responsible for methadone's ability to mitigate opioid-induced tolerance and to treat neuropathic pain.

Methadone has lipophilic properties; therefore, it has slow elimination and delayed clearance. There is extensive inter-individual variation in the relationship between plasma methadone concentration and analgesia. The unique characteristics of analgesia during one phase of elimination, and the prevention of withdrawal during another phase of elimination, account for the need of analgesia dosing every 6–12 h and once daily dosing for opioid maintenance therapy.

Methadone has no known active metabolites. It undergoes hepatic metabolism by the cytochrome P450 enzyme; therefore, multiple potential drug interactions can result. Methadone is not excreted renally and does not accumulate in renal failure or appreciably filter during hemodialysis; however, its metabolism and rate of absorption and/or excretion are altered with poly-pharmacy, changes in gastric pH, and urinary pH, all of which are important to consider when prescribing this medication. Ultimately, methadone's pharmacodynamic properties make it beneficial for those with impaired GI absorption, and ideal in patients with renal impairment.

The pharmacological complexity of methadone increases the risk of side effects, especially in patients with cardiac issues, concomitant illness, or those on multiple medications. Methadone has a pro-arrhythmic potential, with prolongation of the Qtc interval resulting in torsade de pointes. Patients should be monitored with a baseline EKG and an annual follow up EKG if being prescribed long term.

In the opioid-tolerant patient, the exact equi-analgesic dose of methadone, as a conversion from morphine equivalents, is uncertain. A recommended safe starting dose in most opioid naive adults is a 2.5 mg orally, every 8 h, with subsequent dose increases no more frequently than weekly. Opioid-tolerant patients should generally start at doses no higher than 30–40 mg/day. Methadone presents the inexperienced clinician with a challenge due to un-reliable equi-analgesic dosing ratios and fluctuations related to hepatic metabolism, drug–drug interactions, protein binding changes, and altered renal clearance.

Conclusion

Opioids have been widely used in the treatment of both malignant and non-malignant acute, sub-acute, and chronic pain. These opioids come in oral, transdermal, intravenous, and epidural/intrathecal formulations. In addition to providing analgesia and pain relief to patients, the administration of opioids comes with unwanted side effects. These side effects include itching, nausea, sedation, respiratory depression, confusion, and constipation. One must be aware of these side effects with the use of opioids. Some of these side effects decrease with continued use; however, some, such as constipation, may not resolve and dosage may need to be adjusted.

With regular use, opioid tolerance and physical dependence must be considered. Tolerance occurs when there is a need to increase an opioid dose to maintain the same analgesic effect. Recent work by Dr. Jay Grider at the University of Kentucky on opioid-induced hyperalgesia indicates that the unexplainable pain exacerbation following increased opioid doses may be modulated by the NMDA receptor [8]. So, when prescribing opioids, one needs to be aware of tolerance, hyperalgesia, and unwanted side effects.

Patients need to be completely screened for risk factors and evaluated for functional benefit before being started on opioids and also while being maintained on opioids. Opioids have a role in the treatment of acute and/or chronic pain usually as an adjunct to other non-opioid treatments in a multi-disciplinary treatment algorithm. With the recent FDA alerts and concerns over the safe use of opioids, it is important to prescribe the lowest dose possible to achieve functional benefit and minimize risk.

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Chapter 31
Opioid-Induced Hyperalgesia Syndrome in the Rehabilitation Patient

Keith A. Scarfo

Introduction

Opioids remain one of the most common medications prescribed in the treatment of moderate to severe pain of both cancer and non-cancer patient populations [1]. Despite the numerous potential side effects including addiction, dependence, respiratory depression, and chronic constipation, opioid-induced hyperalgesia is frequently overlooked and remains largely misunderstood. Opioid-induced hyperalgesia syndrome is the result of a paradoxical response to opioids where neuroplastic changes in the peripheral and central nervous systems are sensitized to nociceptive stimuli [2]. The therapy, which was intended to ameliorate the patient's chronic pain, results in increased sensitivity to stimuli or exaggeration of the patient's underlying painful disorder.

Brief History

In the 1880s, Rossbach had incredible foresight when he first described the syndrome that we now refer to as opioid-induced hyperalgesia. In his essay, he stated "dependence on opioids finally becomes an illness of itself, opposite effects like restlessness, sleep disturbance, hyperesthesia, neuralgia, and irritability become manifest" [3]. It would be another 60 years until Himmelsbach would publish his observations of opioid withdrawal. It is at this point that medicine began to

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recognize that the treatment of pain with opioids could alter the nervous system. In fact, the opioid therapy itself could have a paradoxical effect and patients could become more sensitive to nociceptive stimuli [4]. It would not be until the early 1970s that the scientific community would start to vigorously explore the underlying pathophysiology in an attempt to explain this phenomenon.

Pathophysiology

Although evidence continues to mount, there are currently only proposed theories as to the mechanism of opioid-induced hyperalgesia syndrome. These can be described broadly as involving the peripheral terminal of primary afferent neurons, the spinal cord, and the supratentorial structures of the central nervous system. More specifically, medical research has been focused on multiple potential etiologies, which includes the role that genetic predisposition may play, decreased reuptake of neurotransmitters, descending facilitation, the role of the central glutaminergic system (glutamate and NMDA receptors), and spinal dynorphins. The glutaminergic system and the role of spinal dynorphins [5] may play a primary role in the mediation and maintenance of opioid-induced hyperalgesia.

Basic Principles of Diagnosis and Treatment Options

Clinicians are faced with the daunting task of making the correct, albeit difficult, diagnosis of opioid-induced hyperalgesia syndrome as it may mimic an exacerbation of the patient's underlying pain, further progression of the patient's injury/disease, or tolerance to opioid therapy. There are several defining characteristics of opioid-induced hyperalgesia which set it apart from the remaining differential diagnoses. Pain associated with opioid-induced hyperalgesia tends to be diffuse, spreading beyond the areas in which treatment was originally initiated, and its presentation may include diffuse allodynia. The constellation of symptoms also mirrors those of opioid withdrawal, as was first noted in the 1880s by Rossbach [6]. Additionally, if the pain is the result of an exacerbation of the patient's underlying disease, further progression of the patient's injury/disease, or tolerance to opioid therapy, an escalation of opioid dosage will result in decrease of the patient's pain. This is in direct contrast to what happens in opioid-induced hyperalgesia, where pain is exacerbated in the face of escalating opioid therapy.

Overall, treatment of opioid-induced hyperalgesia requires a reduced dosage of opioid, or an opioid rotation. If symptoms persist, weaning off opioids is recommended. If the patient's underlying pain persists, alternatives including NMDA

receptor antagonists have been shown to reduce tolerance and to reverse opioid-induced hyperalgesia and therefore should be initiated.

Application to Patients in the Rehab Setting

Opioid-induced hyperalgesia can have significant implications in the rehabilitation setting as many patients who have sustained an injury will require opioid therapy. During rehabilitation, a patient's physical exacerbation/demands metabolically, physically, and emotionally will most likely increase. Thereby, patients may require additional opioids to maintain a level of comfort to be able to actively engage in therapy. Differentiating between increased pain associated with the demands of rehabilitation, the development of tolerance to current opioid levels, re-injury, or opioid-induced hyperalgesia may be challenging. This makes the responsibility of the provider to discern the correct clinical diagnosis difficult, yet critical.

Evidence

Since the 1970s, there have been over 100 studies attempting to uncover the underlying cause of opioid-induced hyperalgesia syndrome. Although the exact mechanism remains unknown, there are several leading theories, which attempt to explain how pain modulation at the neuronal level in both the peripheral and central nervous systems is altered. Research has been carried out in animal models and human studies including healthy volunteers, former opioid addicts, and post-surgical patients. Animal models involving both intrathecal and subcutaneous opioid administration followed by exposure to mechanical or thermal stimulation have lead to the development of opioid-induced hyperalgesia. These findings suggest a role for both central as well as peripheral neural pathways [5].

Central Glutaminergic System

As evidence continues to build toward a better understanding of the pathophysiology of opioid-induced hyperalgesia syndrome, the central glutaminergic system appears to be taking a prominent role. Glutamate is a major excitatory neurotransmitter in the central nervous system, with receptors found throughout the brain and spinal cord. In the 1990s and early 2000s, Mao et al. advanced our understanding of the role the glutamine receptor, the NMDA receptor, and the interaction it plays in activating and maintaining opioid-induced hyperalgesia [5]. Thermal

hyperalgesia develops in a rat model receiving intrathecal morphine. This effect is blocked partially or completely when morphine is administered with an NMDA receptor antagonist MK801 [7].

Spinal Dynorphins and Descending Facilitation

The work of Vanderah et al., which involved intrathecal delivery of the μ-receptor agonist DAMGO, provides additional insight into the role by which dynorphin promotes abnormal pain. Utilizing a rat model, the μ agonist DAMGO was delivered intrathecally for 7 days, followed by morphine, control serum, or dynorphin antiserum. Thermal and mechanical nociceptive testing was then performed. The antinociceptive effect of morphine after intrathecal DAMGO infusion decreased its efficacy. The efficacy of spinal morphine was restored by the administration of antiserum to dynorphin. This research speculated that decreased μ-receptor expression on primary afferent fibers may promote abnormal pain via an increase in the release of excitatory neurotransmitters [8]. It is the increased synthesis and release of spinal dynorphin that may promote opioid-induced hyperalgesia.

Centrally, the rostral ventromedial medulla may also play a role in sensitizing the spinal cord. Under naive conditions, the rostral ventromedial medulla inhibits transmission of nociceptive signals. Rats subjected to pellet or mini-pump delivery of morphine developed hyperalgesia or thermal allodynia. This suggests that morphine leads to neuroplasticity, resulting in tonic activation of descending facilitation, which in turn causes pain. Blocking the rostral ventromedial medulla via microinjection of lidocaine, or lesioning of the dorsolateral funiculus restores spinal morphine anti-nociceptive potency. Therefore, opioid-induced pain is caused by tonic descending facilitation from the rostral ventromedial medulla decreasing the antinociceptive potency of spinal and systemic morphine [9].

Conclusion

Despite the fact that opioid-induced hyperalgesia syndrome was first recognized and documented in the medical literature over 135 years ago, its underlying pathophysiologic cause remains elusive. To date, clinicians continue to struggle to correctly diagnose this problem, even though opioid therapy has become common place in the treatment of chronic pain. A correct diagnosis remains paramount for effective treatment of the problem, versus exacerbation of the patient's pain by increasing daily opioid consumption. When the loss of efficacy of opioid therapy is coupled with markedly increased pain or unexplained distribution of pain, providers should consider the manifestation of opioid-induced hyperalgesia syndrome. Therefore, upon initiation of chronic opioid therapy, it is prudent to discuss the possibility of opioid-induced hyperalgesia with patients, and the implication it may have on their care.

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Chapter 32
Urine Drug Testing for Opioids in the Rehabilitation Patient

Tahir Tellioglu

Chronic Pain Treatment

Pain is associated with significant impairment of physical and mental health, and performance of social responsibilities, which include both work responsibilities and activities of daily living. In a survey of primary care settings, an average of 22% of patients reported persistent pain (range 6–33%) [1]. Untreated or under-treated pain can cause psychosocial effects, which can lead to a significant increase in physical disability as well as an increased use of healthcare resources [2]. Chronic pain management can be time-consuming, frustrating, and distressing for both clinicians and patients, and may even threaten clinician–patient trust [3]. In an another survey on patients' risk assessment among family physicians, 61.1% reported concern and hesitation in prescribing opioids due to known risks, which include overdose, addiction, dependence, or diversion [4]. It is important for patients to understand their pain condition and to learn strategies for self-management in order to cope better with their condition. Pain providers should have better knowledge, perspective, and experience in managing the pain patient.

Monitoring Opioid Management

Opioids are the most effective drugs in the management of acute, severe pain, as well as chronic pain related to advanced medical illness. Numerous opioids have been used via oral, transdermal, and intravenous administration. The term "*opioid*"

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includes all chemicals that bind to opioid receptors. *Opiates* are alkaloids derived from the opium poppy plant, such as morphine and codeine. Opioids include semi-synthetic opiates, which include drugs that are synthesized from naturally occurring opiates, such as heroin from morphine and oxycodone from thebaine, as well as synthetic opioids, such as methadone, fentanyl, and propoxyphene.

The prevalence of opioid therapy for chronic non-cancer pain (CNCP) has increased dramatically in recent years [5, 6]. There has been a massive increase in the number of opioid prescriptions, daily prescribed opioid doses, and overall opioid availability, with a parallel increase in opioid abuse, misuse, and death from accidental overdose. Many more patients with CNCP receive high doses of long-acting opioids; however, the majority of patients with CNCP are dissatisfied with their treatment [7]. Since opioid diversion, addiction, and overdose have become the fastest-growing drug-related problems in the United States, the Centers for Disease Control and Prevention (CDC) has labeled pharmaceutical opioid overdose as a national epidemic [8].

According to the guidelines of American Society of Interventional Pain Physicians (ASIPP), one-third of CNCP patients may not use opioids as prescribed or may abuse them, which is why illicit drug use is significantly higher in this patient population [9]. The majority of prescriptions are written by non-pain physicians. Many patients are on long-acting opioids, and some are provided with combinations of long- and short-acting opioids. (The short- and long-term effectiveness of opioids is discussed elsewhere in the book). Patients themselves may even be reluctant to take an opioid medication prescribed to them for fear of becoming addicted. The prevalence of drug abuse is estimated to be 9–41% in patients receiving opioids for chronic pain [10, 11]. Significant differences were noted in the prevalence of opioid abuse in patients who developed chronic pain following motor vehicle accidents (16 vs. 11% or 4%) and in patients with involvement in three parts of the body, as compared to one region (14 vs. 5%). Illicit drug use was seen predominantly in patients below the age of 45, with no illicit drug use seen in patients 65 years or older (25 vs. 13% or 0%) [10].

In clinical practice, it is imperative to incorporate methods to identify patients who are non-compliant or who are abusing prescription or illicit drugs. Screening for prescription drug abuse can be incorporated into routine medical visits. Irregular behaviors, such as rapid increases in the amount of medication needed, frequent and/or unscheduled refill requests, and involvement of multiple providers should alert the clinician to possible abuse or misuse. Since self-report of prescribed or illicit drug use among patients with chronic pain treated with opioids is often unreliable, interviews with spouses, review of medical records, or input from prescription monitoring programs, may improve patient management.

Urine Drug Testing (UDT) in Clinical Settings

There is limited evidence for the reliability and accuracy of screening tests for opioid abuse, due to the lack of high-quality studies. The various biological specimens used in laboratory drug testing, which include urine, blood, sweat, saliva, hair, and

nails, have different levels of specificity, sensitivity, and accuracy. Among those, routine urine drug testing has become standard in clinical practice. Urine samples allow quick and practical determination of the presence or absence of certain drugs to be evaluated with good specificity, sensitivity, ease of administration, and low cost [12, 13]. However, UDT is under-utilized in clinical practice. In a survey of 248 primary care practitioners, only 6.9% reported obtaining UDT before prescribing opioids and only 15% performed UDT on patients already prescribed opioids [14]. It is expected that random UDT will deter the use of illicit drugs and will also improve compliance. In a study of 500 consecutive patients on opioids, adherence monitoring combined with random drug testing resulted in significant reductions in overall illicit drug use [15].

Methods for accurate UDT have been available for several decades, and such methods are useful in assessing and identifying substance use. Issues related to UDT collection are important, since there is a time limit to detecting certain drugs in the samples (Table 32.1). Random UDT is therefore preferred to detect illicit use, since many of the patients with addiction tendencies are familiar with the detection time frames of the illicit substances [16]. In addition, certain measures such as close monitoring of sample collection, temperature of the sample, etc., may be necessary to avoid adulteration and subversion of UDT, and to ensure validity. In case of suspicion or inconsistency, these methods can specifically be requested from the laboratory.

Various factors of drug pharmacology, such as drug absorption, metabolism, or excretion, can affect UDT findings by influencing the quantity of the drug excreted in urine. Drug detection in urine samples is performed by a **cut-off** threshold, which is the predetermined drug concentration in the sample. Any value equal to or above the amount found in the sample is considered a *"positive result"*. Typical screening and confirmation cut-off concentrations and detection times for drugs of abuse are seen in Table 32.1. Depending on the cut-off levels of the testing, or of the laboratory standards, there may be more false-positive or false-negative results.

Blood concentrations of the active drug may be influenced by genetic polymorphisms on metabolism and clearance, which cause variabilities. For instance, a prodrug, such as codeine, can be converted to morphine, and its presence in the urine may misguide the clinician to falsely believe that there was an abuse of morphine [17]. In addition, urine pH is known to affect methadone excretion, which causes lower urine concentrations of methadone at higher urine pH, as seen in conditions such as urinary tract infection, a vegetarian diet, and others [18]. Oxycodone, a semisynthetic opiate derived from thebaine, has minimal cross-reactivity with opioid screening assays. However, specific immunoassay strips are commercially available. Regular opioid UDTs are unable to detect fentanyl, or its analogs, in the urine because these compounds do not have cross-reactivity against the immunoassay antibodies designed for opioids in the urine samples. These chemicals are only be measured using gas or liquid chromatography with mass spectrometry (GC/MS, LC/MS) techniques [19].

Cross-reactivity with other chemicals that have similar structural and chemical properties as the original substance, which include over-the-counter diet agents, some antibiotics, and decongestants, are also common and can be misleading in the

Table 32.1 Urine drug testing: typical screening and confirmation cut-off concentration and detection times for drugs of abuse (from Christo et al. [22])

Drug	Screening cut-off concentrations ng/mL urine	Confirmation cut-off concentrations ng/mL (non-regulated)	Confirmation cut-off concentrations ng/mL (federally regulated)	Urine detection time
Opioids				
Morphine	300	50	2000	3–4 days
Codeine	300	50	2000; 300	1–3 days
Hydrocodone	300	50	2000	1–2 days
Oxycodone	100	50	2000	1–3 days
Methadone	300	100	2000	2–4 days
Benzodiazepines	200	20-50	NA	Up to 30 days
Cocaine	300	50	150	1–3 days
Marijuana	50	15	15	1–3 days for casual use; up to 30 days for chronic use
Amphetamine	1000	100	500	2–4 days
Methamphetamine	1000	100	500	2–4 days
Heroin*	10	10	NA	1–3 days
Phencyclidine	25	10	25	2–7 days for casual use; up to 30 days for chronic use

*6-MAM, the specific metabolite is detected only for 6 h

UDT. Similarly, NSAIDs may make UDT positive for marijuana. Bupropion, desipramine, and cold medicines may make UDT positive for amphetamines. Finally, poppy seeds, chlorpromazine, and rifampicin may make UDT positive for opioids [20]. One should realize that screening methods detect the presence of a certain chemical in the sample (above or equal to the cut-off value), and not the actual concentration of the chemical. Therefore, all positive results should be confirmed by further laboratory techniques.

Types of UDT

Two types of urine drug tests are commonly used, which include: (1) immunoassay (IA); (2) laboratory-based testing, such as gas chromatography/mass spectrometry (GC/MS), liquid chromatography tandem mass spectrometry (LC/MS), or high

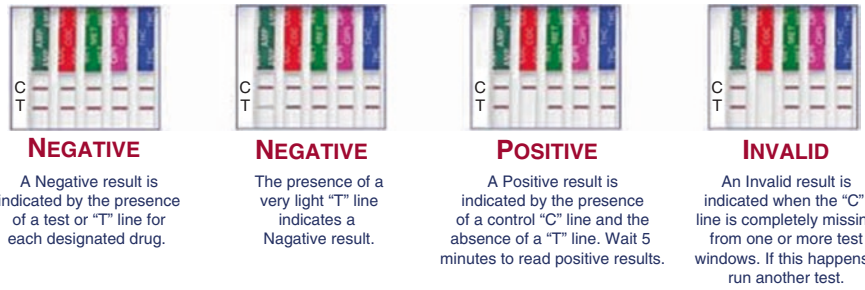

Fig. 32.1 Example of a reading guide for urine immunoassay (IA) testing results

performance liquid chromatography (HPLC). IA tests that are practical, fast, and low cost, are frequently used in home-testing kits and in point-of-care (POC) screenings at outpatient clinics. IAs can detect numerous drugs and their metabolites within minutes of collection by using a pre-arranged, reactant-absorbed strips. If the sample contains any chemical that reacts with those strips, the results appear as a line on the screen. If the sample does not contain that particular substance, no reaction occurs (Fig. 32.1). The reaction of a chemical is dependent on the predetermined cut-off levels. Therefore, any chemicals in the sample, which are above or equal to the cut-off value, would make the result positive. IA test results should always be considered as *presumptive* until confirmed by a laboratory-based tests (GC/MS, LC/MS, or HPLC) for the specific drug. Several studies report false-positive results for cocaine and THC, in contrast to false-negatives for opiates and amphetamines [21].

Monitoring for Compliance

UDT is a useful tool in all phases of chronic pain management to detect noncompliance, prescription abuse, illicit drug use, or diversion. Random drug testing was shown to decrease illicit drug use significantly [15]. Although several algorithmic steps in UDT were suggested [22], there is no consensus as to the frequency of UDT. Initiation of opioid therapy generally requires a baseline drug test. Patients who have higher risks for opioid misuse and addiction as well as aberrant drug-related behaviors should be monitored and tested more frequently. Interpretation of the results should be done with caution due to multiple limitations of the tests as discussed earlier. Random testing is the preferred method to prevent patients from figuring testing patterns and thereby potentially altering their drug utilization [16]. A "*normal*" result for a patient being maintained on opioids includes a UDT positive for opioids and negative for the other substances tested (unless prescribed). Issues with semi-synthetic (oxycodone) or synthetic (fentanyl) opioids were discussed above. A confirmatory laboratory analysis would specify the type of the

opioid making the UDT positive. Additionally, it should be kept in mind that the dose taken cannot be extrapolated from drug screen results, even if a quantitative result is obtained.

Abnormal or unexpected results should not be considered as definitive, or have bearing on clinic decision-making [13, 16]. In such cases, UDT may be repeated and confirmed with additional laboratory tests. In cases whereby the prescribed opioid is not present in the UDT, nor in confirmatory lab analysis, it may indicate abnormal utilization, such as when the patient is sharing or selling the drug. Due to a fast-developing tolerance to opioids, some patients have the tendency to use bigger and/or more frequent doses of their prescription, which results in them being out of medication before their next scheduled refill, which in turn, leads to a negative test result for the prescribed opioids [23, 24]. These patients may require a reassessment for the appropriate opioid dosing to prevent under-treatment. It is well accepted that patients who use illicit drugs are at an increased risk for opioid misuse, abuse, and diversion. Therefore, such patients who show no improvement in repeated testing should not be allowed to continue opioid management, and may be referred to addiction treatment.

Conclusion

Chronic opioid management requires providers to overcome the challenge of preventing abuse of controlled prescription drugs, while providing the appropriate treatment for those patients who are in need of treatment. UDT represents a useful and practical testing method, which is currently under-utilized in clinical settings. UDT should be performed in tandem with other forms of patient monitoring, such as regular follow-up visits, behavioral observation, risk assessment, and review of the patient's prior history of addiction or substance abuse. Clinicians should avoid making final judgments about patient compliance based solely on the results of a urine test. Both knowledge and performance of UDT in clinical practice would result in better adherence to, and compliance with opioid therapy.

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Part VII
Multi Modal Approach: Injections and Procedures

Chapter 33
Trigger Point Injections for the Treatment of Pain in the Rehabilitation Patient

Vishal Kancherla and Amir Ahmadian

Introduction

The term "trigger point" was coined in 1942 by Dr. Janet G. Travell, MD, an internist and White House physician, who focused her clinical interest on dysfunction of the myofascia [1]. A trigger point (TrP) is an area of taut, ropey, boggy skeletal muscle, which is both hyper-excitable and hyper-irritable and can result in a twitch response to palpation. A twitch response is a transient contraction of the muscle that can be elicited by needle or manual manipulation [2]. Trigger point injections (TPI) have been used as one of the methods of treating non-malignant chronic pain syndromes, which annually affect 10–20% of North Americans [3]. Most practice guidelines recommend TPI as a form of adjunctive therapy for management of non-malignant chronic pain syndrome related to myofascial pain. Other treatment modalities that are similar to TPIs include indirect wet needling, direct dry needling, and indirect dry needling.

Pathophysiology

While the exact etiology of a trigger point is unclear and at times controversial, it is hypothesized that a dysfunctional neuromuscular junction (NMJ) is the pathophysiologic cause of a trigger point. It is believed that the neuromuscular junction

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becomes flooded with excess acetylcholine, which triggers the postsynaptic motor endplate to perpetually fire, leading to both acute and chronic muscle dysfunction. If the NMJ chemical milieu normalizes, it is thought that muscle firing regains its normalcy and can lead to the resolution of intrinsic hyperactivity. Introduction of injectate into the muscle belly, or TPI, has been known to have diluting effects on the NMJ, normalizing its firing presynaptically, which can lead to a decrease in pain and normalization of muscle function postsynpatically. Trigger points may be active or latent. Latent trigger points hold the cellular characteristics of a dysfunctional NMJ, but the associated muscle is not painful unless palpated.

The etiology of NMJ dysfunction can be multifactorial, most commonly related to environmental or postural factors. Environmental factors include poor ergonomic set-up, improper sports technique, and hobby-driven or work-related repetitive use of a muscle group. Postural factors include deviation from the normal physiological curves of the axial spine in the sagittal plane. Other more common changes in anatomy that can influence trigger point development are protraction or rounding of the shoulders, forward positioned cervical spine over a plumb line, pelvic obliquity, leg length discrepancy, valgus/varus deformity of the knee, and coronal plane abnormality of the spine, which most commonly includes adult degenerative scoliosis.

Common Symptoms

The clinical picture of an active trigger point is variable. A trigger point can present clinically with a mixed nociceptive and neuropathic picture. Often, patients will complain of tightness, muscle spasm, and deep/ache-like pain. Trigger points may also cause tingling, burning, and radicular pain. Symptoms can temporarily respond to myofascial release or to massage. Often, pain can be accompanied by limitations in range of motion, a sense of muscle weakness, an autonomic response, and often a predictable referred pain pattern (Fig. 33.1).

Diagnosis

Currently, there is no accepted gold standard to diagnose a trigger point. The utility of electromyography remains controversial. EMG studies of trigger points reveal spontaneous activity, while adjacent muscle remains electrically silent [4]. Palpatory examination is of paramount importance, as it will help to identify painful foci as well as a potential twitch response. **TART** is a mnenonic for palpation criteria to help diagnose muscle and somatic dysfunction: **T**issue texture abnormality; **A**symmetry; **R**estriction of motion; **T**enderness. Usually, trigger points will lie within the muscle belly. When disrupted by palpation, they can lead to reproduction of pain in a specific referred pain pattern (Fig. 33.2).

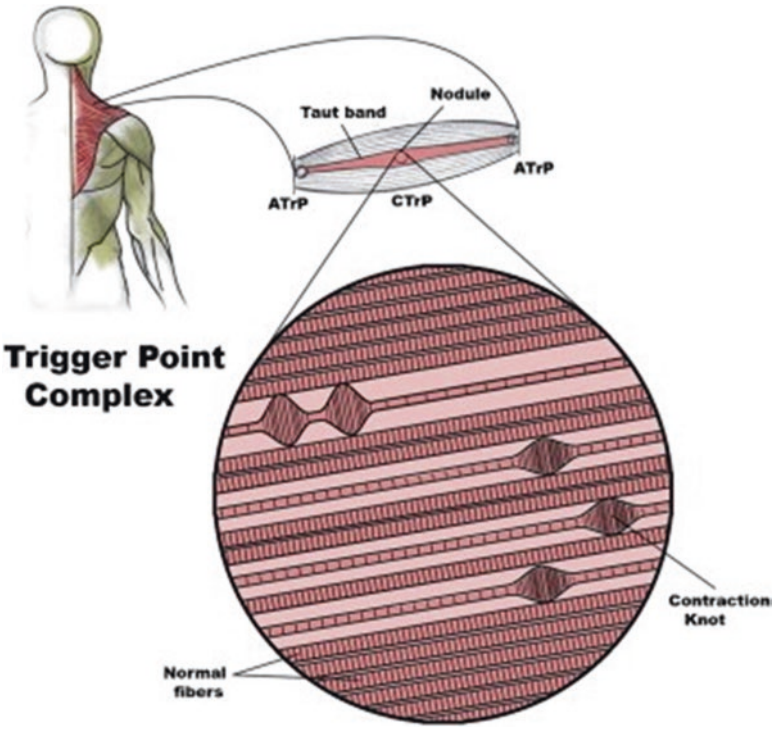

Fig. 33.1 Schematic of trigger point complex. Permission from Elsevier

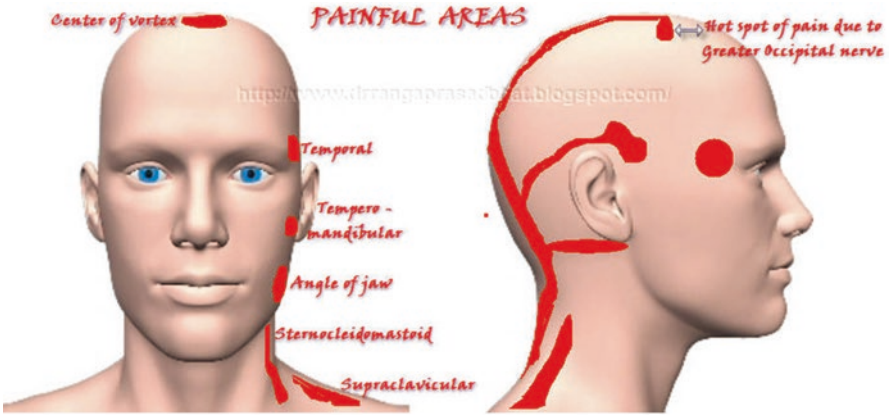

Fig. 33.2 Head and face trigger points. Permission from Dr. Rangaprasad Bhat

Treatment

Treatment of trigger point-induced pain should be multimodal. Correction of the precipitating factor, along with active and passive physical therapy modalities coincident with TPI have been shown to be most effective. The following modalities are important in the treatment of trigger points: TPI, myofascial release techniques, modalities including heat, ice, ultrasound, and spray and stretch technique, which is the application of flouri-methane or ethyl chloride spray topically followed by active stretching. It is important to ensure that mimickers of trigger point-induced pain are ruled out prior to treatment. These may include, but are not limited to large and small joint dysfunction, systemic arthritides, radicular pain, peripheral nerve compression, tempero-mandibular joint dysfunction, and even visceral pain. It is also important to differentiate trigger point pain from fibromyalgia as both can have superimposing patterns.

The injectate can be a mixture of corticosteroid and local anesthetic or normal saline alone. An anesthetic or normal saline can be used as a solitary injectate as well. Additionally, a variety of other fluids have been used in direct wet needling including vitamin B solutions, acetylsalicylate, ketorolac, and botulinum toxin [3].

Technical Considerations

A trigger point injection is performed under aseptic technique. Prior to prep, the muscle belly can be found via palpation using two fingers to centralize the muscle belly, which is the target of the injection. A small gauged needle is aimed directly into the trigger point and can be used to mechanically "break" the trigger point prior to injecting. Typically, if the trigger point is appropriately reached, the patient's pain is reproduced, and a local twitch response is elicited. Anywhere from 0.1–0.3 cc [5] to 1 cc [2] of injectate should be injected into the trigger point, after aspiration reveals no evidence of blood. Multiple trigger points may be injected at each encounter. Post-treatment care should include icing of the area for 15–20 min, every 4–6 h, and observation for infection. Stretching after the injection is encouraged, preferably through the entire range of motion of the treated muscle [6]. The use of ultrasonography and/or electromyography to guide TPIs may reduce risks associated with injections and may help to confirm needle position in muscle; however, this is not currently not the standard of care (Fig. 33.3) [7, 8].

Complications

TPIs are relatively safe; however, some rare adverse outcomes have been reported, which include pneumothorax, epidural abscess, muscle atrophy, infection, allergic reaction, vasovagal events, and nerve injury.

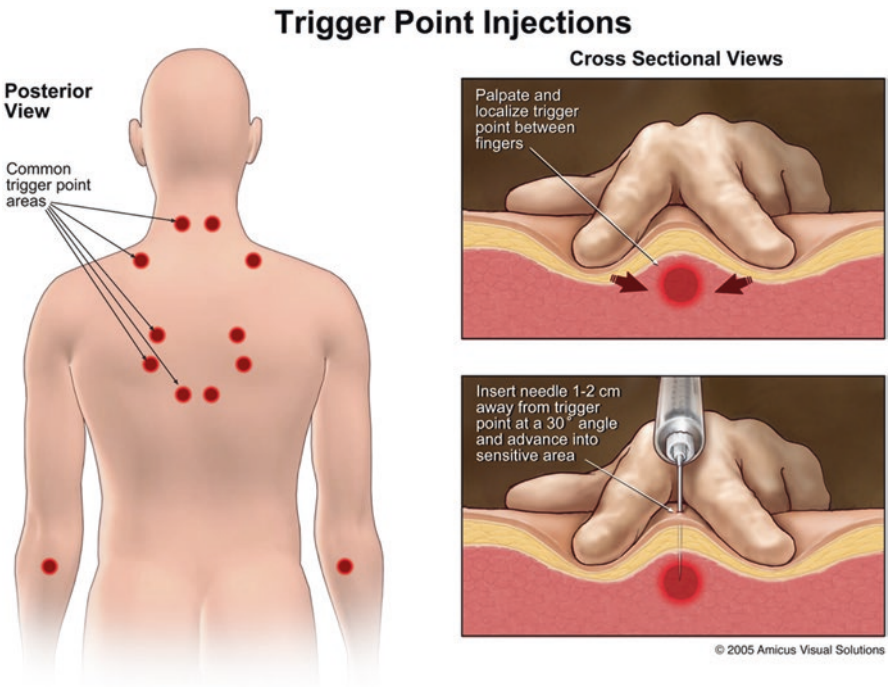

Fig. 33.3 Trigger point injection. Permission from Amicus Visual Solutions

Conclusion

Myofascial trigger points constitute a common source of pain, and the use of TPIs, in conjunction with other treatment modalities, has been shown to be an effective and safe option for managing these pain syndromes.

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Chapter 34
Intra-articular Joint and Bursa Injections for the Treatment of Pain in the Rehabilitation Patient

Vishal Kancherla and Angela Cortez

Introduction

Intra-articular injections were first recorded in 1792 by Jean Gay using Goulard's extract astringent, and refined by Joseph Hollander in 1951, who pioneered hydrocortisone injectate, describing successful clinical responses in over 100,000 injections for rheumatic disease [1, 2]. Rheumatic joint disease, particularly osteoarthritis, is one of the leading causes of disability in adults, and currently accounts for over one million in yearly total hip and total knee replacements and over $50 billion in annual hospital costs in the United States [3]. Intra-articular injections are both diagnostic and therapeutic, provide conservative treatment of arthritic disease, and remain the principal therapy for bursitis.

Pathophysiology

The large and small peripheral joints of the appendicular skeleton can undergo transformative changes that lead to inflammation and pain. These destructive changes can stem from osteoarthritis, rheumatoid arthritis, repetitive and overuse use type injuries, trauma, sport-related injuries, crystalline arthritides, and spondyloarthropathies to name a few. The hallmark of most of these changes in anatomy is an inflammatory

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cycle that initiates with cell wall damage and the release and production of proteolytic enzymes, prostaglandins, interleukins, and thromboxanes [4]. The rationale behind introducing and exposing a large or small joint to corticosteroids is to halt the inflammatory cycle. Clinically, this equates to increased range of motion, reduction in pain, and ultimately increased functionality.

Bursas, which are also a part of the appendicular skeleton, are common pain generators of musculoskeletal-induced pain syndromes. When this synovium-filled sac, which provides a surface and cushion for tendons gliding over joints during motion of a limb, is inflamed it can become a pain generator. The etiology of bursitis or inflammation of the bursal wall includes body habitus, muscle and skeletal imbalance such as a pelvic obliquity, trauma, and repetitive frictional stress over the bursa. Injection of corticosteroid into the bursa and peri-bursally can lead to pain relief [5].

Indications

Intra-articular and bursa injections are an integral part of multimodal therapy and are both diagnostic and therapeutic in nature. An appropriately placed intra-articular or bursa injection can support a preliminary diagnosis and aid in guiding treatment. Injection therapy should be considered before surgery and in conjunction with or after a trial of NSAIDs, activity modification, and physical therapy. By reducing pain and improving range of motion, active therapy comes with more ease and tolerance. This can lead to potential reduction of analgesics, which can help to mitigate the common side effects associated with medications.

Technical Considerations

There are several joints and bursas in the appendicular skeleton that are typically targeted. The knee, hip, ankle, and glenohumeral joints are the more common joints; however, essentially any joint that has an intra-articular space can be injected. The bursas that surround the knee, pelvis, and shoulder are the more common bursas that may require interventional treatment (Figs. 34.1, 34.2 and 34.3). The axial spine has its own articular joints and can potentially refer pain in similar distributions as the large joints of the body, but is referenced in a different chapter.

General technique for any joint or bursa injection is relatively standard. Consent should be obtained. The patient should be positioned in a manner that would minimize injury from a potential vasovagal reaction, as well as optimizing entry into the joint space or bursa. This can usually be achieved with the patient seated or supine, depending on the target. The procedure can be performed blindly or may be guided most commonly with use of fluoroscopy or ultrasound. Aseptic technique and universal precautions are recommended to avoid introducing infection.

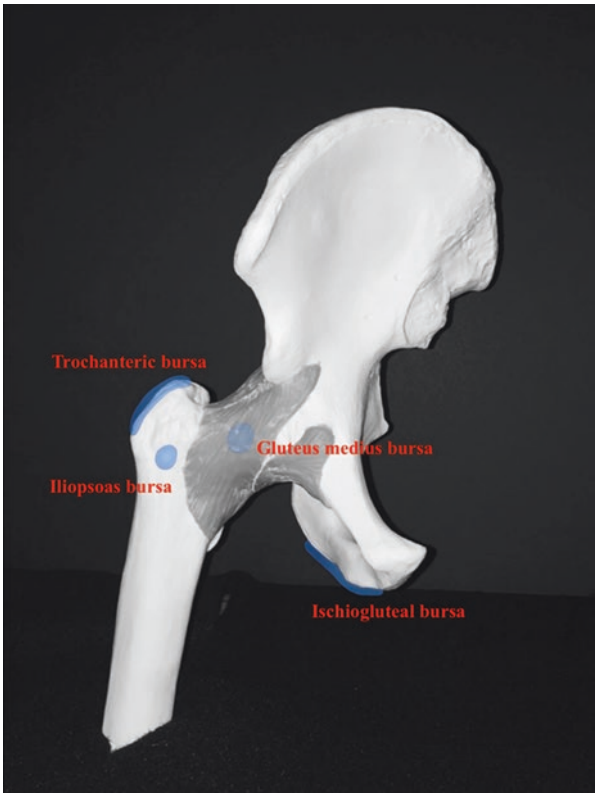

Fig. 34.1 Bursas in the pelvic area

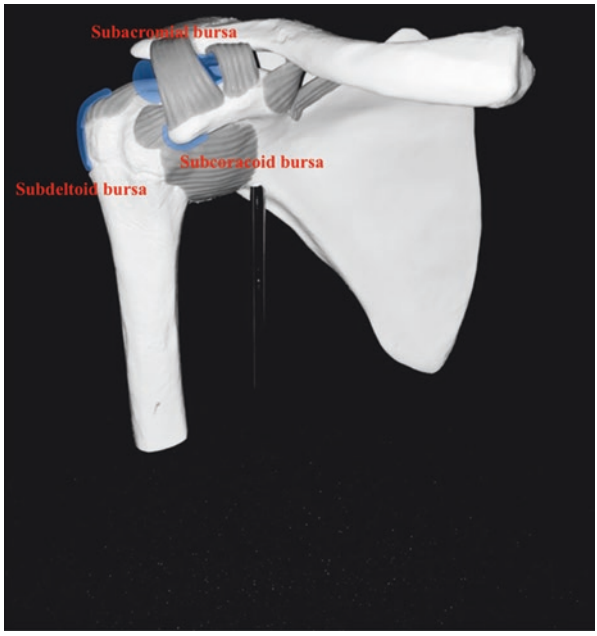

Fig. 34.2 Bursas around the shoulder

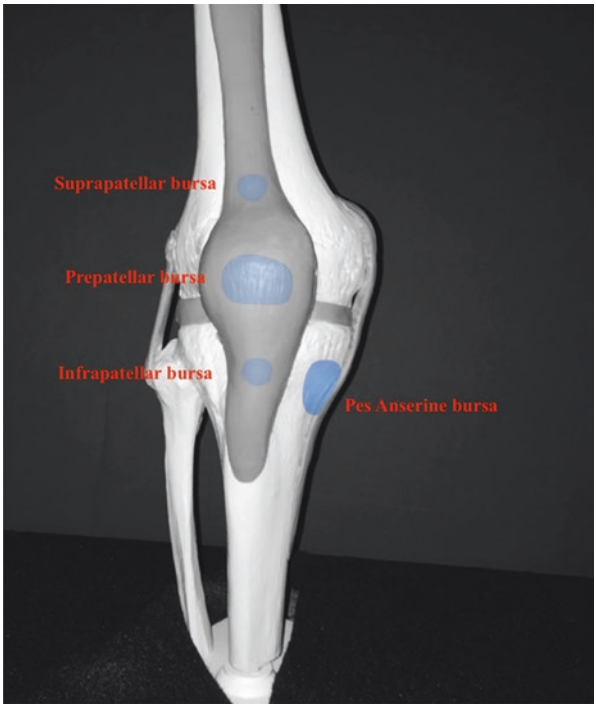

Fig. 34.3 Bursas surrounding the knee

The type of injectate is variable. Injectate usually consists of mixture of a local anesthetic and a corticosteroid. The most common anesthetics, bupivacaine and lidocaine, temporarily leaves a joint insensate, aiding in determining a primary pain generator and may be used alone for diagnostic purposes. Corticosteroid injectates are most commonly triamcinolone and methylprednisolone and vary in half-life and solubility [5]. Hyaluronic acid is FDA-approved as an injectate for the treatment of osteoarthritis in knees. Hyaluronic acid makes up part of the molecular matrix of synovial fluid, which gives the knee viscous and elastic properties and a smooth gliding surface to help the joint move and articulate [6]. In addition, it serves to provide nutrients, remove waste products, increases lubricating ability and has anti-inflammatory properties [6, 7].

Contraindications to joint injection include bacteremia, bleeding disorder, prosthetic joint, osteochondral fracture, infectious arthritis, uncontrolled diabetes, osteomyelitis, adjacent or overlying cellulitis [8]. Post-injection care includes applying a sterile adhesive dressing over the injection site with added pressure to halt any bleeding. Icing the area 15–20 min every 4–6 h can have an analgesic response and aid in post-injection discomfort. Relative rest and avoidance of vigorous activity immediately after the injections will help prevent washout of the corticosteroid.

Conclusion

With sound knowledge of anatomy and proper procedural technique, intra-articular and soft-tissue bursa injections can be safely performed to provide a means for both therapeutic treatments and definitive diagnostic tools.

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Chapter 35
Interlaminar and Caudal Epidural Steroid Injections for the Treatment of Pain in the Rehabilitation Patient

Joseph William and Ai Mukai

Introduction/History

The first epidural injection was performed utilizing a caudal approach with administration of cocaine for the treatment of low back pain and sciatica in 1901 [1]. Fifty-one years later, corticosteroids were first injected into the lumbar epidural space for the treatment of lumbar radicular pain [2]. Back and neck pain continue to be prevalent today and represent the first and fourth most common causes of disability in the United States, respectively [1]. Back and neck pathology also represent a significant financial burden in the United States, with the economic impact (directly and indirectly) estimated to be in excess of $86 billion annually [3]. There are numerous modalities utilized in the treatment of spine pain and epidural cortisone injections can be an important part of a multimodal treatment plan.

Glucocorticoids are endogenous molecules that are produced by the adrenal glands and are regulated by the hypothalamic–pituitary–adrenal (HPA) axis [4]. Glucocorticoids have many effects on the human body, but their effect to decrease pro-inflammatory substances can be utilized in order to reduce inflammation. Steroids given intravenously (IV), intramuscularly (IM), or by mouth (PO) may increase the systemic effects of glucocorticoids. Utilization of these medications in the epidural space creates a localized anti-inflammatory response, which minimizes the unwanted systemic effects of the medication.

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Epidural steroid injections can be administered as a single procedure or in a series of up to three; however, more recent evidence does not support the use of "series of three" injections [5]. Additional injections may not be indicated if the initial injection does not relieve symptoms or improve function [6]. Typically, no more than three to four epidural steroid injections should be given during the course of a year, as there are concerns for an increased risk of osteopenia as well as cortisol suppression [7]. There are several approaches to the epidural space including transforaminal, interlaminar (also called translaminar), and caudal (see Figs. 35.1, 35.2, 35.3, 35.4, 35.5, 35.6, 35.7, 35.8 and 35.9). This chapter will cover the cervical, thoracic, and lumbar interlaminar approaches as well as the caudal approach.

Epidural steroid injections introduce glucocorticoids, typically mixed with an anesthetic agent, via spinal needle into the epidural space (a potential space that lies between the ligamentum flavum and the dura) to relieve pain. Generally, it relieves radicular symptoms more than axial symptoms. Pain relief can also be attributed in part to the "wash out" effect, whereby the volume of injected material disperses the inflammatory molecules as well as the anesthetic agent that the steroid is mixed with [8].

Most guidelines recommend utilization of image guidance, typically in the form of fluoroscopy, with use of a non-iodinated contrast agent administered prior to injection of glucocorticoid, to ensure proper needle placement as well as lack of vascular uptake [5]. Image guidance is utilized in conjunction with the "loss of

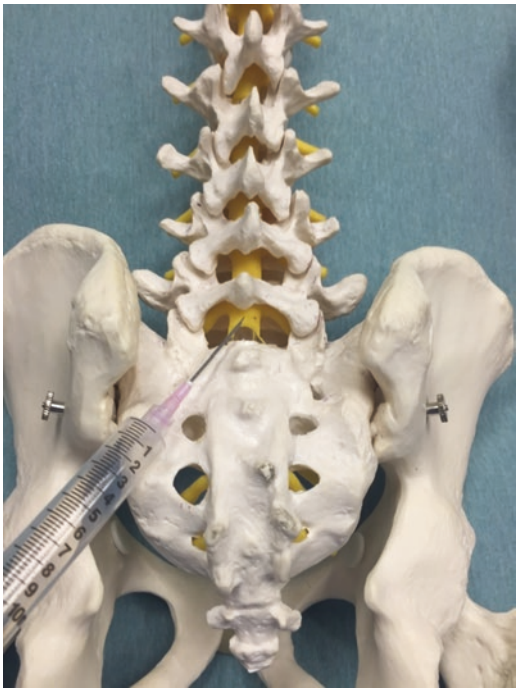

Fig. 35.1 Posterior view of an anatomic model depicting the insertion site for an interlaminar epidural injection at the L5-S1 level

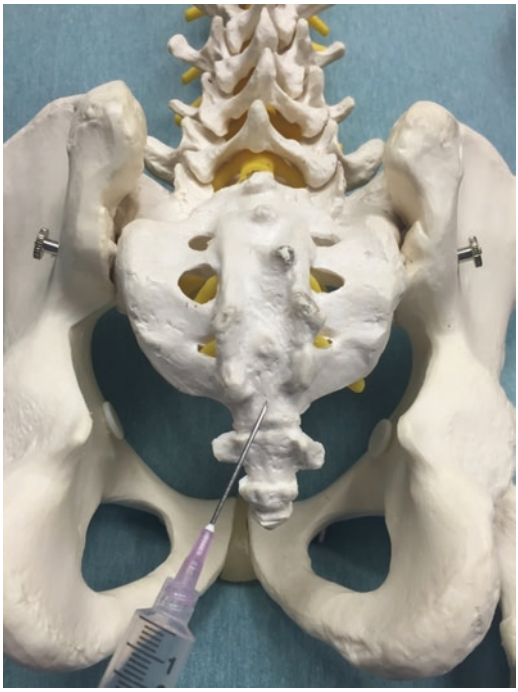

Fig. 35.2 Posterior view of an anatomic model depicting the insertion site for a caudal epidural injection

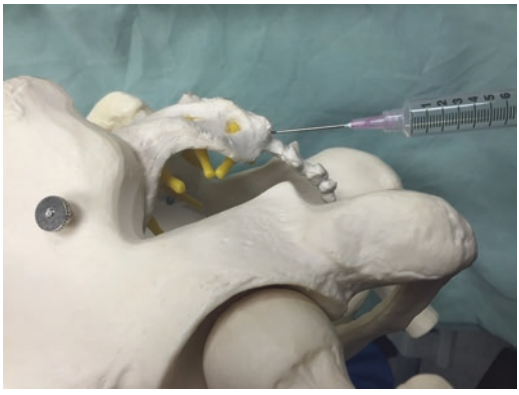

Fig. 35.3 Lateral view of an anatomic model depicting the insertion site for a caudal epidural injection

resistance" technique in interlaminar injections. The loss of resistance method can be performed with a glass or plastic syringe, using either air or saline, or with no syringe at all (hanging drop technique). Guidelines recommend cervical interlaminar injections be performed at the C7-T1 level and no higher than the C6-C7 level, as the cervical epidural space is widest at the C6-T1 levels and gaps in the ligamentum flavum become more common in the ascending cervical levels [9].

Caudal epidural injections can be guided with either fluoroscopy or ultrasound. A caudal epidural injection is considered to be the least specific modality of the

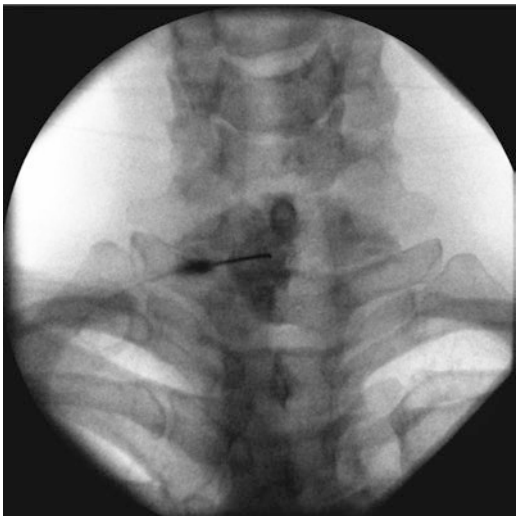

Fig. 35.4 AP fluoroscopic image, post-contrast, of an interlaminar epidural injection at the C7-T1 level

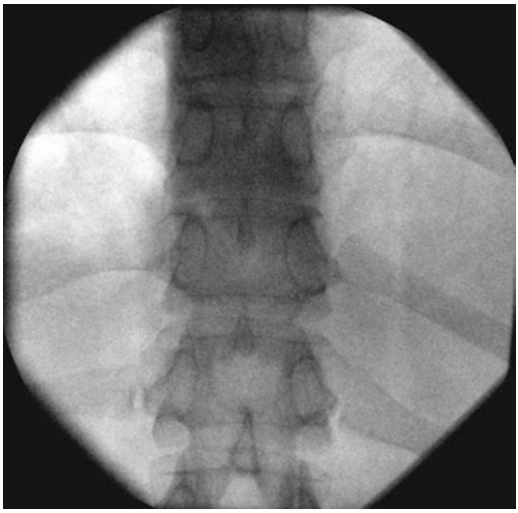

Fig. 35.5 AP fluoroscopic image of the thoracic vertebrae

three epidural options, requiring high volumes of medication to reach the pathological area in the spine [10]. What caudal epidural injections lack in specificity, it makes up for in ease and safety, as these procedures can typically be performed in the outpatient clinic setting under ultrasound guidance with minimal risk of dural puncture [1]. Trained specialists, many with fellowship training in pain and/or interventional spinal procedures, typically perform epidural injections including but not limited to anesthesiologists, physiatrists, and interventional radiologists. Indications for epidural glucocorticoid injections include: acute radiculopathy, subacute/chronic radiculopathy, spinal stenosis, and post-spine surgery syndrome [1].

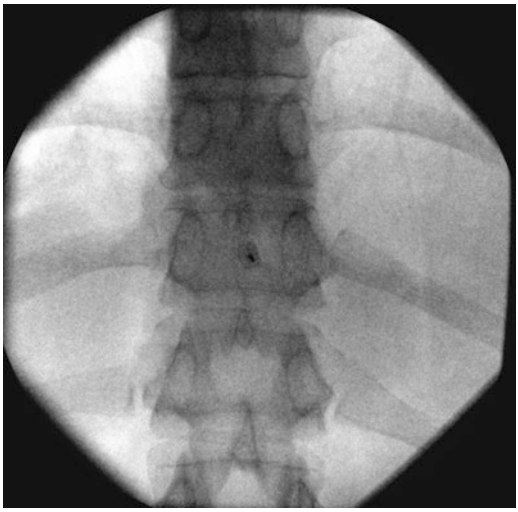

Fig. 35.6 AP fluoroscopic image of the thoracic vertebrae depicting proper interlaminar needle placement at the T10-T11 level

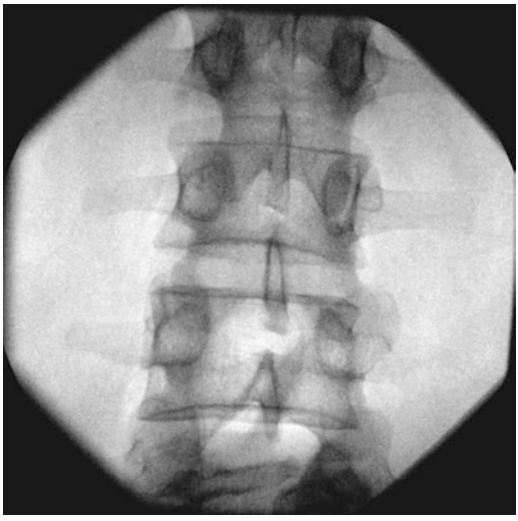

Fig. 35.7 AP fluoroscopic image of the lumbar vertebrae

Multiple glucocorticoid agents have conventionally been utilized for epidural injections, which include dexamethasone, hydrocortisone, methylprednisolone, triamcinolone, and betamethasone. For many interventionalists, the steroid preference is based on personal preference as well as spinal level of the procedure. Triamcinolone and betamethasone have particles that can form aggregates, which can occlude a blood vessel if inadvertent intravascular uptake occurs [11]. Interventionists may prefer dexamethasone, which is non-particulate and thereby does not aggregate, depending on the spinal level injected and/or proximity to the vasculature.

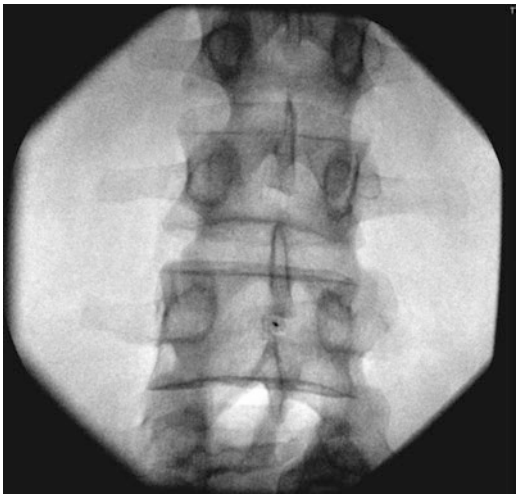

Fig. 35.8 AP fluoroscopic image of the lumbar vertebrae depicting proper interlaminar needle placement at the L3-L4 level

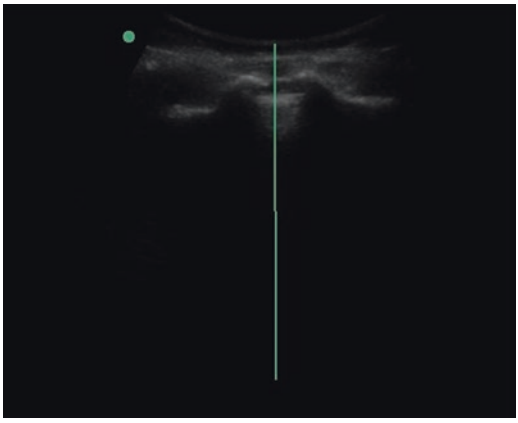

Fig. 35.9 Ultrasound image of the Sacral Cornua and the Sacral Hiatus for placement of caudal epidural steroid injection

Pathophysiology

Anatomy

Spinal nerves roots exit posterolaterally through the neural foramina, above the vertebral level in the cervical spine and below the vertebral level in the thoracic and lumbar spine. Neural impingement can occur from spinal canal and foraminal stenosis, from spondylosis and spondylolisthesis, as well as from disk herniations and other structures compressing the nerve root along the path of exit.

Radiculopathies

Greater than 95% of lumbar disk herniations occur at the L4-L5 and L5-S1 levels, followed by the L3-L4 and L2-L3 levels. Consequently, the L5 and S1 nerve roots are most commonly affected [12]. Additionally, posterolateral disk herniations of the nucleus pulposus are the most common form of disk herniation, as this is the weakest area of the annulus fibrosus. This can result in nerve root irritation proximal to the neural foramen, as it descends in the lateral recess [12]. In contrast, lateral or extra-foraminal herniations affect the nerve root after it exits the neural foramen which can result in nerve root irritation at the same disk level. For example, a far lateral L4-L5 disk herniation would cause L4 neural impingement, not L5 as in posterolateral herniation.

In addition to disk herniation causing foraminal narrowing, spondylosis can also decrease the diameter of the foramen, which results in similar symptomatology. Lastly, central disk herniations, as well as spondylosis and congenital canal stenosis can affect any portion of the spinal canal [12]. It is thought that a localized inflammatory reaction or mechanical compression leads to radicular symptoms. This allows for a potential intervention to halt the inflammatory cascade in acute, subacute, and chronic radiculopathies.

Spinal Stenosis

Much like a radiculopathy, spinal stenosis pain can result from mechanical compression and/or local inflammation of the nerve root. With spinal stenosis, however, nerve root ischemia can also occur, which results from venous congestion and arterial insufficiency. This can lead to symptoms of neurogenic claudication (i.e., leg numbness, heaviness, tingling, pain, and/or weakness with walking and/or standing) [12].

Post-Laminectomy Syndrome (Failed Back Surgery Syndrome)

This chronic pain syndrome, that persists despite surgical intervention predominantly effecting the lumbar spine, has multiple names (e.g., failed back syndrome, post-laminectomy syndrome) and has a constellation of etiologies that result in continued low back and/or leg pain. Typically, the surgery that precedes this syndrome is a spinal fusion or laminectomy and the differential diagnosis of the resulting pain can be grouped based on whether the predominance of pain is in the back or in the leg(s) [13].

Clinical Considerations

Much like any pain complaint, back/neck pain should be evaluated with a thorough history and physical examination, which can often lead to the diagnosis before any additional imaging studies are utilized. “Red Flags” with respect to spinal pain require prompt management to reduce morbidity and mortality. These include, but are not limited to, history of trauma or cancer, suspected fracture, unintentional weight loss, progressive leg weakness, urinary/bowel incontinence, unremitting pain, suspected myelopathy, suspected cauda equina syndrome, and saddle anesthesia [12]. The presence of such signs and symptoms may also indicate the need for a surgical referral.

Based on the history and physical examination, additional diagnostic studies may be warranted to further narrow the differential diagnoses and/or to rule out “Red Flag” pathology. These typically include plain x-ray films, magnetic resonance imaging, computed tomography, myelography, electromyography, and nerve conduction studies. Some form of imaging is recommended prior to considering an injection, especially in the cervical spine, to ensure adequate epidural space for needle placement [9]. Laboratory studies may also be warranted if an inflammatory disease or neoplastic process is suspected [12]. For technical considerations, please see appendix.

Comprehensive Multimodal Approach

Current treatment guidelines recommend using epidural steroid injections as an adjunct to other conservative treatments in an effort to shorten the duration of symptoms and to improve functional outcome. Epidural steroid injections can help to facilitate therapeutic exercise, in the form of patient education, aquatherapy, and physical therapy. Functional movement therapies, as well as directional preference therapies such as the McKenzie method, have been shown to help with acute radicular pain. Other adjuvant options include modalities such as heat, ice, and electrical stimulation as well as medications such as NSAIDs, muscle relaxers, neuropathic pain medications, certain classes of antidepressants, and opioids. In general, long-term opioids are not indicated for spine pain [14, 15]. Research has also shown that earlier “return to work” produces better outcomes in terms of work function and disability [16, 17].

Potential Treatment Complications

Although epidural steroid injections have become a safe and relatively common tool for the interventionist, rare treatment complications do unfortunately occur. Potential complications can be divided into two categories, which include immediate and delayed. The immediate treatment complications can include intravascular

uptake of local anesthetic causing seizures/arrhythmias, spinal headache, nerve injury, hemorrhage (both intraspinal and extraspinal), vasovagal reaction, allergic reaction, and dural puncture. Extremely rare complications may include spinal cord injury, stroke, and death. Delayed complications can include slow hemorrhage, infection, steroid side effects, delayed allergic reaction, CSF leak/spinal headache, and diabetic complications, which are typically in the form of elevated blood glucose levels or difficulty in controlling blood glucose after an injection [18]. Significant hematomas have also been noted in patients with an underlying coagulopathy and those taking anticoagulant medications [19, 20]. The American Society of Regional Anesthesia (ASRA) guidelines recommend holding most prescription anticoagulants prior to axial spinal procedures [21]. Exceptions could be considered for ultrasound-guided caudal injections.

Evidence of Efficacy

Multiple studies have supported the efficacy of interlaminar and caudal epidural steroid injections in patients with cervical, thoracic, and lumbar radicular pain secondary to disk herniation, spinal stenosis, and post-lumbar surgery syndrome [1, 22, 23]. The true short and long-term efficacy of these injections is more controversial, with more recent research showing limited value in the context of lumbar spinal stenosis [24]. These injections have shown benefit in allowing patients to participate in physical therapy, reduce disability/off-work status, and possibly avoid surgery, emergency room visits, and opioid addiction.

Conclusion

Epidural steroid injections can play a role in the context of a multimodal treatment approach to the patient with spinal radicular and occasionally axial pain. The risks and benefits should be weighed and discussed with the patient to create an individualized treatment plan that optimizes symptom relief as well as functional independence.

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Recommended Reading

Atlas of Image-Guided Spinal Procedures, 1st Edition, Furman
Braddom's Physical Medicine & Rehabilitation, 5th Edition, Cifu
Interventional Spine: An Algorithmic Approach, 1st Edition, Slipman
Guidelines: SIS, ASRA, and ODG

Chapter 36
Transforaminal Epidural Steroid Injections and Selective Nerve Root Blocks for the Treatment of Pain in the Rehabilitation Patient

Mehul Sekhadia

Introduction

SNRBs were first described in the literature in the early 1950s and were eventually re-introduced in 1992 by Richard Derby [1, 2]. In practice, the terms SNRB and TFESI are used interchangeably, as the technique for both procedures is very similar. The selectivity of the block is debatable in that even a small volume of medication injected at the nerve root may spread to an adjacent level via the epidural space [3]. The majority of these procedures are performed for both diagnostic and therapeutic purposes; therefore, depositing medication close to the source of the pain can provide pain relief beyond the duration of the local anesthetic medication initially injected. In the setting of multi-level disease, the source of pain can be determined by utilizing a low volume of medicine at a particular nerve root. For example, if there is disease at both the C4-5 and C5-6 levels, and if symptoms do not correlate exactly with either levels, then serial diagnostic blocks can be done to determine the source of pain and to provide both pain relief and staging for surgical correction. If partial pain relief is achieved at both levels, then both levels may need to be corrected.

Pathophysiology

The nucleus pulposus of intervertebral discs contains a high concentration of phospholipase A2 [4]. When phospholipase A2 is released into the epidural space, there is a high concentration of the inflammatory mediator prostaglandin in the neuraxis.

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Corticosteroids targeted to this area will inhibit phospholipase A2, which will thereby decrease prostaglandin levels as well as pain. This mechanism of action has remained the premise behind using epidural steroid injections for over 100 years. This has been proven in animal models but still remains controversial in vivo. Part of the controversy surrounds the fact that non-steroid injections also provide pain relief, which include both local anesthetic and saline [5–11]. Additionally, there is controversy as to the utility of this procedure because it unknown whether mechanical compression of the nerve is the source of pain, or whether it is truly a chemical reaction, as described earlier, that is the source of pain. Interestingly, studies reveal that 36% of some patients with mechanical compression of nerves remain asymptomatic [12]. Furthermore, mechanical manipulation of nerve roots most likely causes paresthesias or numbness, rather than pain. Finally, 10–20% of patients who undergo surgical correction of anatomy still have persistent radicular pain [13].

Despite the controversies and debates regarding the evidence and efficacy of this procedure, injection of corticosteroid into the epidural space is a mainstay of conservative, non-surgical management of radicular pain [14]. Many patients ask if the injection of corticosteroid will "fix" their anatomic pathology. Current opinion suggests that the use of steroid does not "fix" the pathology, as a large number of patients who do not undergo steroid injections are still able to avoid surgery, even in the setting of a large disc extrusion.

Common Diagnoses/Symptoms

Pathology in the spine can cause axial and radicular pain. Painful conditions in the spine can include disk herniations, facet arthropathy, ligamentum flavum hypertrophy, primary and secondary cancers, facet synovial cysts, infections, post-laminectomy pain syndrome, and others. The SNRB/TFESI is performed most commonly in the setting of pain related to an irritated nerve root in one of these settings. Successful pain relief is best obtained when the subjective complaint is consistent with objective findings. That is, if MRI or CT myelogram reveals a disk herniation with neural impingement, it is highly likely that an injection near the pathology will provide pain relief. Pertinent positives seen on exam may include decreased spine range of motion in any plane, sensory abnormalities, motor deficits, decreased deep tendon reflexes, muscle atrophy, and positive provocative testing, which includes straight leg raising or Spurling's maneuver.

If multiple areas of pathology are seen on imaging, or if subjective findings are not consistent with objective findings, the block can be utilized to determine which potential pathologic finding is truly the source of the pain. While a temporary response to local anesthetic can be achieved at any targeted level, the response to corticosteroid might be more predictive of determining the "source" of pain, as well as the possible response to surgical intervention. For example, if the complaint of pain is in the L5 dermatome, but more severe findings are seen at the L3 nerve root, the L3 nerve root can then be injected to provide both pain relief as well as a diagnostic confirmation as to the source of pain. This can also be used as a "negative" study if pain relief is not achieved [15, 16].

A thorough history and physical examination should always be performed prior to any spinal intervention. Appropriate imaging such as CT scanning or MRI of the spine is absolutely necessary if there is any objective neurologic finding or progressive deficit noted. A plain X-ray may suffice in some situations, such as recurrent symptoms in the setting of stable neurological findings on examination. For example, a patient who does not have any recent imaging, but has had interventional treatments in the past for similar complaints concordant with previous imaging, with benefit, without complication, without progressive neurological deficit, then history or physical exam alone may be considered sufficient to re-engage in interventional treatment.

Functional Limitations Addressed

As mentioned, the primary purpose of the SNRB/TFESI is pain relief. Relief from radicular pain will improve quality of life measures and will also enhance participation in rehabilitation, which will inevitably address restrictions in the range of motion. Common reasons for patients presenting to pain management clinics involve the inability to perform normal activities of daily living (ADLs), which include sitting, standing, walking, and sleeping. In some cases, time and pain medications may provide enough relief to allow performance of ADLs, but if there are side effects from the medication, or if symptoms do not remit with time, injections can be essential to facilitate the rehabilitation paradigm.

The diagnostic capability of the injection is very much dependent upon the "spread" of medication along the nerve root. To avoid false positive responses, focus is placed on the amount of medication injected, as studies have shown that as little as 0.3 mL of volume can spread to the adjacent root, even in the lumbar spine [3]. As such, the procedure should be performed with a non-iodinated contrast agent, to maintain diagnostic integrity and to determine the potential for a false positive result. Furthermore, the volume of injectate should be adjusted to avoid potential spread to an adjacent nerve root.

Monitoring success of the block is dependent upon the patient's ability to participate in normal ADLs, restoration of quality of life, and basic exercise, as well as use of objective standardized outcome assessment tools, such as the Oswestry Disability Index (ODI). Repeat procedures should be considered if partial or temporary success has been attained for any of these measures. If there is no improvement in any measure, then a different cause of pain should be considered, which should suggest targeting a different part of the body or another neurologic level in the spine.

Technical Considerations

All SNRB/TFESIs should be performed with image guidance. The majority of these procedures are performed with fluoroscopy but recently, the use of ultrasound has also been employed with success [17].

Required materials:

- Imaging:
- C-arm fluoroscope with fluoroscopic table, or CT scan, or ultrasound machine
- Monitors:
- Pulse oximetry, oscillometric blood pressure cuff, EKG, and end tidal CO_2 (for conscious sedation)
- Needles:
- 2 or 25 gauge Quincke needle, variable length from 3.5 to 7 in., depending on patient's body habits
- Medication:
- Corticosteroid—preferably non-particulate (dexamethasone) or particulate (depomedrol, triamcinolone, betamathasone) and non-iodinated contrast agent.

Figures 36.1, 36.2, 36.3, 36.4, 36.5, and 36.6 demonstrate the various fluoroscopic angles utilized for the SNRB/TFESI. The usual volume of injectate for therapeutic purposes is 2 mL, which is composed of 1 mL of the corticosteroid and 1 mL of either saline or local anesthetic. In a recent review published in JAMA, Benzon et al. suggested that dexamethasone should be utilized for the "first" injection, as it has demonstrated equivalent efficacy and no catastrophic consequences. Until recently, particulate steroids were more commonly utilized, as it was thought the particles would provide longer lasting relief or effect as compared to the water-soluble steroids such as dexamethasone [18].

For the lumbar spine below the L2 level, some experienced practitioners will typically utilize particulate steroids based mostly on anecdotal experience (this writer included). However, above the L2 level, it makes more sense to use water-soluble steroids because of the risk of catastrophic complications, which will be discussed in the next section [19]. To account for the higher risk of injury above the L2 vertebral level, mostly stemming from vascular penetration, the use of digital subtraction angiography can be added to confirm safe needle placement without vascular uptake. If vascular penetration occurs, the needle should be repositioned and repeat angiography should be performed. If vascular uptake is shown twice, especially in the cervical spine, the procedure should be aborted [19].

Complications

Relative to the number of procedures reported, the risk of complications remains very low. Short-term complications include bruising at the injection site, possible site-related pain, numbness in the distribution of the nerve being blocked, and sometimes neuritis, which can cause more pain temporarily after the procedure. Most of these complications are transient.

Catastrophic complications have also been described [20–25]. Therefore, the procedure should only be performed by those who have completed proper training.

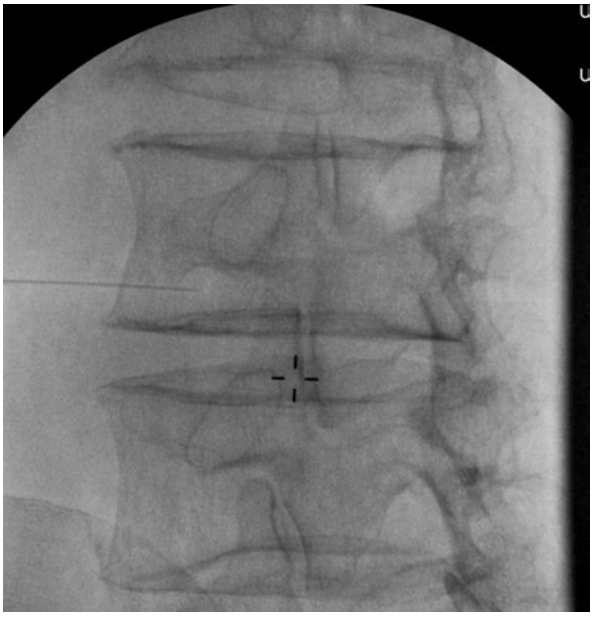

Fig. 36.1 Square off end plates of the desired level to be injected (in this case, L3). Fluoroscope is rotated oblique 20–35° to obtain the "foraminal" view. Local anesthetic is injected via a 25 gauge needle as shown in the figure

Complications are often related to the failure to recognize abnormal needle placement, failure to abort a procedure in the setting of patient intolerance, vascular penetration of the needle, and excessive sedation whereby the patient cannot respond. Depending on the location in the spine, vascular penetration has a relatively high incidence (11–19%); thus, recognition is paramount to procedural safety [26]. The use of particulate steroid has also been implicated as the cause of the spinal cord injury in the setting of vascular uptake. Nevertheless, even though vascular penetration occurs frequently, clinical sequelae are uncommon. In many settings, severe central, foraminal, or lateral recess stenosis is present; thereby, it is imperative to have the patient awake and responsive during the procedure as many catastrophic complications such as permanent nerve damage have been reported in this setting, most likely related to severe nerve ischemia.

Evidence

There is a paucity of "level 1" evidence for the use of SNRB/TFESI for both diagnostic and therapeutic purposes. Level 1 implies randomized, prospective, double-blinded, placebo controlled outcome studies. Because pain is such a subjective experience, with a significant amount of patient-to-patient variability, it is a difficult measure to standardize. As such, most studies will include outcomes based on more objective measures such as ODI, quality of life measures, and avoidance of surgery. Since epidural steroid injections are performed so frequently, there are a plethora of

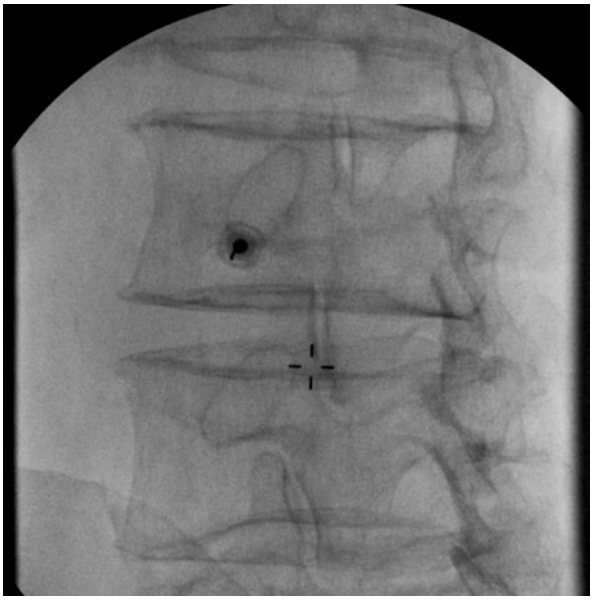

Fig. 36.2 A spinal needle is placed sub-pedicular, outer edge of the pedicle. Note the coaxial view of the needle where the hub is over the tip of the needle in the oblique plane of the fluoroscope

opinions regarding their utility and place in the overall management of pain. SNRB/TFESIs frequently get grouped into all spinal interventions when meta-analyses are done, which includes interlaminar and caudal epidural steroid injections.

Recently, Chou et al. published a review in the Annals of Internal Medicine, which essentially concluded that there is no evidence to support the use of epidural steroid injections for the management of pain related to disk herniations [27]. This contradicts many studies published in both pain management and rehabilitation medicine journals [28–32]. Most of the specialty-specific articles agree that these procedures do work for the management of pain related to disk herniations. There is more uncertainty as to how to perform them (interlaminar, caudal, or transforaminal), when to perform them, and how frequently they can or should be performed. Since the majority of these procedures are performed in the lumbar spine, the majority of the literature is relative to blocks performed in this region. There are retrospective reports of success in the cervical spine, which have been recently published by the Cleveland Clinic [33].

Conclusion

SNRB/TFESIs are a useful adjunct in the diagnosis and treatment of painful spinal conditions as outlined earlier. As with most procedures in medicine, success is related to patient selection as well as the use of a comprehensive management approach. Improvement in ODI, quality of life measures, and participation in a rehabilitation program are methods to monitor progress of patients with pain. A

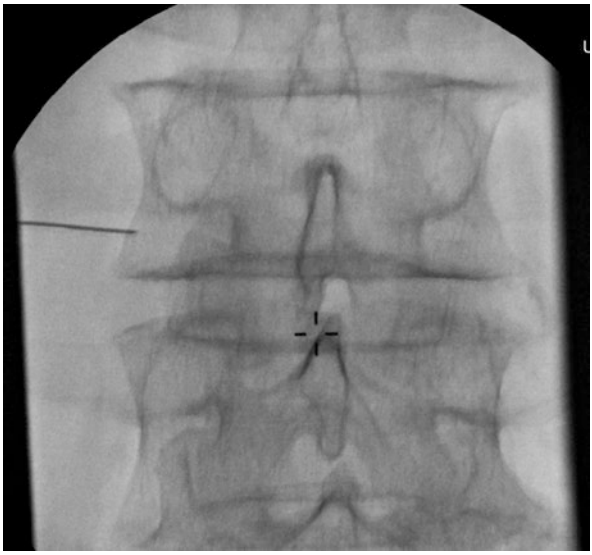

Fig. 36.3 The fluoroscope is rotated back to anteroposterior view and the needle tip is located at the outer edge of the foramen

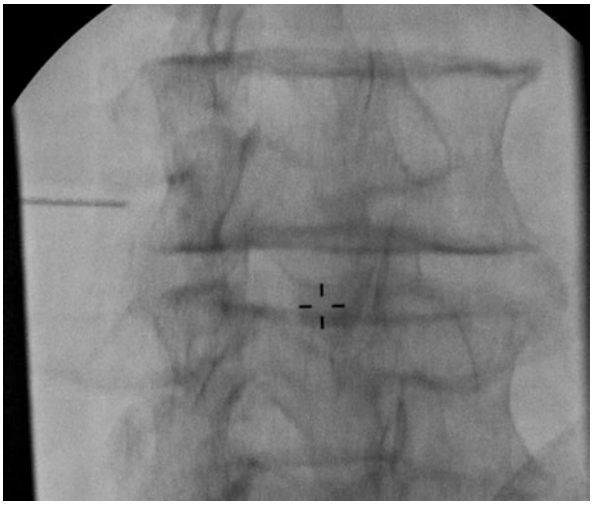

Fig. 36.4 Reverse oblique view is taken and the needle tip has not yet entered the foramen

thorough evaluation of the patient should be performed prior to the procedure, ideally including an MRI unless contraindicated.

Image guidance should be utilized for all procedures. While fluoroscopy is the most frequently utilized, recent advances in ultrasound position it as potentially useful as well. The technique has to be adjusted in the setting of severe spine degeneration. Recognition of proper needle placement and more importantly improper needle placement are important to prevent catastrophic complications such as spinal cord

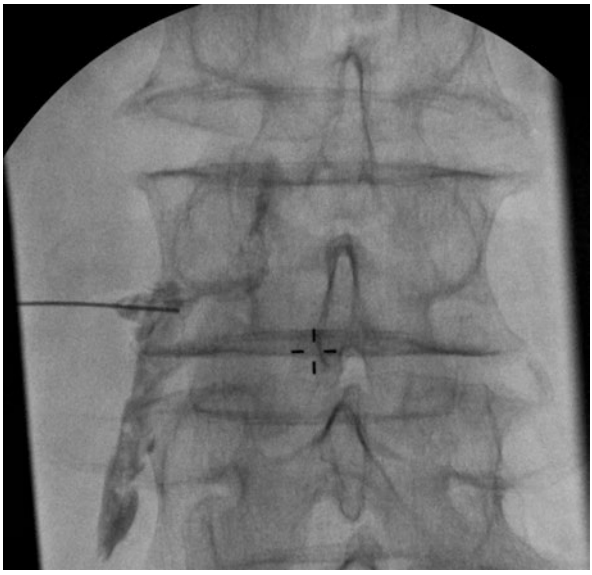

Fig. 36.6 Injection of 2 mL of iodinated contrast outlining the L3 nerve root without any vascular or cerebrospinal fluid uptake. The contrast can be seen proximally in the spine as well as extra foraminally

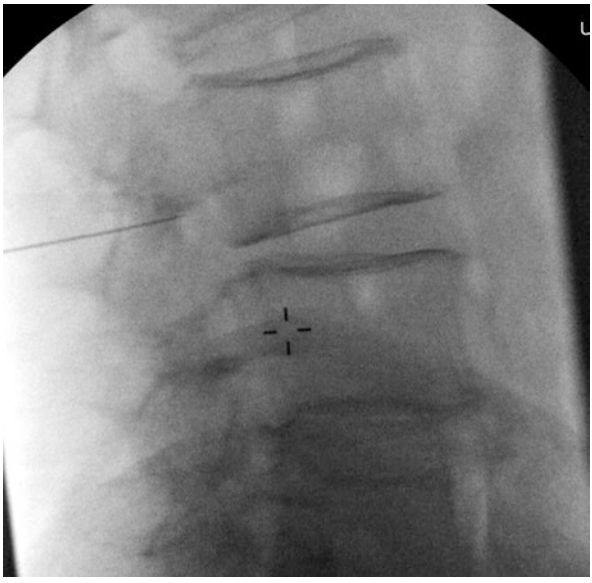

Fig. 36.5 Lateral view with needle seen at the posterior edge of the foramen, just under the pedicle. For more of an epidural injection, the needle would be advance to the anterior portion of the foramen. For the selective nerve root, the final position of the needle tip should be dependent upon the outline of the nerve with the injection of the iodinated contrast

injury. The risk of catastrophic complications is extremely low relative to surgery, assuming the patient has a normal coagulation status, there is absence of systemic or local infection, and proper technique is utilized. There is evidence to support the use of this procedure for the management of spine-related pain, and the potential benefit significantly outweighs the potential risk.

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Chapter 37
Sacroiliac Joint Injections for the Treatment of Pain in the Rehabilitation Patient

Miguel D. Attias, Olena Zhukova, and Nomen Azeem

Introduction/History

Following Glodwaith and Osgood's reports in 1905 [1], "joint sprains" were considered as the predominant cause of "sciatica". In the year 1930, Mixer and Barr described a ruptured disc and nerve compression discovered during surgery in a patient who was being treated for a "sacroiliac joint sprain" [2]. Thereafter, attention became focused on the degenerated/herniated disk as the predominant source of low back pain. In 1956, Norman and May became the first physicians to fluoroscopically inject the sacroiliac joint (SIJ), but it wasn't until the work of groups led by Fortin, Schwarzer, and Maigne in the 1930s that the objective data necessary to regain the subsequent acceptance of sacroiliac joint dysfunction (SIJD) as a progenitor of low back pain (LBP) was established [3–6].

Pain originating from the SIJ is estimated to affect from 15% to over 30% of patients with axial LBP [7]. Despite the significant variability in prevalence rates, there is general agreement that the SIJ is positioned, along with the intervertebral discs and the facet joints, as one of the major causes of LBP, with or without lower extremity pain. Frequently, multiple concomitant spinal and non-spinal sources are involved in generating low back pain syndromes, making diagnosis and management even more complex.

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In a cross-sectional study, which included 202 patients with image-proven lumbar disc herniation, it was reported that 72.3% of patients satisfied the criteria for SIJD. Thus, it was recommended that regardless of intervertebral disc pathology, SIJD must be considered in clinical decision making [8].

The prevalence of SIJ pain is at least 2–3% in patients with failed back surgery syndrome and may be higher in patients who had fusion of the sacrum [9]. It is likely that the joint becomes painful secondary to bone harvesting or due to transfer of stress after fusion [10]. Additionally, SIJ-mediated pain may have been present before surgery, but went unrecognized [11].

Currently, the consensus is that history, physical examination, and radiological imaging are insufficient to diagnose SIJ pain and that only the combination of multiple tests can increase diagnostic validity. Multiple publications have shown moderate levels of evidence supporting the accuracy of provocative physical examination maneuvers. Furthermore, some studies advocate performing diagnostic blocks when further treatments like interventional procedures may be appropriate.

If the patient's history, palpation, and provocative tests generate suspicion, the most commonly used method to verify the SIJ as a pain generator involves a local anesthetic injection into the sacroiliac joint, using fluoroscopic guidance. This procedure remains a "reference standard", despite arguments against the validity of controlled local anesthetic blocks [7, 8, 12–20]. When steroids are added, the injection may become therapeutic, if an acceptable time period of relief is obtained.

The management of this potentially disabling entity involves multiple disciplines and specialties. The main focus of this chapter will be on the interventional aspects of pain management, taking into consideration the intricate relationship between procedures and rehabilitation.

Pathophysiology/Mechanisms of Action

SIJ pathology is not the same as SIJD, as both entities may occur independently or may coexist [13]. Pathologies of inflammatory nature, like the spondylo-athropathies, are well-described and relatively easy to demonstrate as sources of SIJ pain, and this is also true for infectious states, tumors, and metabolic bone disease. These etiologies generally do not generate diagnostic uncertainty, given that imaging and laboratory tests are available to demonstrate a causal relationship. Traumatic events can also trigger pathology and SIJ pain, both of which can be easily deducted from history and imaging. By contrast, SIJD is a syndrome caused by a combination of pelvic asymmetry, joint locking, hypo/hypermobility, and/or muscular imbalance; and typically, there is no demonstrable radiographic joint pathology [15].

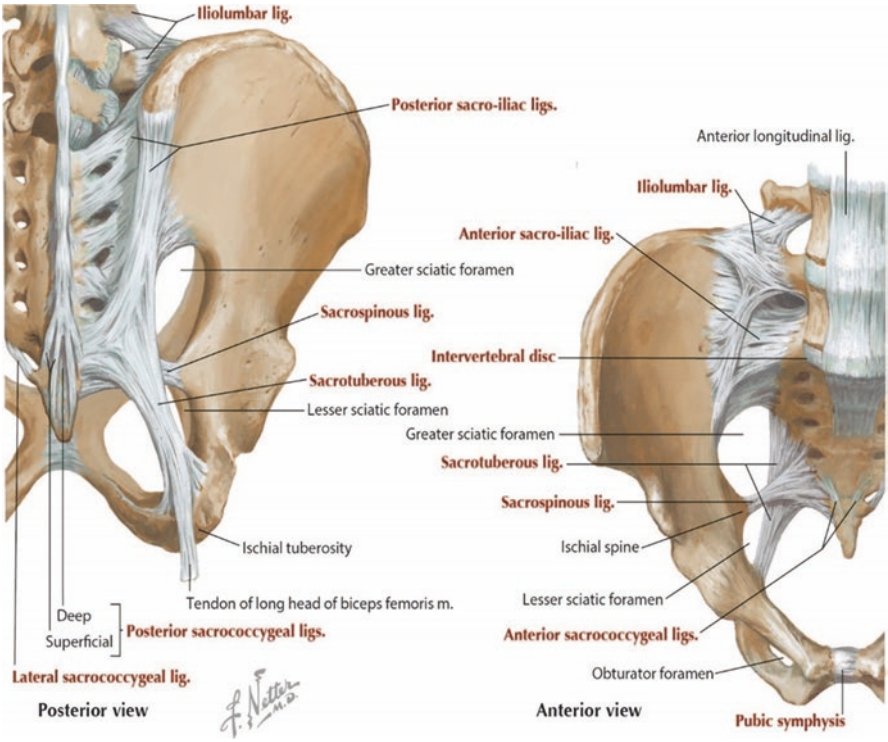

Fig. 37.1 Ligaments of the Sacroiliac Joint

Anatomy and Biomechanics

The SIJ is considered the largest axial joint in the body, although there is great variability in size, shape, and surface contour within and among individuals. [15, 16] It is an auricular or C-shaped diarthrodial joint, but it has elements of amphi-arthrodial joints, like the symphysis pubis. Only in the anterior third of the contacting surfaces, between the sacrum and ilium, is it a true synovial joint, where it is approximated by a fibrous capsule [21]. The posterior portion of the joint has only a rudimentary capsule, if any, and is considered a fibrocartilage syndesmosis, which is reinforced by ligamentous structures that prevent motion in all planes. The joint's articular surfaces contain several ridges and depressions that further impede movement and increase stability, and these seem to develop in response to stress and vary among individuals. Of all factors involved in joint stabilization, the multiple adjacent ligaments are believed to be the most important (Fig. 37.1).

There are several myofascial structures that influence movement and stability, the most notable of which includes the latissimus dorsi via the thoracolumbar fascia, the gluteus maximus, and the piriformis. Multiple studies suggest that SIJ stiffness increases with muscle activity, supporting the notion that effective load transfer

from the spine to the legs is possible when muscle forces actively compress the SIJ, therefore preventing shear. Altered motor control of deeper muscles, like the transversus abdominus, internal oblique, multifidus, diaphragm, and pelvic floor muscles, plays an important role in both lumbo-pelvic support and pain generation [22].

The SIJ allows movement of the pelvis about the axis of the sacrum, which serves the important functional role of transferring forces in a bidirectional manner. These forces occur during standing and ambulation, between the upper body and the lower extremities, and in the sitting position, between the trunk, ilia, and ischial tuberosities. Although little joint motion exists, it appears to be sufficient enough to decrease the cost of ambulation by storing and releasing energy, which thereby diminishes stress on the pelvic ring by absorbing shock [23]. Nutation denotes sacral base movement in an antero-inferior direction in relation to the ileum that occurs during lumbosacral extension. During lumbosacral flexion, the sacral base moves postero-superior. This opposite movement is termed counter-nutation. There are conflicting reports regarding the position of the instantaneous axes of rotation, the extent of movement, and the existence of motion in other dimensional planes [16].

Under the special physiologic conditions of pregnancy, hormone-induced laxity of the sacroiliac and pelvic ligaments allows for the mobility necessary for gestation and parturition. The hormone-induced ligamentous laxity, pregnancy-associated weight gain, exaggerated lordotic posture, and the mechanical stress associated with parturition, all predispose women to SIJ pain [24].

The variable distribution of referred pain from the SIJ can be attributed in part to its size and heterogeneity, but also to the variable nature of its sensory innervation, which remains controversial. The literature suggests that the posterior SIJ is supplied by lateral branches of the S1 to the S3 dorsal rami, with some evidence of contributions by the dorsal rami from L3 to S4 (Fig. 37.2) [21]. The anterior joint might receive contributions from different combinations of the ventral rami of L2 through S2, and even from the obturator and superior gluteal nerves; however, it is also believed that the SIJ might be devoid of innervation [16, 25].

Pathophysiology

Injury and pain generation from the SIJ generally results from a failure of its stabilizing ligaments, as well as dysfunction of the joint's anatomical relationships. Destabilizing compressive and torsional shearing forces, which result from excessive axial loads and rotation, can injure the SIJ and associated myofascial structures. Acute, high velocity, repetitive, and asymmetrical forces will have significant impact, but whether acute or insidious, the injury may trigger capsular or synovial disruption, capsular or ligamentous tension, ankylosis or hypermobility, micro or macrofractures, chondromalacia, soft-tissue injury, and inflammation. All these factors are usually followed by abnormal joint mechanics and altered or maladaptive regional biomechanics that can further exacerbate SIJ pathology, dysfunction, and pain [21, 26].

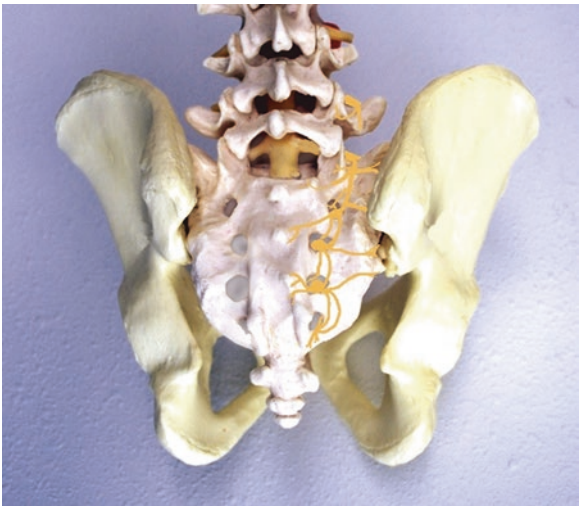

Fig. 37.2 Innervation of the posterior SIJ. Original figure by Attias et al.

Common Diagnoses/Symptoms Treated

LBP is defined as such pain occurring within a region limited by the outer borders of the erector spinae laterally, the imaginary line through the T12 spinous process superiorly, and a line through the S1 spinous process inferiorly. Sacral pain is defined as that being confined within a region overlying the sacrum and contained between the imaginary vertical lines drawn through the posterior-superior and posterior-inferior iliac spines, and within the transverse lines passing through the S1 spinous process superiorly, and by the posterior sacro-coccygeal joints inferiorly [27].

Pain originating from structures in these regions typically crosses these boundaries. Thus, SIJ pain is often perceived in the lower back, groin, buttocks, lower extremities, and abdomen. Pain caused by SIJ dysfunction can be similar to pain from a discogenic or radicular source. More commonly, it presents unilaterally, below the belt line, in the groin, and over the postero-lateral thigh (Fig. 37.3). It might present with associated crepitus or popping. A study reported that in 22.5% of the involved population with SIJ pain, the radiation pattern was toward the calf and foot [12]. This frequent observation generates confusion given the similarity in referral patterns between SIJ pain and discogenic or radicular pain. It has been noted that any pathology in the SIJ, which causes spasm of the piriformis muscle, may also lead to sciatic nerve irritation as well as a broad spectrum of symptoms, in addition to a variety of radiation patterns [27]. Very frequently, symptoms are perceived and described by the patient as “sciatica”.

Common mechanisms causing traumatic disruption of the SIJ include motor vehicle accidents, falls, athletic injuries, as well as childbirth. Pain is exacerbated with SIJ loading, which can occur after prolonged sitting, standing, walking and climbing stairs, or by transition from these positions [28, 29].

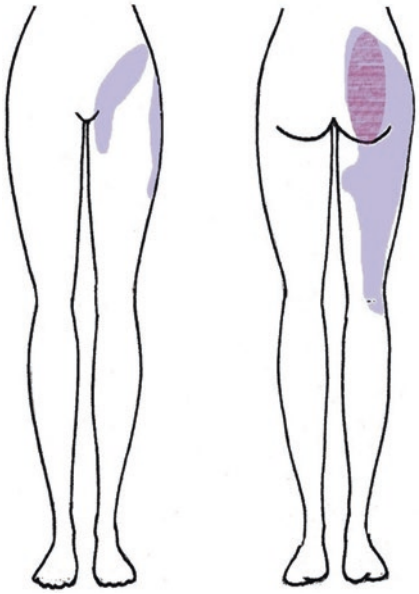

Fig. 37.3 Common pain referral patterns from the SIJ. Original figure by Zhukova-Attias

Table 37.1 Differential diagnostic categories of SIJ pain generators

Intra-articular sources	Extra-articular sources (more common)
Spondyloarthropathy	Fractures
Metabolic and endocrine disorders (crystal-induced joint disorders, hyperparathyroidism)	Trauma
Arthritis (osteoarthritis and inflammatory)	Ligamentous injuries
Infection	Myofascial components
Malignancy	Pregnancy (hypermobility)
Joint trauma	Malignancy
	True and functional leg length discrepancy
	Spinal surgery
	Transitional anatomy

Modified from Cohen SP, Chen Y, Neufeld NJ. Sacroiliac joint pain: a comprehensive review of epidemiology, diagnosis and treatment. Expert Rev Neurother. 2013;13(1):99–116. doi:10.1586/ern.12.148

Multiple etiologies are associated with SIJD and pain (Table 37.1). The HLA-B27 gene is strongly associated with ankylosing spondylitis (AS) and other inflammatory diseases like psoriasis, inflammatory bowel disease, and reactive arthritis. Seronegative and HLA-B27-associated spondylo-arthropathies are notable for producing inflammation at one or both SIJs. Unlike other forms of arthritis and rheumatic diseases, onset of AS commonly occurs in younger people, between the ages of 17–45. However, it can affect children, as well as an older population. AS is more

Table 37.2 Clinical features of SIJ pain

Lower back pain (below L5)
Pelvic/buttock pain
Hip, groin, postero-lateral thigh pain
Lower extremity pain, numbness, tingling, weakness
Unilateral (4:1 vs. bilateral)
Subjective leg instability (buckling, giving way)
Decreased tolerance to sitting positions and side-sleeping
Exacerbation with transitional activities (i.e. rising from a seated position and climbing stairs)

Table 37.3 IASP criteria for SIJ pain

Positive Fortin finger test, i.e. pain located within 1 cm inferior-medial to the PSIS
Pain that is relieved by injection of the SIJ
At least three positive provocative pain tests (0.82 for sensitivity, 0.88 for specificity, 0.86 for positive predictive value of a test, and 0.84 for negative predictive value) (2015-04-16)

Merskey H, Bogduk N. Classification of chronic pain: syndromes and definitions of pain terms. Seattle, WA: IASP Press; 1994. p. 190–1

common in men, but occurs in women as well. Infection can be a source of SIJ pain and etiologies include reactive arthritis in HLA-B27 carriers, reactive arthritis associated with HIV-positive individuals, and other rare local infections [26]. Tumors infiltrating the SIJ with resulting pain have been reported, and regional malignancies can certainly trigger or mimic SIJ pain [30]. Regardless of the etiology, both pain and proprioception are transmitted from the SIJ. This is supported by anatomical studies demonstrating the articular presence of both myelinated and unmyelinated nerve fibers, as well as mechanoreceptors [31–34].

The differential diagnostic categories for SIJ pain are summarized in Table 37.1. The most common presenting clinical features and pain patterns of SIJD are outlined in Table 37.2. Fig. 37.3 shows common pain patterns. The International Association for the Study of Pain diagnostic criteria for SIJ pain [35] are outlined in Table 37.3.

Treatment Options

This chapter section will focus on technical aspects of the therapeutic modalities used for SIJ pain. Additionally, it will provide suggestions regarding their position in the treatment algorithm, once the correct diagnosis is made. The available supporting evidence will be discussed further in section “Potential Treatment

Complications". Medical management of individual etiologies will not be discussed, but we encourage the reader to refer to the recommended reading list, as well as to the pathology section of this chapter.

Conservative Management/Physical Therapy

Once SIJD has been appropriately diagnosed, the initial treatment often begins with conservative management, similar to other types of joint-associated pain. Conservative management of SIJD may include medication, physical therapy, manual therapy, and durable medical equipment.

The basic principles of medical pain management apply to the treatment of SIJD, including the use of oral steroids, non-steroidal anti-inflammatory drugs, non-opiate analgesics, antidepressants, anti-spasmodics, and other adjuvant medications [36]. Often the combination of these medications, along with other conservative treatment options, provides better outcomes. Physical therapy can provide a structured exercise program with a specific focus on SIJD, to help ease stress on the SIJ, reduce inflammation, remedy associated muscular dysfunction, and to improve functional status. This is accomplished by exercises focused on strengthening and stretching of the musculature surrounding the SIJ (i.e. gluteal muscles, hamstrings, hip flexors/extensors), pelvic floor muscles, and core muscles in the lower back, which help to offload tension on the SIJ [37]. Combining both passive (i.e. application of stretch by therapist) and active (i.e. resistance exercise) physical therapy treatment provides the best outcomes.

Manual methods for correcting SIJD fall into three broad categories, which include the following: direct mobilization, direct manipulation, and indirect techniques. No single discipline (osteopathic, chiropractic, or manual physical therapy) has been shown to be superior to another [36]. The overall goal of these techniques is to restore physiologic motion of the SIJ.

Direct mobilization includes both soft tissue mobilization (SMT) and joint mobilization (JMT). SMT addresses muscle tension and attempts to break up inelastic or fibrous muscle tissue (myofascial adhesions) and to relax muscle tension. This procedure is applied to the musculature surrounding the SIJ by placing traction force on the tight area in an attempt to restore normal texture to tissue and to reduce associated pain. JMT involves loosening up the restricted joint, increasing its range of motion by providing slow velocity, and increasing amplitude movement directly into the barrier of a joint, which moves the actual bone surfaces over each other in ways patients cannot otherwise move the joint themselves.

Direct manipulation introduces high velocity, low amplitude thrusting, which aims to restore the gliding motion of joints, enabling them to open and close more effectively. It is a more aggressive technique than joint mobilization and muscle energy techniques, which thrust a joint to its restrictive barrier, but not past it. If utilized properly, increased mobility and decreased muscle tone about the joint should be noticed [38].

Indirect techniques include muscle energy techniques (METs) and are designed to mobilize restricted joints and to lengthen shortened muscles. The mechanism of action utilizes a voluntary contraction of the patient's muscles against a distinctly controlled counterforce, which is applied by the therapist, from a precise position and in a specific direction. Following a 3–5 s contraction, the therapist takes the joint to its new barrier, where the patient again performs a muscle contraction. According to a study done by Visser and associates, out of 51 patients identified with SIJD-associated leg pain, manual therapy had a significantly better success rate with improved pain scores and increased function when compared to physical therapy and intra-articular SIJ injections [39].

Durable medical equipment such as SIJ (Pelvic) belts can help to stabilize the SIJ, provide biofeedback, and give pain relief for patients with SIJD. Proper positioning of the belt is important, which should be placed directly superior to the greater trochanter [40]. Pelvic belts can help to decrease sacroiliac joint motion by approximately 30% [41].

Interventional Management

SIJ Injections

As mentioned previously, SIJ anesthetic injections are considered a reference standard to diagnose SIJ-related pain. As a therapeutic intervention, most studies agree that analgesic effects from the addition of corticosteroids are significant in the short term, but decline over time, generally 3–6 months. Injections may be directed inside the joint (intra-articular injections), may be directed to the supporting ligaments and muscles that comprise the articulation (extra-articular injections), or may combine both targets. In younger, more active patients, extra-articular pathology with unilateral pain is more common. In the elderly, intra-articular pathology and bilateral pain is more frequent [18, 19]. Depending on the patient, either technique might be of benefit. In our opinion, most patients will benefit from a combination approach.

It is now common practice to utilize either fluoroscopy or CT-guidance to perform SIJ injections, the latter of which is restricted by higher radiation exposure and availability in the pain clinic setting. Ultrasound-guided techniques are becoming increasingly incorporated into pain clinic practices, but are highly dependent on operator experience [42]. For fluoroscopy-guided sacroiliac joint injections, a common technique involves advancing a 22-gauge spinal needle into the inferoposterior aspect of the joint, an area 1–2 cm cephalad to the joint's most caudal end. The needle is advanced, while rotating the C-arm approximately 30° caudal to the axial plane, to better visualize the area inferior to the posterior superior iliac spine and the iliac crest. Contralateral oblique angulation may be added to further demarcate the joint space. Penetration of the posterior capsule is usually felt as a change in resistance. This may not be felt in all patients, in particular those with significant osteoarthritic changes and ankylosis. In such cases, an extra-articular injection

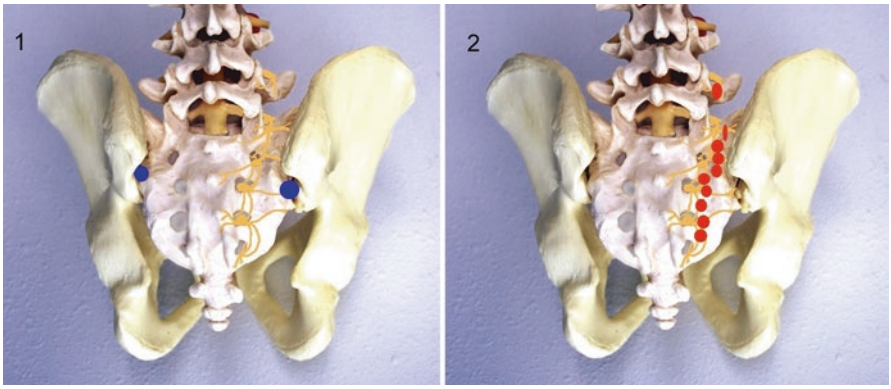

Fig. 37.4 Target locations for SIJ injections (**1**) and RFA ablations (**2**). Original figure by Attias et al.

might be necessary. Contrast media can be used to verify placement and to rule out intravascular injection. The total amount of steroid and/or local anesthetic injectate volume should not surpass 3 mL to avoid painful joint distention (Fig. 37.4-1).

Instillation of neurolytic agents like phenol has been tested, in an attempt to prolong the relief obtained with corticosteroids. However, phenol is rarely used in clinical practice due to the high risk of extra-articular spread to susceptible structures [43]. Although visco-supplementation with hyaluronic acid may also represent a reasonable alternative, given the demonstrated benefit in osteoarthritis of the knee and hip, only small series exist studying subgroups of patients with degenerative SIJ arthritis [44].

Radiofrequency Denervation

For patients who obtain good, yet short lived, response from SIJ steroid injections, radiofrequency (RF) lesioning of the lateral branch nerves that innervate the SIJ should then be considered. In conclusions derived from a randomized trial by Dreyfuss et al., Cohen et al. [7] support the notion that lateral branch denervation should be more effective in alleviating extra-articular SIJ pain; additionally, either lateral branch or extra-articular blocks are thought to serve as better predictors of RF denervation response than intra-articular injections.

As previously noted, the posterior aspect of the SIJ is innervated by the L5 dorsal ramus and the lateral branches of S1, S2, and S3, with possible contributions from the L4 dorsal ramus. Anesthetic blockade of these structures can predict response to RF ablation of the same nerves. This can be achieved by guiding a needle to a point 5 mm lateral to each foramen, between the 2 and 5 o'clock positions on the right side, and the 7 and 10 o'clock positions on the left side. These targets will correspond to the path of the lateral branch, as it travels laterally toward the joint. The L4 and L5 dorsal ramus can also be included by using the same technique required for medial branch blockade.

Standard monopolar RF ablation of the sacral lateral branches will result in a restricted lesion. Given the size and variable location of these nerves, multiple techniques have been described to increase the chance of achieving denervation. For example, utilizing multiple probes and creating bipolar RF "strip lesions" can be considered, and targets may be expanded to include the terminal fibers innervating the joint. This requires the placement of multiple successive probes, with a separation of less than 1 cm, in a trajectory parallel to the path of the nerves, which are targeted as described for the diagnostic blocks. Therefore, this creates multiple lesions in a "leapfrog" manner (Fig. 37.4-2). Addition of normal or hypertonic saline solutions before lesioning and proper lesion time may increase the size of the lesions, while diminishing the spread of tissue destruction beyond the electrodes [45]. Prior to lesioning, sensory and motor nerve stimulation should be performed to verify concordance and absence of muscle contraction in a radicular distribution. Finally, the addition of anesthetic and steroid mixtures after the lesioning will provide post-procedural analgesia and may prevent neuritis.

There is higher level evidence that cooled RF neurotomy is beneficial to treat SIJ pain, presumably due to the larger lesion size attainable with this technique, with a higher analgesic response at 3 months when compared to traditional radiofrequency, but no significant difference between both modalities at 6 months [19]. Other tools capable of creating multiple lesions with a single device have entered the market (Fig. 37.5) with the goal of decreasing procedural complexity, as well as improving outcomes [46, 47].

Neuromodulation

Non-neurolyitic pain modulation therapies like spinal cord, peripheral nerve, and peripheral field stimulation are, in general, considered effective for neuropathic pain syndromes. Predominantly nociceptive pain syndromes, like SIJ pain, are widely considered less responsive to neurostimulation. Despite this assumption, several reports utilizing this therapy targeting different neural targets can be found in the literature, with the goal of treating intractable SIJ pain. [47–49]. Intrathecal opiate and non-opiate infusion pumps are traditionally considered better options to control chronic intractable nociceptive pain arising from these structures, but still typically require ongoing interventional strategies and physical therapy to maintain function, and to keep medication infusions within the recommended dosages.

SIJ Fusion

SIJ arthrodesis, or fusion, is a surgical technique used to treat back or leg pain caused by SIJD that remains controversial. Arthrodesis should be considered only in patients with joint pain proven by controlled diagnostic anesthetic blocks and without any source of pain from the lumbar spine. It also should be reserved for those patients who continue to have disabling symptoms that have not responded to aggressive conservative care [36]. Numerous techniques exist for the surgical fusion

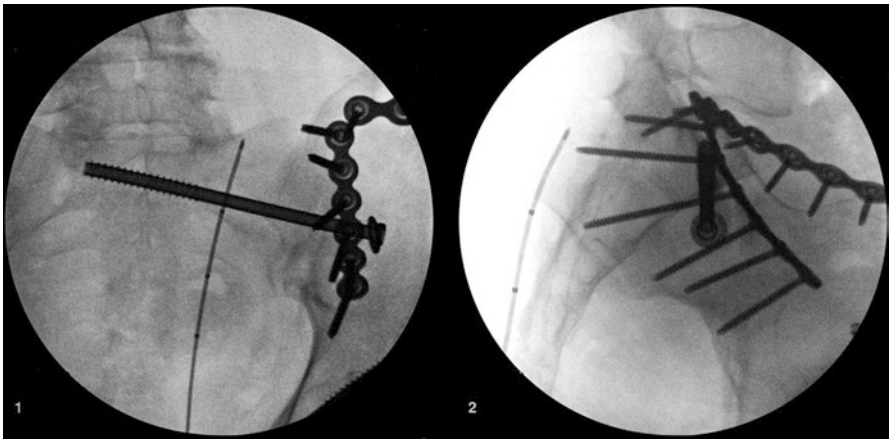

Fig. 37.5 Sacroiliac joint radiofrequency ablation with a multi-lesion probe. Images courtesy of Dr. Stanley Golovac

of sacroiliac joint. The main goal is to stabilize the joint by using implants and/or instrumentation that can be accomplished by an open surgical procedure (OS) or by a minimally invasive surgery (MIS).

Smith-Petersen first reported SIJ arthrodesis in 1921 [50]. Studies that followed included non-instrumented approaches to achieve arthrodesis and most required either long periods of immobilization, or casting and bracing for a substantial period of time [51]. In the mid-1980s, there were reports of internal fixation using metal plates and screws [52–55]. Reports of minimally invasive surgical (MIS) techniques to address the SIJ began appearing in 2008. However, instrumentation remained limited to threaded screws and cages that rely on autologous bone grafts [56–58]. Recently, new MIS techniques have been introduced with promising outcomes [59–64]. According to a multi-center comparative study done by Smith et al., in which 263 patients underwent either open surgical (OS) or MIS SI joint fusion, patients showed postoperative improvements in pain score. Compared to OS patients, MIS patients had significantly greater pain relief and more favorable peri-operative surgical measures [65]. According to a literature review performed by Zaidi et al., surgical intervention for SIJ pain is beneficial in only a subset of patients. However, with the difficulty in making an accurate diagnosis and with the lack of evidence for the efficacy of SIJ fusion itself, serious consideration as to the cause of pain and alternative treatments should be given before performing the operation [66].

Complementary and Alternative Techniques

Regenerative medicine is considered a paradigm shift in the treatment of degenerative and overuse injuries. Historically, pain symptoms due to these types of injuries were often treated with corticosteroid injections to alleviate the inflammatory

component. The goal of regenerative medicine is to directly or indirectly draw upon growth factors and mesenchymal stem cells to regenerate injured tissue. Regenerative medicine includes novel therapies such as prolotherapy and platelet rich plasma injections (PRP).

Over the past several decades, prolotherapy or proliferative therapy has been mostly performed outside of mainstream medicine by independent physicians. More recently, multi-specialty groups, which include family or sports medicine physicians, physiatrists, orthopedic surgeons, neurologists, and anesthesiologists, have been incorporating prolotherapy as the result of both positive clinical experience and reports in the literature. Dorman et al. observed in vitro that injecting chemical irritants into ligamentous tissue incites collagenous proliferation [67].

Prolotherapy treatment has been advocated for a variety of soft tissue conditions, including non-specific low back pain, chronic musculoskeletal pain, and hypermobility of joints [68]. In the treatment of a hyper-mobile sacroiliac joint, a combination of concentrated dextrose and a local anesthetic is injected into the affected joint. Prolotherapy has been defined as "the rehabilitation of an incompetent structure, which included ligaments or tendons, by the induced proliferation of new cells" [69]. In 1937, Earl Gedney injected a hyper-mobile sacroiliac joint with sclerosing agents, resulting in satisfactory results in pain improvement [67]. According to a study done by Cusi et al., in which 25 patients underwent CT-guided SIJ prolotherapy, 76% of patients had a positive clinical outcome at both 3 and 12 months post-therapy [70]. Kim et al. compared intra-articular prolotherapy to intra-articular corticosteroid for SIJD and found that dextrose injections provided improved analgesia compared to corticosteroid [71]. Drawbacks to this method of treatment include the need for multiple injections, the potential for considerable post-injection pain, and the general lack of research supporting efficacy [72].

Platelets release many bioactive proteins responsible for attracting macrophages, mesenchymal stem cells, and osteoblasts that promote removal of necrotic tissue and also enhance tissue regeneration and healing. Based on this principle, autologous platelets are introduced by injection, to stimulate a supra-physiologic release of growth factors, in an attempt to jump-start healing in chronic injuries. The current literature reveals a paucity of randomized clinical trials. The existing literature is filled with mostly anecdotal reports or case series, which typically have small sample sizes and few control groups [73, 74]. The use of autologous PRP was first reported in 1987 by Ferrari et al., following an open heart surgery, which was utilized to avoid excessive transfusion of homologous blood products [75]. Since that time, the application of autologous PRP has been safely used and documented in many fields, which include orthopedics, sports medicine, dentistry, ENT, neurosurgery, ophthalmology, urology, and wound healing. Additionally, applications have included cosmetic, cardio-thoracic, and maxillofacial surgery. PRP therapy has shown promising results in the treatment of intra-articular arthritic conditions and chronic tendonopathies, but there have been no controlled studies regarding its effect on SIJ pain [76–79].

Functional Limitations

Determining functional limitations from SIJD and the response to treatment is a complex task since it may have an overlapping presentation with other etiologies like disc degeneration and facet arthrosis. Based on the specific anatomic structures affected, functional limitations associated with SIJD may include the inability to walk for extended periods of time, challenges while walking on uneven surfaces, and difficulties with sitting or standing in one position. The measurement of functional limitations caused by SIJD may be based on either patient self-report or on performance tests conducted by physical therapists. Both methods may indicate hypothetical limitations given the complex nature of the process and the numerous variables at play, in particular psychological factors. Furthermore, given the concept of tensegrity, SIJD may also indirectly trigger other musculoskeletal issues.

Combining the tests outlined in Tables 37.4 and 37.5, and in clusters as described in Table 37.6, will yield more diagnostic sensitivity and specificity than any one test alone. Furthermore, it will facilitate the identification of specific structures involved and will thereby help to select specific treatment strategies. Continual re-examination will help to determine the effect of these interventions. Lastly, functional limitations should be appropriately addressed by using a multidisciplinary approach, which will better ensure that each component of SIJD is rehabilitated.

Potential Treatment Complications

Overall, the rate of complications from SIJD treatments is low. It is reasonable to expect that, as the complexity and invasiveness of the management increases, so will the frequency of complications. Manual and physical therapies should be performed with the appropriate force, intensity, and frequency to avoid further injury. Sterile precautions should be employed for any injection technique to prevent infection. Any SIJ injection, regardless of injectate, can pose risk for infection, which can lead to abscess formation in the pre-sacral tissues. Local anesthetic toxicity may be avoided by selecting the appropriate agent, limiting volumes, and by using contrast medium. Due to the potential for intravascular spread during injection, it is advised to use a non-particulate corticosteroid to prevent embolic events. Image guidance and contrast medium should be utilized to minimize spread to susceptible structures like lumbar and sacral nerve roots, vascular structures, and pelvic organs. All intra-articular injections can cause post-procedural pain due to distention of the joint capsule. RF neurotomy, in particular, can increase pain following the procedure. Judicious use of anesthetics and steroids might reduce neuritis. Furthermore, confirmation that the active tip of RF probe is positioned well below the dermis prior to lesioning can prevent undue pain, burns, and potential infection. Complications of SIJ fusion are those inherent to surgical procedures and include infection, radicular irritation, and pseudoarthrosis.

Table 37.4 SIJ pain provocation tests

Clinical test	Description
Patrick test (FABER—femoral abduction external rotation)	With the patient supine, examiner brings ipsilateral knee into flexion with lateral malleolus placed over the contralateral knee, fixates the contralateral ASIS, and applies a light pressure over the ipsilateral knee
Thigh thrust (posterior shear test or posterior pelvic provocation test)	The patient is supine, with the hip flexed to 90°. The examiner applies posteriorly directed force through the femur
Compression test	With the patient on a lateral decubitus and the affected side up, with hips flexed approximately at 45° and knees flexed approximately 9°, the examiner applies a force vertically downward on the anterior-superior iliac crest
Sacral thrust test	With the patient lying prone, the examiner applies force vertically downward towards the center of sacrum
Gaenslen's test	With the patient supine and one leg hanging over the edge of the table, and with the other leg flexed toward the patient's chest, the examiner applies pressure to both the hanging leg and the leg flexed toward the chest
Distraction test	With the patient supine, the examiner applies cross-arm pressure to both anterior-superior iliac spines
Mennell's test	With the patient lying with affected side up and the knee flexed toward the abdomen, the examiner puts one hand over the ipsilateral buttock and iliac crest and the other hand grasps the semi-flexed ipsilateral knee and forces the leg into extension

Modified from Cleland J, Koppenhaver S. Netter's orthopaedic clinical examination: an evidence-based approach. 2nd ed. Philadelphia: Elsevier; 2011

Evidence

Despite limited and sometimes contradicting evidence supporting the use of therapeutic SIJ interventions, the healthcare utilization of these procedures has soared in the recent years. For example, SIJ injections have increased 311% per 100,000 Medicare population from 2000 to 2013 [80–83].

At the time this manuscript, the most recent and complete review of the available evidence supporting the diagnostic and therapeutic value of SIJ interventions, is by Thomas T. Simopoulos et al. [19]. The authors performed an extensive analysis of the available literature supporting the diagnostic and therapeutic interventions for SIJ. This study recognizes the fact that the interventions performed by pain specialists, when summed to numerous other conservative therapeutic modalities and surgical interventions, have resulted in escalation of costs that have been considered to be uncontrollable [83–89].

For diagnostic accuracy, this review found Level II to III evidence (modified grading of qualitative evidence) [90] in favor of sacroiliac joint injections, but high variability was found in prevalence rates, diagnostic criterion, and methods used. For therapeutic modalities, they found that the evidence is Level II–III in managing sacroiliac joint pain with cooled radiofrequency neurotomy and that the evidence

Table 37.5 SIJ motion assessment tests

Clinical test	Description	Positive findings
Gillet's test (Stork test)	With the patient standing, examiner palpates the following landmarks:	Positive if the lateral landmark fails to move posterior-inferiorly with respect to medial landmark
	L5 spinous process and PSIS	
	S1 tubercle and PSIS	
	S3 tubercle and PSIS	
	Sacral apex and posteromedial margin of the ischium	
	The patient is instructed to raise the ipsilateral leg of the side of palpation	
Long-sit test (supine to sit test)	With the patient supine, the length of medial malleoli are compared	Positive if one leg appears shorter in supine and then lengthens when the patient comes into long-sitting position
Standing-flexion test	With the patient standing, examiner palpates inferior slope of PSIS. Patient is asked to forward bend completely	Positive for sacroiliac hypomobility if one PSIS moves more cranially than the contralateral side
Sitting flexion test	With the patient sitting, the examiner palpates the inferior slope of PSIS. The patient is asked to forward bend completely	Positive for sacroiliac hypomobility if one PSIS moves more cranially than the contralateral side
Prone knee bend test	With the patient prone, the examiner looking at heels, assesses leg length. Knees are passively flexed to 90° and leg length are again assessed	Positive if a change in leg length occurs between positions
Click-clack test	With the patient sitting and the examiner's thumbs on the caudal PSIS, the patient rocks pelvis forward and backward	Positive if one PSIS moves slower from cranial to caudal than the other
Heel-bank test	With the patient sitting, an examiner's thumbs are placed on caudal PSIS; the patient raises one leg at a time and places the heel on the bench without using hands	Positive if the test requires any effort
Abduction test	With the patient side-lying with hips flexed 70° and knees flexed 90°, the patient is asked to lift the top leg about 20 cm	Positive if the test required any effort

Modified from Cleland J, Koppenhaver S. Netter's orthopaedic clinical examination: an evidence-based approach. 2nd ed. Philadelphia: Elsevier; 2011

for conventional radiofrequency neurotomy, intra-articular steroid injections, and periarticular injections with steroids or botulinum toxin is limited to Level III or IV. The main limitation is still the paucity of high quality, replicative, and consistent studies.

The authors of a systematic review of the literature [91] aimed at evaluating the available evidence supporting specific physical therapy interventions for the

Table 37.6 Cluster tests

Test cluster	Positive findings
Mennell's Test + Gaenslen's Test + Thigh Thrust	2 of 3 tests need to be positive
Distraction + Thigh thrust + Gaenslen's test + Patrick sign + Compression	At least 3 out of 5 tests need to be positive
Distraction + Thigh thrust + Sacral thrust + Compression	At least 2 out of 4 need to be positive
Distraction + Thigh thrust + Gaenslen's test + Sacral thrust + Compression	A least 3 out of 5 tests need to be positive

Modified from Cleland J, Koppenhaver S. Netter's orthopaedic clinical examination: an evidence-based approach. 2nd ed. Philadelphia: Elsevier; 2011

management of SIJD in adults, including pregnant women, and recommended a combination of specific stabilizing exercises, nonelastic sacroiliac belts in the high position, and ergonomic education as the most beneficial strategy for SIJD and posterior pelvic pain for pregnant women (with SIJD). Little evidence was found supporting specific physical therapy interventions for SIJD in those who are non-pregnant individuals.

Conclusion

SIJD occupies an important place in the generation of low back pain syndromes, and the interrelation is complex, as is the diagnosis and its management. The joint's internal structure, supporting ligaments, surrounding musculature, and neural structures all contribute to its function and dysfunction and are therefore targets for disease prevention and therapy.

In those patients where the SIJ might be the main origin of pain and dysfunction, it is of paramount importance to obtain a reliable diagnosis in order to direct the appropriate therapeutic algorithm and to prevent the morbidity, complications, and costs associated with misdirected invasive interventions of the lumbar spine.

The SIJ has intricate biomechanical relationships with the spine, the pelvic ring, and structures it contains, as well as the joints of the lower extremities. Invariably, pathology in one given structure will alter the function of the others and result in dysfunction. Pain is a salient symptom and may be generated from any dysfunctional structure in the system.

As the condition progresses from onset to chronicity, from involvement of peripheral to central neural systems, and with the addition of psycho-social factors, it becomes more complex. Early diagnostic and appropriate management might prove to be difficult, but it is key to prevent progression of this cascade and to diminish disability.

In the context of the pain management and rehabilitation practice, this condition might be easier to diagnose than to treat, and effective and long lasting outcomes warrant a multimodal approach. Rather than following algorithms that promote

individual steps graded from “conservative” to “interventional or invasive”, concomitant strategic application will more likely yield better results. Patient compliance to physical therapy will certainly increase if pain intensity is improved by early application of an intra-articular injection. Furthermore, this combination might avoid progression to more invasive, costly, and potentially risky interventions. The best efforts should be placed to allow appropriate patient understanding and expectations regarding the treatment plan.

In the current complex healthcare environment, the more these interventions are applied at the wrong time, directed towards the wrong target or patient, or overutilized, the more the reimbursement and healthcare insurance coverage will diminish. It is our collective responsibility to prevent this from happening, to generate and utilize the best medical evidence in order to guarantee continued access to all these impactful treatment modalities.

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Chapter 38
Radiofrequency Neurotomy for the Treatment of Pain in the Rehabilitation Patient

Jason Friedrich and Virtaj Singh

Introduction/History

Spinal pain is ubiquitous worldwide. Low back pain causes more global disability than any other medical condition and neck pain ranks fourth in terms of years of healthy life lost to disability [1, 2]. Once thought to be a self-limited condition, spinal pain is now recognized to be recurrent or chronic in many people. Though estimates vary, epidemiological studies indicate that 30–80% of patients with acute low back pain will go on to have recurrent or chronic low back pain and that the prevalence of chronic low back pain is rising [3, 4]. Similarly, 50–75% of those with neck pain will report recurrence within the next 1–5 years [3, 5]. In any 3 month period, 30% of adults will report back pain and 15% will report neck pain, with annual prevalence estimates reaching 80% and 50%, respectively [3, 6]. Around 10% of adults have chronic, activity-limiting spine pain, and as high as 75% of individuals suffering from both neck *and* low back pain report work limitations [3, 6].

There are multiple potential structural sources of spine pain, including bone, joint, ligament, disc annulus, nerve, and muscle/fascia. The spinal facet joints, more formally known as zygapophyseal joints (or z-joints), were first recognized as a source of back pain by Goldthwait in 1911 [7]. While estimates vary, z-joints are thought to be responsible for approximately 15% of low back pain, 50% of thoracic pain, and 55% of cervical spine pain [8–10]. Mechanical spine pain is often multifactorial; therefore, a comprehensive approach to diagnosis and treatment should be utilized to account for biomechanical influences that may be best addressed through

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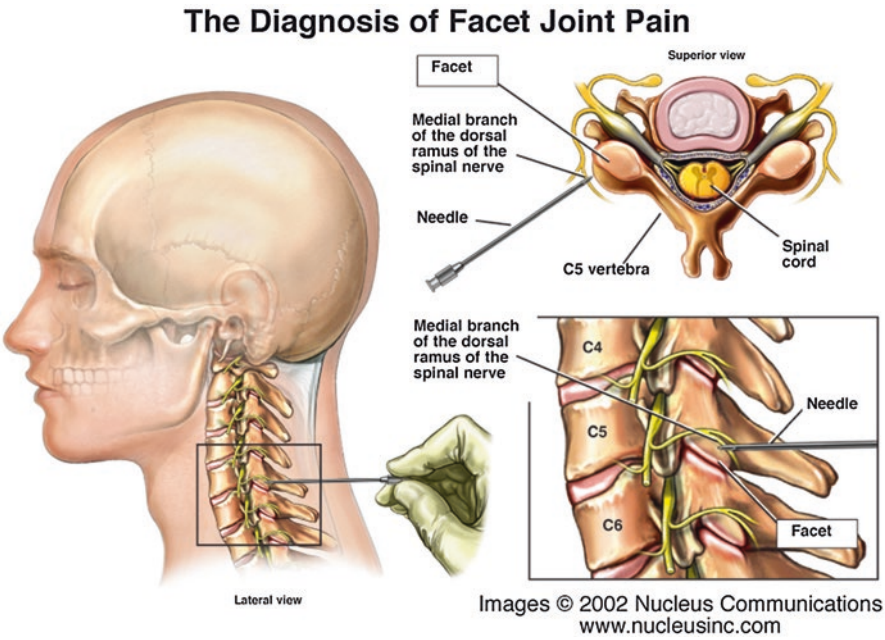

Fig. 38.1 The diagnosis of facet joint pain

targeted therapeutic exercise. Similarly, when psychosocial factors are contributory, then a multidisciplinary approach is certainly warranted.

This chapter will focus on the z-joint as a source of spinal pain and will discuss the pathophysiology, symptoms, and diagnoses related to these joints, as well as assessment and interventional treatment of chronic z-joint pain, with emphasis on radiofrequency neurotomy (RFN). A section in this chapter is also devoted to sacroiliac (SI) joint pain.

Pathophysiology/Mechanisms of Action

The z-joints are paired synovial joints that are formed by the superior articular process (SAP) and inferior articular process (IAP) of the vertebrae (Fig. 38.1). The purpose of these joints is to limit motion and to assist with axial weight bearing. The z-joints accept greater axial loads when disc degeneration is present. Like other diarthrodial synovial joints, they contain hyaline cartilage, a synovial membrane, and a fibrous capsule, and can hold between 1 and 2 mL of fluid. Though avascular, each joint capsule contains nociceptive fibers that can transmit pain with irritation and distention [11, 12]. Normal synovium is also richly innervated and capable of generating pain. Cartilage injury or degeneration can also lead to pain from the innervated subchondral bone. Painful z-joints can result from age-related/

degenerative, traumatic, or inflammatory processes yielding synovitis, spondylosis/osteoarthritis, capsular injury, or spondyloarthropathy. A simplistic view of the degenerative spine cascade can be described in the following sequence: aging, genetic predisposition, biomechanics (obesity, muscle imbalance, abnormal posture/loading), other factors (smoking, trauma, etc.) → disc degeneration with resultant increased z-joint loading → z-joint cartilage micro-injury and synovial inflammation → capsular laxity, joint subluxation, osteophyte formation → cartilage loss, subchondral bone reaction/synovial cysts, and deformed/hypertrophic z-joints with periarticular fibrosis. Symptoms can occur at any stage of the degenerative cascade or with any abnormal loading of the joint.

Common Diagnoses/Symptoms Treated

Common diagnoses relating to the z-joint include cervical, thoracic, or lumbar facet arthropathy, facet syndrome, and spondylosis. Several other diagnoses often implicate the z-joint as a potential source of pain including whiplash syndrome, cervicogenic headache, and degenerative spondylolisthesis. The z-joints can cause a variety of symptoms including both local axial pain and referred extremity pain. In the cervical spine, the z-joints often cause pain in well-known distributions [12] (Fig. 38.2), with the upper cervical joints capable of causing headaches. Referral patterns from the lumbar z-joints are less specific [11, 13]. No historical features have proven pathognomonic for identification of z-joint pain, but these patients often complain of sharp or aching pain that is worse with loading the joint, such as during spine extension or extension with rotation or with stretching the capsule of the joint, such as extremes of flexion or rotation. Isolated z-joint pain should not cause burning, tingling, numbness, or extremity weakness typical of neuropathic processes. Common diagnoses are described in more detail in the subsections below.

Cervicogenic Headaches from the C2-3 Joint

The cervical spine is often overlooked as a potential source for chronic headaches. Cervicogenic headaches are those that appear to emanate from the upper cervical spine and tend to create headaches in the suboccipital region, with occasional radiation into the forehead. They can be unilateral or bilateral and are often mistaken for migraines or tension-type headaches. Cervicogenic headaches can evolve from any of the upper cervical spine segments, including the C0-1 (atlanto-occipital (AO) joint), C1-2 (atlanto-axial (AA) joint), and the C2-3 or C3-4 z-joints. Of these potential sources, the C2-3 z-joint has been identified as the cause of cervicogenic headaches 54% of the time [14] and is considered the most common source of chronic post-whiplash headaches [10, 15]. Biomechanical factors can predispose to upper cervical z-joint pain, including a forward-head position with resultant upper

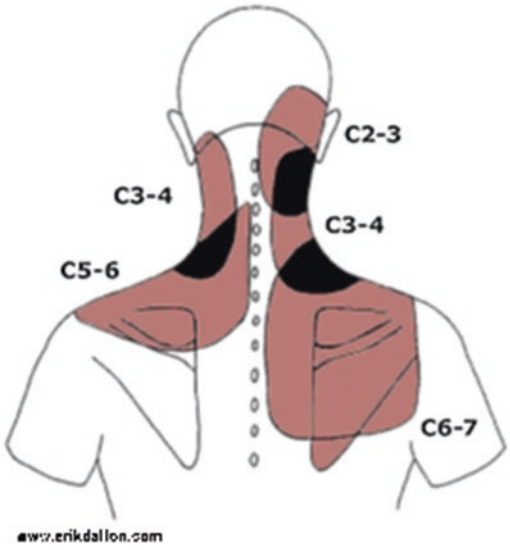

Fig. 38.2 Classical pain referral patterns in cervical z-joints

cervical hyperextension. Cervicogenic headaches from the C2-3 z-joint can be reliably confirmed via third occipital nerve block or well-placed intra-articular injection of anesthetic and treated with RFN.

Neck Pain from Cervical Z-Joints C3-4 to C6-7

The cervical z-joints refer pain in classic referral patterns (Fig. 38.2). These joints should be considered as potential sources of pain in anyone with neck pain referring to the upper trapezius and/or periscapular regions. The cervical z-joints are commonly the source of chronic axial neck pain in older patients or following whiplash-type injuries [15]. The most commonly affected z-joints in whiplash are C2-3 followed by C5-6 [10, 15], while degenerative osteoarthritis most commonly affects C3-4 and C4-5 [13]. Adjacent segments to prior cervical fusions are predisposed to z-joint arthropathy. It is especially important to identify the cervical z-joints as sources of chronic pain because this condition is potentially treatable without surgery.

Low Back Pain from the Lumbar Z-Joints

In a general population, at least 15% of low back pain is z-joint mediated [16]. The prevalence rises to 40% in older patients (median age 59 years) with chronic back pain [16]. Assuming typical anatomy, the lumbar z-joints begin with L1-2 and extend to L5-S1. The most commonly affected joints are L4-5 and L5-S1. Atypical lumbosacral transitional anatomy, such as a sacralized lumbar vertebra or a lumbarized sacral vertebra, occurs 10–20% of the time [17]. The referral patterns of pain from

the lumbar z-joints are less well defined than those from the cervical spine. Pain can refer to the buttock, hip, groin, and proximal thigh [11]. Typically, pain is present along the corresponding paraspinal muscles and less so midline. Pain tends to be worse with loading the joints in standing, extension, and extension-rotation maneuvers, but can also be exacerbated with capsular stretch at end ranges of flexion or rotation. Many find some relief with lying down. Some associated biomechanical factors include lumbar hyperlordosis, tight hip flexors, weak core muscles, and history of lumbar fusion. When properly diagnosed and treated, individuals with chronic z-joint pain can see functional improvements with physical therapy to optimize spine mechanics and interventional treatments, such as medial branch RFN [18, 19].

Thoracic Spine Pain from Thoracic Z-Joints

Thoracic region pain is less common and less studied than cervical or lumbar pain. Among those with chronic thoracic pain, estimates suggest up to 48% emanates from the thoracic z-joints [9]. RFN of the thoracic medial branches is considered a possible treatment option, but should be considered with caution only after careful evaluation to rule out other potential sources of pain. The pain referral patterns from the thoracic z-joints can overlap considerably, which makes it difficult to isolate specific joints to target for intervention. At this time, there is insufficient literature to predict outcomes following thoracic RFN; therefore, this treatment should only be pursued when less invasive options have been exhausted. Those who perform thoracic RFN must be aware of the unique characteristics of the thoracic medial branches, including more lateral anatomic course around the transverse processes compared to the lumbar spine and more cutaneous innervation [20].

Assessment

There are currently no historical features, physical exam maneuvers, or radiographic findings that can definitively and specifically identify z-joint pain. History should focus on identification of red flag conditions, such as cancer, infection, and unstable fracture, and can help to distinguish between mechanical pain and inflammatory arthropathies, as well as to differentiate somatic pain from neuropathic pain. At a minimum, the physical exam should attempt to rule out neurological injury, identify biomechanical factors that may predispose to z-joint pain, such as forward-head position or lumbar hyperlordosis, and should include a manual examination of the painful region. Careful segmental deep palpation can identify a joint level of maximal tenderness, especially in the cervical spine. Localizing signs may be absent in the lumbar spine, but the L4-5 and L5-S1 levels are most commonly affected [16].

Diagnostic imaging options include plain X-rays, dynamic bending X-rays, MRI, CT, and single photon emission CT (SPECT). All of these modalities can demonstrate

z-joint osteoarthritis. Dynamic X-rays, including flexion and extension sequences, can show a mobile spondylolisthesis, which may support a specific joint level as being the pain generator. MRI can show increased signal in the peri-facet bone marrow, or in the z-joint itself especially on STIR sequences. SPECT can demonstrate metabolically active z-joint arthropathy that has been linked to injection response in some studies [21, 22], but involves significant radiation exposure and is not recommended for routine use. Studies continue to look at radiographic predictors of response to diagnostic blocks [23, 24]. While patients with z-joint pain are likely to have imaging abnormalities, many asymptomatic individuals also demonstrate these same findings. Furthermore, diagnostic imaging can often overlook microscopic injuries to the joint capsule or cartilage, and cannot be used to definitively rule out a particular joint as a pain generator. This is especially true in the post-whiplash population [10, 15], where imaging may be more helpful in ruling out competing diagnoses.

The current gold standard to diagnose z-joint pain remains controlled diagnostic blocks to the specific joint in question or its nerve supply [13]. A single anesthetic block has a false positive rate as high as 40% [16]. A dual blockade protocol can be used to improve specificity and is recommended in most situations where RFN is considered. For example, on one occasion a short-acting anesthetic such as xylocaine is used, then at a separate time the block is repeated using a longer-acting anesthetic, such as bupivacaine. Patients are blinded as to which anesthetic was used and should complete a pain diary including percentage of relief from their index pain and duration of response. While a well-placed intra-articular injection and medial branch block (MBB) may be equally efficacious for the diagnosis of z-joint pain, MBBs may be a better predictor of response to RFN [25]. Debate continues regarding the most appropriate cutoffs for a "positive response." Most accept 80% improvement as definitively positive for the lumbar spine, but some argue that 50% is adequate to reduce false-negative responses for selection of patients for RFN [25]. Some studies and insurance companies advocate stricter cutoffs as high as 100% improvement, especially in the cervical spine [15]. A positive concordant response entails a patient demonstrating improvement for a length of time that approximates the duration of action of the anesthetics used. Positive concordant dual blocks reduce false-positives and increase the probability of a successful RFN.

Treatment/Technical Considerations

When pursuing diagnoses and interventional treatments for z-joint pain, some common technical standards should be considered. All procedures should be performed only after thorough informed consent, including a discussion of the procedure, risks, benefits, and alternatives. Sedation should be minimized for any diagnostic procedures. For an effective diagnostic block, patients need to have the index pain at time of the procedure or need to be able to consistently trigger the pain with a movement or activity, such that a pre- and post-procedure comparison can be made. Therapeutic procedures can be performed with or without sedation depending on patient and provider preference, as well as availability of cardiopulmonary

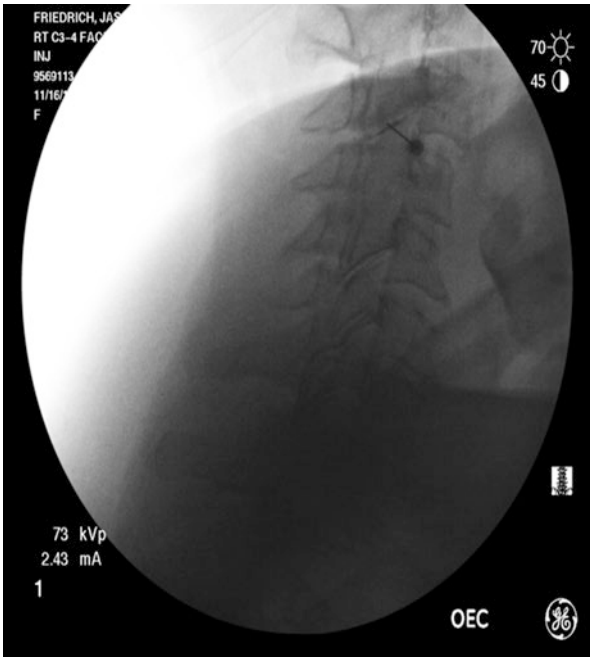

Fig. 38.3 Fluoroscopic image showing successful intra-articular injection of contrast into a cervical facet joint

monitoring and emergency resuscitative supplies. All procedures should be image-guided, most commonly with biplanar fluoroscopy, and should follow strict sterile precautions. Unless contraindicated, radio-opaque contrast dye should be utilized for all diagnostic blocks to ensure accurate placement and to avoid intravascular injection. For diagnostic intra-articular z-joint injections, no more than 1 mL of volume should be used to avoid capsular rupture or extravasation to surrounding structures including the nerve roots and epidural space (Fig. 38.3). For diagnostic MBBs, no more than 0.5 mL should be used to maintain specificity.

After diagnosis, therapeutic interventional options include therapeutic intra-articular injection or RFN. Therapeutic intra-articular injection typically involves instillation of corticosteroid with local anesthetic into the joint itself and can provide primarily short-term pain relief. For chronic z-joint pain, RFN can be considered with goal of more sustained improvement of pain and function. The above procedural setup applies to RFN; however, rather than relying on local anesthetic to block the joint's nerve supply, a radiofrequency electrode is used to heat the needle tip immediately adjacent to the nerve target (Fig. 38.4).

Several techniques of RFN are described including pulsed, conventional, or cooled. Pulsed RFN utilizes a lower temperature (~42 °C) for a longer duration (120 s), compared to conventional RFN (~80 °C for 90 s). The rationale for pulsed RFN is to alter neural transmission without fully coagulating the nerve; it may be considered in higher risk areas, such as the upper cervical spine or when there is concern for aberrant anatomy. Conventional RFN aims to coagulate/destroy the target nerve for a longer therapeutic effect. The RF needle tip can sense temperature and shuts

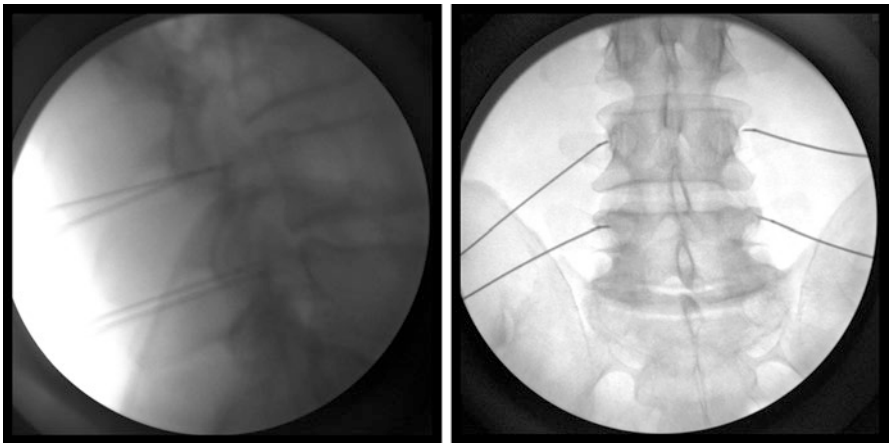

Fig. 38.4 Fluoroscopic images showing lateral and AP images of the radiofrequency electrodes along the L3 and L4 medial branches

off the lesion if temperatures are exceeding 95 °C, a temperature at which surrounding tissues are at risk. Outcomes from conventional RFN are highly dependent on technique, with the best outcomes achieved when the needle tip lies parallel to the target nerve. Cooled RFN is a newer technique that maintains some special advantages over conventional RFN, but carries higher equipment costs that may not be reimbursed by insurance. Cooled RFN utilizes a fluid pump, which circulates sterile water to cool the needle tip and adjacent tissue. With a probe tip temperature of 60 °C, coagulation time is longer (150 s), but the lesion size is larger. Moreover, the lesion extends beyond the needle tip allowing for easier perpendicular needle placement, which is helpful in complex anatomy or SI joint RFN. Added caution is also required with cooled RFN because of the larger lesion size.

Following RFN, the lesioned nerves typically regenerate and can restore nociception to the joint. While duration of effect from RFN varies, positive outcome can be considered at least 50% improvement for at least 6 months.

Cervicogenic Headaches from the C2-3 Joint

Multiple interventional treatments for cervicogenic headaches have been described, with targets including the A-O joints, A-A joints, C2-3 and C3-4 z-joints, C2 spinal nerve, third occipital nerve (TON), C3 and C4 medial branches, greater occipital nerve (GON), lesser occipital nerve (LON), and overlying upper cervical soft-tissue/musculature. Studies estimate about 50% of cervicogenic headaches after whiplash injury emanate from the C2-3 z-joint, which will be emphasized here [14, 15]. The C2-3 z-joint is innervated by the TON. The TON arises from the dorsal ramus of C3 and supplies the C2-3 z-joint capsule, as well as the semispinalis, communicating branches to the GON and LON, and cutaneous innervation of the

midline occiput. Treatment options include intra-articular injections or RFN. The intra-articular injection can be performed as described for the other cervical z-joints below. Due to variable course of the TON, RFN is optimally performed by blockade of three adjacent locations of the TON along the lateral pillars of C2 and C3. Dual blockade protocol is recommended for diagnosis, prior to considering RFN. Successful blockade of the TON can be confirmed by the expected sensory alteration in the occipital region.

Neck Pain from Cervical Z-Joints C3-4 to C6-7

The cervical z-joints are predominately coronal in orientation. Cervical z-joint intra-articular injections or MBBs can be performed in the side-lying or prone positions. Cervical RFN is typically performed with the patient prone. The cervical medial branches are targeted after they split from the primary dorsal ramus and when they wrap around the lateral margin of the articular pillar, as they travel posterior to the joint capsule (Fig. 38.1). The medial branch also supplies the multifidus and interspinales muscles and care should be taken to avoid blocking the lateral branch, which supplies many of the larger paraspinal muscles. The medial branches can occasionally have some segmental cutaneous innervation, thus some local numbness is possible with MBBs or RFN. With the exception of C2-3, each cervical z-joint is innervated by two medial branches, numbered consistent with their corresponding vertebral level. For instance, in order to block the C3-4 z-joint, one must block both the C3 and C4 medial branches (Fig. 38.5). The numbering scheme transitions at the cervicothoracic junction, where the C7-T1 z-joint gets innervation from the C7 and C8 (rather than T1) medial branches. This numbering scheme continues through the thoracic and lumbar spine. Dual block protocol with positive concordant response of at least 80–100% improvement is recommended prior to proceeding with RFN.

Low Back Pain from the Lumbar Z-Joints

The lumbar z-joints are predominately oblique in orientation, with more variability at L5-S1. The patient is prone for lumbar z-joint procedures. Each lumbar z-joint gets innervation from two medial branches, but the numbering scheme is distinct from the cervical spine. For example, the L3-4 z-joint is supplied by the L2 and L3 medial branches, and the L4-5 z-joint is supplied by the L3 and L4 medial branches (Fig. 38.4). The nomenclature changes again at L5-S1, where the L5-S1 z-joint is supplied by the L4 medial branch and the L5 primary dorsal ramus. The lumbar medial branches go on to innervate the segmental multifidi muscles and do not provide cutaneous innervation. Care should be taken to avoid neurotomy of the lateral branches, which supply larger paraspinal muscles and sometimes overlying skin.

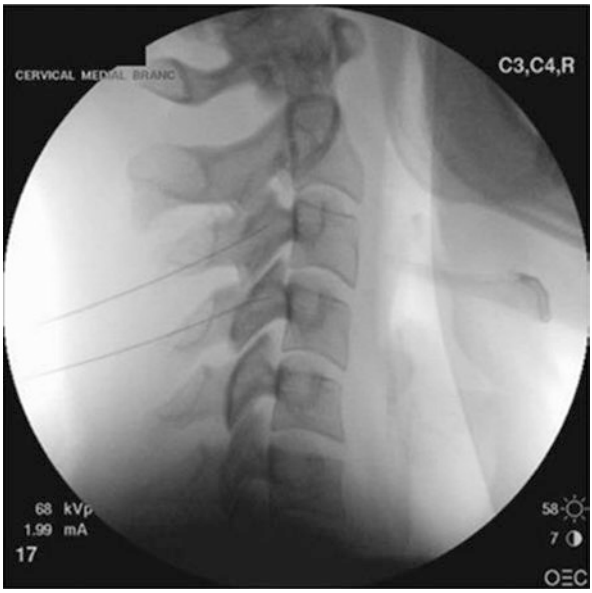

Fig. 38.5 Fluoroscopic image showing the needle placement for cervical medial branch blocks for the C3 and C4 medial branches

Potential Treatment Complications

Serious complications are very rare (<1%) following intra-articular z-joint injections, MBBs, or RFN. All z-joint procedures carry the usual risk of infection, hematoma, allergic or adverse reaction to the medications used, unintended nerve injury, and vasovagal reaction, including syncope. Risk of catastrophic bleeding, which could lead to spinal cord compression, is extremely low as these procedures all remain outside of the spinal canal. RFN carries some additional unique risks including post-RFN neuritis, anesthesia dolorosa, and muscle injury/denervation. Risk to the dorsal and ventral nerve roots is very low when correct technique is utilized. Post-RFN neuritis can occur with perfect technique and typically involves painful dysesthesias in the distribution of the targeted nerve lasting days to several weeks. Anesthesia dolorosa is a rare chronic deafferentation pain, such that an individual experiences neuropathic pain in a region of cutaneous numbness. Both post-RFN neuritis and anesthesia dolorosa are more common in the upper cervical spine (e.g., TON) with neuritis occurring around 20% of the time and lasting 7–10 days on average [26]. Post-RFN neuritis is frequently treated with corticosteroids. An expected side effect of RFN is local, segmental denervation of the multifidi muscles at the levels of the RFN. While multifidi denervation has not been shown to be clinically significant in cases of successful lumbar RFN [27], significant cervical muscle weakness and kyphosis has been reported following multilevel cervical RFN [28].

It is rare to require RFN to more than two joint levels, to achieve clinical benefit and the fewest number of joints possible to achieve good outcome should be targeted.

Evidence

There is a substantial body of evidence that suggests that RFN is an effective treatment for chronic pain emanating from the z-joints. It is important to highlight that these beneficial effects were observed under conditions where patients were carefully selected using a dual block protocol and subsequently treated using anatomically sound techniques. With respect to intra-articular injections, high-quality studies are lacking. There is limited evidence to support the use of intra-articular injections for short-term pain relief of z-joint-mediated pain. Further studies are required to examine the efficacy of intra-articular z-joint injections in patients selected with a dual block protocol and to determine the value added by intra-articular injections when combined with a physical rehabilitation program. The following discussion of relevant research only describes some of the seminal studies and is not an exhaustive summary of the literature.

Cervicogenic Headaches from the C2-3 Joint

The C2-3 facet joint has received a mixed review in the RFN literature. Many of the early RFN studies found lower success rates with the C2-3 facet joint, relative to other facet joints. The seminal positive cervical RFA study by Lord et al. excluded the C2-3 level [29]. Variable course of the TON, multifactorial causes of headaches, and higher risks associated with TON RFN may explain the relative lack of studies and positive reported outcomes compared to other cervical joint levels. Furthermore, double-blinded RCTs are difficult to perform without un-blinding the treatment group given that occipital numbness is associated with successful TON blockade. However, there are several prospective trials suggesting that RFN is an effective treatment for cervicogenic headaches [30–32]. In summary, patients who experience 100% relief of suboccipital pain/headaches following dual diagnostic blocks of the TON have a 60–86% chance of being pain free for a minimum of 10 months following RFN.

The evidence for pulsed RFN and therapeutic C2-3 intra-articular injections is more limited. Small, uncontrolled studies suggest pulsed RFN may also be effective for some patients with occipital neuralgia and cervicogenic headaches [33]. Retrospective evidence suggests C2-3 intra-articular injections can potentially reduce headache frequency in patients with chronic cervicogenic headaches after whiplash [34]. More rigorous prospective studies are needed to clarify the value of these treatments for cervicogenic headaches.

Neck Pain from Cervical Z-Joints C3-4 to C6-7

In 1996, Lord et al. performed the seminal effectiveness study for cervical RFN, excluding C2-3 [15]. This study demonstrated that patients carefully selected via a rigorous dual block protocol had a 58% chance of complete pain relief for an average of 263 days following RFN. Subsequently, multiple prospective studies have confirmed the effectiveness of RFN in the cervical spine [31, 32, 35–39]. Briefly, a summary of the findings of these studies includes the following: using a criterion of 50–80% relief following dual blockade protocol, 62–68% of patients obtain greater than 75% relief for up to 6 months following RFN and 74% obtain greater than 50% relief at 12 months post-RFN. If more stringent selection criteria are used (80–100% relief after dual diagnostic MBBs), then up to 74% of patients experience complete relief for a minimum of 10 months following RFN.

To date, there are no cervical intra-articular z-joint injection RCTs that utilized a dual block protocol for patient selection. The best study was performed by Barnsley et al. in 1994, in patients with chronic neck pain after whiplash [40]. Their findings suggest that about 20% of patients achieve sustained improvement for at least 2–3 months with either local anesthetic or steroid [40]. It is still unknown if the short-term effects of cervical intra-articular injections can facilitate recovery in combination with physical rehabilitation.

Low Back Pain from the Lumbar Z-Joints

The current literature regarding the effectiveness of RFN in the lumbar spine is mixed. However, studies that employed appropriate selection criteria and anatomically correct techniques have consistently shown positive results for RFN in the lumbar spine [18]. Using an inclusion criterion of 80% pain relief with dual block protocol, the data suggest that 60% of patients experience greater than 90% pain relief at 12 months following RFN and 87% of patients experience greater than 60% pain relief at 12 months following RFN [18]. The probability of an effective RFN is reduced if a single diagnostic block is used [41].

While still accepted as a diagnostic tool, the therapeutic effects of lumbar intra-articular z-joints are still debated. Most guidelines do not support the routine use of lumbar intra-articular z-joint injections, due to the lack of high-quality research [42]. No study has selected patients with a dual block protocol typical of the best RFN trials. In uncontrolled studies, intra-articular lumbar z-joint injections with steroid provided long-term relief in 18–63% of subjects [16]. Controlled studies have produced mixed outcomes and all have technical shortcomings, largely due to patient selection [16, 41, 43]. While the value added has not been proven, lumbar intra-articular injections may improve tolerability of active physical therapy for some patients, potentially increasing the chance of success within a comprehensive treatment paradigm [16]. Lumbar z-joint injections should not be used as a stand-alone treatment for low back pain.

Sacroiliac Joint Pain

The sacroiliac (SI) joint is another synovial joint that is an often-overlooked source of low back pain. It is generally accepted that the SI joint is causative in 15–30% of patients with chronic back pain, especially when the pain is below L5 [44, 45]. The SI joint is a C-shaped joint between the sacrum and the ilium, secured by powerful ligaments and built for shock absorption to buffer forces transmitted between the upper and lower body. The thinner anterior SI ligament lies across the front of the joint; the posterior SI ligaments are much stronger and overlap with the even stronger interosseous SI ligament. The attachment of the SI joint to the pelvis is further reinforced by the sacrotuberous and sacrospinous ligaments and to the lower lumbar facet vertebra by the iliolumbar ligaments. Ligamentous disruption of the SI joint, such as by trauma or from pregnancy, are sources of pain and dysfunction originating from the SI joint. Other SI-related sources of pain come about through natural aging and/or disease-related arthritic changes (e.g., sacroiliitis from spondyloarthropathy) to the joint itself, or abnormal loading of the joint in situations of scoliosis or leg length inequality causing pelvic obliquity, or after lumbosacral fusion.

The innervation of the SI joint is still debated, but most accept that the posterior joint/ligaments are innervated by the primary dorsal ramus of L5 and the lateral branches of the dorsal primary rami from S1-S3; conversely, the anterior joint/ligaments are innervated by direct branches of L2-S2 trunks and possibly the superior gluteal and obturator nerves [46]. Perhaps because of this complex innervation, symptoms of SI joint pain can vary substantially. Accepting variability, SI joint pain is often unilateral, aggravated by transitions from sitting to standing, and is predominately below the L5 vertebrae [47]. Pain referral patterns have been delineated [48, 49], and often include the buttock, groin, posterior thigh, and occasionally below the knee (i.e., pseudosciatica).

Clinical evaluation of the SI joint has been well studied and no single physical exam maneuver has high predictive value. However, using the following criteria predicts a positive response to a diagnostic block in 70–80% of subjects: maximal pain below L5 and at least 3/6 positive provocation tests (distraction, compression, thigh thrust, Gaenslen's, FABER, sacral thrust) [50]. Unless true sacroiliitis is present, imaging is of limited use in diagnosing presumed SI pain. Sacroiliitis is represented by periarticular sclerosis on X-ray and CT, and by increased signal on MRI. Among the imaging modalities available, SPECT seems to have the highest specificity for detecting SI joint pain [51], but is not routinely used due to radiation exposure and unknown sensitivity. Imaging is still valuable to rule out competing diagnoses. The gold standard for diagnosis of SIJ pain remains positive response to an image-guided intra-articular block with anesthetic. As with the z-joint injections, false-positive rates are high with single blocks (20–40%).

When SI joint pain has been confirmed, several widely accepted interventional options are available, if active physical rehabilitation has been unsuccessful: therapeutic intra-articular SI joint injection with steroid, conventional RFN, and cooled RFN. All procedures should be performed under image guidance. Intra-articular

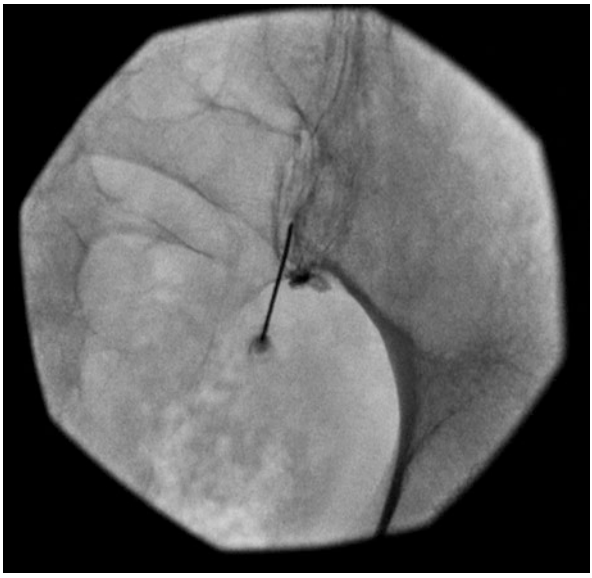

Fig. 38.6 Fluoroscopic image of an intra-articular SI joint injection

injections should be confirmed with radio-opaque contrast (Fig. 38.6). Similar to the z-joint injection studies, most therapeutic SI joint injection trials suffer from loose patient selection criteria. A higher quality study supports intra-articular injections of steroid for spondyloarthropathy, with close to 70% response rate for significant pain reduction beyond 6 weeks [52]. Effects were less for patients with a history of lumbosacral fusion. Results from mostly lower quality, uncontrolled studies suggest variability in both effect and duration of SI joint injections, with the majority supporting short-term improvement in pain [53].

In patients who do not achieve sustained improvement following intra-articular injection, RFN can be considered. Because of the complex innervation of the SI joint, positive response to diagnostic lateral branch blocks should be obtained prior to proceeding to RFN, even in patients with a positive response to the intra-articular block. The most common protocol includes anesthetic blockade of the L5 dorsal ramus and lateral branches from S1-3 (blocked at the lateral aspect of the S1-3 sacral foramina). The ventral innervation of the joint is not accessible. Those with a positive intra-articular block, but negative response to the lateral branch blocks, may still have pain related to the SI joint ligament complex, but are not good candidates for RFN. In multiple uncontrolled trials, 35–70% of those who do have a positive response, which typically includes at least 50% improvement to the lateral branch blockade, achieve at least 50% improvement in pain for at least 6 months [54]. One placebo controlled trial utilizing cooled RFN after >75% response to single diagnostic block yielded a number needed to treat (NNT) of 1.5 for at least 50% improvement for 3 months, with 50% of subjects responding for at least 6 months [55]. A subsequent placebo controlled trial utilizing cooled RFN selected patients on the basis of at least 50% improvement from a dual block protocol, and demonstrated that 59% experienced at least 50% improvement for at least 9 months

[56]. Cooled RFN offers some clear technical advantages over conventional RFN for the sacral lateral branches, including larger lesion size that extends slightly beyond the tip of the needle.

Conclusion

Spinal pain will affect most of us at some point in time and is frequently recurrent or chronic. The z-joints and SI joints are common causes of chronic pain. Before considering interventional treatments, the clinician should develop a high pretreatment probability that a patient's pain is coming from a particular joint (or joints) based on a combination of prevalence, history, examination findings, and diagnostic tests. Although physical examination and imaging studies lack the specificity and sensitivity to definitively diagnose all causes of z-joint and SI joint pain, they can be used to support the case for diagnostic blocks and to rule out competing diagnoses. Intra-articular injections can provide diagnostic information and can be therapeutic in some patients. The gold standard to determine if RFN is an appropriate treatment is a double blockade protocol to anesthetize a particular joint (or joints) and to ascertain if the expected duration of pain relief is achieved. Research suggests that when RFN is used in carefully selected patients who demonstrate positive concordant responses to a double blockade protocol, it is an effective treatment the majority of the time and is generally well tolerated by patients.

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Chapter 39
Neurolytic Injections for the Treatment of Pain in the Rehabilitation Patient

Kenneth D. Candido and Bryant England

Introduction

One of the more challenging aspects of pain management in the patient undergoing rehabilitation has been the management of chronic intractable pain, which includes malignancy. In cancer patients, multiple pain syndromes can occur for a given patient from primary site tumor burden, to contiguous and distant metastatic lesions. Having a multimodal approach for managing pain in these patients is the most effective plan for providing an acceptable level of comfort. One such adjunctive modality of intractable or recalcitrant pain includes incorporating the treatment options of thermal, cold, or chemical neurolysis. Advanced chronic pain alleviated with chemical neurolysis has a long track record dating back to the nineteenth century. Since its inception, there have been a multitude of enhancements in technique, technologic advances in imaging guidance, and newer agents. As a result, outcomes for patients have only continued to improve. With the increasing popularity of using neuromodulation techniques and extended-duration opioid therapy, neurolysis has somewhat fallen out of favor as a first-line therapy for managing chronic intractable pain. However, there remain individuals who are either not accepting of those interventions, or who have prohibitive side effects associated with their use. These patients remain viable candidates for consideration of neurolysis. This chapter focuses on those techniques that are useful in the patient requiring rehabilitation.

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History

Neurolysis is the destruction of nerves via nonspecific disruption of the neuron or spinothalamic tracts (and often others) of the spinal cord. It can be executed using different modalities, which include physical, chemical, or thermal (freezing or heating). Historically, neurolysis was first effectively utilized for chronic benign conditions by Luton in 1863 for sciatic neuralgia [1]. He injected subcutaneous irritants in order to achieve his desired outcome. Luton was able to successfully treat not only sciatic neuralgia, but infraorbital neuralgia as well, by injecting various agents from simple saturated sodium solution to silver nitrate. In 1925, Doppler painted the femoral artery with 7% phenol for peripheral vascular disease [1]. In 1931, Suvansa treated tetanus spasticity using intrathecal carbolic acid (phenol) [2]. That same year, Dogliotti was the first to successfully attempt subarachnoid alcohol spinal neurolysis for treatment of chronic sciatica [3]. He recognized the physical separation of sensory (dorsal root ganglion, DRG) and ventral motor fibers at the neural entry zone and utilized this to attempt selective sensory block, while sparing motor fibers. Maher recognized the hyperbaric nature of phenol in the subarachnoid space and used this agent to provide pain relief in cancer patients [4, 5].

Indications

Neurolysis is useful for blocking pain from the cranial nerves, primarily the trigeminal (CN V). It is also useful for major plexopathies, such as following avulsion injury (brachial, lumbar). Sympathetically mediated pain is amenable to these techniques in Complex Regional Pain Syndrome (CRPS) patients (stellate ganglion, lumbar sympathetic, superior hypogastric plexus). Abdominal pain originating from the pancreas, liver, omentum, gallbladder, mesentery, and the alimentary tract ("PLOGMA") to the transverse large colon is successfully treated using neurolytic celiac plexus blocks. Finally, peripheral joint pain (sacroiliac-SIJ) pain may also be treated with chemical agents when RFA isn't successful or is contraindicated.

Agents

There are numerous agents that can be used for performing chemical neurolysis. These include absolute alcohol, phenol, glycerol, cold saline, hypertonic and hypotonic solutions, and ammonium salts, with contemporary use largely being relegated to alcohol and phenol. Alcohol is typically used for subarachnoid block, cranial nerve procedures, and celiac plexus block. Phenol is typically reserved for use in

Table 39.1 Chemical agents used for subarachnoid neurolysis: A comparison [6]

Agent	Alcohol	Phenol
Concentration	100%	3–12%
Diluent	None	Glycerin
Patient position	Lateral (bedside upwards)	Lateral (bedside down)
Added tilt	Semi-prone	Semi-supine
Painful side	Uppermost	Lowermost
Injection causes	Immediate burn	Painless warmth
Neurolysis occurs at:	Immediate	Delayed (15 min)
CSF uptake ends at:	30 min	15 min
Full effect occurs at:	3–5 days	1 day

lumbar sympathetic nerve block, peripheral procedures (SIJ), ganglion impar block, superior hypogastric plexus block, and genicular nerve block (after knee reconstructive surgery, for example) (Table 39.1).

Wallerian Degeneration

Named for Dr. Augustus Volney Waller (1816–1870), this is the major pathophysiologic mechanism underlying chemical neurolysis. It is a process that results when part of the axon, which has separated from a neuron's cell body, degenerates distal to the injury. This is also known as anterograde or orthograde degeneration. Between the central nervous system (CNS) and the peripheral nervous system (PNS), there are vast differences that characterize Wallerian Degeneration. The process will typically occur within 24 h from initial injury, whereby the axon will degrade stepwise; however, as noted above, the effects of alcohol and phenol subarachnoid neurolysis will typically demonstrate marked physiological changes at a much earlier time than 24 h.

In the PNS, after application of a chemical neurolytic drug (alcohol or phenol), it is the macrophages that will initiate degradation by removing myelin and axonal debris. After 96 h of initial injury, the basal lamina houses those remaining Schwann cells, which provide nerve growth factors for axonal sprouts to form. From the sprouts, new neuronal tissue will grow through the tube and will continue to advance to its target tissue. A regenerative process occurs over a period of multiple weeks to several months in certain situations under favorable physiological conditions (absence of acidosis) [1].

By comparison, the CNS does not contain Schwann cells, but oligodendrocytes that produce a myelin sheath. The macrophage removal of debris occurs over weeks, instead of days. This is due to inhibitor factors that hinder the progression of debris removal. For the regenerative process, it is not the myelin producing oligodendrocyte

that provides the network lattice for the axon; rather, it is the astrocytes. Glial filaments are produced and form a glial scar, which fills the void created by the degraded axon and myelin from the initial injury. As a result, the normal axonal pathway is permanently disrupted and new neuronal tissue does not replace that scar [1].

Alcohol

One of the two primary agents used for neurolytic procedures, alcohol, exerts its mechanism of action through dehydration. As a result, phospholipids, cerebrosides, and cholesterol are extracted from neuronal cells. Additionally, mucoproteins are precipitated, and sclerosis of the nerve fiber and myelin sheath itself occurs. The primary mode of injury is through Wallerian degeneration. Alcohol will spare the Schwann cell tubes, leaving the possibility for neuron regeneration, the exception being the dorsal root ganglion. Indirectly, it acts on modulating pain perception via production of arterial vasospasm in a concentration-dependent manner [1].

One will observe inflammatory changes in the nerve roots, Lissauer's tract, posterior columns, and meninges with subarachnoid alcohol chemical neurolysis. Individuals treated with ethanol will often complain of intense burning dysesthesias secondary to chemical neuritis when receiving the injection, or just afterwards. Another commonly encountered, potentially concerning complication is the potential for toxicity. One significant issue with alcohol is that toxicity is not dose dependent; individuals can develop toxicity even with standard dosages are injected intravascularly [1].

Phenol

The other widely used compound for neurolysis is phenol (carbolic acid). A unique added benefit to neurolysis with phenol is its local anesthetic properties. This affords additional analgesia for individuals receiving the injection because it is more tolerable. The effects include neurolysis via a different mechanism of action, in addition to Wallerian degeneration. Local anesthesia is achieved at concentrations of <1%, with no neurolysis. To attain maximal neurolysis, one would have to inject 12% phenol, which is the highest concentration that can be placed into solution. As a result, phenol has a biphasic action, wherein warmth and numbness occur initially from the local anesthetic properties, and nonselective degeneration with neurolysis follows shortly thereafter [1].

There is a direct correlation between concentration and neurolysis, unlike what is observed with alcohol chemical neurolysis, which is essentially complete at concentrations above 33% [7]. At concentrations <5%, primarily sensory block of A-delta and C-fibers occurs, and concentrations >5% beget both motor and sensory blockade. Protein degeneration is another outcome of using concentrations >5%,

but coagulation of proteins occurs specifically at concentrations between 5 and 6%. More importantly, orthograde Wallerian degeneration ensues at the same concentration as protein coagulation. A-delta and C-fibers (cold, pressure, and nociceptive receptors) and A-beta fibers (stretch receptors) are destroyed, but the dorsal root ganglia are spared with phenol at these higher concentrations [1].

Unlike its counterpart alcohol, phenol damages the neural tube because it is directly neurotoxic, so nonspecific regeneration of the axon takes place. The greatest afforded benefit of phenol is that there is predictable toxicity and adverse outcomes, which are concentration dependent. With concentrations >6%, there are predictable neural adverse events, including the potential for spinal cord infarcts, development of adhesive arachnoiditis, and meningitis when the chemical is used intrathecally. The most concerning toxicities occurring after intravascular injection include central nervous system depression and cardiovascular collapse. Other organ systems may be affected, which include development of hepatic toxicity, and chronic poisoning, which can cause skin eruptions, gastrointestinal, and renal toxicity. In general, clinical applications are the same as for alcohol, but also include use of phenol for the splanchnic nerve, peripheral nerve roots, as well as for sympathetic block of the celiac ganglion and lumbar sympathetic chain.

Selected Techniques

Applications are vast, which include performing neurolytic blocks at the head and neck, subarachnoid, epidural, transforaminal, celiac plexus, lumbar sympathetic, SI joint, ganglion impar, and superior hypogastric plexus nerves as targets of nociception. With subarachnoid, and to a lesser extent epidural block, there is predictable segmental sensory loss for precise targeting of dorsal roots, while avoiding ventral root motor deficits. This chapter will focus on the technical aspects of nerve blocks with chronic pain treatment for the rehabilitation patient. When performing a neurolytic block at any site, imaging (ultrasound, fluoroscopy, CT scan, MRI) is mandatory for both medical–legal reasons, to assure appropriate technique and procedure-related approach, as well as to assure competent assessment and negotiation of the relevant anatomy.

Head and Neck Blocks

The trigeminal nerve and Gasserian ganglion blocks are two different techniques used in targeted neurolysis for chronic facial pain conditions. Interventionists have at their disposal fluoroscopic, ultrasound, and CT-guided access to the foramen ovale to execute the block. CT has advantages in offering views in rostral, sagittal, and axial sections. This is not to say fluoroscopy cannot be effectively used, as high success rates are observed when utilized; however, it is at the discretion of the

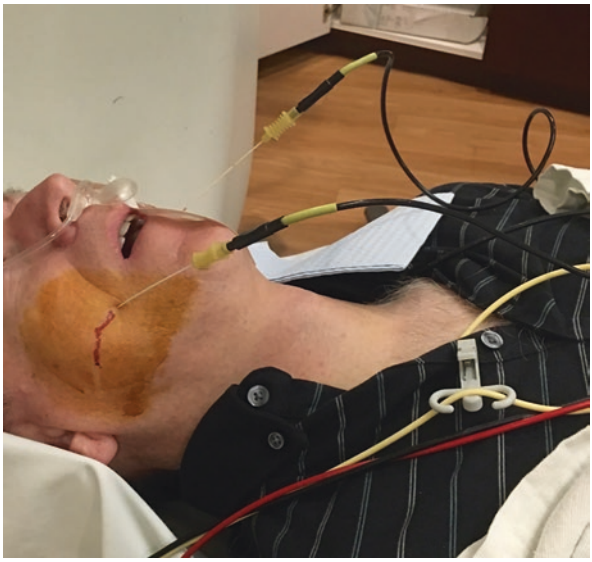

Fig. 39.1 Patient positioned for neurolytic (radiofrequency thermocoagulation) Gasserian ganglion block for chronic intractable facial pain due to idiopathic trigeminal neuralgia. Bilateral subzygomatic 15 cm cannulas have been placed into the foramen ovale under CT scan guidance in a lightly sedated patient who provides verbal feedback (Photo courtesy of Kenneth D. Candido, M.D.)

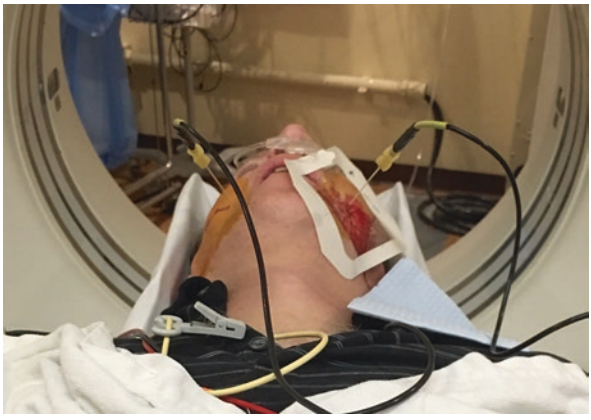

Fig. 39.2 Caudal-cranial view of bilateral subzygomatic 15 cm cannulas placed into the foramen ovale using CT scan guidance. Radiofrequency (RFA) electrodes have been placed through the cannulas and continuous RF energy is being applied at 80°C for 90 s for thermocoagulation of the Gasserian ganglion (Photo courtesy of Kenneth D. Candido, M.D.)

individual performing the block as to how to best carry it out. Pain secondary to cancer, which can occur in the V1, V2, and V3 trigeminal nerve distributions, can be treated in this manner (see Figs. 39.1, 39.2, 39.3, 39.4, and 39.5 below).

Careful patient selection is mandatory, and patients should be offered surgical options such as microvascular decompression prior to proceeding. Contraindications include bleeding diatheses, use of anticoagulant medications, localized skin infection, and patient refusal. All patients require advanced hemodynamic monitoring and a functioning IV prior to proceeding.

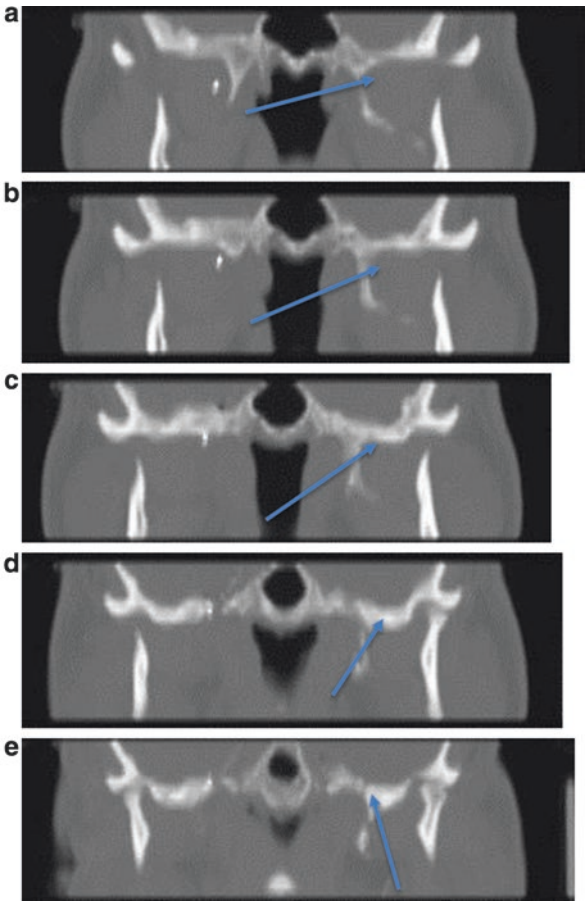

Fig. 39.3 (**a–e**) CT scan images of needle entering the foramen ovale: rostral views; *arrows* indicate needle tip (Photos courtesy of Kenneth D. Candido, M.D.)

After disinfecting the skin and performing a local anesthetic skin wheal, needles are placed subzygomatically, 3 cm from the lateral border of the lower lip, as shown in Figs. 39.1 and 39.2. Using image guidance (fluoroscopy, ultrasound, CT scan, MRI), needles are advanced into the foramen ovale [8]. The cavernous sinus is medial; the temporal bone is superior; the brain stem is posterior; V1, V2, and V3 are anterior, with V1 and V2 being medial in the ovale and V3 being lateral. Sometimes, clear and free flow of CSF will be obtained as the needle tip enters Meckel's Cave. Water-soluble, iodine-based contrast is useful to assure appropriate placement and to minimize needles being situated in non-targeted structures, such as the foramen spinosum. For neurolysis, 0.5 mL of absolute alcohol in a tuberculin syringe can be injected; after which, the needle needs to be re-styletted to prevent backflow.

Subsequently, the patient should be observed to assure no hematoma formation, and no spillover onto other, nearby structures including the facial nerve (CN VII). Individual branches of CN IV (ophthalmic-V1, maxillary-V2, mandibular-V3) can also be blocked either at the foramen ovale or for V2, at the foramen rotundum. Additionally, the superficial branches of V1 (supratrochlear; supraorbital nerves),

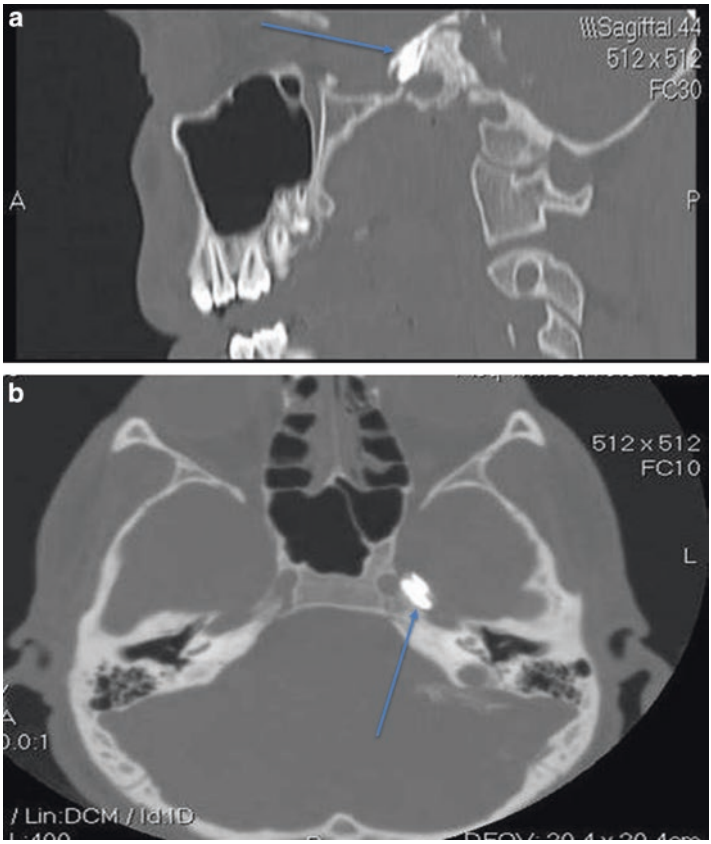

Fig. 39.4 (**a**) Sagittal view of contrast injection into foramen ovale for TGN block (Photo courtesy of Kenneth D. Candido, M.D.). (**b**) Axial view of contrast injection into foramen ovale for TGN block (Photo courtesy of Kenneth D. Candido, M.D.)

V2 (infraorbital nerve), and V3 (submental nerve) can be blocked using small quantities of phenol for individuals who are not found to be suitable candidates for central cranial nerve neurolysis.

Celiac Plexus Neurolysis

There are several well-accepted approaches to celiac plexus blockade, which include the anterior approach (Fig. 39.5). This may be a more technically demanding technique reserved for more experienced interventionists and for patients who cannot assume the prone position, which is necessary for posterior block. The needle must traverse the liver, stomach, intestine, vessels, and pancreas before the desired agent can be injected into the celiac plexus. More opportunity for injury exists as a result,

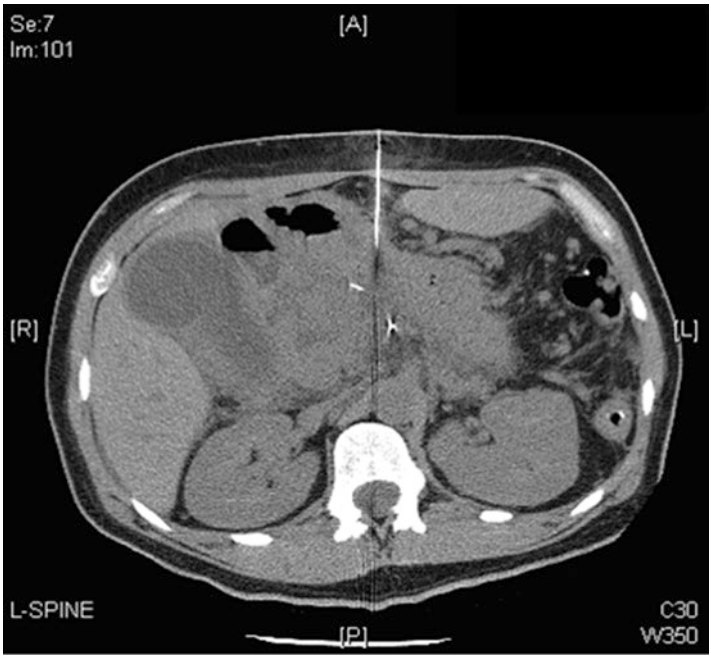

Fig. 39.5 Needle approach to anterior celiac plexus block using CT scan guidance (Photo courtesy of Kenneth D. Candido, M.D.)

with potential complications arising to include peritonitis, abscess formation, hemorrhage, and fistula formation. Additionally, it is essential for fluoroscopic, CT, ultrasound, or MRI image confirmation of needle location, because it has been associated with higher success rates [9–11].

Endoscopic ultrasound-guided celiac plexus neurolysis offers a more direct route of blockade with favorable outcomes [12]. Since fewer structures need to be traversed, the side effect profile is allegedly not as severe and includes hypotonia, post-procedure pain, and increased frequency of bowel movements. Patients with pain from unresectable tumor masses, or those with intractable pain from pancreatic cancer, are among the primary indications for celiac plexus neurolysis to effectively provide pain relief when other less aggressive medical modalities have been exhausted.

For posterior approaches, either a unilateral or bilateral needles can be placed (Fig. 39.6). The relationship of the block needle to the crus of the diaphragm determines whether the procedure is a "pure" celiac plexus block ("antero-crural") vs. being a splanchnic nerve block ("retro-crural"). With the patient prone, a bolster is placed beneath the abdomen to minimize the normal lumbar lordotic curve. After disinfecting the skin and performing a local anesthetic skin wheal, a 22-gauge, 5- or 6-in. Quincke type subarachnoid needle is advanced to the anterolateral surface of the T12–L1 junction. This can be determined using one of the visualization

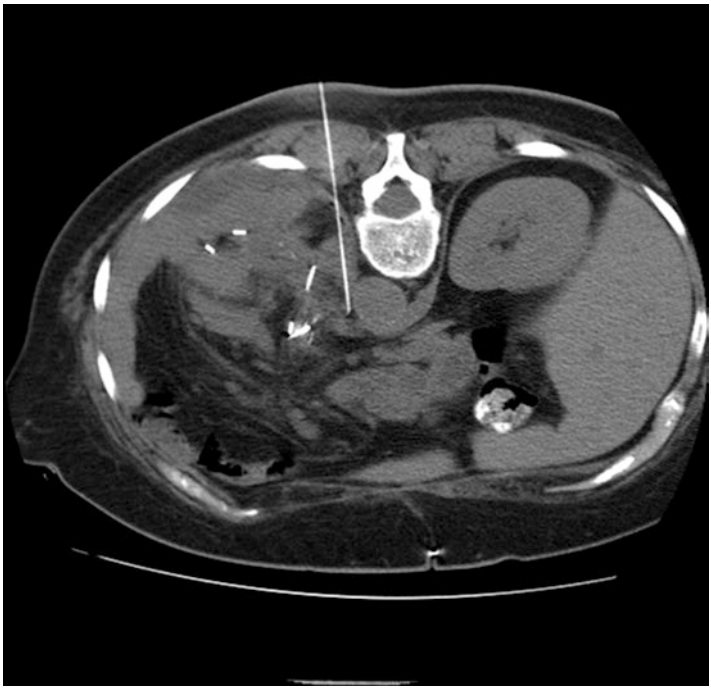

Fig. 39.6 Posterior approach to celiac plexus block using a single-needle technique on the right side. Needle approaching the anterior-lateral surface of the abdominal aorta (Photo courtesy of Kenneth D. Candido, M.D.)

techniques described above. Once the needle tip has been seen to pass the anterior cortex of the selected vertebrae, it is advanced 2–3 cm more anteriorly, until one of the following end-points occurs: (a) There is bright red blood noted in the hub of the needle once the stylet of the needle is withdrawn; under these circumstances the needle should be re-styletted and advanced a cm further to remove it from the lumen of the aorta; (b) There is radiographic (CT scan) evidence that the needle tip is ventral to the abdominal aorta, as confirmed using contrast agents; (c) ultrasound imaging shows the needle tip to be extravascular (not in the vena cava or aorta). At this point, for fluoroscopic or CT scan or MRI techniques, contrast is injected in 5 mL aliquots until the spread appears to be satisfactory to proceed to neurolysis. Once this has been determined, a volume of neurolytic agent, alcohol being the most common, in the same volume as the contrast used to define the anatomical boundaries, is injected into the abdominal space, ventral to the abdominal aorta. The needle(s) is then re-styletted, withdrawn, and then removed. Sterile bandage is applied over the injection site and the patient is observed for a minimum of 30 min to assess the presence of orthostatic hypotension, a common occurrence following successful blockage.

Potential complications include the possibility of spinal or epidural neurolysis resulting in paraplegia, quadriplegia, or death; renal damage; vascular damage; infection; orthostatic hypotension; increased bowel motility; severe backache; and protracted nausea and vomiting.

Intrathecal and Epidural Neurolysis

Intrathecal and, to a lesser extent, epidural neurolysis are seldom-used techniques to provide long-term analgesia for individuals suffering from intractable lower extremity pain, who are not deemed to be reasonable candidates for neuromodulation (spinal cord stimulation) or intrathecal drug delivery systems (IDDS). The technical challenges and absolute need for precision associated with the performance of these techniques, the low margin for error, and the devastating potential consequences of neurolytic spillover onto non-targeted structures have relegated these techniques to those possessing advanced interventional pain management skills. Nevertheless, there remains a role for these approaches in the armamentarium of managing chronic intractable pain in those undergoing rehabilitation efforts to improve functionality, without a primary reliance upon opioid analgesics.

Prior to considering use of these techniques, it is mandatory to comprehend the takeoff of the respective nerve roots from the spinal cord itself. For example, blockade does not occur at the intervertebral space, but rather at the interlaminar space; therefore, an intimate knowledge, attained from consulting standard anatomical, dermatomal, and sclerotomal charts, cannot be overemphasized. For example, in many lower extremity pain syndromes manifesting as pain from the lower limb to the foot, needle placement will not be at the L5-S1 level; rather, it will occur much higher at the T9-T10 level. Pre-neurolytic diagnostic blocks, using a discrete amount (<1.0 mL) of a short-acting local anesthetic for subarachnoid blockade, is essential to assure that analgesia will be forthcoming after the neurolytic procedure is complete.

For intrathecal, also known as subarachnoid neurolysis, there are many technical differences between alcohol and phenol (Fig. 39.7). For alcohol, which is hypobaric relative to the cerebrospinal fluid (ratio of the density of alcohol to CSF is <1.0), the patient is positioned in the lateral decubitus position, with the painful, affected side uppermost, with a semi-prone tilt (rolled anteriorly 45°). The painful dorsal root ganglion side will need to be the uppermost side as well. Neurolysis with alcohol is virtually immediate, with cerebrospinal fluid (CSF) uptake ending 30 min after injection so the patient must remain in the position post-block, and full effect observed for a minimum of 45 min post-procedure. In comparison, with phenol, which is hyperbaric to cerebrospinal fluid (ratio of density of phenol to CSF >1.0), the patient is semi-supine (rolled posteriorly 45°) in the lateral decubitus position. Therefore, the painful side is the lowermost part. Neurolysis is delayed by up to 15 min, and occurs when cerebrospinal fluid uptake of phenol ends; the full effect of

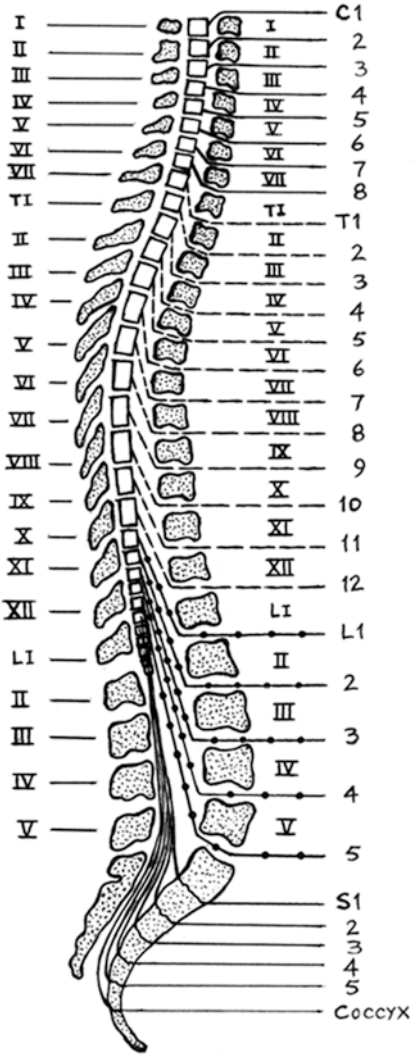

Fig. 39.7 Schematic demonstrating takeoff of spinal nerves from the spinal cord for selecting appropriate interlaminar needles for needle insertion when considering subarachnoid neurolysis (Picture courtesy of Kenneth D. Candido, M.D.)

neurolysis is realized after 1 day. It is important to mention that with phenol, the bevel of the needle must be directed inferiorly.

Epidural neurolysis is best suited for patients with midline pain and impending loss of motor function. This is a result of the fact that epidural injection cannot be utilized for patients requiring unilateral analgesia; separation of motor and sensory block is much less likely to occur. This technique is gravity independent, so multiple levels could theoretically be affected by injecting the requisite larger volumes of neurolytic agent. Phenol is typically used because of its relatively greater ease of use via continuous catheters. It is mandatory that advanced imaging techniques be utilized, including either fluoroscopic vs. CT scan techniques to determine

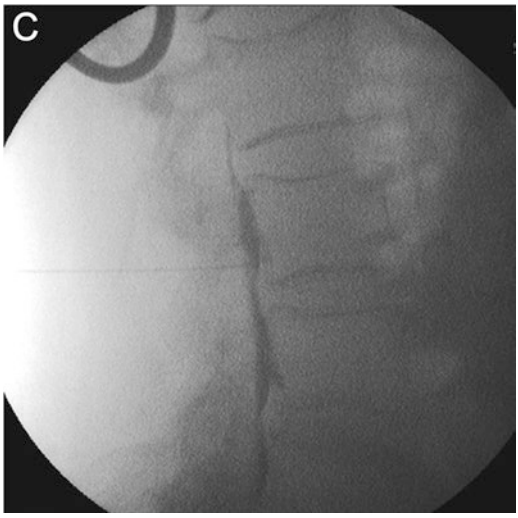

Fig. 39.8 Lateral fluoroscopic image in patient undergoing a transforaminal contrast injection as a prelude to injecting 5% phenol for neurolysis in the management of chronic, intractable lower extremity pain and weakness (Photo courtesy of Kenneth D. Candido, M.D.)

appropriate catheter location and to assure correct delivery into the epidural space. Recently, a transforaminal epidural technique of neurolysis has been described for intractable lower limb pain management [13] (Fig. 39.8).

Comparative advantages of epidural vs. intrathecal neurolysis injection include less risk of bladder or bowel dysfunction (urinary retention, bowel incontinence), loss of sphincter tone, option for daily injections, and incremental injection using a catheter. The risks are actually higher with epidural phenol vs. alcohol and are greater with lumbosacral blockade. Blockade of the S2, S3, and S4 anterior nerve roots interrupts parasympathetic innervations leading to bowel and bladder complications. Other potential complications include nausea, vomiting, central nervous system stimulation, burning pain in nerve distribution, cardiac arrhythmias, respiratory arrest, flaccid paralysis, and paraplegia.

Ganglion Impar Neurolysis

Also known as the Ganglion of Walther, this is the solitary terminal ganglion of the sympathetic chain (Figs. 39.9 and 39.10). It is located anterior to the sacrococcygeal junction. The interventionist will need to use fluoroscopy, CT scan, or ultrasound guidance in order to appropriately assess needle location. Indications for ganglion impar neurolysis include intractable perineal pain secondary to rectal cancer, bladder cancer, or cervical cancer. Rarely, neurolysis may be undertaken for severe, intractable perineal pain resulting from benign conditions.

The technique is performed with the patient prone, and with a bolster placed beneath the hips. After appropriate skin disinfection has been performed and a skin wheal of local anesthetic has been injected, a short-beveled, 1.5 in. needle can be

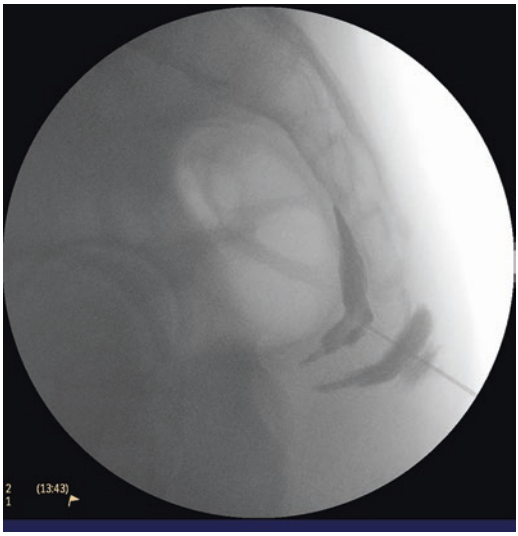

Fig. 39.9 Ganglion impar (ganglion of Walther) neurolysis technique; lateral fluoroscopic image: needle seen traversing the sacrococcygeal joint space (Photo courtesy of Kenneth D. Candido, M.D.)

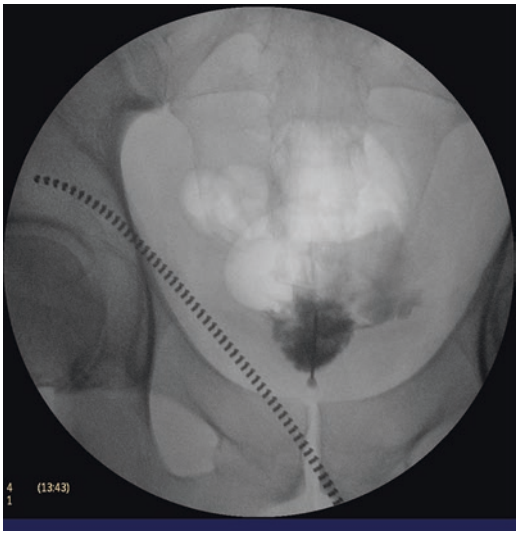

Fig. 39.10 Anterior-posterior fluoroscopic image in patient undergoing ganglion impar neurolysis; needle seen above the symphysis pubis, which defines the anatomical midline (Photo courtesy of Kenneth D. Candido, M.D.)

advanced from posterior to anterior, at the level above the symphysis pubis, through the sacrococcygeal junction, taking great care not to puncture the nearby rectum. Although the rectum cannot be visualized using fluoroscopy, it can be seen on ultrasound. With fluoroscopy, the surrogate of identifying air in the rectal vault has occasionally been considered to be confirmation of where that anatomical structure is located. Once the ventral cortex of the joint has been negotiated. 2–3 mL of contrast may be injected, followed by an equivalent volume of phenol 5–6%. Complications include bleeding, infection, rectal injury, perineal numbness, and vascular injection.

Outcomes

Neurolysis is a useful technique to provide prolonged analgesia and in many cases, to cause a reduction in opioid consumption (and the attendant side effects associated with opioid use, which include nausea, vomiting, pruritis, constipation, urinary retention, and respiratory depression. Fortunately, chemical neurolysis does exactly that. Unfortunately, its use has no bearing on cancer patient prolonged survival [12]. Providing pain relief to intractable, recalcitrant, or inoperable patients is just as important as quality of life improvement. The prevalence of pain in cancer patients is roughly 50%, and of those, two-thirds have advanced cancer [1]. It should be mentioned when comparing alcohol to phenol that the duration of efficacy following subarachnoid neurolysis has been observed to be longer with alcohol, up to more than 6 months in duration, but no study has specifically evaluated superiority between the two in a head-to-head prospective comparison.

Success rates with epidural and intrathecal neurolysis vary based on the spinal level of pain, with the greatest success in thoracic, then lumbar, then cervical locations. Motor loss following thoracic neurolysis is less of a consequence following injection, in comparison to the lumbar region wherein the proximity of the sensory and motor nerve roots calls for intense precision of needle placement and injection. Somatic pain responded in 78–84% of cases, while only 19–24% of patients with visceral pain responded favorably. As many as 81% of cancer patients in pain had complete pain relief after subarachnoid neurolysis, 60% demonstrating relief for a month or more while 19% had poor pain relief [1, 6]. When comparing ethanol to phenol in intrathecal neurolysis, there is little difference with regard to favorable outcomes; however, poorer outcomes were slightly higher with phenol as compared to alcohol (25% vs. 18%). Many patients will reduce opioid use significantly, with elimination of dependence in some.

Celiac plexus neurolysis is one last resort treatment option for patients with inoperable pancreatic cancer pain and pain due to any pathological process in the PLOGMA organs. Up to 86% have been observed to have improvement in pain after 1–2 weeks, with substantial improvement after 2–3 months following endoscopic approaches. Pain relief has been observed to be greater in multiple studies at 1 and 3 months post-blockade. One study even found that patients had a longer survival rate compared to non-endoscopic approaches.

Chemical neurolysis is an outstanding option for patients with pain secondary to cancer. It offers a long-lasting treatment that is both safe and effective, and can improve quality of life.

Conclusion

Contemporary pain management has seen explosive growth in the use of techniques of neuromodulation with the recent developments of high-frequency stimulation, pulsed stimulation, and dorsal root ganglion stimulation, each of which is being critically evaluated as a potential long-term strategy for managing chronic, moderate-to-severe pain. Additionally, extended-duration opioids are becoming more favored by pain physicians due to their stable pharmacokinetics and dynamics, which minimize the peaks and troughs associated with immediate-release preparations, felt by many to contribute to aberrant drug utilization and therapeutic failures.

However, in light of these advances, and in light of the push by society and oversight agencies to minimize or to eliminate opioid use and to curb expenses incurred by using neuromodulation, there does remain an underutilized and extremely viable technique of neural destruction using chemical, thermal, or mechanical methods to provide sustained analgesia in select cases. Neural ablation and chemical neurolysis in particular are techniques which demand extreme attention to detail, both anatomically and physiologically. These techniques rely upon the use of advanced imaging modalities for successful placement of chemicals (primarily alcohol or phenol) in intimate approximation of targeted neural structures deemed responsible for nociception. The relative inexpensive acquisition of these chemical agents and techniques makes them ever more attractive in contemporary interventional pain practices, and the future is beckoning in terms of providing a perfect storm of opportunity for resurgence in their respective use. Clinicians will undoubtedly seek to expand upon our knowledge and scope of practice to involve greater use of neurolysis in future pain applications. This chapter forms a basic framework upon which to commence that journey.

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Chapter 40
Kyphoplasty and Vertebroplasty for the Treatment of Pain in the Rehabilitation Patient

Tory McJunkin, Moustafa Maita, Edward Swing, and Paul Lynch

Introduction

Osteoporosis and resultant vertebral compression fractures (VCFs) are a major worldwide healthcare concern and healthcare expenditure. Osteoporosis affects over 10 million Americans, with approximately 80% of them being female. In addition, over 30 million Americans have osteopenia. Osteoporotic disease is more common in the elderly, but over 55% of Americans over the age of 55 have osteoporosis (see Fig. 40.1). There is an increased incidence of vertebral compression fractures in those with lower bone marrow density. Because of our aging population, the prevalence of osteoporosis is expected to double in the USA by 2040 and to quadruple in the world by 2050. These statistics suggest that there will be an osteoporosis epidemic in the future.

VCFs typically arise in an area with fewer bony trabeculae, which leads to a decrease in tensile strength, endplate compression, and finally a wedge compression deformity. Most often, VCFs are spontaneous, with little to no inciting event or trauma (see Fig. 40.2).

Approximately 85% of detected vertebral compression fractures cause moderate to severe pain. On average, the pain lasts for approximately 6–9 months, although many people have pain that lasts much longer. Not only do VCFs cause significant pain, but they also contribute towards a downward trend in daily activities and overall health (see Fig. 40.3). This has been called the vertebral compression fracture spiral. The downward spiral can include the following: pain leading

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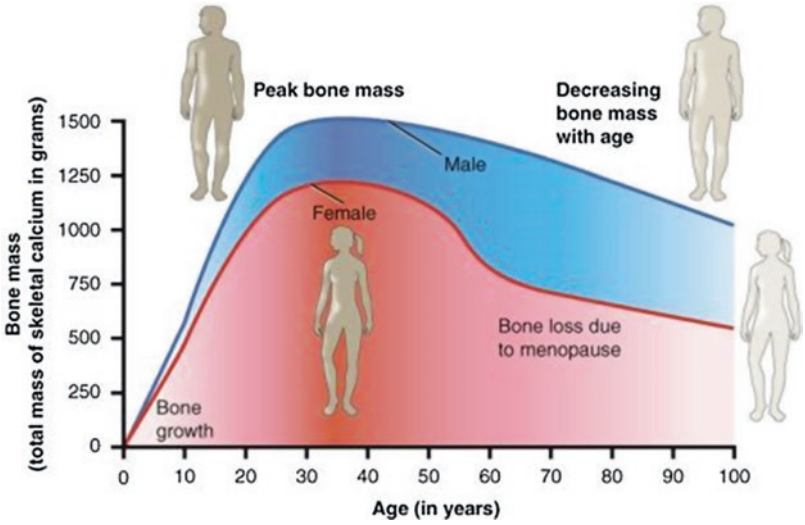

Fig. 40.1 Incidence of osteoporotic disease

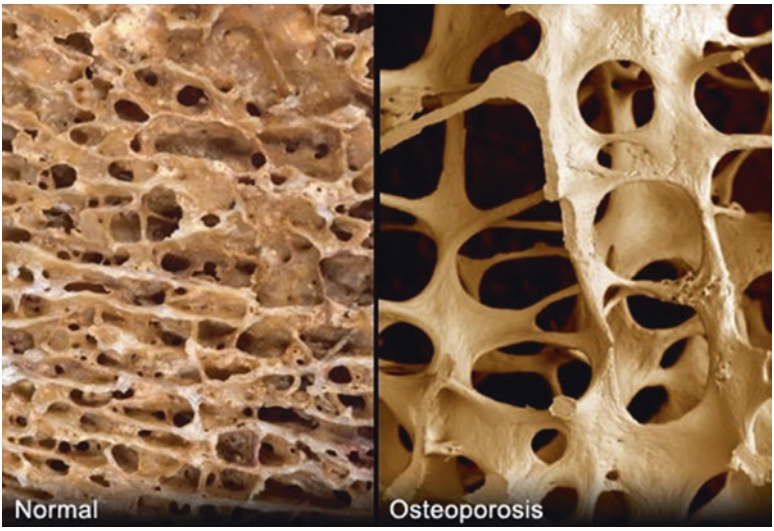

Fig. 40.2 VCFs typically arise in an area with fewer bony trabeculae, which leads finally to a wedge compression deformity

to a reduction in ambulation, a reduction in exercise tolerance, a further decrease in bone density, additional compression fractures, a decrease in pulmonary function, rib crowding, decreased lung capacity, pneumonia, DVTs, other morbidities, and sometimes even death.

Vertebral compression fractures are often undiagnosed. In many people, height loss from vertebral body fracture is very gradual and is often under-recognized until

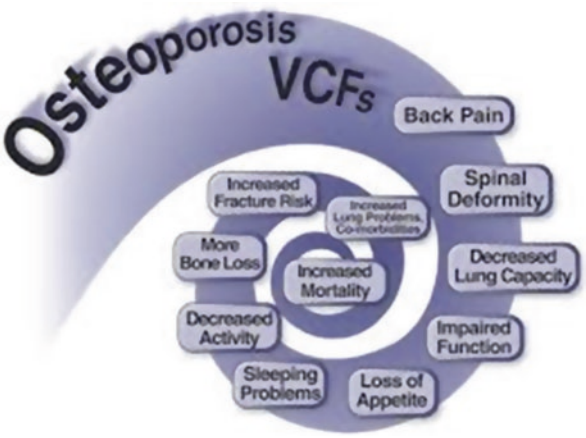

Fig. 40.3 VCFs contribute towards a downward trend in daily activities and overall health

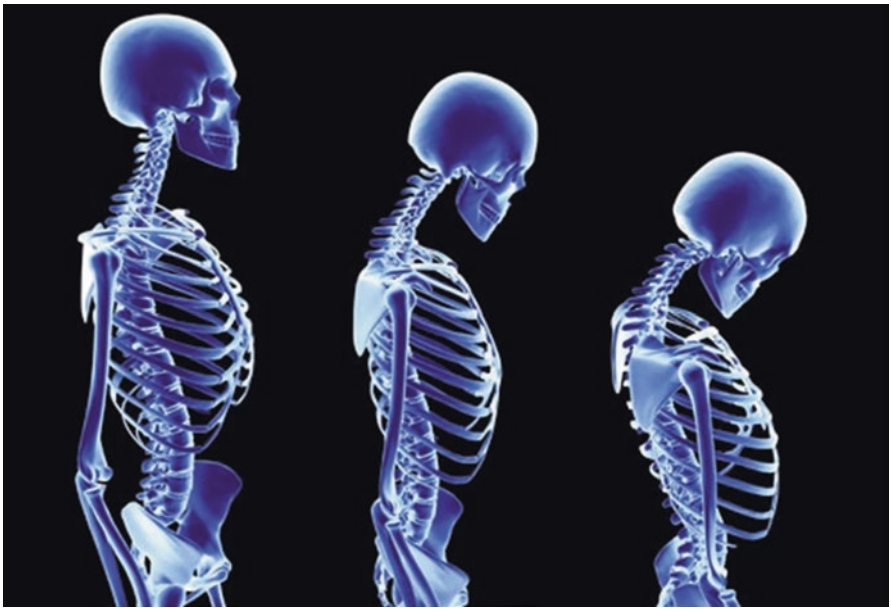

Fig. 40.4 Height loss from vertebral body fracture may be very gradual and is often under-recognized until one has a high enough level of clinical suspicion to obtain a MRI

one has a high enough level of clinical suspicion to obtain a MRI (Fig. 40.4). Plain film X-rays are often initially ordered to evaluate new onset spinal pain. Unfortunately, X-rays do not always show a clear demarcation between fracture and non-fracture. Older chronic fractures often look the same as acute or subacute fractures; mild compression deformities are often not seen at all. One must remember that osteoporosis is a generalized disease and often affects other vertebral bodies, as well as other bones. If someone has one vertebral compression fracture, they may have another, and are certainly more susceptible to having future fractures as well.

Osteoporotic vertebral compression fractures (VCFs) have become an increasingly important disease, not only due to their significant socioeconomic impact, but also due to the increasing age of our population [1]. Approximately 4% of patients presenting in the primary care setting with low back pain have a vertebral compression fracture [2, 3]. The painful progressive collapse of the vertebra and subsequent loss of posture are associated with a series of clinical consequences leading to an increased morbidity and mortality rate [4]. Many patients heal with conservative treatment, which consists of rest or activity modification, analgesics, and bracing. However, persistent severe pain compels some patients to seek a minimally invasive intervention via one of two procedures: vertebroplasty or kyphoplasty [1].

Vertebroplasty (VP) and kyphoplasty (KP) are minimally invasive percutaneous procedures, whereby an interventionist injects polymethylmethacrylate (PMMA) into fractured osteoporotic vertebral bodies, with the aim of immediate stabilization and pain relief [4]. PMMA, also known as "bone cement," is injected at low viscosity directly into the cancellous bone in the VP technique [4]. Kyphoplasty differs from VP through its inherent mechanism; KP is performed by inserting a hollow needle consisting of a contrast-filled inflatable balloon into the vertebral body, which is then carefully inflated to create a hollow space within the fracture (Fig. 40.5). This method allows a degree of fracture and pressure reduction, while leaving a cavity that is immediately filled with high-viscosity PMMA [4]. Both procedures provide a treatment for VCFs and exhibit a significant postoperative decrease in pain, as well as an increase in function [5–8].

Background

The first percutaneous vertebroplasty was performed in France by Dr. Deramond in 1984 to fill a painful cervical hemangioma. Other physicians around the world later adopted this technique to treat VCFs. Revisions to the procedures helped physicians in the United States to address growing concerns of VCFs. While VCFs affect approximately 25% of postmenopausal women, the prevalence increases to 40% for women aged 80 and older [5, 9–11]. However, decreased bone mass, which is often seen in postmenopausal women, is not the only cause of VCFs. VCFs can also arise from metastatic cancer and trauma. Consequently, VCFs can cause the spine to progressively become weaker, rendering it unable to bear body weight. This sequence

Fig. 40.5 (continued) pedicle and verify the trajectory of the needle. (**b**) When the needle tip arrives at the medial border of pedicle, verify entrance to the vertebral body on a lateral view. Advance the needle to approximately 4 mm past the posterior cortical wall. (**c**) Drill channels for balloons. (**d**) Insert balloons. (**e**, **f**) Inflate the balloon. (**g**) Maximum balloon distention is safely achieved. (**h**) Balloon deflation. (**i**) Deliver the cement. (**j**) Fill the cavities and then interdigitate. (**k**) In terms of cement volume, the trend is towards smaller volumes, but the volume delivered depends on the level treated (less for high thoracic and more for low lumbar), the caliber of vertebral body, and clinical goals. Typical volumes range from 1 to 4 cc

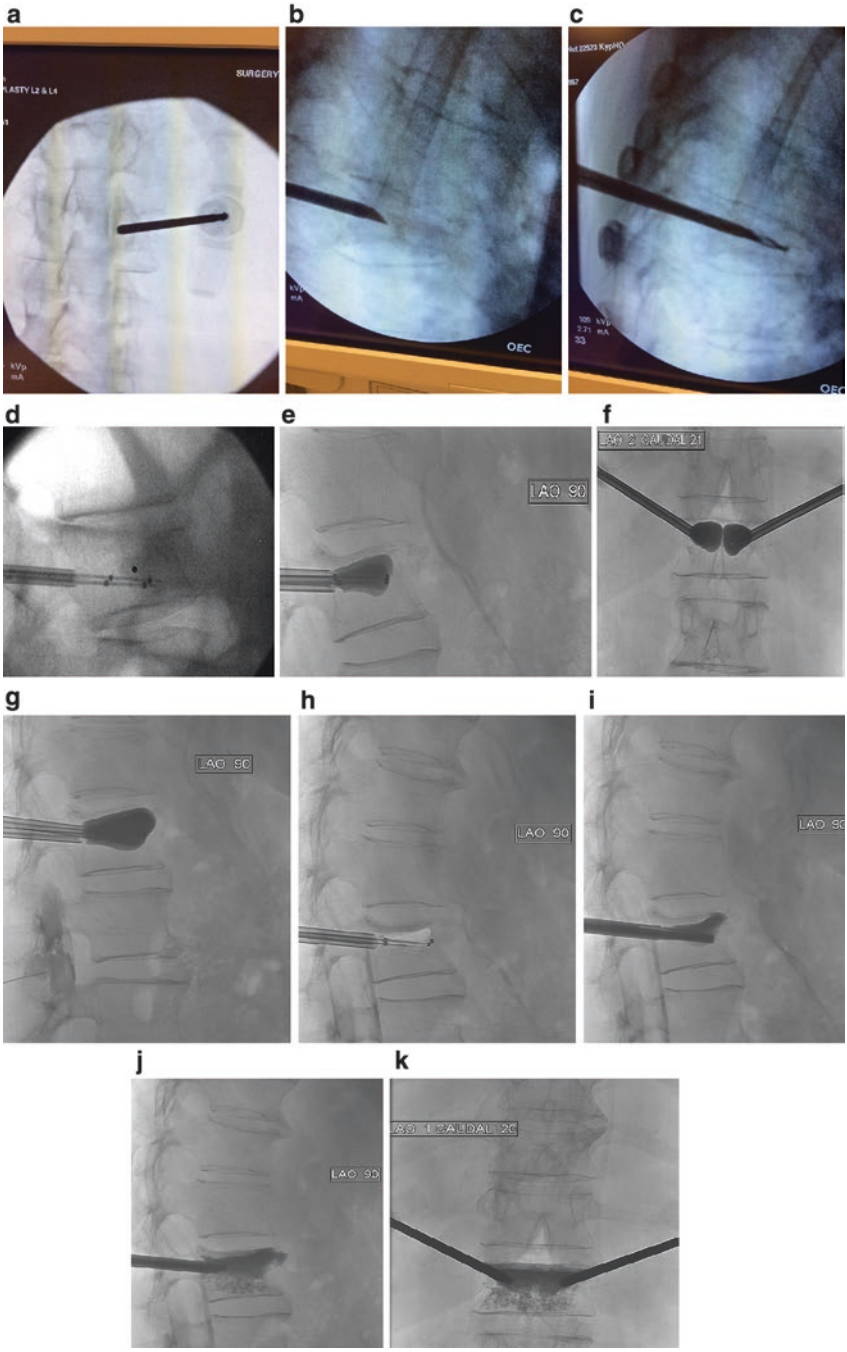

Fig. 40.5 Image sequence of kyphoplasty (KP) for vertebral fracture repair. Images courtesy of Arizona Pain and Wayne Olan, M.D. (**a**) Align the tip of the needle with the lateral and superior aspect of the pedicle. Verify on a lateral image that the tip is placed on the posterior wall of the

of events may lead to poor mobility, weight gain, depression, and a host of other side effects. Moderate to severe back pain subsequently develops, and a progressive loss of height may ensue.

Pathophysiology

Acute vertebral compression fractures occur when the weight of the upper body exceeds the ability of the bone within the vertebral body to support the load. Progressive reduction in trabecular bone mass from osteoporosis or inflammatory mediators creates porous bone, which subsequently increases the risk of fracture [12]. Poor diet, decreased estrogen (menopause), and lack of weight-bearing exercises can increase yearly bone loss, resulting in progression to osteoporosis. Patients with severe osteoporosis may experience a VCF from activities of daily living (ADLs) and from minor movements, such as stepping out of a vehicle, vigorous sneezing, or lifting light objects [13]. A healthy spine can sustain a compression fracture from severe trauma, such as an automobile accident, sports injury, or hard fall.

After sustaining an injury, the applied force usually causes the anterior portion of the vertebral body to crush, forming what is known as a "wedge fracture" (Fig. 40.6) [9]. The middle column usually remains intact and can act as a hinge. Loss of anterior height of the vertebra ensues while the posterior height usually remains unaffected. As the collapsed anterior vertebrae fuse together, the spine bends forward, causing a kyphotic deformity [9]. Since the extent of damage is localized to the anterior vertebrae, the fracture is usually stable and is rarely associated with neurologic complications. A "burst fracture" is considered when the entire vertebral body collapses (Fig. 40.7).

Other causes of VCFs included malignancies, long-term corticosteroid use, trauma, and adolescents suffering from chronic rheumatologic disorders. Malignancies such as multiple myeloma can cause high serum levels of IL-6, which stimulates plasma cell growth and production of osteoclasts that in turn lead to vertebral body destruction [12]. Adolescents suffering from chronic ankylosing spondylitis (AS) for 20 years or more are prone to vertebral compression fractures due to rigidity and decreased bone mineral density [14]. Chronic AS releases inflammatory mediators, such as TNF-α and IL-6, which activate osteoclasts that may lead to osteopenia/osteoporosis; thereby, this increases fracture risk [14]. Long-term corticosteroid usage inhibits bone formation by altering osteoblast activity while causing osteocytes to undergo apoptosis, reducing bone formation, and inhibiting development of the cytoskeleton [15, 16]. Although the most common cause of vertebral compression fractures is osteoporosis [1], osteoporotic fractures are not the only cause of VCFs. It is incumbent to include VCFs as part of the differential diagnosis when a patient presents with back pain.

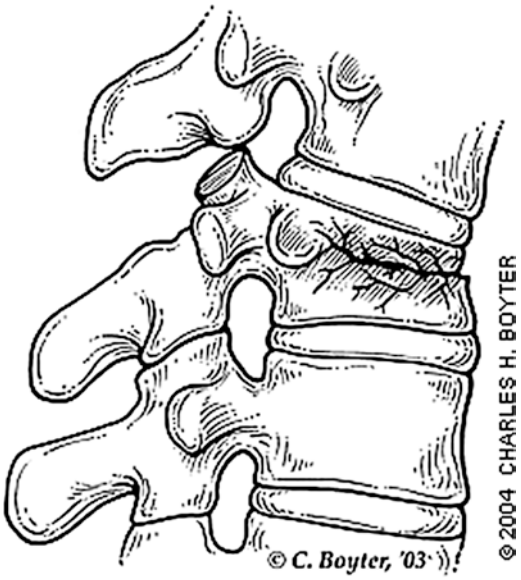

Fig. 40.6 "Wedge fracture"

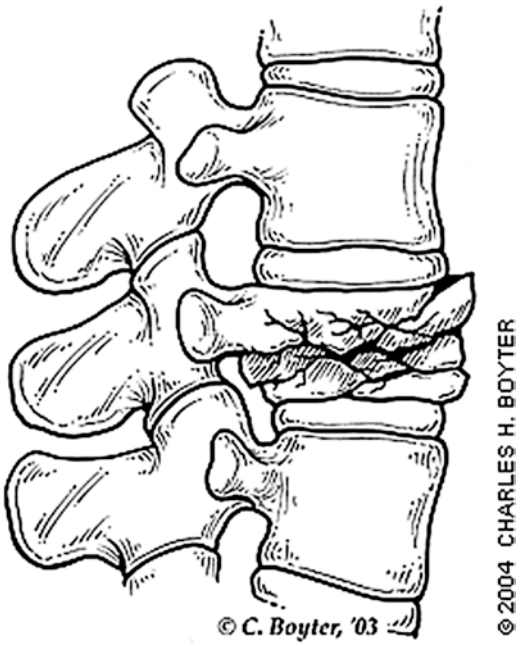

Fig. 40.7 "Burst fracture"

Diagnosis

Vertebral compression fractures cause characteristic signs and symptoms that may be revealed upon careful history and physical examination. In particular, patients usually present with constant and focal pain, which appears to be axial or non-radiating. Thoracic spine pain may transfer to the ribs and the patient may demonstrate some difficulty with large inspiratory and expiratory movements. The pain may also radiate to the abdomen, but this is less common. Upon physical examination, direct percussion or palpation along the spinous process of the affected level may reproduce or worsen the patient's pain. Some also use a tuning fork over the affected spinous processes to see if the patient has concordant pain. In addition, careful history may reveal that the patient has pain that is worse while standing, sitting, and driving in a car. Pain may be partially relieved while lying down flat. Symptoms that radiate to the upper or lower extremities are likely due to another pathology.

Vertebral compression fractions are most commonly located in the mid-thoracic region from T6-T9, as well as the thoracolumbar junction from T11-L1. In the mid-thoracic region, spinal thoracic kyphosis is the most pronounced, which induces loading stress during flexion, making these vertebral body levels more susceptible to fracturing. In the thoracolumbar junction, the more rigid thoracic spine gives way to the mobile lumbar region, which makes these vertebral bodies more susceptible to fracture as well.

In the USA, 1.5 million vertebral compression fractures occur each year [17]. Only a third of these fractures are diagnosed [18, 19]. Patients typically present with acute back pain after sudden sneezing, coughing, stretching, lifting, or after minor trauma [13]. Even something as seemingly benign as riding over a speed bump can precipitate a fracture [20]. Palpation or percussion of the midline spine often reveals tenderness that may refer to the paravertebral musculature, flank, or abdomen. Often presenting without pain, height loss of >6 cm can be very specific (94%) for VCFs [21]. When using baseline height as a comparison, a 20% decrease of vertebral height or decrease of at least 4 mm identified on radiographs may be considered as a positive finding for a VCF [22]. Fractures may occur anywhere along the occiput to the sacrum, and careful imaging of the entire spine should be taken.

Plain frontal and lateral radiographs of the thoracolumbar spine can diagnose fractures through the lumbo-dorsal junction, mainly T8-T12, L1, and L4 [23]. Though radiographic imaging can reveal a fracture, *magnetic resonance imaging (MRI) using the short tau inversion recovery (STIR) sequence is the gold standard for VCF assessment*. MRI allows the documentation of the number of fractures. The STIR sequence is preferred for determining the age of a fracture (see Fig. 40.8). Specifically, presence of a fat signal surrounding a fracture indicates an older VCF that has healed. The presence of vertebral body marrow edema, bright white on T2 STIR sequencing, indicates an acute or subacute fracture that is unhealed. MRI can also reveal the extent of spinal canal encroachment and can be used to identify or to rule out other possible pain generators or malignancies.

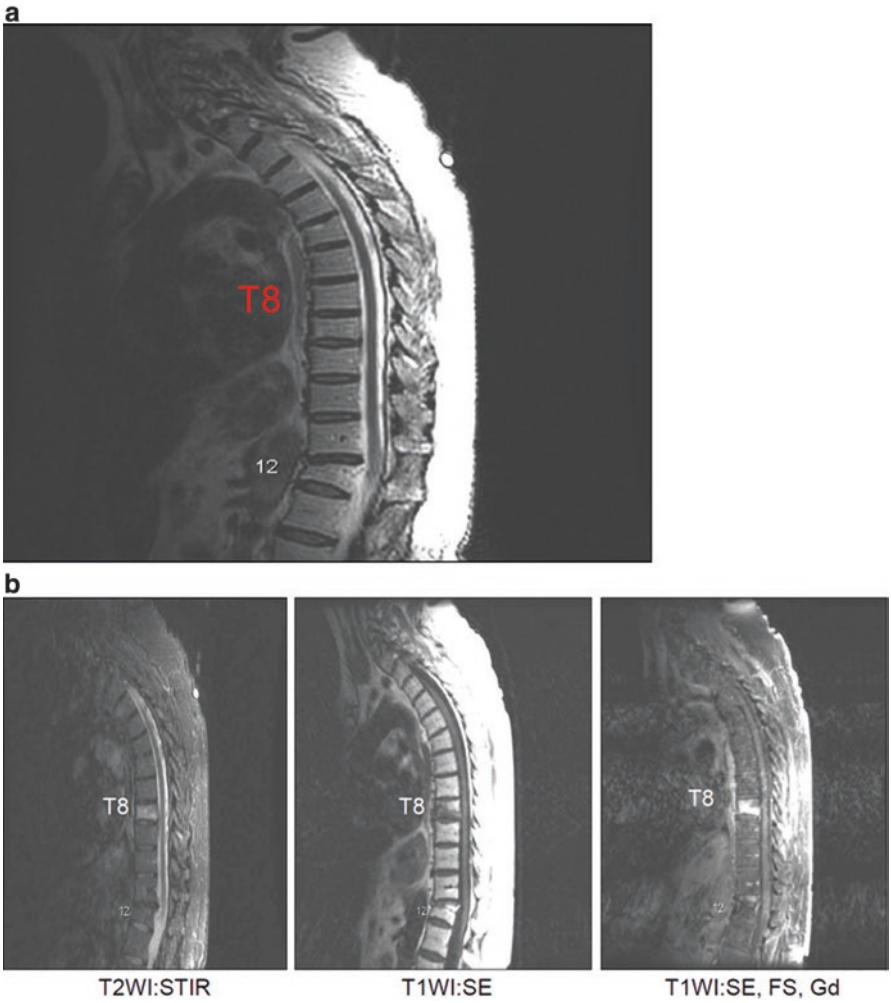

Fig. 40.8 Magnetic resonance imaging of a patient with fractures of the T8 and T12 vertebrae. Images courtesy of Wayne Olan, M.D. (**a**) MRI T2 images show T8 and T12 fractures. Acute and subacute fractures are not differentiated. (**b**) MRI STIR sequence images reveal an acute T8 fracture and chronic, healed T12 fracture.

If one is unable to obtain a MRI (e.g., patient with cardiac pacemaker, spinal cord stimulator device), a combination of CT and bone scans are typically performed to diagnose and to classify the acuity of VCFs (see Fig. 40.9). On bone scans, bone uptake is markedly increased in acute fractures. It may be near normal in older, healed fractures. Caution is needed in interpreting bone turnover, as bone turnover tends to be low in older adult patients. Computerized tomography (CT) imaging, using sagittal and 3D reconstruction (if available), can be useful in such patients.

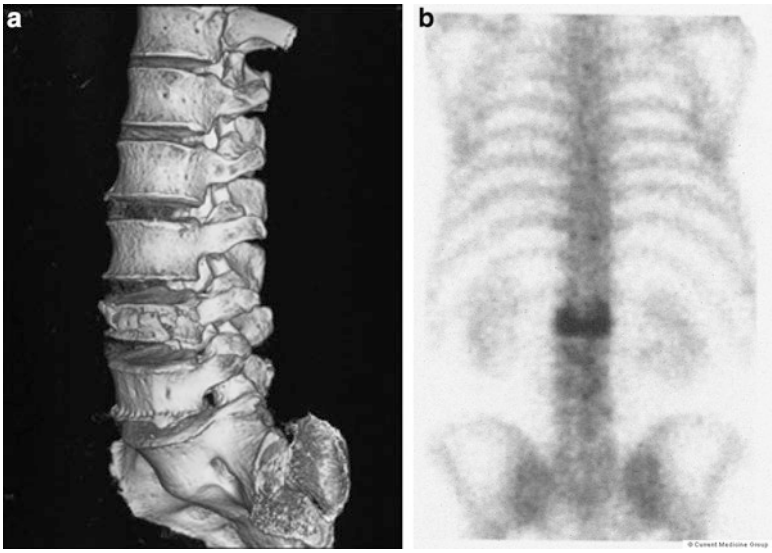

Fig. 40.9 (**a**) CT scan with 3D reconstruction of an L4 VCF. (**b**) Bone scan showing uptake at an acute or subacute VCF

Treatment Techniques

Traditionally, VCFs have been treated non-operatively and conservatively with analgesics, bed rest, bracing, and correction of underlying osteoporosis. Patients who don't experience relief from these treatments may continue to have persistent pain. Furthermore, kyphotic deformities lead to a lower quality of life. Left untreated, VCFs can progressively worsen, leading to severe spinal canal stenosis and neurological compromise (see Fig. 40.10). If refractory pain persists, is moderate to severe in intensity, and if a patient fails conservative treatment, VP or KP is likely warranted.

Both percutaneous VP and KP typically utilize PMMA (polymethylmethacrylate) injections to provide an alternative to a more invasive procedure, such as anterior and/or posterior spinal fusion, which have significant risks due to general anesthesia and the invasiveness of the surgery [24, 25]. During immediate postoperative treatment, a meta-analysis reported a 5-point decrease in VAS pain score for patients treated with KP or VP [1]. Neither technique was superior to the other at decreasing VAS scores in the immediate postoperative period or at long-term follow-up [1]. A separate meta-analysis of RCTs showed no improvement with VP and KP two weeks after treatment ([26], Table 40.1). However, a subgroup analysis of a RCT exhibited that VP was more effective than KP at decreasing the VAS score during the initial postoperative period [27, 28]. Complication rates also differed between the two procedures. VP was associated with an increased risk of cement extravasation and procedure-related complications more often than KP [29]. Conflicting evidence regarding which procedure is safer or more effective warrants further evaluation with additional randomized controlled trials.

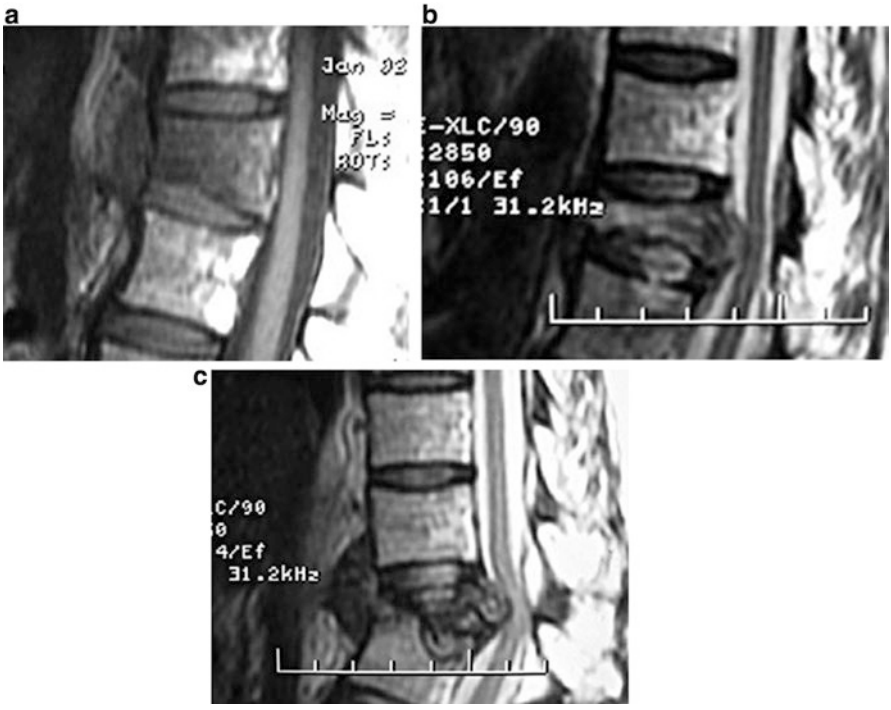

Fig. 40.10 A series of radiographic images showing progressive canal compromise in a patient with an untreated vertebral compression fracture. Images courtesy of Wayne Olan, M.D. (**a**) January—no central canal stenosis. (**b**) February—50% stenosis. (**c**) May—75% stenosis

Rehabilitation

Patients treated in a rehabilitation setting should be considered for possible VCF. When an acute or subacute painful VCF is identified, conservative treatment modalities including the use of appropriate medications should be considered first. Patients whose pain is severe and refractory should be referred for VP or KP. There is evidence that, even after VP or KP, patients benefit from rehabilitation exercises [30]. Rehabilitation should favor a flexion-biased approach.

Evidence

Dozens of studies have examined the efficacy of VP and KP for treating VCFs. The results of these studies have been summarized in at least two large medical database reviews and in seven meta-analytic reviews (see Table 40.1). Most of the studies conducted to date are non-randomized trials. Overall, the non-randomized studies have found that patients with painful VCFs have substantially lower pain after VP

Table 40.1 Large medical database and meta-analytic reviews of vertebroplasty (VP) and kyphoplasty (KP) for treating vertebral compression fractures (VCFs)

Study (type)	Methods	No. of of studies	No. of patients	Conclusions
Retrospective [1]	Systematic/meta-analysis research articles	21	VP—1046 KP-263	5 point drop post-op for VP and KP
Retrospective, qualitative and quantitative [5]	Database search ICD-9 codes from California, Florida, and New York		KP—35,805 VP—26,046	KP used more than VP due to financial incentives, perceived safety. Kyphoplasty patients had more comorbidities than VP patients
Retrospective, quantitative and qualitative [27]	Systematic/meta-analysis of randomized/non-randomized controlled trials, computerized databases	8 studies	848 patients	VP showed better short-term (1 week) results, whereas KP showed better intermediate term (3 months) results. Long-term results were similar. VP was recommended due to lower cost
Retrospective [30]	Analysis of medical records in Rochester, MN		57	The addition of rehabilitation of osteoporosis program-exercise (ROPE) after VP extended time before refracture
Retrospective and prospective, qualitative [29]	Systematic/meta-analysis, computerized database of Pubmed and Ovid	121 total reports, 29 prospective reports	121	VP and KP were effective for VCFs and had a low rate of adverse events. VP had a higher rate of procedure-related complications and cement extravasation than KP
Retrospective, qualitative [26]	Systematic/meta-analysis of randomized controlled trials using Medline through Pubmed, Cochrane, CINAHL, EMBASE	5 randomized controlled trials	529	Though the significance varied across time points, VP reduced pain more than conservative treatment at 3, 6, and 12 months
Retrospective, qualitative [33]	Systematic review analysis of RCT and NRCT through Pubmed	27		Pain reduction in KP/VP was superior to nonsurgical treatment in pain relief and subsequent VCFs. KP was superior to VP in cement leakage, disability improvement, and kyphosis correction
Retrospective, qualitative [34]	Systematic/meta-analysis	9	886	VP was superior to noninvasive treatment in pain and quality of life (QoL) and superior to sham injection in QoL. New fracture risk was similar across groups
Prospective, retrospective [35]	Systematic/meta-analysis of prospective and RCT on comparative studies comparing VP and KP	10	783	VP and KP reduced pain and disability. Compared to VP, KP reduced long-term kyphosis angle and risk of cement leakage

or KP, as compared to those same patients' pain levels before the procedure. There are considerably fewer RCTs comparing VP or KP to noninvasive treatments, but many of these RCTs provide support for the efficacy of these procedures. Two notable studies were taken as unsupportive of VP for the treatment of VCFs [31, 32]. However, in the study by Buchbinder et al., only 71 subjects were in the 6-month follow-up analysis, which is a small sample size for a RCT with a sham procedure control [32]. Additionally, there were trends toward greater pain relief in the VP group at all follow-up time points. Though Kallmes et al. included a somewhat larger sample of 125 patients in follow-up analyses, they also obtained evidence of greater pain relief (64% of VP patients got 30% relief, as compared to 48% for control, $P = 0.06$) and a higher crossover rate for the control group (43% vs. 12%, $P < 0.001$) [31]. Overall, the published literature, as reviewed in several meta-analyses including these and other published studies, is supportive of a therapeutic benefit for VP and KP.

Though some studies have found differences in the efficacy and in the rate of complications (e.g., cement leakage) between VP and KP, comparisons between VP and KP are difficult, in part because patients receiving VP and KP tend to differ on potentially relevant characteristics. Specifically, KP is often used over VP in patients with more extreme fractures that have resulted in a loss of height or in those patients for whom height restoration is the goal.

Conclusion

Vertebral compression fractures (VCFs) are a common and potentially debilitating condition, particularly among women and older adults. Most VCFs are associated with osteoporosis, but they can also occur in cases of cancer or trauma. VCFs are often painful, but in some can be managed with rest, conservative care, and medication management. In more severe cases where conservative treatments do not control pain or improve function, vertebroplasty (VP) and kyphoplasty (KP) should be considered. These procedures can produce substantial pain relief and can potentially prevent further fractures by stabilizing the fractured vertebra. Though additional randomized controlled trials (RCTs) are necessary to further prove the efficacy of VP and KP, the existing evidence indicates that these procedures are effective in relieving pain and in improving symptoms for patients suffering from painful VCFs.

In a patient with new onset axial spinal pain, one must have a high clinical suspicion of VCFs. Once diagnosed, if a patient has persistent moderate to severe pain after conservative care has been attempted, the VCF should be addressed with KP or VP. In addition, one must recognize that VCFs are usually caused by osteoporosis. If undiagnosed, osteoporosis must be diagnosed and aggressively treated to prevent further fractures and morbidity.

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Part VIII
Multi Modal Approach: Behavioral Management

Chapter 41
Psychological Interventions for the Treatment of Pain in the Rehabilitation Patient

Lucille A. Rathier

Introduction

Chronic pain affects more than 100 million Americans [1]. According to the IOM, it is the most common reason that individuals seek medical care. IOM reported that the societal cost, in terms of annual direct economic affect, is estimated to be approximately $600 billion.

Significant impairment in physical, psychological, social, and vocational functioning is frequently associated with chronic pain [2]. Indeed, it can be a challenging medical condition with physical, behavioral, social, emotional, and cognitive elements [3]. The experience of chronic pain frequently requires individuals to adapt to a daily life that can include episodes of pain exacerbation, disability, and psychological distress [4]. Moreover, high rates of stress, depression, anxiety, and sleep disorders are often the result of chronic pain disorders [5, 6].

Medications and surgical interventions alone have limited benefits for many patients [3]. Analgesics are typically a first-line treatment for chronic pain. However, controversy regarding the use of opioid medications has increased awareness of the need for treatment alternatives [7].

Psychological approaches have a long-standing record of success in the treatment of chronic pain [8]. These approaches have emerged as a common component of multidimensional and interdisciplinary treatment of patients with chronic pain [9]. These approaches are well suited to the rehabilitation team approach. A wide

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variety of psychological interventions aim to reduce the impact of chronic pain disorders by helping patients to develop greater self-efficacy in coping with their condition, to regain a sense of purpose, to reduce pain-related disability, and to improve their quality of life [10]. Empirically supported psychological treatments of patients with chronic pain that are informed by the biopsychosocial model of pain [2] are reviewed. This chapter is meant to be complementary to the physiatric approach in treating pain across the rehabilitation continuum.

Cognitive Behavioral Therapies

Cognitive Behavioral Therapy (CBT)

More recent iterations of CBT for pain management incorporate the biopsychosocial conceptualization of pain [11]. This posits that pain is a complex experience that is influenced not only by its underlying pathophysiology, but also by an individual's cognitions, affect, behavior, and sociocultural status. CBT aims to improve coping, self-efficacy, psychological and physical symptoms, and functional health [12]. Two principles in this approach are: (1) Problems with functioning related to pain can be addressed even if the pain is not targeted directly and remains unchanged and (2) Psychological factors can influence the experience of pain itself [8].

In CBT for pain, clinicians provide a treatment rationale that helps patients to better understand the role of cognitions and behavior in the pain experience and emphasizes the role that individuals play in managing their pain [13]. One underlying mechanism of treatment is changing the content of thoughts from maladaptive (e.g., catastrophizing) to adaptive thoughts that render one able to deal with situations effectively and to improve adjustment to the pain condition [14]. Another underlying mechanism of CBT is the use of more effective coping strategies to address the overwhelming stressor, chronic pain [14]. Coping skills training includes activity pacing and pleasant activity scheduling to help individuals maximize their daily functioning and quality of life [13]. Relaxation training is used to decrease muscle tension, to reduce psychological distress, and to divert attention away from pain. Individuals are also taught problem-solving methods that enable them to develop plans for dealing with pain exacerbations. As more effective coping strategies are consistently used, psychological distress will be reduced and functioning will be improved.

Several meta-analyses have demonstrated that cognitive behavioral therapy in the treatment of chronic pain and associated disability and psychological distress has been regarded as the most efficacious in terms of reduced pain and improved daily functioning [15–19]. Additionally, CBT for the treatment of chronic pain has been regarded as a cost-effective approach, especially when compared with commonly utilized medical approaches ([20, 21]).

Contextual Cognitive Behavioral Therapy (CCBT)

Recently, specific developments in theory and methods have resulted in approaches in the wider field of CBT that regard suffering as inherent in the human condition, which is built into the design of human experience and behavior [8]. Within the framework of Contextual Cognitive Behavioral Therapy (CCBT; [22, 23]) are acceptance-based and mindfulness-based approaches [24]. These approaches emphasize experiential methods and changing responses to symptoms rather than to symptoms themselves.

Acceptance and Commitment Therapy (ACT; [25]) is a CCBT approach that includes a combination of acceptance and mindfulness methods along with activation and behavior change strategies. In addition, it emphasizes cognitive processes and emotional experiences, similar to other CBT approaches [25]. The central treatment process within ACT is *psychological flexibility,* which is the capacity to continue with or to change behavior guided by one's values and goals despite the presence of interfering thoughts, emotions, and bodily sensations [26].

Psychological flexibility includes the subprocesses of acceptance, cognitive defusion, flexible attention to the present, self-as-observer, values-based action, and committed action [25]. Cognitive defusion methods aim to reduce the influence of maladaptive thoughts without necessarily changing the content of the thought [8]. Using acceptance methods, one engages in values-based behaviors despite unwanted feelings. One refrains from controlling feelings when these attempts block success [8]. Mindfulness processes include non-defensive, moment-to-moment, and non-judgmental awareness [27]. It helps individuals to pay attention to current experiences without suppressing or elaborating those experiences [12]. This approach may be integral to decreasing automatic, maladaptive responses including hypervigilance to perceived threats and catastrophizing [28, 29].

Six randomized, controlled trials provide support for the use of ACT in treating patients with chronic pain [26, 30–34]. Consistent results include increased physical and social functioning as well as decreased pain-related medical visits [8]. A meta-analysis of studies of acceptance-based and mindfulness-based treatments for chronic pain found that these approaches seem at least equally effective as traditional CBT [35]. A study comparing CBT, mindfulness and acceptance treatment, and arthritis education found that the mindfulness and acceptance treatment yielded greater reductions in daily pain-related catastrophizing, morning disability, fatigue, and daily stress-related anxious affect than the other two conditions [12]. McCracken and Vowles [8] point out that ACT is a form of CBT that includes many similar methods.

Investigation of treatment process in an ACT trial for chronic pain reveals important findings related to pain, disability, and psychological distress. Increases in the acceptance of pain have been associated with improvements during treatment, which include reduced anxiety, depression, and disability [36]. Moreover, increases in values-based action correlate with improvements in anxiety, depression, and disability at 3-month follow-up [37]. Additionally, increases in acceptance of pain, mindfulness, and values-based action during the active phase of treatment significantly correlate with improvements in anxiety,

depression, and disability, independent of changes in pain at 3-month follow-up [38]. Research supports that mindfulness-based methods are effective in chronic pain by virtue of symptom reduction and improved emotional functioning [27, 39]. Psychological flexibility mediates treatment effects on life satisfaction and disability [40].

Relaxation Training

Relaxation training is an adjuvant method that is frequently used in biofeedback training as well as a part of cognitive behavioral therapy for pain management [9]. Both physiological and emotional stresses are produced by pain. The authors note that these stresses collectively feed into a cycle, which results in increased pain perception and continual modification of the physiology of the body in ways that increase pain (e.g., muscle tension or spasm, constriction of blood vessels). Relaxation training focuses first on gaining awareness of states of tension within the mind and body. Then, the application of systematic relaxation methods (i.e., diaphragmatic breathing, progressive muscle relaxation, guided imagery, or autogenic relaxation) is used to reduce tension and to change the perception of physical pain [9].

The foundation of all relaxation techniques is diaphragmatic breathing. When we are fully asleep or relaxed, we breathe correctly. Our abdomens expand when inhaling and contract when exhaling. Many of us restrict our breathing to our upper chest when awake or under stress. One may repeat a relaxing word such as "calm" or "peaceful." Individuals should limit the pace of breathing to 6–8 breaths per minute [41].

Progressive Muscle Relaxation (PMR) is a widely used method that was developed by Jacobson [42]. The PMR procedure teaches individuals to relax their muscles through a two-step process. First, one deliberately applies tension to certain muscle groups, and then one stops the tension and turns attention to noticing how the muscles relax as the tension flows away. By tensing muscles in this way, one is forcing them to be relaxed. Frequently, 14 muscle groups from head to toe are utilized in this procedure. However, it can be reduced to 4–6 muscle groups with practice.

Guided imagery [43] is the use of mental images (e.g., a peaceful scene) to create a sense of relaxation and reduce stress. Individuals decide their destination (e.g., the beach, the mountains). They make the image as rich as possible using all five senses. For example, if they imagine the beach, they allow themselves to *see* the clouds floating in the sky, to *hear* the waves rolling in, to *feel* the warm sand under their feet, to *smell* the ocean mist, and to *taste* the salt on their tongue. Finally, they are asked to carry this experience with them throughout their day.

Autogenic relaxation [44] is a meditational form of relaxation, which focuses on giving oneself specific self-instructions, such as *"My whole body feels comfortable, relaxed, heavy, and warm"* and *"I feel quite quiet."* The therapist gives a series of relaxing phrases in the first person. Individuals repeat the phrase and are given an opportunity to generate that feeling in their bodies.

Relaxation training has been used to help individuals cope with chronic pain and pain-related psychological distress more effectively [45, 46]. The treatment utility

of relaxation training has been shown in studies of various pain conditions. Relaxation training has been effective in treating migraine and tension type headaches [47]. In addition, these techniques have been shown to be effective in managing musculoskeletal pain in neck, back, joints, and upper extremities [45, 48, 49].

Biofeedback Training

Biofeedback is an interactive process in which individuals can receive real-time information from psychophysiological recordings about the levels at which physiological systems are functioning [50]. The aim is to develop an awareness of when processes change, so that the individual can learn to exert control over the bodily reactions associated with these processes [9]. For pain management, the physiological targets are typically factors that are directly associated with exacerbations of pain or emotional responses to pain [9].

Biofeedback training uses safe, painless, electronic equipment to display the level of a system visually and/or audibly. Most electronic biofeedback devices record from the skin surface [50]. Physiological parameters most frequently recorded for biofeedback include muscle tension (the surface electromyogram [sEMG]), near surface blood flow (done by recording skin temperature), heart rate, galvanic skin response, brain waves (EEG), and respiration [50]. Biofeedback training includes practicing the techniques learned during biofeedback treatment sessions while at home and at work. Much of the home training is done while listening to audio-recorded relaxation exercises.

A randomized, double-blind, controlled study found that 7.5 hours of respiratory biofeedback over 15 days was more effective than placebo biofeedback for treating chronic low back pain [51]. Meta-analyses have demonstrated empirical support for biofeedback methods (i.e., sEMG, near surface blood flow, EEG, galvanic skin response) for chronic headaches [52, 53]. Combined sEMG and EEG biofeedback effectively treats fibromyalgia [54]. Extant research has demonstrated that most individuals with amputations and concomitant cramping pain are helped by sEMG biofeedback [55].

Clinical Hypnosis

The interest in hypnotherapy as a treatment for pain management is increasing [56]. Elkin and colleagues proffer that hypnotherapy can provide analgesia, reduce stress, relieve procedural anxiety, improve sleep, improve mood, and reduce the need for opioids during and after painful medical procedures [3]. Moreover, hypnotherapy can enhance the efficacy of existing treatments for pain [14].

Assessment of the nature of the patients' pain as well as cognitive appraisals and core beliefs is critical in treatment planning for the use of hypnotherapy for pain management [57]. The influence of social factors and current coping strategies being utilized should also be assessed [58]. Patients should be evaluated for

drug-dependent or drug-seeking behaviors, which can confound treatment [3]. The authors recommend cognitive hypnotherapy as part of an overall psychological and medical treatment plan.

Cognitive hypnotherapy for pain management usually involves a hypnotic induction that includes suggestions for changes in perception, behavior, and coping [3].

The authors note that posthypnotic suggestions may be used after treatment sessions for the reduction of pain and the return to a state of comfort. Additionally, the authors indicate that it includes teaching patients how to use hypnosis to reduce pain throughout their daily lives via the use of audio-recording or self-hypnosis.

Hypnotic techniques for treating pain can utilize suggestions for relaxation, dissociation, analgesia, alteration in sensation, safe-place imagery, cognitive restructuring, distraction, and pain metaphors [3]. For instance, the relaxation response can be facilitated by direct suggestion such as *"*notice a wave of relaxation that begins at the top of your head and spreads across your forehead, face, neck, and shoulders. Every muscle and every fiber of your body becomes more and more completely relaxed. More and more, notice a feeling of letting go and becoming so deeply relaxed*"* [59]. An example of using hypnosis for pain intensity reduction is *"*it is possible to experience a change in sensation in your lower back … to experience more comfort … perhaps a numbness, a coolness, or perhaps a warmth … as the pain becomes less and less … Your lower back can relax and become numb in sensation, as if it were to go to sleep for a few minutes … As you become deeper relaxed, drifting into a deeper hypnotic state the area of your lower back becomes numb, an analgesic feeling ….*"* [60].

Research is supportive of the adoption of cognitive hypnotherapy as an evidence-based adjunctive treatment for pain, which is acute, chronic, and related to procedures [3]. A meta-analysis of 12 clinical studies using hypnosis for chronic pain problems [61] found that hypnosis provided a moderate treatment benefit when compared to standard care during a post-intervention phase. The meta-analysis also revealed that hypnosis showed a moderate superior effect as compared to other psychological interventions (i.e., guided imagery, progressive muscle relaxation) for a non-headache group during a post-intervention phase. Effect size analysis indicated that autogenic training had a slightly greater effect when compared to hypnosis during the post-intervention phase. In a randomized, controlled trial targeting fibromyalgia, CBT with hypnosis was more effective that CBT alone [62]. The authors concluded that hypnosis is efficacious for managing chronic pain.

Conclusion

The field of psychology has made significant contributions to understanding the multidimensional nature of chronic pain and how it affects the person who lives with pain. This chapter has reviewed the various psychological methods that have been empirically supported in the treatment of individuals with chronic pain. Health care providers are encouraged to continue to be informed about psychologically

based interventions and consider them in their treatment planning for their patients who suffer from chronic pain. Psychological management of pain is integral and complementary to the physiatrist across the rehabilitation continuum.

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Chapter 42
Medical Perspectives of Psychological Management of Pain in the Rehabilitation Patient

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Despite our impressive knowledge of the neurophysiology of pain and the multitude of options we have to treat it, chronic suffering and disability from pain are more prevalent than ever. There is growing awareness of the need to understand both the physical and psychosocial factors that deeply affect pain. Chronic pain is now understood to be a disease of the central nervous system, a problem of overactive pain perception and/or under active pain modulation. When treating the chronic pain patient, the provider must acknowledge the psychological environment that directly precipitates, magnifies, and prolongs a pain experience. In certain cases, the notion of permanently "curing" a patient's pain is an unrealistic goal for both the individual patient and the provider, a goal that may remain forever elusive. The disease of chronic pain should be considered, for some, from a more psychological perspective, which may lend insight into the root causes of a patient's recurrent suffering and disability.

The goal of psychological management is not just to treat pain symptoms by targeting nociceptors of pain, but also to delve into the individual psychology of pain. This can be accomplished by teaching rehabilitation patients self-efficacy and independence through better pain management coping strategies. This process may not only enable pain sufferers to feel more in control of their lives, but also less dependent on medications and procedures.

Pain is experienced as an emotional as well as physical experience. Psychological therapy implies treatment of underlying mood disorders, which are commonly involved in chronic pain disorders. We know through functional MRI and other brain scanning tools that the perception of pain involves up to ten brain regions at once, which transmit information back and forth. Thereby, it is imperative to understand the role and principles of psychological management to attempt to address the "brain" part of pain.

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The physiatrist, who sees a range of chronic, painful conditions, including devastating cases of musculoskeletal, brain, and spinal cord injury, already understands that the rehabilitation patient must be treated with a comprehensive multidisciplinary approach. An inpatient rehabilitation patient works with a team of providers, which may include a physical therapist, occupational therapist, speech therapist, social worker, and medical specialist. The job of the physiatrist is to oversee this team, with an ultimate goal of helping the patient to achieve both short- and long-term functional goals to maintain independence. A chronic pain patient should be addressed with a similar multidisciplinary team-based treatment paradigm. This team may involve the pain management specialist, medical provider, physical therapist, social worker, and, ideally, the pain psychologist.

There has been extensive research and interest in the field of psychological pain management, and progress has been made in understanding what works and what doesn't to improve pain and mood. Before a discourse on the most well-known form of psychological treatment, **cognitive behavioral therapy**, or CBT, an historical background, is warranted. Beginning in the 1960s, Wilbert Fordyce pioneered the concept of pain, moving its management domain from a purely biomedical model to a biopsychosocial model. The biopsychosocial model involves operant conditioning, which involves an understanding that behavior is always affected by the environment in which it exists. That is, there is a reciprocal relationship between pain behaviors (i.e., hobbling, grimacing, groaning, contorting posture, activity avoidance) and the responses they elicit, the latter of which can either reinforce or blunt future behaviors. The result of this model was to draw the treatment focus away from the experience of pain sensation and instead towards achieving life goals and functional independence. In fact, Fordyce proposed that we systematically ignore pain behaviors and instead encourage well behaviors, such as activity tolerance and graded exercise.

In the CBT model, the provider must understand the crucial role he or she plays in helping to formulate a patient's conceptions about pain. Christopher Eccleston, a prolific writer in the field of psychological approaches to pain management, stated, "Beliefs about the cause, meaning, and consequence of pain are often at stake in any consultation". He enforced the notion that the treating physician is a powerful cocreator of a patient's beliefs about pain. How the physician listens, empathizes, and reacts to a patient in pain can alternatively negate or reinforce a patient's own behavior regarding pain. For instance, a patient who reports 10/10 pain intensity on the numeric rating scale (NRS) and displays dramatic pain behavior at a medical clinic is often treated with more potent drugs, sent for more tests at an urgent pace, and offered invasive treatments, including surgery, regardless of the underlying cause of pain. Such a response may validate a patient's belief that his or her illness is overly dire to deserving of so much attention. This perception persists even if the working diagnosis is common and relatively benign. Similarly, family members of patients who display severe pain behaviors feel obliged to express sympathy, to excuse their loved ones from household responsibilities, and to encourage passivity or helplessness. Secondary gain isn't necessarily the prime motivator of the sufferer, who may only seek empathy, understanding, and pain relief. However, overattention

to chronic somatic pain symptoms without acknowledgement of social context can negatively reinforce pain behaviors, inactivity, and attention to nociceptive stimuli.

In cognitive behavioral therapy, there is an optimistic notion that people can learn more adaptive ways of thinking, feeling, and reacting to pain. Pain patients can become active collaborators in changing maladaptive beliefs and can thereby become more present, focused, active, and efficient managers of their own symptoms. CBT therapists are educators and coaches. Spouses and loved-ones can also become involved in the therapy, and can learn to react to the pain patient's pain in ways that support function and coping, rather than passivity and helplessness. In the following paragraphs, particular psychological strategies are discussed.

In 1969, Neal Miller demonstrated that through **biofeedback**, it was possible to teach people to gain control over their autonomic peripheral nervous system and stress hormones, both of which may play a role in maintenance of pain and pain-related anxiety**.** Biofeedback is a useful psychological strategy, which is often used in combination with other therapies. It involves controlling pain through monitoring a patient's peripheral physiological responses, including respiratory rate, breath quality, heart rate, blood pressure, skin temperature, and muscle tension. With biofeedback, the patient learns and practices self-regulation of these physiological variables. Neurophysiologist, Christopher deCharms, studied headache using EMG feedback to help patients decrease tension in their frontalis muscles and to thereby alleviate tension-type headache pain. In a contemporary example of biofeedback, functional MRI studies designed by Sean Mackey and deCharms have shown that patients can gain voluntary control over the activation of the rostral anterior cingulate cortex (involved in pain perception and regulation). Biofeedback can enhance the relaxation response and can also diminish muscle tension, both of which are both helpful in pain treatment.

Relaxation therapy is a psychological coping strategy that generally involves muscle relaxation and controlled breathing. There are a plethora of relaxation techniques, which involve various activities and senses, including meditation, aerobic exercise, imagery, sound therapy, water therapy, engagement in pleasurable activities, massage, tai chi, and yoga. Relaxation therapy involves invoking the relaxation response, which decreases stress hormones, improves brain function, and distracts attention away from pain. Because there is no one proven superior relaxation strategy, making use of one or many of the senses while individualizing treatment is most useful.

Hypnosis is another psychological tool that can be learned and applied to some pain patients. Although studies suffer from low enrollment and poor long-term follow-up, this strategy has been shown to be effective in small studies when compared to physical therapy and education alone. In hypnosis, there is a direct suggestion of anesthesia, called "glove anesthesia," which can lead to displacement of pain through physical dissociation. Hypnosis sessions usually run about 30 min, and involve a trained hypnotist who induces an altered state of consciousness in the patient. The patient is alert and awake, but distanced from the outer world and focused on inner thoughts and emotions through the therapist's suggestions and

guided imagery. Hypnosis has been shown to help with relaxation, sleep, and quality of life. Instruction in self-hypnosis and home practice is essential.

Mindfulness-based stress reduction, or **MBSR**, popularized by Jon Kabat-Zinn in 1979 and derived from Buddhist teachings, is a secular mind–body strategy involving the theoretical constructs of non-judgement, patience, the beginner's mind, trust, non-striving, acceptance, letting go, and being in the moment. The goal is to uncouple the physical sensing of pain from the emotional suffering it causes. One practices to become desensitized to pain through acceptance of pain as a purely physical state. The practitioner of mindfulness therapy learns to regulate one's emotions and reactions to pain. Instead of cognitively reconstructing "what" one thinks about pain, as in CBT strategies, the focus is on "how" one thinks about pain.

Cognitive coping models of psychological therapy involve teaching patients to become aware of their maladaptive thoughts and behaviors in relation to their pain. Cognitive models were formally developed in the 1970s–1980s, and advanced from the purely behavioral strategies used previously, including relaxation therapy and biofeedback, into a broader package; thus, cognitive behavioral therapy, or CBT, was born. Cognitive behavioral therapy involves a combination of stress management, problem-solving, goal setting, activity pacing, and self-efficacy techniques. There is an understanding that, similar to other chronic medical conditions including diabetes and hypertension, patients must learn to manage symptoms over extended periods of time.

The goal of CBT is *not* to find a "better diagnosis" or "miraculous cure" for pain, which often becomes a futile and self-defeating process, but rather to teach the patient better self-management skills through an understanding that cognitive perceptions and emotions directly affect the pain experience. Hopefully, this will also uncover the very real and difficult underlying psychological and/or social problems involved in chronic pain, which include a patient's access to social support, mood counselors, and other resources. The correlation between mood disorders and refractory somatic presentations is well documented and studied, but unfortunately mood disorders are still undertreated. This may be secondary to underreporting from social stigma regarding mental illnesses, lack of patient trust, or presence of both medical and psychological conditions, which often neglects the psychological over the medical.

The psychological approach, like any treatment approach, has its pros and cons. It is by no means a simple "fix it" approach. Rather, it takes time, effort, practice, and patient compliance to be successful. The analogy can be made to physical therapy, which is commonly a mainstay in the pain rehabilitation treatment program. Behavioral and psychological approaches may improve a patients' compliance to and treatment responses from a pain rehabilitative pain program.

The evidence is stronger for CBT over other purely behavioral strategies. In a Cochrane Review of 42 randomized control trials involving 4788 participants, CBT was effective in decreasing short-term disability and mood, which persisted at 6-months follow-up [11]. It was also helpful in diminishing negative thoughts about future pain (catastrophizing). Review articles and meta-analyses agree that outstanding questions still need to be better understood, including the timing, frequency,

and specific components of optimal treatments as well as the specific characteristics of patients who obtain the greatest benefit from treatment.

In Dennis Turk's text on the "Cognitive-Behavioral Approach to Pain Management," the specific details of the psychological or "talk" approach to pain therapy and the underlying rationales behind each are outlined.

> The cognitive behavioral approach to treatment and rehabilitation are concerned with both helping patients and residual pain after treatment, presuming the physical pathological process has been assessed, understood, and resolved, in so far as known available treatments have been offered and or already been applied.

Turk gives a step-by-step approach to the process of patient assessment, reconceptualization, coping skills training, and practice implementation involved in the cognitive behavioral therapy approach to pain.

The first task of the cognitive behavioral psychologist is to assess how the patient feels regarding his or her pain. The provider starts by listening to the patient and learning what the patient's own ideas might be about the cause of suffering and disability. Patients often have negative beliefs and expectations about their own abilities to cope with pain. They may have exaggerated or ill-perceived notions about the cause, cure, and prognosis of their pain. Such notions include: (a) pain always implies tissue injury, (b) recommended drugs/interventional therapies are "only going mask the pain" temporarily, and (c) pain "will never get better."

The provider tries to identify incorrect notions about pain and provide new insights into a patient's maladaptive pain behaviors. Habitual and over-rehearsed thoughts can lead to permanently negative beliefs about one's condition. The idea of catastrophizing comes into play, which is to say, one believes and focuses on the worst possible outcome. For example, when a patient is diagnosed with a "degenerative" or "arthritic" spine or rheumatological condition, which is most often attributed to the aging process, the patient prone to catastrophizing patient may conclude that he or she is "falling apart," or that the pain will inevitably get worse with time. Catastrophizing has been the subject of much research. It directly affects treatment outcomes, increases pain severity, and correlates directly with depression and disability. Furthermore, it may result in an increased attention to pain, which has been demonstrated by increased fMRI activity in the anterior cingulate cortex and insular cortex. It is unclear whether catastrophizing is associated with an inherent personality trait or not, but it is clearly modifiable with CBT. Similar maladaptive concepts include overgeneralizing, all-or-none attitudes, selective attention to negative outcomes, and mind reading.

Initial patient assessment should include a detailed patient history based on surveys of mood and function, interviews with patients and family members, and pain diaries. Then, the provider and patient must begin the long work of reappraisal of pain experiences, cognitive restructuring of maladaptive thoughts, and development of new coping skills and more adaptive behaviors. The main goal of this process is to teach the patient to play an active role in the healing process. The patient should learn to maintain control over pain symptoms and treatment responses, and not to surrender to being a helpless, passive recipient of medical interventions.

Common psychological tools used for skills acquisition in the cognitive behavioral therapy world include:

- Distraction/attention diversion: Decreases pain perception and stress arousal by diverting attention to other sensory information. Creative use of all the senses is helpful in achieving this, as is reengagement in activities once thought to be pleasurable.
- Assertiveness/Communication training: Helps patients to confront social problems, especially useful in patients who use pain to avoid stressful social situations or interpersonal problems.
- Muscle relaxation and controlled breathing: Includes relaxation strategies to control stress and pain through positive mind–body concepts. Meditation and yoga have been used in this setting.
- Exposure to Feared Activities: Employs systematic desensitization by gradual, progressive exposures to a feared activity or related environmental factor. There is growing evidence that exposure-based, counterconditioning treatments focused on fear of physical activity are effective.
- Graded Exercise/Activity Pacing: Works by contradicting the sedentary behaviors of many chronic pain patients, who often fall into a vicious cycle of disuse atrophy, deconditioning, and subsequent increased vulnerability to pain and disability. Exercise activates the endogenous opioid system, which is healthier and safer than depending on pharmaceutical opioids. Exercise can bring a sense of control back to the patient who feels helpless, and can also decrease pain-avoidant behavior. Patients must learn to incorporate an appropriate and individualized exercise regimen, to plan and review individually determined and realistic exercise goals, and to be able to deal with setbacks. Exercise can always be modified, but the patient should not give up simply because of a history of bad experiences or because new pain may arise from exercise, especially initially.

CBT is the most common and widely accepted form of psychological therapy and has the greatest empirical evidence compared to other behavioral therapies. The 2009 Cochrane Review of 40 studies comparing CBT to usual care found small but positive effects on pain, disability, and mood. Future steps should include determination of which patients respond best to this kind of therapy, and when and how to deliver it in a feasible, accessible, and reliable manner.

There is a need for more trained pain counselors and resources for patients, including outreach programs for chronic pain, substance abuse resources, support groups, and community-based programs. The idea of indirect or remote delivery is controversial among some experienced pain psychologists, who argue that the experience of personal contact and developing a relationship between psychologist and patient is invaluable. However, the development of web-based/electronic psychological treatment tools can help expose the larger community to CBT. One Cochrane review assessing internet delivery of psychological treatments determined that pain, depression, and disability were decreased in multiple chronic pain conditions, but the effect size was modest.

Psychological counseling and management for pain relies on patient education. Education is not only the responsibility of the trained psychologist, but every physician, therapist, and allied health practitioner treating pain on the multidisciplinary team. In the setting of chronic pain, there is a definite place for psychological assessment, treatment, and management. Although this may not cure chronic pain, it can help to modify the affect that pain has on the individual. This may give a sense of control back to the patient, may improve the patient's ability to self-manage pain, and may help the patient in pain to cope better.

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Part IX
Multi Modal Approach: Complimentary and Alternative Medicine

Chapter 43
Osteopathic Medicine for the Treatment of Pain in the Rehabilitation Patient

Athina Giovanis and Claudia Wheeler

Introduction

Osteopathic medicine is a distinctive form of western medical care, which focuses on the whole person, and is founded on the philosophy that all body systems are interrelated and dependent upon one another for good health. Osteopathic physicians are taught to apply the tenets of osteopathic medicine to the prevention, diagnosis, and treatment of disease, including pain. Osteopathic physicians are fully trained and licensed to prescribe medicine. Furthermore, DOs are credentialed to practice in all medical and surgical specialties and subspecialties in the United States through completion of either allopathic or osteopathic training programs. They may also use OMM techniques to evaluate and diagnose pain and injury, to relieve pain, to restore range of motion, and to enhance the body's capacity to heal.

Brief History

Osteopathic medicine was developed on the Missouri frontier in 1874 by Andrew Taylor Still, MD. Dr. Still was an army surgeon and an abolitionist during the Civil War, who became discouraged with the ineffectiveness of medicine at the time.

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In response, he founded a new approach to medicine, with a focus on anatomy, finding health, and looking at the body as a whole unit.

Today, while attending their own medical schools, Doctors of Osteopathic Medicine (DOs) have the same academic requirements as their allopathic colleagues and receive additional hours of study in the musculoskeletal system. Currently, DOs provide comprehensive medical care to patients in all 50 states and the District of Columbia, and have unlimited practice rights in more than 65 countries. There are more than 74,000 DOs practicing in the United States in a wide range of medical specialties including surgery, anesthesiology, physical medicine and rehabilitation, neuromusculoskeletal medicine, sports medicine, geriatrics, and emergency medicine. Almost 25% of today's medical students are enrolled in osteopathic medical colleges. The American Association of Colleges of Osteopathic Medicine (AACOM) represents the 31 accredited colleges of osteopathic medicine in 45 locations in the United States.

As noted above, Osteopathic medical schools have a strong emphasis on the musculoskeletal system and all students learn osteopathic evaluation and treatment. In addition to common recommendations for pain management, such as imaging orders, prescribing medications and exercise, or administering various injections, osteopathic physicians are also trained to use osteopathic manipulation techniques for the treatment of somatic dysfunction. Some osteopathic physicians incorporate osteopathic techniques into their medical practice, while others may be more specialized in these techniques and their application. Osteopathic physicians that tend to incorporate these techniques commonly are in various specialties like Neuromusculoskeletal Medicine/Osteopathic Manipulative Medicine, Physical Medicine and Rehabilitation, Family Practice, and Internal Medicine.

Basic Principles

The Basic Principles of Osteopathic Medicine are:

(a) The body functions as a unit, whereby the person is a unit of body, mind, and spirit. An osteopathic diagnosis will focus on the unity of the person, as opposed to breaking the body down into separate parts.
(b) The body has an inherent ability to heal itself. It is capable of self-regulation, self-healing, and health maintenance.
(c) Structure and function are inseparable, and reciprocally related. Understanding the inseparable connection of anatomy and physiology is helpful for evaluation and treatment.
(d) A rational therapeutic approach is based upon an understanding of body unity, self-regulatory mechanisms, and the interrelationship of structure and function.

These are universal osteopathic medicine principles providing a basic structure for medicine, which are helpful when treating pain. Osteopathic manipulation is the specific, hands-on treatment that applies these osteopathic principles directly, and may be used to decrease pain and to optimize a patient's function.

Pathophysiology

Osteopathic physicians identify somatic dysfunction by history and palpation. Somatic dysfunction is the impaired or altered function of related components of the body framework. The palpatory examination involves identifying areas of tissue texture change, asymmetry, restriction of range of motion, and tenderness. Acute somatic dysfunction is characterized by vasodilation, edema, tenderness, pain, and tissue contraction. Chronic somatic dysfunction is accompanied by tenderness, itching, tissue fibrosis, paresthesias, and tissue contraction. A complete osteopathic structural examination can include assessment of somatic dysfunction of up to ten body areas, including the following: head, neck, thoracic spine, lumbar spine, sacrum, pelvis, lower extremities, upper extremities, ribs, and abdomen.

Common Techniques

Indications for osteopathic manipulative treatment include identification of somatic dysfunction, resulting in some combination of restricted range of motion, asymmetry, tissue texture changes, and pain. Contraindications to osteopathic manipulative treatment depend on the type of treatment and the patient's condition; however, the patient must always consent to whichever treatment is used and in all conditions. Each type of manipulation carries its own absolute and relative contraindications. Thrust techniques have the greatest number of absolute contraindications, including: malignancy, osteoporosis, severe rheumatoid arthritis, carotid or vertebrobasilar vascular disease, fracture, history of a pathological fracture, connective tissue disease, aneurysm, and anticoagulant therapy.

There are seven care modalities of osteopathic manipulation (see Table 43.1). There are over 40 individual techniques noted in the American Association of Colleges of Osteopathic Medicine Glossary of Osteopathic Terminology. Osteopathic techniques are described as being direct or indirect approaches. Direct techniques engage the restrictive barrier. Indirect techniques move toward the direction of ease in the affected tissues. Some techniques require active participation of the patient, requiring the patient to follow specific directions. Passive techniques are performed to the patient and do not require any additional effort from the patient.

Table 43.1 The seven care modalities of osteopathic medicine

Technique	Direct or Indirect	Active or Passive
HVLA (thrust)	Direct	Passive
Muscle Energy	Direct and Indirect	Active
Soft Tissue	Direct or Indirect	Passive
Counterstrain	Indirect	Passive
Myofascial	Direct or Indirect	Passive
Lymphatic	Direct	Passive
Cranial Osteopathy	Direct or Indirect	Passive

High velocity-low amplitude (HVLA), or thrust technique, is a direct technique of mobilization with impulse. Thrust techniques comprise the majority of studies on spinal manipulative therapy (SMT) for low-back pain. Acute pain often responds well to this technique.

Muscle energy is a direct technique that involves moving the patient toward the restrictive barrier. The patient is then instructed to contract the muscle group that moves away from the barrier, while the practitioner resists the movement, performing a series of isometric contractions.

Soft tissue technique is a direct, passive technique that involves rhythmic stretching, deep pressure, and traction to mobilize fluid in the soft tissues, relax hypertonic muscles, and to mobilize the fascial layer of tissue.

Counterstrain is an indirect technique, in which the patient is passively moved away from the restrictive barrier, toward a position without pain. This technique creates a strain in the direction opposite to the reflex that is causing the symptomatic strain. It can be used in all pain conditions, including very acute pain.

Myofascial release technique can be performed in a direct or indirect fashion. In a direct technique, the myofascial barrier is engaged and the tissue is loaded with force until a change occurs. In an indirect technique, the tissues are guided in the direction of ease, until a freedom of motion occurs.

Lymphatic technique promotes circulation of lymphatic fluids, which can be helpful in the presence of infection or acute injury.

Cranial osteopathy involves assessment of the primary respiratory mechanism through the cranial sutures and at the sacrum. This technique is passive, and is performed by applying specific pressures over the sacrum and at the cranio-cervical junction in an effort to impact the flow of cerebrospinal fluid. It can be performed in a direct or indirect fashion.

Specific Applications

Acute Pain

The post-operative lower extremity joint replacement patient is in acute pain in the days to weeks following surgery. The controlled trauma of surgery results in edema, lymphatic stasis, and acute muscle spasm in the surrounding muscles. The osteopathic manipulative treatment plan would include lymphatic techniques to improve drainage of the lower extremity, by first clearing a path proximally, and then working distally to drain the affected limb. Once the lymphatic channels have been opened, pedal pumping would help to mobilize fluid from the extracellular space. Increasing the range of motion around the post-operative joint would be achieved with reducing spasm in the hypertonic muscle groups. Counterstrain technique would be an ideal choice for reducing muscular pain in this patient. These techniques can all be performed at the bed level in the acute or rehabilitation hospital setting.

Subacute Pain

The ventilator-dependent tetraplegic patient with tracheostomy and limited jaw range of motion may experience pain due to myofascial and articular dysfunction. The osteopathic manipulative treatment plan would include trigger point pressure release of spasms in the medial pterygoid muscle. Addressing temporomandibular joint dysfunction with muscle energy, soft tissue, and cranial osteopathy would improve functional jaw excursion to reduce pain and to improve ability to communicate.

Chronic Pain

The amputee with hip flexion contracture experiences iliopsoas spasm due to the prolonged period of wheelchair use prior to an amputation caused by a wound. This pain may present as back pain, limited tolerance of the prone position, and impaired ability to tolerate a prosthesis. The osteopathic manipulative treatment plan would include counterstrain technique to address the acute on chronic aspects of the related low-back pain. Muscle energy and soft tissue treatment of the hip flexor and lumbar paraspinals would help to lengthen the shorten muscles. An exercise prescription would be provided as part of the comprehensive treatment program with therapy.

Evidence

There are several pitfalls with osteopathic manipulative treatment research. Osteopathic manipulation encompasses more than just spinal manipulative therapy (SMT), however this is the topic most published. Large reviews, such as the Cochrane Systematic Reviews of SMT pool studies, include treatments performed by many types of practitioners, such as chiropractors, manual therapists, and osteopathic physicians. However, patients under the care of an osteopathic physician are often receiving more than just SMT, including exercise, self-management, nutrition, prescription medication, and soft tissue injections, as part of a comprehensive treatment program. Studies on SMT for low-back pain are at high risk for bias, lack quality data, have small sample sizes, and often include publication bias.

The RCTs do not reflect the experience of a true individualized evaluation and treatment experience with an osteopathic physician. One of the constraints of RCTs is in utilization of protocols and generic treatment plans as part of the research process. In practice, osteopathic physicians provide individualized treatment, which is based on the patient's source of somatic dysfunction, with thought given to prioritization and the interrelationship of dysfunction.

Cochrane Systematic Reviews of Spinal Manipulative Therapy (SMT)

Acute Low-back Pain

No high-quality evidence was provided for any comparison, outcome, or time interval; therefore, no strong conclusions or recommendations can be made for the use of SMT for acute low-back pain. SMT appears to be no better than other existing therapies for pain reduction and improvement in functional status. It is the review's conclusion that the decision to refer for SMT in patients with acute low-back pain should be based upon costs, patient preference, and safety of treatment options.

Chronic Low-back Pain

High-quality evidence suggests that there is no clinically relevant difference between SMT and other interventions for reducing pain and improving function in patients with chronic low-back pain. It is the review's conclusion that the decision to refer for SMT should be based upon costs, patient preference, and safety of treatment options.

The conclusion of the Cochrane Systematic Reviews of Spinal Manipulative Therapy (SMT) is that there is need for future research. Relatively few studies follow patients long enough to identify chronicity of pain. The authors point out that there are currently more than 100 RCTs of SMT for low-back pain with disappointing quality of evidence. They propose research to address the prevention of the onset of chronic low-back pain, which is disabling and expensive. This is a more clinically relevant question. SMT for chronic low-back pain should be studied for its role as an adjuvant in a multi-modal treatment plan. There is a need for cost-effectiveness studies. If SMT is equal to other presumed effective interventions for chronic low-back pain, it may be more cost-effective.

Conclusion

Osteopathic manipulative treatment is a valuable tool in the diagnosis and management of pain given its inherently holistic approach to the entire person and interrelated factors that may be contributing to the pain. Osteopathic manipulative medicine can serve as an adjuvant at any point along the continuum of care in the pain patient. The skill set of each osteopathic physician is unique and will need to be considered in the efficacy of pain treatment for the patient. More research is needed, particularly evaluating cost-effectiveness and the role of osteopathic manipulation in the prevention of the progression to chronic pain.

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Recommended Reading

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Chapter 44
Chiropractic Medicine for the Treatment of Pain in the Rehabilitation Patient

Robert D. Vining and Sean Mathers

Abbreviations

DC doctor of chiropractic
SM spinal manipulation

Introduction

Chiropractic is a growing health profession comprising approximately 70,000 licensed professionals within the United States [1]. After medical and dental physicians, chiropractic represents the third largest group of health professionals of which patients have direct access [2]. In the United States and Canada, graduates of chiropractic institutions receive a degree entitled Doctor of Chiropractic, abbreviated as DC. Seventeen accredited chiropractic educational institutions exist within the United States, with an additional 26 located in Australia, Asia, Europe, Africa, and South America [3]. Approximately 80 countries license or otherwise regulate the practice of chiropractic, a number that has steadily grown since the mid-twentieth century.

Chiropractic is a distinct healthcare profession that shares some similarities with other specialties. Because most patients can access chiropractic services without a referral, many educational and practice elements are similar to those experienced by primary care practitioners. However, more like the professions of dentistry, podiatry, and optometry, chiropractic training and practice focus primarily on a distinct area, the neuro-musculoskeletal system, with special emphasis on the spine and related conditions. Increasingly, doctors of chiropractic (DCs)

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are identified as primary (referring to: portal of entry or primary access) spine care practitioners [4–6].

Within the United States, professional privileges vary somewhat by country and by state. In most jurisdictions, the chiropractic scope of practice includes full diagnostic test ordering privileges and the same level of diagnosis, case management, and referral responsibility as other primary level providers. Prescription and surgical privileges are usually outside the scope of practice because the primary focus of the profession is non-surgical, non-pharmacological diagnosis, management, co-management, and prevention [7] of neuro-musculoskeletal conditions, especially those of the spine [5]. Treatment is primarily delivered through a variety of manually-based therapies, consistent with the Greek origin of the root word "chiro," meaning "hand."

Brief History

Spinal manipulation (SM) and other manual therapies have been a part of the healing arts for millennia, as evidenced by historical Chinese and Greek writings and those of Hippocrates. However, it was not until 1895 that the chiropractic profession and the first college (1897) were officially founded by a man named Daniel David Palmer. During the early twentieth century, chiropractic educational programs gradually matured. Entrance and program requirements became more rigorous [8] and similar to that of medicine, especially in the basic science and foundational clinical coursework. Today, individual coursework between medical and chiropractic education systems vary in a few key areas, mostly due to differences in professional focus and treatment patterns. For example, medical schools tend to dedicate more formal training time to public health topics and pharmacotherapy, while chiropractic schools devote more time to musculoskeletal diagnosis and manual therapies [9].

The medical and chiropractic professions developed a competitive and sometimes fierce adversarial relationship during the early twentieth century, likely driven by the goal of generating credibility for chiropractic and the desire to increase cultural authority for medicine [8]. Other factors that contributed to conflict between the professions included different health paradigms, a separate chiropractic educational system, exaggerated claims from both sides, and confusing terminology [8].

Historically, the chiropractic profession has also endured internal ideological struggles between vitalistic and biomedically based health paradigms. Gradually gaining predominance over time, biomedically based practitioners now represent the mainstream of the profession, likely aided by scientific research, rigorous and accredited educational programs, and a professional identity as conservative spine care specialists. However, DCs with alternative health paradigms are still a part of the profession, as evidenced by a survey of Canadian DCs reporting 19% of respondents held views other than those considered standard for biomedically based practitioners [10].

The public perception of the chiropractic profession has evolved into one of cultural legitimacy. A 2015 survey of over 5400 US adults reported more than 60% of respondents considered chiropractic care as effective for treating neck and back pain [11]. Now in the second century of existence as an organized health profession, this positive perception has probably been aided by many factors including the practitioners and patients who account for more than 190,000,000 visits per year in the United States alone [1].

The majority of chiropractic practitioners function within single or multiple provider private practices. Nearing the twenty-first century, DCs began integrating into multidisciplinary settings in substantial numbers. Currently, many hospital and corporate-based healthcare systems within the United States offer chiropractic care. U.S. military health treatment facilities [12], US Olympic training centers [13], and Veterans Affairs hospitals and outpatient clinics also provide chiropractic care to their respective constituencies [14, 15]. Additional professional training is available for DCs in many clinical areas such as nutrition, radiology, and sports injuries. Advanced training in rehabilitation is also available to DCs in the form of graduate degree programs, continuing education courses, and certificate level training. Residency programs exist within the United States Veterans Health Administration. Other residency programs are available at chiropractic educational institutions in specialty areas such as radiology and rehabilitation.

Perhaps the most distinctive aspect of the modern practice of chiropractic is the unique skill set and corresponding care delivered by providers focused on the structure and function of the musculoskeletal system, especially of the spine, and its inter-relationships with other systems. Care is delivered using multiple therapeutic techniques, commonly with one of many widely adaptable spinal manipulative procedures.

Pathophysiology

The founders of the chiropractic profession proposed a pathophysiological model of spinal dysfunction consisting of vertebral malposition causing direct or indirect pressure on spinal nerve roots leading to sensory, motor, and/or autonomic dysregulation and pain. The term "vertebral subluxation," signifying minor malposition leading to a wide range of spinal and extraspinal pathology became part of the chiropractic lexicon. However, the chiropractic use of the word "subluxation" was adapted from a term already in use, defined as the loss of joint integrity, but short of dislocation or "luxation."

Simultaneously, the osteopathic profession developed the term "somatic dysfunction" signifying impaired function of joint, myofascial tissues, nerve, or vascular structures resulting in compromised function. This broad definition is congruent with the term "vertebral subluxation complex," which incorporates or acknowledges myofascial, nerve, vascular, and joint dysfunction as clinically important.

The use of multiple vague and overlapping terms with distinct professional definitions fostered confusion among members of different health disciplines. Other terms signifying spinal pathophysiology have subsequently been introduced, such as "segmental dysfunction," which also lack clarity. The search for a single term to define the multidimensional pathophysiology underlying spinal-related dysfunction may not be successful. The complex functional inter-relationships existing between the spine and other systems (muscular, nervous, and vascular) suggest that a single comprehensive term must encompass a wide array of pathology affecting each system component. Such a term would likely be vague and confusing.

The vertebral malposition model leading to nerve root compression was eventually shown to be a physiologically errant concept in most circumstances and by the mid-twentieth century, other models developed to explain the physiology behind clinical effects observed following SM [16].

Pain Reduction and Spinal Manipulation

Short-term reduced pain sensitivity due to altered neural processing within the brain and spinal cord following SM has been demonstrated in numerous studies [17–19]. Research is ongoing to further elucidate the specific central nervous system mechanisms responsible for this phenomenon. Reduced pain sensitivity due to central nervous system mechanisms in the short term suggests that manual therapies including SM might be effective for some individuals experiencing chronic neuropathic pain. Long-term pain reduction mechanisms are less clear and more research is needed to better identify patients most likely to respond to treatment.

Motor Programming and Spinal Manipulation

Clinical research has demonstrated increased muscular strength following SM due to motor neuron facilitation or disinhibition [20, 21]. Thrust manipulation also reduces paraspinal muscular tone, suggesting one mechanism whereby patients with abnormally hypertonic musculature (those suffering from muscular strain, inflammation, spasm) may achieve symptom reduction [22, 23]. Trunk muscle thickness (multifidus, and transversus abdominus) has also been shown to increase following SM. Changes in the size of trunk muscles following SM have been shown to be predictive of disability improvement.

The exact mechanisms responsible for muscular changes following SM are complex, involving interactions between multiple systems and are not yet fully understood [16, 24]. What is known of spinal manipulative mechanisms affecting muscular function has largely been determined from the results of studies conducted with laboratory animals and asymptomatic humans. Researchers continue to investigate the intricate neurological mechanisms influenced by SM to further elucidate their individual and collective therapeutic contributions.

Joint Function and Spinal Manipulation

SM disrupts adhesions formed from joint disuse, injury, or degenerative disease [25]. Through this mechanism, SM is thought to increase spinal joint mobility; thereby, facilitating improved range of motion, the performance of rehabilitative exercise, and motor retraining, which is aimed at reducing aberrant spinal joint loading. Improving joint mobility also increases the potential for proprioceptive sensory input, which is thought to contribute to improved motor programming and to inhibit pain through gating mechanisms within spinal and supraspinal circuits [26].

Basic Clinical Principles

The Diagnostic Process

The diagnostic process for musculoskeletal conditions including the spine is complex [27] and guided by answering three basic questions. Answers to these questions serve as foundational information that informs management decisions. The three basic questions are: (1) "Are the symptoms with which the patient is presenting reflective of a visceral disorder or a serious or potentially life-threatening disease?", (2) "From where is the patient's pain arising?", and (3) "What has gone wrong with this person as a whole that would cause the pain experience to develop and to persist?" [28–30]. These three diagnostic questions include the two components of traditional diagnosis, screening for serious or concealed disorders, and a condition-specific label. The third component includes evaluation of factors that lead to or contribute to the continuation of the problem, consistent with a biopsychosocial approach.

Many factors can contribute to perpetuating symptoms. Factors thought to be important for patients with spine-related pain include: (1) impaired motor control or movement patterns, contributing to symptoms; (2) neuroplastic changes leading to central pain hypersensitivity; (3) oculomotor dysfunction for patients suffering from cervical injury; and (4) psychosocial factors such as fear, passive coping, depression, and catastrophizing [29]. Identifying factors contributing to pain perception or symptom perpetuation facilitates clinical decision-making.

Chiropractic patient evaluation typically begins with an interview focused on obtaining a general health and problem-oriented history. Examination often consists of palpation, directional movement preference, orthopedic, and neurological testing, gait evaluation, and spinal mechanics analysis. Each evaluation procedure is designed to help the DC better understand how symptoms behave, to answer each of the three basic diagnostic questions so as to inform management decisions, and to help develop an appropriate management plan.

Table 44.1 Commonly employed chiropractic care goals [31, 63]

Acute and subacute conditions	Chronic conditions
Reduce/eliminate symptoms	Minimize lost work time
Restore to prior functional status	Support current functional levels
Prevent chronicity	Pain relief or control, minimize/prevent disability
Prevent disability	Minimize/prevent exacerbation frequency and severity
Educate to prevent recurrence	Enhance patient satisfaction with care and self-efficacy
Promote self-efficacy	Reduce or minimize reliance on medication

Care Goals

Some of the overarching goals of chiropractic care are to improve functional capacity, educate patients regarding the importance of actively participating in theirhealth recovery, and reduce or eliminate the need for treatment [31]. Specific goals commonly employed for chiropractic patients with acute/subacute or chronic pain conditions are listed in Table 44.1.

Chiropractic care often involves several treatments, which are scheduled over sequential visits. In general, recommendations suggest that patients with initial or recurrent acute and subacute conditions should generally be treated up to three times weekly over a period of 2–4 weeks before re-evaluation [31]. Patients with chronic conditions are usually treated one to three times per week for 2–4 weeks prior to re-evaluation [31]. Patients requiring continued care following an initial course are usually treated at a slightly reduced frequency, for periods of up to 12 weeks depending on individual factors. Treatment frequencies usually reduce as patients respond and either approach or achieve care goals. An evidence-based management guideline for chiropractic care of patients with chronic low back pain is presented in Fig. 44.1 to demonstrate the complex decision-making that is involved in the chiropractic management of individuals suffering from chronic spinal-related pain.

Common Treatment Techniques

Spinal and Other Joint Manipulation

SM is the most easily recognizable therapy associated with chiropractic care. SM is often employed because of the wide range of available techniques and delivery modes, and because SM has several known or suspected physiological mechanisms, making, it broadly applicable as a primary or supportive treatment procedure.

Spinal and extremity joint manipulations can be performed with patients in the prone, side-lying, supine, seated, or standing positions. A wide variety of manipulative

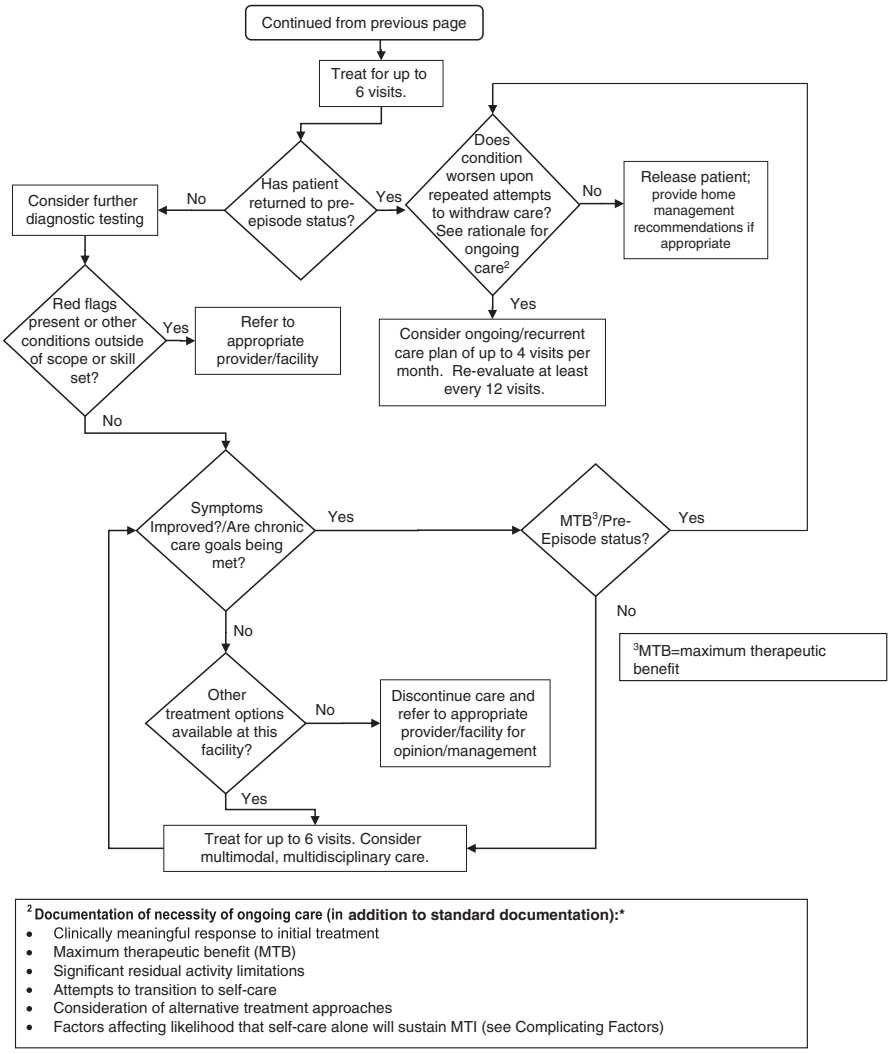
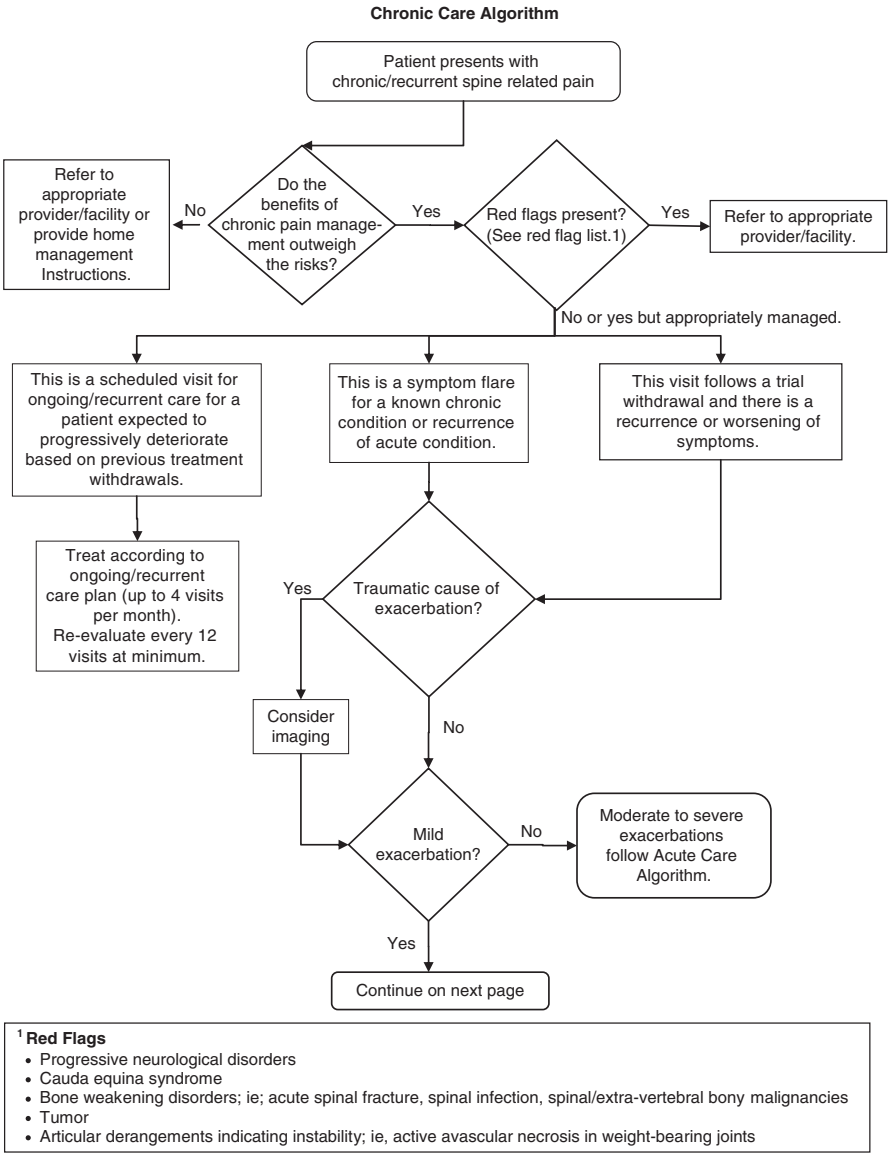


Fig. 44.1 Chiropractic management algorithm demonstrating complex decision-making involved in chiropractic management of patients with chronic spinal conditions. This figure has been reprinted with permission from Globe G, Farabaugh RJ, Hawk C, Morris CE, Baker G, Whalen WM, Kaeser M, Dehen M, Augat T. Clinical Practice Guideline: Chiropractic Care for Low Back Pain. *J Manipulative Physiol Ther* 2016. doi.org/10.1016/j.jmpt.2015.10.006



techniques are available. Those chosen for treatment are dependent on practitioner training and skills, diagnosis, co-morbid conditions, care goals, and patient preferences. Manipulative techniques are broadly classified as either thrust or non-thrust [32], with many subcategories existing under each label. Most manipulative techniques can be delivered in a wide range of force applications, from robust to gentle, depending on patient tolerance, goals of care, and other factors. Though there are numerous named chiropractic techniques, the most common SM thrust intervention used by DCs is called “Diversified” technique. Diversified technique is reported to

Table 44.2 Examples of myofascial and neurologically oriented therapeutic techniques used by doctors of chiropractic

Techniques	Application	Purpose/possible mechanism(s)	Potential indications
Manual friction massage	Manually applied friction technique	• Disrupt adhesions that restrict or cause painful range of motion • Increase short-term blood flow • Stimulate sensory nerves, contributing to pain reduction through pain-gating mechanisms and altered muscle tone • Facilitate lymphatic circulation	• Reduced joint mobility • Painful range of motion • Myofascial adhesions
Manual friction techniques applied to soft tissues, typically with stainless steel tools (e.g., Graston technique®, FAKTR®)	Manually applied friction technique with specially shaped tools and emollient to prevent or reduce skin irritation		
Active Release Technique® (ART®)	Manually applied pressure to myofascial tissues usually with active or passive stretching	• Disrupt adhesions that restrict or cause painful range of motion • Improve range of motion • Increase pain-free range of motion • Stretch contracted tissue(s) • Facilitate lymphatic circulation	
Myofascial release	Manually applied pressure to myofascial structures often with joint movement		
Neural mobilization	Slowly guided passive or active movement of the spine, head, neck, or limbs causing repetitive nerve stretching (or flossing) through constricted spinal or peripheral regions	• Reduce aberrant nerve tension, compression, adhesions • Facilitate blood and lymphatic circulation for neural tissues	• Spinal and peripheral nerve entrapment syndromes • Spinal and peripheral mechanical nerve compression syndromes
Proprioceptive neuromuscular facilitation (PNF)	A wide array of rehabilitative techniques involving stretching, strengthening, mobility, and motor control training	• Influence neurological signaling to alter muscle activity, coordination, contraction patterns, range of motion, joint stability and overall function	• Joint instability • Motor control compromise • Motor weakness • Injury prevention during motor tasks • Gait training

(continued)

Table 44.2 (continued)

Techniques	Application	Purpose/possible mechanism(s)	Potential indications
Trigger point therapy, Nimmo® Technique, Receptor Tonus Technique, Ischemic compression	Manually applied pressure (or with special hand-held tools) to localized areas of muscle contraction (trigger points)	• Disrupt self-perpetuating localized muscle contraction • Stimulate increased reflex local muscle circulation • Facilitate disbursement of inflammatory chemicals from muscle tissue	• Referred pain from muscles • Confirmed active trigger points

be used at least some of the time by over 95 % of DCs [33]. A common non-thrust intervention used by DCs is called Flexion-Distraction, or Cox technique [34–36]. Most techniques are manually applied, sometimes with the use of specially designed treatment tables.

Myofascial Therapies

Fascia is composed of connective tissues containing important sensory components. The tissues comprising fascia surround, connect, and infiltrate organs, muscles, bones, and nerves throughout the body [37–39]. Fascial pathology can affect the function of most body tissues, and thus, it is an important tissue/organ system considered by DCs when treating patients with musculoskeletal conditions.

Myofascial therapies represent a broad range of treatment techniques used by practitioners within the physical therapy, occupational therapy, and other healthcare professions including chiropractic. Primarily targeting fascial dysfunction or pathology, myofascial therapies are applied manually, sometimes with the aid of specialized tools and active contraction or with stretching on the part of the patient. Common application methods, mechanisms, and indications for using myofascial therapies and other manual therapy techniques used by DCs are listed in Table 44.2.

Therapeutic Exercise

Therapeutic exercise is not novel to rehabilitation settings. It is used by several professional groups including DCs. Exercises are prescribed by more than 95% of DCs, often designed to improve spinal stability and function [40, 41]. However, many other exercises are used depending on the condition and other individual factors. DCs commonly incorporate team-based care plans that encourage patients to

partake in symptom management and recovery activities using therapeutic exercise [30]. Exercises may be employed to reduce pain, increase available motion, increase strength, and to improve coordination in the performance of athletic movements or daily living activities. The performance of therapeutic exercise by patients may also aid recovery by facilitating personal involvement and commitment to recovery, and by enhancing self-efficacy [42].

Specific Applications

General Protocols

Chiropractic rehabilitation protocols for patients with spinal conditions follow a general model that typically begins with passive modalities, gradually transitioning to more active therapies, unassisted exercise, and self-management/independence [43]. Care for patients with acute spinal conditions often incorporates thrust or non-thrust SM, traction, and directional preference exercises. Active therapies including basic exercises designed to promote self-efficacy and to reduce symptoms may be employed immediately, or delayed until the patient can tolerate them. Exercises such as directional preference movements, consistent with McKenzie diagnosis and treatment principles, are often employed for acute spinal conditions to facilitate symptom reduction and promote movement [44]. As symptoms improve, care plans tend to focus more on improving function for daily living activities or sport-specific tasks, often by progressively implementing additional or advanced exercises.

Treatment for patients with subacute or chronic conditions will often consist of SM and active exercises oriented toward joint mobilization and stabilization as well as strengthening symptomatic or related areas. Similar to acute care principles, treatment focus usually transitions from symptom management to improving function for daily living activities as patients improve. Monitoring treatment progression and effectiveness is accomplished through the use of established outcome measures such as the Oswestry Disability Index [45]. Those patients who fail to meet rehabilitative goals, or show substantive change on outcome measures, may require additional diagnostic testing, an altered treatment plan, and/or referral to another healthcare provider.

Patient education is an integral part of chiropractic care. Education carries the potential to influence and to address psychosocial factors contributing to health conditions [46]. Regardless of the disease, DCs are trained to help patients understand their condition and to develop strategies that enable patients to manage or to resolve it, including recognizing when referral to other providers with expertise in cognitive behavioral therapy and mental health is appropriate [6]. Examples of chiropractic rehabilitation goals and treatment strategies are listed in Table 44.3.

DCs use the broad array of treatments to treat patients with a wide range of neuro-musculoskeletal conditions. Individualized care plans are necessitated by

Table 44.3 Chiropractic rehabilitation goals and typical intervention strategies used [6, 43, 79]

Goals	Intervention strategies
Improve locomotor system function	• Spinal manipulation • Joint/muscle retraining to reverse/reduce antalgic postures/pain guarding movements • Other passive modalities (e.g., ice, heat, massage) • Education to promote self-efficacy and prevent/reduce fear-avoidance behaviors
Improve automatic stabilization responses	• Spinal manipulation • Training proper movement patterns and postures through proprioceptive neuromuscular facilitation exercise • Sensorimotor training on stable, then progressing to labile, surfaces • Education to promote self-efficacy and prevent/reduce fear-avoidance behaviors
Reverse, prevent central sensitization	• Therapies designed to reduce pain and increase physiological mechanoreceptor signaling • Education on chronic pain mechanisms • Graded exercise • Myofascial therapies • Spinal manipulation
Improve strength in key muscles and in overall physical fitness	• Proprioceptive neuromuscular facilitation exercise • Work/sport specific physical fitness exercise • Isotonic, isometric, aerobic, and graded activity training • Encouraging quick return to normal or near-normal work
Prevent or reverse ineffective illness behavior	• Education to prevent/reduce fear-avoidance behaviors, passive coping, catastrophization, and promote self-efficacy • Encouraging quick return to normal or near-normal work • Graded exercise • Refer for cognitive behavioral therapy or other specialty

unique patient presentations, even for those with similar conditions. Therefore, few detailed protocols for specific diagnoses are described in the literature. Most commonly, rehabilitation principles, goals, and strategies are applied based on individual elements.

For example, shoulder pain is a common disorder following stroke [47] and spinal cord injury. Contributing factors include poor seated posture, spasticity, and upper extremity overuse [48]. Patients recovering from spinal cord injury and stroke may benefit from multidisciplinary rehabilitation, which includes chiropractic care. Treatment could include manual shoulder manipulation to disrupt adhesions, reduce pain, and to increase mobility. Other treatments that may be employed include strength training for functioning muscles, myofascial therapies to improve mobility and to reduce pain, and graded exercise to improve posture and the coordination of the remaining functioning muscles. Selective SM may also be employed to help reduce pain or to aid mobility in appropriate cases [49]. Examples of condition-specific chiropractic care protocols that have been described in the clinical literature are displayed in Table 44.4.

Table 44.4 Examples of chiropractic clinical protocols for specific spinal conditions [34, 35, 80, 81]

Condition	Spinal manipulation (SM)	Passive therapies	Active therapies	Education/home exercise and ADL advice	Treatment frequency
Lumbar spinal stenosis/ neurogenic claudication	Non-thrust and/or thrust procedures as tolerated	• Passive neural mobilization • Muscle stretching	• Active neural and lumbar mobilization exercises • Unassisted exercise	• Education about condition • Home exercise ADL advice/self-management strategies	• 2–3×/week for up to 6 weeks • Re-evaluate • Reduce frequency to 1–2×/week • Reduce frequency to 0 or to treat exacerbation
Post spinal surgery/injection	Following surgical clearance, performed as indicated and/or tolerated	• Myofascial therapies • Electrical modalities, heat, and ice	When tolerated: • Assisted exercise • Activity and/or exercise to strengthen weakened extremity and trunk muscles	• Education about condition • When tolerated: • Basic home exercise to promote self-efficacy • ADL advice/ self-management strategies	• 2–3×/week for up to 3 weeks • Re-evaluate • Frequency varies by co-morbidity, severity, and response to care
Radiculopathy (cervical or lumbar)	Subacute or chronic stage, thrust or non-thrust procedures as tolerated	• Passive neural mobilization	When tolerated: • Active neural mobilization • Education and performance of directional preference exercise(s)	• Education about condition • When tolerated: • Basic home exercise to promote self-efficacy • ADL advice/ self-management strategies	• 2–3×/week for up to 3 weeks • Re-evaluate • Reduce frequency to 1–2×/week • Reduce frequency to 0 or to treat exacerbation

Clinical Case Examples

An elderly male experiences episodic sacroiliac joint area pain. Gradually worsening symptoms characterize the current episode, which has lasted approximately 6 weeks. The case is complicated by a history of cerebrovascular accident (post 6 years), left-sided hemiparesis, and anticoagulant use. Sacroiliac joint injection has been considered, but the treating physician wishes to avoid this procedure because it carries an increased risk due to the current medication regimen. A more conservative treatment with lower risk is sought.	*A female in her 30s experiences chronic, frequent, and severe headaches originating in the suboccipital region and radiating forward to both orbits. Topomax®, an anti-epileptic drug used to treat migraine headaches, is the primary pharmaceutical management strategy. Topomax® use reduces symptom severity and headache frequency to approximately 1–2 per week. The patient is seeking to become pregnant and wishes to discontinue the medication regimen due to the increased risk of birth defects associated with this medication.*
Chiropractic evaluation of this type of case will typically begin with a clinical interview and evaluation leading to a working diagnosis. Using validated diagnostic procedures, the working diagnosis of sacroiliac joint pain or other diagnosis can be confirmed or otherwise evaluated [27, 50]. *Following the initial evaluation, the DC can communicate to the referring physician the working diagnosis and proposed treatment plan, including information that anticoagulant use is not a contraindication to spinal/sacroiliac manipulation.*	*Chiropractic evaluation of this type of case will typically begin with a clinical interview and examination that first seeks to reveal evidence for pathology requiring referral or other emergent conditions. If no indication for obvious pathology is present, evaluation will include examination of the spine and posture, to determine if the headaches have a cervicogenic component that can be treated with conservative chiropractic methods.*
Clinical evaluation will note the hemiparesis and unilateral steppage gait that typically accompanies it. Evaluation will include the process of ruling in or ruling out a recent cause of the steppage gait. Other movement patterns and their causes will also be assessed. Compensatory movements may be the inevitable result of hemiparesis. They can also represent movement adaptation/maladaptation to low back pain, or instability and/or fear of falling.	*When cervicogenic headache is present, postural faults are common. Abnormal postures often include a forward head position, rounding/protraction of the shoulders bilaterally, loss of lumbar lordosis, and posterior pelvic tilt. Muscle trigger points are typically present in the suboccipital region and upper trapezius musculature. Patients with cervicogenic headache may also demonstrate reduced cervical muscle endurance, assessed with tests such as the chin tuck neck flexion test* [51], *reduced lumbar stability, and a relatively high Neck Disability Index score.*
Assuming diagnostic confirmation of sacroiliac joint pain and long-standing hemiparesis, the patient will likely be treated with spinal manipulation oriented toward the lumbar spine and sacroiliac joints. Spinal manipulation will most likely be employed to reduce pain, improve mobility, and facilitate the performance of spino-pelvic stabilization exercises. An ankle foot orthosis to support weak ankle dorsiflexor muscles on the side of hemiparesis may also be prescribed.	*Patients with cervicogenic and migraine headaches may also exhibit findings of cervical muscle weakness, dynamic spinal instability, and chronic low-intensity cervico-thoracic muscular strain, complicated by postural faults.*

The ankle foot orthosis is designed to help normalize gait, reduce falling anxiety and risk, and to alter the abnormal biomechanical loads traversing the symptomatic sacroiliac joint. As symptoms improve, intermediate level stabilization exercises and progressive resistance exercises will be prescribed to further reduce abnormal gait patterns.	*Chiropractic treatment for this type of case is typically provided at 2–3 visits/week for 6 weeks. Treatment will likely consist of:* *1. Spinal manipulation to the cranio-cervical and cervico-thoracic regions* *2. Myofascial release therapy applied to the suboccipital and upper trapezius musculature bilaterally* *3. Cervical spine and scapular regional exercises* *4. Basic lumbar core stabilization exercises*
Care for this type of case would likely be provided 2–3 times/week for approximately 4 weeks, at which time the case would be re-evaluated for further care, discharge, or referral. If the symptoms are controlled and the patient's goals achieved, the patient would be discharged from chiropractic care.	*At the conclusion of the initial treatment plan, a clinical re-evaluation will determine the need for further care, discharge, or referral. If symptoms are controlled and the patient's goals achieved, the patient would likely be discharged with a self-management program consisting of basic postural and core stabilization exercise.*

Evidence

Research studying the effectiveness of specific rehabilitation protocols for all disciplines, including chiropractic care, is limited due to the challenges of studying many available techniques that can be modified and applied differently for individuals with diverse conditions and wide ranges of symptom severity, chronicity, and co-morbidity. However, many clinical trials involving spinal manipulation and other treatments provided by DCs have been conducted, resulting in a body of evidence that demonstrates the safety and effectiveness of these procedures [52]. Several studies have consistently reported high levels of patient satisfaction with chiropractic care [53–55], while other evidence suggests that the benefits of chiropractic care may include protection against declines in functional and self-rated health status, as well as in activities of daily living for Medicare patients [56, 57]. Though research focused on spine care including chiropractic is relatively new, some studies have reported that evidence-based integrated teams can contribute to improved functional outcomes, reduced cost, and high patient satisfaction [58, 59].

Numerous clinical guidelines recommend chiropractic care, including SM and other procedures commonly used by DCs, for neuro-musculoskeletal conditions [60–63]. For example, low back pain guidelines from the American College of Physicians and the American Pain Society recommend SM for patients who do not improve with self-care options [64].

Safety

Adverse events associated with chiropractic care including SM are similar to those experienced by patients receiving other manual therapies (exercise, massage, physical therapy). Most reactions are mild, short lasting, and consist of musculoskeletal symptoms [65]. Approximately 34–61% of patients experience an adverse event associated with chiropractic treatment at some point during care according to several studies. However, evidence suggests that many reported adverse events are not caused by chiropractic treatment; rather, by the natural variations in symptoms inherent to a wide variety of musculoskeletal conditions [65]. Common and rarely reported adverse events described in the scientific literature are listed in Table 44.5 [66, 67].

The Question of Stroke

Considerable debate has arisen over the role cervical or neck SM plays in vertebral artery dissection, which has been shown to lead to cerebrovascular accidents, including stroke. This debate is founded on several case reports describing patients suffering a stroke following cervical SM. However, determining causality is not possible from case reports and no research has been able to causally link cervical SM to strokes [68].

Biomechanical research has demonstrated that cervical SM causes less strain on the major cervical arteries than normal range of motion [69, 70]. These findings bring into the question the long-held belief that excessive carotid and vertebral artery stretching or kinking occurs during cervical SM, leading to micro tears, thrombus formation, and stroke.

Several epidemiological studies have consistently demonstrated that patients experience the same, extremely low, risk of suffering a cerebrovascular accident following cervical manipulation as they do after visiting a primary care practitioner [71–73]. While epidemiological studies cannot determine causality, it is unlikely that both chiropractic and primary care providers engage in procedures that equally increase the risk for stroke. Instead, these studies, combined with biomechanical research data, provide evidence suggesting that cervical SM is more likely incidental to, rather than causal, to strokes. Patients experiencing a stroke following a visit to

Table 44.5 Common and rarely reported adverse events associated with chiropractic care

Commonly reported	Rarely reported
Increased musculoskeletal symptoms	Dizziness
Radiating symptoms	Nausea
Joint or muscle Stiffness	Tinnitus
Headache	Anxiety
Fatigue	Muscle spasm

either provider type are likely visiting for unrelated health reasons prior to an event, experiencing concurrent musculoskeletal neck/head pain, or prodromal symptoms masquerading as neck pain and/or headache [74].

Collaboration

Collaborative care occurs when multiple provider types and patients actively work together to manage a distinct care plan with mutually agreed upon goals and coordinated treatments [75]. When this approach is used in a single institution, it is often termed "interdisciplinary care." Including chiropractic as members of a collaborative or interdisciplinary care team can be beneficial. As primary spine care practitioners, whose expertise is the evaluation and conservative treatment of spinal and other musculoskeletal-related conditions, DCs can address conditions responsible for, or co-occurring with the need for rehabilitation.

Because chiropractic is a portal of entry healthcare profession, some patients attending outpatient rehabilitation also receive concurrent chiropractic care [76]. Co-occurring care can be beneficial, but the lack of care coordination between providers of different disciplines can also create the potential for poor inter-provider communication [77], misunderstanding, and slowed recovery (see Table 44.6). Team-based rehabilitation can be superior to concurrent, but separate, care from providers of different disciplines [78]. This may be due to a more coordinated approach employed by rehabilitation teams as they manage severe or complex conditions.

Integrated Care Pathways

Several healthcare systems have initiated, or are in the process of initiating, integrated spine care pathways consisting of multiple provider types including DCs [58, 59]. In some settings, DCs serve the role of first contact provider or as a "Primary Spine Provider," performing triage assessment for individuals who present with spine-related and other musculoskeletal disorders [59]. Following initial screening for conditions or symptoms indicating the need for immediate referral (i.e., fracture, osteomyelitis, cancer, acute progressive neurological deficits) and other diagnostic evaluation, DCs may facilitate patient self-management, begin conservative rehabilitative management, or direct referral to another provider for evaluation, primary, or co-management.

Conclusion

DCs are uniquely trained in neuro-musculoskeletal diagnosis and management enabling them to evaluate patients, perform primary level conservative care, initiate referrals, and co-manage care with other providers. Within the field of rehabilitation,

Table 44.6 Potential implications of co-occurring and collaborative/interdisciplinary care models

Co-occurring uncoordinated care	Collaborative/Interdisciplinary care
Possible redundant treatments/diagnostic tests	Potentially reduce treatment/test redundancy
Increased potential for conflicting care goals and treatment(s)	Avoid/reduce conflicting care goals and treatment(s)
Possible uncoordinated delivery of care	More coordinated delivery of care
Potential for confusion among providers/patients from lack of communication	Reduce/avoid confusion due to increased communication
Few or no resources expended on care coordination	Requires additional resources to support an interdisciplinary team and care coordination
Individual providers more free to use all aspects of their discipline and skillset	Potential to utilize disciplines according to greatest strength(s) and individual skillset
Patients potentially more able to choose individual providers	Providers able to reinforce recommendations of other caregivers

success is not always accurately measured by correct disease management; instead, goals and treatments are usually oriented toward appropriately managing the consequences of a disease [46]. Chiropractic care protocols are consistent with the general principles of the rehabilitation environment by naturally progressing along care plans beginning with symptom reduction/control, transitioning toward functional restoration of movements and activities, and encouraging self-management.

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Chapter 45
Acupuncture for the Treatment of Pain in the Rehabilitation Patient

Rocco Chiappini

Introduction

Acupuncture is an ancient medical treatment with potentially powerful applications in the management of pain in the rehabilitation patient. Acupuncture can trace its origins to the Shang dynasty in China over 3000 years ago [1]. It is now practiced throughout the world for the treatment of pain, as well as many other medical problems. Acupuncture has increased in popularity and acceptance in the West over the last few decades. It is practiced by doctors of Chinese Medicine, medical doctors, dentists, and therapists. Many rehabilitation patients suffering from painful conditions have benefitted from acupuncture treatments. Anything as old and as geographically widespread as acupuncture is bound to be practiced with various distinct differences. With the understanding that there is a wide diversity in acupuncture styles and schools of thought, this chapter will focus on a modern approach to the management of pain.

Brief History

Acupuncture is a component of the larger corpus of Chinese Medicine, which also includes herbal medicine, massage (Tui-Na), Qi Gong, and nutritional treatments. The origins of Chinese medicine are seen in texts from the Shang Dynasty (1500-1025 BCE). Shen Nong is said to have discovered the curing virtues of plants. Huang Di, the so-called "Yellow Emperor", wrote the Nei Jing or "Canon of Internal Medicine" at this time. The first known mention of needles was during the Zhou

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Dynasty (500 BCE), during which time texts called the Shan Hai Jing "The Classic of Mountains and Rivers" mentions the use of needles in medical treatment [1].

The practice of acupuncture evolved over long stretches of time and geography, in the hands of countless practitioners who were trained in small schools or in master-apprentice relationships. Acupuncture was not well-known in the United States until president Nixon's opening of China. In 1971, the journalist James Reston, a correspondent with the New York Times, was in China when he came down with acute appendicitis. He underwent an emergency appendectomy in Beijing and received acupuncture to manage his postoperative pain. Mr. Reston wrote about his experience in the New York Times and this account received widespread attention [2]. Acupuncture has since burst on the scene as an intriguing alternative treatment option for pain. As a result of the opening of China, many Americans went to China to train in acupuncture and brought back their knowledge upon their return.

In addition to the James Reston article, two other events helped to move acupuncture more into the mainstream of American medical practice. Prior to 1996, acupuncture needles were classified by the FDA as Class 3, or investigational. In March 1996, the FDA reclassified acupuncture needles to Class 2, which meant that they were deemed to be safe and effective, but requiring certain restrictions [1]. This classification is no different than for other medical devices, such as surgical scalpels or syringes.

The other occurrence was the publishing of a NIH Consensus Statement on acupuncture in 1997. The NIH convened a Consensus Conference, which brought together national and international experts in the fields of acupuncture, pain, psychology, psychiatry, physical medicine and rehabilitation, family medicine, internal medicine, substance abuse, health policy, statistics, epidemiology, biophysics, physiology, and representatives of the general public. After a thorough review of the available literature on acupuncture, the panel concluded that there were many flawed studies and that there were inherent difficulties in studying acupuncture, such as finding appropriate controls for acupuncture treatment. Despite this, the panel noted promising results revealing efficacy for the use of acupuncture to treat postoperative nausea and vomiting, as well as postoperative dental pain. In addition, the panel stated that the literature supported acupuncture as an adjunct or alternative treatment for headaches, tennis elbow, addiction, stroke rehabilitation, menstrual cramps, fibromyalgia, myofascial pain, osteoarthritis, low back pain, asthma, and carpal tunnel syndrome. The panel concluded that "there is sufficient evidence of acupuncture's value to expand its use into conventional medicine and to encourage further studies of its physiology and clinical value" [3]. This stamp of approval from the NIH went a long way in paving the path for acupuncture to become a more accepted mainstream medical treatment in the United States.

Basic Principles

Chinese medicine developed from ancient Chinese philosophy, with ideas about balance and harmony in the natural world, as well as the human body. The two main concepts behind these ideas are that of Yin and Yang, and the energy or life force or

Table 45.1 Examples of Yin/Yang correspondences

Yin	Yang
Ventral	Dorsal
Internal	External
Lower	Upper
Flaccid	Spastic
Hypofunction	Hyperfunction
Deficiency	Excess
Cold	Warm
Relaxed	Agitated

Table 45.2 Categorization of organs in Chinese Medicine

Yin Organ	Yang Organ
Lung	Large Intestine
Spleen	Stomach
Heart	Small Intestine
Kidneys	Urinary Bladder
Pericardium	San Jiao (Triple Warmer)
Liver	Gall Bladder

"Qi", pronounced "chee". These are concepts with which many Westerners are now well-acquainted. Yin and Yang represent two different manifestations of all things in nature and human experience, including the body itself. Yang is warm, active, rising, or energetic, while Yin is cool, quiet, sinking, or quiescent. Therefore, spring and summer are Yang, while fall and winter are Yin. Day is Yang, while Night is Yin. In human physiology, hypertension is Yang, while hypotension is Yin. See Table 45.1.

These ideas are very closely related to the concept of Qi. In Chinese medicine, Qi is the life force; every life process or organ function is an expression of the action and movement of the Qi. In Chinese medicine, there are three important sources of Qi. Each person inherits the Yuan Qi or source Qi. The Zong Qi is received from respiration, while the Yin Qi is obtained through food.

The Qi flows through the body in pathways, which are called meridians or channels. The meridians correspond to the organs of the body. In Chinese medicine, the organs are lung, large intestine, stomach, spleen, heart, small intestine, urinary bladder, kidney, pericardium, san jiao (triple warmer), gall bladder, and liver. The organs in Chinese medicine are not only the physical organs, but the larger functions that they are thought to govern. For example, the kidney functions in filtering impurities and in the creation of urine, but is also involved in sexual function. In addition, it influences a person's will. The lung governs respiration as well as proper functioning of the skin. It is also related in some way to mood, especially depression. See Table 45.2.

Acupuncture points are discrete pin-point areas found along the meridians. There are anywhere from 350 to 400 acupuncture points on the body. Many sources list 361 as the exact number. In Chinese medical theory, placement of needles at these points influences the flow of Qi through the corresponding meridians. In turn, this

influences the health or functioning of the corresponding organ. There are meridians corresponding to each organ of the body. In addition, there are two other meridians called Du mai and Ren mai, which do not have corresponding organs. Therefore, there are a total of 14 standard meridians of the body (see Fig. 45.1).

Western researchers have tried to determine whether there are unique anatomical structures at acupuncture points. Melzac et al. found that 71% of acupuncture points correspond to trigger points. Deung listed structures found in the vicinity of acupuncture points. He found the structures to be as follows: large peripheral nerves; nerves emerging from a deep to a more superficial location; cutaneous nerves emerging from deep fascia; nerves emerging from bone foramina; motor points of neuromuscular attachments; blood vessels in the vicinity of neuromuscular

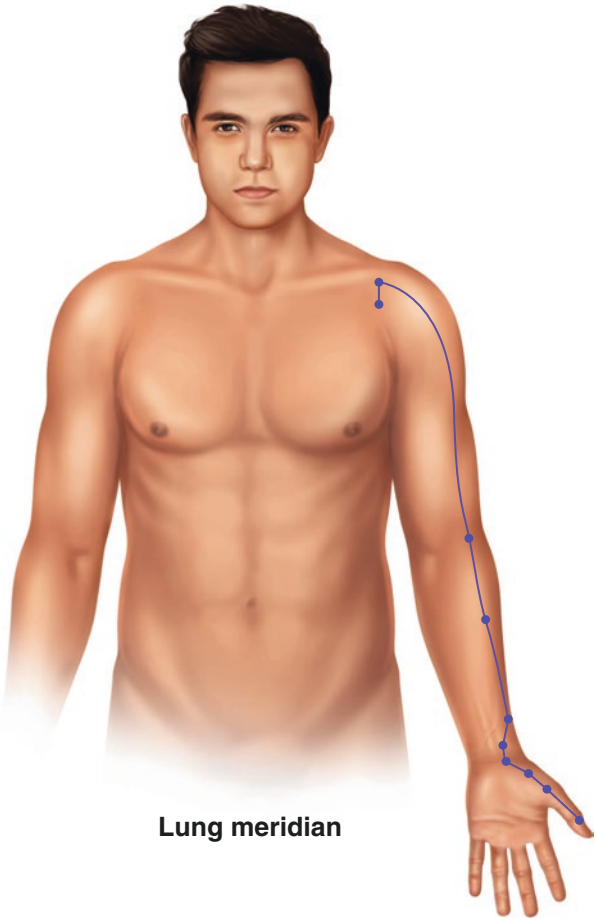

Fig. 45.1 a,b Acupuncture points are discrete pin-point areas found along the meridians. There are anywhere from 350 to 400 acupuncture points on the body. There are meridians corresponding to each organ of the body, totaling 14. A: Lung Meridian. B: Large Intestine Meridian

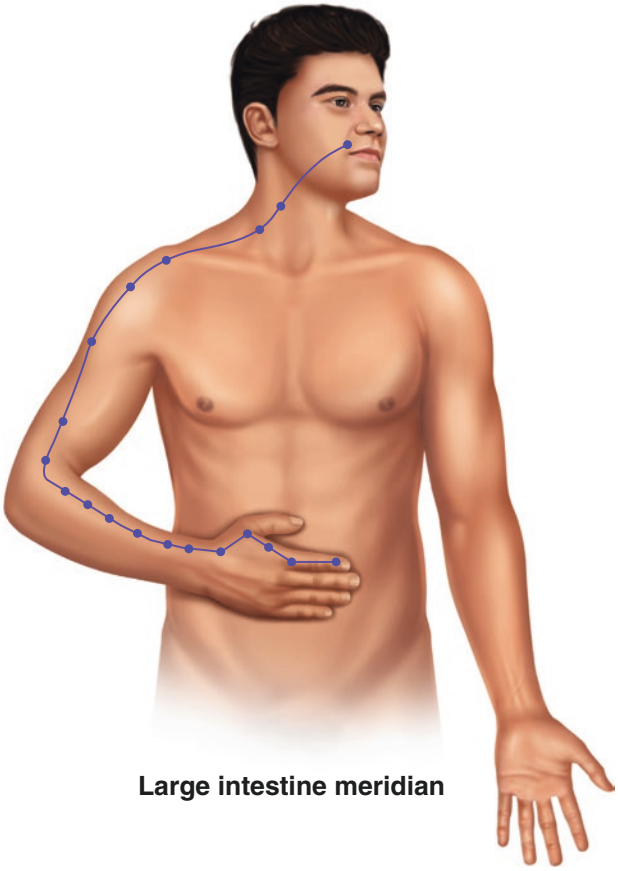

Fig. 45.1 (continued)

attachments. Heine found that 80% of acupuncture points correlate with perforations in the superficial fascia of the cadavers he studied [4]. In the majority, acupuncture points correlate with anatomical structures and, in fact, correlate with nerves or fascial layers.

Common Techniques

The acupuncture approach to the rehabilitation patient with pain should begin with a complete history and physical exam. It is important to know where the pain is, whether there is radiation of the pain, and exactly where it radiates to. The clinician should use his/her knowledge of the acupuncture points and meridians to determine whether the pain corresponds to them. It is important to find out what elicits the pain and what alleviates it. The clinician should also find out how long the pain has been present and what other treatments have been attempted. The best approach to pain

management is multimodal, with a focus on removal of any factors that interfere with full resolution of the pain. For example, muscular imbalances in strength or flexibility and/or improper posture need to be addressed in order to achieve the best outcomes. In the case of sports injuries, technique should be assessed to ensure that the athlete is using proper form and body mechanics when practicing or playing their sport.

Once the clinician has completed his/her assessment and finds the pain to be amenable to acupuncture, it is then important to determine point selection. The selection of acupuncture points is more of an art than a science. There are many different schools of thought, but basic principles are common in most cases. Pain treatment with acupuncture involves needling a combination of local points, distant points, and ah shi points. Local points are acupuncture points in the region of the pain. For example, LI 10 and LI 11 would be local points for the treatment of lateral epicondylitis, or tennis elbow. Distant points are points along the same or related meridians, which can influence the pain. In this same example of the treatment of lateral epicondylitis, distant points would be LI4 and SJ5. Ah shi points are tender areas in the region of the pain that do not correspond to any official acupuncture points. Often a technique called a "flower pattern" can be used when needling ah shi points (Fig. 45.2).

In addition to the needling of local, distant, and ah shi points, auricular or ear points can also be helpful in treating pain. Auricular points are points on the ear that correspond to different parts of the body. There are charts indicating all of these corresponding points, which can be used as a guide. Auricular points are treated with smaller needles placed in the auricular cartilage. The palm of the hand and the sole of the foot also have points, which correspond to different parts of the body.

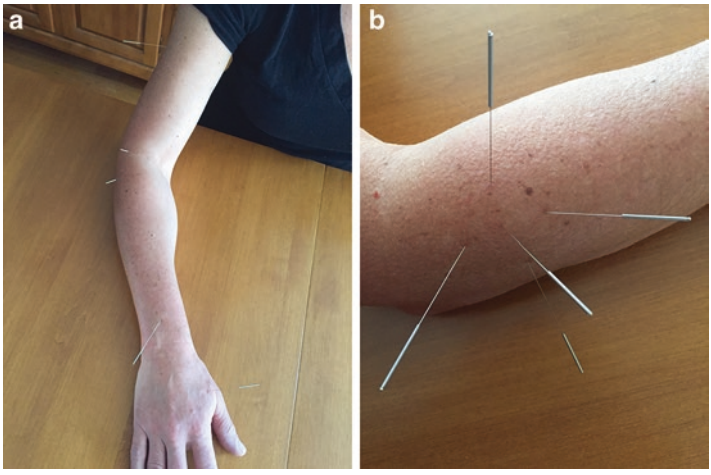

Fig. 45.2 (**a**) Ah shi points are tender areas in the region of the pain that do not correspond to any official acupuncture points. (**b**) The "flower pattern" technique can be used when needling ah shi points

These can be treated with needles, but more often, acupressure is used in these sensitive areas. Acupressure is the application of pressure to acupuncture points in order to achieve a similar effect as with placement of a needle. Pressure is usually applied with the hand.

Different practitioners have various techniques for needle stimulation. Manual stimulation of the needle, by spinning the needle once it is placed and periodically during the treatment, is the most traditional technique. Electrostimulation is also a popular technique for needle stimulation. Regardless of the type of needle stimulation used, it appears that the best pain relief results are obtained when the patient reports a de qi sensation. This is described by patients as a feeling of fullness, dull ache, or tingling sensation. The de qi sensation seems to be elicited by a combination of needle stimulation and proper placement of the needle over the acupuncture point. Electrophysiological evidence indicates that acupuncture stimulation of muscle afferent fiber types ll and lll are responsible for production of the de qi sensation [4].

Most acupuncture treatment sessions involve the patient lying down, although some areas such as the neck are more easily treated with the patient seated. The needles are placed either free-hand, or more commonly, with use of an insertion tube. The needles are left in place for 20 to 30 minutes. A course of treatment is usually about ten sessions, with treatments occurring once to twice each week; however, courses of treatment can vary considerably, depending on the condition being treated.

Acupuncture has potential applications in all aspects of rehabilitation practice. It can be used in both the inpatient and the outpatient settings, although the majority of treatments take place in an office setting. An increasing number of hospitals allow physicians with appropriate training to apply for privileges to provide acupuncture to inpatients. The types of conditions that are treated on inpatient units include headache, neck and back pain, nausea, insomnia, muscle spasms, and anxiety. Patients treated in the inpatient setting usually receive a few treatments each week, if not daily. Many inpatients benefit from these treatments and can continue these treatments at a lesser frequency when they are discharged to the community

Evidence

There has long been controversy about the mechanism by which acupuncture works to relieve pain. Many skeptics have argued that the entire treatment effect of acupuncture is obtained through the placebo effect. The current thinking, by those who practice and study acupuncture, is that the release of endorphins may explain how acupuncture helps to decrease pain. One of the earliest studies looking at this endorphin-acupuncture analgesia hypothesis was performed by Mayer et al. and published in 1977. This group studied acute laboratory-induced dental pain in human volunteers. They were able to achieve pain control with the LI4 point in the first dorsal interosseous muscle in the hand. In a double blind design, they gave the study group IV naloxone, an opiate receptor blocker, and the control group IV saline. The naloxone group showed no acupuncture analgesia, while the saline

group maintained the acupuncture-induced pain control. The interpretation of this study was that it showed a connection between the release of endorphins and acupuncture analgesia and that these endorphins could be blocked to eliminate the pain-relieving effect [5]. Since the publication of this study, there have been numerous studies in which systematically administered endorphin antagonists have been used to test the endorphin-acupuncture analgesia hypothesis.

Many studies have since been performed, which have shown that there is definitely a component of the placebo effect in the response to acupuncture for the treatment of pain. These studies use sham acupuncture, which generally includes placement of needles in non-acupuncture points, or making it appear to the subject that a needle has been inserted when it has not actually been. These studies usually involve three groups, which include an acupuncture group, a sham acupuncture group, and a group that receives usual care. These studies usually show significant pain relief with acupuncture, intermediate relief with sham, and the least pain relief with usual care.

A large meta-analysis published in JAMA in 2012 revealed this pattern of response to acupuncture. The authors reviewed 29 eligible high-quality randomized control trials, with a total of 17,922 subjects studied. They found that acupuncture was superior in pain control when compared to sham acupuncture and to no acupuncture for all pain conditions, which included chronic neck pain, osteoarthritis pain, and chronic headache. The differences between the acupuncture and sham groups were statistically significant, but relatively modest, which indicated that non-acupuncture effects were an important component of the treatment effect. The authors went on to say that "… the clinical decision made by physicians and patients is not between true and sham acupuncture, but between a referral to an acupuncturist or avoiding such a referral". The total effects of acupuncture, as experienced by the patient in routine practice, include both the specific effects associated with correct needle insertion according to acupuncture theory, the nonspecific physiologic effects of needling, and the nonspecific psychological (placebo) effects related to the patient's belief that treatment will be effective [6].

Conclusion

Acupuncture is a valuable treatment for pain in the rehabilitation patient. It is a potentially powerful component of a comprehensive approach to pain management. It has an exceptionally long track record across vast stretches of time and geography. There has been scrutiny by the FDA and the NIH and there is a growing evidence base for efficacy and mechanism of action.

The integration of acupuncture into all aspects of rehabilitation practice has great potential to improve pain control, outcomes, and patient satisfaction with the care that is delivered to them.

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Chapter 46
Yoga for the Treatment of Pain in the Rehabilitation Patient

Sarah Schmidhofer

Introduction

The word "yoga" (loosely translated from Sanskrit to English as "union") refers to a system of physical, meditative, and spiritual practices designed to help people experience a sense of wholeness within themselves and within the universe. In modern usage, this word has been misappropriated to refer to a set of athletic movements and postures. However, the meditative and spiritual aspects of yoga are essential to pain management strategies, and as such, throughout this chapter the term "yoga" is meant to emphasize non-physical aspects of its practice.

When most people are in pain, the natural reaction is to want to separate from it, or to extinguish it physically. Yoga encourages exactly the opposite: pain control with yoga requires reinhabiting and befriending the body, acknowledging that pain is present, and reintegrating with it in a loving way, by unraveling existing patterns of mind and body. This chapter helps to outline some of the theory, practice, and techniques behind this approach, and how this is possible through yoga. This can be applied to all patients in the acute, sub-acute, and chronic rehabilitation care continuum.

How Can Yoga Help in Pain Management?

Yoga is not meant to erase pain, but rather to change the way it is experienced, reducing the suffering caused by pain. It imparts a sense of comfort within one's own skin, allowing a better sense of integration and control over pain and one's life.

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Even when pain is present, it does not have to rule a person's life. This is accomplished by the following: (a) reducing **suffering**, (b) reducing **stress**, (c) allowing for a conscious **reinterpretation** of pain, and (d) **befriending the body**.

Yoga Reduces Suffering

Pain and suffering are distinct entities that are often, but not necessarily, linked. *Pain* is the physical component of an injury, and *suffering* is the emotional component. The emotions invoked by chronic pain contribute greatly to the amount of suffering experienced. Emotional pain is experienced in same parts of the brain as physical pain [1], so when the emotional pain is continuously activated, the physical pain is likely perpetuated as well. For example, increased anger is associated with worsening chronic back pain [2]. Yoga helps people to deliberately reinterpret the thoughts and emotions caused by pain, thus reducing suffering, and often, reducing the experience of pain itself through this means. When practiced regularly, it can allow a person to consciously relax while experiencing pain, thereby helping the brain to uncouple the physical pain from the mental suffering.

Yoga Reduces Stress

Pain and stress (mental or emotional discord) both activate the sympathetic nervous system. As a result, constant stress causes muscles to tense, breathing to become erratic, and mood to deteriorate. It also contributes to weight gain and systemic inflammation. Muscular tension, dysthymia, weight gain, and inflammation all independently contribute to the experience of pain, and therefore, control over stress is a key component of pain management.

Yoga excels at reducing stress and the physiologic responses to stress, increasing parasympathetic tone [3, 4]. The mechanism by which parasympathetic tone is increased and stress is decreased in yoga is unclear, but some mechanisms that have been postulated, which include inhibition of the posterior hypothalamus, decrease in endogenous glucocorticoid production, increase in positive affect, and increase in self-compassion [5]. When parasympathetic tone in increased, muscles can relax, hyper-vigilance is reduced, blood flow is redistributed, and inflammation is reduced. This is the state that yoga can help people induce at will.

Yoga Allows for a Conscious Reinterpretation of Pain

In acute injury, interpreting pain as a threat is appropriate, and taking the body through the sympathetic response (complete with neurologic, immunologic, and endocrine responders) is adaptive, in order to remove the self from a harmful

situation. When the pain is chronic, however, it no longer represents a threat to reality. Thereby, the brain has difficulty in learning to experience pain without invoking the panic response. In a way, chronic pain is a pain that can no longer be trusted to serve a protective function; the body's cumulative response to enduring pain is to "overprotect" the system by maintaining this sympathetic response. Because of what the brain has learned through experience, the pain threshold decreases, and non-threatening situations can be misinterpreted as threatening.

Yoga helps people to understand and to make choices about how to respond to, and how to conceptualize continued pain (i.e., Is the pain dangerous? Is the pain "everywhere", or is it more localized? Is it constant, or does it actually change over time?) In bringing some of the connections to conscious awareness, the body and mind can begin to alter their relationship to pain perception. In this way, components of a yoga practice can actually decrease the brain's sensitivity to incoming pain signals from the body [6–8].

Yoga Encourages a New Relationship with the Body

People who experience chronic pain often come to view their pain and their body as enemies, even as separate entities altogether. Yoga teaches people to love again and integrate the body into the sense of self. It can help to transform emotions that worsen pain, can teach people to listen to their bodies, and can help to tease out the actual extent of the physical pain. This will lead to remapping pathways that were previously devoted to learned suffering, and to awaken joy in everyday experiences. These experiences teach people how to consciously have an influential role in the way pain is experienced; they teach people to remind themselves that pain is just a small part of who they are, even when it feels all-consuming. Yoga helps people learn how to live a fulfilling life with pain and despite it.

The Practice of Yoga in the Chronic Pain Patient

Movement/Asana

A painful limb causes disuse, and disuse causes dysfunction. Yoga encourages gentle movement, which can help to loosen muscles/fascia and to develop strength in order to support problem areas.

There are two main types of movement in yoga, called vinyasa and asana. *Vinyasa* refers to the act of linking breath with movement and helps to create a state of moving meditation. It also helps to increase awareness of how the breath, mind, and body affect each other. *Asana* refers to poses that are held for longer periods of time. These focus on creating stretch and strength, while using good alignment to allow proper flow of energy through the body.

When practiced correctly, yoga is individualized and therefore very safe. Patients will likely have to modify physical poses depending on personal limitations, which should be instructed on an individual basis. In a rehabilitation setting, clearance by a medical provider in advance of postural adjustment is important to rule out the potential for creating further structural damage. Furthermore, no movements should be made without first asking the body what it needs and what it can tolerate. This helps people to learn and to listen to their bodies.

Patients should be encouraged to learn the difference between harmful sensations and helpful sensations (e.g., a stretch or a working muscle). Learning to tolerate intense sensations, such as a working muscle, in a controlled environment with even, calm breathing can help to provide the tools for handling pain in other situations. This can also help patients to recognize worsening pain or acute pain episodes earlier, and to make adjustments accordingly.

Breathwork/Pranayama

In yoga, the word *prana* refers to both the breath and the body's energy. The practice of *pranayama* ("drawing out the breath") consists largely of breathing work. Meditative and deliberate breathing is often the anchor in a yoga practice; it provides a way to connect to what is happening in the body and to help to alter the activation of the parasympathetic and sympathetic nervous systems.

The rate, depth, and character of breathing change in response to stress and autonomic nervous system input. However, because breathing can be both unconsciously and consciously regulated, it is possible to deliberately induce the parasympathetic response through breath work [9, 10]. Some evidence suggests that a person can invoke specific emotional states by voluntarily engaging in corresponding types of breathing [11]. Furthermore, *pranayama*, or breath work, can allow people to selectively attend to the experience of breathing over the experience of pain.

Meditation

In classical theory, the *asana (*physical*)* and *pranayama (*breath work*)* components of yoga are simply a means to prepare the body for meditation. Meditation refers to the act of focusing on one point, first with great effort, and eventually, effortlessly. It can help the brain to unlearn maladaptive habits of the mind and to replace them with healthier ones. Meditation has been shown to induce relaxation and to increase pain tolerance [7, 8, 12]. For a nice review of how meditation may modulate pain perception, please refer to Nakata's article: "Meditation reduces pain-related neural activity in the anterior cingulate cortex, insula, secondary somatosensory cortex, and thalamus" [6].

Meditating allows a person the space and tools required to be able to become aware of his or her automatic/negative thoughts, which include fear, criticism, anger, and despair, and to consciously direct them towards helpful ones, which include gratitude, joy, and love.

It is important to advise patients that the goal of meditation is not to empty the mind completely. Rather, it is to build attention and compassion, and to learn to befriend and to guide the mind in adaptive ways. When patients find the mind wandering, which may happen many times a second, they should be advised to simply notice this and to gently bring it back. Each and every time this happens, the brain is being trained. There is no way to be "bad at" meditation.

Conclusion

Yoga helps people learn to respond to pain differently, and learn to live fulfilling, joyful lives, even in the presence of pain. It can empower people to gain power over the feeling of pain and to give them tools to combat it consciously. It helps people to tune into the ability to feel joy and peace for no reason at all. A yoga practice builds the capacity to foster and to nurture happiness that is distinct from life events. In the yogic philosophy, wisdom, joy, and love are the core elements of the natural human condition, and a yoga practice allows people to reconnect to this. People are perfect and whole, even when pain is present.

Reminders and Quick Tips: When Recommending Yoga to a Patient for the First Time, It Is Worth Emphasizing the Following

- The effects of yoga, while perhaps providing immediate relief, are cumulative and are most noticed after months or years of regular practice.
- There is no need to know what is causing the pain for yoga to help.
- In a group class, avoid looking in the mirror while doing poses, or looking at others in the room. It doesn't matter what you look like as yoga is about learning to sense what is happening from within.
- Most yoga classes offered in studios focus heavily on movement. Some classes are much safer than others. It is critical to tell instructors ahead of time about any medical conditions or physical limitations so that modifications can be suggested for some movements.
- In general, for a beginner with chronic pain, use the following as a rough guide for class titles:

Words to look for	Words to avoid
Restorative	Bikram
Gentle	Hot yoga
Therapeutic	Ashtanga
Viniyoga	Vinyasa flow

Words to look for	Words to avoid
Meditative	Power yoga
Yin yoga	Forrest yoga
Ishta yoga	
Yoga nidra	

Beginning Practices

While it is optimal to begin a yoga practice under the guidance of a professional, there are some simple techniques described here, which can have powerful effects when practiced regularly. Try reading them to patients, or photocopying them and giving them to patients to take home. Before beginning any of these practices, help your patient find a relatively comfortable position. This can be sitting in a chair, against a wall, or on a cushion, but it is important to maintain a neutral spine position as much as possible, using cushions or blankets as needed for support. The techniques can also be practiced lying on the back or with a rolled blanket or pillow under the knees for support. It is reasonable to try all of the techniques, then pick one or two that resonate most strongly, working up to practicing for 20 min, twice a day, every day.

A Simple Vinyasa, Linking Breath and Movement

Inhale while lifting the arms up; exhale while lowering the arms down. This can be a big or a small movement, using one or both arms. The important part is to move in *one direction for the entire duration of the inhale*, and *another direction for the entire exhale*. If the arms have limited mobility, any body part and/or movement can be selected, such as lifting and lowering the chin, bending and straightening the knee, rotating the palms up and down, and separating the hands, then bringing them together. Inhale, moving in one direction; exhale, moving in the other direction, concentrating on linking breath with movement.

Cat/Cow

This movement helps to gently mobilize the spine and to loosen the muscles used in breathing fully. From sitting, standing, or balancing on the hands and knees, inhale and bring your chest forward, arching the back, looking up slightly, and opening the chest muscles, like a cow, then exhale and round your back, moving your chin towards your chest, and tucking your tail bone, like a cat. Repeat this movement with each breath. *Make the length of the movement match the duration of the breath*. This is a good practice to do before starting any of the other techniques.

Mindfulness/Breath Awareness

Close your eyes and tune into your breath. Don't try to change anything, just notice what is happening. Notice the quality of the breath … is it shallow or deep? Where do you feel it the most? Is it in your nostrils, your lips, your belly, or your chest? See if you can feel your ribs moving, or the way your clothing feels on your skin as you breathe. Notice the length of the breath to see if your inhalation and exhalation match, or if one is longer. *Any time your mind wanders, just bring it back to the breath*, noticing that the breath is a reflection of the mind and vice versa. See if you can *become curious about each breath* as it occurs. Don't worry if the mind wanders; every time you notice it and bring it back, you are training the mind to be with the present, while learning to notice thoughts/emotions without getting carried away by them.

Lengthen the Exhale

This breathing pattern increases parasympathetic tone and is very calming. Close your eyes, and tune into the natural rhythm of the breath. Next time you inhale, count the length of the inhale. On you exhale next, see if you can lengthen the exhale. For example, if you breathe in for a count of 4, see if you can breathe out for a count of 6. Continue breathing in this way, making the exhalation longer than the inhalation. If you become short of breath or anxious during this practice, just take a few breaths without counting, until you are ready to begin again. A slow, steady exhale can help you to calm your nervous system.

Nadi Shodana (Alternate Nostril Breathing to Balance Brain Activity)

Close your eyes. Notice the flow of breath from your nostrils, which will most likely be more dominant on one side over the other. This practice will aim to even out the flow of air through the nostrils. On an inhalation, imagine breath flowing only through the right nostril, pause, and then imagine exhaling only through the left nostril. Pause again, then inhale through the left nostril, pause, and then exhale through the right nostril. Pause. Repeat this pattern, until it feels as if air is flowing equally between both nostrils. If imagining this is difficult, you can use your right hand to open and to close each nostril as you breath, using your thumb and ring finger to alternate the flow of breath, resting the index and middle fingers on the forehead. When the breath feels as though it is flowing evenly through both sides, lower the hands and rest in this state of balance for several minutes, or as long as you'd like.

Sat Yam (Purification of Emotional Expression)

This technique may help to connect emotions to breathing and helps to tune into a natural state of compassion and joy. In turn, this can release pent up emotions. Close your eyes. Bring your attention to your heart; not the organ, but the spiritual heart, in the center of your chest. Try to visualize or to imagine a small glow in the center of your chest. As you inhale, imagine that glow expanding outward in all directions. As you exhale, allow the glow to draw back into your heart. At first, the light may expand a bit, just to fill your body, then contract back to the center of the heart. As you continue practicing, when you inhale, allow the light to expand further and further. First, fill the space around you, then the room, then the whole building, and then maybe even the whole universe. On each exhalation, be sure to allow the light to contract back to the center of your chest. *Inhale, let the light expand; exhale, the light contract*. Eventually, your breath may become slowed and much more subtle. At this point, rest in this state of balance for several minutes, or as long as you'd like.

Yoga Nidra

This term loosely translates to "yogic sleep", and can be used for deep relaxation, to help you to fall asleep, or to release deep unconscious patterns in the body and mind. This is a wonderful practice designed to be practiced lying on the back, with the aid of an audio guide. Many free versions can be found online and in the links in the section "Recommended Reading".

Body Gratitude/Loving Kindness Meditations

This type of meditation can be particularly helpful in redefining strong emotions that surround chronic pain. For more information, please see Sharon Salzberg's link the section "Recommended Reading".

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Recommended Reading

An excellent, in depth review on the subject of yoga for chronic pain: Vallath, Nandini. Perspectives on yoga inputs in the management of chronic pain. Indian J Palliat Care. 2010; 16(1): 1–7.

http://yogaforpainrelief.com/: book on yoga for pain relief, as well information on further resources and free guided audio practices, such as the ones described in this chapter.

http://www.sharonsalzberg.com/: information about loving kindness meditation, and links to recordings.

http://www.freemindfulness.org/download: information and free audio recordings of mindfulness meditations.

http://marc.ucla.edu/body.cfm?id=22: information and free audio recordings of mindfulness meditations.

http://www.yoganidranetwork.org/: a source of free yoga nidra recordings online.

http://itsbetterwithyoga.com/: information about how to safely begin a yoga practice.

https://www.irest.us/: information and research around learning and practicing a modified form of yoga nidra.

Chapter 47
Alternative Medicine for the Treatment of Pain in the Rehabilitation Patient

Sagar S. Parikh, Yuriy Shepelyak, and Sara Cuccurullo

Introduction

As clinical practice continues to encounter variations in pathology, the scope of medical treatment continues to evolve. For some, this means looking toward novel research; however, for others it encourages revisiting medical techniques from alternative schools of thought. By definition, complementary medicine deals with non-mainstream practices that are used together with conventional medicine when treating a patient. In contrast, alternative medicine deals with non-mainstream practices that are used in place of conventional medicine. Acupuncture is a fine example of an alternative medical practice that has gained a wider acceptance. It is now considered complementary, as it is used alongside modern medical practices. It is important to know that by definition, true alternative medicine is uncommon. Most non-mainstream approaches are now used alongside conventional treatments.

A National Health Interview Survey (NHIS) done in 2012 revealed that yoga, chiropractic and osteopathic manipulation, meditation, and massage therapy are among the most popular alternative practices. Other mind and body practices include acupuncture, relaxation techniques such as guided imagery or mindfulness

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therapy, eastern energy arts such as tai chi or gi qong**,** healing touch**,** hypnotherapy, and movement therapies. Even though they do not require significant resources, alternative medicine is not universally available. The use of alternative medicine seems to be more prevalent in affluent communities [1]. It is also frequently utilized in terminally ill patients. Pain and anxiety are among the most common complaints treated with alternative medicine. Specifically in the rehabilitation population, patient's seek alternative therapies most commonly for the treatment of pain, depression, anxiety, insomnia, and headaches [2]. To unravel the complexities of modern medical management, we realize that a combination of modern medical techniques and alternative medicine may hold the key for pain relief and function restoration.

Brief History

The roots of what some may consider holistic modern medical practice can be traced back to 1977, when George Engel, M.D. introduced the biopsychosocial model. Prior to this, the majority of treatment approaches had been focused on the biomedical model, looking for what could be treated primarily from an anatomic perspective. Introducing the psychological aspect of a patient's wellness emphasized the link between the mind and the body with regard to pain and function, which was aligned with the IASP's definition of pain as "an unpleasant sensory and emotional experience…"

Many alternative medicine therapies employ the mind-body principle. Mind-body therapies are types of treatments employed for the sole purpose of strengthening the mind's control over emotions, bodily functions, and other symptoms. Why mind-body techniques work is not immediately intuitive; however, one prolific pain expert devised a theory. Ronald Melzack, best noted for his contribution to the Gate Control theory of pain, proposed the Pain Neuromatrix in the 1970s. This theory dictates that a combination of sensory, emotional, and cognitive inputs run through a truly unique and individual circuitry, which then provides a particular output. This output includes a combination of emotional, motor, pain, and stress responses, that in summation, create our pain experience [3].

Data from the past decade has revealed a correlation between involvement of the autonomic nervous system, which includes the sympathetic and parasympathetic divisions, and regulation of the cortisol stress response, anxiety, and pain. Regulation of the stress response is pertinent to rehabilitation, as stress is defined as a state in which homeostasis is or has been perceived as threatened [4]. Unregulated stress responses can result in energy depletion. Many alternative medicine therapies focus on promoting activity of the parasympathetic nervous system to reduce stress by reducing heart rate, reducing blood pressure, and overall promoting a state of relaxation, which indirectly leads to a state of pain relief. Our pain perception can be affected and modified by our mental state, which is why mind-body therapies are quite helpful for managing pain. There are various approaches to mind-body therapy and many of these therapies overlap in their emphasis on meditation and relaxation.

Mindfulness-Based Therapy

The basis of mindfulness-based therapy is a set of techniques geared toward accessing one's awareness of sensory perception and then using that harnessed awareness as a facilitator or inhibitor of the pain response. The technique is difficult to master and requires patients to exert a major effort. The goal is to attain a state of "detached observation" and to observe one's own cognitions, perceptions, and emotions without judgment, or without intention to control. The rationale for this type of therapy in pain management involves detachment of the sensory and cognitive emotional components of pain, whereby the experience of pain becomes more spontaneous and the overall pain perception is thereby diminished. This assumes that low rates of awareness lead to increased pain perception due to the emotional overlay that patient's place on their feelings of pain. Theoretically, low levels of mindfulness or awareness can be correlated with higher levels of pain catastrophizing, which is significantly associated with fear and anxiety caused by pain [5]. In turn, this can result in diminished levels of function. Detachment of this association can therefore reduce catastrophizing and pain. Reiner et al. characterized mindfulness-based interventions into three core features as follows:

- Observing the reality of the present moment by attending to objective qualities of present experience or situation existing in one's inner or outer world
- Maintaining one's attention to a single aspect of awareness and to accept it as it is, without acting, judging, or elaborating on its implications
- Remaining open to everything that is currently salient, without attachment to any particular point of view or outcome

The technique of mindfulness-based interventions varies, however the aforementioned goal remains the same. The patient may be asked to engage in different forms of meditation or even yoga practices during the sessions and is encouraged to utilize these techniques in their daily living. Dr. Jon Kabat-Zinn is well-known in the study of "mindfulness meditation" and created a collection of techniques called mindfulness-based stress reduction (MBSR). He demonstrated significant decreases in the Pain Rating Index scores of a subset of 51 chronic pain patients of various diagnoses that had undergone his 10-week stress reduction program, in addition to improvements in behavioral symptomatology [6]. Since then, MBSR has been studied in various pain and psychological conditions and has been shown to be beneficial. Similar studies have also shown significant benefit in overall pain severity and quality of life measures with respect to the chronic back pain population [7]. A more recent randomized controlled study looking at 40 patients with migraine or tension-type headaches also found significant improvements in pain intensity perception after an 8 week course of MBSR [8]. This course included understanding pain and its etiology; discussions on relationship stress, anger, and emotion with pain; identifying and understanding negative automatic thoughts; introducing the concept of acceptance; breathing exercises; behavioral activation; mindfulness of routine activity; meditation; mindful walking; and reading literature related to mindfulness.

Though treatment sessions typically last from 8 to 12 weeks, the effects of mindfulness-based therapies and meditation are presumably long lasting, especially in reference to neuroplasticity. One particular study looked at the potential benefits of long-term meditation in Zen masters and found positive correlations with increased meditation practice and decreased pain sensitivity with anatomically larger cortical size [9]. This association of larger cortical thickness to meditation has also been moderately reported; however, the actual specific neuroplasticity effect on stroke rehabilitation has not yet been demonstrated.

Nevertheless, mindfulness-based therapies have also shown benefit in post-stroke survivors. Improvements in mental fatigue and depression have been demonstrated [10]; however, studies of this nature have been limited in sample size and power. Mindfulness-based training has been proven to show benefit in attention-related behavior, judgement and memory, as well as decreases in cognitive rumination. Application of these principles to stroke victims is the subject of future research.

Guided Imagery

Meditation provides a means to relaxation by focusing one's mind for a period of time. Much like mindfulness-based practices, guided imagery, in particular, is a commonly employed meditative technique that uses visual cues to promote relaxation. Simply put, the relaxation technique of guided imagery includes "imagining scenes, pictures, or experiences to help the body heal". Guided imagery can include a variety of techniques from visualization and direct imagery-based suggestion through indirect metaphor and storytelling. Much like most forms of meditation and relaxation, guided imagery can influence the autonomic nervous system and can affect major physiologic control systems of the body, which include respiration, heart rate, and blood pressure. This is mainly achieved through physiologic relaxation, which is the result of decreased sympathetic and increased parasympathetic nervous system activity.

Pain and anxiety were cited as the most common reasons to start guided imagery. In the post-operative population, if pain and anxiety go unchecked, a resultant protracted early rehabilitation in joint replacement will ensue, in addition to increased rate of morbidity, decreased utilization of physiotherapy, increased state of anxiety, and decreased level of patient satisfaction [11]. The introduction of these endeavors in this population has lead to decreased rates of opioid use and increased rates of patient satisfaction [12] in many studies.

Yoga

Yoga has become a growing trend in fitness and wellness and has been studied in the context of mindfulness and relaxation. According to the National Center for Complementary and Integrative Health, yoga is a mind-body practice with its origins

in ancient Indian philosophy. It comes in many varieties, all of which utilize physical postures, breathing techniques, and meditation or relaxation. Though the practice of yoga was first rooted in meditation and deep breathing, Hatha Yoga and Iyengar Yoga have become the more commonly practiced forms in the United States and Europe and its mainstay is the emphasis on physical postures and core stability. Though many use this practice for fitness, studies have shown a correlation between yoga practice and pain relief, especially with respect to certain diagnoses.

Pathophysiology

Hatha Yoga practice aims to improve strength, endurance, and flexibility, while promoting relaxation and initiating mental awareness. Like most relaxation practices, yoga aims to physiologically increase relative parasympathetic activity, decrease heart rate, decrease blood pressure, and increase breath volume. The sustained postures necessitate a state of active mental awareness. Generally speaking, yoga practitioners were found to be more accepting of their bodies, more accepting of physical pain, more understanding of their body's condition, less likely to "catastrophize" over current or future symptoms, and better able to detach from their psychological experience of pain.

Lower Back Pain

Lower back pain is the most common pain complaint in the United States, with billions of dollars spent on treatment strategies to alleviate it, and almost 80% of the population experiencing it at least once in their lifetime. One study in particular looked at the effectiveness and efficacy of a 24-week long Iyengar Yoga program. Significant improvements were noted with respect to functional disability, pain intensity, and depression [13], as well as a significant difference when compared to a control group of patients who underwent non-yoga-based usual back pain treatments. Subjects also tended to utilize less pain medication after completing the Yoga program.

Knee Osteoarthritis

Yoga therapy has been shown to successfully decrease pain and stiffness in the knee osteoarthritis (OA) population, especially with treatment durations lasting between 6 and 12 weeks. A study looking at the effects of Hatha Yoga on patients with knee OA, in comparison to those undergoing therapeutic exercise, revealed that as a complement to normal physical therapy, the yoga treatment group exhibited significant improvements in pain intensity, joint tenderness, swelling, and crepitus, as well as a significant decrease in morning stiffness [14, 15] at 90 days post treatment. Similarly, other studies have also demonstrated this improvement, especially with respect to

pain intensity and stiffness long term, even as far as 20 weeks post treatment. Though gait speed, strength, endurance, and flexibility are the goals for most knee rehabilitation practices, there have been mixed results when it comes to yoga treatments in the knee OA population.

Post-stroke

Yoga has been shown to provide benefit to post-stroke patients as well. One of the most common causes of anxiety in the post-stroke patient is the loss of independence and the fear of imbalance or falling. During an 8-week pilot study looking at veteran stroke survivors after yoga therapy, an improvement in overall balance scores and an improvement in the fear of falling measures were recorded [16]. This result, with respect to balance, has been demonstrated in other studies; however, limitations in these studies included observation that the severity of balance deficits or the degree of aphasia had an impact on participation in therapy [17]. Nevertheless, in follow-up studies, pain scores, neck and hip range of motion, upper extremity strength, and 6-min walking scores have showed significant improvements [18]. In addition to functional gains and improvements in dexterity, post-stroke patients have also shown a greater degree of acceptance with their changed functionality as well as a greater sense of calm.

Massage Therapy

Massage therapy is commonly prescribed within physical therapy programs for most myofascial pain conditions. One of the advantages of massage therapy is that it is the least likely modality to be harmful. It has become increasingly utilized in sports medicine clinics and has become a regular part of athletic training and sports rehabilitation programs. It can be an effective tool to decrease stress, tension, and pain, in addition to increasing lymphatic drainage. Before discussing the benefits of massage therapy, the pathophysiology of muscle tension and pain must be addressed. Myofascial pain is likely the most common of the muscle tension pain syndromes. It is characterized by the presence of myofascial trigger points, of which the most distinct features are tender nodules that are part of a palpably tense band of muscle fibers. The physical attributes of a taut contracted muscle band with tightly contracted sacromere segments have been studied, but how this came to be is still unknown.

One of the most regarded theories involves integration of the trigger point hypothesis, which describes an “energy crisis” within the muscle, caused by overloading, contraction, and fatigue. Prolonged muscle contraction can subsequently yield pockets of micro-ischemia, which is the result of a temporary blockage of capillary blood flow within the muscle, thus causing an inflammatory and painful milieu. Massage can relieve these pockets of micro-ischemia and can even cause

reflex vasodilation, with subsequent improvements in circulation. By applying dynamic pressure to facilitate loosening of these contracted muscle fibers, massage can thereby relieve pain. Massage also reduces pain perception through the gate control theory of pain. The nervous system is provided with afferent A-beta nerve stimuli, which can effectively "close the gate" and inhibit afferent pain stimuli.

There are various techniques employed in therapeutic massage. Effleurage is a relaxation technique that employs gliding movements of the skin without deep palpation. Petrissage refers to kneading of tissue to increase circulation. Tapotement refers to performing light percussion to help with tissue desensitization. Soft tissue mobilization is a forceful deep tissue massage done with the fascia muscle in a stretch position, which is often used to reduce contractures. Myofascial release is used to perform a prolonged stretch to focal areas of muscle or fascial tightness [19]. For the purposes of the hospital setting, the type of massage employed is a mixture of myofascial release, deep tissue massage, and fluid stroking of the muscle and support tissue, which is often seen in Swedish massages.

Massage integrated into the acute care setting has theoretical and proven results in pain reduction. Potential benefits of massage include decrease in pain perception via the gate control theory; psychological benefit includes increases in parasympathetic activity, which can result in reduced heart rate, reduced blood pressure, and increased endorphin release [20]). With regard to post-operative pain, one randomized controlled trial found higher degrees of pain reduction and anxiety relief when massage was added to the post-operative period of a patient's hospital stay [21]; however, pain reduction did not correlate with a significant decrease in post-operative opioid use or length of stay.

Hypnosis

Hypnosis is an effective tool that has been recognized by the medical community since the late 1950s. Hypnosis is a state of focused attention in which a person has an enhanced capacity for suggestion; in turn, the patient is able to achieve behavioral modifications that he/she desires. The hypnotic state can be achieved in various ways, especially with the help of a physician, a therapist, or a guided self-recording. Contrary to popular belief, most people are susceptible to hypnosis. There are even "depth scales" to grade people into "high", "medium", or "low" susceptibility level of responsiveness to suggestion under hypnosis. Approximately 80% of the population are medium, 10% are high, and 10% are low susceptibility levels; it is controversial whether the distribution is on a "normal" bell-shaped curve or rather on a bi-modal shaped curve [22].

Furthermore, like many other alternative therapies, modern hypnotherapy has been shown to have various clinical uses. For example, it has been shown to be effective in treating fears and phobias [23], psychotherapy [24], and relaxation [25]. Of particular interest is its application to pain management; various studies have shown that hypnosis can be used to decrease the experience of or can be used to

alleviate pain from a wide spectrum of causes spanning diffuse pain secondary to cancer treatments through oral pain experienced by patients with mucositis [26]. Furthermore, hypnotherapy can also be effectively used before painful medical procedures to decrease pain levels, such as wound debridement [27]. Finally, hypnosis is helpful for patients who are living with a terminal diagnosis of cancer. In addition to alleviating pain, it has also been shown to decrease some patients' level of anxiety and to improve their sleep [28].

Reiki

Biofield therapies, such as Reiki, therapeutic touch, and healing touch, have gained increased popularity in the past decade. Despite limited data to support the efficacy of these therapies, numerous patients have found them to be effective and have turned to them for a source of relief when everything else has failed. Some of these therapies are ancient, such as qi gong, while others were developed more recently, such as Reiki, which was developed in 1922 by Japanese Buddhist Mikao Usui. Reiki uses a technique commonly called palm healing in which a practitioner transfers "universal energy", also known as "chi" from his/her palms to the patient, thus encouraging healing of the area that is affected. Numerous studies have been conducted to prove the effectiveness of Reiki, but clinical research has not shown Reiki to be effective as a medical treatment for any medical condition [29]. Nevertheless, it has been shown to be effective in reducing stress and in generating a relaxation response, which may be therapeutic, as in other similar mind-body interventions. It is effective when the patient receives the treatment and also when the patient is taught to be the practitioner.

For example, in a study of 30 HIV patients with numerous disease-related symptoms, the subjects were taught to be first degree Reiki healers, whereby patients could treat themselves and others of their ailments. The patients reported a significant decrease in their pain and anxiety levels. Furthermore, Reiki is particularly effective in hospice and palliative care settings. There are ten million cancer patients in the United States and more than one-third of these patients describe their pain as moderate or severe [30]. A systematic review of seven randomized trials found Reiki to be effective in improving symptoms of pain and anxiety in cancer patients, post-surgical patients, and community dwelling adults [31]. A randomized controlled clinical trial to investigate the effect of Reiki on the effect of pain and anxiety on hemodynamic parameters on postoperative days 1 and 2, in patients who had undergone cesarean delivery, revealed a significant decrease in the time needed to provide pain therapy as well as the number of analgesics required [32]. It seems that touch alone is effective in healing patients with cancer. In an interesting review done by Jackson et al., using an analysis of 12 studies, the authors showed that the therapeutic touch is an effective complementary form of care for the oncologic population in reducing both pain and anxiety.

Conclusion

Pain, anxiety, and motivation are important obstacles to overcome in rehabilitation of the patient in the acute, subacute, and outpatient setting as these factors directly impede functional goals. Alternative medicine provides a cost-effective, minimally invasive, and relatively harmless option for the rehabilitation patient to overcome these obstacles. Alternative medicine does require the patient to take direct ownership of the treatment process. Only a motivated patient will be able to effectively undergo mindful meditation, relaxation, exercise-based movements, and dietary changes; however, if sustained, the effects of alternative medicine can be long lasting.

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Recommended Reading

Fundamentals of complementary and alternative medicine. 5th ed. Marc S. Micozzi MD PhD.
Mayo clinic book of alternative medicine: integrating the best of natural therapies with conventional medicine. 2nd ed. Mayo Clinic.

Chapter 48
Lifestyle Modifications for the Treatment of Pain in the Rehabilitation Patient

Nelli I. Pavlotsky

Opening Statement

Pain is something that needs to be managed across the rehabilitation spectrum. Acute, subacute, or chronic pain is a disturbance to the rehabilitation patient's life, thought processes, activities of daily living, and inter-personal interactions within the world. The rehabilitation patient's immediate inner circle (family and friends), outside circle (job and professional relations), and activities of daily living are all affected by pain.

Some pain is "artificially inflicted"; if the rehabilitation patient does not engage in therapy, or does not progress through activities with a realistic perspective and staged approach, damage to the neuromusculoskeletal system can occur. For example, if a patient has inadequate or excessive caloric intake, or has a diet, which is not appropriate (too spicy or too fatty), his/her body and organs will reflect the incongruity through pain in the gastrointestinal tract. Thereby, the healing process will be affected since the body is like a litmus paper; it will indicate what is right and what is wrong, through pain.

Pain is a language. Every rehabilitation provider should listen to communication from the rehabilitation patient's body, throughout each phase of rehabilitation. Helping the rehabilitation patient to achieve and to maintain a pain-free body is a continuous effort.

The following pain management strategies have been suggested [1, 2]:

Breathing slowly
Relaxing with use of biofeedback

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Obtaining regular exercise
Reducing emotional triggers
Venting emotions
Correcting posture
Eating regular meals
Sleeping well

The rehabilitation patient in pain should be prepared both mentally and physically, consciously and subconsciously to understand and to implement lifestyle modifications to affect pain control [2].

Lifestyle modifications should be individualized because every patient has hereditary factors and life experiences, which influence pain. These include professional influences such as specificity of vocation, as well as mental and physical activities, which affect avocational and recreational activities. The rehabilitation patient's personal circumstances, emotional health, and injury and accident history are important to review frequently. Lifestyle modifications require the patient to be educated and engaged, and as such, require active participation [1–4].

Goals

The first and most important goal is to prevent pain. When pain occurs, the rehabilitation provider needs to understand the course of pain through an appropriate diagnosis. The diagnosis should be treated, not the symptoms.

It is important to understand a patient's family history. For example, if a patient has a family history of arthritis, instead of waiting for arthritis to create further disability or impairment, preventive strategies can be undertaken to prevent or delay further progression for a number of years and to reduce the severity of arthritic sequelae. This can occur through education on modification of personal habits, nutrition, exercise, and stress management. The ultimate goal is to manage pain through the rehabilitation continuum. In the case of debilitating chronic disease, improvement in quality of life and return or progression toward a more productive life can be realized through the help of the rehabilitation professional, through an appropriate support network, and through the patient's own efforts. The rehabilitation patient needs to be instructed on the importance of planning and discipline.

Components of Lifestyle

Lifestyle modification is multi-faceted. Each lifestyle component should be addressed; however, flexibility exists to individualize these components within the different phases of rehabilitation. The main components include the following:

1. Daily schedule
2. Habits
3. Balanced nutrition
4. Weight control
5. Discipline and goal setting
6. Exercise and physical activity
7. Stress management

Daily Schedule

Throughout rehabilitation, it is important that the patient's daily schedule be realistic. Patients should be instructed on the importance of maintaining a routine, which includes maintaining regularity in the sleep-wake cycle as well as routine times for meals. This is more difficult in the acute phase of rehabilitation where patients undergo 3 h or more of intense rehabilitation. However, maintaining consistency as much as possible will help the body to establish certain reflexes; if a person wakes up and goes to bed at the same time day after day, the body will work as a clock and will establish a ritual to function optimally. It is hard to underestimate the importance of sleep. People are different, and not everybody needs 9 h of sleep. Seven to eight continuous hours of good deep sleep will help the body to heal, to manage pain, to restore energy, to improve immunity, and to manage stress [5, 6]. Care should be given when using medications in the rehabilitation setting which cause either inadequate sleep or alternatively excessive somnolence.

In the chronic phase, helping the rehabilitation patient early on to plan meals, and to plan daily tasks such as exercise and food shopping, will help to emphasize the importance of a daily schedule, which should be as efficient as possible. Patients in all phases of rehabilitation often complain that they do not have time for specific tasks, which mostly involve self-care activities. The patient's daily schedule should allocate time for certain activities in regular increments, such as 15 min. Table 48.1 will demonstrate how to optimize the daily schedule:

Habits:

It is difficult for patients to change old habits, or to establish new ones, especially if there has been physical or emotional trauma with cognitive challenges, which are frequently seen in the rehabilitation setting. Behavior modification should be implemented incrementally. Patients should be discouraged from attempting sudden or dramatic change. Incremental lifestyle modification should begin with realistic goal setting, followed by analysis of current habits, and finally by strategizing how to implement chosen modifications.

Table 48.1 Activity table

Time of day	Activity	Notes
	Wake up	
	Breathing and stretching exercises	
	Breakfast	
	Work/other activities	
	Lunch (anytime from 12 noon to 1:30 pm)	
	Outside walk (15–30 min)	
	Work/other activities	
	Dinner (anytime from 6 pm to 7 pm)	
	Outside walk (15–30 min)	
	Activities	
	Bed time	

In the chronic outpatient setting, for example, if a patient does not regularly eat breakfast, the patient should be instructed to start with a cup of yogurt or a piece of fruit and then to build it up over a few weeks to a full hot breakfast.

If a patient does not regularly exercise, the patients should be instructed to initiate a chosen new physical activity once a week for 2 weeks, then increase frequency and intensity to twice a week until physical activity goals are realized. This should be carefully balanced with physical and/or occupational therapy objectives in the particular phase of rehabilitation the patients is in as well as realistic expectations based on the patient's impairment.

Development of new habits should be established over time, not overnight and should be accompanied by gradual reduction of bad habits (eating late at night, overeating, not having daily regular physical activities, not having enough sleep, etc.). These behavioral activities can also be extended to the patient's bad medical habits, which may have negative influences on their overall recovery.

Patients should be encouraged to maintain a journal where daily progress can be charted and analyzed retrospectively to analyze trends and to make adjustments as needed.

Patients should be counseled not to get discouraged if goals are not achieved as initially planned. Patients should be encouraged to acknowledge and to reflect upon positive progression and reminded of the importance of pacing to realize substantive and meaningful change.

Balanced Nutrition

Patients should be advised to maintain good eating habits, and off-cycle or excessive consumption of any food should be avoided. Nutrition should include a balanced spectrum of nutrients, which are the building blocks for cells, and should come from

a variety of food sources. Given global agricultural trade, availability of fresh produce has grown in most developed countries. However, when possible, patients should be advised to try and eat locally. In general, sourcing of food locally is most beneficial for patients, because of the following:

1. Bee pollination can lead to strengthened immunity and better tasting produce.
2. It is better to consume naturally ripened food, at its peak taste, and not food, which is preserved or matured artificially with ethylene gas.
3. It is better to follow seasonal eating, which means consuming foods that are grown naturally outdoors, instead of in a season-defying greenhouse.
4. The best nutrients are obtained when local produce is on the table very soon after it was harvested, which is when its nutritional value is still high [7].

When a person is generally healthy, lifestyle modifications include *nutrition management*. When a person is sick or in pain, lifestyle modifications include *diet therapy*. In both situations, attention should be paid to portion sizes, to consistency in food consumption, to quality of food, to combination of different foods, and finally in food preparation.

Patients should receive specific counseling on appropriate hydration. Liquid consumption should be adjusted to a patient's physical and mental load throughout the day, gender, weight, and height, and based on climate.

Many health issues can be treated by addressing nutritional intake through appropriate consumption of the vitamins, minerals, and amino acids, which are essential for proper nutrition. Table 48.2 illustrates the effects of some vitamins and minerals on some functions of the body [8–10]:

Weight Control

It is a fact that diets do not work [11]. However, behavior modification does work, because it is a long-term approach, which changes habits and challenges lifestyle. It works through the patient's mind [12–14]. Excessive or insufficient body mass affects all body systems. Improper weight has serious implications for the mind and psychological state of a person. Furthermore, it limits activity level because it influences energy level and vitality. To address weight control, one should start with assessment of digestive and endocrine systems.

If our digestive tract is not functioning properly, it is very difficult to regulate weight. For example, if a patient's natural flora is destroyed by medications, drugs, smoking, alcohol, or stress, bowel movements and elimination of toxins are not regular, and heartburn, irregularity, or change in consistency of urine and/or stool can result. If the endocrine system is imbalanced, such as when the thyroid gland does not work properly, it is hard to control weight as well.

For proper assessment, it is initially recommended to perform blood work, including CBC with auto differential, Lipid Panel with Direct LDL, Comprehensive Metabolic Panel, Vitamin B12, Vitamin D, Thyroid. Consultation with an endocrinologist

Table 48.2 Vitamins and minerals

Vitamin/mineral	Food sources	What it does in your body
Vitamin A	Low fat or skim milk dairy products; fortified cereals; green, deep yellow, and orange vegetables; deep yellow and orange fruits	Keeps skin, hair, and nails healthy; helps maintain healthy gums, bones, glands, and teeth; helps ward off infection
Vitamin B1 (thiamin)	Pork, fortified grains and cereals, seafood	Enhances energy by promoting metabolism of carbohydrates; promotes normal appetite, digestion, and proper nerve function
Vitamin B3 (niacin or nicotinic acid)	Poultry and seafood, seeds and nuts, potatoes, fortified whole grains and cereals	Required by many enzymes that convert food to energy; promotes normal appetite and digestion; promotes proper nerve function
Vitamin B5 (pantothenic acid)	Almost all plant and animal foods; also manufactured by intestinal bacteria	Essential in converting food to molecular forms needed by body; needed to manufacture adrenal hormones and chemicals to regulate nerve function
Vitamin B6 (pyridoxine)	Meats, fish, poultry; grains and cereals; spinach, sweet potatoes, white potatoes; bananas, prunes, watermelon	Essential to protein metabolism; helps form red blood cells; promotes proper nerve function
Vitamin B12 (Cobalamin)	Meat and poultry (especially calf's liver, venison, lean beef, lamb), seafood (especially sardines, snapper, salmon, scallops, shrimp, halibut), cheese, eggs	Builds genetic material; Needed by all cells; helps form red blood cells
Calcium	Dairy products, canned salmon (with bones), oysters, broccoli, tofu	Helps build strong bones and teeth; promotes proper muscle and nerve function; helps blood to clot
Phosphorus	Dairy products and egg yolks; meat, poultry, fish; legumes	Works with calcium to build and maintain healthy bones and teeth; helps maintain chemical balance; promotes proper muscle and nerve function
Copper	Lobster, organ meats, nuts, dried peas, beans, prunes, barley	Stimulates iron absorption; needed to make red blood cells, connective tissue, and nerve fibers

should be considered to rule out hypo- or hyperthyroidism, as well as consultation with a gastroenterologist to rule out disorders of the digestive system. Particular attention should be paid to frequency of bowel movements, which should be at least daily, proper hydration, exposure to probiotics (good bacteria), proper eating habits and nutrition, exercise routine, stress management, and pain management (if applicable).

Discipline and Goal Setting

Every patient is unique. Some patients need close instruction, some patients need a support group, and some patients are self-motivated and disciplined and do not need external support. In any case, there should be a systematic approach to all lifestyle modifications.

Secrets to Success

Pick the right time in your patient's rehabilitation path to suggest and to implement change. That is, the patient should be ready mentally to take an active role not only in the treatment but also in his/her lifestyle modification, despite having pain. There should be a conscious goal to feel better.

Help the patient with realistic goal setting.

Document all changes/goals first, then subdivide into categories, ranging from easy to difficult.

Advise the patient to select one difficult goal and one easy goal for 2 weeks and focus only on these two goals. If goals are met, advance to the next set of goals. If goals are not met, re-focus for an extended period of time, for approximately 1 month. The behavior modification program should take at least 6 months to a year.

Have your patient maintain a daily journal of food intake and exercise activities, which should include subjective assessment at the end of each day. Help your patient to plan grocery shopping, cooking times, meals, and activities, both social and physical.

Read food labels, to assess the following:

Serving size
Calories
Saturated fat content
Cholesterol
Sodium
Fiber
Sugar
Protein
Vitamins and minerals

Avoid daily weight assessment because it creates mental stress; when a patient participates in a proper exercise program and body composition changes, the muscles weigh more than fat. Perpetual use of a scale might be misleading and discouraging

Assess progress regularly through review of patient's daily journal and acknowledge progress in achieving goals.

Exercise and Physical Activitiy

Exercise should not cause persistent pain or increase the level of baseline pain. Pain is the language a body uses to communicate with the mind. To reduce pain, if available, water therapy can be used to facilitate exercises in a vertical (functional) position in the deep part of a pool to reduce gravitational forces. Once a patient's level of pain is significantly reduced or eliminated, exercises should be progressed to the shallow part of a pool, and then finally to land-based exercise program. Land-based exercises should include a dynamic progression from supine, to sitting, to standing-position [15].

Physical activity should be initiated by simple breathing and stretching exercises, which increase lung capacity and improve systemic blood circulation, which should occur over 5–10 min. Patients should be encouraged to engage family and friends in physical activities such as walking, which will increase likelihood of regular participation. Special attention should be paid to ergonomics, body alignment, and posture. In addition, patients should be advised to avoid damaging repetitive motion. Improper posture puts too much stress on the back and can lead to discomfort and damage. Good body mechanics mean practicing good posture during daily activities [15–17].

Stress Management

Most advanced Western lifestyles lead to an accumulation of stress. Unfortunately, stress management is not considered nor implemented as much as it is needed. In fact, stress relief is essential to achieving a healthier lifestyle. For example, therapeutic massage, which can be a very useful tool to combat stress is often viewed as a luxury, not a necessity. Massage affects the following:

1. Lowers heart rate, and cortisol and insulin levels
2. Encourages relaxation
3. Improves posture
4. Improves circulation
5. Lowers blood pressure
6. Relaxes muscles
7. Improves flexibility and range of motion
8. Promotes deeper and easier breathing
9. Relieves headaches
10. Strengthens the immune system
11. Enhances post-operative rehabilitation
12. Improves rehabilitation after injury [5, 16, 18].

Patients should be encouraged to create a list of "little pleasures", including activities that illicit joy, and should be advised to reference their list frequently, to

be reminded of its importance. For some patients, stress-relieving factors might include music therapy, yoga, exercise, or travel, and should be incorporated on a regular basis.

Acute, subacute, and chronic pain, whether it be constant or intermittent, contributes to stress. Proper pain management techniques using different approaches to reduce stress should be implemented. Stress and tension affect emotions and feelings. By expressing feelings to others, patients are able to better understand and to cope. Crying can also relieve tension. After exercise and physical activities, stress level is usually lowered and more manageable. Deep muscle relaxation reduces muscle tension as well as generalized mental anxiety. Patients should use meditation, deep breathing, acupuncture, and massage to enhance stress management.

It is important to emphasize the importance of sleep, which should include adequate quality (deep REM sleep) as well as adequate quantity of sleep. Sleep deprivation affects the body's immunity, concentration, and mood, and will increase level of stress [5, 6]. Patients should not wait for the cumulative effect of sleep deprivation to occur before adopting change.

The Effect of Nature

Nature provides a lot of remedies, which can be incorporated into lifestyle modification. Such natural remedies have been studied and accumulated by thousands of years and by different cultures. These include use of climates, mineral waters, muds, herbs, mineral salts, and plants. Specific examples include use of valerian root or kava-kava to improve sleep, use of *Aloe vera* to heal a scar tissue, use of calcium phosphate to relieve a sore throat, use of a dry climate to relieve asthma symptoms, use of mineral waters for digestive problems, and finally, use of mineral mud applications for arthritis [10].

Closing Statement

Planning is essential for lifestyle modifications. Use education and an arsenal of toolsto reduce and eliminate pain.

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Part X
Multi Modal Approach: Neuromodulation

Chapter 49
Spinal Cord Stimulation for the Treatment of Pain in the Rehabilitation Patient

Jonathan D. Carlson, Tory McJunkin, Kyle Walters, and Edward Swing

Introduction and Brief History

Inhibition of pain via electrical stimulation has a long history. As early as the first century A.D., the electric ray was used for treating pain resulting from conditions such as gout [1]. More recently, early eighteenth century electrotherapist John Wesley observed successful analgesic effects using light electrical shocks to treat the symptoms of conditions such as gout and sciatica. Further, electroacupuncture gained prevalence in the nineteenth century, as the combination of needling and electricity provided benefits for painful conditions [1].

Melzack and Wall's Gate Control Theory [2] provides the framework for the use of spinal cord stimulation in the treatment of chronic pain. The theory posits a system, in which pain signals traveling up the spinal cord are either blocked or allowed to continue to the brain. This system occurs in the dorsal horn of the spinal cord, where small-diameter fibers carry pain signals and large-diameter nerve fibers carry signals for skin senses such as touch. Increased activity of large-diameter fibers increases the activity of inhibitory interneurons in the dorsal horn. These inhibitory cells prevent pain signals from being sent to the brain. Conversely, the increased activity of small-diameter fibers decreases the activity of inhibitory interneurons, which opens the gate and allows pain signals to pass to the brain. Thus, the theory suggests that rapid stimulation of large fibers can control pain.

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Shealy and colleagues applied this theory in stimulation of the dorsal columns [3]. In their first case report, an electrode was implanted over a patient's dorsal column, which provided electrical stimulation. The patient reported paresthesia and significantly controlled pain [3]. Since then, spinal cord stimulation (SCS) has shown favorable effects for several indications. One study found that effects were most notable in neuropathic pain conditions, such as failed back surgery syndrome (FBSS), complex regional pain syndrome (CRPS), and multiple sclerosis (MS), in addition to peripheral vascular disease (PVD) [4]. This study found the syndromes with the poorest responses to SCS included cauda equina syndrome, as well as predominantly nociceptive bone and joint pain syndromes.

Pathophysiology

In the United States, spinal cord stimulation is most commonly used in patients with failed back surgery syndrome (FBSS), also known as post-laminectomy syndrome [5]. These are patients who, despite being treated surgically with procedures such as laminectomy, discectomy, and fusion, are still suffering from persistent pain in the back, neck, legs, or arms post-operatively. The rate of failure for such surgeries is surprising. A study by Javid and colleagues found that lumbar laminectomy was unsuccessful for 30% of patients with central canal stenosis [6]. Furthermore, a meta-analysis found that nearly three quarters (74.6%) of patients had residual pain after back surgery and that 12.5% underwent revision surgery [7]. Evidence suggests that SCS can be a favorable treatment modality in patients with FBSS. For example, SCS in addition to non-surgical conventional medical management was shown to significantly improve health-related quality of life compared to non-surgical conventional medical management alone [8]. Another study showed that SCS was more effective and less costly than repeat surgery in patients with FBSS [9].

SCS is also a common treatment option for complex regional pain syndrome (CRPS). CRPS, which was previously referred to as reflex sympathetic dystrophy, is a chronic pain condition characterized by intense burning and skin sensitivity, and is often accompanied by abnormal sweating, swelling, and discoloration of the affected limb. While the exact causes of the condition are not currently known, dysfunction of the central or peripheral nervous systems seems to be involved. In a randomized controlled trial, SCS in CRPS patients led to pain reduction at 24 months of follow-up, compared to no change of pain in the control group [10]. A study by Kumar et al. showed that 100% of patients receiving SCS for CRPS had successful long-term pain relief. This rate of success was higher than patients receiving SCS for treatment of FBSS, peripheral vascular disease, peripheral neuropathy, and multiple sclerosis [4].

Aside from providing relief from pain, evidence suggests that SCS may also improve blood flow in patients with peripheral vascular disease. In a review that included six studies and about 450 patients, treatment with SCS resulted in amputation occurring less often [11].

Basic Principles

Neuropathic pain, as defined by the International Association for the Study of Pain (IASP), involves pain that is caused by a lesion or disease of the somatosensory nervous system, whereas nociceptive pain arises from actual damage to non-neural tissue. According to the Gate Control Theory's explanation of the effects of SCS, whereby a nociceptive signal in the dorsal horn is inhibited by activation of fibers in the dorsal columns, nociceptive pain should be treated most effectively with SCS [12]. However, the literature suggests that SCS, and electrical stimulation of large nerve fibers more generally, is more effective for neuropathic than nociceptive pain [13, 14]. Many patients experience neuropathic pain that coexists with a nociceptive pain component [15].

Another distinction in types of pain can be drawn between axial and radicular pain. Axial pain refers to pain located specifically in the spine, such as the neck or back, whereas radicular pain involves persistent pain in the arm, shoulder, leg, buttock, or hip. SCS generally shows greater success in treating radicular pain, as opposed to axial pain [15, 16]. This is due, in part, to axial pain having a nociceptive component. However, advances have been made in treating axial pain, such as in the use of dual, parallel electrodes, and multipolar configurations [16, 17].

Because the effects of SCS can vary substantially from patient to patient, selection and screening are of the utmost importance. Aside from pathology and clinical symptoms, psychological testing is an important tool, which can be utilized to rule out major psychiatric disease and substance abuse, as these diagnoses are not conducive to successful SCS therapy [12]. Once a patient is evaluated physically and psychologically and deemed to be an appropriate candidate, it is common to implement a trial phase before implantation of a permanent system. The trial can be extremely short, in cases where testing is done via an open incision minutes before permanently implanting the system. In longer trials, percutaneous leads are placed that the patient can use for up to 1 month. The general consensus is that a trial of 3–8 days provides sufficient information for predicting success with a permanent implant [15]. One study concluded that acute 15-min intraoperative and prolonged 5-day screening trials have equivalent success in predicting long-term success of SCS for chronic low back or lower extremity pain [18]. If more that 50% relief is obtained from the trial, the patient is usually considered for implantation of the permanent system. After implantation, the device is often reprogrammed several times in an effort to optimize coverage of pain.

Common Techniques

Providing optimal stimulation coverage of targeted dermatomes involves appropriate lead placement. For example, it has been noted that stimulation delivered between T8 and T11 can provide effective therapy for low back pain [19]. Lower

extremity dermatomes can also be targeted with lead location between T9 and T11 [4]. Delivering stimulation to the neck and upper extremities involves electrode placement in the cervical region. Upper extremity CRPS has been successfully treated with electrode placement at C5-6 [20].

There are several stimulation technologies that can be used for SCS, including tonic, high-frequency, burst, and dorsal root ganglion stimulation. Each technology has its advantages and disadvantages.

In tonic stimulation, percutaneous or paddle electrode leads are connected to an internal pulse generator, which delivers tonic pulses that can be adjusted by altering frequency, amplitude, and pulse width. The goal is to make adjustments until paresthesia is felt by the patient in the painful area. Until the advent of more recent technology, it was widely held that the presence of paresthesia was required for pain relief [21]. While some patients do not mind the paresthesia, or even find it pleasant, others do not enjoy the feeling. Another disadvantage to tonic stimulation is that it has prevented the ability to conduct randomized, placebo-controlled studies as patients cannot be blinded to their condition [22].

Burst stimulation involves intermittent high-frequency stimulation, without the onset of paresthesia. This stimulation consists of closely spaced pulses of electrical energy. Compared to traditional stimulation, burst stimulation has produced better relief for both leg as well as back pain [22].

High-frequency stimulation is achieved by producing continuous stimulation at a particular frequency (e.g., 10 kHz) of electrical energy, which is higher than the range used in tonic stimulation. The mechanism behind this technology is that overactive wide dynamic range neurons, which are overactive in chronic pain conditions, are stimulated by high-frequency electrical energy. These neurons become desensitized, resulting in relief of pain [23]. Like burst stimulation, high-frequency stimulation produces no perceivable paresthesia in the patient. This technology has also shown evidence of effective treatment for both back and radicular leg pain [23]. In a study comparing high-frequency stimulation to conventional stimulation, 88% of patients preferred high frequency [19]. Aside from better pain relief, it is suggested that better sleep could account for this preference. It may be the case that patients using high-frequency stimulation are able to sleep without experiencing uncomfortable stimulation that results from body position changes [19].

Dorsal root ganglion (DRG) stimulation is a technique that can be beneficial for patients with pain in very specific or isolated dermatomes. An electrode is placed adjacent to the spinal ganglion, which produces paresthesia to a single dermatome [12]. With its ability to selectively target areas of pain, DRG can avoid paresthesia in non-painful areas. For example, for a patient experiencing chronic neuropathic pain in the foot, in order to relieve pain with traditional SCS, the patient would likely feel paresthesia all the way down the leg. This could be avoided with DRG, which would be especially beneficial for those patients who find the paresthesia unpleasant. DRG stimulation has provided effective relief for FBSS, CRPS, as well as localized pain in the back and extremities [24]. A randomized trial comparing traditional SCS and DRG stimulation for 155 patients, suffering from lower

extremity CRPS, found that DRG stimulation provided greater pain relief and less stimulation of non-painful areas than traditional SCS [25].

Historically, one challenge with SCS has been positional sensitivity. Changes in body position, such as with lying, sitting, and standing, can affect electrode contact with the spinal cord, which can result in perceptual changes in stimulation intensity [26, 27]. For example, with such changes, patients need to manually adjust their stimulation when moving from the sitting to the standing position. Recently, position-adaptive technology has been developed, which allows the SCS device to detect postural changes and to automatically adjust stimulation intensity accordingly. One technology uses an accelerometer-based algorithm to automatically adjust stimulation based on position (Restore® or Restore Advanced®, Medtronic Inc., Minneapolis, MN) [27]. In a study with patients comparing automatic versus manual adjustment of stimulation, patients preferred automatic adjustment for transitioning from standing to supine and from supine to standing [27].

Specific Applications to Patients in the Rehabilitation Setting

In most cases, SCS should not be utilized until a patient has experienced at least 6 months of conservative treatment with poor response [28]. Conservative treatment can include modalities, such as physical therapy, chiropractic, acupuncture, medication management, and interventional procedures, which include regional nerve blocks, rhizotomy, and epidural steroid injections. Certain exceptions to this guideline can be made for extreme conditions, such as CRPS, whereby early intervention is essential. In these cases, each step of conservative treatment should be expedited to be no longer than 2–3 weeks [29]. In an analysis of safety, appropriateness, time to fiscal neutrality, and efficacy, it was determined that SCS for CRPS should be considered earlier than opioid medication management in the patient's plan of care [30].

Evidence

In looking at an overview of randomized studies of SCS, the results are generally favorable. In a study on patients with FBSS, who received either SCS plus conventional medical management (CMM), as compared to CMM alone, almost half of SCS patients had more than 50% relief, as compared to 9% of the group receiving CMM alone [31]. In another study of SCS patients with FBSS, treated with either SCS or re-operation, almost half (47%) of the SCS group obtained more that 50% pain relief, as compared to about 12% of the re-operation group [32]. In a randomized prospective study for CRPS, patients being treated with SCS plus physical therapy obtained significantly more pain relief than patients being treated with only physical therapy [33]. In a recent meta-analysis that included 74 studies and over

Table 49.1 The published studies, by level of evidence, supporting the efficacy of spinal cord stimulation (SCS) for failed back surgery syndrome (FBSS), complex regional pain syndrome (CRPS), and peripheral vascular disease (PVD) [34]

Indication	Level of evidence
FBSS	I [9, 31]
	II-1 [16, 23]
	II-2 [28]
CRPS	I [10]
	II-2 [4]
PVD	II-1 [11]
	II-3 [28]

3000 patients with chronic back and leg pain, results revealed that 53% of patients obtained at least 50% pain relief at 24 months of follow-up, with a mean pain relief of 58% [34]. See Table 49.1.

Conclusion

For several decades, SCS has been gaining support and credibility as a safe and effective method for controlling chronic pain. Although debate exists regarding its mechanisms of action and long-term efficacy, its success has been demonstrated with a variety of conditions that usually involve a neuropathic pain component. With careful patient selection and appropriate testing prior to permanent implantation, SCS can provide substantial pain relief, improvement in quality of life, and reduction in use of pain medication. As technical advancements and accurate prognostic factors continue to develop, higher success rates for more patients can be possible in the future.

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Chapter 50
High-Density Spinal Cord Stimulation for the Treatment of Pain in the Rehabilitation Patient

Jay S. Grider and Michael Harned

Introduction

Spinal cord stimulation [SCS] was first introduced in 1967 with the concept that electrical impulses delivered directly to the dorsal horn of the spinal cord could result in depolarization of nociceptors, thereby reducing pain in subjects with neuropathic pain syndromes [1]. The stimulation was accomplished by the production of an electrical field, which transduced the flow of electricity [a faradaic reaction] into the flow of ions [non-faradaic reaction] in biologic tissue, creating depolarization within the targeted structures of the spinal cord and ultimately analgesia. This depolarization of the spinal cord produced what is commonly known as a paresthesia, or the tingling sensation, that is then manipulated to spread across the area of pain in the arms, trunk, lower back, or legs [1]. During trialing, the process of creating a paresthesia and manipulating the paresthesia to clinical advantage is called neurologic mapping and is often referred to as Holshiemer monitoring after Jan Holshiemer, who did extensive computer modeling of paresthesia and paresthetic effects on the spinal cord [1]. The creation of an electrical field resulting in a paresthesia has been, for over four decades, fundamental in the analgesia created by SCS [1].

The paresthesia is created by manipulating the three basic elements of SCS, which include frequency, which is how often the device delivers charge and thus depolarization; amplitude, which is the relative 'strength' of the charge delivered; and pulse width, which is how long the charge delivery lasts [2]. Conventional

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programing of these three parameters typically involves frequencies in the 40–80 Hz range, with occasional higher applications of frequency. Amplitude is adjusted until the patient feels the stimulation, with perception threshold being the amplitude at first detection and discomfort threshold being when the subject feels that the paresthesia transitions from pleasant or tolerable to noxious [2].

The difference between detection threshold and discomfort threshold comprises the therapeutic window of stimulation amplitude for that individual subject. Pulse width is adjusted to widen or to narrow the electrical field. As such, amplitude and pulse width have been the primary parameters adjusted during trialing and maintenance of SCS, with frequency being adjusted only to vary the 'coarseness' or 'smoothness' of the perceived stimulation. Low frequencies [20–40 Hz] result in many subjects feeling the individual pulse, whereas at higher frequencies, the pulses start to blend, which results in a tingling sensation without detection of individual pulses [2]. Increasingly, investigators have examined the effect of manipulating the long neglected parameter of frequency rate, with surprising results [3–7].

The concept of dramatically altering the frequency rate of pulses delivered has recently led to a change in the nomenclature of neuromodulation, describing the existing methods of SCS programming as 'conventional' stimulation, with newer platforms between 500 Hz up to 10,000 Hz, or platforms with higher-frequency bursts of stimulation being referred to 'high-frequency' [HF] stimulation [3–7]. Please refer to other chapters within the text on 10 K stimulation and burst stimulation for expanded details on these programming platforms.

As these HF stimulation platforms were being trialed in Europe and reported in the United States, several investigators in the United States began to independently explore the maximum capabilities of existing stimulation technology to see if the frequencies achieved with currently available systems in the upper frequency ranges benefited patients [7]. While most programming in the United States is in the 20–120 Hz range, existing technology can increase the frequency of currently available systems to >1000 Hz. This capability has expanded the possibility of delivering more charge per second to the spinal cord, often in a sub-perception threshold amplitude, with a net result of greater charge delivered per second than conventional stimulation, without the higher frequencies of 10 K stimulation, or the burst patterns described by DeRidder [3, 5].

This has led many in neuromodulation to begin considering the pulses created by the SCS system as 'charge dose' delivered to the spinal cord, analogous to the more familiar concept of medication dose daily in intrathecal drug delivery (Fig. 50.1) [7, 8]. In this case, the concept of dose would be related to charge [dose] per second. As such, delivery of maximum frequency achievable by a conventional SCS, with manipulation of amplitude and pulse width as needed, would increase the time within any given second that charge [dose] is delivered; therefore, compared to conventional SCS, a higher density of charge delivered would be created. This concept became known as high-density spinal cord stimulation or HD stimulation [Medtronic Inc.; Minneapolis, MN] [9].

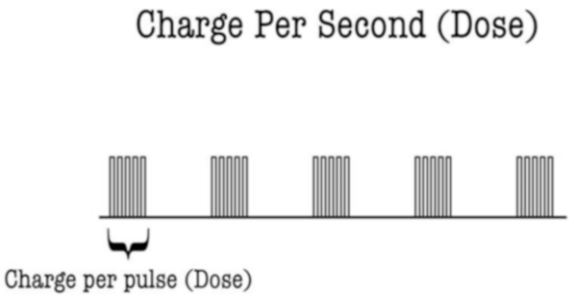

Fig. 50.1 The concept of charge as dose is illustrated. In this example, each pulse can be thought of as a therapeutic dose or the charges per second as a total dose

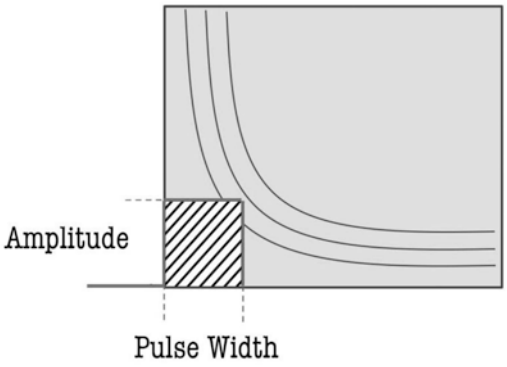

Fig. 50.2 Strength duration curve at a given amplitude or pulse

Description of High-Density Stimulation

As seen in Fig. 50.2, whenever the amplitude and pulse width of various programs are plotted, a strength-duration curve is created. The concepts underpinning the strength-duration curve have been the mainstay of convention SCS programming for several decades. Whenever frequency is added into the framework, the focus begins to shift from strength duration to one of charge delivered per second. Each individual strength-duration pulse added to the number of these pulses in a given second results in a duty cycle [pulse density] or amount of time during each second that charge is being delivered. In conventional SCS, charge is not being delivered during the vast majority of time during a second [Fig. 50.3]. Increasing charge density with higher-frequency stimulation creates more time in charge delivery mode. As can be seen in this example, conventional stimulation at 50 Hz and 400 μs creates charge for significantly lesser time during the 1 s time period than does the subsequent example of 300 Hz at 400 μs. This would be analogous to a radio station that played five songs per hour with no other programming. The time between songs would be dead air. Increasing charge density in SCS decreases the amount of 'dead air', which is hypothesized to change treatment responses.

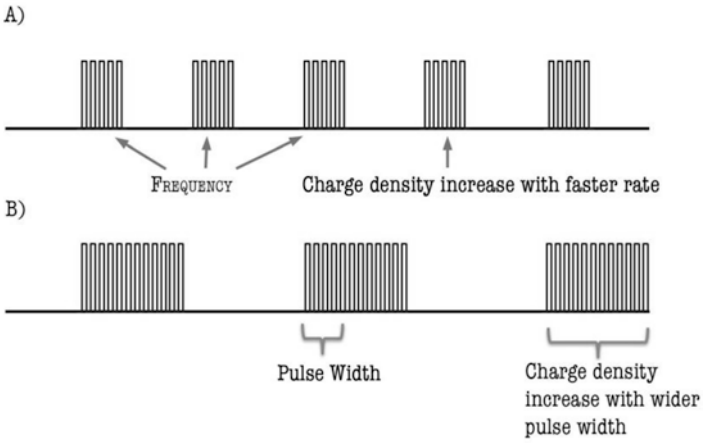

Fig. 50.3 More charge can be delivered per second by (*panel A*) increasing frequency of charge delivered or (*panel B*) increasing pulse width

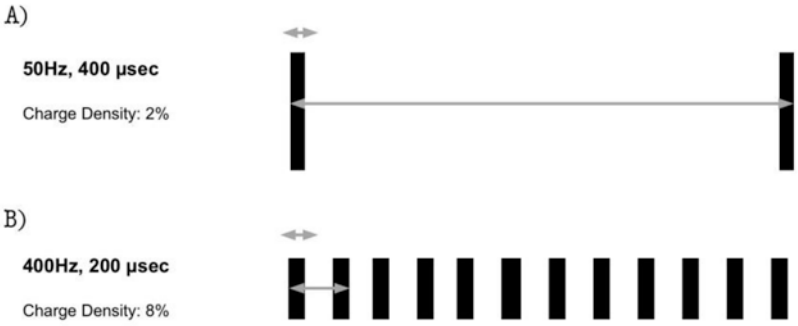

Fig. 50.4 Duty cycle (charge density) can be influenced by increasing frequency, pulse width or both

The duty cycle, demonstrated in Fig. 50.4, can be altered by either increasing pulse width or frequency and either strategy will result in more time during the given second, whenever charge is being delivered. In Fig. 50.5, various scenarios are presented which demonstrate how to calculate the duty cycle [pulse density] of higher-frequency stimulation platforms. For example, a frequency of 200 Hz, with pulse width of 1000 µs per pulse, would result in a duty cycle of 20% [200 Hz × 1000 µs=200,000 µs of charge delivered in 1 s]. Since there are one million microseconds in 1 s, the time of charge delivery [in this example 200,000 µs] divided by the total number of microseconds in 1 s is 0.2 or 20%. This simple calculation allows one to determine the total duty cycle of a stimulation platform. Likewise, example two in Fig. 50.5, with a frequency of 500 Hz and pulse width duration of 500 µs, results in a duty cycle of 0.25 or 25% [{500 Hz × 500 µs}/1,000,000 µs in 1 s= 0.25]. Currently available SCS systems can produce 1200 Hz at 200 µs, resulting in a duty cycle of

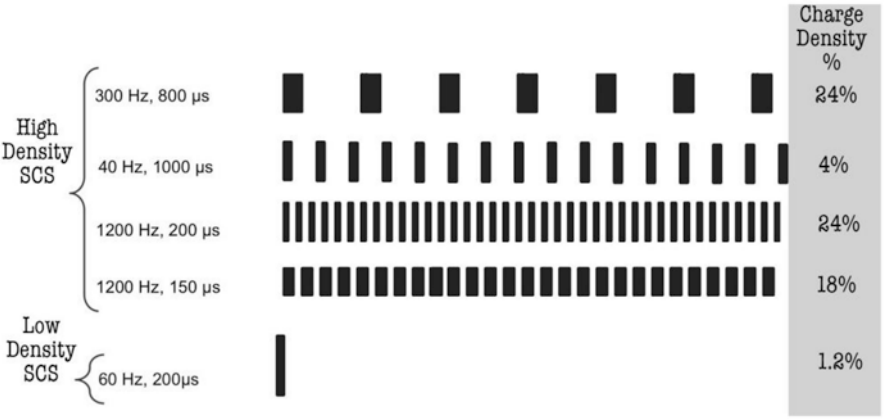

Fig. 50.5 Dosing strategies: point density

24%. Though not displayed in Fig. 50.3, one can easily calculate the duty cycle of the 10,000 Hz stimulation platform and [10,000 Hz × 30 μs] as 30%.

Some investigators began describing conventional or tonic SCS as low density, which would correspond to <5% duty cycle [i.e. less than 5% of a second is occupied by charge delivery], while high-density stimulation platforms deliver charge for >20% of the duty cycle [20% of the second consists of charge delivery] [7]. From a biophysiologic standpoint, the rationale is described as follows: once a nerve was stimulated, it would have a relative refractory period, during which repeat delivery of charge would be non-beneficial. However, investigators discovered that higher-frequency stimulation may activate different neurons within the dorsal horn giving differing clinical results. The higher duty cycle achieved may stimulate the wide dynamic range neurons of the dorsal horn [3, 10]. Other investigators postulate that since some neurons within the nervous system deliver action potentials in bursts, while others produce a tonic pattern, short bursts of high-frequency stimulation may improve clinical outcome [5]. It has been postulated that these patterns of activation within the dorsal horn may account for the observations that better analgesia can be obtained often without the presence or perception of paresthesia. While both 10,000 Hz stimulation and burst stimulation platforms are working through hypothetically differing mechanisms, they each have duty cycles above 20% and fall within the high-density conceptualization.

Literature Review

The higher frequency and ultimately higher duty cycle SCS platforms have increasing evidence, which suggests that multiple approaches can have efficacy. Recent work on the subject comes both from the laboratory and from clinical studies.

Animal Studies

As data began appearing with regard to 10 K Hz stimulation and burst stimulation models, investigators began examining the role of higher-frequency and charge density stimulation in animals. Schecter and colleagues, in an animal model of neuropathic pain, examined the effects of 50 Hz [conventional stimulation], 1 K, and 10 K Hz stimulation [10]. This study suggested that both 1 and 10 K Hz stimulation were significantly different than 50 Hz and sham, with 50 Hz providing some improvement over sham as well. This preliminary report also suggested a latency of onset of maximal result for the 50 Hz group, while the 1 K and 10 K Hz group had relatively immediate effects. Additionally, there was a difference in response to lower- and higher-intensity [corollary to differing amplitudes] stimulation. Taken together, the findings of differing times of onset, which include convention frequencies slower in onset of analgesia than higher frequency, and differing response to intensity of stimulation, which include higher-frequency stimulation responding to lower amplitude application required than the conventional or 50 Hz group, suggest that high-frequency stimulation is acting via a different mechanism to produce analgesia than conventional 50 Hz stimulation. An important implication of this animal study is that 1 K and 10 K stimulation performed similarly to animal models of hypersensitivity and neuropathic pain [10, 11].

In contrast, Song, Linderoth and colleagues, in a series of elegant experiments suggested that in monophasic stimulation, which includes only the positive amplitude stimulation mode, 50, 500, 1 K and 10 K Hz stimulation performed similarly in a 'sub-paresthetic' rat model of inflammation, acute nociceptive pain and neuropathic pain [12–14]. A criticism of this and previous studies from this laboratory centered on the monophasic application of stimulation; however, the group subsequently demonstrated similar lack of difference between conventional and high-frequency stimulation. In the 2015 report, the same authors acknowledge that there are multiple methods to increase charge delivery to the neural interface and that many subsequent experimental designs will be created to conclusively examine the issue [15]. The fact that high-frequency stimulation applied over the dorsal horn and to peripheral nerves gives differing responses also demonstrate that further work is required to fully understand the neuronal effects of increased charge delivery to the neural interface [12–15].

Clinical Studies

The clinical data for 10 K Hz and burst stimulation are covered in other chapters within the book; thus, this chapter centers on studies that fit the description of high-density stimulation, without falling into the 10 K and burst categories. Case studies describing the efficacy of stimulation above 1 K Hz, without paresthesia, have been reported in abstract form at the North American Neuromodulation Society annual

meeting. These reports were soon followed by the first randomized controlled double-blinded fashion [7].

Perrchoud and colleagues performed a small-scale [n=33], randomized controlled trial in which 5 K Hz stimulation, with a pulse width of 60 μs [charge density of 30%], did not have greater effectiveness with regard to VAS and other measures of effectiveness, as compared to the sham non-stimulation period. This study stands in sharp contradistinction to the work done with 10 K and burst stimulation [6].

A more recent study that employs a pure high-density programing platform from a conventional commercially available stimulation system, using parameters of 1200 Hz, 200 μs, and amplitudes set just below perception threshold also demonstrated very mixed results. Of the fifteen subjects enrolled, only four found sub-threshold high-density stimulation to be efficacious [8]. Those four subjects were subsequently enrolled in randomized crossover arm and at the end of the test period the subjects were found to have superior results with high-density stimulation, as compared to the sham non-stimulation period. The authors conclude that the lack of paresthesia is advantageous, as the data from those four subjects demonstrates less preoccupation with pain and focus on treatment of pain, with the absence of paresthesia. While this conclusion is likely true, little mention is made of the high dissatisfaction rate of the larger study population, who rejected high-density sub-threshold stimulation prior to randomization. Taken together, these two small-scale studies suggest that there is a physiologic principle underlying the higher-frequency stimulation systems, which goes beyond mere charge density [8].

Also recently adding to the complexity of analysis of differing stimulation platforms, Knife and colleagues compared 10 K stimulation to burst stimulation and found that they achieved similar results with regard to analgesia for neuropathic extremity pain and also for nociceptive low back pain. Around the same period, De Ridder also published data, which supports the proposed theory that burst stimulation may be working through different neural pathways than tonic stimulation. In this study, both tonic and burst stimulation work through descending inhibitory pathways and ascending lateral pathways; however, burst stimulation may also be working through direct modulation of medial pain pathways of the ascending spinothalamic tract, which provides an important and wholly separate outcome by bringing ascending pain information into better balance with descending pathways; thus, it decreases the spontaneous firing of the hyperdynamic facilitated segments [16].

Interestingly, another recent study has suggested that burst stimulation patterns and 10 K Hz stimulation have similar efficacy, with regard to both low back pain and neuropathic leg pain, in subjects with failed back surgery syndrome [17]. Though admittedly a small study, the similar outcomes for low back and leg pain have important implications for the concept of high-density stimulation [17]. The burst stimulation pattern would have a calculated charge density of 4% [{40 Hz × 1000 μs}/1,000,000 μs], while the 10 K stimulation had the previously demonstrated charge density of 30%. While only one study, this head-to-head comparison would suggest that charge density is not the overriding factor in obtaining clinical efficacy for low back and leg pain in these advanced stimulation platforms.

Conclusion

While the higher-frequency stimulation systems with manipulation of pulse width do increase the charge density and provide the ability to deliver more charge to the neural interface, there is still much that is not known about the biophysiology of these advanced stimulation platforms. The exact mechanisms of how higher frequency or charge density creates differing clinical results from conventional SCS is unknown, as is the ideal frequency range for stimulation parameters in the clinical setting. Animal data has revealed some conflicting results, with one study suggesting no additional benefit above 1 K Hz, while the limited clinical data that is available suggests that higher charge density [>20%] alone does not produce better clinical outcomes.

If the concept of increased duty cycle leading to greater charge density delivered does hold merit, the Perrchoud study is particularly confusing, as a 30% duty cycle [5 K Hz × 60 μs] was not efficacious, whereas others have shown that a 30% duty cycle [10 K Hz × 30 μs] is efficacious [3, 6]. This conclusion is further supported by the head-to-head comparison of burst and 10 K stimulation, with efficacy obtained with low and high charge density [17]. Clearly, further study is required to answer the question of whether the improved clinical outcomes of the non-conventional stimulation patterns are a charge density phenomenon, or if frequency of stimulation truly is a key factor in differential clinical effectiveness for axial low back pain.

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Recommended Readings

Knife TM, Pintea B, Link C et al. High frequency [10 kHz] or burst spinal cord stimulation in failed back surgery syndrome patients with predominant back pain: Preliminary data from a prospective observational study. Neuromodulation. 2016 Jan 13. [Epub ahead of print].
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Chapter 51
Burst Spinal Cord Stimulation for the Treatment of Pain in the Rehabilitation Patient

Lucas W. Campos, Jason E. Pope, and Timothy R. Deer

Introduction

Chronic intractable pain has been present since the human condition came into being thousands of years ago. Acutely, pain is a warning that tissue damage is occurring; spinal reflexes take over to rescue us from the cause of that damage. Chronic pain gives those same warning signals, without actual harm occurring. It is estimated that approximately 100 million Americans suffer from chronic pain [1]. As it is so pervasive, the subject of chronic pain has been the subject of study for philosophers and thinkers, as far back as the ancient Greeks. In fact, the word "pain" is derived from the name of the Greek Goddess of Revenge, Poine, who was sent to punish the mortal fools who had angered the gods. In more modern times, the theory of pain was the subject of bitter controversy. In the late 1800s, there were at least two opposing theories on the processing of pain. The first was the Specificity Theory, which held that pain is a specific modality like vision or hearing, "with its own central and peripheral apparatus." [2] The second was the Pattern Theory, which maintained that the nerve impulse pattern of pain was produced by intense stimulation of nonspecific receptors, since "there are no specific fibers and no specific endings." [3]

These theories were derived from original ideas by von Frey and Goldscheider in 1894. These staunch theories challenged Melzack and Wall as they published their new theory on the transmission of pain signals in the journal *Science* in 1965. Their new idea was called the "Gate Control Theory," which posited that nerve impulses

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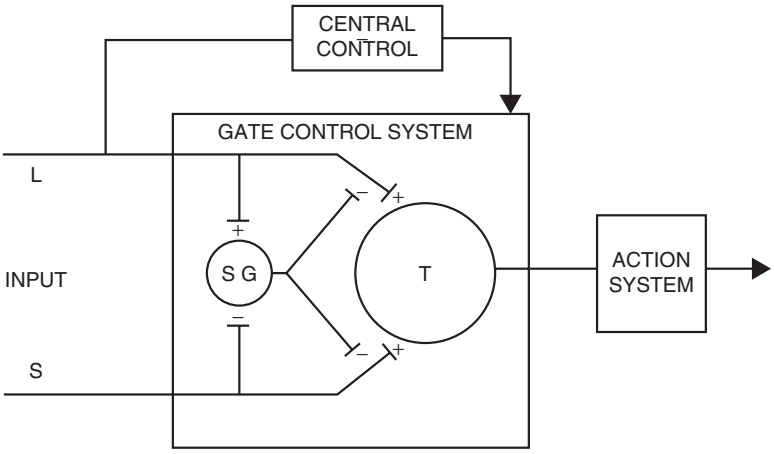

Fig. 51.1 Schematic diagram of the gate control theory of pain mechanisms: *L* the large-diameter fibers, *S* the small-diameter fibers. The fibers project to the substantia gelatinosa (*SG*) and first central transmission (*T*) cells. The inhibitory effect exerted by SG on the afferent fiber terminals is increased by activity in *L* fibers and decreased by activity in *S* fibers. The central control trigger is represented by a line running from the large-fiber system to the central control mechanisms: these mechanisms, in turn, project back to the gate control system. The *T* cells project to the entry cells of the action system. + excitation, − inhibition [3]

entering the spinal cord in large cutaneous nerve fibers came under the influence of a "control mechanism," while the impulses were still in the "terminal arborization of the afferent fiber." (Fig. 51.1) [3] This control mechanism determined the effectiveness of entering nerve impulses on central spinal cord cells in the substantia gelatinosa. Their theory believed that depolarization of the large fibers in lamina II could produce a blockade of the signals transmitted to the terminal central projections of pain fibers [4].

Based on this theory, a new technological application was then forged by the neurosurgeon C. Normal Shealy. Dr. Shealy extrapolated that most chronic pain signals projected from diffusely organized pain fibers in the periphery and concentrated their branches with the larger diameter A fibers upon entering spinal cord. Using the ideas from the Gate Control Theory, he applied electrodes to the spinal cord to focus on stimulating the dorsal columns, where the large fibers were also compactly arranged and could induce an "electronarcosis." [5, 6] When a pulsed D.C. current of 2 mamps, at 0.3 volts, programmed at 50 cycles per second, was applied to a dorsal column electrode over the cervical cord, animals could be awake and could tolerate noxious stimuli, such as tail pinching or intense heat applied to their ears, with no apparent distress [5, 6].

Later research found out just how important the A fibers were in the pathology of medically intractable neuropathic pain. Researchers found that, in the absence of the large A fibers, the small unmyelinated C fibers started to fire spontaneously in a burst pattern or in a series of rapid action potentials, followed by a period of quiescence [7]. Thus, without the inhibitory presence of the A fibers, the spontaneous

firing of the C fibers produced hyperalgesia, which subsequently lead to the development of neuropathic pain. Therefore, by activating these A fibers, as with spinal cord stimulation, the pain generating activity of the C fibers could be overpowered, which would result in analgesia [8]. Electrical stimulation is essential, as these A fibers are normally inactive at baseline.

Neuropathic pain is very well treated using spinal cord stimulation. Conditions that lead to neuropathic pain include diabetic neuropathy, failed back surgery syndrome, complex regional pain syndrome, ischemic limb pain, post-herpetic neuralgia, acute herpes zoster pain, refractory angina, and abdominal pain resulting from chronic pancreatitis [9]. The mechanism of spinal cord stimulation treatment is still not well understood, but it seems to involve a combination of local spinal and supraspinal mechanisms. At the spinal level, the ascending dorsal column fibers, as well as the descending opioidergic and serotoninergic [10] pain modulatory systems, might be implicated in the pain-suppressing effect [11]. Spinal cord stimulation is also associated with enhanced gamma aminobutyric acid, acetylcholine release, and reduced glutamate transmission in the dorsal horn [12].

To achieve pain relief for these painful conditions, factors such as the configuration of active electrodes, the stimulation frequency, pulse width, and pulse amplitude are adjusted to the patient's needs. The electrical stimulation of the large-diameter fibers in the dorsal columns elicits tingling sensations (paresthesias) in most patients. These paresthesia perceptions vary greatly among patients and can be the source of consternation. Some patients reject the device based on these paresthesias and others prefer to feel them so that they know their pain is being treated [13].

After a trial of the implanted electrodes has shown that a patient's pain will be significantly reduced and that the patient's function will be subsequently increased with the epidural lead configuration and amount of electrical energy required, an implantable pulse generator (IPG) is placed. The generator utilizes either a constant current (CC) or a constant voltage (CV) power source. A CC source supplies current to the tissue by adjusting the voltage, in response to impedance resulting from lead positioning, the presence of fibrous encapsulation, and the presence of scar tissue [14]. A CV source adjusts current in response to impedance, thereby maintaining a constant voltage. These changes in impedance will impact stimulation strength during a stimulus pulse, as well as the efficacy of stimulation over the long term [15]. Both systems produce paresthesia and both systems have been shown to effectively treat chronic pain. However, recent evidence suggests that patients prefer CC over CV systems. In a recent study, patients previously implanted with a CV spinal cord stimulation (SCS) system for chronic pain of the trunk or limbs were switched to a CC system, and patient preference was then assessed [9]. Nearly all patients preferred CC stimulation, describing it as more comfortable and noting it to provide better pain relief.

Why patients prefer CC over CV stimulation remains unresolved. One thought is that the pulse shape generated by CV is spiked-shaped and steepens with the rise of impedance at the beginning of the pulse. CC sources produce a smooth, rectangular-shaped voltage pulse in response to increased impedance (see Fig. 51.2). These

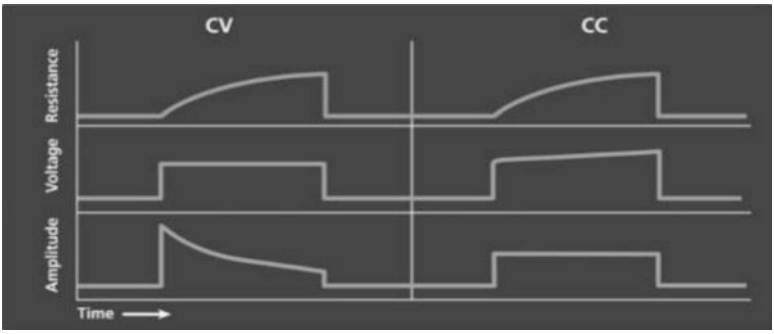

Fig. 51.2 Constant voltage (CV) and constant current (CC) pulse shapes in response to residence

subtle changes in waveforms may selectively activate nerve fibers of varying diameters under specific conditions [16]. For example, spiked-shaped pulses have been shown to selectively activate small myelinated fibers, as well as un-myelinated C fibers, without activation of the larger Aβ fibers [9]. So, large spiked pulses, generated in response to high impedance, may not be tolerable, as they are activating some of C and A-delta fibers, which could result in painful stimulation at the beginning of the pulse.

Pulse shape is one factor that determines nerve fiber response to SCS. Another essential factor is the frequency of the pulses used to activate the large fibers in the dorsal columns. The frequencies of SCS impulses that are most often used are usually in the range of 50 Hz but can vary between 30 and 120 Hz. New types of stimulation paradigms for SCS have used high-frequency stimulation up to 10 kHz [17]. The 10 kHz setting is a very energy demanding form of stimulation, which taxes the IPG battery life, requiring frequent charging of the device. An ideal alternative would be a stimulation paradigm that combined elements of high-frequency stimulation with the less energy demanding requirements of tonic stimulation. Burst stimulation offers a more concise signal transmission, resulting in a waveform that allows for passive discharge during the recovery phase between each pulse within the burst pulse train, and between each group of burst pulse trains. This differs from cycling, as cycling requires an active discharge in the recovery phase. The DeRidder burst waveform uses pulse trains of five high-frequency spike pulses at 500 Hz, occurring 40 times per second [13].

Burst stimulation mirrors some of the neuronal firing patterns in the spinal cord. These neurons fire in groups of action potentials, followed by periods of quiescence, just like the burst program generated by the IPG. Other neurons, at the same stage of sensory processing, fire in a tonic or continuous manner. These neuronal languages are transmitted as firing patterns and allow communication from the spinal cord to the brain. To intervene effectively, an SCS device should speak the same language. The experimental data extracted from laboratory and clinical studies suggests that both bursting and tonically firing neurons efficiently transmit information to the thalamus (Fig. 51.3) [18, 19]. The laboratory animal studies suggest that burst

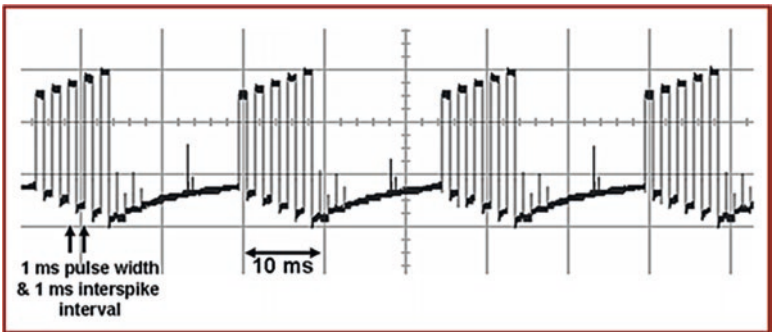

Fig. 51.3 Constant current burst mode (mA): 1-ms spikes with a 1-ms spike interval (500-Hz spike mode) and 5-ms charge balance firing at 40 Hz (40-Hz burst mode). Stimulation delivered by the Eon Implantable Pulse General (Advanced Neuromodulation Systems, Inc., Plano, Texas) via a custom-made program [18]

firing is more powerful than tonic firing in activating the cerebral cortex [20]. These studies have been interpreted as showing that burst activation requires less temporal integration and may activate dormant neurons, not otherwise activated by tonic stimulation [21].

Evidence

When applied to the spinal cord, burst stimulation delivers paresthesia-free stimulation, which some patients find to be more comfortable, as opposed to the vibrations felt during tonic stimulation. The landmark clinical trial, performed in the United States, identified a place for both the paresthesia and the paresthesia-free modality. In addition, this finding allowed for the capability to design double-blind, placebo-controlled studies of this burst pattern, in order to test its clinical effectiveness. The lack of paresthesia meant that patients and researchers would be unable to tell when the IPG was active, allowing for analysis between placebo and burst stimulation [18]. Studies can now be designed to test the hypothesis that the more physiologic burst firing pattern treats neuropathic pain more effectively than tonic firing patterns [8].

One study examined 48 patients, with at least 6 months of conventional tonic stimulation, and changed their IPG programming to burst stimulation for a period of 2 weeks. They were classified into three different groups: one cross-section of patients with painful diabetic neuropathy (PDN), a cross-section of failed back surgery syndrome (FBSS) patients, and finally, a cross section of FBSS patients who had become poor responders (PR) to SCS. Visual analog scale scores for pain were assessed prior to implantation with tonic stimulation, and after 2 weeks of burst stimulation. The results of this study showed that burst stimulation caused pain reduction in almost all patients. On average, burst stimulation lead to greater pain reduction in all three patient groups, as compared to tonic stimulation. In total,

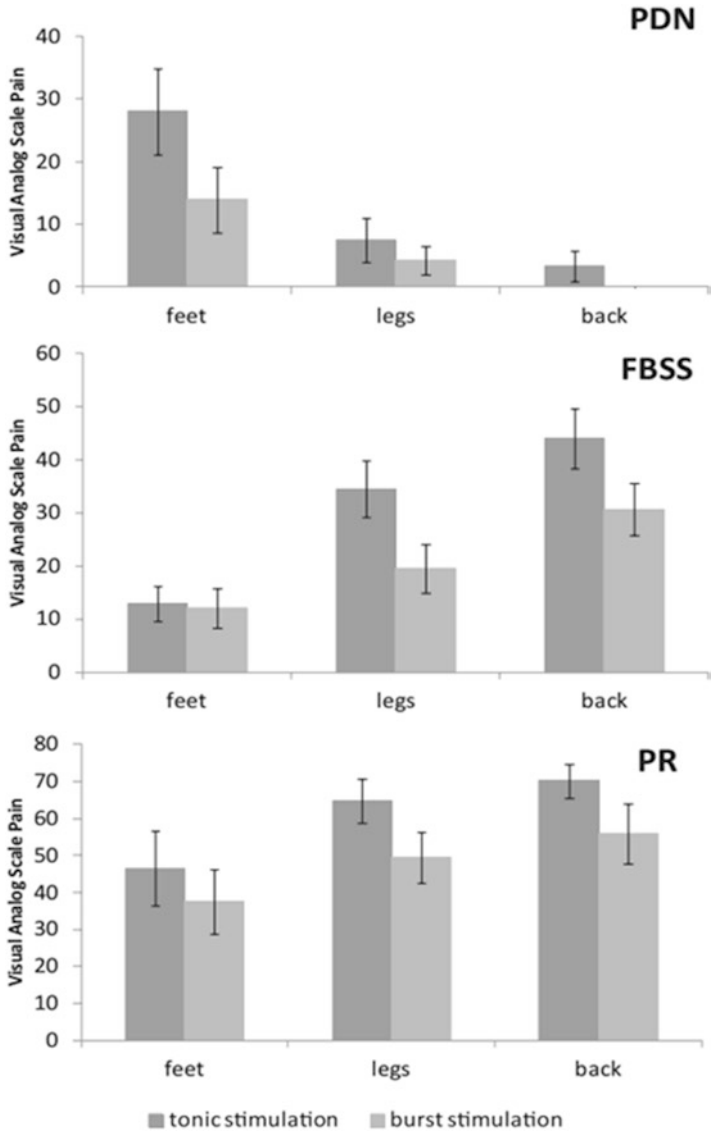

Fig. 51.4 VAS scores for pain of the patients with painful diabetic neuropathy (PDN), failed back surgery syndrome (FBSS), and the poor responders (PR) perceived in their feet, legs, and back, with tonic and burst stimulation. Bars represent the average pain score in a body part; error bars represent standard errors [13]

about 60% of patients (67% for PDN, 58% for FBSS, and 50% for the PR group) experienced further pain reduction when applying burst stimulation, as compared to tonic stimulation. An increase in perceived pain reduction with burst stimulation started after 1–7 days (Fig. 51.4) [13].

In addition to the spinal cord, the thalamus communicates to the cortex in a burst firing pattern [22]. Burst generated activity from the SCS mimics this thalamocortical firing pattern. The activation of specific regions of the thalamus by the burst stimulation initiated in the spinal cord appears to exploit another pathway, which further reduces the patient's affective response to pain. This hypothesis is supported by electroencephalogram recordings made during placebo, burst, and tonic stimulation [23]. This effect takes time to reach its full potential, as seen in examinations during a multi-week trial between burst and tonic stimulation. One study found that in a 1-week trial, burst stimulation was no better than tonic stimulation for leg and back pain; however, over a longer period, burst stimulation was superior to tonic for pain suppression, which was possibly due to the affective mechanism [24].

Burst stimulation seems to have a dramatically different effect on the attention paid to pain and pain changes, analogous to the effect of a cingulotomy [25]. It is known that attention to pain is mediated via the anterior cingulate cortex. In one study, the use of functional magnetic resonance imaging (fMRI), which was performed during SCS, has demonstrated that tonic stimulation modulates, predominantly, the lateral pain system, which includes the primary sensorimotor area, the posterior insula, and the secondary somatosensory cortex [26]. Burst stimulation activates not only the lateral pathway but also the medial pain pathway transmission system, which stimulates the cingulate cortex. Based on these results, it can be hypothesized that burst stimulation not only modulates the lateral discriminatory pain system but also the medial affective/attentional pain system. The mechanisms of pain suppression during burst stimulation combine to allow more patients to find relief when tonic stimulation has failed.

Another study has shown that burst stimulation can rescue about 60% of SCS failure patients who do not respond to tonic stimulation [24]. This predicts yet another benefit of burst stimulation, in that it may be better at improving long-standing pain when tonic SCS becomes dramatically less effective over time [27]. The results from this study by De Ridder et al. suggest that there is no reason to exclude patients with long-term pain from a trial of SCS. Indeed, some patients who had suffered pain for over 20 years prior to implantation had very good pain suppression effects with burst stimulation. Further analysis demonstrated that burst stimulation was superior to tonic stimulation, irrespective of how long the patients experienced pain prior to implantation. This shows that modulating the affective and attentional component of pain, via the medial pain pathway, can bring relief to those with decades of pain. De Ridder's study demonstrated that even though patients were only stimulated for 2 weeks, this duration was long enough to permit a large degree of pain suppression [8].

There are other important factors that predict successful outcomes with burst or tonic stimulation, such as selecting the patients most likely to benefit. There are certain patient characteristics, which make successful pain reduction more likely, and others that predict a less favorable outcome. First, a neuromodulation provider must be sure to establish realistic goals and patient expectations regarding treatment. The patient must understand that success with SCS is typically defined as a 50% or greater reduction in pain, leading to an improvement in function. In addition,

patients must possess the cognitive ability to understand the device's purpose and how to manage the various stimulation patterns and settings available. Without these mental faculties, the therapy is destined to fail.

Cognition is affected by psychological factors, which, in and of themselves, can be predictive of successful therapy. These psychological factors can predict a poor response, even when the procedure is clinically indicated and the procedure is performed perfectly. The analysis necessary to assess psychological readiness for SCS is still highly controversial, because of considerable differences in the design of different studies and the opinions generated by various investigators [28].

This problem has been recognized for some time. One series of recommendations came from the European Federation of IASP Chapters (EFIC), which in 1998 presented a consensus document on neuromodulation treatment, that established exclusion criteria for SCS. The consensus was that major psychiatric disorders, which included active psychosis, severe depression, hypochondriasis, and somatization disorder predicted failure. This was based on earlier studies, which suggested that anxiety (either trait or state), other mood disorders, active suicidal behavior, active homicidal behavior, serious alcohol or drug addiction problems, and severe sleep disturbance should exclude patients from therapy [29]. Other studies predicted therapy failure in patients showing poor medical compliance, lack of appropriate social support, history of drug and/or alcohol abuse, and drug-seeking behavior [30]. Some contraindications can be more insidious than others and can be missed by practitioners performing psychosocial evaluations. One example includes somatoform disorders, which are characterized by the presence of physical symptoms suggesting a medical condition, but in fact are derived from a patient's inability to accept unresolved emotional issues [28]. Another example involves personality disorders, which include borderline, avoidant, dependent, and obsessive-compulsive personality disorders. Thus, effective psychological screening should include both a personal structured psychological interview and appropriate psychometric testing to formalize a meaningful diagnosis; however, providers are still sometimes unable to predict, with certainty, which patients will do well with SCS and which will not [28].

In addition, there are physical characteristics that must be considered prior to electrode implantation. Patients should have thoracic imaging to ensure that there is adequate space to accommodate the device, without producing iatrogenic spinal cord compression. These include flexion and extension X-rays, which should assess for scoliosis, as well as severe anterior or retrolisthesis, which may obviate the need for corrective spine surgery instead of SCS. An MRI would also help to determine the presence of severe soft tissue disturbances, such as ligamentum flavum hypertrophy or severe epidural lipomatosis. Any sign of local infection near the surgical site, sepsis, coagulopathy, or condition that prevents fluoroscopic needle guidance or appropriate consent should be avoided.

Other important patient indications for neurostimulation therapy include selecting patients with conditions that will respond to SCS. Patients with neuropathic back pain must be diagnosed accurately for a proper determination to be made. The differential diagnosis of axial neuropathic back pain, not associated with prior surgery,

is extensive and includes vertebral body compression fracture, discogenic pain, facet arthropathy, and sacroiliac joint arthropathy. Less common causes of chronic low back pain include spinal stenosis, spondylolisthesis, and myofascial pain syndrome [31]. Investigations have found that axial low back pain in the non-operated back affects 60–80% of people at some point in their lives, with approximately 45% of these attributed to a discogenic source, 30% attributed to facet arthropathy pain [25–28], and 10–38% estimated to be from sacroiliac joint arthropathy [32, 33]. Other indications for spinal cord stimulation include radiculopathy, neuropathy, amputation pain, and vascular disease [34].

Recently, the problem has not been with finding conditions that will respond to SCS, but rather with the timing when neurostimulation should be used. Neurostimulation has historically been accepted as a last resort or therapy second line to surgery. Many patients are put on high doses of systemic opioids prior to consideration of neuromodulation. This practice generally occurred before the development of newer innovations, such as high-frequency stimulation, burst stimulation, peripheral field stimulation, and combination or hybrid stimulation. These advances will challenge the order of existing treatment algorithms, surrounding the treatment of chronic pain [35].

Since spinal cord stimulation technology was introduced in 1967, which was initially based on the gate control mechanism proposed by Melzack and Wall. This theory showed that activity in large-diameter cutaneous fibers (type A-beta) inhibits the transmission of noxious information to the brain. Subsequently, application of the gate control theory has shown that electrical stimulation of the dorsal columns activates these large fibers and suppresses secondary neurons that are activated by pain-transmitting small (C and A-delta) fibers [5]. The demand for this therapy outpaced the ability of the technology to deliver the needed pain relief required to restore functionality in patients. To meet the complex demands of the chronic pain population, new research has focused on innovative central axis targets and waveforms [36]. The most effective application of neurostimulation is for the treatment of neuropathic pain, or pain resulting from a nervous system injury. Neuropathic pain associated with FBSS can be due to chronic nerve root compression, irritation, arachnoiditis, or inflammation of the nerve roots. Although the estimated prevalence of neuropathic pain in the general population ranges from 1.5% to 8%, conditions that cause neuropathic pain are often under-diagnosed anvd under-treated [37].

Later work examining pain transmission to the brain found that these signals are processed in parallel by two pathways: (1) a medial affective and attentional pain pathway; (2) a lateral discriminatory pathway [38, 39]. The medial system is triggered by nociceptive-specific neurons, firing in burst mode, and relayed in lamina I of the dorsal horn to the mediodorsal and ventromedial nucleus of the thalamus, and from there to the anterior cingulate cortex, anterior insula, and amygdala [40]. The lateral system is triggered predominantly by the wide dynamic range neurons, firing in tonic mode, and relaying these signals from lamina I and IV–VI of the dorsal horn to the VPL and VPM nuclei of the thalamus. From there, the signals travel to the primary and secondary somatosensory cortex in the posterior parietal area [41].

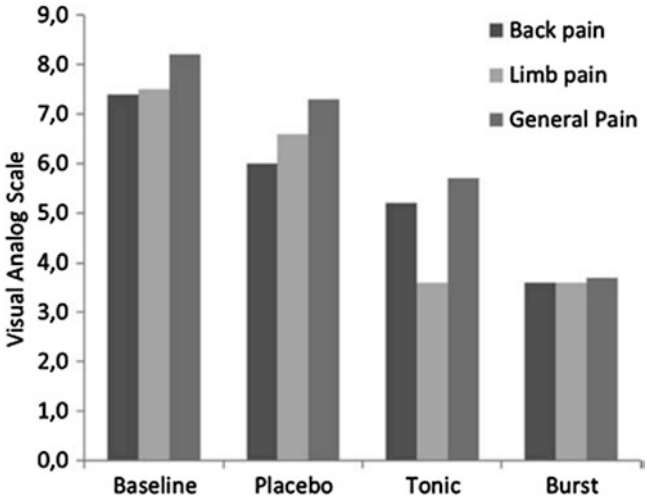

Fig. 51.5 Primary outcome measure. The data represent the mean scores on baseline (placebo, tonic, and burst) for back pain, limb pain, and general pain [23]

In patients implanted with burst stimulation technology, EEG data supports the proposed mechanism that burst stimulation activates the medial system, in addition to the lateral system, with the finding that burst stimulation is characterized by significantly more activity in the dorsal anterior cingulate cortex (medial pain pathway) [23] (Fig. 51.5). Only burst stimulation was better than placebo in altering the subject's attention to pain. Thus, rather than being a more powerful pain suppressor, burst stimulation might therefore exert its main effect by an attention-modulating effect, as evidenced by both the clinical differences between burst and tonic stimulation, as well as the neurophysiological differences at the level of the anterior cingulate [23].

It is possible that activation of the medial system is responsible for the observations which have revealed improvements in patient tolerance to neurostimulation, increase in function, and significantly improved pain relief in patients refractory to tonic spinal cord stimulation. Thus, burst stimulation could be used as a salvage strategy to mitigate tonic spinal cord stimulation failures and could also be used to improve cost-effectiveness by reducing explant rate [42].

With such an advanced technology, cost-effectiveness becomes a key issue. It has been shown that SCS is cost-effective for failed back surgery syndrome, as compared to conventional medical treatment as well as to re-operation, and is associated with better pain suppression [43, 44]. The average cost of a worker's compensation claim of $8300 for back injury is more than twice the average cost of all compensable claims [45]. Researchers estimate that low back pain (LBP) causes 83–149 million lost work days annually, and the cost of lost work is estimated to be equivalent to an annual productivity loss of $28 billion [46]. The Institute of Medicine reported a conservative estimate in 2012 of the compensation costs due to

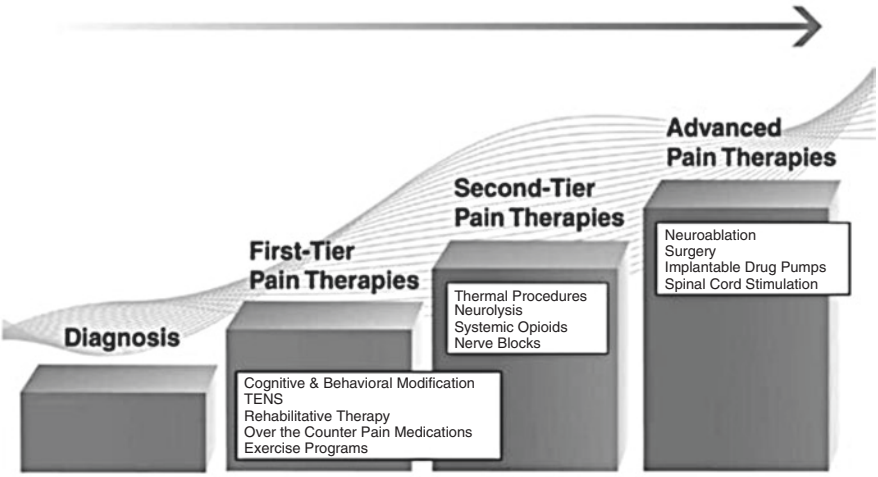

Fig. 51.6 Schematic diagram illustrating how patients with intractable low back pain progress through a treatment continuum. Interventions become progressively more invasive, expensive, and risky with each tier. *TENS* transcutaneous electrical nerve stimulation [45]

low back and upper extremity musculoskeletal disorders to be $50 billion annually due to lost wages and productivity (Fig. 51.6) (National Research Council, Institute of Medicine, 2012; [1]) This enormous cost shows the way we have been treating pain in the past is not sustainable and that new methods of treating pain, such as SCS, must be attempted before more invasive surgical methods are used.

Conclusion

The value analysis of this technology, and the double-blind, placebo-controlled studies demonstrate that advanced waveforms, such as burst and high-frequency SCS, are effective in controlling neuropathic pain. This indicates that burst stimulation will become a mainstream therapy in the near future. The described mechanism of burst stimulation in pain relief is likely related to a combination of a spinal and supraspinal pathways. Mechanistically, through orthodromic activation of ascending dorsal column fibers in both the medial and lateral pathways, and antidromic activation of dorsal horn pain modulatory systems [13]. This approach generates pain relief, without the induction of paresthesias. The lack of necessity for paresthesia gives providers more margin of error in lead placement and reduces the ability of lead migration and scarring to decrease the effectiveness of the therapy. This powerful new waveform will salvage patients failing traditional SCS and will successfully treat axial chronic back pain, as well as many other chronic pain syndromes. With the current level of evidence, burst stimulation will likely become an earlier strategy to treat these debilitating conditions.

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Chapter 52
Dorsal Root Ganglion Stimulation for the Treatment of Pain in the Rehabilitation Patient

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Introduction

Use of neurostimulation of the spinal cord to reduce transmission of pain signals to the brain was first explored by neurosurgeon C. Norman Shealy in 1967 with adult cats. He applied a dorsal column electrode to the cervical cord and found that when direct current was applied, animals could be awake and tolerate noxious stimuli such as tail pinching or intense heat applied to their ears, with no apparent distress [1]. He then took his bench research to the bedside and implanted Vitallium electrodes through a thoracic laminectomy in a 70-year-old patient [2]. The patient had lung cancer and was suspected of having metastases to the pleura and liver. When the leads were activated, the patient noted paresthesias in his back; however, his incisional and original pain was immediately abolished.

DRG Stimulation as a Viable Option

Shealy's work demonstrated that spinal cord stimulation (SCS) could be a powerful neurostimulation technology for the treatment of chronic pain. Since his work began, its usage has grown rapidly to over 27,000 SCS devices implanted per year

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in the United States alone [3]. Several recent systematic reviews have shown that it is a relatively safe and often effective treatment option for patients suffering from chronic, intractable, neuropathic pain [4]. In a large prospective trial, SCS was found to significantly reduce lower limb pain associated with failed back surgery syndrome (FBSS), relative to a conventional medical management control group, over an extended time period [5, 6]. Similarly, SCS can be effective in the treatment of CRPS, though this therapy often has trouble covering CRPS pain in the distal limbs [7].

SCS involves percutaneously placing cylindrical electrical leads through an epidural needle targeting the dorsal columns near the segment of the spinal cord, which is transmitting chronic pain signals. If the lead cannot be placed percutaneously, an open laminotomy method can be used by a spine surgeon and paddle leads can be placed in the epidural space, under direct vision. Both of these methods have been successful in a high percentage of patients; however, each method has limitations. The cylindrical leads inefficiently deliver electrical power and are sometimes unable to penetrate the CSF gradient to strongly affect the desired area in the spinal cord [8]. Once placed, the leads can migrate away from the target area, rupture if under too much stress, and have difficulty in covering distal complex pain patterns. Limitations of the paddle leads include the potential need for surgical laminotomy under general anesthesia, inability to steer the lead once placed to be sure the correct area is covered, and the possible risk of damage to the surrounding neural tissues [9]. Yet, even with these limitations, neurostimulation can offer relief for intractable pain conditions, which not only reduce quality of life but also lead to exorbitant healthcare costs, as well as lost productivity [10].

Despite being labeled as a therapy of last resort, neurostimulation has gradually acquired demand for earlier use in the treatment algorithm of neuropathic pain [11]. There is widespread expert agreement that patients presenting with neuropathic pain, who do not respond to conventional treatments by 12–16 weeks, should be offered a trial of SCS [12]. Earlier use of SCS is further supported by studies demonstrating that the efficacy of neurostimulation is time dependent, with success rates exceeding 80% if implantation occurs within 2 years of symptom onset, compared with 15% for patients whose implants happened 20 years after the onset of pain [13].

Yet, despite the robust evidence for its powerful analgesic effects, real-world SCS utilization remains disappointingly low. A retrospective analysis of 16,455 patients with failed back surgery syndrome (FBSS) disclosed that only 2.4% of eligible patients underwent SCS, while 97.6% received re-operation [14]. It is all too common for otherwise ideal candidates for SCS to be pushed through recurrent cycles of conservative therapies and risky surgeries, with little benefit despite increased possibility of severe complications. Typically, 14% of those with chronic back pain have had back surgery, with 19% receiving re-operation [13]. Other challenges for the use of neurostimulation are compounded by its low public profile. According to a previous European poll survey, 61% of respondents who stood to benefit from SCS were unaware of its existence [15]. The survey also found that 87% of patients had tried four or more treatment options before SCS was ever considered. Among those aware

of SCS, few had been informed by their doctor or specialist, with most relying on self-discovery through television or internet [15, 16].

Other factors regarding the low penetrance of SCS implantation include the finding that 20% of subjects trialing an SCS system do not proceed beyond the trial [17]. For those fortunate enough to have a successful stimulation trial, the treatment has been found to be a successful long-term solution in approximately 50% of patients [6, 18]. Trial failures may be due to difficulty in programming the correct combination of pulse width, frequency, and amplitude of the electrical waveform, trouble finding the correct spinal cord stimulation targets, and unwanted paresthesias due to nerve root stimulation. Areas of paresthesia may also become more intense or may change location, depending on the patient's body position, such as moving from lying to sitting [19].

Body position can largely influence stimulation effectiveness, due to resulting shifts in the distance between the stimulating electrodes and the dorsal columns. This can be due to the effects of gravity either narrowing or widening the CSF gradient, which forces changes in epidural lead position [20, 21]. Additionally, some patients may not tolerate the paresthesias at all, particularly if they are extraneous and located in non-painful areas of the body [22]. Many efforts to improve these bothersome side effects have targeted variables including electrode geometry, programming, and accelerometers, which can automatically adjust the stimulation based on changes in body position [23, 24]. Yet, isolating the neural target that will maximize pain relief can be the most elusive. Thus, there is a need for alternative neuromodulation techniques and targets to address these device challenges.

DRG Stimulation

A recent area of investigation targets neuromodulation of the DRG. The DRG is a cluster of primary sensory nerve cell bodies enclosed in a dural sheath. These cells transmit sensory information, including nociceptive signals, from distal locations in the body to the dorsal columns of the spinal cord [25]. There are other studies that implicate the DRG in the development and maintenance of chronic pain [26]. In animal models of chronic pain, changes observed in the DRG included electrophysiological membrane changes, changes in the expression of integral membrane proteins, and altered gene expression [26–28]. These findings began to elucidate the mechanisms by which the DRG can significantly contribute to chronic pain states.

Converging evidence suggests that the DRG is a rich target for treating chronic pain using neuromodulatory interventions [29]. Stimulation of the somatotopically organized DRG can result in sub-dermatomal patterns of paresthesia coverage. This suggests that recruitment of specific sensory neurons may allow more precise therapy in painful body regions, relative to traditional SCS. Many diseases of the peripheral nervous system are local rather than systemic, which include trauma, cancer, zoster, and radiculopathy. Thus, the neurostimulatory therapeutic approach must also be regional [26]. DRG stimulation would be especially beneficial in cases of

painful regions that are typically difficult to treat with traditional SCS. This includes areas such as the focal distributions in the groin, foot, and hand.

Another advantage of DRG stimulation, compared to traditional SCS, may be in the functional characteristics of the spinal tissue activated by the leads. Traditional SCS recruits multiple fibers in the dorsal columns and causes action potentials to propagate in both orthodromic and antidromic directions, which treats multiple dermatomes including primary sensory neurons [18]. In contrast, DRG stimulation may directly activate the specific cell bodies of the various neurons that innervate the painful regions. This difference gives rise to an alternative possible mechanism of action and thereby, different interventional profiles for these two technologies. It should be noted that because some dorsal column fibers arise from cell bodies in the DRG, it is possible that SCS and DRG stimulation share some cellular targets and have similar mechanisms [30].

The DRG is encased in the bony vertebral foramen, making it possible overcome the over- or under-stimulation artifacts that can occur in SCS patients during various movements and postures. The relative immobility of the bony vertebral environment surrounding the DRG may also help to prevent lead migration. In addition, the cerebrospinal fluid (CSF) layer surrounding the DRG is much thinner than that between the dorsal columns and SCS leads. This means that DRG stimulation targets have more exposure to the electrical impulses generated, making the energy requirements of a DRG stimulator lower than that of traditional SCS systems [31]. Models examining the varying geometric fiber characteristics, the influence of the dorsal cerebrospinal fluid layer, and the electrode configuration affecting the threshold stimulus for axonal excitation have been studied [31]. The results predicted that the curvature of the dorsal root fibers and the angle between these fibers and the spinal cord axis strongly affect their threshold values. Based on these models, the threshold stimuli of dorsal root fibers are relatively low, as compared to dorsal column fibers.

Neuropathic pain is transmitted to the DRG from the periphery. The prevalence of neuropathy originating from the periphery is ill-defined; although, it has been estimated to contribute to 8–10% of adults with neuropathic pain [32]. There are many neuropathic pain states affecting the upper and lower extremity, including diabetic peripheral neuropathy, plexus avulsions, compressive neuropathies of large peripheral nerves, and CRPS types I and II. Conservative therapies for these neuropathic pain syndromes are focused on the disease etiology. Depending on the type of neuropathic pain, different treatment strategies include physical therapy, occupational therapy, diagnostic injections, transcutaneous electrical stimulation, neuropathic pain medications, and opioid analgesics [33]. Unfortunately, less than 50% of neuropathic pain patients find significant improvement in pain control with any pharmacological drug or other conservative therapies [34].

In the past, DRG-specific treatments were used by employing conventional SCS leads [35]. Treating neuropathic targets in certain regions of the body, such as those projecting to the cervical spine, can be technically challenging when using conventional SCS leads. One issue with targeting the cervical DRG with such systems, besides possible compression of nerve roots and blood vessels due to lead diameter, is that placement of these electrodes can result in motor recruitment. Motor

recruitment may occur because of the shape and size of conventional leads, causing ventral, rather than dorsal stimulation. Neurostimulation systems have been specifically designed to overcome these issues, so that targeting the DRG throughout the spinal column yields a more clinically usable and efficacious system, which improves therapeutic outcomes [36].

Common conditions targeted by neurostimulation include low back pain and CRPS. Currently, there is no curative treatment for CRPS and this pathology responds poorly to the previously mentioned conventional treatment strategies. Neurostimulation techniques, such as SCS, have been reported to reduce CRPS pain and improve function [37]. A potential advantage of DRG stimulation in these cases is the ability to selectively bring stimulation to these traditionally challenging spinal cord stimulation targets. Low back pain is also difficult to treat using neurostimulation, due to the challenge in targeting the necessary spinal cord regions specifically innervating this area. In fact, prior studies have observed only a 46% decrease in low back pain using SCS [38]. In a recent prospective study, Deer et al. were able to selectively target DRG stimulation that produced paresthesias in the appropriate location of all low back pain patients [36]. DRG stimulation resulted in an average decrease in back pain of 84%. All subjects achieved greater than 50% back pain relief by the end of their 3–7-day trial, and all requested that the device be implanted long term.

A longer term study by Liem et al. examined patients with multiple neuropathic conditions including CRPS, FBSS, radicular pain, lumbar stenosis, disc-related pain, and pain related to peripheral nerve damage [7]. Measures intended to limit lead migration, such as strain relief loops and use of lead anchors, were employed. Stimulation programming was based on patient feedback, and stimulation amplitude could be adjusted by the patient at any time. The investigators found that stimulation was selective and highly steerable, resulting in discrete paresthesia coverage of painful areas. The location of the paresthesia was assessed at 6 months post implant for stability of intensity across various body positions. Paresthesia intensity ratings were essentially the same for supine and upright positions. The investigators also analyzed VAS pain ratings for overall pain and specific anatomies (back, leg, and foot), quality of life using the EQ-5D-3L [39], psychological stress using the 30-item Brief Profile of Mood States (POMS) [40], and the impact of pain on daily functions using the Brief Pain Inventory (BPI) [41]. After 6 months, back pain was reduced by 69.5%, leg pain was reduced by 69.3%, and foot pain was reduced by 84.5%. Change in quality of life, as measured by EQ-5D-3L remained significantly higher at all follow-up time points, beginning 1 week after stimulation. Similar findings were discovered regarding the POMS and BPI scores.

In 2015, a prospective, open-label clinical trial with an internally controlled reversal design across seven clinical sites was conducted by Liem et al. [30] In this study, researchers examined the effectiveness of DRG stimulation in patients suffering from the same neuropathic conditions as their previous study, which was published in 2013. They followed patients for 12 months, examining DRG stimulation effects on pain level, quality of life, and mood. They observed that patients had 56.3% relief of overall pain, with 60% of patients attaining at least 50% pain relief.

Quality of life, as measured by the EQ-5D-3L, found that patients' EQ-5D VAS showed an improvement of 64.0% and the EQ-5D index score improved by 134.2%. Mood, as measured using POMS showed a decrease in psychological stress by 65.8% at 12 months, with a reversal of the vigor and fatigue patterns measured in the POMS questionnaire. They cautioned that the observational design and small size of the study may have inflated the results. Overall, the study found statistically significant improvements after 12 months of DRG stimulation in ratings of pain, mood, and quality of life. In addition, the coverage of painful areas with paresthesia created high levels of patient satisfaction with the therapy.

Another study, completed in 2015, followed patients with lower extremity CRPS pain treated by DRG stimulation for 12 months [42]. At 12 months, subjects reported an overall pain reduction of 61.7% in both foot and leg pain. Other secondary endpoints included the Brief Pain Inventory Short Form, POMS, and EQ-5D-3 L. All of these secondary outcome measures improved by 50% or more. Some patients had improvements in perfusion and trophic changes in the affected limbs, which investigators attributed to antidromic activation of sensory afferents causing the release of vasodilatory peptides. Some patients reported improved mobility and had remission of symptoms, such as swelling and discoloration. This study demonstrated the promise of DRG stimulation as an excellent therapy for CRPS patients. The authors did note that their study was underpowered for some measures, so they cautioned not to generalize the results of their cohort to the larger CRPS population.

DRG stimulator placement has all the benefits listed earlier; however, there are risks. The most common adverse events (AE) were temporary motor stimulation, cerebrospinal fluid leak with associated headache, and infection [30]. SCS reviews report similar AEs for this more mature therapy [43]. In the DRG studies mentioned, the AEs that occurred were attributed to consequences of the implant procedure or to the programming itself. Investigators noted that this was a novel therapy and there was limited clinical experience with these devices. However, they felt that new refinements, including acute needle incision angles for epidural access and more experience avoiding ventral lead placement, will reduce the incidence of such AEs in the future [30].

Conclusion

Neuromodulation of the DRG has been shown to be effective in relieving many chronic neuropathic pain syndromes. This new therapy is able to consistently provide discretely defined paresthesia coverage in challenging anatomical regions not otherwise covered by traditional SCS, such as the groin, low back, and foot [44]. The advantage of DRG stimulation over SCS may be due to the recruitment of the distally extending sensory neurons [45]. Another advantage of DRG stimulation is the large amount of data demonstrating that the generated paresthesias do not significantly change over different body positions. In SCS therapy, this has been a consistently reported problem [23]. This may be due to different neurophysiological

properties of the neurons stimulated by SCS when the leads move toward and away from the dorsal columns, as gravity causes CSF gradient shifts.

The current DRG device performance demonstrates a good safety profile and consistent improvement in quality of life, mood, and pain symptoms [7]. The improvement in these measures, as well as the coverage of painful sites using DRG stimulation, has been shown to be stable for at least 12 months [19]. In addition, as with SCS, DRG stimulation can be achieved through a minimally invasive operation with relatively short procedure times. In the future, other similarities between SCS and DRG stimulation may appear. SCS has advanced using new waveforms, which have shown significant promise for other neuropathic pain states, such as high-frequency 10-kHz SCS (HF10) and burst stimulation [46, 47]. The question of applying these novel waveforms to a DRG stimulator will likely be a new subject of investigation.

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Chapter 53
High Frequency (HF-10 Therapy) for the Treatment of Pain in the Rehabilitation Patient

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Introduction

The approval of a novel, high-frequency 10 kHz spinal cord stimulation device (SCS) (commercially available as HF10™ therapy) for the treatment of chronic pain by the Food and Drug Administration (FDA; May 2015) was prompted by the results of the SENZA-RCT study [1]. The study demonstrated the superiority of HF10 therapy in controlling chronic back and leg pain, when compared to a traditional, paresthesia-based spinal cord stimulation device. The study was the first of its kind in SCS therapy, as the largest prospective randomized controlled SCS study, which provided level I evidence for both traditional and HF10 therapy. In July 2015, the 12-month outcomes of this prospective randomized controlled study were published. The study demonstrated about 82% of patients using HF10 therapy reported >50% pain relief in their lower back, versus 42.5% of the patients with traditional SCS achieving the same level of improvement with traditional, paresthesia-based SCS [1]. The outcomes of traditional SCS for low back and leg pain in the SENZA-RCT study were in line, or slightly better, as compared to already available published data on traditional SCS for post-laminectomy syndrome patients. However, HF10 therapy demonstrated superiority over traditional SCS in low back and leg pain patients. Moreover, HF10 therapy was about twice as better than traditional SCS within all the subcategories of diagnoses studied with low back and leg pain [1].

Implantation and adjustment requirements of HF10 SCS therapy differ from traditional SCS by an anatomical, midline lead placement, subthreshold 10 kHz frequency stimulation, and algorithmic programming, which differ from traditional

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paresthesia-based stimulation programming paradigms. A few nuances associated with HF10 SCS therapy are further described in this chapter. The consistency of HF10 SCS therapy implantation and its subsequent utilization, associated with superior pain relief, demonstrated in a Level I RCT study, has ushered in a new era in neuromodulation clinical research and treatment for the treatment of chronic pain [1–5].

Although extensive research is currently under way, the mechanism of action of HF10 therapy remains unclear. There is some speculation on attenuation of windup in the wide dynamic range neurons (WDR) in patients with hyper-excitable chronic pain states with this type of therapy; however, the theory warrants confirmation with additional basic research.

The required implantation time interval required for both the trial and the permanent procedure is more consistent and predictable, as paresthesia mapping is not required for this therapy. The in-operating room paresthesia mapping of traditional paresthesia-based devices is arguably the most unpredictable portion of any traditional SCS placement. The patient is awakened and asked to verbalize where they feel the respective paresthesias. The physician will then move the leads in the dorsal epidural space until optimal overlap of paresthesias and pain patterns are achieved. Lack of paresthesias has also been shown to improve compliance with the therapy, likely contributing to the overall efficacy of HF10 SCS therapy [1–5]. Most patients have been shown to keep their HF10 therapy devices turned on constantly, improving pain not only during the wake cycle, but also during sleep.

Lead Positioning for HF10 Therapy SCS

Typical paresthesia mapping is not required with HF10 therapy since the therapy does not elicit paresthesias. As such, the positioning of the SCS leads is always anatomical. In order to cover low back and leg pain using HF10 therapy, leads are positioned at the anatomical midline in a staggered fashion between T8 and T11 [1–3]. For the Nevro SENZA® HF10 SCS system (Fig. 53.1), it is recommended that two 8 contact leads are placed with their tips at the top of the T8 vertebral body and mid-T9 vertebral body, respectively [1–5].

Clinical Studies Demonstrating Efficacy of High-Frequency Stimulation

There is increasing clinical evidence on the efficacy of high-frequency stimulation, which began with the feasibility study by Tiede and colleagues, published in 2013 [2]. The study was performed in 2007–2008, utilizing temporary SCS leads in 24 patients with the diagnoses of low back pain and Failed Back Surgery Syndrome (FBSS). The subjects first received conventional stimulation for 4–7 days, then

Fig. 53.1 Nevro Corp. Senza IPG and SCS leads capable of HF10 therapy

high-frequency stimulation for an additional 4 days via the same percutaneous leads [2]. VAS pain scores were shown to be further improved with high-frequency stimulation, and more patients preferred the high-frequency SCS mode in this study [2].

In 2013, a prospective, open-label, multicenter European clinical trial with 10 kHZ SCS was published [3]. Seventy-two patients with lower back and/or leg pain, along with the diagnosis of Failed Back Surgical Syndrome, were implanted with commercially available HF10 SCS therapy. Most of the subjects suffered from axial low back pain without radiculopathy, which is generally considered more challenging to treat with SCS [3, 4]. Over a 6-month follow-up, study subjects demonstrated significant improvements in VAS pain scores, Oswestry Disability Index scores, and sleep patterns [3]. Similar SCS benefits were also demonstrated at 24 months post-implantation, suggesting that HF10 therapy is likely to produce sustained pain relief without tolerance on a long-term basis [4].

The pivotal study demonstrating the efficacy and superiority of HF10 therapy to traditional SCS was the SENZA-RCT study, published in 2015 [1]. The SENZA-RCT randomized 198 patients with back and/or leg pain to either traditional, low-frequency SCS (Boston Scientific™ Precision Plus), or HF10 SCS therapy, with Nevro SENZA® system [1]. The responder rates to treatment were significantly higher in the HF10 therapy arm for the 12-month duration of the study [1]. The 24-month data also reflected similar results, underscoring the efficacy and durability of HF10 therapy [5]. VAS scores were reported to be much lower for both back and leg pain in the HF10 therapy arm subjects in the SENZA-RCT study [4, 5]. Moreover, HF10 therapy subjects reported improved functional capacity at a statistically significant level, which was superior to the traditional, low-frequency arm subjects. Although both arms demonstrated a reduction in opioid use, the HF10 therapy subjects reduced their opioid usage at a higher rate. Subject satisfaction, reported by the patients, was also significantly higher throughout the entire study [4, 5]. Adverse events were rare in both arms, underscoring the safety of SCS, regardless of device choice throughout the study [4, 5].

Although the evidence for low back and leg pain control has established HF10 therapy as a superior choice for this condition, additional studies are warranted and underway to evaluate the efficacy of HF10 therapy in various other indications.

Trial Procedure for HF10 Therapy

Positioning

The patient is placed in the prone position, in the usual manner for all dorsal column SCS placements. A pillow or two is placed underneath the patient's abdomen to minimize lumbar lordosis. Access to the epidural space is most likely from the upper lumbar area of the spine, using a paramedian approach. The authors prefer L1 and L2, in order of preference, for epidural access.

Anesthesia

For SCS trials, patients may be sedated using IV sedation or other anesthesia, which is based on the surgeon's preference. The patient need not be awake, as paresthesia mapping is not necessary with HF10 therapy. Local anesthetic of choice should be used over the intended trajectory of a 14-gauge Tuohy needle in the deeper fascia, in order to minimize soft tissue discomfort. Although paresthesia mapping in the operating room is unnecessary with HF10 therapy, communication with the patient is critical, in order to allow early detection of adverse incidental events, such as inadvertent spinal cord, or nerve injury during the procedure. Therefore, the authors would recommend refraining from deep anesthesia in the trial patient population.

Lead Placement

Using fluoroscopic guidance, the lumbar interlaminar space is visualized, with the spinous processes positioned at midline. The upper endplate of the target interlaminar level is aligned by tilting the image intensifier on the fluoroscope toward the feet of the patient. This will ensure optimal trajectory and direction toward the epidural space for the surgeon. The entry point for the manufacturer-supplied 14-gauge Tuohy needle is approximately medial to the pedicle, at the level below the target interlaminar space. The Tuohy needle is then advanced in a paramedian fashion toward the target laminae (Fig. 53.2).

The Tuohy needle is advanced slowly into the epidural space using a standard loss of resistance technique. The surgeon may prefer to use AP or lateral fluoroscopy for the approach to the epidural space. Nonetheless, the target epidural entry

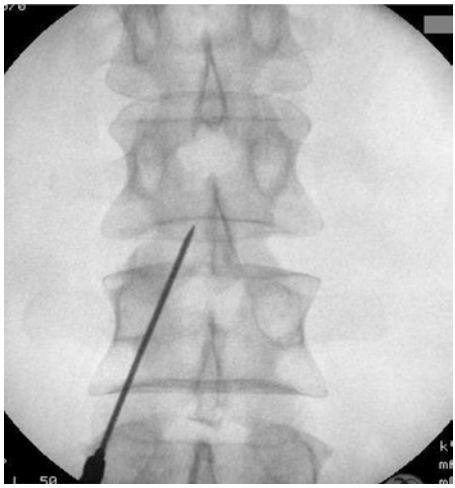

Fig. 53.2 Paramedian approach is used for HF10 therapy similar to traditional SCS needle placement. Needle tip position should be at midline at epidural entry

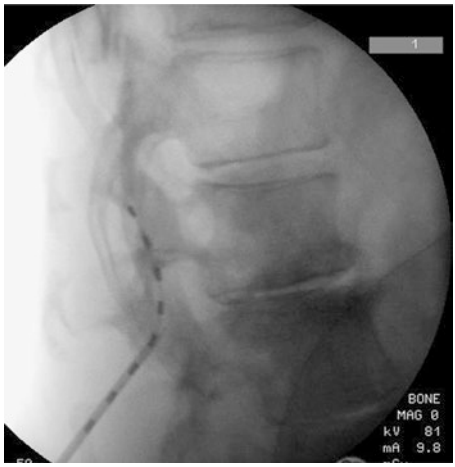

Fig. 53.3 Lateral view of the Nevro SCS lead initial tread into the posterior epidural space

point should be at, or near, the midline, as close as possible to the inferior portion of the spinous process. This approach will allow the most expeditious needle placement, in order to allow the path of least resistance to the epidural midline with the lead (Fig. 53.3). The upper contact of the first lead is placed at the top of the T8 endplate at the anatomical midline. The second lead is subsequently placed in a similar fashion at the anatomical midline, with the uppermost contact at the mid-body of T9 on AP fluoroscopy. Care must be taken to stagger the leads to avoid contact between the leads (Figs. 53.4 and 53.5).

The aforementioned studies have demonstrated the best results in low back and leg pain control with this type of anatomical midline placement. The manufacturer, as well as this chapter's authors, strongly recommend anatomical midline placement of the leads for best results. This is based on the compelling evidence in a number of different peer-reviewed published studies, as well as real world experi-

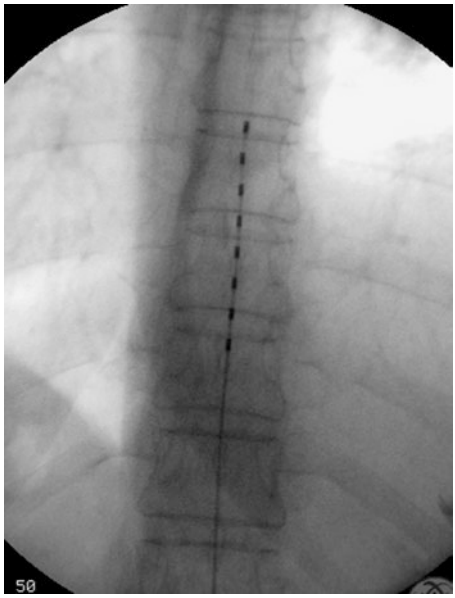

Fig. 53.4 AP view of properly positioned first lead for HF10 therapy with the upper contact at the upper endplate of T8 at the anatomical midline

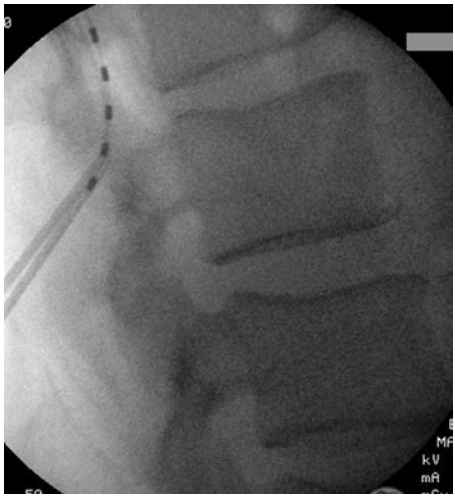

Fig. 53.5 Lateral view of the second lead placement

ence. This recommendation is independent of the laterality of the pain pattern in any patient. This approach is most likely to provide the best and most consistent results in all patients with low back and leg pain, who would be candidates for SCS therapy (Fig. 53.6). The leads are then connected to the programmer for an impedance check. This is typically completed within 5–10 s by the representative of the manufacturer. Once the impedance is confirmed, the Tuohy needles and lead stylets are cautiously removed, under live fluoroscopy in the AP view, to ensure prevention of lead migration.

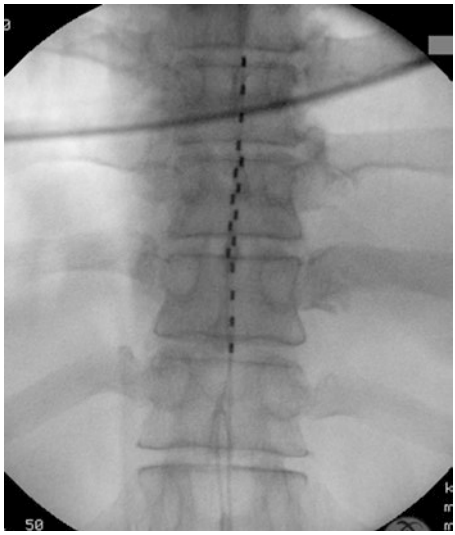

Fig. 53.6 AP view of both leads placed for HF10 therapy at the anatomic midline spanning T8–T11 with the second lead tip at the mid-body of T9

Securing the Leads

The lead anchors (Figs. 53.7 and 53.8), supplied by the manufacturer, are placed over the leads, near the insertion site and sutured into the skin, after application of local anesthetic. Other supporting tools, such as steri-strips or sterile covers, may then be applied to the area.

Permanent Implant

Anesthesia

Anesthesia for permanent SCS implantation may be provided utilizing a similar algorithm to the trial, based on the implanting surgeon's preference. Additional local anesthetic at the incision and lead tunneling sites may be indicated to minimize intra- and post-operative pain. For the permanent implantation procedure, the patients are often kept at a deeper plane of anesthesia with I.V. agents, such as propofol, under monitored anesthesia care (MAC anesthesia). As HF10 therapy does not require paresthesia mapping, patients may undergo deeper anesthesia care, based on the surgeon's preferences and safety precautions.

Lead and Generator Implantation Site Preparation

Using AP fluoroscopy, the interlaminar space is visualized, the spinous processes are adjusted to midline, and the fluoroscopic image intensifier is tilted to align the upper end-plate of the target site vertebrae. The entry point for the Tuohy, medial to

Fig. 53.7 Nevro lead anchor

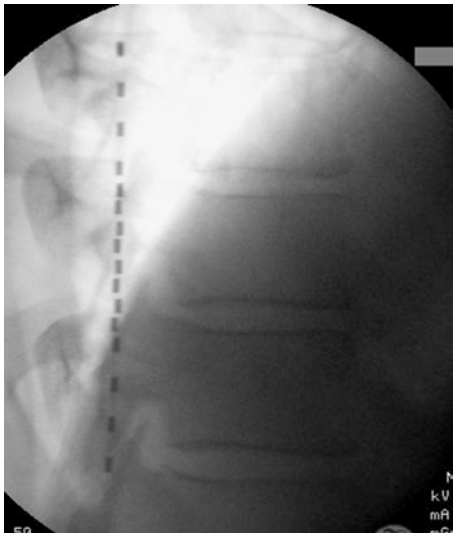

Fig. 53.8 Lateral fluoroscopic view of both leads positioned in the dorsal epidural space

the pedicle below the target site, is marked. This location will be the widest section of the incision to allow a bilateral, or ipsilateral, two needle entry into the soft tissue and toward the epidural space. A 3–4 cm vertical incision is made with this insertion site at the center of the incision, already marked over the skin. The incision site is then dissected with electrocautery toward the thoraco-dorsal fascia, where some undermining is completed with electro-cautery or blunt dissection, in order to allow for the future implantation of the leads and anchors. The 14-gauge Touhy needle is then inserted medial to the pedicle, under AP fluoroscopic guidance, and advanced in a paramedian fashion toward the target interlaminar space, keeping a midline epidural entry at the target site the primary goal. A shallow approach of the needle to the soft tissue and shallow angle of the needle to the midline will provide the best chance for the lead to be placed at midline, taking the path of least resistance cephalad, within the anatomical midline. The Touhy needle is slowly advanced into the epidural space using standard loss of resistance technique. Once loss of resistance is achieved, the surgeon will place the first lead in the epidural space and direct the top of the lead to the upper endplate of T8 at the anatomical midline.

The second Tuohy needle is then placed on the ipsilateral or contralateral position at the level of the first needle, depending on the surgeon's preference. The authors prefer an ipsilateral approach, since such an approach will require a smaller incision for the patient. Once loss of resistance has been achieved, the second lead is placed through the needle and directed to the mid-body of T9 vertebral body, at the anatomical midline. The dorsal positioning of the leads must be confirmed using lateral fluoroscopy. This view is imperative in HF10 therapy due to the lack of paresthesia. The Tuohy needles and lead stylets are cautiously removed under live fluoroscopy in the AP view to ensure prevention of lead migration. See Fig. 53.9.

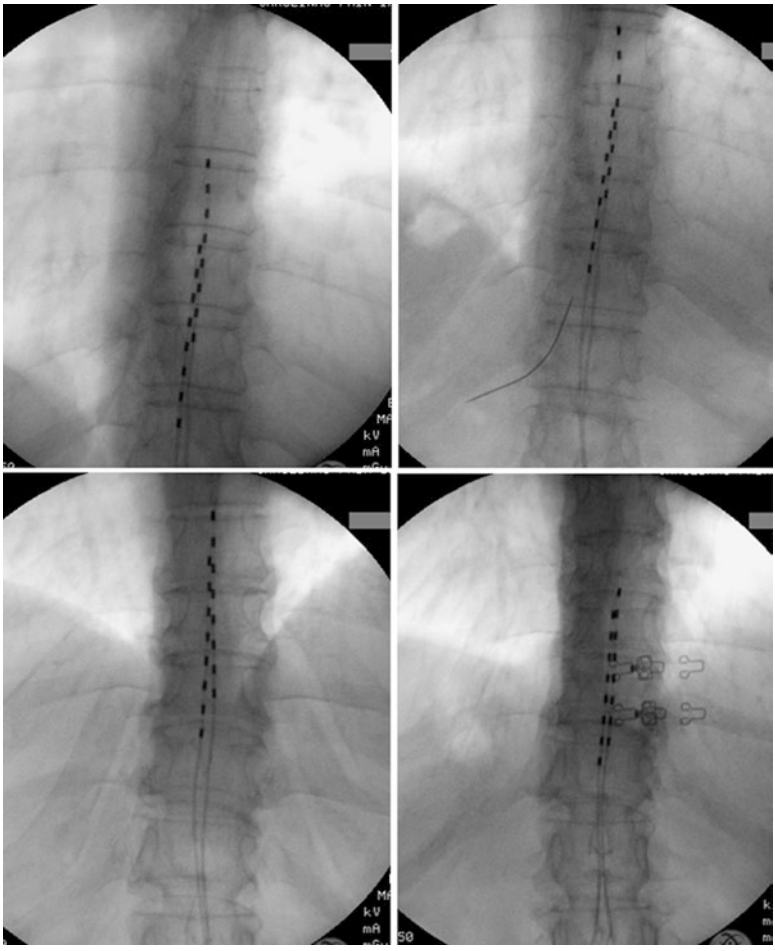

Fig. 53.9 AP view of two leads placed for HF10 therapy trial for two different patients (**a**, **b**). Significant lead migration is noted after at the termination of the trial (**c**, **d**)

Securing the Leads

The lead lock anchors, supplied by the manufacturer, are coursed over the leads and carefully placed slightly through the thoracodorsal fascia. These anchors are then sutured to a ligamentous structure nearby to ensure stability. The surgeon should take an additional AP image, using the fluoroscopy, to ensure prevention of lead migration during the anchoring process. The intended site for the Implantable Pulse Generator (IPG) should be marked pre-operatively, after discussion with the patient for site preferences (i.e., avoidance of areas such as belt lines) and usually marked in both the sitting and standing positions (Fig. 53.10). If the patient's IPG site is marked in the prone position, this may lead to malpositioning of the IPG, either too low or too high in the flank or buttock area. Areas in the flank, above the beltline or in the buttock, are most commonly used. However the buttock area, below the beltline and lateral to the sacroiliac joint may be used for the IPG pocket, based on the physician and patient preference.

After the application of local anesthetic, a horizontal incision is made at the intended IPG site and blunt digital or scissor dissection of the soft tissue below scarpa's fascia is then performed to create a pocket for the IPG implantation. Electrocautery may be used to ensure hemostasis. The site may be preserved using a saline or bacitracin-soaked gauze while the remainder of the procedure is completed.

Tunneling of Leads

The manufacturer-supplied tunneling device is used to connect the paraspinal incision site with the IPG pocket. Tunneling should be done in the subcutaneous tissue in a uniform and instantaneous fashion. Once the tunneling device connects the two sites, the trocar is removed, leaving the tunneling straw in place. The leads are then threaded

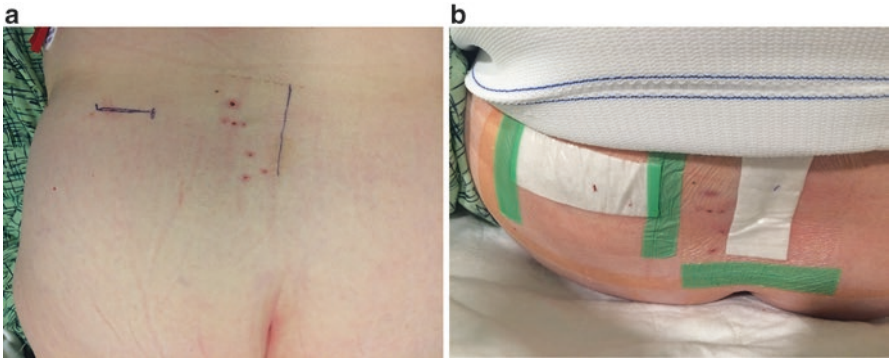

Fig. 53.10 Proposed position of IPG placement incision site in prone (**a**) and sitting (**b**) positions. The IPG incision site appears higher in the hip when prone (**a**)

through the straw, toward the IPG pocket. Care must be taken to leave some lead slack at the midline pocket, in order to form a relief loop at that site. Relief loops have been shown to mitigate the rate of lead migration with patient movement. The tunneling straw is subsequently removed. The leads are then connected to the IPG and the manufacturer's representative performs impedance testing. Once this has been completed the leads are secured in place using a torque screw driver, which is included in the IPG kit. Some physicians will simply place the IPG and some lead slack inside the pocket, taking care to place the lead slack below the IPG. This manner of placement will reduce the risk of interference with the charging device and the remote control. Other physicians prefer to suture the IPG to a fascial layer, in order to ensure its stability.

Wound Repair

The paraspinal and IPG incision sites are irrigated with bacitracin or other antibiotic solution, prior to undertaking the closure. The authors prefer a three-layer closure. The first layer approximates the wound and secures the IPG in place. The second, more superficial layer will bring the skin edges together for future skin closure. The skin edges are finally sutured in a subcuticular fashion, or stapled, per the surgeon's preference. However, the manufacturer recommends refraining from stapling over the IPG, as the metal artifact may interfere with charging in the immediate post-operative period [6]. The dressing of choice is subsequently placed over the suture line. The authors prefer steri-strips followed by Tegaderm, if suture is used. Sterile Vaseline tape may need to be placed over the repaired incision first if staples are preferred.

Post-operative Instructions

The patient may be asked to wear an abdominal binder for up to 7 days, until the first follow-up appointment on post-operative day seven (POD7), in order to mitigate the risk of hemorrhage and hematoma. In order to minimize lead migration risk, the patient should minimize any extension, flexion, or twisting of the spine for up to 6 weeks [9].

Potential Complications of HF10 SCS Therapy

Potential complications reported with HF10 SCS therapy systems are no different than those reported with conventional systems, and occur at similar rates [1]. These potential complications include lead migration, hematoma/seroma, or infection of the operative sites. Pocket pain may also be reported early on, after the permanent implantation [2, 3, 6].

Conclusions

HF10 SCS therapy, at 10 kHz frequency, among other technological advances, is a novel stimulation method, which has demonstrated superiority to conventional low frequency SCS, delivered at frequencies between 50 and 1200 Hz, for treating low back and leg pain in the first ever randomized controlled study comparing the two therapy modes. Furthermore, axial low back pain, which has historically been challenging to treat with traditional low-frequency SCS, has been shown to respond well and on a long-term basis, to HF10 therapy [1, 3, 4]. The SENZA® SCS system from Nevro Corporation is the only device commercially approved to deliver HF10 therapy, at the time of press of this publication. Extensive research is also underway in order to determine the mechanism of action for HF10 therapy. HF10 therapy does not produce paresthesias, obviating the need to emerge a patient from anesthesia during the SCS implantation. This allows for more patient safety and more consistent procedure times. The most optimal placement to treat low back and leg pain requires lead placement between T8 and T11 at the anatomical midline with this technology. Complication rates from HF10 SCS therapy are similar to the rates seen with conventional SCS, based on level I data published in peer-reviewed literature.

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Recommended Reading

Novel 10-kHz High-frequency Therapy (HF10 Therapy) Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain The SENZA-RCT Randomized Controlled Trial. Kapural, Leonardo, et al., Anesthesiology. 2015;123(4):851–60.

High-frequency spinal cord stimulation for the treatment of chronic back pain patients: results of a prospective multicenter European clinical study. Van Buyten, JP, et al., Neuromodulation. 2013;16(1):59–66.

Chapter 54
Intraoperative Neurophysiology for Spinal Cord Stimulation Placement Under General Anesthesia for the Treatment of Pain in the Rehabilitation Patient

Jay L. Shils and Jeffery E. Arle

Introduction

Spinal cord stimulation (SCS) is a common therapeutic technique for the treatment of medically refractory neuropathic back and other painful limb syndromes. Historically, the common practice for placing SCS leads required direct interaction with the patient. This included using a sedative anesthetic technique and awakening the patient at specific time points during the surgery in order to assess response to sensations generated from stimulation and direction from the surgical team. Given the pain patients' variable responses to anesthetics, due in part to prior use/exposure to opioid and anxiolytic medications, patients' pain distributions, ability to respond accurately to differentiate their pain syndrome from the surgical "situation," and positional changes from cord movement, responses have proven to be unreliable or misleading [1–5]. To help minimize these effects, lead manufactures have developed new lead designs that offer more postoperative programming options. These new designs still require the leads to be placed in an appropriate medio-lateral position relative to the cord pathways and dorsal nerve roots. It is also critical that these leads be placed at the appropriate cranial-caudal spine level to maximize the desired pain coverage. The crania-caudal position is easier to locate given the use of trial leads, which are small cylindrical leads that are similar to EEG depth leads, the known segmental peripheral root distributions, and the length of the leads, which

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can cover 2–3 vertebral levels. On the other hand, localization of the dorsal column over the midline is more critical and less reliable using fluoroscopy, alone as parallax, cord rotation, and the potential for patient response unreliability confound the issue.

Sedative and awake procedures are not without their complications. This is due to the fact that patients are typically placed prone, and in some cases patients are placed in the lateral decubitus position on the operative table, which significantly inhibits the anesthesiologist's access to the airway despite receiving significant sedation for the initial and follow-up surgery. Either the patient will be unreasonably uncomfortable, or they can become oversedated, necessitating emergent placement of an airway placed while in the prone position. This risk is not insignificant; it is one of the highest categories of closed claims in the anesthesia field, specifically from loss of airway secondary to oversedation. The use of neurophysiologic mapping techniques allows for the use of a general anesthetic technique, which the aforementioned issues.

The technique that was developed [6] is based on antidromic activation of the alpha-motor neuron (light green arrows in Fig. 54.1) through stimulation of the large Ia fibers of the dorsal column (Fig. 54.1). This in turn will drive the muscle generating the EMG response that is recorded (Fig. 54.2). It is important to note that the stimulation required to generate the compound muscle action potential (CMAP) response is at a higher stimulation amplitude than normally used for pain therapy. Other authors have developed similar techniques for localization of the SCS lead under general anesthetics, yet focus will be on the approach the authors have developed [7–10].

Methods

Bilateral, simultaneous free running EMG (Fig. 54.2) activity was recorded via two subdermal needles (Rhythmlink model RLSND121-2.5, Columbia, SC or Cardinal Health (Nicolet) model 019-409900, Madison, WI) placed into muscle bellies 1–2 cm apart from each other. For cervical leads, the following muscles were studied: (1) trapezius, (2) deltoid, (3) biceps brachii, (4) triceps, (5) flexor carpi ulnaris (FCU), (6) extensor carpi ulnaris (ECU), (7) abductor pollicis brevis (APB), (8) abductor digiti minimi (ADM), (9) gastrocnemius (gastroc). For the upper limb, biceps brachii and triceps are referenced, FCU and ECU are referenced, and APB and ADM are referenced. For thoracic leads, the following muscles were studied: (1) iliopsoas/adductor longus, (2) vastus medialis (Q), (3) tibialis anterior (AT), (4) gastroc (and/or soleus), (5) abductor hallucis, (6) paraspinal (rhomboid and/or erector spinae and/or trapezius—ultimate decisions on which muscles were studied may have depended on the level and amount of adipose tissue), (7) rectus abdominis (or sometimes external oblique depending on amount of adipose tissue). Needle leads were taped to the skin with either silk tape or Tegaderm and the wires secured with a piece of silk tape or a Tegaderm, 5–10 cm from the needle to act as a strain relief.

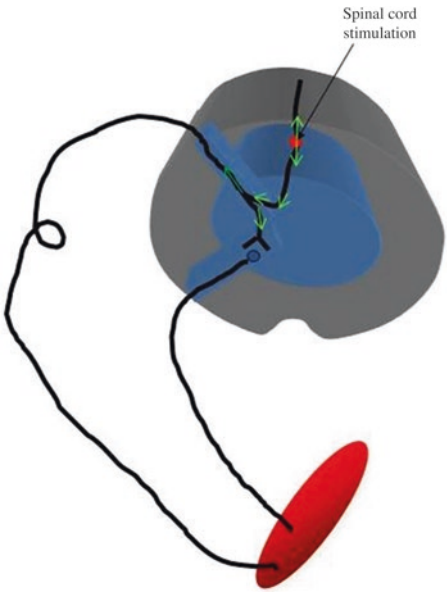

Fig. 54.1 A graphical representation of the activated pathway during this test. The SCS lead stimulates the dorsal column at a level that is strong enough to activate enough fibers to excite the alpha motor neuron and generate a CMAP at the muscle. It should be noted that during normal pain therapy the levels of stimulation are much lower and thus no motor activation since not enough fibers in the specific motor pool are driven to excitement

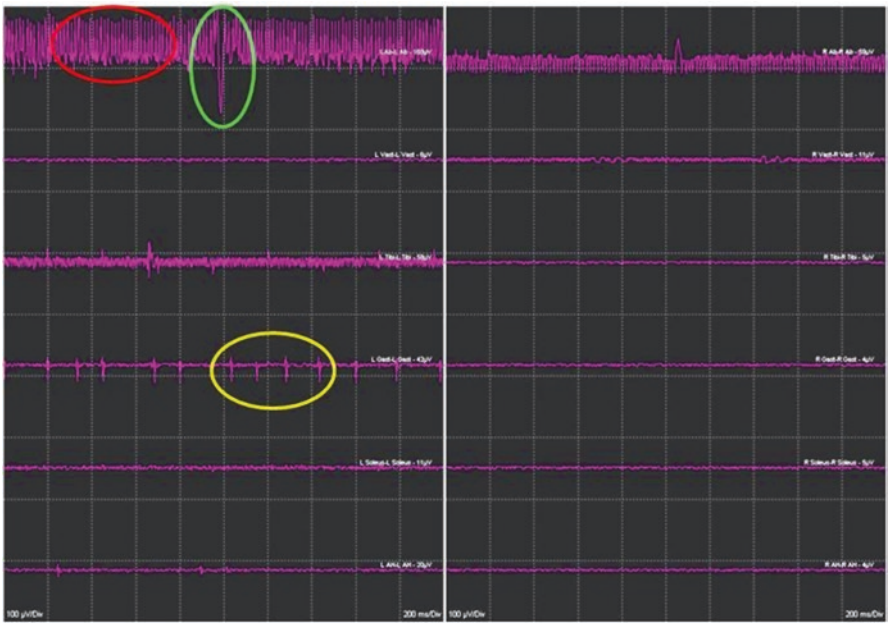

Fig. 54.2 An example of the different types of responses is noted with this technique. The response in the red circle is artifact from the stimulation device. The response in the green circle is from EKG artifact. The responses in the yellow circle are compound muscle action potentials generated by the anhidrotic activation of the alpha motor neuron pool for this muscle group

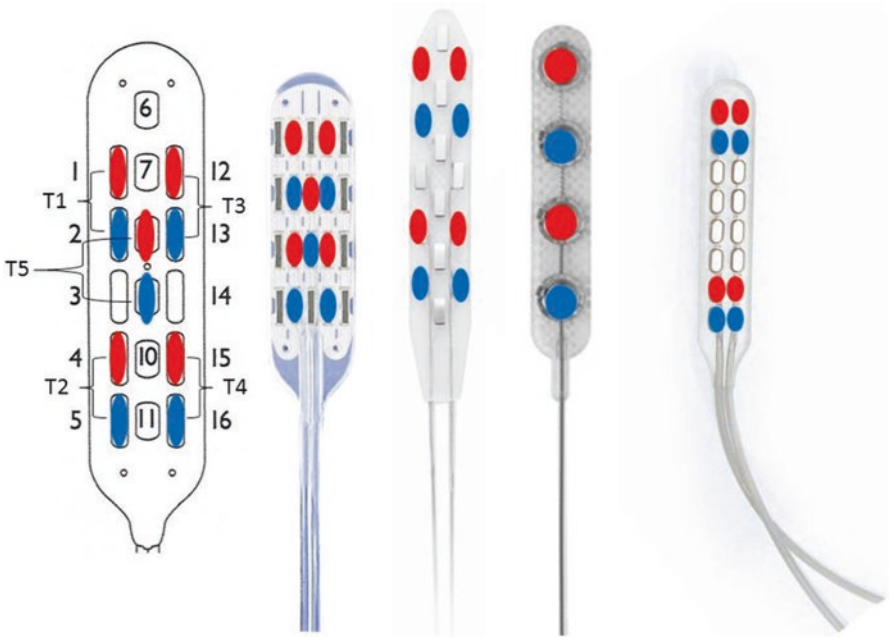

Fig. 54.3 Graphical representation of the stimulation paradigms used for each lead type. The first lead on the left shows the sequence that is used with the left most electrode pair being the first tested and then sequentially going around the lead testing each electrode pair in cranial to caudal/left to right order. A similar pattern is used for the other electrodes

All wires were run to the foot of the bed and connected to the EMG recording system amplifier. A ground pad was placed on the knee, lateral thigh, or chest. For thoracic SCS leads, only lower limbs were examined. For cervical leads, primarily only upper extremities and the trapezius were examined, but on some occasion, both upper and lower extremities were included.

Initial amplifier settings were as follows: (1) gain 100 uV/div, (2) high-cut filter (low pass) 3000 Hz, (3) low-cut filter (high pass) 30 Hz, (4) sweep 200 mSec/div. For spinal musculature, abdominal muscles, and trapezius muscles, the filter bandpass was narrowed to 100 Hz–500 Hz in order to reduce proximity stimulation artifact saturating channels. High- and low-cut filters may also require adjustment, depending upon noise levels in the operating room.

During the testing session, the gain of specific channels was adjusted during testing to account for dynamic range changes (i.e., the number of motor units activated and also the artifact amplitude). As stimulation is increased (see later), channel gains were reduced. Since the goal was to locate real EMG activity, and not the specific amplitude of this activity, such an approach was deemed to be acceptable.

Stimulation was applied through the SCS electrodes. Quadrant testing was performed (Fig. 54.3) on all lead types, except single column leads, wherein cranial (anode) and caudal (cathode) pairings could determine orientation. Stimulation was

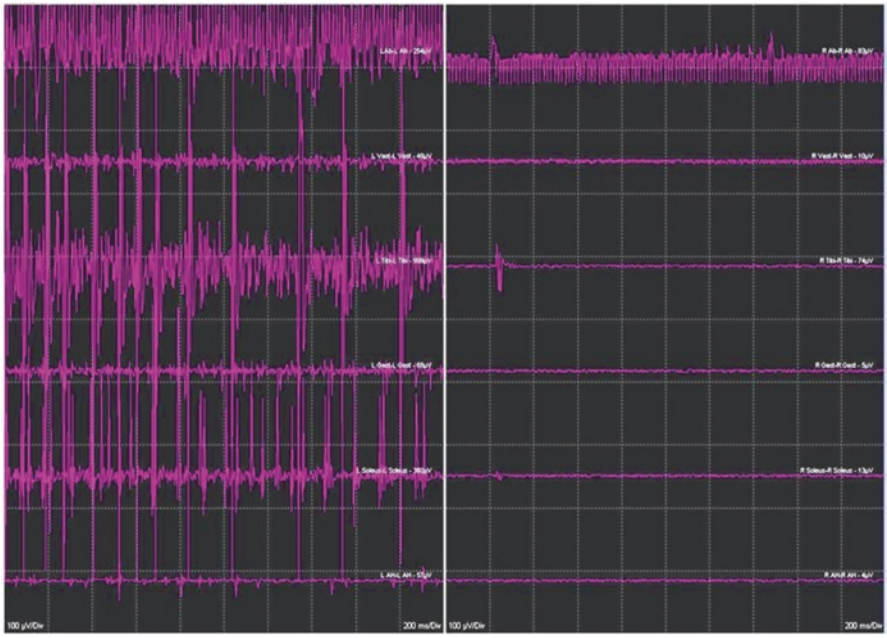

Fig. 54.4 This shows a complete left-sided response with the start of a response on the right side

applied via the specific lead manufacturer's screening device (Boston Scientific "Bionic Navigator", Valencia, CA, Medtronic model 8840, Minneapolis, MN, St. Jude model 6850, Plano, TX). The lead was connected to the device via the screening cables, which were also manufacturer specific. Impedances were tested to make sure the device was working and properly connected.

Initial stimulation testing parameters were 60 Hz and 210 μs. The amplitude was then slowly raised in 0.5 V or 0.5 mA increments until EMG activity was noted (Fig. 54.2) in any channel. Amplitude was then increased in 0.5 V (mA) increments further, until a new location of activity was detected. This process was continued until either one of three things occur: (1) the stimulator reached its maximum output; (2) both sides activated all muscle groups; or (3) one side was "completely" active, and then the stimulation was raised 1.0 V (mA) beyond this level (Fig. 54.4). "Completely" active means that all muscles on one side were firing. It is important to be able to differentiate the noise (red (stimulation artifact) and green (EKG artifact) circles in Fig. 54.2) from the actual EMG response (yellow circle in Fig. 54.2).

For 2-column arrays, testing is performed at each corner (thus 4 tests). For example, if a 2 × 8 electrode lead was being tested, the following test sequence was used: (+1,−2), (+7,−8), (+9,−10), (+15,−16). For three-column arrays, testing was performed at each column and often at some part of the center column. For example, when testing the Tripole or 5-6-5 lead, the following testing sequence was used: (+1(0),−2(1)),(+4(3),−5(4)),(+12(11),−13(12)),(+15(14),−16(15)),(+6(5),−7(6)), (+10(9),−11(10)). For the St. Jude Penta™ lead (5 columns), the center three

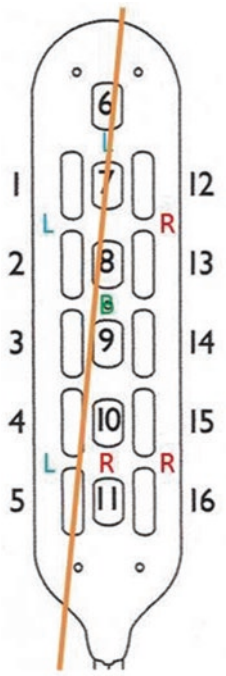

Fig. 54.5 For each electrode pair, a plot is made of the location of the spinal cord midline as determined by the technique. See the text for a detailed description

columns were tested in similar fashion to tripolar leads. On occasion, the lateral columns were also tried, in an effort to determine laterality.

Once all the data was obtained for each test, a midline was calculated, which was based on muscle where the initial response was noted and the strength required to activate muscles on the contralateral side (Fig. 54.5). For example, if the initial muscle was the AT on the left side, and no right-sided activity was noted up to the maximum stimulation amplitude or the point where the stimulation amplitude was 1.0 mA beyond the level where the complete left side activated, then the line for the level would be placed to keep those electrodes on the left side of the dorsal column midline (Fig. 54.2 contacts 1 and 2). Yet, if the initial muscle was the AT on the left side and a muscle on the right side showed EMG activity at a point before the full left side activated, the line would be drawn through the contact pair with the majority of the midline to the right of the electrode pair (Fig. 54.5 contacts 4 and 5). The last condition would occur when the left and right muscle activity started at the same stimulation amplitude. In that case, the midline was drawn so that both contacts overly it figure (Fig. 54.5 contacts 6 and 7).

Several conditions can occur during testing, which require modification to the testing protocol described earlier. In some cases the output of the screening device reaches a maximum amplitude limit (based on the safety parameters of each manufacture's system). This can occur in one of three possible conditions. First, the limit is reached after EMG activity is initiated. In this condition there is sufficient data to continue with the standard protocol. Second, no EMG activity has been recorded

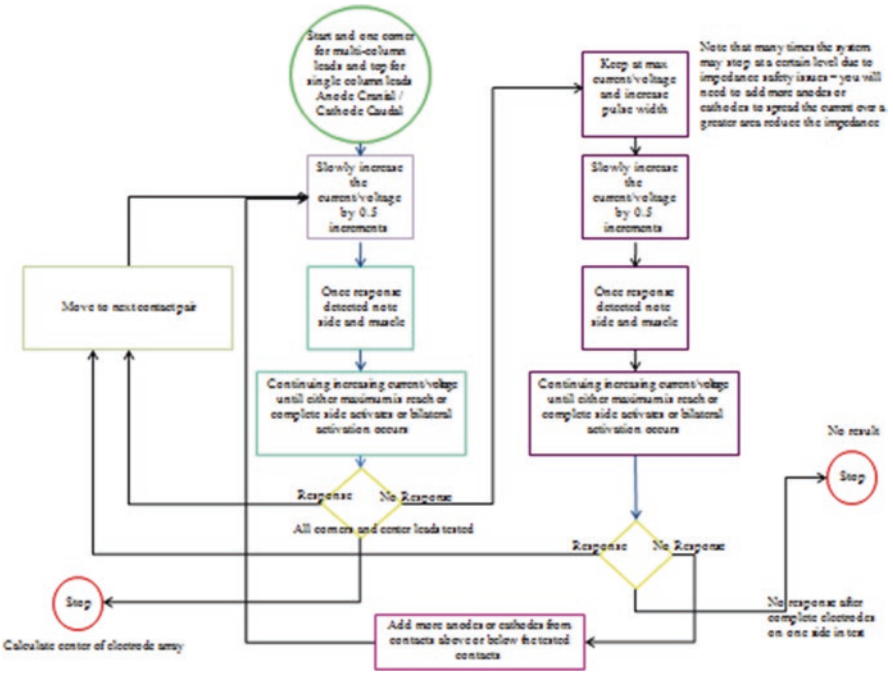

Fig. 54.6 A graphical representation of the procedure

when the limit is reached. When this condition occurs, the pulse width is slowly increased until EMG activity is noted and the standard protocol can be continued. Third, no EMG activity is recorded when both the amplitude limit and the pulse width limit are reached. If this occurs, the numbers of anodal electrodes are increased and dorsal column midline evaluation is based on this new configuration. Anodes are increased instead of the cathode to keep to focality of the stimulation. It appears that these conditions tend to occur in cases where an old electrode is being removed and there is scar tissue or thickened dura. Epidural fat tissue may also contribute to this phenomenon. A graphical representation of the methodology is shown in Fig. 54.6.

Conclusion

Since the implementation of this technique, all patients in our practice have their leads placed under general anesthesia. The outcomes of these patients are the same as the standard sedative anesthetic technique, which is important in the application of any new methodology [6]. Additionally, this technique has reduced the surgical time by an average of 15–30 min, depending upon the amount of time it took to wake the patient and number of lead repositionings necessary. In general, patients

are much happier with this technique in that they do not have to be awake for the procedure. Furthermore, the overall safety of the procedure is improved in not having to perform a sedative anesthetic technique in the prone patient. Finally, this technique does not require any special equipment, and each SCS lead manufacture can use their existing testing technology.

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Chapter 55
Peripheral Nerve Stimulation for the Treatment of Pain in the Rehabilitation Patient

Rabia Tari, Christy Gomez, and Konstantin V. Slavin

Introduction

Peripheral nerve stimulation (PNS) refers to electrical stimulation of the named nerves, plexuses, and branches using implantable hardware; it is a commonly used surgical approach that has many current and potential uses in the care of rehabilitation patients. For example, it has been used to restore breathing in patients with diaphragmatic palsy by stimulating the phrenic nerves, to control seizures and depression by stimulating the vagal nerve, to improve/normalize bowel and bladder function in patients with incontinence and retention by stimulating the sacral nerves, and to control sleep apnea by stimulating the hypoglossal nerve. But, the most established and probably the most underutilized PNS application is related to its ability to control chronic pain.

PNS was introduced for the treatment of chronic pain in the early 1960s [1], even before the "gate-control" theory of pain was conceived and published. As a matter of fact, PNS was used to support this theory when its authors described the pain-relieving effect of PNS with self-experimentation and clinically relevant results in a series of eight patients [2]. Soon thereafter, a novel approach of spinal cord stimulation (SCS) was developed for the treatment of chronic pain. Predictable and reproducible results of SCS lead to its universal acceptance, and by the mid-1970s, SCS eclipsed PNS in clinical practice. The modality was not abandoned completely, and despite the lack of dedicated equipment, there were multiple clinical centers that kept PNS alive, albeit in small volumes and for very specific painful syndromes [1].

Recently, there has been a surge of interest in PNS applications to treat chronic pain for multiple reasons. First, there is a need for a focused neuromodulation approach that would selectively stimulate the nerves that are responsible for pain

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syndrome (see section on indications below); second, technological advances and creative thinking have resulted in the development of dedicated PNS devices that have been designed to facilitate the implant component of the procedure and to improve long-term outcomes (see sections on procedural details and the future directions); finally, there is now a clear understanding that other modalities, which include SCS, may not be uniformly effective in every clinical situation; furthermore, there are multiple instances where PNS may be significantly superior to everything else, in terms of efficacy and safety (see section on evidence).

Mechanism of PNS Action

Although there are many possible theories explaining the exact way in which PNS suppresses pain, the two most plausible explanations have to do with the frequency of stimulation [3].

The conventional frequency of PNS is in the range of 10–100 Hz; it is usually referred to as "paresthesia-inducing stimulation", as PNS at this frequency is capable of and is expected to produce paresthesias, which are usually described as a tingling sensation by patients. The Gate Control theory of pain postulates that the presence of non-painful sensation in the area of pain may suppress transmission of nociceptive information toward the central processing regions. Interestingly enough, it appears that the presence of paresthesias in the painful region does not guarantee pain relief, but the absence of paresthesias is all but certain to result in failure of the modality. This, at least in part, may explain the dismal results of PNS seen in patients with complete numbness in the painful region; another explanation may be in the degree of underlying nerve damage, as the injury that is severe enough to make the area numb is likely to make the affected nerve insensitive to electrical stimulation. Paresthesia inducing PNS has been successfully used on a long-term basis in a variety of neuropathic pain conditions.

Another mechanism is observed in the use of a much higher frequency range of 10,000–12,000 Hz (10–12 kHz). Here, it appears that such high frequency stimulation produces complete (but fully reversible) conduction block, which makes the area supplied by the stimulated nerve numb and painless. This PNS approach, described as "high frequency nerve block", has been successfully used in the treatment of post-amputation pain, with lasting pain relief after intermittent use of stimulation [4].

Indications

Most established indications for PNS include pain in the extremities. PNS has been traditionally used to stimulate large named nerves in the arms and legs for a variety of neuropathic pain syndromes. Traumatic or iatrogenic neuropathies,

as well as complex regional pain syndromes (type 1, formerly known as reflex sympathetic dystrophy, and type 2, formerly known as causalgia), are considered best indications for PNS [5, 6]. In addition to stimulation of individual nerves, peripheral neuromodulation may also target the brachial plexus and dorsal root ganglia.

Pain in the trunk has been evaluated as an indication for PNS on many occasions. Currently, there is CE (Conformité Européenne) mark for PNS in the treatment of low back pain with neurostimulation from two different companies [7]. Moreover, PNS has been successfully used for the treatment of intercostal neuralgia, abdominal, inguinal and flank pain syndromes, as well as pain in the neck due to cervical spondylosis or following cervical spine surgeries [8].

In terms of head and face pain syndromes, PNS has been used primarily for the treatment of occipital neuralgia [9], cluster headaches, migraine headaches, and trigeminal neuropathic pain [10]. Here, occipital PNS is used for the management of pain syndromes that involve posterior aspects of the head and the upper neck, and stimulation of the trigeminal branches is reserved for pain in the face and frontal part of the head. In addition, occipital PNS has been shown to improve whole body pain in fibromyalgia [11]. Based on several publications, it appears that postherpetic neuralgia, which frequently presents with chronic pain in trigeminal distribution, is one of those indications for which PNS is less predictable and probably less effective overall [12].

A distinct and relatively new indication for PNS is in the treatment of post-amputation stump pain that may or may not be associated with formation of amputation neuroma, which strongly interferes with the patient's ability to wear a prosthetic device on the affected limb, and thereby impedes progress in rehabilitation [4]. In these cases, use of a high-frequency nerve block may be a better solution, since making the stump numb does not carry additional functional impairment. Although sometimes considered for the treatment of phantom pain, PNS may not be very effective for this particular indication, which is not unlike other spinal and extra-spinal approaches and is not surprising since it is known that phantom pain is a central phenomenon.

Procedural Details

There are many ways that PNS devices may be implanted into the human body. Although the various equipment options may dictate the different procedural details, the general principles remain the same. The stimulating contacts of the electrode lead have to be either in direct contact or in the immediate vicinity of the stimulated nerve. This is accomplished by placing the electrode next to the target nerve by either direct exposure of the nerve (such that the lead may be positioned next to the nerve, or wrapped around the nerve, depending on the lead geometry) or by inserting the electrode lead in the vicinity of the stimulated nerve(s) using a percutaneous approach.

Usually, the implantation of a permanent PNS device is preceded by insertion of temporary electrodes, as a part of so-called "trial" of stimulation. For this, a percutaneous approach is frequently chosen, with or without ultrasound guidance. At the end of the trial, which usually lasts 5–10 days, the temporary leads are removed, and then a permanent device is implanted at the same time or during a separate session. Design of the electrode lead dictates the procedural details. Cylindrical leads may be inserted through an introducer needle; paddle-type flat leads require direct exposure of the stimulated nerve, with the exception of specially designed narrow paddle leads that may be inserted percutaneously through a dedicated insertion tool (Epiducer, St. Jude Medical) [13]; wrap-around leads require not only exposure of the nerve, but also its circumferential dissection. However, the resulting tight direct contact between the nerve trunk and the electrode contacts creates a much more reliable and energy-efficient interface.

Stimulation devices have to be powered and there are different conceptual models to achieve this. Most commonly, the electrode leads are connected to an implanted generator that contains the battery and telemetry/programming units. Such a generator is usually placed through a separate incision in the patient's abdomen, chest wall, flank, or in the case of smaller devices and larger patients, next to the stimulated area in the patient's paraspinal region or the painful extremity.

Before the invention of implantable generators, there were radiofrequency-coupled systems that included an implanted antenna/receiver and an external power source. Such devices have not been used for several decades, but the concept was resurrected with more compact versions of either radiofrequency-coupled or direct current/induction-based devices. Finally, a new generation of these devices employs nanotechnology concepts to miniaturize the stimulator hardware and to power it via "wireless" approach. Examples of such new devices include StimRouter (Bioness), Reprieve (BlueWind Medical), and Freedom (StimWave) neurostimulators [14, 15]. Insertion of these new devices has become much less invasive, as they do not require tunneling and generator implantation.

Results/Clinical Evidence

Despite a 50-year clinical history of using PNS in a variety of pain syndromes, there is remarkably little evidence of its long-term effectiveness. In 1996, a prospective series by Hassenbusch et al. [5] documented good or fair pain relief in 63% (19/30) patients with reflex sympathetic dystrophy that were followed by 2–4 years. They also noted marked improvement in vasomotor tone chances and the patients' activity levels, whereas improvement in motor weakness and trophic changes was less impressive.

A large multi-center nationwide study in Austria showed that subcutaneous targeted stimulation (frequently called peripheral nerve field stimulation) used in the treatment of focal non-cancer pain in 111 patients resulted in across-the-board improvement in pain intensity by more than 50% (from 8.2 to 4.0 in mean numeric

rating scale measurements) [16]. These results were similar to an earlier US study of 20 patients with chronic back and leg pain, who were treated with a combination of spinal cord stimulation and peripheral nerve field stimulation [17]. Following these promising results, a prospective multi-center observational study in 11 centers across Austria and Switzerland analyzed 105 patients with chronic low back pain who were treated with peripheral nerve field stimulation. The analysis showed that all pain and quality-of-life measures (including pain intensity, depression, disability questionnaires, etc.) improved during the 6 months follow-up period in a statistically significant fashion; the review of medication usage showed highly significant reduction as well [18]. The most recent review of PNS in the treatment of back pain emphasized the importance of proper depth in the placement of stimulating electrodes. Specifically, a lead depth of 10–12 mm from the skin surface appeared to maximize target sensation that was mediated by fast-adapting A-beta fibers [19]. The authors from Australia came to this conclusion based upon analysis of published studies and their own extensive experience in the use of PNS for a variety of peripheral neuropathic conditions.

A multi-center investigation of a novel minimally invasive PNS device (StimRouter) used for the treatment of neuropathic pain of peripheral nerve origin showed that, when tested in a double-blind crossover fashion, this approach resulted in a statistically significant higher response rate (38%), as compared to the control group (10%). The difference in improvement of pain intensity was also statistically significant between the randomized groups (27.2% vs. 2.3%) at 3 months post-implant [14].

Interestingly, PNS seems to have a unique longevity. In a recently published analysis of 5 patients with peripheral neuropathic pain, who were using PNS for more than 20 years, both pain intensity and pain unpleasantness remained significantly improved at the time of follow-up; quality of life measures, which included sleep and daily function, improved as well [20]. Despite earlier concerns, prolonged (>20 years) stimulation of the peripheral nerves did not result in any change of sensory function, as documented by quantitative sensory testing in “on” and “off” conditions [20].

Future Directions

There are several main directions for PNS development, which include new indications, new hardware choices, new paradigms, and new evidence-based guidelines.

In terms of indications, it is conceivable that in addition to “classic” PNS indications, such as pain due to peripheral nerve injury (from neuropathy, traumatic injuries, CRPS type 1 and type 2, amputation neuromas), occipital neuralgia, and truncal pain (intercostal and post-herniorrhaphy neuralgias), there will be new, potentially responsive clinical conditions. Among these, chronic low back pain, neck pain, migraine, and fibromyalgia are probably the most promising.

New hardware choices are expected, not only to improve efficacy and to make PNS more predictable, but also to reduce the rate of re-operations and complications, which was left out of this chapter for brevity reasons. One should keep in mind that most of the experience collected during the last half century was gathered with devices designed for spinal cord stimulation [5, 8–13, 16–20]. Novel, dedicated PNS devices, introduced only recently, have already shown significant promise in improving the clinical outcomes [4, 6, 7, 14, 15].

New stimulation paradigms are expected to bring PNS to a different level, both in terms of efficacy as well as reproducibility. These paradigms include different electrical parameters and waveforms, which include higher frequency, burst, and other irregular patterns that are now explored for spinal cord stimulation applications [21], but will inevitably be tested in PNS applications as well. New paradigms will also include new stimulation targets, such as the dorsal root ganglion, which is the intermediate structure between the central and peripheral nervous system that combines the selectivity and sensitivity of peripheral nerves with the anatomical stability of intra-spinal structures.

Finally, the recent publication of evidence-based guidelines [22, 23] that legitimized the use of PNS for a specific indication, namely occipital neuralgia, paves the way for widespread acceptance of this modality in clinical practice. Development of convincing clinical evidence will further support PNS applications for a variety of chronic pain conditions and is expected to provide scientific base for our clinical applications [24, 25].

Conclusion

Peripheral nerve stimulation (PNS) is an important part of the spectrum of neuromodulation procedures. Shown to be effective for various chronic pain conditions, PNS has a unique ability to control highly localized pain in specific syndromes, such as post-amputation pain in patients with traumatic neuromas, occipital neuralgia, and complex regional pain syndromes (types 1 and 2). Some of these indications play particularly important role in neuro-rehabilitation, as long-term control of severe pain facilitates the patients' ability to participate in the rehabilitation process and makes them more receptive to rehabilitative interventions and procedures. Development of dedicated PNS hardware and the creation of evidence-based clinical practice guidelines are expected to further support the use of PNS in pain management for the rehabilitation patients.

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Chapter 56
Intrathecal Therapy for the Treatment of Pain in the Rehabilitation Patient

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Introduction

The idea of using intrathecal (IT) medication to treat chronic pain began to grow after mu-opioid receptors were found in the dorsal horn of the spinal cord [1]. Since the receptors were located in the dorsal horn, the concept of delivering medications to their appropriate targets, with a catheter placed directly over these receptors, seemed to make sense. Later, in 1991, the Food and Drug Administration (FDA) approved Medtronic's intrathecal drug delivery system (IDDS). This led to an increased use of intrathecal analgesics for the relief of cancer and non-cancer-related pain [2]. This method of treatment was used when conservative medical, interventional, and surgical therapies had failed. Intrathecal delivery was also considered when there were intolerable side effects to oral opioids, such as sedation, constipation, and urinary retention [3].

As the need for IT therapy grew, a number of issues need to be addressed for this to be successful as a long-term solution for chronic pain patients. ITT bypasses the blood–brain barrier, which results in higher cerebrospinal fluid (CSF) concentrations of medications. This allows achievement of equipotent doses of equivalent oral medications to be delivered, so that drugs, such as opioids, can be reduced or even stopped [4]. Variables include which drug or combination of drugs to use, the concentration of medicines, catheter placement, and infusion strategies, such as continuous, bolus, or patient-activated bolus. This called for more research to be done on the dynamic forces present in the IT space. Work began to elucidate the

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complexities in delivering therapy by this means and a new understanding of how best to apply this therapy grew [5, 6]. Based on new data, guideline statements were created to improve patient safety by reducing interprovider variability in catheter placement, medications used, and patient selection [7, 8].

Patients with chronic pain can have separate or mixed pain states and both nociceptive and neuropathic pain qualities. Neuropathic pain is typically described as burning, gnawing, and lancinating, whereas nociceptive pain is commonly described as aching, mechanical, and sharp. Conservative therapies commonly include ultrasound or fluoroscopically guided injections, oral adjuvant medications, such as gabapentin or tricyclic antidepressants, systemic medication trials with IV lidocaine or Ketamine, topical analgesic therapies, and careful use of opioid medications. Chronic opioid therapy has not been found to be beneficial for long-term treatment of neuropathic pain and can actually worsen pain, as in patients with HIV-induced peripheral neuropathy [9]. Failure of patients to respond to conservative therapy obviates the need for advanced therapies, such as spinal cord stimulation (SCS) and ITT. For many chronic pain syndromes, SCS methods of treatment are used before ITT due to data suggesting that SCS is the safer option to start with [10]. When limitations of SCS therapy do not allow sufficient treatment to be obtained, as when paresthesias are unable to entirely cover painful areas, ITT should be the next consideration [11].

IT drug delivery for malignant and nonmalignant pain has become a well-established and effective treatment option for resistant or refractory pain that has failed conservative therapy [12]. Commonly, the safety concerns have placed ITT at the end of the treatment algorithm [10]. Thus, ITT has been viewed as a salvage therapy, due to the risks associated with IT opioids; however, there are nonopioid agents, which have led to its use earlier in the pain treatment algorithm [13]. Despite designation as a last ditch therapy, success has been demonstrated by randomized controlled trials with nonopioid agents [14–16] and opioids for malignant and nonmalignant pain [12].

Patient populations likely to benefit from ITT include those with failed back surgery syndrome, vertebral compression fracture, nonoperative spondylolisthesis and radiculopathy, as well as those patients unlikely to benefit from surgery [11]. This therapeutic option can also benefit patients with visceral, pelvic, and abdominal pain, as well as end-of-life care for cancer patients [17]. In order to be an appropriate ITT candidate, the patient must meet both a disease indication as well as patient selection criteria for optimal outcomes. Patient selection criteria include optimized preoperative management of comorbidities, autonomy and capacity to understand the therapy, ability to be present for medication refills and scheduled visits, no present symptoms of psychosis, and stabilization of any depression, anxiety, or personality disorders [11].

Currently, only two agents are FDA approved for intrathecal use in pain: morphine and ziconotide [18]. Ziconotide is a hydrophilic molecule that acts as a selective N-type voltage-gated calcium channel blocker. This results in limiting the release of nociceptive molecules, such as glutamate, calcitonin gene-related peptide, and substance P [19]. There are also other agents, which are commonly used

off-label, including bupivacaine, clonidine, and fentanyl [20]. There have been studies examining the use of other medications in the IT space, such as sufentanil, methadone, adenosine, hydromorphone, meperidine, gabapentin, baclofen, ketorolac, midazolam, neostigmine, octreotide, ropivacaine, dexmedetomidine, and lidocaine [7]. Critical factors needed for a better understanding of which IT therapy is better to use include the following: catheter location, volume of injectate, kinetic energy of injectate, drug dose, drug concentration, and the physiochemical properties of the drug, including density and hydrophobicity [11].

Intrathecal Medications

Selecting which IT medication to use encompasses many factors. These include the disease state (region of pain, type of pain), pharmacokinetics of the IT space, medication physicochemical properties, and device variables [11]. Physicochemical properties of the drug and its mechanism of action are critical in treating patients with neuropathic pain. The agent's density and hydrophobicity influence the length of therapeutic time when the medications are in the cerebrospinal fluid. The more hydrophobic a medication is, the less it is thought to spread, and the more it is thought to penetrate the lipid dense tissues of the spinal cord [7].

This means that the positioning of the catheter can be critical, especially with use of lipophilic medications [21].

As with opiates, intrathecal agents typically work by binding to particular receptors in the superficial layers of the dorsal horn. Prior to reaching their targets, intrathecal medications may be taken up by both fat tissue as well as blood vessels. The lipophilic agents are more likely to be taken up by the systemic circulation than hydrophilic agents, as the lipophilic agents readily diffuse past fatty cell membranes and into the circulation. Hydrophilic opioids, such as morphine and hydromorphone, can be preferred in certain cases, because they stay in the CSF longer, which allows them to diffuse more slowly into the layers of the dorsal horn not adjacent to the catheter tip.

Much effort in trying to understand the pharmacokinetic characteristics of intrathecally administered medications has revealed that lipid solubility plays a very important role in analgesic responsiveness [21, 22]. For example, unlike other agents used intrathecally, local anesthetics act earlier on sodium channels at the rootlets of nerve fibers in the IT space, rather than targeting spinal cord receptors [5]. Bupivacaine is the predominant local anesthetic used in chronic intrathecal infusion systems and is highly lipophilic.

A randomized double blind cross-over study looking at the addition of bupivacaine to deliver 4, 6, or 8 mg/day, through an intrathecal pump already delivering chronic morphine or hydromorphone, found no added benefit for bupivacaine [23]. On the other hand, a double blind study of 20 cancer pain patients, who failed conservative medical management, found that the combination of intrathecal morphine and bupivacaine blunted the escalation of intrathecal morphine dosing significantly [24].

The high lipid solubility of bupivacaine means that the catheter tip location is likely critical for its effectiveness in regional pain conditions.

Again, while preservative-free morphine and ziconotide are the only FDA-approved medications for intrathecal administration, the treatment of chronic pain often employs combination therapy in clinical practice. These other agents are used off-label or in combination with each other. The lack of FDA approval for these other medications hinders prospective studies and limits ability to adequately investigate their effectiveness when used alone or in combination. Neuraxial administration of a combination of local anesthetics and opioids is synergistic for pain relief in rats [25]; however, such an assertion cannot be easily made in human studies and may involve a number of other variables [26]. Research could demonstrate that combination therapy is superior to monotherapy, given the complexity of pain signaling mechanisms; however, no human studies have shown that potential [4].

The agent that has grown in popularity and is more routinely employed in ITT is the nonopioid medication ziconotide. It is the only nonopioid intrathecal option for IT treatment of chronic refractory pain [27]. There are three randomized placebo-controlled trials that suggest efficacy and another open-label multicenter study that demonstrates safety [14–16, 28]. The use of ziconotide has been shown to be helpful in both neuropathic and nociceptive pain in properly selected patients [14]. The side effects include dizziness, nausea, confusion, ataxia, myalgia, memory impairment, and induced psychiatric disorders. The psychiatric disorders are less frequent but can include auditory and visual hallucinations. This is why it is contraindicated in people with a history of psychosis and schizophrenia.

Ziconotide has been clearly defined in both animal and human studies to have linear kinetics, with a half-life of 4.5 h [6, 29]. Trials for this therapy are usually single-shot boluses; however, chronic ziconotide therapy is routinely begun as a simple continuous rate, with low starting doses and a slow titration schedule. There is a possibility that failure of this therapy after a positive trial may be the result of a pharmacokinetic difference between chronic continuous infusion and bolus delivery. The behavioral side effects, as represented in the dog model, were also altered with intrathecal infusion, but not with the intrathecal bolus [6]. This has been observed in human clinical trials, whereby patients using fast titration schedules consistently reported pain relief at high doses, but the usefulness of this relief was mitigated by side effects [13]. These side effects included neuropsychiatric adverse reactions, reduced level of consciousness, and elevation of serum creatine kinase. Thus, patients with a history of psychosis should not receive ziconotide. Pain physicians must have partnerships with mental health specialists to evaluate ITT candidates with a history of psychological pathology. If a patient has such a history, morphine may be a better choice, assuming the patient meets the other selection criteria [30].

Morphine, and other opiates used in ITT, underwent preclinical safety examination in animals, as measured by the Neurotoxicity Standardized Assessment. In chronically catheterized large animal models, the data showed that continuous infusions of morphine, hydromorphone, methadone, or fentanyl, for at least 28 days, caused no spinal tissue damage at the highest doses and concentrations examined [31].

Morphine monotherapy efficacy clinical data on IT morphine continued to support its use as a first-line therapy. Results from several long-term studies support the efficacy of IT morphine in treating patients with chronic pain, including both cancer and non-cancer pain types [7]. One example is a retrospective study, which examined patients with chronic malignant pain on long-term IT opioid therapy including morphine, hydromorphone, or sufentanil [32]. They noted that the Visual Analog Scale (VAS) scores significantly decreased from baseline up to the time of first refill. These scores remained stable and significantly lower than baseline scores for 3 years.

In a prospective, open-label study of IT morphine infusion, 110 patients with chronic pain were implanted and followed for 1 year [33]. Pain relief was noted within 1 month and was sustained for the 12-month period. Another open-label study examined patients with intractable pain due to chronic pancreatitis. These results showed a reduction in pain scores from an average of 8.3 to an average of 0.75 at the last follow up after 29 months [34]. For patients with vertebral fractures due to osteoporosis, who did not respond to oral opiates, an open-label study of IT morphine was conducted [35]. The mean VAS pain scores decreased significantly from 8.7 cm before IT therapy to 1.9 cm after 1 year. They also saw improvements in quality of daily life, ambulation, and perception of health status. Interestingly, a retrospective study designed to identify characteristics of patients likely to benefit from IT morphine therapy found a greater than 50% decrease in pain in 73% of patients [36]. The study included patients with multiple subtypes of pain, including cancer related, nociceptive, and neuropathic. No differences in responder rates were noted, regardless of pain type, patient age, or morphine dosage.

Many providers struggle with which agents to start with and which ones to add if the previously tried medications fail. The Polyanalgesic Consensus Conference in 2012 defined tiers of therapy in treating neuropathic pain [7]. Tier one for neuropathic pain includes morphine and ziconotide as monotherapy, along with morphine and bupivacaine in combination. If this fails, the second tier includes hydromorphone as monotherapy and combination therapy with bupivacaine or clonidine. Also included in the second tier is a combination of morphine and clonidine. The final tier suggests monotherapy with clonidine or fentanyl, as well as combination therapy using ziconotide with an opioid in combination with bupivacaine or clonidine [7].

Intrathecal Space and Mindful Catheter Placement

The understanding of drug distribution in the CSF has been a large focus of investigation. Textbooks have portrayed CSF in the IT space as flowing cephalad to caudad, by bulk flow, along the posterior surface of the spinal cord, and returning cephalad along the anterior surface [37, 38]. If true, this CSF motion would be expected to move drugs considerable distances. Animal studies have found that this portrayal of CSF movement is incorrect [5]. Numerous human studies using Magnetic Resonance Imaging techniques have shown that CSF oscillates back and forth along the rostro-caudal axis [39, 40]. This motion is driven by cyclic

expansion and contraction of the cerebrospinal vasculature during cardiac systole and diastole. The magnitude of motion is greatest in the upper cervical regions and decreases with more caudal distances from the foramen magnum. The oscillation of CSF becomes negligible at the level of the cauda equina [5].

One detailed examination of drug distribution in the CSF using bupivacaine (lipophilic) and lioresal (hydrophilic) found most of the bupivacaine and lioresal were recovered within 1 cm of the site of administration [5]. Drug concentrations in CSF between these two drugs reached steady state using a continuous infusion before the 8th hour of administration. This suggests that a longer period of drug administration would be unlikely to significantly alter the limited distribution of either bupivacaine or lioresal. Other studies have shown that net CSF motion is limited for multiple reasons, which include the following: CSF being propelled in opposite directions during each cardiac cycle, smaller CSF pulse waves at larger distances from the cranium, and CSF motion only occurring in the rostro-caudal axis—not circumferentially [5]. This could explain why patients can have marked, permanent rostro-caudal CSF concentration gradients for many molecules. These pharmacokinetic properties of medications in the CSF have led to a paradigm shift regarding the importance of catheter position. Yet, there is little published data on region-specific catheter location recommendations. Most practitioners determine catheter placement based on the patient's dermatomal location of pain or based on SCS paresthesia mapping [11].

Intrathecal Trial

There is no historical literature indicating a sound trialing method for predicting long-term success of intrathecal therapy by slow continuous infusion [7]. Trialing was previously thought to be critical, but this has come under scrutiny of late. It is felt that real insight into the success of long-term ITT cannot come from a single-shot trial or even from a brief 72- to 96-h infusion. Trialing may lead to an underestimation of the failure rate with long-term infusion. In chronic noncancer pain patients, it was found that groups of patients who had previously tolerated a drug after a trial bolus were accurately predicted to have long-term success with slow continuous infusion [41]. Yet, explants of IT pumps secondary to refractory pain do happen. In addition, the national trial-to-implant ratio is close to 40%, due to lack of at least a 50% reduction in pain or an improvement in function [42]. Contrary to ITT, positive results with an SCS trial are an excellent predictor of implant success.

Use of a single-shot injection to evaluate candidacy for chronic delivery of ziconotide, or other intrathecal medications, is gaining momentum [43, 44]. Single-shot strategies have been shown to be more cost effective, as compared to hospital inpatient catheter trials [45]. For one time bolus evaluations, a 23 h period of observation is typically all that is needed [13]. Catheter inpatient trials also can also obscure side effect profiles and have an increased potential for infection, since they

typically last 5–7 days [46]. The British Pain Society, which published recommendations for the best clinical practice in IT drug delivery, concluded that trials should always be performed before the implantation of an IT pump. They noted that trials can be done by either bolus or continuous injections; however, they felt that continuous infusion trials were less informative [47].

With opioids, there is little consistency and much disagreement about appropriate conditions for trialing. These trials typically use morphine or hydromorphone. It is felt that an opioid-naive brain is the ideal situation for an opioid trial. Here, IT opioids are more potent at microdoses, which mitigate secondary effects such as respiratory depression seen in higher IT doses. In patients who are not opioid naive, converting a patient's current opioid requirements into an appropriate IT dose for an opioid trial is debatable, because of differences in pharmacology between systemic and IT opioids. Often, a patient's disease process and pain severity will not allow for tapering before the trial. In these cases, a trial can be used to determine whether systemic opioid doses can be reduced [7].

Ziconotide trials can also be difficult because the side effect profile is closely related to the rate of dose increase, rather than the absolute dosage. Bolus trialing with ziconotide has drawbacks, because the side effects seen with bolus dosing may eliminate many patients who could have otherwise benefited from slow infusion therapy. This failure may represent a pharmacokinetic failure, as much as a pharmacodynamic failure, as there are only CSF oscillations providing little distribution of this hydrophilic molecule [48–50]. Trialing as an inpatient with an intrathecal catheter could be a solution to this problem, but this method can be hazardous because of the slow titration required. Here, catheter doses are typically only increased by 0.5–1.0 μg every few days [7]. Alternate trialing methods are needed to avoid trial failure due to intolerable side effects.

Risks

As demonstrated, IT therapy can be a life changing therapy bringing improved quality of life and significant pain relief; however, there are some risks that patients and providers need to consider. IT therapy can have complications secondary to technical, biological, or medication-related issues [17]. Most complications are minor; however, some can be serious. An increased mortality rate in patients with noncancer pain receiving IT therapy was shown to be related to the opioid dose, as well as patient and device issues, especially at the start of therapy [8]. Mortality rates were 0.088% at 3 days after implantation, 0.39% at 1 month, and 3.89% at 1 year after implantation. The possibility of an opioid overdose, due to improper dose calculation or pump failure, carries the risk of fatal respiratory depression. When first initiating IT opioid therapy, and when restarting IT opioids after an interruption in therapy, providers must be vigilant for this complication [51]. It is suggested that clinicians consider a catheter evaluation when taking over the management of an existing pump delivering opioids when the patient is not getting adequate therapy [30].

Other complications of IT therapy include catheter kinking, fracture, leakage, migration, CSF leak, seroma, hygroma, and pump erosion through the skin [4]. However, one of the most insidious complications is granuloma formation. Spinal granulomas are associated with certain chronic intrathecal opioid infusions [52, 53]. Continuous infusions of morphine, hydromorphone, methadone, or fentanyl for at least 28 days were examined, and all these agents, except for fentanyl were observed to produce IT granulomas in dogs at high concentrations [54]. Granulomas are inflammatory masses, which form at the tip of an intrathecal catheter. Animal studies demonstrate that they are related to the concentration of the infused opioid [55]. Possibly, the limited distribution of morphine away from the catheter tip predisposes to the formation of large granulomas, which subsequently increases the risk of spinal cord injuries [5]. Surgical interventions to treat granulomas are not typically needed, as weaning off the IT opiate and running preservative-free saline through the catheter can resolve them [56, 57]. Granulomas may occur in as many as 3% of implanted patients; however, they are usually asymptomatic. A prospective study determined that routine MRIs to rule out intrathecal granulomas were not necessary due to their low incidence [58]. The earliest sign of granuloma may be increased pain, despite increasing opioid infusion, due to obstruction of the catheter tip.

Chronic Intrathecal Infusion

The delivery of IT medications involves anatomical, functional, and fluid dynamic factors occurring in the nonhomogeneous CSF space [22]. Attempting to understand these variables focuses on understanding CSF dynamics in the IT space. One means of having a medication spread in the IT space is by the use of kinetic energy from the act of the injection itself. If injecting from a syringe, as with an IT drug trial, the medication can be rapidly distributed a great distance from the injection site, if the syringe plunger is pushed hard enough. Intuitively, it would seem that faster infusion rates would have the same effect; however, this was found to only create a slight increase in forward distribution of the medication [5]. Another mechanism that is thought to aid in drug distribution includes suspension of the drug in the CSF itself. However, this is unlikely based on MRI investigations demonstrating oscillation of CSF rather than flow [39, 40].

Oscillation can actually impair distribution of medications dissolved in the CSF [5], which suggests that the location of the infusion catheter tip, relative to the targeted spinal cord segment, is critical given the limited distribution from the catheter tip [59]. This is exemplified in cases whereby patients had marked improvement of spasticity and pain after injection of baclofen or morphine during a trial, yet found limited to no relief after the implant. Many of these cases were salvageable by repositioning the catheter tip [5]. Attempting to compensate for poor catheter position by increasing the flow rate seems like a viable option, so the idea was tested with CRPS patients in a study by van der Plas et al. They showed that when the daily dose of baclofen was maintained, and after a fourfold increase in flow rate was implemented, adverse events

increased, but there was no positive effect on dystonia or pain [60]. Another study examined increased flow rates in chronic pain patients and found that a fourfold increase in flow rate, at a constant daily dose, did not result in improved pain scores, but was associated with a significant decrease in quality-of-life scores [59].

The market currently has two implantable delivery systems, which include Medtronic's Synchromed II and Flowonix's Prometra II. The Synchromed II uses a peristaltic rotor delivery system, which has a good track record, but has had past issues including precision with priming bolus, motor corrosion, and over infusion [11]. The Synchromed II also offers patient-controlled bolusing, termed patient therapy manager (PTM), which has been well received. The Prometra pump is a reservoir that works via a valve-gated bellow system. This allows delivery of precise, predetermined volumes, at specific times. A recent study of the Flowonix system found it to be very accurate and best in its class regarding bolus delivery [61]. Another difference between the two systems is shown when patients need an MRI. In the past, it was recommended that all the medication from the reservoir be removed before the scan, as the magnetic field could cause the peristaltic motor to deliver imprecise aliquots and lead to overdosing of the reservoir medications. The Prometra II has a gated outlet, which circumvents the need to empty the reservoir [11]. There are no studies that demonstrate superiority of one delivery device against the other, so the decision of which system to use depends on the patient's condition and surrounding circumstances.

An alternative strategy for trialing and medication delivery has been suggested in the literature with a recent study, which was meant to address the poor translation from trial to permanent therapy due to a pharmacokinetic failure [13]. These investigators proposed a dual bolusing trial and a nocturnal flex dosing chronic infusion strategy. Flex dosing is a daily single programmable dosing strategy. This delivery method is thought to more closely approximate the pharmacokinetics seen during the medication trial. In their study, they hypothesized that the best time to activate their bolus dose for ziconotide was at night. This would help to avoid the cognitive side effects that can be seen when a bolus dose is delivered and the bolus would be delivered with the patient in a horizontal rather than a vertical position [13]. They carried out a small prospective case series showing proof of concept that their dual bolusing strategy of ziconotide may improve its tolerability. The team was able to demonstrate that after 6 months of ziconotide monotherapy using nocturnal dosing, 70% of patients still had benefit. Unexpectedly, they found that the dose of ziconotide needed for pain relief at 6 months was 2.7847 μg/day, which is much less than the 6.9 μg/day reported by Rauck et al., and the 6.48 μg/day that was reported by Webster et al. [14, 62].

Conclusion

Challenges limiting the increased use of ITT include the complex nature of the patient's pain, the various risks associated with the devices and medications, and the possible need to find the correct "recipe" or combination of drugs to treat the pain.

Combination therapy is further complicated by the use of a single-chamber pump to deliver the various drug cocktails. Despite all the work put into performing trials and implants, refilling pumps, and the high level vigilance required, ITT is not well compensated by the current reimbursement system [63]. Poor reimbursement limits the development of advanced devices, novel dosing strategies, and medications, which could offer improved analgesia and safety. The cost effectiveness of IT therapy has been demonstrated to be superior to conventional therapy, with high start-up costs recoverable within 28 months [64]. Additionally, systemic opioid overdoses leading to death were found, by the Centers for Disease Control (CDC), to be nearly 16,000 in 2009. For every one of these overdose deaths, nearly 900 people took prescription painkillers for nonmedical use [65]. Based on these findings, ITT has a permanent place in the pain care algorithm.

The old idea of ITT, which represented a treatment option for patients failing escalating doses of systemic opioid medications, is rapidly fading. Now, this therapy is no longer just considered a salvage strategy when high-dose systemic opioid therapies fail. Pain providers have a responsibility to their patients to provide access to evidence-based care. Clear evidence exists that there is an inherent risk, including death, of doing nothing to manage a patient's pain [66]. New findings, such as the improved efficacy of ziconotide therapy when using a single nocturnal programmable dosing strategy, have begun to significantly improve patient control of their pain. With improved patient satisfaction, demand for this therapy will increase, as will the desire of investigators and private companies to find new ways to improve it.

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Chapter 57
Deep Brain Stimulation for the Treatment of Pain in the Rehabilitation Patient

Steven M. Falowski and William S. Rosenberg

Abbreviations

CCH	Chronic cluster headache
DBS	Deep brain stimulation
PH	Posterior hypothalamus
PVG/PAG	Periventricular/periaqueductal gray area
SF-36	Short Form (36) Health Survey
VPL/VPM	Ventral posterolateral/ventral posteromedial nucleus

Introduction/History

Deep brain stimulation (DBS) involves the delivery of electrical current to subcortical neural targets via implanted electrodes in the intracranial space. Although DBS received FDA approval for the treatment of movement disorders in 1996 and is most often used to treat Parkinson's disease, essential tremor, and dystonia, it has also been used off-label for pain. In fact, one of the first uses of neurostimulation to treat refractory chronic pain involved DBS [1]. A benefit of DBS, relative to other neurosurgical procedures used to treat pain, such as ablation, is that

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it is both adjustable and reversible. It is also less invasive; therefore, it is associated with a lower risk profile. This chapter will review hypothesized mechanisms of action, common indications, impact on functional limitations, patient selection and surgical technique, efficacy, potential complications, and areas for future research.

Pathophysiology/Mechanisms

Although the use of DBS to treat chronic pain has been studied for more than five decades and precedes Melzack and Wall's gate control theory, its exact mechanism of action remains uncertain [2, 3]. Abnormal rhythmic activity in periventricular and periaqueductal gray area (PVG/PAG) and ventral posterolateral and ventral posteromedial nucleus (VPL/VPM) is thought to play a significant role in pain pathophysiology. No standardized algorithms for treatment exist, but decisions regarding DBS targets are typically guided by the specific type of pain reported [4]. For example, treatment of nociceptive pain most often involves stimulating the central gray matter (i.e., the PAG or PVG), because the region is thought to interact with the endogenous opioid system. In contrast, treatment of neuropathic pain usually involves stimulation of the sensory thalamus (i.e., the VPL or VPM nucleus), since the dorsal medial lemniscus pathway travels through that region [5, 6]. Other physiologic targets include the ventrocaudalis thalamic nucleus, the medial thalamic nuclei (e.g., the centromedian–parafascicular complex), the rostral anterior cingulated cortex, the globus pallidus, the subthalamic nucleus, and the ventral striatum.

Common Diagnoses/Symptoms Treated

DBS has been used to treat many different types of chronic pain, both nociceptive and neuropathic. Research evaluating the use of DBS for various chronic pain conditions found that patients with failed back surgery syndrome and peripheral neuropathic pain experienced the best long-term results, with more mixed results observed in patients with trigeminal neuropathic pain and/or anesthesia dolorosa, and in patients with phantom limb pain. DBS for spinal cord injury and post-stroke pain was much less successful [7]. In general, DBS does not appear to be an effective treatment for central pain syndromes, but does have some promise in a largely recalcitrant patient population [8]. DBS has also been used to treat trigeminal autonomic cephalalgias [9] (e.g., chronic cluster headache) [8–11], paroxysmal hemicranias [9, 10], and SUNCT syndrome [9, 10, 12], chronic low back pain [1], and pain secondary to brachial plexus avulsion [1].

Functional Limitations Addressed/Assessed

Chronic pain can have a significant impact on a patients' function, due to its effect on factors such as sleep, health, social interactions, personal relationships, employment status, and other activities of daily living [13]. A number of studies have used the Short Form [14] Health Survey (SF-36), a 36-item, patient-reported survey of functional health, to investigate the effect of DBS on function, as well as on pain. For example, in addition to studying the effect of DBS of the PVG/PAG on 7 patients' intractable head and facial pain (in 4 of the 7, a second electrode was placed in the VPM of the thalamus), Green et al. also evaluated the patients' health-related quality of life by administering the SF-36 pre- and postoperatively. They analyzed each of the eight SF-36 categories individually (physical functioning, physical role limitations, bodily pain, general health, feeling of vitality, general mental health, social functioning, and emotional role limitations) and also calculated a composite physical component score and mental component score. Overall, they found a significant improvement in the mental component score, reflecting better scores in the bodily pain, general health, and social functioning categories; however, there was no improvement in the physical component score [15]. Boccard et al. used the SF-36 to study changes in the health-related quality of life of 39 patients whose chronic pain was successfully treated with DBS of the PVG and/or VPL/VPM for chronic neuropathic pain. During the first year postsurgery, the patients experienced a 26% improvement in SF-36, which increased to 34% at 4 years [2]. The same group also used the SF-36 to study changes in the health-related quality of life of 15 patients who received DBS of the anterior cingulated cortex for chronic pain. They reported that, although total SF-36 scores did not significantly change following implantation, the physical functioning and body pain categories significantly increased by 64.7% and 39.0%, respectively [16].

Finally, Gray et al. followed 18 patients with chronic, neuropathic pain who received DBS of the PVG/PAG and sensory thalamus and also used the SF-36 to evaluate changes in health-related quality of life. The investigators found that, postsurgery, patients experienced significant improvement in two categories: physical role limitations and mental role limitations. However, postimplantation SF-36 scores continued to be elevated on all subscales, relative to a normative sample [17].

Given the few published studies, it is difficult to make any generalizations regarding the impact of DBS on functional limitations in patients with chronic pain, although it demonstrates promise in these few studies. More research is needed to gain a better understanding of the way in which DBS can be used, not only treat pain, but also the effects of pain on a patients' physical and social function.

Techniques

Patient Selection

DBS is generally considered when drug treatment at adequate dosages and for sufficient periods of time is ineffective or is associated with intolerable side effects. Although a neurologist may refer a patient for DBS, preoperative evaluation is usually conducted by a multidisciplinary team and should include a pain specialist, a neurosurgeon, and a neuropsychologist. It involves a detailed history and physical examination to evaluate pain intensity and distribution, as well as psychological screening to rule out psychogenic pain or other psychiatric disorders [6, 10, 18].

No standard inclusion or exclusion criteria exist for patients undergoing DBS for chronic pain, although there are proposed guidelines for some specific conditions. For example, several investigators have recommended that patients with chronic cluster headache consider DBS only if they have experienced near daily unilateral attacks refractory to all medication for at least 24 months [19, 20].

Surgical Technique

The surgery to implant a DBS device takes approximately 2 h and is generally performed using moderate intravenous sedation, as well as local anesthesia for the incisions. High resolution MRI or CT scan imaging and stereotactic navigation (either frame based or frameless) are used to guide implantation of the electrodes. Following the creation of a parasagittal frontal burr hole through a small incision, subcortical targets are localized with the use of intraoperative trial stimulation involving either microelectrode recording, microstimulation (i.e., test stimulation through the microelectrode), or macrostimulation (i.e., test stimulation through the final lead). Some targets, e.g., the cingulate gyrus, do not require intraoperative testing, and the surgery can be performed using general anesthesia. Once the targets are localized, permanent electrodes are positioned and the leads are externalized for postoperative trial stimulation. This is followed by a CT scan or MRI to confirm electrode placement and the absence of intracerebral hemorrhage (Fig. 5.1). Approximately 1–2 weeks of additional trial stimulation takes place. If satisfactory pain relief is obtained during that time, the electrodes are then connected to an implantable pulse generator during a second surgical procedure [1, 5, 8] (Fig. 5.2).

Evidence

DBS appears to be an effective treatment for a number of different types of refractory chronic pain. Much of the evidence to date has focused on the sensory thalamus and the PAG/PVG, although researchers have also studied stimulation of the

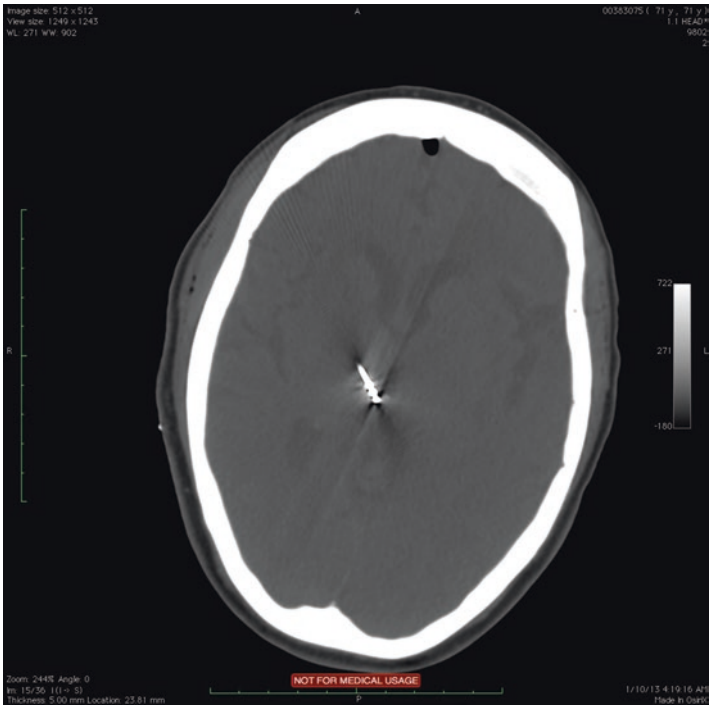

Fig. 5.1 Postoperative CT head demonstrating a right-sided DBS lead

internal capsule, the center median–parafascicular complex, and the posterior hypothalamus. The generally accepted treatment goal is at least a 50% reduction in pain; however, objective assessment of a subjective symptom like pain can be difficult [21]. Other study limitations include the following: lack of randomized or case–control trials; lack of detail regarding patient selection criteria; unblinded assessment; and variation in targets stimulated, parameters used, and pain syndromes included [16, 22].

Sensory Thalamus DBS

The three largest studies within the past decade that focused specifically on DBS of the sensory thalamus include research by Yamamoto et al., Hamani et al., and Pereira et al. [23–25]. Yamamoto et al. reported on a case series in which 18 patients with phantom limb or stump pain received DBS of the thalamic nucleus ventralis caudalis. Fourteen of the 18 achieved long-term satisfactory pain control. The authors noted that bipolar stimulation of wide areas from the anterodorsal part to the center of the ventralis caudalis appeared to be more effective than focal stimulation of a more limited area. They also partly attributed their success to the use of

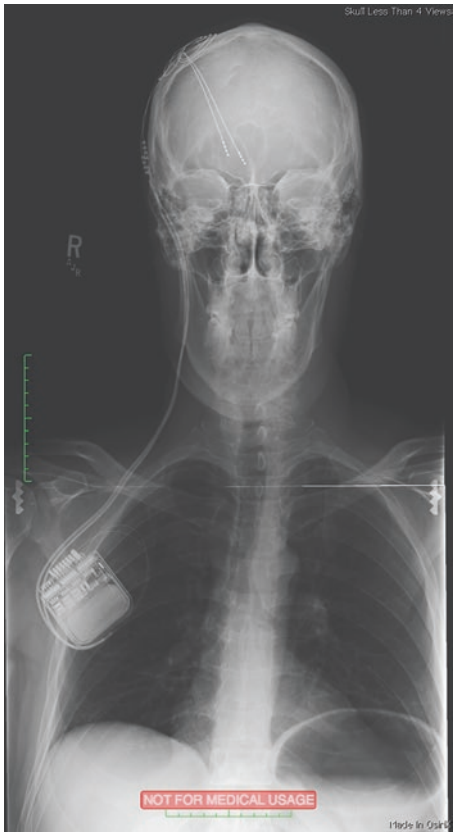

Fig. 5.2 X-ray imaging demonstrating a complete DBS system implant (lead, extension, and pulse generator)

exclusion criteria, which were based on pharmacological classification by the morphine, thiopental, and ketamine tests [23].

A case series by Hamani et al. included 21 patients with chronic neuropathic pain, which was characterized by burning, aching, dysesthesias, and/or allodynia. Of the 13 who had electrodes placed solely in the ventrocaudalis thalamic nucleus, five experienced an insertional effect, and ten had a successful stimulation trial, but only two of the ten experienced relief of pain that lasted for more than 1 year [24].

Most recently, Pereira et al. conducted a one-year prospective case series that included 12 patients with either phantom limb pain or brachial plexus avulsion who received DBS of the VPL sensory thalamus. At the end of the year, 11 of the 12 reported persistent pain relief. The authors noted that they focused on the VPL, instead of the PVG, because the latter is a target with: (1) more clearly delineated intraoperative stimulation effects, (2) less risk of side effects, and (3) a strong connection to appendicular pain syndromes [25].

PVG/PAG DBS

The three largest studies within the past decade that have focused on DBS of the PVG/PAG include research by Rasche et al., Owen et al., and Boccard et al. [2, 7, 26]. Each of these investigators also cotargeted the VPL/VPM during the procedure, which is sometimes considered a second-line approach following unsuccessful PVG/PAG stimulation [2]. Rasche et al. published a case series that included 56 patients with failed back surgery syndrome, anesthesia dolorosa, phantom limb pain, spinal cord injury, poststroke pain, or postherpetic pain. Of these, 32 underwent permanent DBS implantation, with favorable results observed in 22. The best long-term results were seen in failed back surgery patients, the majority of whom preferred to have both PVG and VPL electrodes activated [7].

Owen et al. reported on a case series that included 47 patients, most of whom had pain related to stroke, phantom limb, or brachial plexus injury. Of these, 38 underwent permanent DBS implantation, with six lost to follow-up. Of the remaining 32 patients, PVG stimulation was optimal in 17 and associated with the highest degree of pain relief. A combination of PVG and thalamic stimulation was optimal in 11 patients, and thalamic stimulation alone was optimal in four patients.

Most recently, Boccard et al. published a prospective case series including 85 patients with phantom limb pain, stump pain, plexus injury, poststroke pain, spinal cord injury, or facial pain. Of these, 74 underwent permanent DBS implantation, but 15 were lost to follow-up. Of the remaining 59 implanted patients, 39 experienced favorable results, with 21 receiving only PVG stimulation, five receiving only VPL/VPM stimulation, and 13 receiving stimulation of both targets. The greatest success was observed in patients with phantom limb pain. For most cases of neuropathic pain, the authors recommend targeting the PVG first and proceeding to VPL DBS only if the patient does not experience an intraoperative sensation of pleasant warmth with PVG DBS [2].

Internal Capsule DBS

The most recent research focusing specifically on DBS of the internal capsule includes two studies by Namba et al. and one study by Franzini et al. [27–29]. Namba published two case series focusing on patients with poststroke pain, thalamic pain syndrome, or multiple sclerosis. In the first series, seven patients underwent trial stimulation of the posterior limb of the internal capsule and, of these, six received permanent DBS systems. Three experienced good results, two experienced fair results, and one experienced poor results after follow-up ranging from 9 to 31 months [27]. Based on the results of the second case series, in which 8 of 11 patients experienced fair to excellent pain relief, Namba et al. determined that the most posteromedial part of the internal capsule (i.e., the nucleus reticularis pulvinaris or area

triangularis) is the most effective target [28]. More recently, Franzini et al. published a case report of the successful use of internal capsule DBS for a patient with poststroke pain, based on 5 years of follow-up [29].

Center Median–Parafascicular Complex DBS

Several investigators have published research focusing on DBS of the center median–parafascicular complex [30–32]. For example, Andy et al. reported on a case series, in which five patients with intractable thalamic pain syndrome or headache received DBS of the CM–Pf complex and related intralaminar nuclear structures. All five patients experienced good to excellent pain improvement. The authors hypothesize that the CM–Pf complex and thalamic intralaminar system are both directly and indirectly involved in the mechanisms for both central and peripheral generated pain. Furthermore, they believe that DBS of these targets relieves pain by altering the excitability state and/or the thalamic discharge patterns [30].

Krauss et al. published an abstract comparing CM–Pf stimulation to sensory thalamus stimulation in a prospective case study involving 11 patients with chronic neuropathic pain. Ten of the patients underwent permanent DBS implantation and experienced significant pain improvement with CM–Pf stimulation, relative to both preoperative pain and VPL/VPM stimulation [31]. The same group also published a subsequent study of CM–Pf DBS for three patients with neuropathic pain and concomitant movement disorders. All three patients experienced improvement in their movement disorders, and two of the three experienced improvements in pain that were significant enough to prompt permanent implantation of the DBS system [32].

Posterior Hypothalamus DBS

The posterior hypothalamus (PH) is typically targeted in an effort to treat refractory, chronic cluster headache (CCH). General consensus is that approximately 50–60% of CCH patients have a positive response to DBS of the PH [9, 10]. For example, Fontaine et al. published a randomized, controlled, double-blinded trial, in which 11 patients received active or sham stimulation. At 1 month, there was no significant difference in headache frequency between the two groups; however, after 1 year of active stimulation, six experienced at least a 50% decrease in headache frequency, and three of the six were pain free [33].

More recently, Seijo et al. studied the use of PH DBS in a case series of five patients with CCH, but targeted the posterolateral hypothalamus in an effort to increase the stimulated area and to avoid damage to the third ventricle wall. At 33 months, all five patients experienced at least a 50% decrease in headache frequency, and two of the five were pain free [34].

Potential Treatment Complications

DBS-related complications can occur at any point during the surgical procedure and/or postoperatively, although technological advances (e.g., coaxial DBS electrodes) and increased experience with the procedure have yielded a relatively low-risk profile. The most potentially serious complication is intracranial hemorrhage, which occurs most often at the cortical entry site during electrode insertion or removal. Incidence ranges from 1.9 to 4.1% of cases, and most cases are asymptomatic. Following symptomatic hemorrhage, patients often improve with supportive therapy and typically do not require evacuation or device revision [1, 8]. The incidence of permanent neurological deficits, most of which are associated with hemorrhage, ranges from 2.0 to 3.4% [8, 35, 36].

Infection (e.g., meningitis, encephalitis, or at the scalp or pulse generator site) is another potentially serious DBS-related complication, with an incidence ranging from 2.4 to 13.3%. It is more often hardware related than intracranial and usually requires systemic antibiotics, wound debridement, and device revision although infection can sometimes be resolved with antibiotics alone [1, 8].

Hardware-related complications can occur at any time during the lifespan of the DBS device and have an incidence of approximately 7%. Examples include lead fracture, pulse generator failure, lead migration, and erosion. Other less common adverse events include cerebral edema, venous air embolism, and ischemic events, as well as more minor and transient complications, such as headache, vision changes (e.g., diplopia, blurred vision, vertical gaze palsies, and horizontal nystagmus), and nausea [1, 8].

Conclusion/Areas for Future Research

Although DBS has been successfully used to treat a large number of patients with varying chronic pain conditions, many questions remain unanswered. On one end of the continuum, more basic research is needed to gain a better understanding of the mechanisms of action behind the efficacy of DBS. On the other end, large, well designed, randomized, controlled trials with standardized protocols are necessary to better understand physiologic targets and stimulation parameters, as well as to improve protocols for patient selection. Progress in this area is reflected by a recently published clinical trial design that includes a control arm to investigate stimulation of the ventral striatum and anterior limb of the internal capsule [14].

Another challenge related to DBS for chronic pain is the fact that 25–50% of patients who undergo successful trial DBS do not experience long-term pain relief after permanent system implantation [22]. Further research can help to identify the factors underlying this apparent habituation and the techniques that can be used to address it. Additional research may also help to determine if neuronal signatures based on local field potentials could be used to facilitate patient selection or even lead to the development of pulse generators that automatically respond to physiologic changes [2].

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Part XI
Multi Modal Approach: Neuroablation

Chapter 58
Neuroablative Procedures for the Treatment of Pain in the Rehabilitation Patient

Daniel M. Aghion

Introduction

All tissues of the body are innervated by nociceptors, with the exception of the neuraxis. These are primary afferent neurons that are specialized to detect the presence, intensity, and quality of noxious stimuli. Incoming nociceptive information is then processed centrally by several cortical structures including the primary somatosensory cortex, secondary somatosensory cortex, anterior cingulate cortex, and the insular cortex. Whether the character of one's pain is peripheral or central in nature, surgical interventions for pain may be performed at the level of the primary afferent neurons, through their ascending pathways, within the thalamus, or in areas of the cortex that these fibers project to.

Unlike other physiological processes, pain does not emanate from a single specific organ but rather from a distributed system. Patient selection and psychological assessment is of the utmost importance in evaluating a patient for a surgical pain relief procedure. An individual's integration and affective information is crucial to understanding their pain. All comorbidities should be treated before considering any surgical intervention.

When evaluating a surgical option, one practical approach to discriminate the types of procedures available is to divide them into "Neuromodulation" and "Neuroablation" procedures. Neuroablation is typically a destructive procedure that interrupts afferent input from the nociceptive pathways. Although the lesions themselves are irreversible, the long-term effect on pain perception is often limited to months or years, because of the adaptability and plasticity of the nervous system. Neuromodulation, on the other hand, seeks to decrease pain by modulating

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nociceptive input by either pharmacological or electrical means. This typically requires implantable pumps or electrical stimulating devices and has the advantage of testability, adjustability, and reversibility. Because neuromodulatory procedures are covered in separate chapters of this text, the focus of this charter will be on neuroablative procedures.

Neuroablation: Relieving Pain by Interrupting Pain Pathways

Neurectomy

A neurectomy is the transection or partial resection of a nerve. This can only be considered for small peripheral nerves that are purely sensory. This imparts complete numbness in the distribution of the nerve, but can be useful in the facial region, especially with trigger point areas. Unfortunately, it rarely provides long-lasting relief. Partial resection of a nerve is generally only considered for painful neuromas. The correct nerve is identified, the end-bulb neuroma is resected, and the proximal nerve is relocated to a site that is away from any irritation, usually into a nearby muscle.

Facet Blocks and Denervations

This topic is covered in another chapter of this book.

Dorsal Root Ganglionectomy (DRG), Dorsal Rhizotomy (DR), and Dorsal Root Entry Zone (DREZ) Lesions

The nerve cell bodies of the nociceptive neurons reside in the dorsal root ganglion. Three to ten posterior spinal rootlets enter the posterolateral sulcus of the spinal cord, creating what is thought of classically as the dorsal root entry zone (DREZ). This zone subserves pain perception for that dermatomal distribution, but most areas of the body and peripheral nerves are innervated by multiple overlapping nerve roots. For this reason, these procedures usually require lesioning at multiple levels for adequate pain relief. DRG and DR are sometimes indicated in patients suffering from chronic pain in a particular dermatomal distribution related to cancer or tumor. DRG is still utilized in the cervical region for severe and intractable occipital neuralgia, whereby the C2 ganglion is removed with good long-term results.

Dorsal rhizotomy is most often performed intradurally but may also be carried out extradurally. The intradural technique is performed through standard multilevel laminectomies, allowing for overlap of innervations. After the dura is opened, the

selected sensory roots are followed rostrally to their respective true level, then cauterized, and then transected. However, this technique causes a loss of all sensation within that dermatome. Therefore, modifications of the DR were developed to preserve cutaneous and proprioceptive sensation; namely, the selective DR and the DREZ lesion were developed.

Selective DR implies making small 1–2 mm incisions in to the ventral aspect of the DREZ; thereby, this interrupts small unmyelinated nociceptive fibers, while preserving larger heavily myelinated fibers subserving touch and proprioception, which enter the DREZ dorsally. DR does require a multilevel laminectomy. After the dura is opened, the arachnoid layers must be freed, exposing both the rootlets and the pia mater. The microsurgical dissection then involves creating a longitudinal incision of the dorsolateral sulcus, ventrolaterally to the entry of the rootlets into the sulcus. Microbipolar cautery can then be performed within the sulcus, down to the apex of the dorsal horn in the spinal segments targeted. The average lesion is 2–3 mm deep, at a 35° angle medially and ventrally. Lesions are performed at each selected level that corresponds to the pain dermatome.

DREZ lesions can also be performed using a small radiofrequency needle, which is placed 2–3 mm into the DREZ area of the spinal cord, through its dorsal surface. The tip is heated to 65–70 °C, which thereby preferentially destroys the unmyelinated and ventrally located pain fibers. Approximately 10–12 lesions have to be placed in each spinal segment; multiple segments should be treated for effective pain relief. The goal is to lesion only the dorsal roots, preserving the ventral ones. The procedure is guided by both motor and somatosensory evoked potentials to ensure that no ventral roots are being affected, which is then followed by stimulating each root to identify its functional value. The most common indication for this procedure is a brachial plexus avulsion injury. Others include cancer pain, cauda equina or spinal cord lesions, peripheral nerve lesions, and postherpetic pain.

Extradural rhizotomies are quite similar to a ganglionectomy; however, the ganglion is not resected. Using this technique, the corresponding motor root should be identified and preserved whenever possible, as it sometimes lies within the same dural encasement. Percutaneous radiofrequency rhizotomy or ganglionectomy may also be performed since unmyelinated or small myelinated neurons are sensitive to thermal lesioning. A tip electrode is placed within the neural foramen and heat at 42 °C is passed for 15 s. A more permanent lesion may be performed by using 65–90° of heat for 60–90 s.

Sympathectomy

Historically, sympathectomy was performed to treat epilepsy, glaucoma, goiter, spasticity, and even trigeminal neuralgia. In 1920, it was performed on a patient with hyperhidrosis, yielding superior results; it has become the most common indication for the procedure since. Other indications include sympathetically maintained pain and select cases of vasculitis. The characteristic sympathetic pain is

severe, continuous, and burning in nature with both hyperalgesia and allodynia. Additionally, it may be accompanied by skin changes, temperature changes, and hyperhidrosis. Historically, this was described as reflex sympathetic dystrophy (RSD); however, it is now classified as complex regional pain syndrome (CRPS). Sympathetic blocks are the treatment of choice in this patient population, and the patient may show marked improvement in symptoms, but after repeated blocks, patients tend to become less effective. At this point, sympathectomy should be considered.

For open surgery, supraclavicular, transaxillary, and retroperitoneal flank approaches have all been described, but the most common route is the posterior paravertebral approach. For a thoracic sympathectomy, the procedure is done in a prone or sitting position. The T2-3 costotransverse junction is exposed on the side of the pathology, which is then removed, along with the proximal 3 cm of the head of the ribs. Just deep to this, the sympathetic chain is visualized medial to the pleura. Using a clip, the chain is clipped above the T2 ganglion, to include the inferior portion of the stellate ganglion, and below the T3 ganglion. The chain is then cut between the clips. Rami communicantes adjacent to this are also clipped and cut to ensure a complete sympathectomy. In the case of thoracic sympathectomies, the procedure may also be performed thoracoscopically. Postoperative pneumothorax is a known complication and may require treatment with a chest tube, while Horner's syndrome may be caused by resecting or injuring the stellate ganglion and the fibers that innervate the papillary muscles of the eye.

In the case of lumbar sympathectomies, a retroperitoneal approach is used. This is done through a large flank incision carried down to the abdominal muscles. Using blunt finger dissection, the peritoneum and renal tissue is displaced from the posterolateral abdominal wall. After identifying the quadratus lumborum, medial dissection exposes the psoas muscle and the vertebral bodies with the adjacent aorta, if performed on the left, and vena cava, if performed on the right. The lumbar sympathetic chain is then identified lying on the anterolateral part of the vertebral body, between the psoas and aorta or vena cava. As described earlier, the L2 and L3 regions are clipped and cut along with the corresponding rami communicantes.

Hypophysectomy

In 1952, hypophysectomies were performed for palliation from intractable pain related to metastatic carcinoma. Treatment of this disease entity has evolved tremendously over the past decades, but widespread acceptance for hypophysectomies lasted over 30 years and the indications for such a procedure have broadened. As a better understanding has evolved of hormones and their effect on cancers, such as breast and prostate, surgery to remove target hormone glands, such as the ovaries, adrenal glands, or even part or all of the pituitary gland began in an attempt

to keep the patient's cancer at bay. The results of this were mixed and sometimes included life-threatening complications. However, a marked effect on pain relief was noticed.

Open hypophysectomies transitioned to transsphenoidal approaches in the 1960s, which provided for a much less morbid surgical approach. Stereotactic radiofrequency and cryotherapy hypophysectomies were developed as well, which used radiographically guided instruments into the sella via a transsphenoidal approach. Though pain was usually only a secondary side effect of the procedure, patients continued to report immediate and long lasting pain relief after undergoing their surgery. Also in the 1960s, functional hypophysectomy for prostate carcinoma was attempted using brachytherapy with stereotactically implanted yttrium^{90}, with good pain relief. Additionally, in the late 1960s and 1970s, stereotactic chemical ablation of the pituitary was performed with ethanol. It was not until the 1970s when the focus of reports on hypophysectomy emphasized pain relief and not the effect on tumor control.

Fracchia et al. reported on a series of 203 patients with advanced stage breast cancer treated with various forms of hypophysectomy, and 180 of 203 patients had pain relief with the procedure; although, only 68 patients had no objective tumor response. The mechanism of pain control after hypophysectomy was initially viewed as a result of tumor shrinkage, and removing hormonal stimulation led to an overall decrease in size of the tumor burden, which thereby caused less pain. However, as time passed, it was noticed that pain relief was achieved in nonhormone responsive tumors in the absence of clinical improvement. Although no identifiable pituitary hormone was known as a pain mediator, it was not until 1984 that Ramirez and Levin suggested that the paraventricular nucleus (PVN) in the hypothalamus may be the key anatomic locus for pain control. Projections from the PVN are known to innervate the spinal dorsal horn, perimesencephalic gray, and other structures known to be important pain-modulating centers. Thus, the hypothalamus may in fact be the key to the efficacy of hypophysectomy, but it is only rarely performed today.

Midline Myelotomy

Interrupting ascending pathways that deliver nociceptive signals to the brain has been a mainstay of neurosurgical procedures aimed at the treatment of pain. Several of these procedures are either prone to complications or necessitate bilateral procedures; for this reason, the midline myelotomy is rarely performed today. It was developed in 1926 and the aim was to treat intractable visceral pelvic pain by interrupting the crossing axons of the spinothalamic tract neurons on both sides, by incising the midline of the posterior spinal cord. It was noted that pain relief was achieved at sites well distal to the levels of decussating axons. To this day, it is still unclear as to the mechanism of pain relief in midline myelotomies. The relief from

this procedure is reported to last for 31 months after surgery without sensory, motor, or autonomic complications that are sometimes seen with other procedures.

Anterolateral Cordotomy (AC)

The anterolateral quadrant of the spinal cord contains ascending pathways that are responsible for transmitting nociceptive information to the cerebral cortex. Of these, the most important are the lateral spinothalamic and spinoreticular tracts, which are located in the posterior quadrant of the cord, along with the posterior columns; therefore, pain can be relieved without loss of motor control. The procedure may be performed percutaneously or via open laminectomy.

The percutaneous procedure is performed with radiographic guidance, by inserting a needle into the spinal cord via a lateral C1–C2 puncture. After penetration of the dura, and prior to entering the cord, a small amount of dye is injected to outline the insertion of the dentate ligament. The radiofrequency needle is then inserted 3–4 mm into the anterior quadrant of the cord, and a lesion is thereby created.

The open procedure may be performed unilaterally or bilaterally, depending on the source of the patient's pain, but is obviously only valuable in abdominal and lower extremity pain. The patient is positioned prone and the spinous processes and lamina are removed at the T2-3 levels. The dura is then opened, and the dentate ligament is cut to allow gentle rotation of the cord and visualization of the exiting ventral roots. The pia, over the anterolateral quadrant, is then opened and a cordotomy electrode is inserted into the white matter with EMG guidance. A probe that reflects the dimensions of that specific cord is then used to make the lesion. The probe is swept anteriorly, avoiding the anterior spinal artery. Complications from AC are related to the tracts that are lesioned. Painful dysesthesias; decreased respiratory drive; bowel/bladder dysfunction; and sexual dysfunction, weakness, ataxia, and hypotension have all been reported, but overall, AC can provide excellent short-term pain relief lasting 12–18 months. This makes it especially appropriate for patients with cancer pain.

Mesencephalotomy

Mesencephalotomy, or a lesion into the midbrain, was initially an extended cordotomy procedure intended to lesion the spinothalamic tract at the high level necessary to treat upper extremity or head and neck pain. Unfortunately, patients experienced very high rates of morbidity and mortality, and if they survived the procedure, patients still had severe dysesthetic pain, as well as a loss of sensation on the contralateral part of their body. Nevertheless, mesencephalotomy remains a consideration and treatment option for patients suffering from severe cancer pain, chronic pain, or central pain, at locations too high to treat with an IT pump or anterolateral cordotomy.

Extraocular palsy remains a known risk of this procedure and patients should be counseled on this prior to surgery. Today, the procedure has been modified to account for its prior morbidity and involves lesioning the paleospinoreticular pathway. It incorporates the lateral edge of the central gray and includes the medial part of the reticular formation. This procedure now actually spares the spinothalamic tract and provides bilateral pain relief. Additionally, it has been shown that intrinsic chemical changes occur as a result of severe pain and emotional distress. Therefore, the goal of mesencephalotomy is accomplished by modifying the perception of pain itself.

The procedure itself is carried out using stereotactic MRI guidance and electrode insertion into the mesencephalic spinoreticular tract, avoiding the tectum. Intraoperative stimulation is used to verify location of the lesion site between 5 and 300 Hz. At the target site, a small radiofrequency lesion is made, which usually produces a severe emotional response and a feeling of pain relief at the core of the body. If the electrode is too lateral in the spinothalamic tract, paresthesias on the contralateral body are felt. If the electrode is too close to the medial lemniscus, contralateral tremor is seen.

Medial Thalamotomy (MT)

The spinothalamic tract terminates in the medial thalamus; therefore, it has been postulated that lesioning the medial thalamus might alleviate both chronic and severe pain. Further proof that the medial thalamus is involved in nociceptive processing is that abnormal electrical activity is observed here in patients suffering from chronic pain. Based on electrical recordings, it has been shown that the most intense bursting of activity is in cells located in the posterior aspect of the core of the ventrocaudal nucleus and in the posteroinferior area. It is in these areas that the spinothalamic tract terminations are most dense.

MT was actually the first stereotactic brain operation performed for pain. Given that these areas of the thalamus are the recipient of spinothalamic tract fibers and the main pain-processing center, MT has been used to treat somatic, deafferentation, and central pain. In the medial tier of thalamic nuclei lies the centralis lateralis (CL), a nucleus packed densely with spinothalamic tract terminals. The centromedian and parafascicularis nuclei are other neighboring intralaminar structures of the thalamus that receive a much less dense concentration of spinothalamic tract projections. These nuclei then collectively project to cortical structures and the striatum. Preoperative determination of lesion location is made by stereotactic MRI or CT. Surgical lesioning of the medial thalamus is then made anatomically, based on calculated positions from the anterior commissure–posterior commissure (AC-PC) lines, and physiologically, based on spontaneous or evoked electrical activity.

The most common medial thalamus lesion is made in the centromedian and parafascicularis. Lesions may be placed unilaterally or bilaterally. Pain relief effects are initially quite good but tend to decrease with time and can recur. It is for this reason that malignant pain has been shown to have a much better treatment result after MT,

as compared to central or neurogenic pain. Complications rates for MT are low and mostly due to lesions extending into the lateral thalamus resulting in severe dysesthesias.

Cingulotomy

A cingulotomy refers to ablation of the anterior cingulate gyrus, which includes both the cortical regions and the subcortical regions; namely, this includes the cingulum fasciculus, which is a major association tract of the limbic system, located in the white matter, underneath the cingulate gyrus cortex. Most surgical procedures for pain have aimed at disrupting the neural pathways conveying a painful stimulus, often at the expense of normal somatic sensation. However, the cingulotomy procedure has no influence on somatic nociception. It is thought to produce pain relief by altering the patient's emotional reaction to pain and by increasing the tolerance to the subjective and emotional feelings of pain. No afferent pain pathways are actually lesioned here, as the affective components, such as fear, depression, and suffering are the real targets of therapy. Therefore, cingulotomy has become indicated in patients with affective disorders suffering from chronic pain.

Cancer pain, as well as various nonmalignant types of pain that include a psychogenic element, has also been treated with cingulotomy. Cingulotomy should only be considered in patients suffering from persistent, debilitating, and treatment refractory pain. The mechanism of a cingulotomy is thought to involve the complex fiber pathway that receives and transmits signals to both the limbic and extra-limbic structures in the vicinity of the cingulum. As with other stereotactic lesioning procedures, it is performed under local anesthesia with intravenous sedation, and targets are chosen on preoperative MRI. Heating the electrode tip to 85 °C for 90 s creates lesions. After the electrode tip has cooled, it may be withdrawn and the procedure may be repeated bilaterally. Complications are relatively few but can involve temporary bladder retention or incontinence, isolated seizures, hemorrhage, or unsteady gait. About 25–40% of patients will require repeat cingulotomy, with an attempt to lesion more of the cingulum fasciculus.

Success with this surgery seems to surround the volume of damaged cingulum fasciculus. For best results, bilateral cingulotomies should be performed. Long-term follow-up and adequate pain recording diaries are crucial for these patients and, again noted was an inverse relationship between pain-free patients and survival.

Conclusion

As described here, several neuroablative procedures are available for treating certain pain syndromes. These seemingly destructive procedures act by interrupting input from several pain pathways. A struggle remains because although irreversible,

the long-term effect on pain perception is often limited due to the plasticity of the nervous system. However, the hope is that the effect is beneficial and sufficient in controlling pain to allow for adequate rehabilitation and therapy. Every patient's ultimate goal is to function in a relative pain-free state; with the help of some of the procedures detailed earlier, patients may be able to participate, endure, and supplement the rehabilitation that is so crucial to their recovery and well-being.

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Part XII
Multi Modal Approach: Surgical Management of Pain

Chapter 59
Orthopedic Procedures for the Treatment of Pain in the Rehabilitation Patient

Roy Ruttiman, Adam E.M. Eltorai, and Alan H. Daniels

Introduction

Modern orthopedic procedures are safe and reliable treatment options to alleviate pain stemming from many musculoskeletal conditions [1–4]. Procedures on mobile joints are generally designed to immobilize the joint via fusion, or retain motion via arthroplasty, which often includes replacing the joint with a metal, ceramic, or plastic bearing surface. Decompressive procedures are commonly performed by hand and spine surgeons to take pressure off nerves. Soft tissue reconstruction of injured ligaments, muscles, menisci, and tendons are also common procedures designed to alleviate pain and restore function. Realignment surgery can also be performed to alleviate pain associated with deformity in spine and extremity surgery. Finally, painful traumatic fractures and dislocations are commonly stabilized by orthopedic surgeons to quickly improve pain and hasten recovery. Orthopedic surgery outcomes are generally positive but may vary depending on operative site, invasiveness

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of procedure, and severity of disease. Careful patient selection, preoperative planning, and surgical execution are necessary to avoid complications and achieve optimal results. Each subspecialty has unique traditions, procedures, and risks which rehabilitation providers must be familiar.

Adult Reconstruction: Hip and Knee Replacement

Adult Reconstruction Surgery is aimed at reducing disabling arthritic pain of the hip and knee [5–7]. Osteoarthritis, rheumatoid arthritis, and posttraumatic arthritis can all cause pain and loss of joint function. Most commonly, hip and knee replacement surgery is used to treat osteoarthritis—wear and tear degeneration of articular cartilage in these large, weight-bearing joints. Total joint arthroplasty (TJA) is the preferred surgical strategy to mitigate joint pain.

- TJA of the hip involves the removal of diseased bone and cartilage followed by implantation of a mobile prosthesis made of metal, plastic, or ceramic. Common complications include infection, blood clots, leg-length inequality, and hip prosthetic dislocation. See Fig. 59.1.
- TJA of the knee requires replacing the injured bone and cartilage with a plastic or metal implant to optimize alignment and restore function. Common complications include infection, knee stiffness and loss of range of motion, blood clots, nerve injury, and implant wear. See Fig. 59.2.

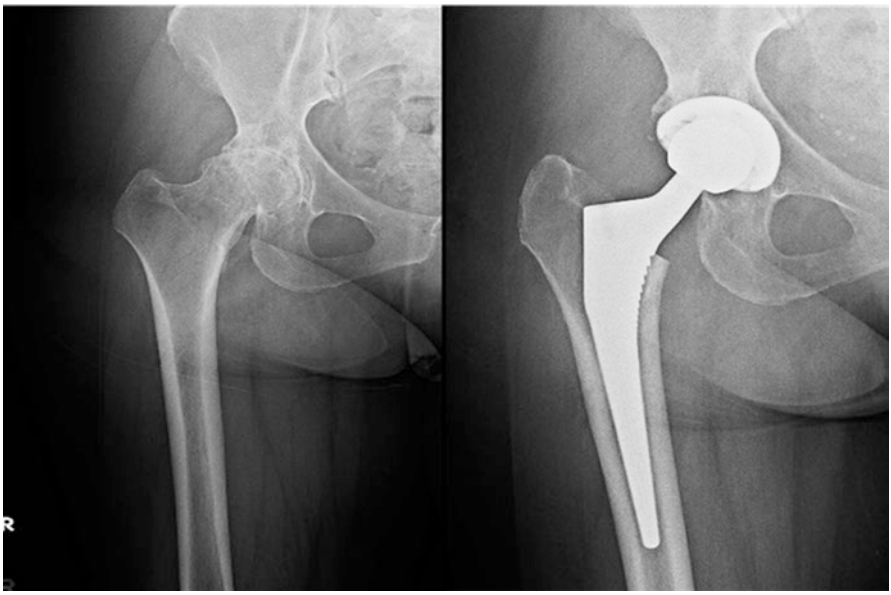

Fig. 59.1 Pre- and postoperative hip replacement

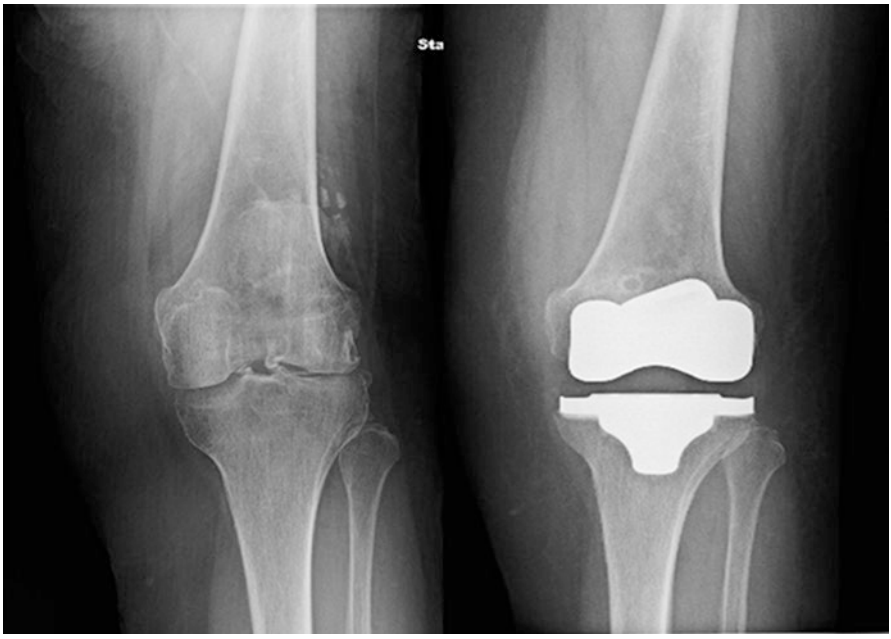

Fig. 59.2 Pre- and postoperative knee replacement

Improvements in technology and clinical management have allowed for effective and safe joint arthroplasty in the aging population. As such, there are no strict age restrictions for TJA. Patients should be evaluated individually, with emphasis on the natural history of experienced pain, its associated limitations on everyday activities, the patient's responsiveness to medical treatment, and existing comorbidities.

Foot and Ankle Surgery

Foot and ankle pain commonly occurs in patients with osteoarthritis, rheumatoid arthritis, or poorly healed fractures. Selective fusion and TJA of the ankle, foot, and toes provides pain relief for the majority of patients [8–10].

- Fusion involves the removal of articular cartilage between adjacent bones and implantation of metal instrumentation to hold bones in the most functional position while the bones heal together (arthrodesis). Bone grafts may also be used to aid in fusion. Fusion of the ankle, foot, or toe joints is indicated depending on the location of pain and joint degeneration. Complications include delayed or poor bone fusion, wound healing issues, infection, hardware irritation, and stiffness in adjacent joints.

- In TJA of the ankle, an artificial ankle consisting of metal and plastic components is implanted to replace the diseased joint. Unlike ankle fusion, joint mobility is maintained and often improved by TJA. Complications include infection, neurovascular damage, blood clots, misalignment, and implant wear.

Fusion and TJA of the ankle should be avoided in patients with bone or vascular illness that may interfere with bone healing, severe deformity of the extremity, markedly impaired leg function, or prior/current bone infection.

Hand Surgery

Carpal tunnel syndrome, osteoarthritis, and rheumatoid arthritis are the main causes of debilitating pain in the hand and wrist. Carpal tunnel release surgery, TJA, and fusion of bones in the hand and wrist are commonly used and effective procedures [11–13].

- Carpal tunnel release involves incising the transverse carpal ligament, which is located on the ventral surface to the wrist. This creates a larger carpal tunnel and decreases pressure on the median nerve thus decreasing pain and optimizing nerve function. Complications include bleeding, median nerve damage, and infection.
- Fusion of wrist and hand bones requires the removal of articular cartilage on surfaces of adjacent bones followed by the insertion of metal pins/plate and screws into the bones, which stabilizes the joint as the bones fuse. Selecting which bones to fuse is dependent on the location of pain and joint pathology. Complications include skin necrosis, irritation related to retained instrumentation, incomplete fusion, and loss of mobility and dexterity.
- TJA of the wrist involves replacing damaged bone and cartilage with a wrist prosthesis, consisting of radial and carpal components. The radial component of the prosthesis is implanted in the distal radius, while the carpal component is inserted into viable carpal bones. These two components are linked by a plastic spacer, which approximates the wrist's natural motion. Prosthetic wear and loosening are common complications, especially in patients with severe wrist deformity or poor bone stock. Infection and wound healing problems are also possible complications, which are more common in patients with rheumatoid arthritis.

Surgical treatments for hand and wrist pain are generally less invasive compared to major joint or spine operations. As such, most can be performed in under local anesthesia and in the outpatient setting.

Shoulder and Elbow Surgery

Shoulder and elbow pain are commonly associated with arthritis, fractures, and tendon inflammation or tears [14–16]. TJA of the shoulder is considered for shoulder fractures and arthritis. Rotator cuff repair is reserved for tendon injuries

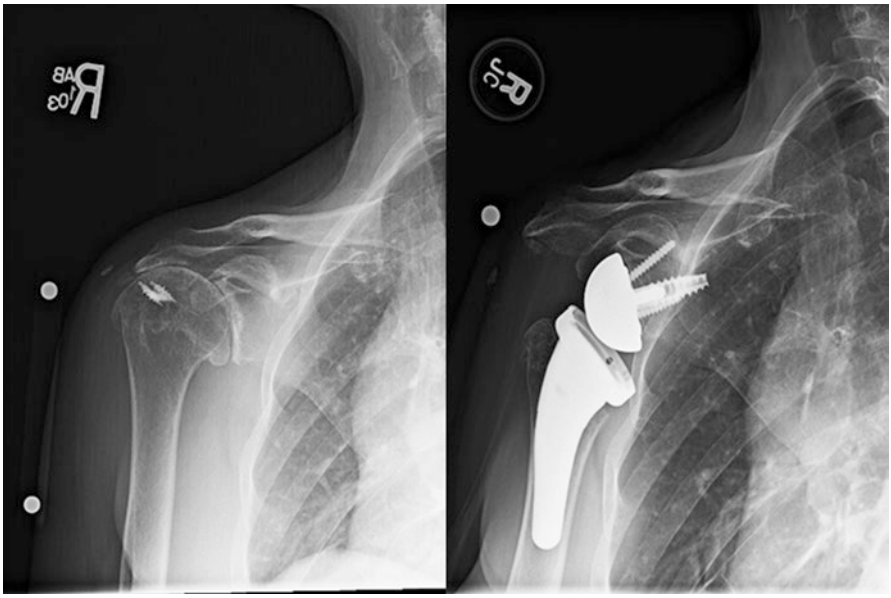

Fig. 59.3 Pre- and postoperative shoulder replacement

- TJA of the shoulder includes substituting the damaged humeral head and glenoid fossa with a polished metal ball and a plastic socket, respectively. This procedure may not be suitable for individuals with torn rotator cuff tendons. Hemiarthroplasty and reverse total shoulder arthroplasty are also viable joint replacement options. Complications include infection, nerve injury, and implant dislocation or wear. See Fig. 59.3.
- Rotator cuff repair most commonly involves reconnecting a tendon to the humeral head. A complete tear within the tendon requires suturing of two ends back together. Partial tears may only involve trimming loose, aggravating tendon pieces. Complications include infection, nerve damage, stiffness, failed deltoid reattachment, and tendon retear.

Open, mini-open, or arthroscopic surgical approaches are suitable for rotator cuff repair and produce comparable outcomes. Arthroscopic procedures have grown tremendously in popularity over the last decade and now account for the vast majority of rotator cuff repair procedures. Patient noncompliance with rehabilitation and postoperative restrictions, old age, and large tendon tears are all linked with suboptimal surgical outcomes.

Spine Surge+ry

Back and radicular arm and leg pain may occur due to disc pathology (degeneration, herniation), spondylolisthesis (vertebral displacement), spinal stenosis (canal narrowing), or deformity (scoliosis, kyphosis). See Fig. 59.4. Discectomy, laminectomy,

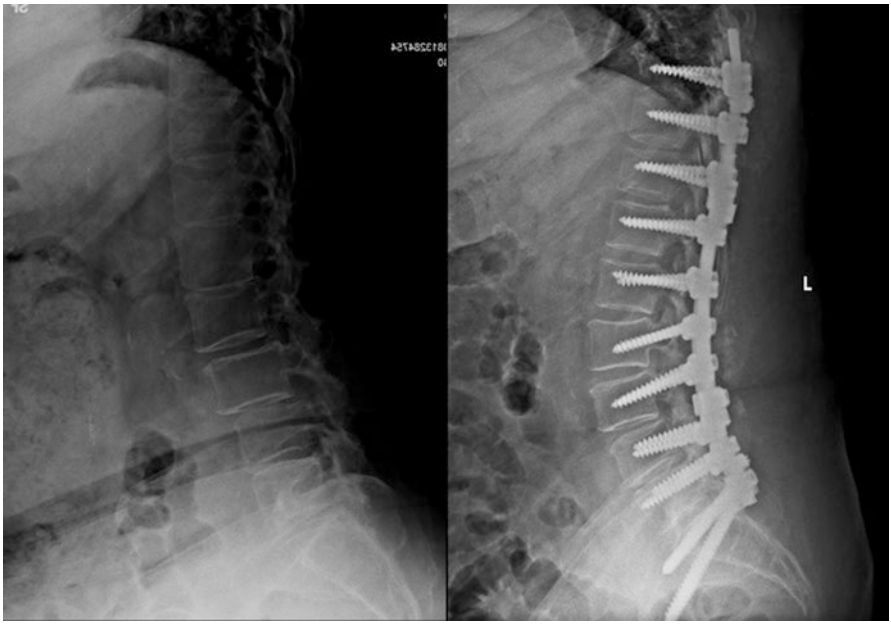

Fig. 59.4 Pre- and postoperative spinal deformity surgery with correction of spinal sagittal balance

fusion, and spinal deformity correction are commonly performed procedures for back and radicular pain [17–19].

- Discectomy normally involves surgical removal of the protruding portion of the herniated vertebral disc that is impinging on nerve roots and eliciting pain in the patient. In the cervical spine, the disc is often completely removed from an anterior approach, thus necessitating reconstruction with either fusion or arthroplasty. In the lumbar spine, the offending fragment of disc is most commonly removed from a posterior approach. Open or minimally invasive approaches may be taken and fusion is not generally required. Complications include infection, neurovascular injury, continued pain, and leakage of cerebrospinal fluid (CSF).
- Laminectomy (spinal decompression) is used to treat nerve impingement by providing more space for the nerve to function. This is achieved by removing a small portion of the bone over and/or disc material from under the nerve root. Complications include nerve root damage, spinal instability, CSF leakage, and infection.
- Fusion of adjacent vertebrae can be accomplished via an anterior, posterior, lateral, or combined approach. To obtain anterior spinal fusion, removal of the intervertebral disc followed by placement of a bone graft (autologous, allograft, or artificial graft) in between two vertebrae is performed. For posterior fusion, the facet joint is decorticated and bone graft is placed in the facet and over the transverse processes. Metal instrumentation is often implanted into involved vertebrae to prevent movement of the spine and to enhance fusion. Complications include infection, pain at autologous graft site, pseudarthrosis, nerve damage,

and degeneration of the adjacent levels (although this may occur due to the natural history of spinal degenerative disease).

Sports Medicine

Pain associated with athletic activity can arise as a result of overuse, fractures, articular damage, or muscle/ligament strains or tears. Knee arthroscopy, anterior cruciate ligament (ACL) repair, and hip arthroscopy are commonly performed procedures to address pain syndromes within orthopedic sports medicine [20–22].

- Knee pain due to meniscal, articular, or ligament pathology may benefit from knee arthroscopy. An arthroscope is inserted through small incisions on the knee to visualize structural damage to the knee. A sterile solution is typically used to clear and better visualize the area of interest. Once a diagnosis is determined, small instruments—scissors, shavers, or lasers—are used to reconstruct or remove damaged tissue (e.g., torn meniscus). Complications include infection, blood clots, and local accumulation of blood.
- ACL repair usually involves the replacement of the torn ACL with a tendon autograft or cadaveric allograft. Tunnels are created in the femur and tibia adjacent to the natural attachment sites of the ACL. The appropriate tendinous graft is then threaded through the bony tunnels and held in tension. Screws, spike washers, and staples are used to fix the graft in place. Before completing the operation, the knee is tested for range of motion, tension, and stability. Patients who undergo preoperative physical therapy to reduce knee stiffness and regain range of motion have been associated with better outcomes. Complications include infections, stiffness, growth plate injury when performed in children, tendon rerupture, and ongoing knee instability.
- Hip arthroscopy requires the femur head to be pulled away from the acetabulum, allowing for the insertion of the arthroscope through a small incision and visualization of the hip joint. If an abnormality is recognized on arthroscopy, scissors or other instruments may be inserted to treat the injured joint. Complications include infection, blood clots, temporary numbness, and neurovascular insult.

Sports medicine patients are often young and healthy, although a growing population of active elderly patients are currently being treated by Sports Medicine surgeons. As such, surgical complications are often limited and easily managed and many procedures are performed on an outpatient basis. The reestablishment or maintenance of athletic performance and short patient recovery duration are associated with patient satisfaction.

Orthopedic Trauma

Although most traumatic fractures can be treated nonoperatively, some more serious fractures require fixation to optimize outcomes and prevent disability [23–25]. Orthopedic trauma patients may develop posttraumatic deformities and experience

long-term disabling pain and dysfunction if fractures are not properly aligned and fixed. Fracture fixation and corrective osteotomies are commonly performed by orthopedic traumatologists to provide relief for trauma patients.

- During an open fracture fixation, the bone pieces are repositioned and secured into place using metal plates, rods, pins, screws, and/or nails. Complications include bleeding, infection, injury, malalignment, nonunion, or osteonecrosis.
- Corrective osteotomy consists of reshaping—shortening, lengthening, or realigning—a deformed bone to achieve proper bone alignment and restore function. Osteotomies may also be used to shift body weight away from deformed bone or damaged cartilage and toward healthier aspects of the joint. Complications include infection, ongoing misalignment of bone, blood clots, nerve damage, and impaired healing of bone.

Advanced age, smoking, severe osteoarthritis, and rheumatoid arthritis can complicate these procedures.

Conclusion

Arthritis, neural compression, fracture, bone deformities, and ligament/tendon tears exist as the main causes of orthopedic pain. Although many orthopedic conditions can be managed medically, other more severe conditions benefit from surgical intervention as a means of alleviating pain and preventing further damage. Complications rarely occur during orthopedic procedures. Nonetheless, careful patient selection, surgical planning, and surgical execution are necessary to reduce risk and optimize outcomes. Orthopedic procedures most often provide excellent pain management, especially when conservative treatments fail to alleviate pain and when surgery is performed by the appropriate surgeon on the appropriate patient.

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Chapter 60
Vascular Procedures for the Treatment of Pain in the Rehabilitation Patient

Lidie Lajoie and Subodh Arora

Abbreviations

AHA	American Heart Association
ASA	American Stroke Association
DRIL	Distal Revascularization and Interval Ligation
DVT	Deep Vein Thrombosis
EVAR	EndoVascular Aortic aneurysm Repair
PAI	Proximalization of Arterial Inflow
PTS	Postthrombotic Syndrome
RUDI	Revision Using Distal Inflow
TOS	Thoracic Outlet Syndrome

Introduction

Vascular causes of pain, while less common than musculoskeletal pain, require a high level of suspicion due to the risk to life or limb, if left untreated. Pain originating from vascular disease may be acute or chronic. The origin of pain may include arterial disease, venous disease, extrinsic compression, or inflammation. The most common arterial etiology of pain is atherosclerotic disease, which results in claudication or rest pain but may also be due to aneurysmal degeneration, dissection, or acute arterial thromboembolism. The most commonly encountered venous etiology of pain is acute deep vein thrombosis, which results in chronic pain secondary to postthrombotic syndrome. Extrinsic compression of adjacent nerves may cause pain in patients with thoracic outlet syndrome, arterial aneurysms, and popliteal entrapment. Inflammatory etiologies of vascular pain include vasculitis and infection.

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Table 60.1 Vascular etiologies of pain

Acute	Chronic
Neck and Upper Extremity	
Carotid Artery Dissection	Subclavian or Axillobrachial Atherosclerosis
Vertebral Artery Dissection	Hemodialysis-Associated Steal Syndrome
Thoracic Outlet Syndrome (arterial or venous)	Thoracic Outlet Syndrome (neurogenic)
Acute Arterial Thromboembolism	Raynaud's Phenomenon
Upper Extremity Deep Vein Thrombosis	Vasculitis (scleroderma, lupus)
Hypothenar Hammer Syndrome	
Chest and Abdomen	
Acute Aortic Dissection	Chronic Aortic Dissection
Aortic Aneurysm (thoracic or abdominal)	Aortic Aneurysm (thoracic or abdominal)
Acute Mesenteric Ischemia	Chronic Mesenteric Ischemia
Lower Extremity	
Lower Extremity Deep Vein Thrombosis	Postthrombotic Syndrome
Acute Arterial Thromboembolism	Venous Insufficiency/Reflux—Varicose Veins
Popliteal Artery Aneurysm with Thrombosis	Aortoiliac or Femoropopliteal Atherosclerosis
Exertional Compartment Syndrome	Popliteal Entrapment Syndrome

The differential diagnosis for acute or chronic pain includes vascular etiologies in virtually every anatomic location. These are listed in Table 60.1.

A general description of the various surgical and endovascular procedures employed by the vascular specialist for the treatment of pain by anatomic region, as well as the outcomes of these interventions will be reviewed in this chapter. The role of the rehabilitation specialist in the management of patients with pain of vascular origin begins with postoperative rehabilitation after vascular intervention. It is important for the rehabilitation specialist to be able to recognize acute pain syndromes and postoperative complications, which should prompt referral to a vascular specialist.

Neck and Upper Extremity

Neck pain resulting from spontaneous or traumatic dissection of the extra-cranial carotid or vertebral arteries is rare but may account for up to 20% of ischemic strokes. A large population-based study found the incidence of spontaneous extracranial internal carotid artery dissection was 1.72 per 100,000 and 0.97 per 100,000 for vertebral artery dissection [1]. The mainstay of treatment for extra-cranial internal carotid or vertebral artery dissection, according to the AHA/ASA guidelines, is anticoagulation for 3–6 months.

Surgical reconstruction or stent placement is reserved for patients with persistent symptoms despite anticoagulation or antiplatelet therapy [2]. Surgical reconstruction

for carotid artery dissection was associated with a 10% postoperative stroke rate and a 40% rate of cranial nerve damage at long-term follow-up in one series [3]. The use of endovascular stents effectively eliminates the risk of cranial nerve injury associated with open repair, without any difference demonstrated in the postoperative stroke rate [4].

Stroke rehabilitation may be initiated within 48–72 h after carotid endarterectomy. Patients may have some tenderness on neck rotation for the first 1–2 weeks, so driving in this time period is not recommended. The operative vascular surgeon should be consulted immediately if sudden neck swelling is observed during rehabilitation. After carotid stent placement, rehabilitation may begin within 24–48 h after intervention without restriction in most cases.

Dual antiplatelet therapy is required for the first 3 months after stent placement, so the assessment of fall risk is essential, prior to discharge home, since a fall with head trauma in these patients may be devastating. The interventionist should be consulted immediately if a sudden, expanding, erythematous, or necrotic groin hematoma is observed. Evaluation in the emergency department should be pursued if any new symptoms of transient ischemic attack or stroke occur during rehabilitation after endarterectomy or stent placement.

Thoracic Outlet Syndrome (TOS) is due to compression of the brachial plexus, subclavian artery, or subclavian vein by fibrous bands to the first rib, or by a cervical rib where these structures exit the thoracic cavity. The syndrome frequently presents with pain. The nonoperative management options for the syndrome should be familiar to the rehabilitation specialist, as more than 80% of cases are neurogenic and treatment is conservative.

Operative treatment is reserved for the <5% of patients who present with arterial or venous TOS, or for those patients who have failed conservative measures aimed at alleviating symptoms for neurogenic TOS. Treatment involves first rib resection via an axillary, supraclavicular, or thoracoscopic approach. Patients who present with arm pain and upper extremity deep vein thrombosis, due to compression of the subclavian vein (Paget–Schroetter syndrome), may be treated with venous thrombolysis and/or thrombectomy prior to rib resection.

Arterial TOS can manifest as acute or chronic extremity pain, absence of pulse, or distal embolization, and may have associated rudimentary or cervical ribs. An arterial reconstruction surgery may be indicated at the time of rib resection if aneurysmal degeneration, stenosis, or occlusion of the subclavian artery has developed. First rib resection is associated with positive long-term outcomes in 95% of patients treated for all indications [5].

Occupational therapy can generally be resumed within 3–5 days after surgery, but sports and strenuous activity should be delayed for at least 2 weeks. Edema is usually successfully managed with arm elevation. While complications are rare, the operative surgeon should be contacted if patients complain of acute pain or if loss of pulses in the arm is noted on exam.

Upper extremity pain of arterial origin may be due to atherosclerotic disease, although this is uncommon. More frequently observed is hemodialysis-associated steal syndrome, which affects up to 10% of patients receiving hemodialysis with an

arteriovenous fistula or graft. As the prevalence of end-stage renal disease continues to rise, prevalence of this syndrome will likely also rise in the rehabilitation setting.

Classically, the syndrome results from excess blood flow through the fistula or graft, which 'steals' blood supply from the distal extremity. It may also result from arterial stenosis of the inflow artery or from failure of forearm collateral circulation to develop after access creation. Symptoms can range from digital pain or paresthesia to ulceration and gangrene. Prompt recognition is essential for prevention of permanent ischemic nerve damage or need for amputation. A vascular surgeon should be consulted urgently for any patient with an arteriovenous fistula or graft who complains of ipsilateral hand numbness or decreased range of motion, or if ischemic changes are noted in the fingertips on exam.

While ligation of the arteriovenous access remains the "gold standard" treatment for hemodialysis access-associated steal syndrome, a number of surgical procedures have been devised to correct the underlying pathophysiology, while preserving the dialysis access for use. Banding involves focally narrowing the graft, either at the arterial anastomosis or mid-portion, in order to reduce flow through the conduit. Additional strategies include the DRIL procedure (Distal Revascularization and Interval Ligation), RUDI procedure (Revision Using Distal Inflow), and PAI procedure (Proximalization of Arterial Inflow) [6].

A large retrospective review found that, with the exception of ligation where the access is sacrificed, these procedures are associated with >90% hemodialysis access preservation. Improvements in steal symptoms were demonstrated in >90% of patients for all procedures except banding (75%). Ligation and DRIL were associated with the lowest 30-day complication rates (8% and 7%, respectively), whereas more than one-third of patients who underwent banding, RUDI, and PAI had complications ranging from infections, hematoma formation, continued steal, or access thrombosis within 30 days of the procedure [7]. Patients may generally return to usual activity within 3–5 days after these procedures. Occupational therapy may be indicated to rehabilitate the previously ischemic hand.

Upper extremity pain of venous origin is typically associated with upper extremity deep vein thrombosis (DVT), with an incidence in the general population of 2 per 100,000 persons per year. Upper extremity DVT may be secondary to venous thoracic outlet syndrome, indwelling central catheters, malignancy, and/or hypercoagulable disorders. In addition to therapeutic anticoagulation and limb elevation, catheter-directed thrombolysis may be utilized to treat postthrombotic pain in the acute setting. This involves inserting a catheter into the thrombus and infusing thrombolytic agent directly into the clot to dissolve it, with or without the adjunctive use of mechanical thrombectomy to break up the clot (Fig. 60.1). At long-term follow up, catheter-directed thrombolysis for upper extremity DVT can be associated with complete resolution of postthrombotic syndrome in up to 80% of patients [8]. Patients will often require arm elevation, while at rest, to resolve the edema from upper extremity DVT, but rehabilitation may continue without restriction.

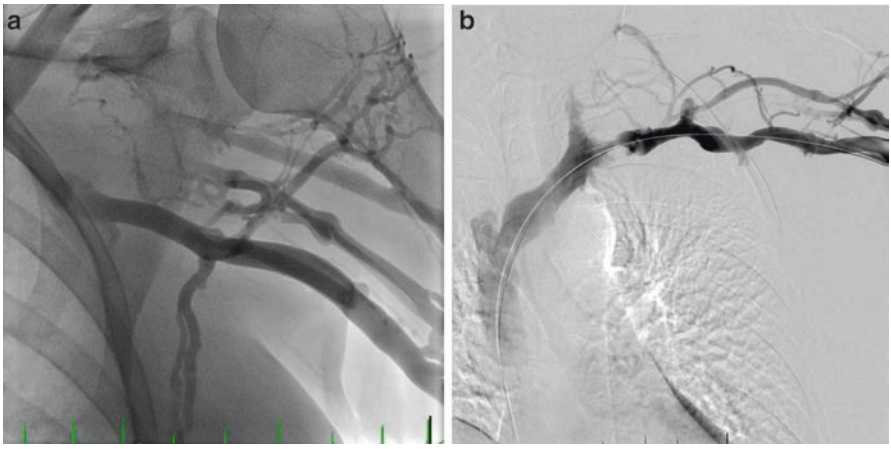

Fig. 60.1 Upper extremity catheter-directed thrombolysis. (**a**) Angiogram prior to thrombolysis demonstrating acute thrombosis of the subclavian vein. (**b**) Angiogram after thrombolysis, with subclavian vein recanalization demonstrating underlying vTOS

Chest and Abdomen

Chest pain of noncardiac vascular origin is most commonly encountered acutely in patients with thoracic aortic dissection, or more chronically in patients with aneurysmal degeneration of the thoracic aorta, with an incidence of approximately 3 and 6 per 100,000 persons per year, respectively [9, 10]. Prompt surgical aortic replacement is necessitated for patients with "Type A" aortic dissections involving the ascending aorta and/or aortic arch. This repair is performed by a thoracic surgeon via a median sternotomy approach and requires total cardiopulmonary bypass with hypothermic circulatory arrest. Surgery of this type is associated with an in-hospital mortality rate as high as 30%. Furthermore, 15% of survivors have a postoperative course complicated by a neurologic deficit (stroke or paraplegia) [11].

For patients with "Type B" dissections involving the descending aorta, surgical or endovascular treatment is indicated emergently for rupture, mal-perfusion (visceral, spinal, or limb), or persistent pain. Patients with known type B dissections, who are being cared for in the rehabilitation setting, should be transferred to an emergency department immediately if sudden hypotension; paraplegia; or severe pain in the chest, back, abdomen, or lower extremities develops.

Open surgery involves a left posterolateral thoracotomy, can lead to profound hemodynamic shifts from aortic cross-clamping, and often requires significant postoperative rehabilitation. Thoracic endovascular stent graft placement (Fig. 60.2) can be performed either percutaneously or via minimal groin incisions, minimizes intraoperative hemodynamic changes, and significantly reduces postoperative pain and recovery time, when compared to open repair. In a meta-analysis, the endovascular

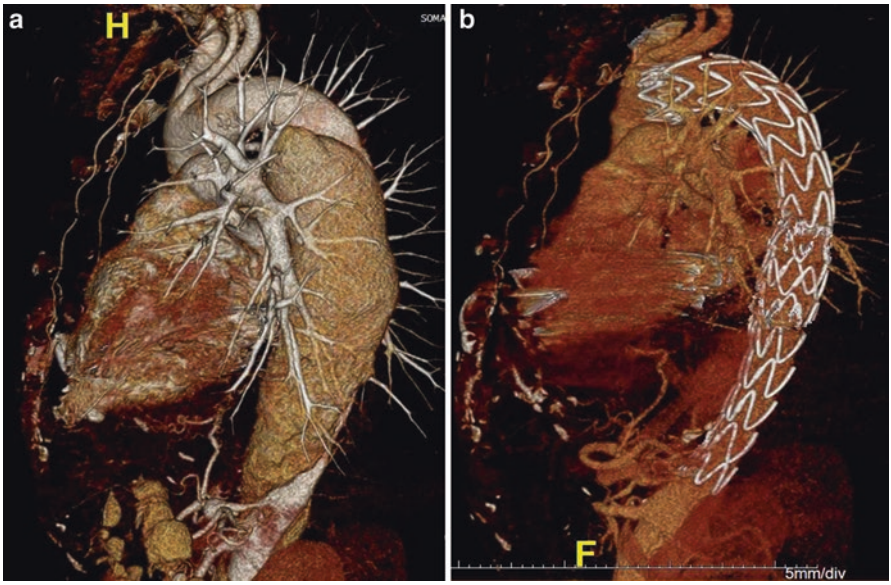

Fig. 60.2 Endovascular repair of thoracic aortic dissection. (**a**) CT 3D reconstruction demonstrating Type B dissection with aneurysmal degeneration. (**b**) CT 3D reconstruction after endograft placement demonstrating exclusion of the false lumen

approach for Type B dissection is associated with a significantly lower 30-day mortality, when compared to open repair (11% vs. 35%, respectively); however, there is no significant difference in the rates of postoperative paraplegia (9% vs. 8%, respectively) [12].

The same surgical and endovascular approaches are employed in the treatment of thoracic aortic aneurysms in an elective setting. Results from the Nationwide Inpatient Sample demonstrate low overall operative mortality (4.5%) for both procedures, with decreased odds of postoperative neurologic, cardiac, and respiratory complications in the thoracic endograft group [13]. In uncomplicated cases, rehabilitation may begin 3–5 days postoperatively. In complicated cases, patients may be severely debilitated by the time they are medically ready for rehabilitation. Postoperative cardiopulmonary rehabilitation is often required after open repair. In patients with postoperative paraplegia, partial or complete recovery of neurologic function with intensive rehabilitation can be expected in most patients.

Abdominal aortic aneurysm is asymptomatic in most patients, but patients who present with abdominal pain require urgent surgical evaluation, since this symptom suggests rapid enlargement or imminent rupture. Similar to thoracic aneurysm repair, abdominal aortic aneurysm repair may be performed open, via a laparotomy or flank incision, or via an endovascular approach.

Similar reductions in postoperative recovery times have been associated with endovascular aortic aneurysm repair (EVAR, Fig. 60.3). For patients requiring urgent repair for pain or rupture treated with EVAR in lieu of open repair, significantly

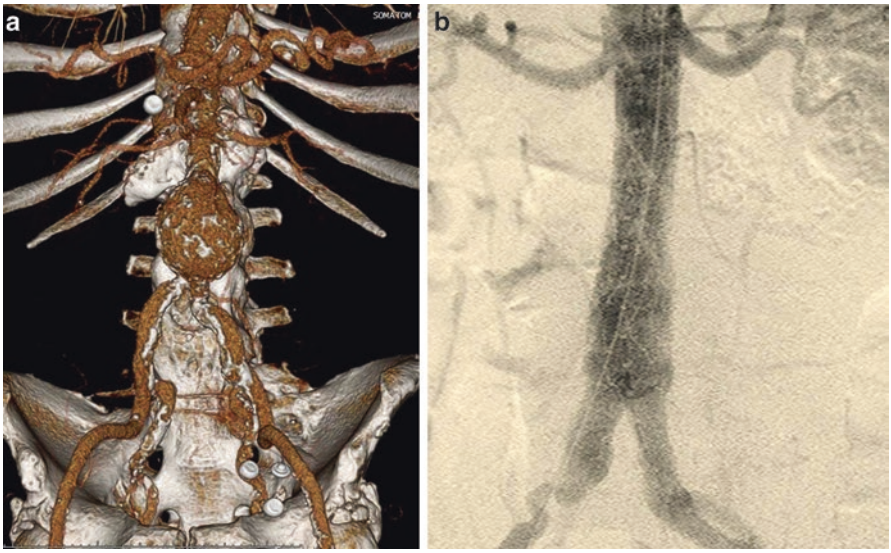

Fig. 60.3 Endovascular abdominal aortic aneurysm repair. (**a**) CT 3D reconstruction demonstrating abdominal aortic aneurysm. (**b**) Angiogram after endovascular repair of abdominal aortic aneurysm

lower 30-day mortality rates (11% vs. 54%) and mean hospital stays (9 days vs. 18 days) have been demonstrated [14]. Rehabilitation may be initiated 24–48 h after endovascular repair and 3–5 days after open repair. Heavy lifting and strenuous activity is restricted for the first 6 weeks postoperatively after open repair to reduce the risk of incisional hernias. The vascular specialist should be consulted if any expanding hematoma, erythema, or drainage is noted in the groin, or if there is a sudden change in the vascular exam.

Lower Extremity

Pain in the lower extremities of arterial origin may be acute, as in acute limb ischemia due to peripheral thromboembolism, or chronic, as in intermittent claudication or rest pain. Acute limb ischemia is uncommon and typically occurs in patients with a history of atrial fibrillation. The treatment includes anticoagulation, surgical thrombectomy, or endovascular catheter-directed thrombolysis and thrombectomy. Patients with intermittent claudication typically present with muscular pain or cramping with ambulation that is relieved by rest. It is one of the more common causes of vascular pain, affecting 6% of the population above the age of 60 [15]. The pain typically affects the muscle groups just distal to the diseased artery, which manifests as buttock claudication in aortoiliac disease, thigh claudication in

common femoral artery disease, and calf claudication in superficial femoral artery or popliteal disease.

The gold standard for the treatment of intermittent claudication is a structured exercise program as well as management of medical comorbidities. However, vascular surgeons are frequently called upon to intervene for lifestyle limiting claudication, failure of conservative treatment, or progression to rest pain. Rest pain is ischemic pain, which occurs in the toes and metatarsal heads, that is aggravated by limb elevation and is relieved by dependency. It is a manifestation of critical limb ischemia, involving two or more segments of the arterial tree, and requires surgical or endovascular management of the aortoiliac or common femoral segments to treat the pain symptoms and to prevent limb loss.

Revascularization for debilitating claudication or rest pain may require an open surgical approach, even in the modern endovascular era. Aortobifemoral bypass involves placement of a bifurcated prosthetic graft from the infrarenal aorta, above the occlusive disease, to the patent femoral arteries below it. This procedure is typically undertaken via a midline laparotomy approach, with bilateral groin incisions. The procedure has excellent durability, with 5-year patency rate of >90%, and a 10-year patency rate of up to 85%.

Rehabilitation in uncomplicated cases may begin 3–5 days after aortobifemoral bypass. The activity restrictions and signs of postoperative complications of aortobifemoral bypass for occlusive disease are the same as observed after the procedure has been performed for abdominal aortic aneurysm.

Axillobifemoral bypass is typically used to treat rest pain in patients with bilateral aortoiliac disease, who are considered high risk for aortobifemoral bypass. Iliofemoral bypass or femoralfemoral crossover bypass may be used to treat unilateral iliac disease. Long-term results of these alternatives are inferior to aortobifemoral bypass, with approximately only two-thirds of grafts patent at 5 years [16].

Rehabilitation, if needed, may begin 3–5 days postoperatively. Heavy lifting above the head should be delayed for 2 weeks to protect the axillary anastomosis. Patients should avoid lying on the flank that the graft is tunneled through, since this area is prone to develop postoperative edema. Hematoma, erythema, or drainage in the groin, or at the chest wall incision, should be evaluated by the operative surgeon.

For patients with disabling claudication or rest pain and atherosclerotic disease in the common femoral artery, femoral endarterectomy, with or without profundaplasty, has been shown to provide long-term relief from pain, up to 95% at 5 years. The procedure involves a groin incision with removal of the atherosclerotic plaque. Then, a patch is typically placed extending onto the profunda femoris artery. Major postoperative complications are rare, and the procedure is successful at alleviating pain, even in patients who have diseased or occluded vessels distally [17, 18].

Many patients with rest pain have limited their activity prior to revascularization and physical therapy may be useful to improve walking distance as well as functional status postoperatively. Rehabilitation may begin within 48–72 h of the procedure and strenuous activity can be resumed within 2 weeks. Groin complications or sudden changes in pulse exam should be evaluated by the operative surgeon.

For patients with aortoiliac disease, endovascular interventions for disabling claudication and rest pain are associated with lower cardiac and pulmonary complications, as well as shorter postoperative recovery. This has led many centers to initially address these pathologies with an endovascular approach, reserving open surgical approaches for disease that is not amenable to this type of intervention. Iliac angioplasty, with or without stent placement, is typically performed for focal disease, with long-term results equivalent to open surgery. Iliac angioplasty and stent placement may also be performed for patients with extensive aortoiliac disease [19].

Endovascular approaches to common femoral artery atherosclerosis are generally not recommended due to the significant risk for stent fracture from flexion at the hip joint and from the morbidity associated with covering the profunda femoris artery. Alternatively, endovascular treatment of disabling claudication for patients with superficial femoral artery and popliteal disease is increasingly common, and comparison of the endovascular to the open approach in this arterial segment has been extensively employed.

Balloon angioplasty with bare or drug-coated balloons, atherectomy, and/or stent placement may be used to treat femoropopliteal disease (Fig. 60.4). Immediate procedural success rates are high. Moreover, with modern technology, even long-segment occlusions, which previously required bypass as the only option, can now be treated with stents. Long-term patency is reduced compared to femoropopliteal

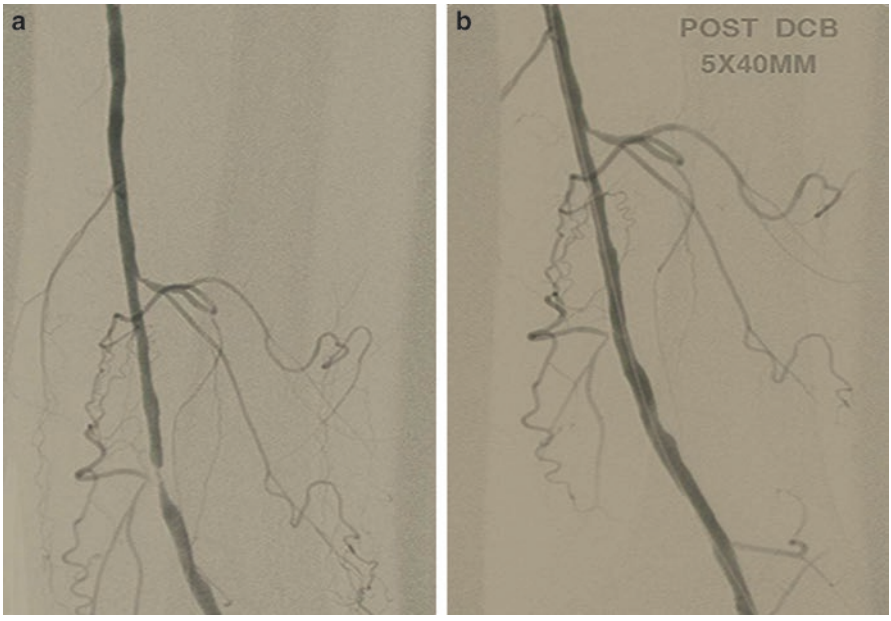

Fig. 60.4 Lower extremity endovascular intervention for rest pain. (**a**) Angiogram demonstrating superficial femoral artery stenosis. (**b**) Angiogram demonstrating resolution of stenosis after angioplasty

bypass, with as many as half of patients requiring reintervention within 1 year after stent placement for extensive disease [20].

Physical therapy and exercise programs usually can be resumed within 3 days of endovascular interventions. Since most interventions involve percutaneous access to the arterial tree from the opposite leg, groin complications at the access site or the sudden pain or loss of previously palpable pulses in either leg may be an indication of a postoperative complication that should prompt evaluation by the interventionist.

Venous insufficiency is often associated with leg pain, both in acute DVT and in venous claudication. Acute DVT affects approximately 1 person per 1000 per year, and up to one-third of affected patients will develop postthrombotic syndrome (PTS). PTS is characterized by pain, heaviness, and swelling of the limb, with hyperpigmentation and venous ulceration seen in severe cases. While the mainstay of treatment for acute DVT remains therapeutic anticoagulation, catheter-directed thrombolysis, with or without mechanical thrombectomy, is increasingly used as an adjunct in patients with iliofemoral DVT. The treatment involves introducing a catheter with multiple side holes into the affected vein, through the thrombosed segment, and instilling a thrombolytic agent into the clot (Fig. 60.5). This therapy has been shown in randomized trials to improve the symptoms of acute iliofemoral DVT and to significantly reduce the incidence of PTS [21].

Venous insufficiency due to great saphenous vein reflux may be alleviated by surgical or endovascular means. Great saphenous vein ligation and stripping

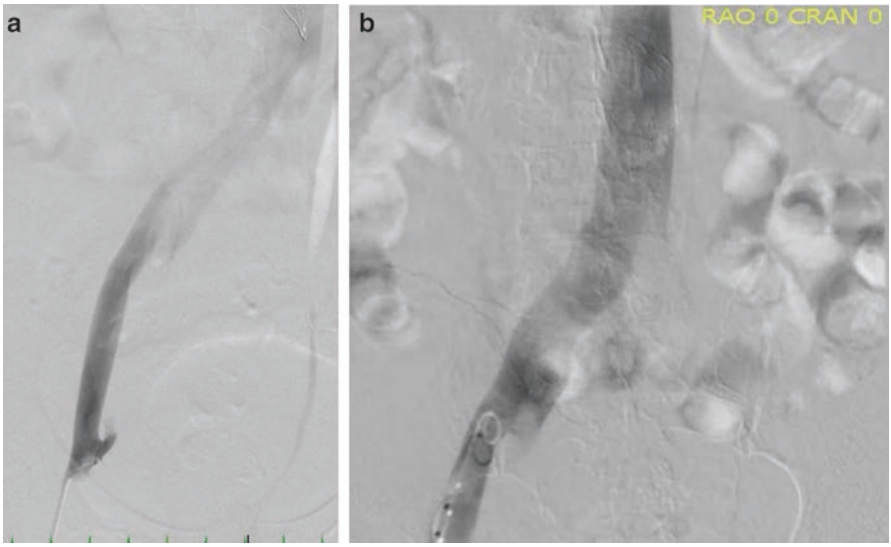

Fig. 60.5 Lower extremity catheter-directed thrombolysis for deep vein thrombosis. (**a**) Angiogram demonstrating acute common iliac vein DVT. (**b**) Angiogram demonstrating successful common iliac vein recanalization after catheter-directed thrombolysis

involves removal of the saphenous vein from the groin to below the knee; however, it may be associated with significant postoperative pain.

Endovascular ablation techniques may use laser, radiofrequency, or sclerosing agents to induce fibrosis and to obliterate the greater saphenous vein, which leads to a significant improvement in postoperative pain, when compared to stripping. These procedures provide acceptable symptomatic relief in a majority of patients with reflux [22]. Venous claudication may also be due to iliac vein stenosis, either from extrinsic compression (May Thurner syndrome) or from postthrombotic fibrosis. Endovascular therapy with angioplasty and stent placement provides long-term symptomatic relief, with two-thirds of patients found to have complete relief from pain at five-year follow up [23].

Patients being cared for in the rehabilitation setting may typically resume therapy in an unrestricted way within 24–48 h after these interventions. Leg elevation, while at rest, can be beneficial to reduce edema and associated pain. Sudden leg pain or swelling may indicate postprocedural DVT and should be evaluated with ultrasound.

Conclusion

Atherosclerosis, thrombosis, extrinsic compression, dissection, and aneurysmal degeneration exist as the main causes of vascular pain. Acute pain and vascular compromise necessitate prompt referral to a vascular specialist and is usually managed surgically. Chronic pain secondary to vascular disease requires a patient-specific approach, which is dependent upon the patient's comorbidities, location of the vascular disease, and rehabilitation potential.

Modern endovascular therapy has allowed vascular surgeons to intervene for disease that was previously treated conservatively due to the prohibitive operative risks and postoperative recovery of open approaches. Endovascular advances have also allowed for the expansion of patients who can safely be treated for arterial and venous claudication. Endovascular and surgical approaches to vascular pain can be life and limb saving in the acute setting, and may be utilized with good results, as well as minimal morbidity in the elective setting.

The rehabilitation specialist plays an important role in the postoperative rehabilitation of vascular patients after procedures for pain and are frequently the first practitioners to recognize postoperative complications. Prompt recognition and consultation with the vascular specialist for acute pain; incisional hematomas; erythema; drainage; or sudden changes in motor, sensory, or pulse exam can be life and limb saving. If the vascular specialist who performed the procedure is not immediately available to determine if the patient should be seen in an office or emergency room setting for evaluation of the aforementioned signs and symptoms, the patient should be sent to the nearest emergency department.

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Chapter 61
Lumbar Spine Procedures for the Treatment of Pain in the Rehabilitation Patient

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Introduction

Lumbago, or lower back pain, is extremely common. Estimated lifetime prevalence has been shown to be nearly 80%, and it is the fourth most common primary diagnosis for office visits in the United States [1, 2]. The presence of activity-limiting low back pain lasting for more than one day is estimated to be 12%, and the one-month prevalence ranges from 22 to 48% [3–6].

The majority of patients presenting with low back pain have nonspecific back pain; the patient has pain in the absence of a specific etiology [7–9]. Patients may present with a wide range of symptoms, with some characteristic findings indicating a potential etiology. Findings may include severe leg pain, claudication or pseudoclaudication, sciatic pain, fever, localized tenderness, gait abnormalities, sensory or motor loss, and numerous other findings [1]. Frequently, patients awaken with morning pain or may develop pain after minor forward bending, twisting, or lifting [10]. Pain can begin very

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ODI Interpretation of Scores

0% to 20%: *Minimal Disability*	The patient can cope with most living activities. Usually no treatment is indicated, apart from advice on lifting, sitting, and exercise.
21%-40%: *Moderate Disability*	The patient experiences more pain and difficulty with sitting, lifting, and standing. Travel and social life are more difficult and they may be disabled from work. Personal care, sexual activity, and sleeping are not grossly affected and the patient can usually be managed by conservative means.
41%-60%: *Severe Disability*	Pain remains the main problem in this group but activities of daily living are affected. These patients require a detailed investigation.
61%-80%: *Crippled*	Back pain impinges on all aspects of the patient's life. Positive intervention is required.
81%-100%:	These patients are either bed-bound or exaggerating their symptoms.

Fig. 61.1 Score interpretation of the Oswestry Disability Index [13, 14]

abruptly as the result of an accident or as the result of lifting a heavy object. Additionally, the pain can develop slowly over time due to age-related changes of the spine [11]. Recurrent episodes are usually more painful, with increased severity of symptoms [10].

Lower back pain can significantly impact a patient's quality of life and may cause substantial time lost from work. Back pain is extremely common in workers 40–65 years of age, and pain exacerbations occur frequently, which has significant impact on productive work time, thereby impacting both the patient and the employer [12]. One commonly used tool to measure pain and disability is the Oswestry Disability Index (ODI) (Fig. 61.1). This index is considered the gold standard for measuring the degree of disability and estimating quality of life in a person with low back pain [13, 14]. The questionnaire is comprised of ten sections, and the patient selects the statement in each section best corresponding to their ability to manage the pain. The score can then be used to interpret the patient's degree of disability related to their pain.

Etiologies

While there are numerous etiologies of lower back pain, the vast majority will have a nonspecific etiology. Many patients presenting with nonspecific pain may have musculoskeletal pain and symptoms may improve within weeks [1].

Mechanical lower back pain is most common and is due to an anatomical or functional abnormality without underlying malignant, neoplastic, or inflammatory disease. Some of the most common causes include [7, 15]:

• Lumbar strain or sprain	• Spinal stenosis
• Degenerative disk disease or facet joint arthropathy	• Osteoporotic compression fracture
• Herniated disk	• Spondylolisthesis

Neurological findings commonly result due to compression of a spinal nerve root, or the spinal cord itself, and include impaired reflexes, sensory loss, and motor weakness in corresponding extremities [1, 16]. Physical findings may help to narrow the differential diagnosis, such as pain that worsens with lower back flexion, which likely indicates compression fracture or herniated disc, and pain that worsens with extension and is relieved with flexion, which likely indicates spondylolysis or spondylolisthesis [10].

Nonmechanical etiologies are various and can include [15]:

• Neoplastic process	• Referred visceral cause:
• Infectious process	– Pelvic organ disease
• Paget's disease	– Gastrointestinal disease
• Inflammatory arthritis	– Renal disease
	– Aortic Aneurysm

Conservative Treatment

Most acute pain, which is less than 4 weeks in duration, and most nonspecific lower back pain resolves over time without any treatment. Controlling pain and maintaining daily function, while symptoms gradually diminish is the goal for most patients [7, 17]. Spontaneous recovery is more than 50–75% at 4 weeks and more than 90% at 6 weeks [7].

There are numerous recommendations to treat acute lower back pain, some of which include the following:

- Patients should remain active and ambulatory:
  - Patients advised to maintain bed rest may have slightly more pain and less functional recovery than those who are advised to remain ambulatory [18]. Activity modification should be minimal, and patients should return to activities of daily living and work as soon as possible [18, 19].
- Providers should target symptom relief:
  - NSAIDs or acetaminophen should be used as needed for up to 2–4 weeks [8, 20]. Additionally, some patients may also benefit from nonbenzodiazepine antispasmodics, but treatment should be limited to short term, 1–3 weeks [21]. Furthermore, evidence shows no benefit to physical therapy in the initial 2–3 weeks of acute low back pain [22–25].

Subacute lower back pain is defined as pain that occurs between 4 and 12 weeks of symptoms, with chronic pain persisting beyond 12 weeks. For those with chronic pain, the goal of treatment involves controlling pain, maintaining overall function, and preventing disability [26]. Some recommendations for subacute and chronic lower back pain include the following:

- Patients should be advised to remain active:
  - For those patients with subacute and chronic lower back pain, it is still recommended to remain active [27]. Exercise programs should be advised for subacute or chronic low back pain, and can help to both alleviate pain symptoms and to improve function [27].
- Providers should target symptom relief:
  - Short courses of NSAIDs and acetaminophen should be used for acute exacerbations of subacute and chronic pain [8]. Additionally, short-term use of opioid analgesics has been recommended for severe acute exacerbations but should not be used for long-term therapy. Opioids may be used in rare circumstances in severely disabled patients with chronic low back pain who have not responded to alternative measures [28]. Muscle relaxants and benzodiazepines have not shown sufficient efficacy for subacute and chronic low back pain [29, 30]. Additionally, depression is common in patients with chronic low back pain, and antidepressant medications may be used as conservative therapy in these patients [31–34].

Some nonsurgical interventional therapies may be considered for patients who have not responded to noninvasive therapies, who are not interested in surgery, or in those who are poor surgical candidates. For further reference, please see the chapter on pain in the spine rehabilitation patient. These may include the following:

- Epidural Steroid Injections:
  - Epidural steroid injections in those with radiculopathy due to a herniated disc may provide moderate improvement in pain and disability at 3 months, but no benefit at 1 year [35, 36]. This is completed through placement of a needle into the epidural space to administer corticosteroids. Intervals for injections should be at least 1 month, and additional injections are generally not indicated if the initial injection does not improve symptoms [36]. Generally, injections may be recommended in patients with radiculopathy who have not improved with conservative treatment over 6 weeks and desire nonsurgical treatment [35, 36].

Surgical Intervention

Only a small minority of patients with low back pain may require surgery. Generally, spinal procedure rates have been rising in the United States, particularly for spinal fusion [37]. The most likely indications for surgery are severe or progressive motor weakness, or signs and symptoms of cauda equina syndrome. In the absence of such indications, there is no evidence that early referral for surgery improves outcomes for disc prolapse with radiculopathy or for symptomatic spinal stenosis [38, 39].

In these patients, surgery may be an elective option for those with persistent disabling symptoms of low back pain and significantly impaired quality of life, who have not responded to conservative management.

In the following section, several types of surgical interventions for lumbar back pain will be discussed, including:

Lumbar laminectomy
Lumbar laminectomy and discectomy
Lumbar instrumented fusion

The section will examine the indications for the procedure, a description of the procedure if appropriate, as well as a discussion of outcomes.

Types of Surgeries

Lumbar Laminectomy

Indications
Lumbar laminotomy and laminectomy is one of the most commonly performed spine procedures. Complications from this procedure have been reducing over the last several years with the advent of microtechniques, magnification, perioperative antibiotics, and better neurodiagnostic testing [40]. One of the most common indications for a lumbar laminectomy is spinal stenosis, or narrowing of the intraspinal canal, the lateral recesses, and/or the neural foramina [41]. Most commonly, this is caused by degenerative arthritis affecting the spine or by spondylosis [41]. Symptoms range from axial low back pain, radiating radicular leg pain, paresthesia, weakness, gait instability, and loss of normal bladder or bowel function. These symptoms typically occur as the result of a chronic, debilitating condition, but may occur acutely, such as with trauma, or disk herniation. The levels most commonly affected are L4–L5, followed by L3–L4, L2–L3, and then L5–S1 [42].

Description of Procedure
Lumbar laminectomy consists of removal of the inferior lamina (hemilaminotomy) or removal of the entire lamina on one or both sides (laminectomy). Frequently, the spinous process is removed as well, and overlying connective tissues, the ligamentum flavum underlying and spanning the interlaminar space, and muscle may be transected in order to gain access to the vertebrae. Further lumbar decompression involves removal of the medial aspects of the inferior articular process of the superior lamina, as well as the superior articular process of the inferior lamina (medial facetectomy and foraminotomy).

Outcomes
Postoperative complications:

- Thecal sac or nerve root injury
  - This can result in complications such as cerebrospinal fluid leak and/or sensory and motor deficits, which occurs from injury to the traversing and exiting nerve roots. Complications frequently occur during dissection of the lateral recess, as visualization is often poor [42].
- Durotomy
  - This is one of the most common complications and may result in postoperative problems such as durocutaneous fistulas, pseudomeningoceles, and arachnoiditis [43, 44]. Incidence has been shown to be around 16%, and in revision spine surgeries rates are high, with a range between 2.1 and 15.9% [45–48].
- Hematoma
  - This can occur from inadequate hemostasis or starting NSAIDs or prothrombotic agents too early in the postoperative period, and should be considered in a patient with progressively worsening back and/or leg pain following the operation [42].

Generally, elderly patients with comorbidities are at a higher risk for complications and adverse outcomes [49].

Pain Control

Several studies have investigated the short- and long-term implications of lumbar laminectomy on pain control. In the short term, some studies have demonstrated variable rates of bodily pain control following lumbar laminectomy, with several finding an overall benefit in the first few months [50–52]. There are conflicting studies regarding long-term benefit on pain control. While some show maintained benefit of surgery for several years, others show a general decline over time, with no statistical significance after a few years [50, 51, 53, 54]. More studies are needed to assess long-term outcomes beyond 2–3 years [52].

Rate of Reoperation

In some patients, the overall benefit from the initial lumbar laminectomy may diminish over time. Prior to reoperation, patients may begin to complain of symptoms such as back pain, radiculopathy, weakness, sensory deficits, and neurogenic claudication. Several studies have analyzed the rates of reoperation, with ranges between 14 and 23% [55–57]. One study showed that approximately 55% of the cohort underwent an additional decompression alone, while 44% underwent decompression and fusion. The lifetime risk of fusion following a first-time laminectomy was 8% [56]. Generally, outcomes vary significantly among studies and centers, showing that local expertise and other procedural factors may influence the outcome [58].

Lumbar Laminectomy with Discectomy

Indications

Degenerative disc disease is extremely common, with an estimated prevalence of 12 million Americans alone. Approximately one million of these patients undergo surgeries each year, with about 200,000–300,000 being lumbar discectomies [59, 60]. The indications for a laminectomy are the same as those discussed in the prior section. A discectomy is typically performed to excise a lumbar disc herniation. The purpose of surgery in this situation is to remove the portion of the disc impinging upon a nerve root, causing radiculopathy, and in extreme cases, cauda equina syndrome. The most important determinant supporting surgical intervention for discectomy is the correlation between the distribution of the radicular leg pain and the nerve root compression seen on preoperative imaging studies [61].

Outcomes

Postoperative complications:

- Dural injury
  - This occurs in roughly 3% of cases [62]. Even if treated intraoperatively, there can be effects on the postoperative course, such as prolonging bed rest for 48 h or longer [62].
- Nerve root or vessel damage
  - Nerve root injury has been reported to occur in about 0.2% of cases, and anterior vessel damage is rare, occurring roughly 0.045% of the time [63, 64].
- Recurrence of disc herniation
  - This results in reoperation, ranging from 3 to 18% in those undergoing first-time surgery [65]. Some postoperative patients may initially maintain a pain-free interval prior to presenting with recurrence of pain in the original distribution. One study showed that at 2 years, roughly 23% of patients demonstrated radiographic evidence of recurrent disc herniation at the level of prior discectomy on serial imaging, with 10.2% of these patients with symptoms [66].
- Infection
  - Infection of the disc space may range from 0.12 to 0.9%. Deep infections typically present as epidural abscess or discitis, possibly involving adjacent vertebral bodies, which results in spondylodiscitis [67, 68].

- Thromboembolic complications
  - Complication rates are reported from 0.1 to 1%, with rates of lower extremity thrombosis likely higher [69].
- Other
  - Nerve palsies may occur, which are often related to positioning during surgery, or symptoms may persist, which is typically due to inadequate removal of the herniated disc, wrong-level surgery, or nerve injury due to retraction.

Pain Control

Robust evidence exists for early improvement in pain or function at 2–3 months following lumbar laminectomy and discectomy [70]. Most patients have pain reduced to a point of clinical irrelevance, though roughly 14% of patients report persistent pain between 6 months and 2 years [65]. Benefits of surgical intervention may diminish over time. One study indicated that after 2 years, between 11.6 and 27.8% of patients reported persistence of pain, depending on the extent of disc resection [65]. Generally, a majority of patients who undergo the procedure maintain resolution of presurgical pain in the long term [65, 71].

Rates of Reoperation

At roughly 2 years, approximately 23% of patients demonstrated radiographic evidence of a recurrent disc herniation on serial imaging, at the level of prior discectomy. However, risk can vary, frequently depending upon the size of the defect in the annulus [51, 65, 71, 72]. Generally, the reoperation rate following an initial discectomy is around 14% [55, 73, 74]. One study indicated roughly 63% of the reoperations are discectomies, 14% are fusions, and approximately 23% are decompressions. Additionally, patients with one reoperation after a lumbar discectomy had approximately a 25.1% cumulative risk of further spine surgery in the 10-year follow-up [73].

Lumbar Instrumented Fusion

Indications

One of the most common procedures for chronic, nonspecific lower back pain with apparent degenerative disc changes is lumbar vertebral fusion. Though controversial, some of the most common indications for fusion include the following:

mechanical pain; grade II or higher spondylolisthesis; ischemic spondylolisthesis; history of repeated (>2) discectomies; history of bilateral facetectomy; spinal stenosis without spondylolisthesis if unstable; radiographically documented instability, with associated pain or progressive neurological deficits [75–78]. Other indications may be even more controversial, including decompression with grade I spondylolisthesis, chronic axial low back pain of unknown etiology, and following a unilateral facetectomy. However, more recent data suggests improved outcomes with fusion as opposed to laminectomy alone in patients with grade I spondylolisthesis and stenosis [78–81]. Additionally, fusions are indicated for treatment of patients with deformity, spinal trauma, and oncological conditions [80].

Various approaches are possible, including posterior, lateral, and anterior approaches:

Posterior:

A posterior fusion is generally considered the gold standard of spinal fusion for spondylolisthesis. It requires only one incision over the lower back. However, only a limited portion of the disc space can be accessed from the posterior approach, as the dural sac is in the way, thus limiting the size of the interbody fixation device that can be placed. Additionally, placing a device from the posterior approach has the added risk of injury to the exiting and traversing nerve roots [80, 81].

Anterior:

This approach permits the best exposure of the disc space, and allows large devices to be used for fusion, increasing the surface area for a fusion, which may enhance postoperative stability. Additionally, an anterior approach permits the ability to enhance lumbar lordosis by an additional 5–10°. However, an anterior approach requires two incisions, which include one in the abdomen and the other in the lower back, and as such, there is an added risk of injury to the aorta or vena cava, as both lie anterior to the spine.

Lateral:

This approach provides a unique corridor to the spinal column, but has significant risk of nerve injury to the exiting lumbar nerves as they traverse the psoas muscle. A lateral approach may be used for trauma or tumor, but traditional indications are rare. More recently, minimally invasive lateral approaches have been developed that may minimize risk and have helped to reinvigorate this approach over the past decade [80].

Outcomes

Some of the more common complications seen more specifically with lumbar fusion include the following:

- Hardware irritation and failure
- Cage displacement
- Adjacent segment disease (ASD)

Additionally, there may be complications of vertebral body destruction, and excessive bone growth into the spinal canal, especially with the use of recombinant human bone morphogenetic protein [82].

Lumbar fusion has shown varying success, but significant long-term functional improvement has been shown in approximately 70% of patients undergoing lumbar fusion, though rates may depend on the procedure performed [83, 84]. A successful result from lumbar fusion can depend on numerous factors, including the diagnosis and procedure, as well as the patient's overall health and lifestyle. Such factors include obesity and smoking status. Generally, the goal of lumbar fusion surgery is to achieve solid ossification between two or more vertebrae; overall, patients who are successfully fused have significantly better clinical outcomes [85].

Conclusion

Lumbar back pain is very common and can substantially limit a patient's quality of life. Though there are numerous etiologies of lower back pain, the vast majority will have a nonspecific etiology. In those with a clear mechanical or nonmechanical etiology, a multimodal strategy of conservative and/or surgical interventions may be appropriate. Surgical intervention of lumbar pain may be necessary in select patients, with varying effects on short- and long-term pain relief. Successful management of patients presenting with lower back pain requires a thorough understanding of this spectrum of available interventions.

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Chapter 62
Transforaminal Endoscopic Surgery for the Treatment of Pain in the Rehabilitation Patient

David B. Choi and Albert E. Telfeian

Introduction

The surgical treatment of spinal canal stenosis started with open procedures to decompress structures, such as intervertebral discs, that impinge upon the spinal cord. In 1934, Mixter and Barr described a laminectomy and fragmentectomy of an intervertebral disc to treat lumbar and sciatic pain [1]. In the following decades, surgeons began to pioneer less invasive techniques. Smith first employed chemonucleolysis in 1963 to treat disc herniations without direct visualization of bony and soft tissues of the spine, later using chymopapain as the nucleolytic agent [2]. In 1975, Hijakata used intra-operative fluoroscopy to perform a percutaneous discectomy [3]. Kambin was the first surgeon to employ a single-port arthroscopic discectomy [4].

Yasargil's use of the operative microscope in 1967 for lumbar disc herniations ushered in an era of minimally invasive techniques in spine surgery [5]. In the 1990s, spine surgeons further adapted endoscopic procedures performed by cardiothoracic surgeons and applied them with the principles of minimally invasive surgery [6–8]. The goal of minimally invasive surgery, as described by Fitzpatrick and Wickham in 1990, is "to reduce the physical trauma inflicted upon the patient and on structures to achieve a maximum therapeutic result." Spine surgeons elaborated upon this definition to include the requirement of preservation of biomechanical spinal stability, giving rise to modern-day minimally invasive spine surgery [9, 10].

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Traditional endoscopic spinal approaches required at least three ports: an endoscopic port, a working port, and a suction port [11]. This technique, however, has evolved to involve only a single port through which the surgeon can access the transforaminal space with an endoscope and a series of fixed and malleable forceps to remove tissues compressing the neural structures.

Advantages and Disadvantages of Endoscopic Spine Surgery

Advantages

Endoscopic spine surgery can benefit the elderly or patients with multiple medical comorbidities, who may not be able to tolerate general anesthesia. Patients undergoing this approach require only conscious, monitored anesthesia care (MAC) and can provide the surgeon with instantaneous and accurate feedback regarding their symptoms during the procedure [11].

Open posterior spinal approaches require mobilization of paraspinal muscles, which can cause tissue devitalization and devascularization. Extensive bony work to access the spinal canal or lateral recess creates biomechanical instability that may require additional instrumented fusion. The transforaminal endoscopic approach requires only focused, in-situ drilling of the caudal pedicle and medial aspect of the superior articular facet of the caudal vertebral body to widen the lateral recess, which offers the surgeon a clear view of the surgical site while preserving biomechanical stability [19].

These procedures are performed in the outpatient setting, and patients are able to ambulate immediately postoperatively. There is no prolonged hospitalization or convalescence.

Disadvantages

Success of this procedure may depend upon the surgeon's experience, as there is a steep learning curve involved in mastering the nuances of endoscopic spine surgery [12]. There is no direct view of the surgical field in this percutaneous approach, and the surgeon must rely upon anteroposterior (AP) and lateral intra-operative fluoroscopy to dock onto the neural foramen; adjacent critical structures include the exiting nerve root in the superior aspect of the neural foramen and the thecal sac within the spinal canal.

Equipment can also be a cause for concern, as the endoscope my offer only a limited field of view. Angled-opening beveled cannulas allow retraction of critical structures away from the surgeon's working field, while probes can help the surgeon to confirm current location relative to the pedicles, and malleable curved grasping forceps can allow the surgeon to remove disc material that would otherwise be

inaccessible via a straight-line trajectory. An arsenal of instruments, including a malleable curved grasping forceps, angled-opening beveled cannulae, along with intra-operative fluoroscopy, allows the surgeon the maneuverability necessary to access the ventral spinal cord without inflicting damage on neural structures.

Indications

General Considerations

Criteria for endoscopic approaches, as defined by Kambin, include [4, 13]:

- Positive straight-leg raise test.
- Correlation between radiologic findings and clinical signs and symptoms.
- Radiating pain with or without neurologic deficits on exam.
- Radiating pain which is worse in the lower extremities than the back.
- Failed conservative treatment of 8 weeks' duration.

Degenerative Disc Disease with Radiculopathy

Contained disc herniations include bulges and protrusions, while non-contained discs refer to migrated fragments and include extrusions and sequestrations [14]. The percutaneous transforaminal endoscopic approach can be used for central and transligamentous disc herniations, but also sequestered disc herniations. Non-contained disc herniations protrude from the intervertebral disc space and cause radiculopathy from chemical irritation to and mechanical compression upon the exiting nerve root. Patients may present with major motor weakness and may have failed conservative treatment for a minimum of 2 months' duration [15]. Hoogland et al. demonstrated excellent or good results in 91% of patients, defined as the ability to resume activities of daily living, resume one's occupation, and discontinue prescription analgesics and anti-inflammatory medications [15, 16].

Lateral Recess Stenosis

A study of neurological and orthopedic surgeons, led by Burton et al., concluded that "failed-back" syndrome resulted from inadequate decompression of the lateral recess in up to 58% of patients [17]. Lateral recess stenosis can be caused by degenerative processes, such as intervertebral disc herniations, spondylolisthesis, osteophytosis of the vertebral bodies and articular processes, and collapse of the posterior longitudinal ligament into the neural foramen [13]. Congenital conditions, such as

short pedicles, can also result in stenosis of the lateral recess. Kambin performed transforaminal endoscopic decompression of lateral recess stenosis in a series of 40 patients and demonstrated that 82% of patients achieved good or excellent results, defined as resolved leg symptoms with occasional back pain, along with ability to continue modified work and activities of daily living [13].

Operative procedures to address lateral recess stenosis include laminectomy with facetectomy, impaction of posterior vertebral osteophytes, and complete facetectomy and arthrodesis. The main disadvantage of these procedures is loss of biomechanical stability. Percutaneous endoscopic procedures can maintain biomechanical stability while also addressing neurologic pathology.

Degenerative Spondylolisthesis

Spondylolisthesis is the translation of one vertebral body relative to an adjacent vertebra, resultant from a degenerative process, and presenting mainly in the elderly population [18]. This translation of the anterior spinal elements can result in neuroforaminal narrowing, causing patients to experience mechanical back pain, neurogenic claudication symptoms, and radiculopathy [19]. Surgical management of this pathology consists of spinal canal decompression, along with instrumented fusion. Although these fusions may provide biomechanical stability, up to 40% of patients may experience significant and debilitating residual pain [20].

A patient's advanced age can potentially create peri-operative complications from general anesthesia, inpatient hospital stay, spinal hardware, and existent medical morbidities. These factors have encouraged exploration of less invasive techniques to relieve stenosis. Jasper et al. reported the use of the transforaminal endoscopic approach to treat symptoms resulting from L4–5 and L5-S1 spondylolisthesis [19]. This approach allowed the authors to focus upon the individual anatomic pathologies compressing the nerve root, such as disc herniations, shingling of the superior articular facet of the caudal vertebra, and posterior displacement of the caudal vertebral body compressing the inferior aspect of the exiting nerve root. The transforaminal endoscopic approach addresses each of these pathologies without destabilizing the spine, as would be done in an open approach.

Spine surgeons have also recently performed successful transforaminal lumbar interbody fusions (TLIF) using the percutaneous transforaminal endoscopic approach. Jacquot and Gastambide performed transforaminal endoscopic fusions on fifty-seven patients, with an average fusion time of 6 months postoperatively [21]. Advantages of this method of fusion include: (1) short operative time, less than one-and-a-half hours, (2) awake sedation, thus minimizing anesthesia risks, (3) reduced postoperative hospital stay, and (4) patient's ability to ambulate immediately postoperatively.

The main disadvantage of this approach is migration of the interbody device, occurring in up to 25% of patients during a period of 8 months postoperatively.

Secondary procedures are necessary in these cases. Passage of instruments and hardware through the neural foramen also creates a risk of postoperative radiculopathy, occurring in up to 12% of patients [21].

Intraspinal Tumors

Limited literature addresses the utility of the transforaminal endoscopic approach in the treatment of spinal tumors. Neoplastic processes can arise from the spinal cord glial or neural tissues, the vertebral body, or paraspinal tissues; the resultant malignant spinal cord compression presents as pain, motor weakness, or bowel or bladder incontinence. Traditionally, open surgical approaches are used in malignant spinal cord compression. Recently, however, Joo et al. reported the case of a patient with metastatic colon cancer with a T11 ventral epidural thoracic spinal metastasis [11]. A minimally invasive transforaminal procedure was performed to decompress the ventral spinal cord; this palliative measure allowed the patient to ambulate and live pain-free for over one month.

In addition to preserving a patient's functionality, the minimally invasive transforaminal endoscopic approach can also preserve biomechanical stability. Telfeian et al. reported the case of a pediatric patient with recurrent ventral extradural thoracic tumor who underwent a minimally invasive transforaminal endoscopic surgery [32]. The primary goal of this surgery was to decompress the spinal canal. A second, and equally important, goal was to preserve biomechanical stability in a patient who had undergone a prior laminectomy for tumor resection; a repeat open approach would further destabilize the facet joints, necessitating an instrumented fusion.

As surgeons' expertise in the treatment of spinal tumors increases, minimally invasive endoscopic spine surgery may be a first-line procedure for biopsies and tumor resection and decompression.

Contraindications

Relative contraindications to the percutaneous transforaminal endoscopic approach include: extruded or sequestered disc fragments that are out of reach of endoscopic instruments, disc herniations at more than one level, severe neuroforaminal stenosis, recurrent disc disease, and spondylolisthesis [22].

However, some of these limitations and technical difficulties can be overcome by the surgeon's experience. When assessing multi-level herniations, the surgeon can determine, by reconciling the clinical exam and radiographic findings, the appropriate level at which to operate. Preoperative nerve root blocks can also determine the offending level [23].

Procedure Description

Preoperative Considerations

Examination of preoperative imaging can help the surgeon to plan a procedure that will effectively address a patient's individual pathology. Spinal MRI can show a paracentral or foraminal disc [24]. In the case of lower lumbar discectomies, the surgeon must consider the height of the iliac crest when deciding upon a skin entry point; for example, the skin entry point for an L5-S1 disc must be above the iliac crest to allow for a trajectory that will safely and properly lead to the neural foramen. See Fig. 62.1.

Relevant Anatomy

Kambin's triangle is a space created by the following borders [25]:

- Medial edge of the exiting nerve root.
- Lateral edge of the superior articular process of the caudal vertebra.
- Superior edge of the caudal vertebral body.

This triangle is also called the "safety working zone," and surgeons can safely access and remove herniated disc material in this region.

Anesthesia

The procedure is performed with conscious MAC sedation, consisting of midazolam and fentanyl.

Patient positioning

The patient can be positioned either prone, with chest and hip bolsters, or in the lateral decubitus position, based upon the surgeon's preference. In the lateral position, pillows can be placed under the contralateral hip to flex the neural foramen open, while gravity causes the dura to retract away to the contralateral side. There is also less blood loss due to decreased abdominal pressure in the lateral decubitus position [26].

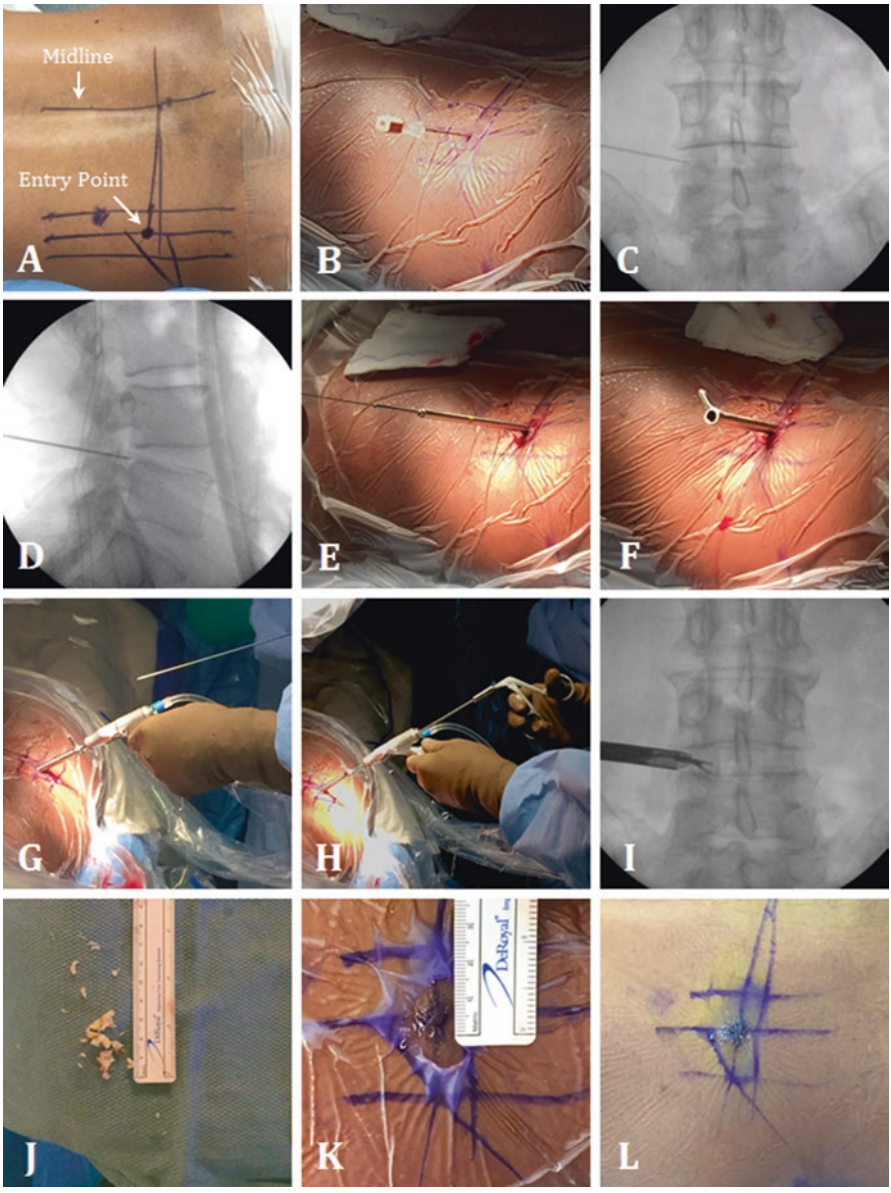

Fig. 62.1 (**a**) Skin marking for spinal needle trajectory. (**b**) Spinal needle entry point 10 cm lateral to midline. (**c**). AP view fluoroscopy demonstrating spinal needle traversing neural foramen and terminating above caudal pedicle. (**d**) Lateral view fluoroscopy confirming depth of spinal needle, terminating at the intervertebral disc space. (**e**) K-wire replaces spinal needle with tube dilators in place. (**f**) Beveled cannula in place after tissue dilation. (**g**) Endoscope enters beveled cannula. (**h**) Grasping forceps in working channel of endoscope. (**i**) AP view fluoroscopy demonstrating grasping forcep removing intervertebral disc material. (**j**) Intervertebral disc material removed. (**k**) Skin incision closed with absorbable suture. (**l**) Dermabond placed over skin incision

Skin Entry

The skin entry point is 10–14 cm lateral to midline, at the operative level, on the ipsilateral side of the disc herniation. The correct spinal level can be confirmed with fluoroscopy. The trajectory for levels below L3-4, however, is limited by the iliac crest. The entry point in this case, therefore, will be above the level of the iliac crest. After injecting the skin with local anesthetic, an 18-gauge spinal needle is advanced towards the neural foramen, and position is continuously confirmed with AP and lateral view fluoroscopy. The needle should traverse the neural foramen and dock into the disc space. At this point, the needle tip will be at the inferior border of the neural foramen and at the midpoint position of the caudal pedicle.

Discography

The surgeon can opt to inject indigo carmine dye into the disc space to assess for presence of a herniation, degree of opacification, epidural leak, and degree of disc degeneration [24].

Dilating Tubes and Foraminoplasty

The skin entry point is incised lengthwise to approximately 5 mm and to a depth just beyond the thoracodorsal fascia to allow adequate space for the dilating tubes. At this time, the spinal needle stylet is removed and replaced with a K wire, and this position is confirmed on fluoroscopy. A series of dilators help to expand the fascia to make space for the endoscope apparatus. The dilating tubes and reemers give the surgeon more easy access through the neural foramen and into the disc space by removing the medial portion of the superior articular facet of the caudal vertebral body. The position of each series of dilators and reemers is confirmed continuously with AP and lateral fluoroscopic imaging.

Endoscopic Discectomy

The dilators are now removed, and a beveled cannula is docked onto the inferior aspect of the neural foramen. The 30-degree-angled endoscope traverses through this cannula, and a single 2.7 mm working channel built into the scope apparatus allows the surgeon to use grasping forceps, bipolar cautery, and pedicle finders through the endoscope for constant visualization. The beveled cannula can be used to retract away critical structures, such as the exiting nerve root, allowing the surgeon to freely grasp disc material. Serial rotation of the cannula allows inspection of the thoroughness of the foraminal decompression.

Closure

Closure with an absorbable suture is performed on the skin only.

Complications

Complications of the transforaminal endoscopic approach for discectomies include recurrence of herniation, with a reported rate of 2.4% of patients during a 3-month postoperative period [27]. Gastambide et al. have reported a 3% disc re-herniation rate during a 2-year postoperative period [24]. Redo procedures can be performed once again with the endoscopic approach or via an open microdiscectomy.

Close proximity to the exiting nerve root can result in iatrogenic radiculopathy. Approximately 1 to 6.7% of patients experience postoperative radiculopathy, with resolution several months after surgery [14, 27]. Choi et al. demonstrated that increased operation time and shorter distance between the exiting nerve root and lower margin of the disc were the two factors that significantly increased the risk of nerve root injury [14]. Inferior displacement of the exiting nerve root creates a smaller "safety working zone," leading to increased risk of nerve root injury and subsequent postoperative radiculopathy [14].

Vascular injury is another feared complication of the endoscopic approach. Retroperitoneal hematoma after an endoscopic procedure most commonly presents as sudden inguinal pain after a pain-free interval immediately postoperatively [28]. Arterial branches of the segmental lumbar artery have been postulated as sources for these hemorrhages. Yong et al. recommend using lateral fluoroscopic images when first advancing the spinal needle into the neural foramen. This step ensures that the needle does not advance deeper than the posterior vertebral line, also known as the line of Ahn [29]. Inspection of preoperative CT or MRI can also ensure that blood vessels do not cross the spinal needle trajectory.

Other Endoscopic Approaches to the Spine

The procedures described in this chapter describe a transforaminal approach, but endoscopic surgery continues to evolve to include more approaches. The transforaminal approach is not limited to the lumbar spine, but has also been applied to the thoracic spine [11, 32]. In the lumbar spine, interlaminar approaches are also used to access more central disc herniations. Endoscopic spine surgery is also performed in the cervical spine to address both anterior and posterior pathology. Hsu et al. performed an anterior cervical endoscopic approach to resect a recurrent cervical chordoma [30]. A recent comparison of anterior and posterior cervical endoscopic discectomies demonstrated no significant difference in functional outcomes [31].

Conclusion

Endoscopic spinal surgery is a less invasive mode to address spinal pathologies that would otherwise require more traditional approaches with larger incisions, intrusive muscle and soft tissue dissection, and longer recovery times. Through proper patient selection, this modality can be effective in addressing spinal disc disease.

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Chapter 63
Upper Extremity Peripheral Neuropathies in the Rehabilitation Patient

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Introduction

Upper extremity peripheral neuropathies occur along various points through the course of each nerve, as it exits the brachial plexus and continues distally to the hands. The epidemiology and clinical presentations of upper extremity peripheral neuropathies vary greatly, depending on the nerve that is involved and the location of pathology.

The ulnar nerve at the elbow is susceptible to external trauma in the post-condylar groove and at the cubital tunnel; ulnar nerve compression at the wrist occurs within the ulnar/Guyon's canal. Carpal tunnel syndrome is the most common upper extremity neuropathy and is multifactorial in origin. Pronator teres syndrome occurs as the median nerve is subject to abnormal pressure under the pronator teres muscle. Anterior interosseous syndrome, also known as Kiloh-Nevin syndrome, is a rare neuropathy involving the anterior interosseous nerve. Radial neuropathy at the spiral groove is also known as Cheiralgia paraesthetica. Posterior interosseous syndrome involves the posterior interosseous nerve, a branch of the radial nerve. This chapter discusses more in detail the epidemiology, anatomy, etiology, clinical presentation, diagnosis, and the management of these various neuropathies.

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Ulnar Neuropathy at the Elbow

Epidemiology

Ulnar neuropathy at the elbow (UNE) is the second most common upper extremity mono-neuropathy, after carpal tunnel syndrome. Its annual incidence is 24.7 cases per 100,000 [1], affecting more men than women (25.2 men and 18.9 women per 100,0000 [2]).

Anatomy and Etiology

The ulnar nerve is comprised of fibers from the C8 and T1 (sometimes C7) spinal nerves and is a continuation of the medial cord in the brachial plexus. In the upper arm, the ulnar nerve runs medial to the brachial artery and runs along the anterior border of the intermuscular septum. The ulnar nerve pierces the intermuscular septum proximally and may become enveloped within the anteromedial aspect of the medial head of the triceps, becoming less mobile. Down the arm, the ulnar nerve runs under the Arcade of Struthers, which is an extension of the intermuscular septum that is present in 50% of the population. As the medial head of the triceps narrows into a tendon, the ulnar nerve emerges and enters the post-condylar groove with the inferior ulnar artery. The post-condylar groove is a bony canal between the medial epicondyle of the humerus and the olecranon of the ulna. Within this groove, the ulnar nerve can be subject to external trauma.

Distal to the elbow, the ulnar nerve enters the humeral and ulnar heads of the flexor carpi ulnaris. Distal to the post-condylar groove, the ulnar nerve enters the cubital tunnel, which has two segments. The first segment is where the ulnar nerve passes under the aponeurosis that connects the two proximal tendons of the flexor carpi ulnaris, which is called Osborne's band. The second segment is where the ulnar nerve passes between the two muscular heads of the flexor carpi ulnaris. Depending on the thickness and the extent of Osborne's band, the ulnar nerve can be compressed. Elbow and wrist flexion can mechanically compress the ulnar nerve within the cubital tunnel, which can precipitate the symptoms of ulnar nerve entrapment.

Smoking [3, 4] and male gender [5] are risk factors associated with ulnar neuropathy at the elbow.

Clinical Presentation

Patients with ulnar neuropathy at the elbow often present with intermittent numbness or tingling in the ulnar nerve distribution, which is often brought on by pressure or flexion of the elbow. It has been reported that 92% of patients with ulnar

neuropathy at the elbow present with sensory disturbances of the fourth and fifth digits [6], whereby 80% and 72% of such cases involve the palmar and dorsal surfaces of the hands, respectively [6]. Medial elbow ache or pain, with or without referred pain along the medial forearm, can also be present. Although subjective symptoms are useful to make the diagnosis, there is poor correlation between symptoms and the electrodiagnostic criteria for UNE [7].

Motor symptoms are less common, but when present, there is weakness or wasting of the intrinsic hand muscles or a claw hand deformity. Weakness of finger flexors of the fourth and fifth digits can occur from the flexor digitorum profundus, which is innervated by the ulnar nerve in the forearm. Provocative tests include Tinel's and elbow flexion with or without direct pressure. If positive and if symptoms are reproduced with these maneuvers, diagnosis of UNE is likely. Palpation for local nerve thickening and tenderness can also be performed. However, the clinical utility of these tests is limited and have a low sensitivity [8, 9].

Diagnosis

The diagnosis can be made based on the clinical picture and results of electrodiagnostic studies. Electrodiagnostic studies include nerve conduction velocities (NCV) and needle electromyography (EMG). The goal of electrodiagnostic studies is to localize the lesion and to determine the character, severity, and prognosis. They can be particularly useful if the clinical presentation is not straightforward in patients with coexisting musculoskeletal disorders, radiculopathy, or other peripheral nerve syndromes. Please see the chapter on Electrodiagnostics for more details.

Motor nerve conduction studies are obtained from the hypothenar eminence or from the first dorsal interosseous muscles, with stimulation at the wrist, below the elbow, and above the elbow. The amplitudes of the maximum compound muscle action potential (CMAP) in response to stimulation are recorded. Diagnosis for UNE is made if there is focal slowing or conduction block across the elbow.

The sensory nerve conduction from the fourth or fifth digits with the sensory nerve action potential (SNAP) can provide evidence of sensory axonal involvement. The sensory response of the dorsal ulnar cutaneous nerve can be used to distinguish ulnar neuropathy at the elbow or at the wrist. The exact sensitivity and specificity is uncertain due to a small number of patients in existing studies. However, one study of 109 arms revealed that the sensitivity of motor conduction studies for localizing UNE was 78% [10]. The sensitivity is highest at 98% if electrodiagnostic studies and sonography are combined [10]. MRI is a useful diagnostic tool for UNE, especially in cases with non-localizing electrodiagnostic studies [11–13]. The features suggestive of UNE on MRI include nerve enlargement and increased signal intensity on T2-weighted or T1 inversion recovery sequences [11–13]. Ultrasonography is also useful and measures thickening or increased cross-sectional diameter as well as altered echogenicity, with a sensitivity of 80% and a specificity of 91% [14–16].

Management

Management of ulnar neuropathy can be conservative or surgical. In practice, conservative treatment is recommended as the initial treatment for most patients, especially those without strong clinical or electrophysiologic evidence of neuropathy such as severe weakness, sensory loss, or significant axon loss on electromyography. Conservative treatment typically involves the use of splints, pads, activity modification, avoidance of provoking factors, and nerve gliding exercises. Rehabilitation focuses on strengthening of the pronator and flexor muscles. The benefit of conservative treatment is unproven [17]. However, with an understanding of the underlying pathogenesis, patients are generally recommended to avoid leaning on the elbows or to remain in a position of prolonged elbow flexion [18].

The main surgical options are in situ decompression, transposition, or medial epicondylectomy. An indication for surgical intervention is moderate-to-severe ulnar neuropathy, which presents with clear weakness, sensory loss, or significant axonal loss on EMG. This is caused by trauma, structural abnormality, or nerve compression. Another indication is moderate-to-severe stable ulnar neuropathy of less than 6 months, despite conservative measures. Chronic ulnar neuropathy of 2 or more years or presentation in elderly or medically unwell patients is relative contraindications to surgery, as the benefit of surgery is doubtful in this patient population.

Simple decompression for UNE is performed by cutting the flexor carpi ulnaris aponeurosis (the humero-ulnar arcade or Osborne's fascia). Transposition is carried out by cutting Osborne's fascia, mobilizing the ulnar nerve from the retrocondylar groove, and moving the nerve anteriorly to achieve transposition. Medial epicondylectomy is performed by cutting Osborne's fascia and by removing the humeral medial epicondyle. The best surgical approach for UNE is controversial [17, 19, 20]. Therefore, the choice of procedure depends highly on the surgeon's experience and preference.

The available data indicates that ulnar nerve decompression and transposition result in similar clinical outcomes [21–24]. Transposition is associated with a higher rate of complications than decompression (31.1% versus 9.9% [22]). Transposition is associated with higher deep wound infections than decompression [23]. There is a trend to favor decompression over transposition for idiopathic UNE, as transposition is associated with higher complication rates and is more technically demanding than decompression.

The natural history of UNE is poorly understood, largely due to the fact that there are no standardized case definitions, electrodiagnostic processes, and outcomes. Patients with more severe clinical presentations undergo a higher rate of surgical intervention [18].

Ulnar Neuropathy at the Wrist

Anatomy and Etiology

At the wrist, the ulnar nerve first passes through the ulnar canal (also known as Guyon's canal), along with the ulnar artery, between the pisiform and hamate bones. The ulnar canal is a triangular canal formed by the volar carpal ligament anteriorly, the transverse carpal ligament posteriorly, and the pisiform and flexor carpi ulnaris tendon medially [25–28]. More distally, the ulnar nerve passes through a second canal called the pisohamate hiatus [29, 30]. The pisohamate hiatus is located just distal to the ulnar canal and contains only the deep branch of the ulnar nerve. The pisohamate hiatus is bound by a fibrous arch anteriorly and the pisohamate ligament posteriorly [31]. The fibrous arch is a bundle of the hypothenar muscle fascia, which connects the pisiform and the hook of hamate. Just before entering the pisohamate hiatus, the ulnar nerve then divides into superficial and deep terminal branches. The superficial terminal branch supplies the cutaneous ulnar border of the palm and then divides into two digital branches that innervate the palmar or volar surfaces of the fifth digit and ulnar half of the fourth digit. The deep branch innervates the opponens digiti muscle, the remaining hypothenar muscles, interossei, and the third and fourth lumbricals, adductor pollicis, and flexor pollicis brevis.

The 3-zone theory was proposed by Gross and Gelberman in 1985 [32] to better understand the clinical anatomy of the ulnar nerve:

- Zone I: begins from the proximal edge of the volar carpal ligament and ends distally at the ulnar nerve bifurcation.
- Zone II: runs from just distal to the bifurcation of the ulnar nerve to the fibrous arch of the hypothenar muscles and contains the deep branch of the ulnar nerve.
- Zone III: begins just distal to the bifurcation of the ulnar nerve and contains the superficial branch of the ulnar nerve.

It is important to recognize that there are numerous anastomoses between the ulnar and median nerves, and the division of the three ulnar nerve final divisions or zones helps to avoid mistakes during diagnosis and surgery [33].

Ulnar neuropathy at the wrist (UNW) is far less common than UNE. The etiology of UNW can be extrinsic factors such as bone fractures, especially involving the hook of hamate, or lacerations. Direct or repetitive pressure or trauma to the ulnar wrist or hypothenar area, as in certain occupational settings, can predispose to UNW. Intrinsic causes include ganglia from the wrist joint or the ulnar nerve itself, ulnar artery aneurysms, lipomas, or other tumors. However, many cases are idiopathic.

Clinical Presentation

Symptoms of UNW can be similar to that of UNE, such as sensory disturbances of the ulnar nerve territory. Motor symptoms such as hand weakness, atrophy of the intrinsic hand muscles, and loss of dexterity tend to me more prominent in UNW than UNE. Compared to UNE, the clawing of digits four and five can be worse with lesions in UNW, due to the fact that the flexor digitorum profundus is spared in UNW, as it innervated by the ulnar nerve in the arm.

Injury to the ulnar nerve at the wrist can be anatomically divided into four sites and the clinical presentations tend to differ accordingly. The following subtypes have been described:

- Proximal canal lesion: All branches of the ulnar nerve, including the proximal and distal deep palmar motor and superficial branches to the palmaris brevis, are affected.
- Proximal deep palmar motor lesion: All ulnar-innervated hand muscles, including the hypothenar muscles, are affected. Sensory fibers and motor innervation of the palmaris brevis are spared.
- Distal deep palmar motor lesion: All ulnar-innervated hand muscles except the hypothenar muscles are affected. Sensory fibers and motor innervation of the palmaris brevis are spared.
- Superficial branch lesion: Only the superficial branching containing the sensory fibers are affected. The palmaris brevis is affected, but not clinically apparent.

Clinical utility of percussion over Guyon's canal is limited. Although the zones of the ulnar canal anatomy and the clinical classifications are useful, there can be a lack of correlation with the exact location of the lesion, due to the fact that not all the fascicles are affected at the injury site. Regardless, a thorough physical examination is important to guide further investigations.

Diagnosis

As with UNE, electrodiagostic testing is often used. Detection of focal motor or sensory nerve conduction slowing or block with stimulation at the wrist, with no evidence of proximal nerve involvement, is highly indicative of UNW. A normal dorsal ulnar cutaneous sensory potential and the presence of normal needle EMG findings in the flexor carpi ulnaris and flexor digitorum profundus muscles are useful to rule out more proximal lesions. As with UNE, both MRI and ultrasound are useful to rule out ganglia or cysts.

Management

Similar to the UNE, UNW can be managed conservatively or surgically. As in UNE, conservative treatment is recommended as the initial treatment for most patients, especially those without strong clinical or electrophysiologic evidence of neuropathy, such as severe weakness, sensory loss, or significant axonal loss on electromyography.

Conservative treatment typically involves the use of splints, pads, activity modification, avoidance of provoking factors, and nerve gliding exercises. Rehabilitation by a physical or occupational therapist in these patients is important to maintain or to improve functional range of motion and strength of the affected muscles, such as the interossei and lumbricals [34]. Patients should be encouraged to use the affected hand. Various splinting methods, such as static splinting and ulnar gutter, may be used. Use of a dorsal metacarpophalangeal block or lumbrical bar to the fourth or fifth fingers may also be used in cases of ulnar claw deformity. However, the benefit of conservative treatment is unproven [17]. Often, surgical exploration of the ulnar canal and subsequent decompression of the ulnar nerve is indicated [35].

Carpal Tunnel Syndrome

Epidemiology

The carpal tunnel syndrome is the most common upper extremity mono-neuropathy. The incidence of carpal tunnel syndrome is 324–542 per 100,000 population in women, and 125–303 per 100,000 population in men [36]. The prevalence is 1–5% and there is a female predominance, with a female-to-male ratio of 3:1 [37]. It is rare in children [38, 39]. It affects more obese females than those with normal to low BMI [40].

Anatomy and Etiology

The carpal tunnel is an anatomic space that is formed by the carpal bones inferiorly and the flexor retinaculum (or transverse carpal ligament) superiorly, in an anatomic position. The retinaculum is about 3–4 cm wide and inserts into the scaphoid tuberosity as well as into the pisiform in the proximal carpal tunnel [41]. Distally, the retinaculum inserts into the trapezium and the hook of hamate [41]. The carpal tunnel contains the median nerve, four tendons of flexor digitorum profundus, four tendons of flexor digitorum superficialis, and a tendon of flexor pollicis longus.

Although the pathophysiology is multifactorial, the leading theory involves increased pressure in the intra-carpal canal [42]. Increased pressure in the intra-carpal canal may cause direct nerve injury, impair axonal transport, and may compress the vessels of the perineurium, resulting in median nerve ischemia [43–45]. Fibrosis of sub-synovial connective tissue, congenitally small anatomic space, mass lesions such as cysts, neoplasm, and a persistent median artery can all contribute to increased pressure on the median nerve. Inflammation or fibrosis of the nine flexor tendons that enter the carpal tunnel or systemic illnesses, such as rheumatoid arthritis, can also increase intra-carpal pressure [42]. Positioning of the wrist is also associated with the intra-carpal pressure, with the lowest carpal pressure in a neutral or slightly flexed position of the wrist [46–48].

Risk factors for carpal tunnel syndrome include obesity [49], female gender [49], and coexisting conditions such as diabetes [50], pregnancy [51, 52], rheumatoid arthritis [50], hypothyroidism [50], and preexisting median mono-neuropathy [53, 54]. There is also evidence to implicate a genetic predisposition and a history of aromatase inhibitor (e.g. anastrozole) use [55]. Occupational exposure to excess vibration, increased hand force, and repeated flexion and extension increase risk for carpal tunnel syndrome [56]. Construction workers are at an increased risk of CTS, and targeted awareness and preventive intervention should be targeted to this group [57].

Clinical Presentation

Patients often present with pain and paresthesia of the hands in the median nerve distribution, typically involving the radial three digits and radial half of the fourth digit, with or without radiation. Sensation over the thenar eminence is not affected in carpal tunnel syndrome, as the palmar cutaneous branch of the median nerve branches off the median nerve prior to entering the carpal tunnel. Symptoms are frequently more prominent nocturnally and are reportedly relieved by shaking or wringing the hands or by putting them under warm water. Sensory testing should be done in the hands, forearm, and upper arm. Fixed sensory deficits occur late in the course of the disease. Motor symptoms such as weakness and decreased dexterity of the hands present typically after the onset of sensory symptoms. On neurologic exam, there can be decreased strength of thumb abduction and opposition. Atrophy of the thenar eminence can also be seen. Bilateral carpal tunnel syndrome is common and is seen in 65% of affected patients [58]. Provocative tests for CTS include Phalen's, Tinel's, manual carpal compression (also called Durkan's test), and hand elevation tests. These can all aid in the diagnosis of CTS in the context of clinical presentation, but the sensitivity and specificity are limited. Phalen's maneuver is positive if there is reproduction of symptoms on flexion of wrists for 1 min. The sensitivity and specificity of Phalen's test are 68% and 73%, respectively [59]. Tinel's test is positive if one can reproduce symptoms with firm percussion over the

course of the median nerve proximal to or over the carpal tunnel. The sensitivity is 50% and the specificity is 77% [59]. Manual carpal pressure (Durkan's test) is positive if direct pressure over the transverse carpal ligament reproduces symptoms within 30 seconds of applying pressure. This test has a sensitivity of 64% and specificity of 83% [59]. The hand elevation test is positive if elevating the hands above the head for 1 min reproduces symptoms. The sensitivity and specificity are 75.5 and 98.5%, slightly better than those for Phalen's or Tinel's test [60].

Diagnosis

Carpal tunnel syndrome is a clinical diagnosis based on the signs and symptoms as discussed above. Electrodiagnostic testing is useful to diagnose or to measure the severity of carpal tunnel syndrome, which can be used to assess for surgical need. Nerve conduction studies (NCS) are a standard part of CTS diagnosis and evaluation to assess the severity of median nerve involvement. NCS has a high sensitivity and specificity [61]. Electromyography (EMG) in conjunction with NCS is useful to exclude other causes such as polyneuropathy, plexopathy, or radiculopathy and also to aid in assessing the severity of the nerve denervation. The use of MRI for CTS may be indicated in select patients if a specific location is detected on NCS/EMG, or if the patient presents with an acute onset. MRI can help to assess for structural abnormalities such as tumor, bone, or joint disease [62]. Ultrasound can be utilized as an ancillary tool; a cross-sectional area of more than 8.5–10 mm^2 indicates CTS [63]. CT with myelography can be used for patients with contraindications to MRI; such patients with ferromagnetic implanted devices (e.g. pacemakers).

Management

Treatment modality depends on various factors, such as the severity of nerve denervation as assessed by electrodiagnostic studies, patient preference, patient risk factors, and availability. Patient risk factors such as obesity, female gender, and coexisting conditions such as diabetes, pregnancy, rheumatoid arthritis, and hypothyroidism should be evaluated and treated. However, there is a lack of evidence to suggest that CTS is reversible with treatment of these risk factors.

Conservative measures are recommended as initial therapy for patients with no evidence of significant axonal loss or denervation, or for those who did not yet receive electrodiagnostic testing in the presence of mild clinical symptoms. Patients with severe clinical symptoms, in the absence of significant axonal loss or denervation, can also be treated conservatively initially. Most studied conservative treatment options in CTS are splinting, glucocorticoid injections, and oral glucocorticoids.

Wrist splinting or braces that maintain the wrist in neutral position are shown to be effective in reducing symptoms for mild CTS [64, 65]. Wrist splinting is the first line of conservative therapy, as evidenced by its effectiveness and safety profile. The prognostic indicators of success for nocturnal splinting are shorter duration of symptoms (1 year or less) and less nocturnal paresthesia [66]. Splinting, however, when compared to surgery, is not as effective for symptom relief [67, 68].

Local glucocorticoid injections are a non-surgical option that reduces tissue inflammation. Glucocorticoids can be injected near the carpal tunnel either proximally or distally. Studies have shown that glucocorticoid injections appear effective in reducing subjective short-term symptomatic relief of CTS for about 1–3 months [69–71]. Although glucocorticoid injections are considered generally safe, there are associated risks such as CTS exacerbation, nerve or tendon damage [72, 73]. While glucocorticoids can offer better short-term symptom relief than surgery, it is not as effective as surgery to offer sustained symptom relief [74, 75].

Oral glucocorticoids are effective for short-term symptom improvement of CTS, but there is limited evidence to suggest that there is any long-term benefit [76]. Furthermore, local glucocorticoid injections are more effective than systemic oral glucocorticoids [77].

Limited data indicate that yoga can be effective for symptom relief in CTS [78]. Carpal bone mobilization, which includes physical and occupational therapy that mobilizes the wrist joint, has limited data to suggest efficacy for CTS [65, 79]. Nerve gliding, which involves nerve and tendon gliding maneuvers directed by a hand or occupational therapist, also has limited evidence to support its effectiveness [65, 80]. Ultrasound or electrical therapy is used to promote tissue healing. However, there is limited evidence to support benefits of ultrasound therapy [65]. Use of NSAIDs or other oral medications are not effective for CTS [76, 81]. Electrical, magnetic, or laser therapy are shown to have no benefit and only anecdotal evidence exists.

There is strong evidence to support the effectiveness of surgery in CTS, both subjectively and objectively [82–87]. A systemic review indicated the success rate of surgery to be 75% [88]. Indications for surgery include persistent sensory symptoms with motor dysfunction such as thenar eminence atrophy and diminished grip or pinching. It is important to make the correct diagnosis with confirmatory electrodiagnostic studies before pursing surgical intervention. In patients with CTS who have normal electrodiagnostic studies, there is no statistically significant difference in the success rate of surgery or the incidence of complications compared to those with CTS and abnormal electrodiagnostic studies [89]. Therefore, in the right clinical setting with physical signs of CTS, confirmatory electrodiagnostic studies are not necessary to elect a surgical option.

There are two main surgical techniques, which include open carpal tunnel release and endoscopic carpal tunnel release. Both techniques can be performed under local anesthesia, with or without sedation, and with the use of a tourniquet. Open carpal

tunnel release is performed through a standard or limited incision. The open approach has the advantage of better exploration of the anatomy. The median nerve is identified through division of the transverse carpal ligament and antebrachial fascia longitudinally. Subneural reconstruction of the transverse carpal ligament has been shown to improve grip strength [90].

The endoscopic technique involves preservation of the palmar fascia, subcutaneous fat, and skin, which can lead to less post-operative pain, less scar formation, fewer complications, and faster return to work. It is important to obtain excellent visualization in both open and endoscopic techniques. Endoscopic carpal tunnel release is performed through a single or double portal. There is no difference in success rates between the use of a single or double portal, and it depends highly on the surgeon's preference and experience [91, 92]. General post-operative care involves a soft dressing with active motion of the digits and the wrist.

Incomplete release of the transverse carpal ligament is the most common complication of carpal tunnel release. Incomplete release is secondary to the inadequate exposure or suboptimal incision site [88]; the rate of incomplete release is 6% [93]. This complication is the most common reason to pursue a re-operation [94]. Re-operation rate is 1.8% [95]. Other complications include neurovascular injury involving the recurrent motor and palmar cutaneous branches of the median nerve, as well as the superficial palmar arch, post-operative wound infections, painful scar formation, and complex regional pain syndrome. However, long-term disability does not exceed 1–2% [88]. The possible complications that ensue from both open and endoscopic techniques are similar [96–98]. The evidence to compare the rate of complications in open versus endoscopic technique is controversial. However, there is evidence to suggest that there is less post-operative pain and earlier return to work for the endoscopic approach [96, 99, 100]. The endoscopic approach depends highly on the experience of the surgeon and the overall complication rate might be higher for that reason [101, 102].

The outcomes of surgery are favorable, both with open and endoscopic approaches. Surgery results in subjective symptom improvement [96, 103–105]. It is important to educate patients about the temporal patterns of symptom improvement after the surgery. One study obtained self-questionnaires of the post-operative patients at 6 weeks, 3 months, 6 months, and 2 years [106]. Sensory symptoms improved within 6 weeks post-operative; however, motor symptoms initially worsened, but improved over a period of 2 years [106]. Ninety percent of patients reported pain relief [106]. Seventy-seven percent of patients returned to work within 6 months of carpal tunnel release [107]. Other studies have shown high satisfaction rates of 86–88% [104, 105]. The outcomes are equivalent in open versus endoscopic techniques [108–110]. As discussed earlier, there is evidence to suggest less post-operative pain and earlier return to work with the endoscopic approach [96, 99, 100], with faster recovery of digital flexor tendon mechanics, versus the open approach [111].

Pronator Teres Syndrome

Epidemiology

Pronator teres syndrome is very rare and is four times more common in women than in men [112].

Anatomy and Etiology

At the elbow, within the cubital fossa, the median nerve lies medial to the brachial artery. It subsequently passes the lacertus fibrosus, a thick fascial band that extends from the biceps tendon to the forearm fascia [113]. It then passes between the two heads of the pronator teres muscle and under the flexor sublimis muscle by entering the sublimis bridge, which is at the proximal edge of the flexor sublimis muscle [114]. The nerve continues down the forearm between the flexor digitorum profundus and the sublimis [115]. Pronator teres syndrome occurs when the median nerve in the proximal forearm is subjected to abnormal pressure as it passes through or under the pronator teres muscle. This pressure can be due to hypertrophy of the pronator teres muscle, tenosynovitis, muscle hemorrhage, fascial tear, scarring, anomalous median artery, or giant lipoma [113, 116, 117]. In some cases, abnormal fibrous bands or thickening of the lacertus fibrosus have been also reported. Patients who are affected by this are usually physically active individuals, such as cyclists.

Clinical Presentation

Patients with pronator teres syndrome can present with forearm aching, pain, or heaviness, as well as sensory loss of the lateral palm often involving the thenar eminence. This is different from carpal tunnel syndrome, in which sensation over the thenar eminence is typically spared. Often, sensory deficits are not as severe or localized as in carpal tunnel syndrome [113]. Repetitive elbow motions provoke symptoms. However, in many cases of mild, intermittent, or partial compression, the signs and symptoms may be vague and the physical findings may not be straightforward [118, 119]. The most important physical finding is tenderness over the proximal forearm. Pressure over the pronator teres muscle may elicit tenderness and reproduction of sensory symptoms. Weakness of the intrinsic hand muscles and weakness of muscles innervated by the median nerve can also be seen. The pronation test is positive, as pain is elicited by pronation of the forearm. Tinel's sign over the point of entrapment may also be seen.

Diagnosis

Electrodiagnostic testing can reveal slowed conduction velocity, or conduction block in the median nerve distribution in the forearm, and is essential in confirming the diagnosis. EMG may reveal abnormal findings in the muscle groups innervated by the median nerve, such as flexor carpi radialis, but with sparing of the pronator teres [120, 121].

Management

Conservative management is the first step, which involves reducing or avoiding movements or activities that induce symptoms. Other nonsurgical measures include non-steroidal anti-inflammatory drugs or analgesics. Low-dose tricyclic antidepressants or anti-seizure medications, such as carbamazepine and gabapentin, may be considered for adequate pain control [113]. Injection of corticosteroid (e.g. methylprednisolone acetate) or local anesthetic agents (e.g. 1 mL of 1% lidocaine hydrochloride) may be delivered directly into the median nerve or pronator teres muscle.

Surgery aims to decompress the nerve and to release any bands. The open method with an S-shaped incision is used for full visualization and exposure of the anatomy [122]. Recently, endoscopic methods have been carried out [123–125]. The clinical results after endoscopic-assisted decompression of the median nerve are excellent. However, there is no current study comparing open versus endoscopic techniques for the pronator teres syndrome [126].

Anterior Interosseous Syndrome (Kiloh-Nevin Syndrome)

Epidemiology

Anterior interosseous syndrome is very rare and accounts for less than 1% of all compression syndromes in the upper limb [127].

Anatomy and Etiology

The anterior interosseous nerve arises from the median nerve, 5–8 cm distal to the lateral epicondyle and distal to the pronator teres muscle. The anterior interosseous nerve is a purely motor branch with no cutaneous sensory fibers of superficial sensation [113]. It descends through the anterior forearm to innervate

muscles such as the flexor pollicis longus, flexor digitorum profundus to the second and third digits, and the pronator quadratus. Isolated injury to the anterior interosseous nerve is very rare. However, it can be injured in direct trauma as in forearm fractures, humeral fracture, supracondylar facture [128], injections [129], mechanical compression with fibrous bands, enlarged bursae, tumors, vessels [130], or muscle abnormalities. It can also be present in patients with neuralgic amyotrophy, brachial neuritis [131], cytomegalovirus infection, or a bronchogenic carcinoma.

Clinical Presentation

The onset of anterior interosseous syndrome can be either exertional or spontaneous. Typically, patients present with acute pain in the proximal forearm or arm, which lasts for hours or days. The patient with anterior interosseous syndrome may complain of muscle weakness and an inability to make a standard "O" ("Okay" sign) with the thumb and forefinger, due to the affected flexor pollicis longus and flexor digitorum profundus of the forefinger; thus, the forefinger remains straight. Resisted supination can test pronator quadratus. The patient should not have any sensory symptoms with this syndrome [132].

Diagnosis

It is common to have normal electrodiagnostic findings on both motor and sensory studies. On electromyography, findings of membrane instability isolated to the muscles supplied by the anterior interosseous nerve can be seen.

Management

Management depends highly upon the etiology of the anterior interosseous syndrome. In cases of penetrating wounds and in the presence of Volkmann's contracture, an immediate surgical exploration with repair is warranted. Otherwise, conservative management is first-line in non-urgent cases. Use of NSAIDs, analgesics, low-dose tricyclic antidepressants, or anti-epileptic medications can be utilized for adequate pain control. Surgical exploration is recommended despite conservative measures after 6–12 months [133, 134]. Minimally invasive endoscopic decompression is an alternative to conventional open surgery and is associated with less scarring and less morbidity [135].

Radial Neuropathy at the Spiral Groove (Cheiralgia Paresethetica

Epidemiology

Radial neuropathy is relatively uncommon, as compared with other upper peripheral neuropathies. A study in 2000 showed that the annual age-standardized rates per 100,000 new presentations in primary care were 2.97 in men and 1.42 in women for radial neuropathy [2].

Anatomy and Etiology

All trunks of the brachial plexus branch distally to either an anterior or posterior division. The posterior divisions form the posterior cord. The posterior cord gives off nerve branches before becoming the radial nerve. Then, the radial nerve gives off various cutaneous branches, such as the posterior cutaneous nerve of the arm, the lower lateral cutaneous nerve of the arm, and the posterior cutaneous nerve of the forearm [136]. Then, the motor branches to the triceps and anconeus are given off, before the radial nerve descends medially down the upper arm and before wrapping around the mid-humerus to travel a posterior course in the spiral grove. The radial nerve is predisposed to compression in the spiral groove, where the nerve is directly adjacent to the humerus. Prolonged compression at the site can cause radial neuropathy. Other causes include humeral fracture, strenuous exercise, or a systemic illness like vasculitis.

Clinical Presentation

Traditionally, this syndrome is known as “Saturday night palsy”, as it frequently affects inebriated individuals after prolonged draping of an arm over a chair or bench. The patient might present with a wrist drop, as evidenced by weakness of the wrist extensors. The patient also has weakness of the finger extensors and brachioradialis. However, the triceps is intact. Weakness of the brachioradialis can be assessed by forearm flexion midway between the pronation and supination positions. Thumb abduction is weak because the abductor pollicis longus is innervated by the radial nerve. Sensory loss is isolated to the dorsum of the hand. It is important to distinguish this from a central nervous system lesion, as arm weakness can be caused by both central and peripheral nervous systems. The preservation of the triceps and localized sensory deficit are more indicative of a radial neuropathy at the spiral groove than a central nervous system lesion.

Diagnosis

Electrodiagnostic testing is important to establish a diagnosis, localize the neuropathy, and to aide in prognosis [136]. The test is typically performed 3 weeks after symptom onset [137]. Radiology and magnetic resonance imaging can be used to rule out anatomic abnormalities or fractures.

Management

Conservative treatments such as physical therapy, wrist splinting, and pain control are recommended for one-time compression. The prognosis for compressive radial neuropathy is generally good, with complete resolution of symptoms over a mean of 3.4 months [138]. In cases of trauma, regular follow-up visits with physical examination and electromyography are recommended. If there is either worsening or no improvement, additional investigations, such as imaging or surgical exploration, are recommended.

Posterior Interosseous Nerve Syndrome

Epidemiology

Like radial neuropathy at the spiral groove, posterior interosseous nerve syndrome is uncommon [2].

Anatomy and Etiology

After exiting the spiral groove, the radial nerve gives off motor branches to the brachioradialis and to the extensor carpi radialis. The radial nerve then bifurcates into the superficial radial sensory nerve and the deep radial motor branch. The superficial radial sensory nerve receives sensory information from the lateral dorsum of the hand extending over part of the thumb and the dorsal proximal phalanges of the second, third, and fourth digits [136]. The deep radial motor branch innervates the extensor carpi radialis brevis and the supinator muscles before entering the Arcade of Frohse, a tendinous border of the supinator. Once it enters the Arcade of Frohse, the radial nerve is known as the posterior interosseous nerve. The posterior interosseous nerve then supplies the majority of the extensors of the wrist, thumb, and fingers. These extensors include the extensor digitorum communis, extensor carpi ulnaris, abductor pollicis longus, extensor indicis proprius [EIP], extensor pollicis

longus, and the extensor pollicis brevis [136]. The posterior interosseous nerve does not receive superficial sensory information, but contains some sensory information, which includes deep sensation from the interosseous membrane and the radial and ulnar join capsules [136]. Compression by the Arcade of Frohse or mass lesions, trauma, and brachial neuritis can lead to the posterior interosseous nerve syndrome.

Clinical Presentation

Pain is the main significant symptom. Compression of the posterior interosseous nerve at the proximal arm qualifies the radial tunnel syndrome. Provocative pain with extension of the middle finger and relief of pain with nerve block can be used to diagnose posterior interosseous nerve syndrome [139]. Motor symptoms include weakness of the finger extensors sparing the more proximal muscles, including the brachioradialis. Physical examination may show radial deviation of the wrist with the wrist in extension due to relative preservation of the extensor carpi radialis longus and brevis that are supplied before the posterior interosseous nerve. There is no superficial sensory loss with posterior interosseous neuropathy.

Treatment

Compression radial neuropathies can be managed conservatively. Conservative measures include avoidance of aggravating activities and adequate pain control with appropriate medications. Local injections of hydrocortisone may be attempted. Surgical intervention to decompress the nerve can be helpful [139]. Radial tunnel release may be used in patients with posterior interosseous neuropathy refractory to conservative measures [140]. The posterior interosseous nerve can be approached dorsally or anteriorly and involves release of all potential sites of entrapment, as well as complete release of the superficial head of the supinator muscle [141]. Surgical treatment generally results in favorable outcomes [141, 142]. However, poor post-operative prognostic factors include associated lateral epicondylitis or patients who are involved in workers' compensation cases [141].

Conclusion

Peripheral entrapment neuropathies can occur from compression at various points along a nerve's course through the upper extremity. Symptom constellations vary due to proximal or distal positions relative to points of compression. Conservative management remains a first-line treatment for many of these conditions.

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Chapter 64
Lower Extremity Peripheral Neuropathies in the Rehabilitation Patient

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Introduction

Lower extremity neuropathies can occur at multiple sites along each nerve pathway and may present with unique signs and symptoms. However, diagnosis may not always be certain, as some conditions may be diagnoses of exclusion. A thorough history and physical examination can lead the clinician to a more accurate diagnosis and effective treatment.

Compressive Peroneal Neuropathy at the Fibular Neck

Epidemiology

Peroneal nerve palsy is the most common entrapment neuropathy of the lower extremity. Injury site may be anywhere along its course, from the sciatic origin to the terminal branches in the foot and ankle. The most common site is at the level of fibular head [1].

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Anatomy and Etiology

The L4-S1 nerve roots form the lumbosacral plexus. The sciatic nerve from the lumbosacral plexus divides into the common peroneal nerve and the tibial nerve, just above the popliteal fossa. The common peroneal nerve fibers within the sciatic nerve supply the short head of the biceps femoris in the posterior compartment, before entering the level of knee. The common peroneal nerve gives off a branch called the lateral cutaneous nerve of the knee, which receives sensory information from the lateral knee. Then, the common peroneal nerve enters the fibular tunnel between the peroneus longus muscle and fibula. At the fibular neck, the deep peroneal nerve fibers lie adjacent to the fibula and the fibers leading to the superficial peroneal are more lateral to the fibula. The common peroneal nerve divides into superficial and deep branches. The deep peroneal nerve supplies mainly the dorsiflexors of the ankle and toes, which are the tibialis anterior (TA), extensor digitorum longus, extensor hallucis longus (EHL), and extensor digitorum brevis (EDB) [2]. The deep peroneal nerve receives sensation of the web space between the first and second toes. The superficial peroneal nerve supplies the ankle everters, which are peroneus longus and peroneus brevis, and receives sensory information from the mid and lower lateral calf, the dorsum of the foot, and the dorsal medial three or four toes up to the interphalangeal joints.

The most common site of injury to the common peroneal nerve is where it wraps around the fibular neck below the knee, just before the division into its deep and superficial branches. External factors such as prolonged lying or squatting, crossing the legs, and leg casts can cause compression leading to peroneal neuropathy. Epineural fibrosis or fibrous bands can also lead to nerve entrapment [3]. Other uncommon causes include traumatic knee dislocation [4], popliteal artery pseudoaneurysm [5], ganglia [6], nerve tumors [7], hematomas [8], and knee osteoarthritis [9].

Clinical Presentation

Acute foot drop, secondary to difficulty with foot dorsiflexion, is typical. Patients may have a “steppage” gait due to the need for flexing the hip higher, to compensate for foot drop and the tendency to trip over. Paresthesias with or without complete sensory loss over the dorsum of the foot and lateral shin over the superficial peroneal nerve territory are seen in 79% of the patients [10]. Pain is not a common symptom, affecting only 16.5% of the patients with common peroneal neuropathy at the fibular neck [10]. Physical examination reveals weakness in foot dorsiflexion and eversion. It is important to note that plantar flexion and inversion are intact, as the corresponding muscles are innervated by the posterior tibial nerve. Sensory deficits are localized to the dorsum of the foot, including the web space between digits 1 and 2 and the lateral shin. The reflexes are normal.

Diagnosis

Diagnosis can be made clinically. Electromyography and nerve conduction studies are very useful to aid the diagnosis. Conduction block on motor studies can be identified at the site of compression. Needle electromyography of the short head of the biceps femoris can help to determine if the lesion is proximal or distal to the fibular head [11]. Signs of axonal injury can be evident in severe cases. Magnetic resonance imaging is most frequently used to see if there are structural defects responsible for the symptoms.

Management

Removing pressure on the nerve, such as avoidance of leg crossing or use of padding or cushioning at the site of compression, is the initial management. Other measures include use of an ankle-foot orthosis splint and physical therapy. Physical therapy involving passive assistive, active, and active resistant exercise can be helpful. Walking is highly encouraged. Prognosis depends on the severity of neuropathy. Those with complete loss of dorsiflexion and eversion tend to make little recovery, while those with signs of nerve preservation tend to recover fully [12]. Surgical decompression is considered if symptoms and signs plateau or worsen, despite 2 months of non-surgical treatment. Other surgical indications include patients with compressive masses, acute lacerations, or severe conduction changes [1]. The surgical outcome is favorable and 97% of the patients reported subjective and functional improvement postoperatively [1, 13].

Tarsal Tunnel Syndrome (Posterior Tibial Nerve Compression)

Epidemiology

Tarsal tunnel syndrome is considered rare, but this condition may be underdiagnosed [14].

Anatomy and Etiology

Tarsal tunnel syndrome occurs when the posterior tibial nerve is compressed as it passes through the tarsal tunnel, underneath the flexor retinaculum (or lacinate ligament or transverse tarsal ligament) on the medial side of the ankle. The tarsal tunnel

contains the tendons of the flexor digitorum longus, flexor hallucis longus, the posterior tibial nerve and its branches, and the medial and lateral plantar nerves. The most common cause of tarsal tunnel syndrome is trauma such as a fracture or dislocation involving the talus, calcaneus, or medial malleolus, as the bony fragments or spurs can mechanically compress on the nerve directly. Other causes include inflammatory processes, such as rheumatoid arthritis, or tumors such as ganglia, lipoma, neurofibroma, [15] and schwannoma [16]. Diabetic peripheral neuropathy and plantar fasciitis [17] are associated with tarsal tunnel syndrome. Idiopathic tarsal tunnel syndrome is rare.

Clinical Presentation

Patients typically present with paresthesia and/or pain involving the sole, toes, and sometimes the heel of the foot. The discomfort tends to worsen at night and with standing. Tinel's sign is positive if the reproduction of sensory symptoms is isolated to the plantar surface of the foot, but does not include the dorsum of the foot. A useful provocative test is the triple compression stress test (TCST), which is carried out by having the patient plantarflex and invert the affected foot, while applying pressure on the posterior tibial nerve [18]. It has a sensitivity of 85.9% and a specificity of 100% [18]. Atrophy of intrinsic foot muscles may be associated with severe nerve injury.

Diagnosis

Electrodiagnostic testing can be useful in confirming suspected tarsal tunnel syndrome [19]. Prolongation of the tibial motor distal latencies and slowing of the conduction velocities across the flexor retinaculum are indicative of tarsal tunnel syndrome. Electromyography has limited clinical significance. Imaging studies, especially magnetic resonance neurography (MRN), is not only useful in the diagnostic process, but also can detect focal fibrosis or injury to the nerve branches in patients with persistent symptoms after surgery [20]. Ultrasonography may be useful to detect ganglia or talocalcaneal coalition in patients with tarsal tunnel syndrome caused by space-occupying lesions [21].

Management

Conservative treatment with nonsteroidal anti-inflammatory drugs, shoe modification, and use of orthotics is initially recommended. Corticosteroid injection is considered for those who do not respond to conservative measures. Surgical decompression is reserved for patients with clear evidence of entrapment who have failed conservative

therapy. The surgical option is associated with subjective symptom improvement in 61–72% of patients [22, 23]. The peri-operative complication rate is 30% [23]. The favorable prognostic factors include a short history of illness, the presence of a ganglion, no history of sprains, and light work demands [22]. Ultrasonic improvement of the tibial nerve was not observed in patients with presumed coexistence of diabetic polyneuropathy and tarsal tunnel symptom after surgical decompression [24]. Ninety-three percent of patients undergoing tarsal tunnel release have excellent postoperative outcomes [25]. Revision surgery involving neurolysis of tibial nerve branches or correction of inadequate release may improve neurosensory measurements after failed tarsal tunnel surgery [26, 27].

Sciatic Neuropathy

Epidemiology

Piriformis syndrome is mostly seen in middle-aged adults with a mean age of 38 years [28]. The female-to-male ratio is 6:1 [28]. Data regarding the incidence and prevalence of sciatic neuropathy due to other causes is not available.

Anatomy and Epidemiology

The sciatic nerve is derived from the L4-S3 nerve roots in the lumbosacral plexus. It leaves the pelvis through the sciatic notch (or greater sciatic foramen) and passes under the piriformis muscle. The sciatic nerve runs medial and posterior to the hip joint, between the ischial tuberosity and the greater trochanter, under the gluteus maximus. The sciatic nerve supplies the semimembranosus, semitendinosus, biceps femoris, and the lateral division of the adductor magnus. The sciatic nerve supplies sensation to the lateral knee (lateral cutaneous nerve of the knee), lateral calf (superficial peroneal nerve), dorsum of the foot (superficial peroneal nerve), web space of the great toe (deep peroneal nerve), posterior calf and lateral foot (sural nerve), and the sole of the foot (distal tibial nerve) [29]. Sciatic neuropathy can arise in two major regions: [1] in the sciatic notch (gluteal region); [2] in the mid-thigh. Sciatic neuropathy in the sciatic notch or gluteal region is most commonly caused by trauma [29]. Other causes include acute external compression, infarction, gun shot wound, hip fracture, hip dislocation, or femur fracture [30]. Sciatic neuropathy in this region is also noted as a rare complication of cardiac surgery, secondary to the intra-aortic balloon pump used ipsilaterally in the presence of peripheral vascular disease [31]. The piriformis syndrome occurs as a hypertrophied piriformis muscle at the sciatic notch compresses the sciatic nerve. The diagnosis of piriformis syndrome is difficult and controversial. It is a diagnosis of exclusion [32, 33]. Rarely, sciatic nerve lesions can occur in the mid-thigh.

Clinical Presentation

Pain is the most common presentation involving the affected leg. Sensory loss involving the peroneal, tibial, and sural territories may be seen. Sensation of the medial calf and arch of the foot may be spared as the saphenous nerve, a branch of the femoral nerve, remains preserved. Weakness of the lower musculature, particularly the hamstrings, can be seen in severe cases with weak knee flexion. Knee extension and hip movements are spared. Also, if the sciatic neuropathy occurs at the mid-thigh, some preservation of hamstring function is commonly seen. Knee jerk is typically normal, but ankle jerk can be difficult to elicit.

Diagnosis

Clinical diagnosis is important. Electromyography is an ancillary test. In severe cases, the peroneal and sural sensory response may be reduced, and the saphenous sensory response is spared. The tibial and peroneal motor response may also be reduced. No definitive diagnostic test or universal criteria exist to establish piriformis syndrome. Prolongation of the H reflex by 1.86 milliseconds on electrodiagnostic studies, pain with the FAIR (Flexion, Abduction, Internal Rotation of the hip) maneuver, and clinical response to nerve block injections into the piriformis muscle may aid in confirming diagnosis of piriformis syndrome [28].

Management

The initial treatment for piriformis syndrome is at least 6 weeks of physical therapy using piriformis stretching and isometric strengthening, as well as analgesic medication. For patients who do not respond to physical therapy, anesthetic and corticosteroid can be injected directly into the piriformis muscle or sheaths of the muscle or the sciatic nerve. Botulinum toxin injections have gained popularity recently [32]. The prognosis of sciatic neuropathy, in the absence of severe motor axonal loss, is generally favorable even without treatment [30]. Surgery must be reserved for patients with intractable or disabling symptoms refractory to conservative measures and injections [34]. Other surgical indications include the presence of abscess, tumors, hematoma, or gluteal varicosities [34]. Surgery involves decompressing the sciatic nerve by releasing the fibrous band or other compressive lesions; it is rarely necessary due to favorable clinical outcomes with botulinum toxin injections.

Femoral Neuropathy

Epidemiology

Femoral neuropathy is uncommon. In one study, two in 27,004 primary hip arthroplasties resulted in femoral neuropathy [35].

Anatomy and Etiology

The femoral nerve arises from the L2-4 nerve roots and passes over the anterolateral border of the psoas muscle, down the posterior abdominal wall and pelvis, until it emerges under the inguinal ligament [36, 37]. The femoral nerve innervates the anterior thigh muscles or quadriceps (sartorius, pectineus, rectus femoris, vastus medialis, vastus lateralis, and vastus intermedius), psoas, and iliacus muscles in the pelvis [36]. The femoral nerve provides sensory innervation to the anterior thigh. The saphenous nerve, which branches off just distal to the inguinal ligament, provides sensory information to the anterior patella, anteromedial leg, and the medial foot [36]. Hip or pelvic fractures or masses within the iliacus, such as hematoma, can result in a femoral neuropathy. Femoral neuropathy is also associated with hip replacement, abdominal or pelvic surgery, childbirth, inguinal lymph node biopsy, femoral nerve block, and femoral artery puncture [38–40]. The underlying mechanisms include compression, transection, diathermy, toxic injury, and ischemia [39, 40]. There has been some debate over the development of femoral neuropathies among patients with diabetes mellitus.

Clinical Presentation

Weakness involving the quadriceps is common [41]. Hip abduction is spared, as the obturator nerve innervates the hip abductor. In some patients, the iliopsoas may also be weak [41]. Sensory loss over the femoral nerve territory, involving the anterior thigh and the medial thigh extending from the medial shin to the region of the arch of the foot, is typical [41]. The knee jerk reflex is usually unobtainable.

Diagnosis

Needle electromyography may be helpful. Involvement of the musculature and sensory response innervated by the femoral and saphenous nerves is seen in sciatic neuropathy. Imaging studies, such as a CT scan of abdomen, may help to exclude hematoma, tumors, aneurysms, or other structural abnormalities [41].

Management

Physical therapy and adequate pain control are important. Prognosis in most cases with incomplete femoral nerve injury is good. The prognostic factor is the degree of axonal loss; more axonal loss, determined by electrodiagnostic studies, results in less successful outcomes [42]. Some are left with permanent residual neurologic deficits [39]. In some patients with direct traumatic nerve injury, nerve repair or grafting is needed [39, 43]. Other surgical indications include psoas hematoma or abscess requiring drainage [44], or when surgical decompression of the nerve is essential.

Meralgia Paresthetica/Lateral Femoral Cutaneous Neuropathy

Epidemiology

The age- and sex-adjusted incidence of meralgia paraesthetica is 32.6 per 100,000 patient years [45]. The adjusted incidence of meralgia paresthetica in people with diabetes mellitus was seven-fold greater than that of the general population, which is 247 per 100,000 people [45]. The mean age at meralgia paresthetica diagnosis is 50 years [45].

Anatomy and Etiology

A pure sensory nerve called the lateral femoral cutaneous nerve is a direct branch of the lumbosacral plexus. It is particularly susceptible to compression as it enters the thigh under the inguinal ligament. The associated comorbidities with meralgia paresthetica include obesity, diabetes mellitus, older age, large abdomens [46], tight belts or garments around the waist, scar tissue around the inguinal ligament, and pregnancy [45, 47–51]. Injury during local or regional surgery can also cause meralgia paresthetica [52]. Long distance walking and cycling and seat belt injury [53] are other causes.

Clinical Presentation

Presentation includes a burning pain, paresthesia, and hypesthesia involving the anterolateral aspect of the thigh. The sensory loss is sharply demarcated. There is debate about whether the pain changes with position or activities such as walking,

standing, or thigh extension [45, 54]. The pain tends to worsen with Valsalva maneuvers or other activity that increases intra-abdominal pressure.

Diagnosis

Meralgia paresthetica is a clinical diagnosis [55, 56] and electrodiagnostic studies are of limited utility. In cases of severe axonal loss, reduced response amplitude may be observed, but for most cases of meralgia paresthetica, electrodiagnostic studies are normal. Clinical diagnosis is based on the unique history, physical examination, and the absence of neurologic abnormalities of the lower leg. On physical examination, pinprick and light touch tend to be abnormal (hypoesthesia, or dysesthesia) over the anterolateral aspect of the thigh, which is approximately 10 × 6 inches and oval-shaped [55, 56]. Also, there should be negative straight leg raise and preserved deep tendon reflexes and motor strength of the lower libs. There is no radiographic finding with meralgia paresthetica. Radiography can be used to exclude other causes such as spondylolisthesis, herniation, or spinal stenosis. Diagnostic nerve blockade via a conventional blind or ultrasound-guided injection can also be performed [55, 56]. If there is relief of pain with injection inferior to and within 1 inch of the anterior superior iliac spine along the inguinal ligament, meralgia paresthesia is likely [55, 56].

Treatment

Meralgia paresthetica is generally self-limited and benign. Conservative measures such as weight loss and avoidance of external pressures over the inguinal ligament are effective in 90% of patients [57]. However, the recurrence rate is high. It is important to counsel patients that the disease is benign and that conservative measurements and weight loss can help significantly. Physical therapy is not useful. In recalcitrant cases, in which symptoms are persistent for more than 1 or 2 months of conservative therapy, anticonvulsants such as carbamazepine, phenytoin, or gabapentin can be used for adequate pain control. Local nerve blocks with a local anesthetic agent, glucocorticoid, or both can be useful [58, 59].

Surgical decompression is only necessary in patients with severe persistent symptoms that are not responsive to conservative measures. Decompression of the nerve can be achieved by sectioning the inferior slip of the attachment of the inguinal ligament to the anterior superior iliac spine. This maneuver can preserve the nerve, but it is not always successful.

The definitive surgical option is neurectomy, which involves sectioning the lateral femoral cutaneous nerve exiting the pelvis. However, this produces a permanent anesthesia. The most common procedure is neurolysis and transposition, which does not permanently cause anesthesia postoperatively. Neurectomy has higher

success rates than neurolysis. Neurectomy produced 87.5% pain relief versus 60% in neurolysis [60]. Also, most neurectomy patients (62.5%) were not bothered by the permanent anesthesia [60]. Some case reports suggest that pulsed radiofrequency nerve ablation of the lateral femoral cutaneous nerve is effective in refractory cases [61–63].

Conclusion

A thorough history and physical examination can elucidate the diagnosis, and in many cases, conservative measures can result in better outcomes. An understanding of the anatomical structures encountered through the course of each nerve can also help to pinpoint the etiology of a neuropathy. In refractory cases, more invasive surgical interventions may be necessary.

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Chapter 65
Glossopharyngeal Neuralgia in the Rehabilitation Patient

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Introduction

Glossopharyngeal neuralgia is defined as a "rare facial pain syndrome characterized by paroxysms of excruciating pain in the sensory distribution of the auricular and pharyngeal branches of the glossopharyngeal and vagus nerves" [1]. This condition was first described as "tic doloureux" in 1910 by Weisenberg, in a 35-year-old patient with a right cerebellopontine angle tumor, while the term "glossopharyngeal neuralgia" was coined by Harris in 1921 [2].

The International Headache Society Guidelines define glossopharyngeal neuralgia as a "severe transient stabbing pain experienced in the ear, base of the tongue, tonsillar fossa or beneath the angle of the jaw" [25]. The condition consists of two types: classic and symptomatic. The classic type is characterized by intermittent pain with no underlying cause or associated neurologic deficit. The symptomatic type consists of the classic type plus either sensory deficits in the glossopharyngeal distribution due to a structural lesion, or an aching pain that persists between episodes of neuralgia.

Glossopharyngeal neuralgia affects mainly adults only, with the age of presentation greater than 50 years. Females are more frequently affected than males.

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Signs and Symptoms

The quality of pain is sudden with an abrupt onset, occurring as clusters of unilateral pain attacks. The pain has been characterized as sharp, stabbing, shooting, and lancinating. The pain is located in the posterior tongue, tonsils, oropharynx, larynx, auditory canal, middle ear, the angle of the mandible, and sometimes in the retromolar region. Throat pain can radiate to the ear and vice versa. The left side is more frequently affected than the right [3]. Attacks can last from a few minutes to a few hours, occurring mainly during the daytime. Clusters of attacks can last weeks to months. The time between these clusters of attacks can be days to years, but it is difficult to predict this inter-ictal period [1].

The pain occurs in the cutaneous distribution of the glossopharyngeal nerve and can be triggered or exacerbated by chewing, swallowing, coughing, yawning, sneezing, throat clearing, nose blowing, ear rubbing, talking, and laughing. Two clinical classifications of glossopharyngeal neuralgia, tympanic and oropharyngeal, describe the location of the pain [4].

A special case of glossopharyngeal neuralgia, vagoglossopharyngeal neuralgia, is described as syncope without an associated pain syndrome [5]. Symptoms include pallor, hypotension, and bradycardia, with associated tonic-clonic limb-jerking movements.

Anatomy of the Glossopharyngeal Nerve

Pathway

The glossopharyngeal nerve exits the brainstem in the medulla, between the inferior olives and inferior cerebellar peduncles [6]. The nerve traverses the subarachnoid space in the cerebellomedullary cistern, and prior to exiting the skull at the jugular foramen, it gives off the tympanic nerve to the middle ear. The nerve lies in the anterior pars nervosa within the jugular foramen, while the vagus and accessory nerves lie posteriorly in the pars venosa. The superior and inferior glossopharyngeal ganglia also lie within the jugular foramen. The tympanic branch (Jacobsen nerve) arises from the inferior ganglion. This nerve carries sensory fibers of the middle ear and also provides parasympathetic innervation to the parotid gland via the lesser petrosal nerve and otic ganglion [7]. The nerve lies posteromedial to the styloid process after exiting the jugular foramen. In the carotid space, the glossopharyngeal nerve lies between the internal carotid artery and the internal jugular vein. At this level, the nerve supplies the stylopharyngeus muscle before penetrating through the pharyngeal constrictor muscles. The terminal portions of the glossopharyngeal nerve convey somatic sensory innervation and taste from the posterior third of the tongue [7].

Vascular Supply

The intracranial portion of the glossopharyngeal nerve is supplied by the vertebral, basilar, and middle meningeal arteries. The vertebral (55%) or basilar artery (45%) gives rise to the artery of the glossopharyngeal nerve, also known as the artery of the lateral fossula [8]. A peripheral branch from this artery accompanies the glossopharyngeal nerve to the jugular foramen [9].

The extracranial portion of the glossopharyngeal nerve is supplied by branches of the external carotid artery. The ascending pharyngeal and occipital arteries provide supply to the carotid body. The descending palatine and sphenopalatine arteries (branches of the maxillary artery) supply the tonsillar portion of the glossopharyngeal nerve. The terminal portion of the glossopharyngeal nerve is supplied by the dorsal lingual artery (branch of lingual artery) [9].

Functions of the Glossopharyngeal Nerve

Special Visceral Efferent (Branchial Motor)

The nucleus ambiguous in the rostral medulla innervates the stylopharyngeus muscle and part of the superior pharyngeal constrictor [6].

General Visceral Efferent

Pre-ganglionic parasympathetic fibers from the inferior salivatory nucleus join the glossopharyngeal nerve at its tympanic nerve to enter the tympanic plexus, giving rise to the lesser superficial petrosal nerve (LSPN). The LSPN enters the skull through the petrous temporal bone and exits the skull through the foramen ovale, synapsing in the otic ganglion. Post-ganglionic fibers travel with the auriculotemporal branch of the trigeminal nerve to the parotid gland for salivation and vasodilation [6].

General Somatic Afferent

Glossopharyngeal fibers relaying sensation from the posterior tongue, posterior ear, tragus, soft palate, oropharynx, and nasopharynx travel to the superior glossopharyngeal ganglion in the jugular foramen, and then to the caudal spinal trigeminal nucleus. Fibers relaying sensation from the tympanic membrane, eustachian tube, and mastoid travel via the tympanic nerve to the inferior glossopharyngeal nucleus in the jugular foramen, and then to the spinal trigeminal nucleus [6].

General Visceral Afferent

Baroreceptors in the carotid sinus, located at the carotid bifurcation, sense increases in blood pressure. These signals travel via the carotid sinus nerve to the inferior glossopharyngeal ganglion and synapse on the caudal nucleus solitarius. Interneurons synapse on the dorsal vagal nucleus, causing a decrease in blood pressure, heart rate, and force of cardiac muscle contraction. This response is known as the carotid sinus reflex [6].

Chemoreceptors in the carotid body detect blood concentrations of oxygen and carbon dioxide. The signals are transmitted via Hering's nerve to the inferior glossopharyngeal nucleus, and then to the caudal nucleus solitarius. Interneurons synapse on the medullary respiratory center to control respiratory rate and depth [6].

Special Sensory Afferent

Taste from the posterior one third of the tongue, along with sensation from the posterior pharynx and eustachian tube, are transmitted to the inferior glossopharyngeal ganglion to the rostral solitary nucleus. The signal then travels to the reticular formation, and then to the contralateral thalamic ventral posteromedial (VPM) nucleus via the central tegmental tract [6].

Pathophysiology

Glossopharyngeal neuralgia is usually idiopathic, with no radiographic evidence of compression upon the glossopharyngeal nerve, and head and neck examination reveals only trigger points [4]. Secondary glossopharyngeal neuralgia is caused by compression upon the glossopharyngeal nerve by structures such as blood vessels, tumors, and infectious processes.

Blood Vessels

Gaitour and Kawashima have demonstrated the posterior inferior cerebellar artery (PICA) and anterior inferior cerebellar artery (AICA) as causative agents, respectively [10, 11] (Fig. 65.1). In other cases, a dolichoectactic vertebral artery can also exert pressure on the glossopharyngeal nerve. Direct carotid puncture can also result in glossopharyngeal neuralgia [1].

Tumors

The first description of glossopharyngeal neuralgia by Weisenberg was caused by a cerebellopontine angle tumor [2]. Other neoplastic causes include laryngeal and nasopharyngeal carcinomas, tongue and oropharyngeal cancers, and skull base tumors that can compress the jugular foramen and foramen ovale [1].

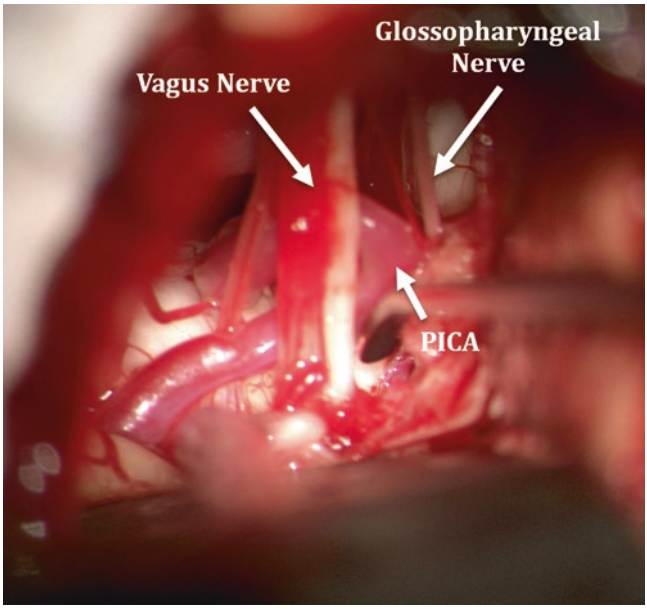

Fig. 65.1 Intra-operative microscopic image showing posterior inferior cerebellar artery (PICA) inferior to glossopharyngeal nerve (CN IX) and deep to vagus nerve (CN X)

Infectious and Inflammatory Processes

Parapharyngeal abscesses can compress the distal glossopharyngeal nerve. Causative inflammatory processes include multiple sclerosis, Paget's disease, and Sjogren's syndrome [1].

Anatomic Variants

Occipital-cervical developmental malformations and calcified stylohyoid ligaments can cause compression upon the glossopharyngeal nerve. Calcified stylohyoid ligaments, as well as elongated styloid processes, can cause glossopharyngeal compression, known as Eagle syndrome.

Diagnosis

No specific test can establish a diagnosis of glossopharyngeal neuralgia. This condition has been mistakenly diagnosed as trigeminal neuralgia or geniculate neuralgia [1]. One difference between the two conditions includes the side of the face that is affected; glossopharyngeal neuralgia more commonly affects the left side, whereas trigeminal neuralgia more commonly affects the right side [3]. The differential diagnosis also includes superior laryngeal neuralgia, affecting the vagus nerve, and

nervus intermedius neuralgia, which affects the facial nerve. Patients may benefit from evaluation by an otolaryngologist to exclude other causes of glossopharyngeal neuralgia.

Topical anesthesia can help the clinician to identify specific trigger zones and can also help to establish a diagnosis of glossopharyngeal neuralgia, if the patient's pain is relieved after a nerve block [1]. Imaging studies can help to identify anatomic causes of glossopharyngeal neuralgia. For example, CT can identify an elongated styloid process causing Eagle syndrome [1]. MRI can also help to identify blood vessels, tumors, or infectious and inflammatory processes that are causing glossopharyngeal neuralgia.

Treatment

Conservative Management

Non-surgical, conservative measures remain the first-line treatment of glossopharyngeal neuralgia. Pharmacologic agents include carbamazepine, oxcarbazepine, gabapentin, pregabalin, and tricyclic antidepressants. Opioids are not effective in alleviating glossopharyngeal pain.

For the vagoglossopharyngeal variant, atropine is the first-line medication for treatment by preventing cardiac sequelae [12]. In addition, carbamazepine can address both the cardiac and neurologic symptoms.

Extra-oral glossopharyngeal nerve blocks have recently been used to treat glossopharyngeal neuralgia [13]. Non-neurolytic agents include local anesthetics, steroids, and ketamine. Neurolytic agents include phenol, alcohol, and glycerol. Singh et al. concluded that this treatment modality works best when combined with pharmacologic agents [13].

Surgical Management

Singleton and Dandy were the first neurosurgeons to describe intracranial sectioning of the glossopharyngeal nerve [14, 15]. In 1977, Laha and Janetta treated the underlying cause of glossopharyngeal neuralgia by performing microvascular decompressions [16].

Microvascular decompression (MVD) of the glossopharyngeal and vagus nerves remains the surgery of choice in the treatment of glossopharyngeal neuralgia, with the highest success rate of any surgical modality [17] (Fig. 65.2). In a series of 217 patients, Patel et al. [18] reported complete pain relief without the need for medication in 58% of patients after an average period of 4 years [18].

Eagle syndrome, caused by elongation of the styloid process, is treated by minimally invasive resection of the styloid process [19].

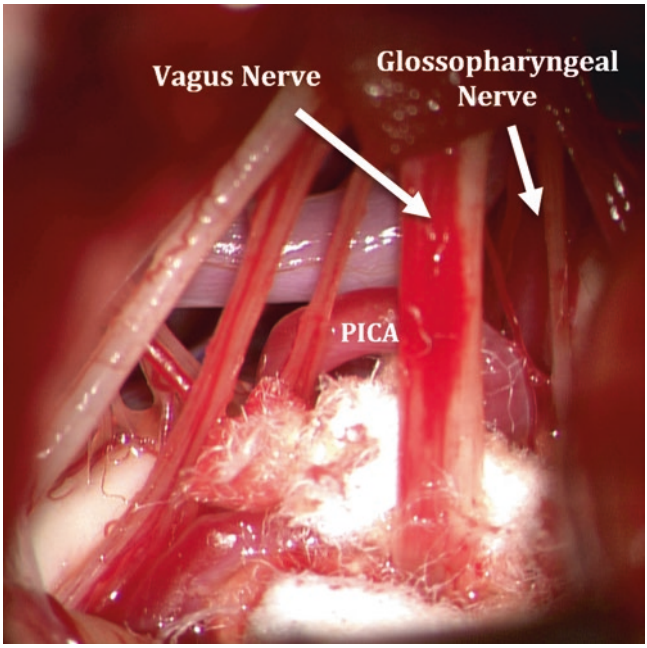

Fig. 65.2 Intra-operative microscopy demonstrating cotton plegets placed between vagus nerve (CN X), PICA, and glossopharyngeal nerve (CN IX)

Rhizotomy of the glossopharyngeal nerve can be a safe alternative surgical procedure when microvascular decompression fails [1]. If an offending blood vessel cannot be identified, the surgeon can section the glossopharyngeal and vagus nerves [17, 20]. Potential complications, however, include dysphagia and vocal cord paralysis, which result from damage to the recurrent laryngeal branch of the vagus nerve [21]. Other open surgical procedures include radiofrequency ablation of the glossopharyngeal nerve and balloon compression.

Stereotactic radiosurgery includes proton beam therapy and Gamma Knife ablation of the glossopharyngeal nerve. In a report by Martinez-Alvarez et al. [22], five patients undergoing Gamma Knife radiosurgery experienced improvement in their symptoms within 3–6 months, but three patients had to continue taking their medications after the procedure [22].

Neuromodulation is not a first-line surgical treatment for glossopharyngeal neuralgia and includes motor cortex stimulation and high cervical spinal cord stimulation. Anderson et al. [23] reported the case of a patient with glossopharyngeal neuralgia, trigeminal neuralgia, and dysphagia who successfully underwent placement of a motor cortex stimulation system; the patient demonstrated improvements in her facial pain and swallowing ability [23]. Low temperature radiofrequency and pulsed mode radiofrequency are two non-destructive methods for treating glossopharyngeal neuralgia. Shah and Racz [24] described the first successfully treated case of glossopharyngeal neuralgia occurring after a tonsillectomy [24].

Conclusion

Glossopharyngeal neuralgia can be caused by compression from blood vessels, tumors, or anatomical variants in bony anatomy. This condition may be confused with trigeminal neuralgia, but close attention to the constellation of signs and symptoms can lead to the correct diagnosis. Treatment consists of conservative, non-invasive measures, as well as more invasive surgical interventions.

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Chapter 66
Trigeminal Neuralgia in the Rehabilitation Patient

Francesco G. Pucci, Wael F. Asaad, and Curtis E. Doberstein

Introduction

The first written description of what may plausibly be a case of trigeminal neuralgia is found in *De causis et signis diuturnorum morborum* by the ancient Greek physician Aretaeus of Cappadocia in the first or second century [1]. The condition can also be inferred from the writings of ancient physicians including Celsus, Galen, and Avicenna [2]. A more reliable description of trigeminal neuralgia was provided by John Locke in 1677, in which he treated the condition using laxatives and purging [3]. In the eighteenth century, the French physician Nicolas André described two cases of trigeminal neuralgia, which he grouped together with other cases of facial convulsions and spasm [4]. He coined the term *tic douloureux* and ascribed the condition to nervous humors. André and the French surgeon George Maréchal attempted to chemically lesion the infraorbital nerve as a treatment for this condition, albeit unsuccessfully [5]. John Fothergill, shortly thereafter, reported a series of 14 patients with symptoms recognizable as classic trigeminal neuralgia, which he described as a sudden onset of excruciating paroxysmal unilateral facial pain, instigated by chewing or light touch with a handkerchief [6]. Although Fothergill lacked a clear understanding of the functional anatomy of the trigeminal nerve and therefore the syndrome's etiology, it is because of his early description that trigeminal neuralgia earned the appellation "Fothergill's disease."

Trigeminal neuralgia is a somewhat rare disease, with an overall incidence of 4.3/100,000 persons/year. Extrapolating the data to the United States, with a cur-

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rent population of 318 million, there are approximately 34,000–64,000 people with trigeminal neuralgia and 13,000 new cases annually. The incidence increases with age, particularly when greater than 60 years old. Females outnumber males by a factor of approximately 1.7 [7, 8]. Despite its relatively low incidence, it is the most common facial pain syndrome and is an easily recognizable clinical entity. Patients with trigeminal neuralgia invariably seek medical care due to frequent severe and debilitating pain. Here, we seek to outline the common clinical presentation of and treatment options for trigeminal neuralgia.

Clinical Presentation and Diagnosis

The trigeminal nerve is the paired fifth cranial nerve, containing both a general somatic afferent component and a special visceral efferent component. The latter comprises the motor functions of the nerve, namely innervation of the muscles of mastication (masseter, temporalis, medial pterygoid, and lateral pterygoid) as well as innervation of the tensor veli palatini, mylohyoid, anterior belly of the digastric, and tensor tympani. The afferent fibers innervate the face and centrally project to one of three brainstem nuclei, which are divided on the basis of their particular sensory modality. The mesencephalic nucleus receives group Ia and Ib fibers, which transmit proprioceptive information from the mandible and also form the afferent limb of the "jaw jerk" reflex. The principle sensory nucleus in the caudal pontine tectum receives input principally from Aβ fibers, which transmit cutaneous discriminative epicritic sensory information from the face, and then projects via the ventral trigeminothalamic tract to the contralateral ventral posteromedial nucleus of the thalamus (VPM). Lastly, the spinal trigeminal nucleus resides in the medulla and receives nociceptive and thermoceptive information from the face mediated by both Aδ and C fibers.

The fifth nerve may be divided into six segments [9]. The nerve exits the pons at the level of the brachium pontis; the smaller motor root, or *portio minor*, lies superior to the much larger sensory root (*portio major*) in the prepontine cistern. These first two segments (i.e., pontine and cisternal) contain the so-called trigeminal root entry zone (TREZ), which is defined by the transition from myelination by peripheral Schwann cells to central oligodendrocytes. The nerve courses towards the petrous apex and then pierces the dura to enter Meckel's cave in the floor of the middle fossa, where the Gasserian or semilunar ganglion contains the somata of the pseudounipolar sensory neurons. In the postganglionic segment, the nerve separates into three distinct divisions: the ophthalmic nerve (V1), maxillary nerve (V2), and mandibular nerve (V3). Each exits a distinct skull base opening: the superior orbital fissure (V1), foramen rotundum (V2), and foramen ovale (V3), respectively. In the extracranial segment, each division contains branches, which ramify in three distinct, non-overlapping dermatomes of the face.

Trigeminal neuralgia is a severe and often debilitating episodic facial pain that occurs within these dermatomes of the trigeminal divisions. It is characterized by

lancinating paroxysmal pain, which must be confined to one or more of the three dermatomes, most commonly that of the second or third division. It is most often unilateral but is bilateral in <10% of cases. If the condition is bilateral, however, it is never characterized by simultaneous bilateral paroxysms. The pain does not cross from one side to the contralateral side of the face. Episodes are very often triggered by sensory stimuli, such as light touch, brushing one's teeth, talking, or chewing. Alternatively, it may have "trigger zones" on the face, or cutaneous areas where stimulation elicits paroxysms in a reproducible way. Sharp pain, such as pinprick, sometimes suppresses the paroxysms. Each episode is short-lived, on the order of seconds or rarely minutes. There are no neurological deficits. These paroxysms of pain are usually so severe and debilitating that trigeminal neuralgia has been called the "suicide disease."

Care must be taken to distinguish trigeminal neuralgia from other types of facial pain. The Burchiel classification of facial pain identifies seven syndromes, including classic trigeminal neuralgia and other closely related syndromes [10, 11]. Type 1 trigeminal neuralgia ("classic" or "typical"), described above in detail, is spontaneous facial pain predominantly episodic in nature. Type II trigeminal neuralgia ("atypical") is similar to classic trigeminal neuralgia except that <50% of episodes are paroxysmal, and the pain is much more constant in nature; this subset includes a minority of patients with trigeminal neuralgia, but it is a group that is important to recognize nonetheless. Type 2 trigeminal neuralgia may represent the natural progression of untreated type 1 trigeminal neuralgia as the nerve is progressively damaged. Thirdly, trigeminal neuropathic pain is similar to trigeminal neuralgia, but is not spontaneous. Rather, it results from unintentional trauma to the trigeminal nerve. Fourth, trigeminal deafferentiation pain is an idiopathic condition resulting from nerve injury after peripheral nerve ablation, gangliolysis, or rhizotomy. Fifth, postherpetic neuralgia is a syndrome of persistent episodic pain in the setting of a history of herpes zoster involving a trigeminal dermatome. Sixth, symptomatic trigeminal neuralgia is a facial pain syndrome secondary to multiple sclerosis. Lastly, atypical facial pain, or persistent idiopathic facial pain, is a somatoform disorder. It is neither secondary to another disease process, nor is it characteristic of a true neuralgia. It is often comorbid with depression or anxiety, is non-dermatomal in distribution, may involve cervical dermatomes, is not stereotyped, and can be migratory or may cross to the contralateral side.

The diagnosis of type 1 or classic trigeminal neuralgia is made clinically. The International Headache Society (IHS) has developed diagnostic criteria to aid the clinician and is now in its third edition [12]:

1. At least three attacks of unilateral facial pain fulfilling criteria 2 and 3
2. Occurring in one or more divisions of the trigeminal nerve, with no radiation beyond the trigeminal distribution
3. Pain has at least three of the following characteristics
   (a) Recurring in paroxysmal attacks lasting from a fraction of a second to 2 min
   (b) Severe intensity
   (c) Electric shock-like, shooting, stabbing, or sharp in quality

(d) Precipitated by innocuous stimuli to the affected side of the face
(e) Intense, sharp, superficial, or stabbing
(f) Precipitated from trigger areas or by trigger factors

4. No clinically evident neurological deficit
5. Not better accounted for by another ICHD-3 diagnosis.

The guideline goes on to comment that effort should be made to exclude secondary causes, that pain never crosses to the opposite side but may rarely occur bilaterally, and that there is usually a refractory period following a painful paroxysm.

The subjective nature of facial main makes it difficult to measure. In order to better make sense of outcomes after intervention, the Barrow Neurological Institute (BNI) has devised a facial pain severity scale ranging from grade I–V [13]. Patients without pain and requiring no medications are classified as grade I. Patients with occasional pain but not require medication are classified as grade II. Patients belonging to grade III require pain medications—those in group IIIa are pain-free on medications; whereas those in grade IIIb have persistent pain, which is controlled by medications. If pain is not adequately controlled by medical therapy, then the grade is IV. Grade V is for patients with severe pain and no relief with intervention.

Since Fothergill's observations were supplemented by Charles Bell's detailed pathoanatomic description of the trigeminal nerve, *tic douloureux* has been understood to be a true cranial neuralgia. The observations of Walter Dandy in the twen-

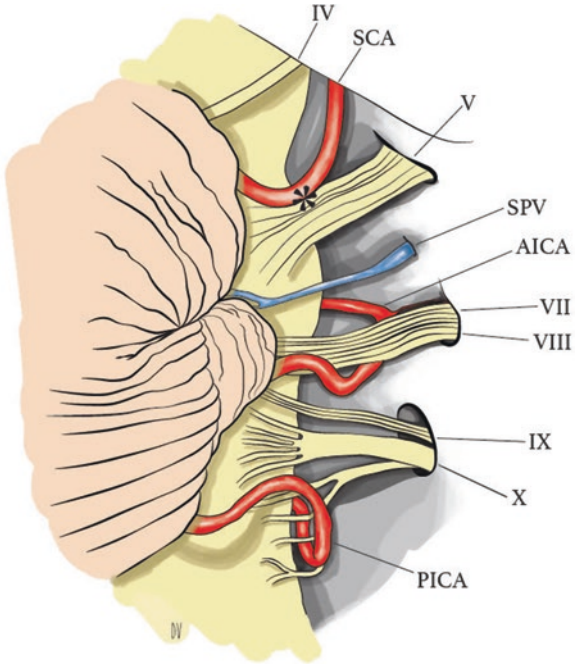

Fig. 66.1 Microvascular compression. A view of the right cerebellopontine angle including cranial nerves and vascular structures. Abnormal contact of a vessel (*asterisk*) with the trigeminal root entry zone, is thought to underlie trigeminal neuralgia. The most common offending artery is the superior cerebellar artery. *SCA* superior cerebellar artery, *SPV* superior petrosal vein, *AICA* anterior inferior cerebellar artery, *PICA* posterior inferior cerebellar artery

tieth century implicated microvascular compression of the nerve root in the pathophysiology of classic or typical trigeminal neuralgia (Fig. 66.1) [14]. Peter Jannetta and colleagues would confirm and deepen Dandy's hypothesis in multiple landmark publications [15]. With microsurgical exploration, an offending vascular structure can be found compressing the nerve in approximately 90% of cases or more. The most common offender is the superior cerebellar artery. The usual site of compression is at the trigeminal root entry zone, at the most proximal part of the cisternal segment. Here, there are more sensitive central oligodendrocytes rather than peripheral Schwann cells. Alternatively, the root entry zone may be understood as the transitional region of the nerve root lying between oligodendrocytes and Schwann cells where there is a relative paucity of myelin, also known as Redlich-Obersteiner's zone.

Two factors contribute to the increasing likelihood of vascular compression of a cranial nerve with age: the first is the increasingly dolichoectatic nature of cerebral arteries with age as the result of vascular disease; the second is the fact that the brain settles within the cranial vault in advanced age. The hypothesis that demyelination is crucial to the pathophysiology of the disease was generated by early observations that a disproportionate number of patients with multiple sclerosis suffered from trigeminal neuralgia [16]. Indeed, ultrastructural histological studies of trigeminal nerve root specimens in subjects with vascular compression demonstrate focal loss of myelin, oligodendrocytes, and astrocyte processes, with close proximity of axons to each other [17, 18]. These closely opposed axons without any substantial myelin sheath are prone to ephaptic coupling, which then leads to either stimulus-induced or constitutive activation [19, 20]. It is this aberrant firing of constituent peripheral neurons that is likely responsible for the stabbing paroxysms of facial pain. Furthermore, it is likely that the pulsatile compression of demyelinated axons by an artery is the instigating factor for these aberrant impulses.

While trigeminal neuralgia is the most common microvascular compressive disorder, there are a host of other cranial nerve compression syndromes thought to share a common pathophysiology. These include the following: hemifacial spasm (facial nerve), glossopharyngeal neuralgia (glossopharyngeal nerve), geniculate neuralgia (nervus intermedius), superior oblique myokymia (trochlear nerve), vestibular paroxysmia or hyperacussis or tinnitus (vestibulocochlear nerve), spontaneous gagging (vagus nerve), spasmodic torticollis (accessory nerve), and even neurogenic hypertension (lateral medulla) [21–28].

Trigeminal neuralgia is a clinic diagnosis; however, magnetic resonance imaging should be performed in all patients with neuralgic facial pain in order to exclude secondary causes such as aneurysm, vascular malformation, demyelinating disease, or various tumors, which can include vestibular schwannoma, meningioma, epidermoid cyst, etc. In many cases, the affected trigeminal nerve can be found to be thinned-out on high resolution T2-weighted MRI cisternography. Additionally, an offending dolichoectatic vessel is often found to be in contact with, or in close proximity to, the cisternal segment of the trigeminal nerve (Fig. 66.2). The diagnostic accuracy of MRI to identify a source of vascular contact with the fifth nerve has variable reports in the literature [29–35]. In one pooled analysis of seven studies,

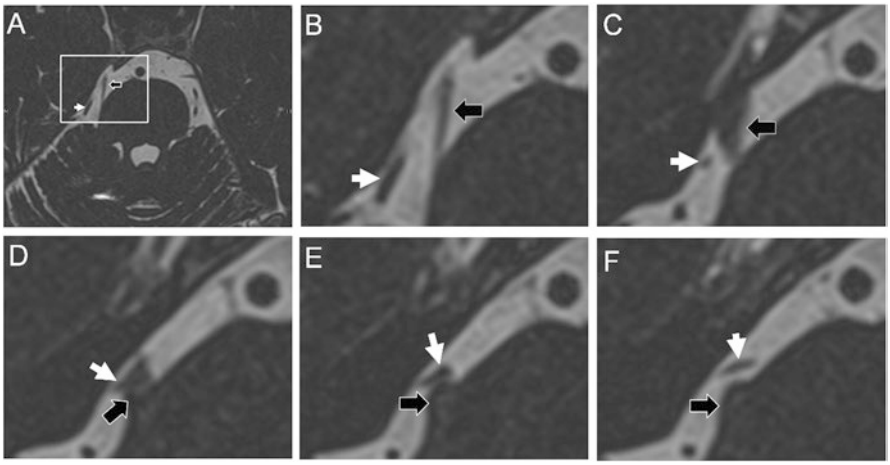

Fig. 66.2 High-resolution MRI. In many cases, the affected nerve can be seen to be thinned-out in the prepontine cistern. High resolution T2 weighted sequences often reveal loop of vessel in close proximity to the nerve. Absence of this finding, however, should not exclude patients from undergoing surgical exploration of the posterior fossa. In image (**a**) a high resolution T2 weighted image demonstrates the superior cerebellar artery (*white arrow*) in close contact with the trigeminal nerve (*black arrow*). Figs. (**b**–**f**) are sequential axial sections of the area demarcated by the inset in Fig. (**a**)

abnormal vascular compression was found in 131/170 cases, with an overall sensitivity of 77% and specificity of 71% [36]. Conventional computed tomography cisternography, with intrathecal contrast administration, may be helpful in patients unable to undergo MRI. The presence of a vessel in contact with the trigeminal nerve may aid in pre-surgical planning. However, the abscess of such a finding on imaging should not exclude a patient from neurosurgical exploration of the posterior fossa, as the offending vessel may often be a small and unnamed artery. Endoscopically assisted surgical exploration of the superior cerebellopontine cistern may aid in the identification of a neurovascular conflict [37, 38].

Medical Therapy

Early pharmacologic therapies for trigeminal neuralgia were severely limited. Fothergill proposed administering the bark of the cinchona tree, which contains quinine [6]. Other therapies specifically proposed for trigeminal neuralgia include ether, opium, arsenic, and conium maculatum [39]. Patients treated with stilbamidine for visceral leishmaniasis were known to experience bilateral trigeminal neuropathy, which led to the use of this agent as a treatment for trigeminal neuralgia despite significant side effects [40, 41]. Michel Bergouignan drew parallels between the paroxysmal nature of *tic douloureux* and epilepsy and began to treat the disease

with phenytoin with some success [42]. The sodium channel blocker carbamazepine was shortly thereafter found to be even more effective [43].

Carbamazepine remains today the first-line treatment for trigeminal neuralgia. To date, four trials have prospectively compared treatment with carbamazepine versus placebo, altogether examining 147 subjects [44–47]. In these studies, 58–100% of participants achieved complete pain relief, with a number needed to treat (NNT) of two. The drug is typically initiated at 100–200 mg twice daily and is then escalated in increments of 200 mg daily until pain relief has been achieved, with the maximum recommended dose being 1200 mg daily. Typical adverse effects of carbamazepine include nausea and drowsiness; more concerning but rare side effects include agranulocytosis, aplastic anemia, and Stevens-Johnson syndrome. Oxcarbazepine is a derivative of carbamazepine which may be better tolerated. Two randomized controlled trials have demonstrated that both drugs are equally efficacious, with 88% of patients attaining a reduction of paroxysms by >50% [48, 49].

Second-line medical therapies are baclofen, lamotrigine, tizanidine, and pimozide—all of which have class I or class II evidence for therapeutic benefit in trigeminal neuralgia [50–53]. Open-label studies with class III or IV evidence suggest some benefit from multiple other antiepileptic drugs including phenytoin, valproic acid, gabapentin, clonazepam, pregabalin, and topiramate. Opioid medications and non-steroidal anti-inflammatory agents are generally not efficacious against neuropathic pain, but opioid pain medication may be helpful in patients with acute exacerbations as an adjuvant therapy to antiepileptic drugs. Intravenous administration of phenytoin or fosphenytoin, lidocaine, or carbamazepine may also be used for acute exacerbations.

Surgical Treatment

The paucity of early effective pharmacological therapies for neuropathic pain, coupled with the often debilitating nature of the disease, created an historical environment that invited creative surgical solutions for trigeminal neuralgia. In the mid-eighteenth century, George Maréchal, first surgeon in the court of Louis XIV, and his contemporary Nicolas André, both attempted to lesion the infraorbital nerve in patients with *tic douloureux* unsuccessfully. Shortly thereafter in 1768, Dussans and Veillard similarly transected the infraorbital nerve in two patients with facial pain, but without clinical effect [2]. In the early part of the next century, anatomists Charles Bell and François Magendie meticulously described the anatomy of the trigeminal nerve and thereby allowed for renewed efforts by surgeons. The first successful surgery for trigeminal neuralgia was performed by the American surgeon John Murray Carnochan in 1856 [54]. Carnochan hypothesized that the Gasserian ganglion was a "generator of nervous power of which, like a galvanic battery, it affords a continuous supply; while the branches of the ganglion under the influence of the diseased trunk, serve as conductors of nervous sensibility" [55]. Thus, he performed a trans-facial approach through the infraorbital foramen and maxillary

sinus to extirpate the second division of the trigeminal nerve and the trigeminal ganglion. The first of Carnochan's patients, who was himself a French physician, reported back over a year later that he remained pain-free [56].

By the end of the nineteenth century, the world's prominent surgeons and indeed founders of neurosurgery had taken interest in the disease. Subsequently, they incrementally developed more refined approaches to the semilunar ganglion and the trigeminal nerve root. In 1890, William Rose published a report describing an infratemporal fossa approach to the foramen rotundum and foramen ovale [57]. Victor Horsley accessed the trigeminal ganglion for resection through a middle fossa craniotomy and intradural route [58], although this technique was prone to bleeding from the cavernous sinus. Frank Hartley and Fedor Krause contemporaneously with each other contributed to reducing the morbidity of the operation significantly by performing a subtemporal extradural exposure of Meckel's cave for neurectomy and ganglionectomy [59, 60]. Harvey Cushing performed a similar extradural subtemporal procedure to Hartley and Krause, but approached the trigeminal ganglion partly through the infratemporal fossa, below the middle meningeal artery [61]. Finally, Charles Frazier at the University of Pennsylvania improved upon the technique in several ways. First, he performed a retrogasserian neurotomy of the trigeminal nerve rather than a complete ganglionectomy, allowing for preservation of the portion of the sensory root and ganglion supplying the first division and ophthalmic nerve as well as reducing the incidence of anesthesia dolorosa. Second, he was meticulous to preserve the *portio minor*, at times even using direct electrical stimulation to identify the motor root. The so-called Spiller-Frazier technique remained a favorite and durable treatment for trigeminal neuralgia in the following decades.

Walter Dandy, however, invented an entirely different way to access the trigeminal root through the posterior fossa, which he termed a "cerebellar approach." Dandy performed a lateral sub-occipital craniectomy to enter the superior cerebellopontine cistern. There, he could visualize the cisternal segment of the trigeminal nerve from the root entry zone at the pons up to its entry into Meckel's cave. Dandy's original operation described partial sectioning of the *portio major* [62, 63]. His operation was a technical feat in this early era of neurological surgery before the advent of the operating microscope and microsurgical techniques. Indeed, the inability of most contemporary surgeons to successfully operate in the cerebellopontine angle limited the so-called cerebellar approach from replacing the Spiller-Frazier technique. Dandy's unique vantage point in the posterior fossa, however, allowed him to discover vascular compression of the trigeminal nerve in 66 out of 215 cases [14]. This crucial observation would fall into relative obscurity for years to come.

Armed with the operating microscope, Peter Jannetta and colleagues described compression of the trigeminal nerve at its root entry zone at the pons by tortuous arteries in his series of neurotomies for trigeminal neuralgia [15] and prompted a re-examination of Dandy's initial hypothesis. Additionally, the trigeminal root was often observed to be thinned-out at the site of compression, which correlated with some hypotheses that demyelination might play a key role in the pathophysiology of trigeminal neuralgia.

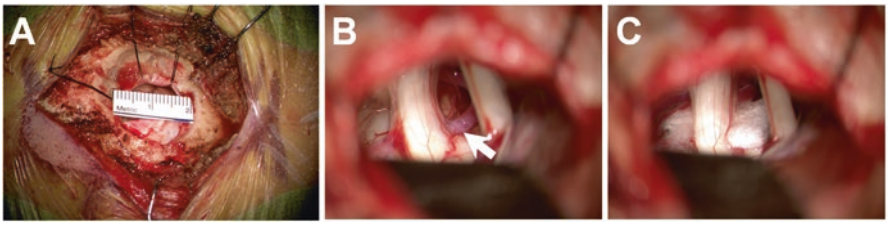

Fig. 66.3 Microvascular decompression. The cerebellopontine cistern can be accessed through a small retrosigmoid craniotomy (**b**). The fifth nerve (*left*), and seventh-eighth nerve complex (*right*) can be easily visualized. An ectatic loop of the superior cerebellar artery (*arrow*) can be seen making contact with the ventral aspect of the trigeminal root entry zone near the pons (**b**). A PTFE cushion is placed between the offending artery and the nerve in order to decompress the nerve and dampen pulsatile transmission (**c**)

Based upon his observations, Jannetta conceived of a procedure to decompress the trigeminal nerve as an alternative to creating a destructive lesion. He approached the nerve through either a retrosigmoid craniotomy similar to Dandy's operation or with a middle fossa transtentorial approach. In nearly every case, Jannetta claimed that an abnormal dolichoectatic vessel, or a small normal appearing vessel, contacted the fifth nerve at its root entry zone. He placed a cushion of polytetrafluoroethylene (PTFE) between the nerve and the offending artery, in order to decompress the nerve and to dampen pulsatile transmission (Fig. 66.3) [23, 64]. Over time, any skepticism within the neurosurgical community was overcome, and microvascular decompression (MVD) became overall the most effective and resilient procedure for trigeminal neuralgia. Subsequent neurosurgeons such as Takanori Fukushima further refined the technique and became effective at decompressing the trigeminal nerve through increasingly smaller craniotomies [65]. Its principle was extended to include other cranial nerve compression syndromes including hemifacial spasm, glossopharyngeal neuralgia, and more.

Subsequent studies demonstrate that both short- and long-term outcomes from microvascular decompression for trigeminal neuralgia are excellent. The largest series studying this operation was a prospective trial published in 1996, which included 1885 patients [66]. In the vast majority of cases (75%), the aberrant artery compressing the fifth nerve was found to be a loop of the superior cerebellar artery (SCA). Other possibilities included the anterior inferior cerebellar artery (AICA) (10%), the posterior inferior cerebellar artery (1%), the basilar artery (1%), and the labyrinthine artery (<1%). In up to 15% of cases, however, there was a small and unnamed artery at the root entry zone. Also, in 68% of cases, the petrosal veins were found to be compressing or abutting the nerve, although the significance of this is unclear given that these veins transmit no pulsatile force, which is thought to be a key component of the underlying pathophysiology.

In this large prospective study, over 98% of patients experienced pain relief in the immediate post-operative time frame, and there was complete freedom from any neuropathic pain in 82% of subjects. At 1 year post-operatively, 75% of patients remained completely pain-free, and an additional 9% had a good outcome with only

occasional episodes of pain requiring no medication. At 10 years, 68% of patients persisted with an excellent or good outcome.

These data demonstrate the durability of microvascular decompression without necessitating any destructive lesion of neural tissue. The lack of immediate post-operative relief, female sex, venous compression without arterial compression, and long-standing pre-operative symptoms (>8 years) are all significant predictors of recurrence of *tic douloureux* after microvascular decompression. Prior radiofrequency ablation of the nerve or ganglion did not influence the primary outcome; however, patients with prior ablative procedures were more likely to experience persistent post-operative dysesthesias. Recurrence of symptoms after microvascular decompression is most commonly associated with recurrence of vascular compression, or more rarely with PTFE-induced granuloma [67, 68]. The majority of recurrences occur early on within the first 2 years.

With operator experience, microvascular decompression is a safe operation. In a meta-analysis of six studies prospectively examining the procedure, the mortality rate was 0.2% [36]. Other significant but rare complications include cerebellar hemorrhage or edema (0.6%), hearing loss from cranial nerve eight palsy (3.7%), facial weakness from cranial nerve seven palsy (0.6%), cerebrospinal fluid leak (1.7%), and venous sinus thrombosis (0.3%). Both intraoperative monitoring of auditory-evoked potentials [69–71] and minimizing cerebellar retraction [70, 72] may reduce the incidence of hearing loss. Minor complications include chemical aseptic meningitis (10.9%), which is easily treated with steroids, and decreased facial sensation (3.8%) [36]. There is virtually no incidence of corneal numbness or keratitis. As with any technically difficult operation, operator experience and volume of procedures performed at the institution may also have an important bearing on reducing perioperative morbidity [73]. The long-lasting durability of pain relief, relative paucity of facial numbness or facial dysesthesias, and the elimination of anesthesia dolorosa are all important advantages of microvascular decompression over destructive procedures [74, 75].

Percutaneous Rhizotomy

If early surgical techniques were focused on creating destructive lesions, such as neurotomies and ganglionectomies, then it would make sense to pursue less invasive means of creating lesions, ultimately leading to percutaneous rhizotomy by various methods. At the end of the nineteenth century, there were multiple reports of chemoneurolysis using chloroform, osmic acid, and alcohol [2]. Cutaneous injections of alcohol into the peripheral divisions of the nerve would effectively cause anesthesia, but the injection was painful. Furthermore, temporary motor weakness was common and pain relief was often only transient.

Thereafter, attention was turned to chemical destruction of the ganglion. In 1910, Wilfred Harris performed a completely percutaneous injection of alcohol into the trigeminal ganglion and cistern. In a large cohort of 1433 patients, he reported

excellent rates of complete anesthesia and freedom from pain [76]. Glycerol was fortuitously found to be an effect neurolytic agent, since a combination of glycerol and tantalum dust was injected into the trigeminal cistern and used as a localization technique for stereotactic radiosurgery [77]. Chemical neurolytic techniques all inject the trigeminal cistern, which is a cerebrospinal fluid-filled space, and are not selective for particular divisions. Weakness of the muscles of mastication, anesthesia dolorosa, keratitis, and unilateral loss of taste were common if not ubiquitous. If alcohol spread out of Meckel's cave, or if the needle was not at the precise target, then other cranial neuropathies would occur, potentially presenting with facial weakness, hearing loss, or oculomotor palsy. Glycerol rhizotomy is an effective procedure with respect to pain relief, but of all the surgical techniques in the treatment of trigeminal neuralgia, it has the highest incidence of both pain recurrence (54%) and of anesthesia dolorosa (approximately 2%) [78–83].

In order to minimize the risks of chemoneurolysis, the technique was refined over the following decades. Fritz Härtel described a percutaneous method of accessing the ganglion through the foramen ovale [84], and multiple clinicians reported

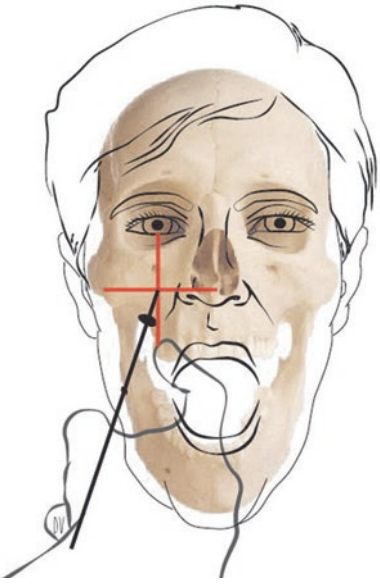

Fig. 66.4 Percutaneous trigeminal rhizotomy. The trigeminal ganglion and retroganglionic root in Meckel's cave can be accessed percutaneously through the foramen ovale under fluoroscopic guidance. Rhizotomy may be performed with radiofrequency ablation, or more rarely now chemical gangliolysis or mechanical balloon compression. The skin is punctured 1–2.5 cm lateral to the labial commissure. The operator often places a finger in the mouth on the pterygoid process to guide the needle or cannula just lateral to this landmark. The target is initially determined by external landmarks: the intersection of a horizontal line at the level of the tragus and a vertical line at the mid-pupil. Fluoroscopy is used to access the foramen ovale and to determine the target site relative to the clival line and sellar floor

the use of x-ray imaging to confirm accurate needle position [85, 86]. Today, the foramen ovale can be percutaneously targeted under fluoroscopic guidance with the assistance of external landmarks (Fig. 66.4). The skin is punctured at a point 2.5 cm lateral to the labial commissure. The operator inserts a finger into the mouth and touches the pterygoid process in order to guide the needle to the skull base. The target can be found at the intersection of two imaginary lines: the first being a horizontal line extending from the tragus to the tip of the nose, and the second being a vertical line extending down from the mid-pupil. Using lateral fluoroscopy, the needle is advanced until it meets the clival line, 5–10 mm below the sellar floor. Aspiration of cerebrospinal fluid confirms location in the trigeminal cistern. Alternatively, contrast media can be injected into the cistern and viewed on fluoroscopy.

Sean Mullan and Terry Lichtor introduced mechanical balloon compression as an alternative to chemical destruction of the sensory root or ganglion in 1983 [87]. This technique was inspired by an older Taarnhøj-Sheldon-Pudenz procedure, in which the ganglion or sensory root was operatively exposed and deliberately compressed in order to elicit pain relief; however, recurrence rates were extremely high. In Mullan and Lichtor's operation, general anesthesia is required as mechanical compression of the trigeminal ganglion can be excruciatingly painful. In the original description of the procedure, the foramen ovale is accessed percutaneously under fluoroscopic guidance. After cannulation of the foramen, a no. 4 Fogarty catheter with a 0.75 mL balloon is inserted into Meckel's cave and is then inflated with 0.5–1 mL of contrast fluid for 5–7 min. A review of the major reports of balloon decompression [88–93] demonstrates excellent initial pain relief with an expected high incidence of facial numbness. However, the primary limitation of this technique is the prohibitively high incidence of trigeminal motor dysfunction (66%).

Thermal coagulation of the trigeminal ganglion is a superior alternative to chemical neurolysis or balloon compression. Additionally, it has been shown to allow for some degree of selection of a particular division. Initially, a monopolar current was applied to an insulated needle [94]. William Sweet and James Wepsic developed a novel approach whereby radiofrequency was used to thermocoagulate the preganglionic nerve fibers [95, 96]. By the time of their report in 1974, multiple advancements and adjunctive techniques had made this a much safer procedure. First, prior to any destructive procedure, they injected local anesthetic in order to create a temporary diagnostic nerve block, which facilitated adequate patient selection. Second, electrical stimulation was used to map out the area of putative lesion, which allowed for selection of a specific division of the trigeminal nerve and avoidance of the motor root. Third, a dual temperature monitoring probe was used concurrently with the application of radiofrequency, which allowed for control of the lesion size and avoided unintended damage to the motor root or first division. Altogether, these changes led to a lower incidence of loss of corneal reflex and subsequent keratitis.

Radiofrequency rhizotomy was at one time the most common procedure performed for trigeminal neuralgia. At least four reports can be found in the literature, which include cohorts of 1000 patients or more [97–100]. In particular, one pooled analysis of 6205 patients who underwent percutaneous radiofrequency ablation pro-

vides an excellent analysis of outcomes [101]. Initial and immediate pain relief was outstanding (98%) after radiofrequency ablation, and the result was durable; however, 20% of patients did have recurrence of pain. Nearly all patients had facial numbness, which was a correlate and marker of an efficacious procedure. This may be considered a potential disadvantage of the procedure compared to non-lesional treatments, such as microvascular decompression, yet <10% of patients have bothersome dysesthesias. Corneal anesthesia occurs in 7% of patients, but anesthesia dolorosa or keratitis occurs in only 1–2%. Major perioperative morbidity is low (1.2%), and there is virtually no mortality.

Today, percutaneous rhizotomy has largely been replaced by microvascular decompression and stereotactic radiosurgery. Nonetheless, it may still have a role in treating trigeminal neuralgia, particularly in non-classical cases where the etiology may not be microvascular compression.

Stereotactic Radiosurgery

Hermann Moritz Gocht was the first to use radiation therapy in the treatment of trigeminal neuralgia in 1897 [102], and although the patient only had significant pain relief for 2 days, it provided a proof-of-principle. Nearly a century after this first attempt, Lars Leksell's gamma knife would provide the means for both a high radiation dose and a very precise delivery to the trigeminal root entry zone, both of which are thought to be necessary to provide meaningful clinical benefit [103]. Stereotactic radiosurgery utilizes either multiple stationary radiation sources around an isocenter or a single dynamic linear accelerator to deliver a high dose of radiation, with a high degree of conformality, to the target tissue with a steep dose gradient. The cranial nerve tissue is relatively radio-resistant and requires a high dose to create a functional lesion in the pain generator. Putatively, focal axonal degeneration of the more vulnerable Aδ and C fibers within the nerve is responsible for pain relief, while damage to the Aβ fibers may lead to facial numbness. Notwithstanding its limitations, the noninvasive nature of the intervention and the low morbidity make this an attractive option for many providers and patients (Fig. 66.5).

The precise target has been the subject of some debate. Generally speaking, the cisternal segment of the nerve is targeted in the pontine cistern, where it can be delineated well on MRI and where it is surrounded by cerebrospinal fluid to minimize collateral damage to surrounding nervous tissue. One hypothesis holds that the trigeminal root entry zone contains radiosensitive oligodendrocytes rather than Schwann cells, making this the optimal target [104, 105]. An alternative strategy, which may minimize dose to the brainstem, is to target the nerve more distally at the pars triangularis as it approaches the ganglion. A more proximal target may result in slightly improved pain control, but may also increase rates of facial numbness. However, such numbness may be predictive of pain relief [106]. The prescription dose is typically 70–90 Gy, which is delivered in a single fraction. Similarly, patients

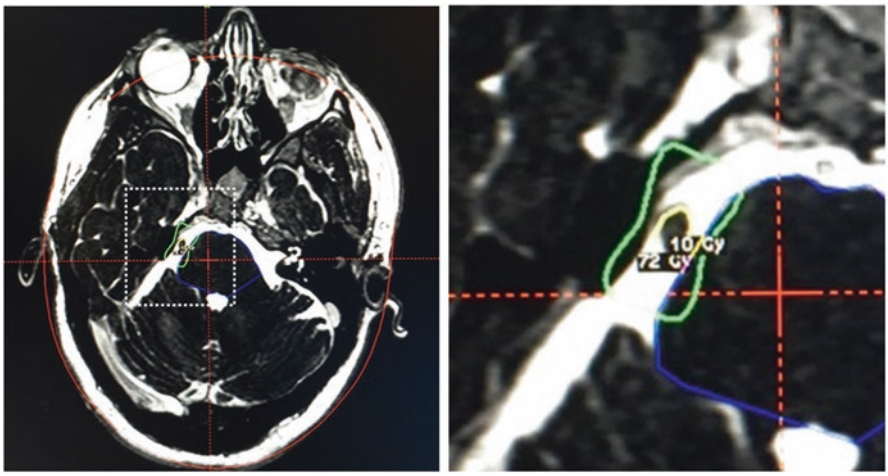

Fig. 66.5 Stereotactic radiosurgery. Using a high resolution MRI performed in a Leksell stereotactic frame, precise targeting of the trigeminal root entry zone can be performed for gamma knife radiosurgery. A 4 mm isocenter (*yellow*) is placed at the cisternal segment of the nerve, and a single fraction of 70–90 Gy is delivered. In the figure, the *yellow line* is the isodose at 72 Gy, and the *green line* demarcates the isodose for 10 Gy. Care is taken to limit the dose of radiation delivered to the brainstem (*blue*)

receiving the higher end of the dose range may have slightly greater pain relief, but also increased numbness [107].

Several centers have performed large retrospective reviews of outcomes after gamma knife stereotactic radiosurgery for trigeminal neuralgia. The largest single review was performed on a cohort of patients at the University of Pittsburg in 503 medically refractory patients [108]. In 98% of patients, a single 4 mm isocenter was targeted at the trigeminal root entry zone and in most cases treated with a single fraction of 80 Gy. Up to 40% of patients achieved complete initial pain relief, and 89% of patients had some improvement after radiosurgery. Other large retrospective series of patients report similar rates of response to gamma knife treatment in the range of 76–92% [104, 106, 108–113]. Facial numbness after radiosurgery, no history of previous surgery or ablation, and evidence of vascular compression on imaging all increase the likelihood of a good outcome.

Severe radiotoxicity is rare in these series (<1%); however, the rate of any trigeminal nerve dysfunction, including facial paresthesias and numbness, is in the range of 5–44%. The mechanism of action is likely directly linked to facial paresthesia, which is one potential disadvantage of stereotactic radiosurgery, and other destructive procedures, relative to microvascular decompression.

Stereotactic radiosurgery for trigeminal neuralgia has additional shortcomings. First, there is a significant latency after radiosurgery before treatment effect, with a median interval of approximately 1 month. Thus, radiosurgery is not an appropriate choice of treatment for patients requiring urgent pain relief. Second, the pain relief afforded by radiosurgery is not entirely durable, as only

70–80% of patients maintain treatment effect at 1 year. Third, a depreciating effect is generally noted, such that at 5 years roughly only half of the population has maintenance of pain relief; by 10 years, only a third of patients retain a good outcome. Taken together, these data suggest that microvascular decompression is a superior option to radiosurgery for trigeminal neuralgia on the basis of initial effect, long-term outcomes, and incidence of trigeminal nerve dysfunction. Nonetheless, the noninvasive nature and the relative safety profile of gamma knife make this an attractive treatment option. Furthermore, response rates make it a viable option, which is particularly well suited for elderly patients, those with comorbidities prohibitive of general anesthesia and craniotomy, or those who are adverse to surgery.

Conclusion

Trigeminal neuralgia causes severe and incapacitating pain. Coupled with an increasing understanding of the disease's etiology, this has created an historical environment, which has encouraged the development of creative surgical treatments. Modern and safe antiepileptic drugs have provided a pharmacologic alternative. Care must be taken in the diagnosis of trigeminal neuralgia to exclude secondary causes. In patients with typical or classic trigeminal neuralgia, the first-line treatment is carbamazepine or oxcarbamazepine, followed by other second-line agents. In patients who have an inadequate response to medical therapy, microvascular decompression is the treatment of choice because it is not destructive to the neural elements, has a high rate of durable freedom from pain, and has a low morbidity. Patients who are elderly, who have significant comorbidities, or who are adverse to surgery should undergo stereotactic radiosurgery, which is noninvasive, safe, and has an acceptable rate of pain relief. Radiosurgery, however, takes approximately 1 month after treatment to have therapeutic benefit and is associated with higher rates of recurrence than microvascular decompression. Percutaneous lesioning of the trigeminal nerve, ganglion, or root by chemical neurolysis or balloon compression is rarely performed currently due to the risk of adverse events. Percutaneous radiofrequency rhizotomy is safer and more effective than neurolysis or mechanical compression of the ganglion, and it may be a good therapeutic intervention in select cases.

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Chapter 67
Pain in the Spinal Oncology Rehabilitation Patient

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Introduction

Pain is the most frequently reported symptom in patients with spinal tumors, affecting up to 80% [1]. Pain is multifactorial in patients suffering from spinal tumors. It can be subdivided into neurogenic, mechanical, and oncological pain.

Oncologic pain develops as the tumor invades the vertebral body and decreases its strength and integrity, thereby making the patient more susceptible to pathologic fractures. Expansion of the tumor in the vertebral body causes bone re-modeling and thinning of the cortex. A major source of oncologic pain is from the periosteum, as it is stretched from the expanding tumor burden. Eventually, the tumor causes pathologic fracture and invades into the paravertebral structures. Minor trauma could accelerate the process of pathologic fracture. The pain from pathologic fracture may be subtle initially, then gradually worsening to the point that it is persistent, even in a recumbent position. One of the most characteristic features of spine tumors is back pain that is persistent, even when the patient sleeps. The type of biologic pain associated with tumor oncology presents with pain in the evenings and mornings, which is usually responsive to steroids and radiation [2]. This type of biologic tumor pain is different from the pain of mechanical instability, which improves with the recumbent position.

According to the Spine Oncology Study Group (SOSG), spinal instability is defined as the "loss of spinal integrity as a result of a neoplastic process that is

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associated with movement-related pain, symptomatic or progressive deformity, and/or neural compromise under physiologic loads" [3]. Pain from mechanical instability is an independent indication for surgical stabilization, regardless of the grade or radio-sensitivity of the tumor. Spinal instability is dependent on both radiographic and clinical criteria.

Clinically, mechanical pain differs from biologic tumor pain, in that it is exacerbated by activity and is problematic during the day. Mechanical instability in the subaxial spine is manifest by pain with flexion and extension [4]. Pain associated with thoracic instability is elicited with extension that causes unremitting pain as the patient straightens out an unstable kyphosis. Additionally, pain associated with mechanical instability in the lumbar spine is elicited with standing, which can cause severe radicular pain. Radiographically, instability can be assessed with dynamic imaging such as flexion/extension films.

Lastly, neurologic pain can occur from tumor compression of the spinal cord or nerve roots. Compression and invasion of the nerve roots by the tumor may result in nerve root irritation and radicular symptoms. This most commonly occurs with extramedullary-intradural tumors, such as schwannomas and neurofibromas. However, it can also occur with pathologic fractures from extra-dural tumor invasion of the vertebra with subsequent neural foraminal narrowing. In addition to causing neurogenic pain, tumor compression of neurologic structures may lead to motor weakness, loss of sensation, and bowel/bladder incontinence. For patients, who are presenting with neurologic deficits, it is important to evaluate the processes that resulted in the development of the deficit. Those who have been living with a deficit chronically from compression are less likely to regain any neurologic function. Conversely, neurologic decline must be treated promptly with decompression, as it halts further deterioration and may help to regain some of the lost neurologic function.

Indications for Surgery

The primary goal of surgery with spine tumors is local control of the oncologic disease. As spine tumors include a wide variety of lesions from primary tumors of the bone to metastases of the spine, this discussion will focus on general concepts in the treatment of spinal oncologic processes. Surgery is the best treatment option for those patients with spinal instability, who are experiencing acute neurologic deficits or uncontrollable pain. Surgery is also indicated for patients with neurologic deficit before, during, or after radiotherapy. Goals of surgery are to decompress the spinal cord and nerve roots and to stabilize the spine. Gross total resection of the tumor is the primary oncologic goal of surgery. However, depending on the tumor, separation surgery may also be a reasonable option. This consists of creating a free plane between the tumor and the neural elements such that radiation may be administered to the tumor safely without risking radiation toxicity to the spinal cord [5].

Limitations of Surgery

Appropriate patient selection is critical when considering whether someone is a candidate for surgery. Factors that are considered include neurologic status, radiosenstitivity of the tumor, mechanical stability of the spine, and systemic tumor burden. Patients with heavy systemic tumor burden, in poor medical condition, and with short life-expectancy are not surgical candidates.

Surgery is most effective for acute symptoms [6, 7]. Treatment within 48 h of neurologic decline has been shown to result in a significantly better neurologic outcome [6]. Surgery is less successful when symptoms have been more chronic. Surgery is also effective for pain control, especially mechanical and oncologic pain [8]. With regard to neurogenic pain, it is important that surgery is performed in a timely fashion before permanent neurologic changes can occur, as chronic pain is more challenging to treat.

Technical Considerations

It is essential to understand where the spinal tumor is located in relationship to the spinal cord and dura. The three major categories of spinal tumors are: (1) intramedullary-intradural, (2) extramedullary-intradural, and (3) extradural. Understanding the location of the tumor is critical in planning treatment as well as in understanding the differential diagnosis. If a tumor is intramedullary-intradural, then the clinician must consider ependymoma, astrocytoma, or hemangioblastoma. If the tumor is extramedullary-intradural, then the clinician must consider schwannoma, meningioma, and neurofibroma in the differential. Lastly, extradural tumors are most often metastases or primary tumors of the spine, such as chordoma, osteosarcoma, and Ewings tumor.

Depending on the location of tumor, treatment strategies may differ. The preferential treatment of intradural tumors is neural decompression. These tumors rarely cause mechanical instability of the spine, unlike extra-dural tumors. Treatment of extra-dural tumors of the spinal column includes anterior/posterior decompression of the spinal canal, restoration of vertebral body height loss with cement augmentation techniques (vertebroplasty or kyphoplasty), and instrumentation with anterior and posterior stabilization [9]. For primary tumors of the spine, laminectomy, total/partial vertebral body resection, piece-meal resection and curettage, and en bloc spondylectomy are all treatment options. Total en bloc spondylecotmy gives the patient the greatest chance of tumor-free survival with primary tumors of the spine.

Potential Treatment Complications

Although surgical treatment of spinal tumors may effectively improve pain, multiple potential complications are associated with surgery that the clinician must be aware of. Careful patient selection is important prior to surgery to minimize risks.

Surgery for spinal tumors may be very physiologically stressful on the patient, and it is important that the patient be medically cleared to undergo surgery. As with any tumor of the nervous system, there is always risk for potential neurologic deterioration, including motor strength, sensation, or bowel/bladder function.

CSF leak is also a risk, especially with the treatment of intra-dural tumors. One must monitor drain output for any signs of CSF post-operatively. Hemorrhage is another known risk factor with any surgical procedure. Meticulous hemostasis intra-operatively, as well as close monitoring of vitals post-operatively, is important. Other potential complications associated with surgery include wound dehiscence and/or wound infection. It is important to monitor the wound post-operatively to ensure that healing is appropriate.

Evidence in the Literature

Until the mid-1980s, the literature suggested that decompressive laminectomy alone did not have significantly better outcomes than conventional radiotherapy. Posterior decompression combined with fusion was later introduced and gained popularity in the surgical treatment of spinal tumors that cause epidural compression. There are now randomized trials in support of this practice, which have demonstrated that direct decompression, combined with stabilization surgery, results in better functional outcomes in patients with metastastic spinal cord compression [7]. Surgery is most effective at treating acute symptoms [6, 10]. Surgery performed within 48 h of neurologic decline has been associated with higher rates of improvement in neurologic function, including bowel/bladder control [7]. Surgery may also result in improved ambulation rates, especially if performed within 48 h of symptom presentation [11].

Conclusion

Surgery can be very effective in providing local tumor control, as well as treating the symptoms associated with tumors of the spine. When assessing pain in a patient with a spinal tumor, it is important to determine the etiology of the pain and to distinguish among oncologic, mechanical, and neurogenic sources of pain. In the evaluation and treatment of spinal tumors, it is important to understand the three general categories of spine tumors, which consist of intramedullary-intradural, extramedullary-intradural, and extradural tumors. Lastly, surgical treatment has been shown to be the most effective at restoring neurologic function when performed within 48 h of symptom onset.

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Chapter 68
Intraoperative Neuromonitoring of the Spine in the Rehabilitation Patient

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Introduction

Inquiries into the ability to record electrical responses from neural structures can be traced back to Richard Caton's 1875 publication in the *British Medical Journal* [1]. One hundred years later, Clyde Nash and Richard Brown's seminal 1977 article [2] on neuromonitoring during surgeries of the spine ushered in the modern era of intraoperative neurophysiological monitoring (IONM). Today, techniques have been refined to identify and to monitor numerous discrete afferent and efferent neural pathways in the peripheral and central nervous systems; these techniques are becoming the standard of care for more types of surgical procedures, beyond the spine [3]. IONM has burgeoned into an accepted and critical element during the delivery of surgical care to the patient.

Intraoperative neurophysiological monitoring as a phrase contains separate components, each of which is salient to a comprehensive understanding of the subject. The broadest component, neurophysiology, refers to the branch of physiology dealing with the functions of the nervous system. The most common modalities associated with the clinical interrogations of this system will be discussed here.

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Modalities

Somatosensory Evoked Potentials

Recording of somatosensory evoked potential (SSEP) responses is achieved through the stimulation of afferent peripheral nerves and recording the responses elicited by this stimulation, mitigated proximally via the ascending sensory fibers in the dorsal column to be processed in the primary sensory cortex.

Since the dorsal sensory tracts are to be engaged, theoretically any (somatic) stimulation would be effective in provoking the desired ascending volley. One might reach under the drape and continually tap the ankle posterior to the medial malleolus and be able to record an SSEP response. However, practicality demands a stimulation technique that is simple, effective, and efficient. This is achieved through the use of surface electrodes to deliver an electrical current of a given frequency and intensity to the skin area superficial to large sensory nerves. Common sites for this stimulation are the posterior tibial nerve (PTN) in the ankle, and the ulnar or median nerve in the wrist, with sites at the common peroneal notch and ulnar groove as less frequent alternatives.

Recording sites should include something peripheral as a control to indicate that the stimulation has effectively "gotten in," such as the popliteal fossa for PTN stimulation, and the supraclavicular notch for recording an Erb's point response from median or ulnar nerve stimulation. Parameters for stimulating and recording settings are well established and are presented in Table 68.1.

The responses generated from somatosensory stimulation are exceedingly small, dwarfed by other physiologically generated electrical signals such as the cardiac node pulse and even the passive EEG activity of the brain. These other organic generators act as a source of electrical "noise" in a recorded SSEP just as would artificial 60 Hz contamination. However, because SSEP responses occur at the same time relative to each stimulation, a mathematic technique using signal averaging may be employed to resolve the response signal out from the background noise. Since the noise generated by other sources tends to be of a random polarity for a given time period, over the course of many mathematical averages the time-locked response will additively increase while the random activity will cancel itself out. Ultimately, after a number of repetitions, this allows for a signal-to-noise ratio that is adequate to appreciate the SSEP response.

Table 68.1 Parameters for stimulating and recording settings

Stimulation	Intensity	Duration	Rate
	30–40 mA	100–300 μs	3–6 Hz
Recording	Low frequency filter	High frequency filter	Repetitions
	5–30 Hz	1000–3000 Hz	250–1000

Primary interpretation of the SSEP involves measuring the amplitude and latency of the responses. Because these responses are going to be used as their own control, rather than compared to a theoretical norm based on absolute values, it is essential that preincision, or premanipulation baselines are established. Discovering a significantly abnormal latency or amplitude value after the fact, without an established baseline generated prior to any surgical risk being incurred to compare to, there is no value to the surgeon or to the patient. Indeed, significance is only established as a delta between the baseline values and the ones recorded during the surgical procedure.

The well-known criterion for determining significance in latency shift is an increase of 10% or more from baseline. For amplitude, significance is reached after a 50% or greater amplitude reduction from baseline. It is important to remember that anesthetic drugs commonly used during surgery can alter SSEP responses by both increasing latency and decreasing amplitude.

Motor Evoked Potentials

As stated previously, a known limitation of SSEP is the fact that it cannot directly measure the integrity of the descending corticospinal motor pathways. Rather, in an SSEP-only paradigm, indirect inference must be made concerning the integrity of the anterior and lateral motor pathways; such inference is fraught with potential danger. Indeed, reports of postoperative motor dysfunction in the context of preserved intraoperative SSEP are not uncommon. Dinner et al. report a 2% incidence of false-negative SSEP detection for new-onset motor deficit [4]. Because general consensus reveals that a motor deficit is regarded as a much more severe sequela than a sensory loss, Motor Evoked Potentials (MEP) were therefore developed as a way of more comprehensively monitoring the spinal cord by including the vital motor pathways within the neurophysiologists scrutiny.

Typically, the stimulating electrodes are placed over the C3 and C4 locations, based on the standardized international 10–20 measuring system. This scalp location puts them in close proximity to the precentral motor gyrus, beneath the bone of the skull. A more medial placement, designated as C1 and C2, is located halfway between C3/C4 and Cz. Using these placement locations may help to improve responses, especially from the lower extremities. Recording electrodes are typically placed in muscle, thus allowing for the recording of a compound muscle action potential (CMAP) as the derived response. In determining which muscles to record from, consideration should be given to the expected spinal levels at risk. Where possible, a TcMEP response should be recorded from a muscle whose innervation is not directly involved with the operative level, in order to act as a control relative to responses at and distal to the at-risk levels.

Delivering 200 V or more to the surface of the head does more than produce a descending corticospinal depolarization. Superficial muscles in the scalp, face, and neck are also activated. This can lead to moderate to strong contraction of the

mastication muscles, essentially creating a bite. Therefore, every care should be taken to avoid the adverse side effect of tongue or lip laceration due to this motor activation. Soft bite blocks, such as rolled 4 × 4 gauze pads should be placed bilaterally between the molars so that no travel is possible between the maxilla and mandible. Even in edentulate patients, bite blocks are recommended so as to prevent bruising of the lips or gums on the endotracheal tube.

Criteria for reporting a significant change in TcMEP responses are not yet as readily agreed upon as for those of SSEP. Currently, two major proposed paradigms vie for consensus: the so-called presence–absence (PA) model and the stimulus threshold (ST) model.

The Presence–Absence (PA) Model

Complete loss of TcMEP response certainly indicates a significant change. However, as we have seen with the intramedullary spinal cord tumor example, the clinical outcome from such a loss cannot be known without corresponding data from d-wave recordings. While the preservation of some TcMEP response, even if dramatically lower in amplitude, indicates least some level of remaining integrity of the corticospinal tract guidance of the surgical or anesthetic regimen intervention remains problematic under this model.

The Stimulation Threshold (ST) Model

This model is based on the knowledge that damage to the corticospinal tract will necessitate increasing the stimulation threshold in order to obtain the same TcMEP response as prior to such damage. Therefore, measuring the required threshold intensity may be taken as an indication of the integrity of the corticospinal tracts intraoperatively. However, it is known that stimulation intensity thresholds gradually increase over time and are also affected by anesthesia drugs. Assessing the significance of changes under this model is therefore multifactorial and not binary.

Other criteria for significance have been proposed, but none have yet become standardized across the IONM landscape [5].

Electromyography

Electromyography (EMG) records spontaneous or triggered electrical activity in muscle. The presence or absence of EMG activity, as well as the pattern of firing, are all indicators of the function or integrity of the nerves innervating a given muscle. However, it should be emphasized that these indicators are indirect [6], and caution must be taken in the interpretation of both positive and negative responses.

Intraoperatively, EMG is commonly used for localization of nerves, as well as some assurance of the integrity of these nerves, albeit cranial or peripheral.

EMG needles are typically placed in a bipolar fashion into the muscles chosen for examination by a review of the patient's clinical symptoms and the type and location of the surgical procedure to be performed. It is important to understand that many muscles receive multisegmental innervation and that sometimes this is from root levels not commonly associated with the muscle [7].

Alcohol swabs are used to prepare the skin surface prior to insertion of the needles, and they are placed into the belly of the muscle, where possible. More superficial or shallow muscles require a more acute angle of insertion. Once placed, the needle electrodes are secured in a manner so as to prevent accidental displacement or removal from the muscle during patient positioning and other manipulation. As with all modalities, care should be taken to ensure that all of the electrode wires are free from contact with electrically contaminating sources and do not hang loosely in a way that would allow them to become entangled with surgical personnel or equipment, which might include foot pedals, C-arm fluoroscopy machines, Mayo stands, etc.

A shielded amplifier is used to convert and to amplify the EMG signal, and continual recordings of the amplified activity are made. Recording parameters are commonly accepted as follows for standard Spontaneous EMG (S-EMG): high frequency filter (HFF) of 1–3 KHz, low frequency filter (LFF) of 20–30 Hz, a sensitivity of 50–500 μV, a gain of 500–5000, and a sweep speed of 10–200 ms per division [8]. These recordings are displayed visually so that EMG morphology can be distinguished from electrical, as well as other physiologic artifact, i.e., ECG. A speaker may be used to provide auditory feedback, which is useful to the surgeon. The surgeon can then hear EMG activity without having to look up from the operation.

During Triggered EMG (T-EMG) a sterile stimulating probe is used for the localization of cranial or peripheral nerves. The probe is typically monopolar, so a reference electrode must be placed, either sterilely in soft tissue adjacent to the operative site, or substerilely prior to draping. Stimulation parameters vary depending on the nerve being interrogated, the degree of existing pathology in that nerve, and other factors. In general, cranial nerves have much lower stimulation threshold intensities than spinal peripheral nerves. Cranial nerve stimulation typically ranges from 0.05 mA to 1 mA, while direct spinal nerve stimulation should be delivered with 2–3 mA.

S-EMG characteristically takes on four distinct firing patterns. In general, the clinical significance of this firing can be considered proportional to the frequency, persistence, and amplitude of the pattern [9]. The firing patterns in ascending order of significance are as follows: Spikes, or isolated motor units; Bursts (activation of several motor units); Trains; and Neurotonic Discharge. See Fig. 68.1.

T-EMG responses are recorded as compound muscle action potentials (CMAPs) from muscles innervated by the salient spinal or cranial nerves. See Fig. 68.2 showing an example of T-EMG responses being recorded from the patient's right-sided vastus lateralis and tibialis anterior, with a small response also seen on the gastrocnemius.

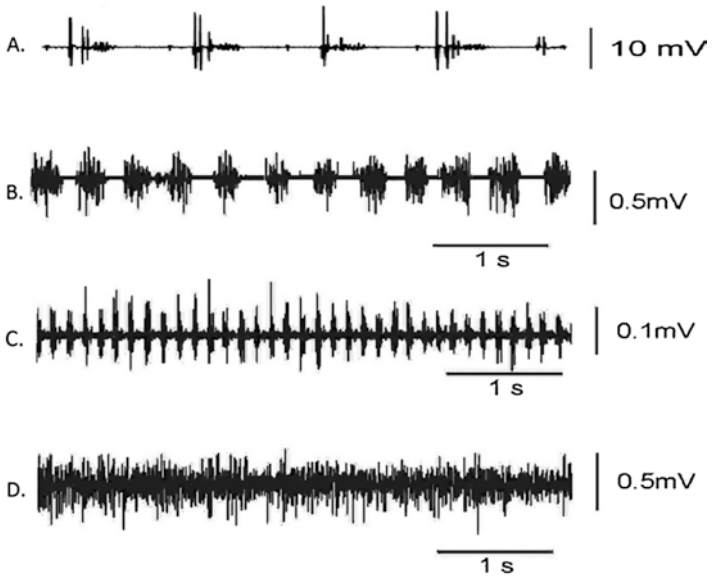

Fig. 68.1 Firing patterns in ascending order of significance: Spikes, or isolated motor units (**a**), Bursts (activation of several motor units) (**b**), Trains (**c**) and Neurotonic Discharge (**d**)

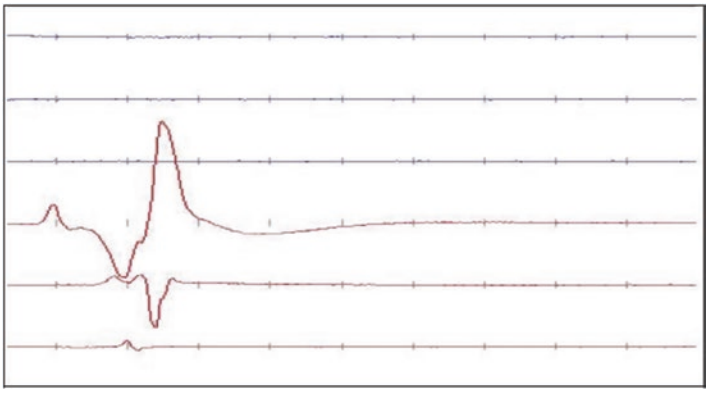

Fig. 68.2 T-EMG responses recorded from right-sided vastus lateralis and tibialis anterior

EMG and Pedicle Screw Testing

By the 1990s, the use of pedicle screws in posterior spinal instrumentation surgeries was emerging as the standard of care [10], replacing sublaminar hooks and wires as the preferred method for achieving internal fixation. Since these devices are threaded deeply into the vertebral body, pedicle screws provide a stronger platform for fixation rods [11]. However, they do so at the incursion of greater risk of neurologic injury due to their more invasive nature. Specifically, spinal nerves egress medial to

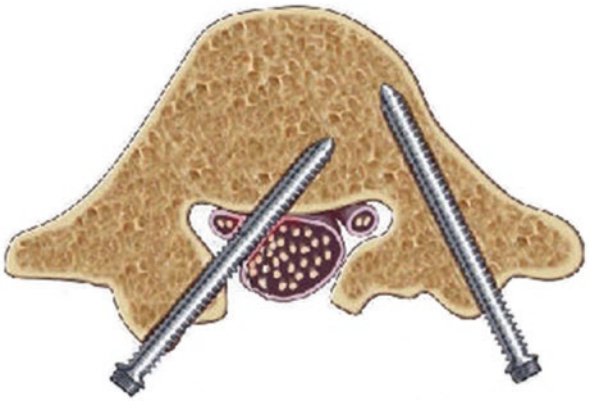

Fig. 68.3 (*Left*) A malpositioned screw impinging on neural structures. (*Right*) Correctly positioned pedicle screw

the pedicle, and the spinal canal is adjacent to these roots. A malpositioned screw may breach the pedicle wall, resulting in mechanical injury to either the spinal roots or the spinal canal itself. In turn, this could lead to significant iatrogenic sequelae, including radicular pain, foot drop, and other related deficits. See Fig. 68.3.

Various techniques have been developed to ensure that the trajectory of the screw implant remains within the bony confines of the pedicle, thereby avoiding damage to neural tissue. Intraoperative fluoroscopy in one or more planes may be used to provide visual guidance for the screw trajectory. Once a starter hole has been made, surgeons may also use a metallic probing instrument to examine the internal wall of the pedicle tactilely.

IONM may also be employed in evaluating pedicle screw placement, as an adjunct to, or in place of, some of the earlier techniques. Indeed, today IONM using S-EMG and T-EMG is "well recognized in numerous publications for improving both the accuracy and safety of pedicle screw implantation" [12].

Efficacy of these EMG techniques relies on the fact that a breach in the bony confines of the pedicle, as induced by a malpositioned pedicle screw, will result in a lower intensity response threshold than in that of an intact pedicle. Literature suggests that stimulation intensities of 8.0 mA or lower that result in a positive T-EMG response should be investigated for potential pedicle breach. Using the techniques outlined earlier in this chapter, pin electrodes are placed in salient muscle groups relative to the operative levels.

SSEP and Spinal Cord Injury

Somatosensory evoked potentials were the first modality utilized clinically to monitor the integrity of the spinal cord during surgeries of the spine. Because they record signals mediated by the ascending dorsal column pathways, they have always been

regarded as an indirect indicator of descending corticospinal tract function. Indeed, the literature is well stocked with case reports describing postoperative motor deficits in patients whose SSEP responses remained stable throughout the operation.

Now, with the maturation of TcMEP as a reliable technique for monitoring motor function, one may ask whether SSEP retains utility within the IONM provider's arsenal. We argue that they do. Studies show that SSEPs have a sensitivity of 52–92% and a specificity of 98.9–100% in detecting new-onset neurological deficit, with a positive predictive value of 100% and a very low false-negative rate [13, 14].

For correction of spinal deformity, which remains one of the most common indications for IONM, SSEP retains utility relative to other monitoring techniques, such as the placement of epidural electrodes to record direct spinal responses (d-waves). The d-wave recording electrode requires a consistent position relative to the corticospinal tracts in order to evaluate its responses. However, derotation and other manipulations of the spine during corrective surgery may cause the electrode to be displaced from its initial position, rendering this consistency problematic. Subsequently, this can lead to a high rate of false-positive changes in the d-wave recordings [15]. SSEPs avoid this pitfall since their stimulation and recording sites are independent of the surgical field and therefore not affected by mechanical manipulation.

Additionally, in rare cases the ascending sensory pathways may be affected by an iatrogenic injury, while the corticospinal tracts are spared and motor responses are unchanged [16]. Reliance on TcMEP monitoring would only miss these rare, but possible, situations.

However, one need not rely on anecdotal findings to favor a continued use of SSEP as a primary modality for monitoring the spinal cord. As Errico et al. advocate, "…one should not dismiss the SSEP outright in favor of the TcMEP. There will be instances when motor system neuromonitoring is unavailable, contraindicated, or unobtainable, so the need for good-quality SSEP data acquisition and interpretation will always remain" [17].

MEP and Vascular-Related Injury

Vascular-related injury to the spinal cord (VR-SCI) accounts for 3–5% of nontraumatic injury rehabilitation admissions [18]. Surgeries involving the spine, the cord itself, or the vasculature related to the spinal cord can lead to VR-SCI through a variety of direct and indirect mechanisms affecting the perfusion of neuronal tissue. Accordingly, a brief review of salient anatomy is appropriate.

The vertebral arteries and aorta give off multiple radicular (or segmental) arteries to the spinal cord. The anterior spinal artery originates bilaterally, as two branches off the vertebrals, which then supplies the anterior two-thirds of the spinal cord. Posterior circulation is supplied by two posterior spinal arteries, arising from either the posterior inferior cerebellar or vertebral arteries, which run the entire posterolateral aspect of the spinal cord, anastomosing with the anterior spinal artery and are

reinforced by the radicular branches. The largest of these branches is the artery of Adamkiewicz, which is responsible for perfusing the lower thoracic and lumbar region of the cord. Compromise to the artery of Adamkiewicz may lead to watershed ischemia in that region.

VR-SCI is most common in patients undergoing thoracoabdominal aneurysm repair, with incidence of ischemia ranging from 4 to 16% [19]. However, vascular complications may occur in surgeries for spinal deformity as well, especially those with an anterior approach [20].

Transcranial motor evoked potentials may be employed to detect potential VR-SCI intraoperatively. In particular, TcMEP are highly sensitive to hypotension resulting from hemorrhage [21], with an associated loss of amplitude in the TcMEP responses. Relative to SSEP, TcMEP changes are detected more quickly, and with more sensitivity [22].

Conclusion

In general, each of the three modalities described here should be considered as individual elements of a comprehensive IONM plan, rather than separate and independent entities. An understanding of what neural structures are at risk from any given surgical procedure, as well as an understanding as to how best identify and to evaluate those structures should guide the neurophysiologist in deciding which IONM modalities to draw from his armamentarium.

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Part XIII
Novel Techniques

Chapter 69
Percutaneous Needle Tenotomy and Tenex Health Therapy in the Rehabilitation Patient

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Introduction

Chronic tendinopathy, or tendinosis, refractory to conservative management may be an indication for surgical treatment. Surgical tenotomy, which involves the division of a tendon, aims to remove fibrotic and degenerative tissue in hopes of improving blood flow to promote an active healing environment [1]. While these techniques have historically been effective, invasive surgical intervention can lead to a multitude of complications including wound infections, skin necrosis, scar formation, and even tendon rupture, in addition to a prolonged recovery period [2]. Less invasive approaches, with the goal of reducing recovery periods and improving safety have more recently been studied with promising outcomes. In addition, patients undergoing percutaneous intervention have been shown to have therapeutic benefits earlier in the postprocedural period than those treated with an open procedure [3].

Percutaneous Needle Tenotomy (PNT), also known as tendon needling or tendon fenestration, involves creating multiple small perforations within the chronic affected tendon. This is in contrast to traditional surgical tenotomy or release, in which tendons are cut. The goal of tendon fenestration is to shift a chronic degenerative injury into an acute process. Increased localized bleeding releases growth factors activating fibroblasts, which induce collagen formation. This process helps to promote tendon healing and pain relief.

Another percutaneous treatment for chronic tendinopathy, which has more recently been studied in the literature, is the Tenex Health TX procedure (Tenex Health, Lake Forest, California). This novel device, which has been approved by the U.S. Food and Drug Administration, is also referred to in the literature as "fasciotomy and surgical tenotomy," or FAST [4]. Tenex Health TX is a procedure which involves the utilization of ultrasonic energy, delivered by the TX1 device through

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low-amplitude high-frequency oscillations, directed at diseased tendon tissue under ultrasound guidance [5]. The theory behind the Tenex Health TX procedure is based on the phacoemulsification more commonly used to treat cataracts. Tenex Health TX, similar to percutaneous needle tenotomy, aims to remove degenerative tendon tissue to stimulate an active healing process. However, in contrast to needle tenotomy, the TX1 device actually has little effect on normal collagen and tissue, instead microresecting only pathological scar tissue within the tendon [6].

Indications

First-line treatment for tendinopathy remains conservative nonoperative management with activity modification, physical therapy, NSAIDs, and eccentric exercises. Additionally, bracing and corticosteroid injections may provide symptom relief in some patients. Both needle tenotomy and the Tenex Health TX procedure may be appropriate for patients with approximately 6 months of symptoms refractory to conservative management. In the studies assessing for therapeutic benefits with these minimally invasive procedures, patients generally had symptoms for greater than 6 months that interfered with their ability to function and were progressively worsening [5, 6]. Although, this time frame is not a requirement, as a few studies utilized patients with symptoms for greater than 3 months, rather than 6 months [7–9].

The diagnostic utility of ultrasound has become more popular in recent years. Ultrasound guidance allows for direct visualization of diseased tendons and ensures greater accuracy for treatment during a percutaneous approach. The reliability of ultrasound to diagnose tendinous injuries is well documented, with one study finding an equal sensitivity and specificity to that of MRI in the case of patellar tendinopathy [6]. Given that chronic tendinopathy is a result of a failed healing process with degenerative changes rather than a true inflammatory process, certain tendon characteristics are evident with ultrasound. Studies have described the sonographic assessment of tendons prior to percutaneous treatments with four features, which include the following: tendon size, tendon echotexture, interstitial tendon tears, and neovascularity [10].

Tendon size is usually increased with chronic tendinopathy. Hypoechoic areas within the tendon, as well as interstitial tears, indicate collagenous disruption. Additionally, tendon hypervascularity is thought to correlate with symptoms. These findings on ultrasound examination support the diagnosis of tendinopathy and can additionally be monitored posttreatment

Percutaneous Needle Tenotomy Technique

No standardized protocol for the treatment of tendinopathy with needle tenotomy or fenestration has been identified in the literature. In fact, even the use of ultrasound to visualize tendon fenestration is not considered a requirement, although this may

bring into question the accuracy of tendon needling [8]. A large majority of the studies available for review did utilize ultrasound for tendon visualization. The advantage of a percutaneous approach compared to open surgery is that patients may be treated in an office-based ambulatory setting, as opposed to the operating room. Additionally, complications associated with general anesthesia can be avoided as only local anesthetic treatment is required.

After patient screening and selection, a preprocedural ultrasound assessment is usually performed to identify the areas of tendinopathy. With patient agreement and consent, the percutaneous tenotomy can even be performed the same day as the ultrasound assessment. Patients are placed in correct positioning and a sterile field is created. Probe covers are used for the ultrasound machine to ensure sterility. Using ultrasound guidance, the patient is injected with a local anesthetic for pain control in the procedural area. Most often, the ultrasound probe is placed longitudinally near the tendon insertion site for an in-plane approach [7]. A variety of needle sizes have been described for actual tendon fenestration. One study, in which patients with elbow tendinopathy were treated, utilized a 16-gauge needle for fenestration [9]. Other studies used hypodermic needles between 18-gauge and 25-gauge [7, 11, 12]. There are currently no studies available comparing the therapeutic effects of different needle sizes or different methods for actual tendon fenestration. Once the procedure is completed, hemostasis is achieved with manual pressure and patients only require a simple dressing.

Tenex Health TX Technique

The development of the Tenex Health TX procedure (Tenex Health, Lake Forest, California) has allowed for a minimally invasive ultrasonic energy debridement tool as an alternative to open tenotomy procedures. Tenex Health TX utilizes a needle-like device, which is approximately the size of an 18-gauge needle [5]. The pencil-like hand piece is connected to the Tenex Health TX console, which provides energy to produce an oscillating "jackhammer" type movement to emulsify tendinopathic tissue [13]. The working tip of the TX1 device has an outer and inner cannula that allows for continuous irrigation and aspiration, respectively. As the oscillating frequency breaks up necrotic tendon tissue, the tenotomized debris is aspirated from the procedural field. Similar to needle tenotomy, the TX1 device allows for a safe and effective treatment that can be implemented in an ambulatory setting rather than operating room.

The Tenex Health TX protocol is slightly more standardized than typical needle tenotomy [5, 13, 14]. Similar to needle tenotomy, the first step involves a confirmatory ultrasound assessment to evaluate for hypoechoic regions within the tendon to target. The patient is positioned to allow for easy access and direct approach to the tendon of focus. Standard surgical site preparation and drapes are used to prepare the sterile field. The ultrasound transducer is placed in the longitudinal axis to allow for greatest tendon visualization. Local anesthetic is injected through an entry point

slightly distal to the area of focus, which is similar to needle tenotomy. An 11-blade scalpel is then used to create an approximately 4 mm puncture site, through which the TX1 probe will be inserted. The TX1 hand piece tip is then introduced with ultrasound guidance into the area of tendinopathic tissue. A foot pedal connected to the Tenex Health TX console is then used to activate the device, allowing for ultrasonic energy debridement. During the ultrasonic energy treatment, concurrent irrigation and aspiration help to remove pathologic tenotomized tissue. Debridement time varies slightly depending on the amount of pathologic tissue that is visualized by ultrasound, but studies reviewed typically used between 30 and 60 sec of ultrasonic energy. The incision may then be closed with a Steri-Strip and covered with a Tegaderm dressing. An additional compression sleeve may be added for comfort.

Postprocedural Considerations

Percutaneous treatments allow for patients to be treated in an outpatient office-based setting without a prolonged postoperative recovery phase. Postprocedural management after needle tenotomy or Tenex Health TX depends on the tendon that is treated. Precautions after treatment of rotator cuff or elbow tendinopathy may be different than those for patellar tendinopathy or plantar fasciitis. The current literature has not proposed a standardized postprocedural rehabilitation protocol. A study employing the use of needle tenotomy describes a 10–12 week rehabilitation protocol based on upper extremity vs. lower extremity tendinopathies as the treatment focus [7].

For lower extremity procedures, it was recommended that patients be nonweight bearing for roughly 48 h, whereas upper extremities were placed in slings. After this, patients were weight bearing as tolerated, with gradual increase in range of motion over 2 weeks. Patients then began isometric exercises and gradual stretching up to week 4. More aggressive isotonic and eccentric exercises with progression from walking to jogging were then implemented over weeks 4–12. This describes one of the more detailed and extensive postprocedural rehabilitation protocols. After the completion of the Tenex Health TX procedure, one study recommended only gentle range of motion for the first 48 h. Patients were instructed not to lift objects greater than 5 lbs for approximately 6 weeks [5]. Normal activity was resumed after 6 weeks.

In general, patients are recommended to rest for the first few days following the procedure to avoid exacerbations or injury. Ice may be used to help reduce discomfort in the area and over-the-counter medication is usually sufficient for pain control. Early but gradual range of motion is also encouraged. After the first week, patients may slowly increase activities as tolerated. Physical therapy is not necessarily a requirement after needle tenotomy or Tenex Health TX but may be provided for patients on a case-by-case basis. Patients are recommended to be cautious, as a loss of reflex inhibition due to pain relief may lead to overconfident use in the early days after the procedure [6].

Therapeutic Effects

Both percutaneous needle tenotomy and Tenex Health TX have been shown to have therapeutic benefits for patients with chronic tendinopathy. These procedures are less invasive than an open surgery and can be done in an outpatient office-based setting.

In 2008, a retrospective study of 52 patients with extensor elbow tendinopathy treated with needle tenotomy reported a 57.7% excellent outcome after the procedure [12]. The study utilized a subjective questionnaire to assess clinical and functional improvements after treatment. A year later, a prospective study expanded the area of focus to multiple tendons throughout the body, including the patellar, Achilles, proximal gluteus medius, proximal iliotibial tract, proximal hamstring, extensor elbow, and proximal rectus femoris [11]. Utilizing a Visual Analog Scale (VAS) to assess for changes in pain level, patients reported a statistically significant change from 5.8 to 2.4 at 4 weeks after treatment with needle tenotomy. Patients continued to have a significant pain reduction at 12-week follow-up compared with the baseline.

Studies employing Tenex Health TX have noted comparable results, not only with pain reduction postoperatively but also with improvement in function as well. The Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire is a validated and reliable outcome measure that assesses for the ability to complete common activities of daily living. A case series including 20 patients with extensor elbow tendinopathy treated with Tenex Health TX found a statistically significant improvement in the DASH-Compulsory (from 21.7 to 11.3) and DASH-Work (25.0 to 6.3) scores at 1 month [4]. The improvement in both scores was sustained at 12 months. This study also noted a reduction in the VAS score from 5.5 to 3.3, as early as 1 week after the procedure. At 3 months, the pain score further improved to 2.0, and at 12 months was down to 0.5, which was a clear change from the baseline. Similar results were seen in a different case series of 19 patients also treated with Tenex Health TX for elbow tendinopathy, where VAS scores improved from 6.4 to 0.7 at 12 months [5]. In addition, the study utilized an alternative validated questionnaire, the Mayo Elbow Performance Score (MEPS), but the pattern of improvement remained the same.

Postprocedural assessment of tendons under ultrasound also showed improvement as early as 6 months after Tenex Health TX in a case series of 20 patients treated for elbow tendinosis [4]. Ultrasonographic changes included decreased tendon thickness (19 patients), reduced hypervascularity (17 patients), and reduced hypoechoic regions (18 patients). Necrotic tendon tissue is thought to induce a cytokine response that produces pain in the patient [6]. With removal of this degraded tissue, almost immediate pain relief is experienced by many patients. Percutaneous tenotomy helps to stimulate induction of bleeding, which helps to transition the chronic nonhealing tendon into an acute process with greater healing potential.

The use of injected blood products introduced after percutaneous tenotomy has also been studied [7, 8, 10]. Products may include autologous blood, platelet-rich

plasma (PRP), or autologous conditioned plasma. A prospective cohort study utilized needle tenotomy and autologous blood injection to treat 47 knees with patellar tendinopathy [10]. Pre- and postprocedure Victorian Institute of Sport Assessment (VISA) scores were collected, which showed a significant improvement from 39.8 to 74.3 after a mean follow-up of 14.8 months.

There were very few complications noted in the literature following a percutaneous approach. There is a theoretical risk of tendon rupture, as the result of fenestration of the tendon, but a single case has not been reported thus far. For comparison, open surgical treatments have been shown to be associated with a variety of complications postoperatively [2]. Common side effects after percutaneous tenotomy may include postoperative drainage, which was reported in only a few patients for about 2–3 days after the procedure [6]. Some patients also experienced residual soreness in the area, but this resolved with time.

Conclusion

With a multitude of treatment options available for patients with chronic tendinopathy, no single treatment has gained widespread acceptance. Percutaneous tenotomy, whether by needle or the TX1 device, provides a minimally invasive treatment option for patients with chronic tendinopathy. The procedure provides a safe, reliable, and effective treatment option for patients who are refractory to conservative management. It is well tolerated, with rapid recovery time, and an improvement in symptoms early in the postprocedural period.

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Chapter 70
Percutaneous Peripheral Nerve Stimulation for the Treatment of Pain in the Rehabilitation Patient

John Chae, Richard Wilson, Maria Bennett, Amorn Wongsarnpigoon, and Joseph Boggs

Abbreviations

EOT	End of treatment
LBP	Low back pain
PNS	Peripheral nerve stimulation
PSSP	Poststroke shoulder pain
RCT	Randomized controlled trial
SIS	Subacromial impingement syndrome
TKA	Total knee arthroplasty

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Introduction

Percutaneous peripheral nerve stimulation (PNS) was originally developed at Case Western Reserve University to reanimate paralyzed limbs following central nervous system injury [1]. Temporary leads were placed percutaneously, adjacent to motor points or nerve trunks innervating the paralyzed muscle, to generate functional movement of the upper and lower limbs. In the early 2000s, this technique was used for the first time to treat pain [2]. Chronic stroke survivors with poststroke shoulder pain (PSSP) received percutaneous leads adjacent to the motor points of muscles surrounding the shoulder joint. Electrical stimulation causing muscle contractions produced significant and sustained pain reduction. This same approach was subsequently used to treat non-stroke-related chronic musculoskeletal pain, such as subacromial impingement syndrome (SIS) [3], and chronic axial low back pain (LBP) [4]. At present, research is being conducted to demonstrate the feasibility of percutaneous PNS for the treatment of residual limb and phantom pain following lower limb amputation [5] and postsurgical pain following total knee arthroplasty (TKA) [6]. Ultrasound guidance is used to place leads adjacent to the femoral or sciatic nerve to generate paresthesias at their respective distributions. This chapter reviews the stimulation system and parameters, clinical indications, implantation procedure, and clinical efficacy data.

Stimulation System and Parameters

The percutaneous PNS system consists of the percutaneous lead, external stimulator, return surface electrode, and cables connecting each component. The power source is encased in the external stimulator or embedded in the return surface electrode. The percutaneous lead is composed of 316 L. stainless steel wire, PFA insulation, and silicone adhesive as shown in Fig. 70.1. The stainless steel wires are wound in a 7-strand, single helix coil configuration, with a diameter of 0.2 mm. Ten millimeters of the insulation is removed at the tip, resulting in a 10 mm^2 stimulating surface. The deinsulated tip is angled to form a barb to facilitate lead stabilization. The lead is preloaded in an introducer needle and placed percutaneously with the externalized lead connected to an external stimulator. The safety profile of the lead for short-term (< 6 weeks duration) use has been well documented [7].

A variety of stimulators were used in the various studies during the developmental course of this technique, with the most recent version shown in Fig. 70.2. Stimulation parameters were tailored to the specific clinical application. Applications that require muscle contraction delivered a biphasic, charge balance waveform of 12 Hz at 20 mA, with intensity of muscle contraction modulated by adjusting the pulse duration between 20 and 200 μs. Applications that require sensory paresthesias delivered the same biphasic waveform but at 50 Hz and at 1–2 mA. The pulse duration was adjusted between 20 and 200 μs to modulate the intensity of the paresthesia.

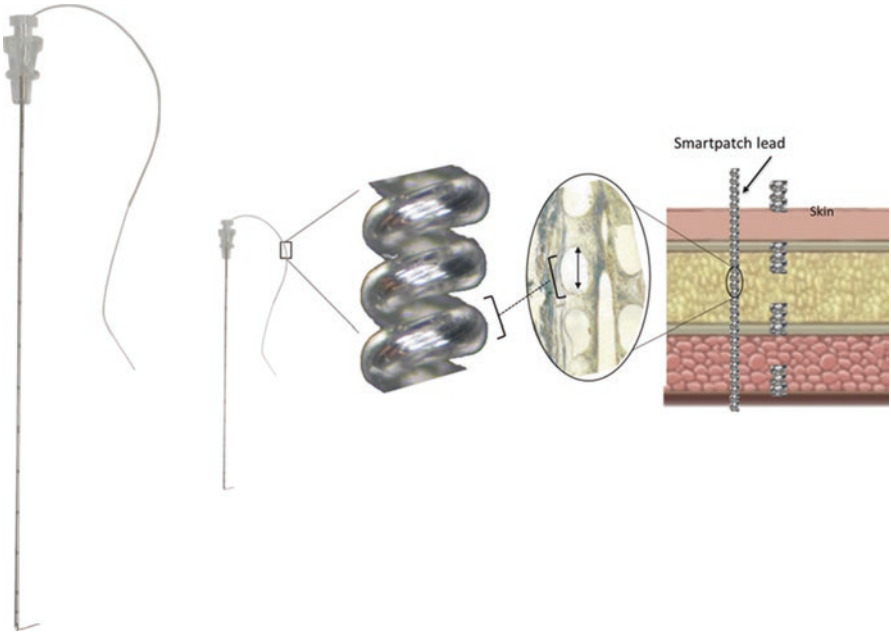

Fig. 70.1 Percutaneous peripheral nerve stimulation lead

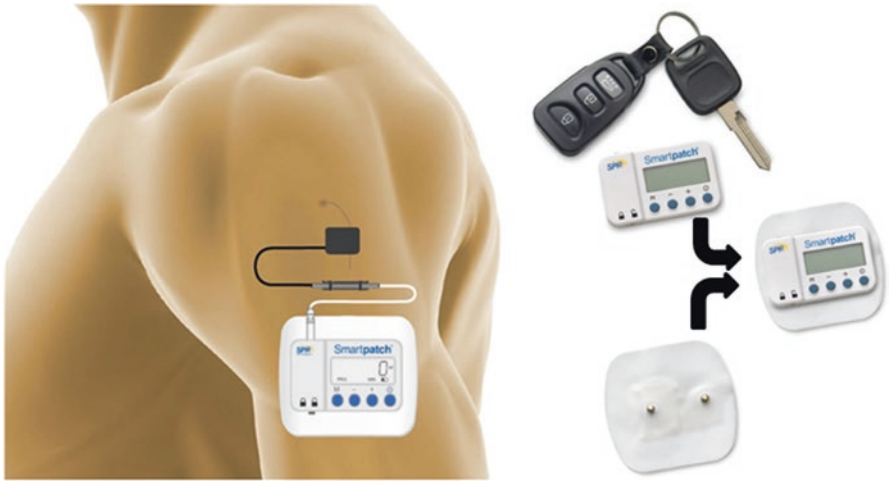

Fig. 70.2 Percutaneous peripheral nerve stimulator

Poststroke Shoulder Pain

PSSP is a debilitating complication of stroke, affecting a great majority of stroke survivors with moderate to severe hemiplegia. The glenohumeral joint is the most mobile joint in the human body; therefore, this joint is also the least stable, relying

primarily on the rotator cuff for stability. With the onset of hemiparesis, the initial inciting cause of PSSP is glenohumeral instability. However, as pain transitions to the chronic phase, PSSP is likely mediated by central sensitization, a mechanism responsible for many chronic musculoskeletal pain conditions. PSSP is associated with depression, reduced motor and functional recovery, and poor quality of life.

PSSP was initially thought to be due to impaired glenohumeral biomechanics manifested by glenohumeral subluxation. Therefore, percutaneous PNS was initially developed to reduce glenohumeral subluxation and early trials only enrolled chronic stroke survivors with PSSP and glenohumeral subluxation. Leads were subcutaneously tunneled under local anesthesia and placed within the substance of the target muscle. Specifically, they were placed adjacent to the motor points of the supraspinatus, middle deltoid, and posterior deltoid to reduce the subluxation, and of the upper trapezius to stabilize the scapula. Participants were treated for 6 h daily for 6 weeks. Uncontrolled case series demonstrated significant reduction in pain and glenohumeral subluxation, which were sustained for up to 6 months after the end of treatment (EOT) [8, 9]. A follow-up multicenter randomized controlled trial (RCT) comparing PNS to a sling demonstrated significant pain reduction in the PNS group compared to the sling, with the treatment effect lasting for up to 12 months after EOT (Fig. 70.3) [10, 11].

An important observation from the RCT, however, was the lack of significant reduction in glenohumeral subluxation, motor impairment, or hypertonia in the PNS group compared to controls. This suggested that improved biomechanics was not the mechanism responsible for the PNS-mediated pain reduction. Emerging data now suggest that while the pain mechanism during the early phase of PSSP is nociceptive, as pain transitions to chronic, central sensitization is the more likely mechanism sustaining the pain experience [12]. Thus, we now theorize that PNS reduces PSSP by the modulation of central sensitization. Accordingly, glenohumeral subluxation is no longer an inclusion criterion for this treatment protocol.

Other important changes were also implemented. Given that the improvement in biomechanics was unlikely to be the mechanism of action, the upper trapezius lead was removed from the protocol. Both the middle and posterior deltoids could be activated with a single lead. Thus, the 4-lead system evolved into a single-lead system. The reduction to a single lead obviated the need for tunneling and the introducer could now be inserted perpendicular to the skin surface, similar to the way needle EMG electrodes are placed. Review of the RCT data further revealed that most of the treatment effect was realized by the third week of stimulation. Thus, the duration of treatment was reduced by half. Overall, these changes have dramatically simplified the treatment protocol and have reduced the risk and discomfort to patients.

The revised treatment protocol was tested in two studies. The first study enrolled eight chronic stroke survivors with PSSP in an open-label case series [13]. Participants were treated with a single lead to the deltoid for 3 weeks and followed for 12 weeks. On average, the participants experienced 70%, 61%, and 63% pain reduction relative to baseline at EOT and at 4 and 12 weeks after EOT, respectively. In a follow-up single-blinded pilot trial [14], 25 chronic stroke survivors with PSSP

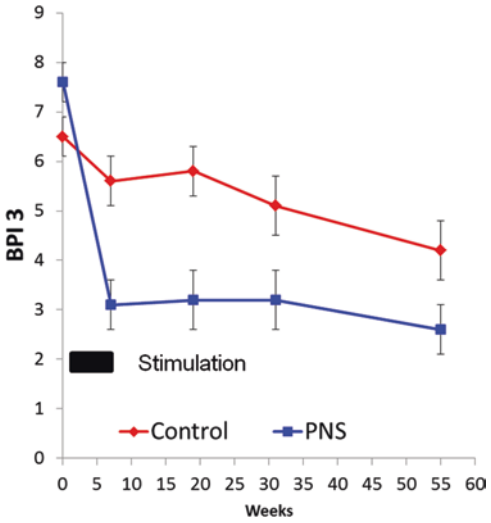

Fig. 70.3 Results of multicenter, single-blinded, RCT of percutaneous peripheral nerve stimulation vs. hemisling for the treatment of chronic poststroke shoulder pain

were randomized to 3 weeks of percutaneous PNS or a course of physical therapy. As shown in Fig. 70.4, both groups experienced pain reduction by the EOT. However, the physical therapy group experienced pain recurrence, while the PNS group maintained their pain reduction. The revised protocol is presently undergoing a pivotal RCT in support of an application for FDA clearance for commercialization.

Chronic Musculoskeletal Pain

The mechanism of percutaneous PNS-mediated pain reduction in PSSP is not known. However, the effect may be similar to the pain-reducing effect of exercise on chronic musculoskeletal pain [15]. We theorize that as muscles contract, the muscles themselves serve as a "translator" of information from the periphery to the central nervous system, the locus of maladaptive neuroplasticity of central sensitization. That is, as PNS induces comfortable muscle contractions, proprioceptors (Golgi tendon organ and muscle spindles) respond by sending physiologic information to the central nervous system, leading to modulation of central sensitization or dissensitization. This theory remains to be validated. There is now strong evidence that the convergent mechanism behind chronic musculoskeletal pain is central sensitization [16]. If percutaneous PNS reduces chronic PSSP by modulating central sensitization, and if all chronic musculoskeletal pain is mediated by central sensitization, then percutaneous PNS should reduce non-stroke-related chronic musculoskeletal pain.

To test this hypothesis, chronic SIS in the nonneurologically impaired population was selected as the test clinical condition. A 57-year-old male, with 20 months history of SIS, unresponsive to available conservative management, including ultrasound-guided subacromial corticosteroid injection, was implanted with a percutaneous lead to

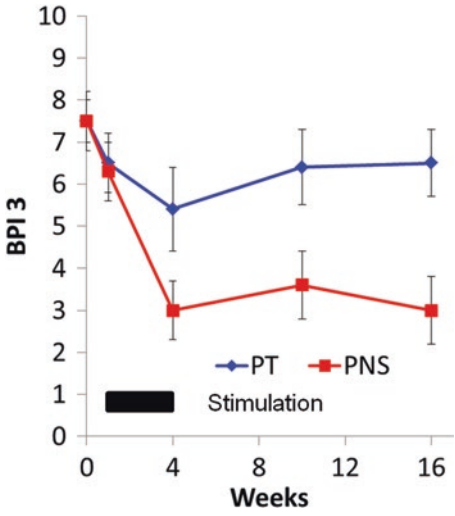

Fig. 70.4 Results of a single-site, single-blinded, RCT of percutaneous peripheral nerve stimulation vs. physical therapy for the treatment of chronic poststroke shoulder pain

the deltoid and treated for 3 weeks [3]. His pain was reduced by 75% at the EOT and was pain free at 4 and 12 weeks after EOT. He reported similar improvements in pain interference with daily activities, and self-reports of function and quality of life. A follow-up open-label case series [17] among ten participants with chronic SIS showed significant reduction in pain and pain interference with daily activities (Fig. 70.5). This case series also reported preliminary evidence of PNS modulation of central sensitization.

In order to further evaluate the earlier hypothesis, two participants with chronic axial low back pain were treated with multiple percutaneous leads for 6 weeks [4]. A 44-year old male with a 6-year history of axial low back pain received eight leads. Three pair of leads were placed over the erector spinae muscle superficial to the posterior thoracolumbar fascia at L1, L2, and L3 bilaterally, and a pair within the substance of the gluteus maximus bilaterally. The participant reported 50%, 40%, and 40% pain reduction at EOT, and at 6 and 12 weeks after the EOT. He experienced significant pain reduction by the end of the first week of treatment and he began to exercise for the first time in 6 years. At 1-year follow-up, he maintained his exercise regimen (swimming and triathlon) and his pain reduction was also maintained. The second case was that of a 28-year old female, with a 10-year history of axial low back pain. She received the same set of leads, except the erector spinae leads were placed within the substance of the muscle. She experienced an 88% pain reduction at the EOT, which was maintained at 6 and 12 weeks after EOT. With the pain reduction, she also began to exercise (kickboxing). However, at 1 year, when she stopped exercising, her pain returned.

Percutaneous PNS is a promising approach to the treatment of chronic musculoskeletal pain. While there is an abundance of evidence of treatment efficacy for PSSP, additional trials are necessary to establish the treatment effect for these other chronic musculoskeletal pain conditions. Fundamental basic science studies are also necessary to elucidate the mechanism of action and to refine and to optimize the treatment paradigm.

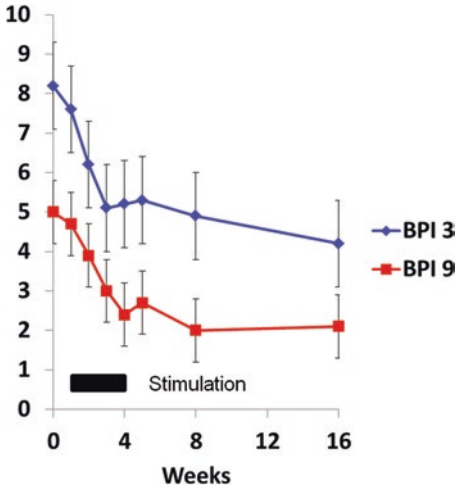

Fig. 70.5 Results of an open-label case series of percutaneous peripheral nerve stimulation for the treatment of chronic subacromial impingement syndrome

Postamputation Pain

There are two types of pain following amputations: residual limb pain and phantom limb pain. Both types can be extremely debilitating and are associated with significant reduction in overall function, societal participation, and quality of life. Oral pharmacological agents, which have been the mainstay of treatment, can be associated with serious side effects and are often ineffective. The application of percutaneous PNS for the treatment of lower limb postamputation pain is different from that of PSSP and chronic musculoskeletal pain in several ways. The postamputation pain application requires the generation of comfortable paresthesias without muscle contractions. The lead is placed adjacent to the femoral nerve to achieve paresthesia coverage of the anterior aspect of residual limb and or the sciatic nerve to cover the posterior aspect. The lead does not need to be in intimate contact with the nerve trunk and may be as far as 1 to 3 cm away. Finally, the implantation procedure requires subcutaneous tunneling under local anesthesia and ultrasound guidance.

The first participant to receive percutaneous PNS treatment for postamputation pain was a 49-year-old male, who exhibited severe chronic residual limb pain following a traumatic below knee amputation, 33 years prior to enrollment [5]. After 2 weeks of baseline pain assessment, he received the PNS treatment for 2 weeks, 24 h a day. The participant experienced an average pain reduction of 60% during the 2-week treatment phase. Pain returned during the 4-week follow-up period, but not to the level at baseline. The participant also reported complete resolution of pain interference on daily activities during the 2-week treatment phase. In a follow-up open-label case series [18], 14 participants received percutaneous leads adjacent to the femoral and or sciatic nerves. The nine participants who completed the 2-week treatment phase reported 72% reduction in residual limb pain and 81% reduction in phantom limb pain (Fig. 70.6). Similar improvements were noted for pain interference and pain disability. As with the initial case report, pain worsened during the

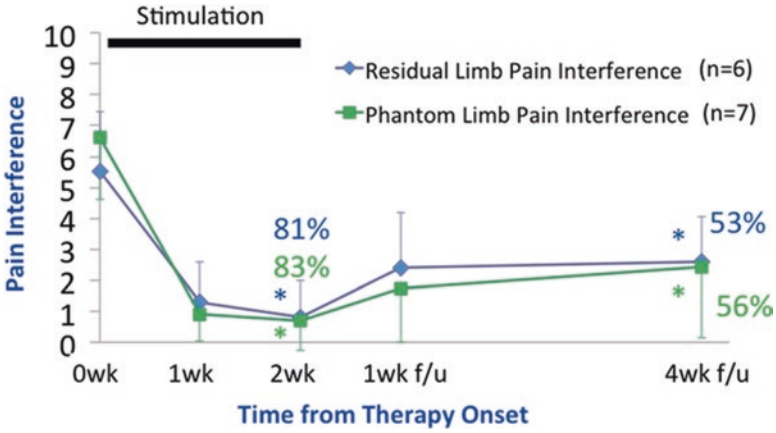

Fig. 70.6 Results of an open-label case series of percutaneous peripheral nerve stimulation for the treatment of residual limb and phantom limb pain following lower limb amputation

4-week follow-up phase, but not to the level at baseline. Based on these encouraging preliminary results, a RCT is presently underway. A permanent implant [19] is also being considered for those who experience substantial pain reduction with percutaneous PNS, but in whom longer term pain reduction is needed.

Postsurgical Pain

Percutaneous PNS is a novel approach for moderate to severe postsurgical pain that could obviate the need for catheter-based analgesia and oral opioids. The approach could revolutionize postsurgical pain management by reducing catheter and opioid-related complications, facilitating mobility and reducing lengths of stay. Postsurgical pain following TKA was selected to investigate the feasibility of this approach.

Five participants who were 8 to 58 days post-TKA surgery received a femoral lead using the implantation method described earlier for postamputation pain [6]. Pain was assessed before and after lead insertion. Percutaneous PNS decreased pain an average of 93% at rest, with 4 of 5 participants reporting complete pain resolution. Pain decreased an average of 27% and 30% during passive and active flexion range of motion, respectively. Leads were removed after completion of pain assessment.

With demonstration of initial feasibility, the efficacy of pain reduction for up to 60 days post-TKA surgery is being investigated.

Conclusions

Percutaneous PNS is a novel application of an electrical stimulation system that utilizes an open-coiled helical lead for the treatment of pain. The lead is temporarily placed for 4–6 weeks adjacent to motor points innervating a muscle to generate muscle contractions or adjacent to a nerve trunk to generate paresthesias. The application of percutaneous PNS for the treatment of chronic musculoskeletal pain requires muscle contractions with therapeutic effect lasting up to 12 months after completion of treatment. The level of evidence is strongest for PSSP, but clinical efficacy for other chronic musculoskeletal conditions, such as SIS and axial low back pain, is being investigated. The application of percutaneous PNS for the treatment of postamputation and post-TKA pain requires the generation of paresthesias without muscle contractions. Preliminary data for these indications are very encouraging and additional studies are presently underway to establish their treatment efficacy. Of all the potential clinical indications for percutaneous PNS, the postsurgical pain indication will likely have the greatest overall impact on clinical practice.

Disclosures The devices presented in this article were investigated under an Investigational Device Exemption from the United States Food and Drug Administration (FDA) and were not approved for commercial use when the final draft was submitted. However, since that time the percutaneous PNS device reviewed in this chapter has received FDA clearance

SPR Therapeutics has a commercial interest in the devices presented in this article

John Chae, MD is a consultant to and Chief Medical Officer for SPR Therapeutics

Richard Wilson, MD is a consultant to SPR Therapeutics

Maria Bennett, MS, Amorn Wongsarnpigoon, PhD, and Joseph Boggs, PhD are employees of SPR Therapeutics

John Chae, MD, Maria Bennett, MS and Joseph Boggs, PhD have ownership interest in SPR Therapeutics

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Chapter 71
Biologic and Regenerative Therapy for the Treatment of Pain in the Rehabilitation Patient

Ian D. Dworkin, Juewon Khwarg, Daniel A. Fung, and Timothy T. Davis

Introduction

Low back pain is one of the most debilitating conditions worldwide, associated with substantial socioeconomic and healthcare implications [1], and is strongly associated with degenerative disk disease (DDD) [2, 3]. Providing effective treatment for DDD has proven to be difficult. Current therapies range from conservative treatments, which include medications, physical therapy, physical modalities, and injections, to more invasive surgical options, which include disk arthroplasty, spinal fusion, and disk decompression [4, 5]; however, these current therapies rarely stop the progression of degeneration and do not restore the native functional state of the disk, focusing instead on management of symptoms and not their etiology [6].

A novel approach to the treatment of DDD utilizes regenerative therapies with the aim of both treating and reversing degeneration, as well as enhancing current treatment modalities. Regenerative therapies, including stem cell therapy, biologic growth factors, and gene therapy, have demonstrated promising results in reversing the degenerative process [7]. In this chapter, we will discuss their role in DDD, peripheral joint disease, and musculoskeletal injuries.

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Stem Cell Therapy Overview and Clinical Applications

Stem cell injection into disks aims at repairing lost cells and matrix, while increasing proteoglycan (PG) content responsible for the disk's organization [8]. These injections have also demonstrated to have both anti-inflammatory and immunosuppressive properties [9, 10]. Mesenchymal stromal cells (MSCs) are one available source for this cell-based repair [11–13]. MSCs are a heterogeneous population of multipotent cells that are capable of differentiating into chondrogenic, osteogenic, and adipogenic lineages but are not associated with hematopoietic cell lines. Sources for these MSCs include the bone marrow (BM-SC), synovial membrane, and adipose tissues [14–17].

The most common source of MSCs is from the bone marrow and is often harvested at the posterior iliac crest, which has a high MSC density and provides similar culture expansion potential compared to other tissue sources [18–20]. MSCs are obtained either from the patient themselves (autologous transplantation) or from other donors (allogenic transplantation). The MSCs are harvested, concentrated, and in some cases, induced and differentiated with the help of growth factors. Disk cells can also be harvested to seed the scaffolding that will assist the MSC in regenerating the affected disk.

With the patient lying prone, local anesthetic is administered at the injection site. A 22-gauge needle is placed via fluoroscopy in the standard posterior lateral discogram approach with two-needle technique [21]. Approximately 2–3 mL of stem cells is then injected into the symptomatic disk. Patients may require a short-term pain medication regimen following the procedure as well as use of a back brace; restricted physical activity is recommended.

A common indication for stem cell use in DDD is moderate-to-severe discogenic low back pain, which is unresponsive to other nonoperative management, with the goal of avoidance or delay of progression to lumbar fusion or disk replacement [21]. Additional criteria for inclusion into previous investigations include Pfirrmann scores (score of 4–7), Modic grade changes on MRI, disk height loss compared to nonpathologic disks, Oswestry Disability Index (ODI), and Visual Analog Score (VAS).

General exclusion criteria include an abnormal neurologic exam, symptomatic compressive pathology due to stenosis or herniation, and significant spondylolysis or spondylolisthesis [21]. Some postulate that a Thompson score of 4–5 would be a contraindication for stem cell therapy, because the extreme microenvironment would impair successful stem cell regeneration. Additionally, grade V annular tears, with full thickness radial tears and leakage of contrast on discography, may be considered a contraindication for cellular injections.

There have been encouraging results from several clinical trials. A 2011 study investigating injection of autologous bone marrow MSCs (BM-MSCs) into the nucleus pulposus (NP) of affected disks revealed 90% improvement in pain relief and water content of the injected disk [11, 14]. A subsequent study injecting autologous stem cells into symptomatic degenerative disks in surgical candidates

demonstrated statistically significant improvement of ODI and VAS at all follow-up time points, sustained pain relief, and overall improvement in modified Pfirrmann scores [21]. A retrospective study demonstrated that 67% of patients got pain relief from stem cell injection at 5–12 months, and 42% continued to have relief at 13–24 months [22]. The safety profile of bone marrow concentrate injections in 101 patients with various bone healing abnormalities was also investigated. No complications were discovered including new bone formation, injections, tumor induction, or morbidity related to extraction on the iliac crest [22, 23].

Stem Cell Use in Orthopedic, Peripheral Joints, and Musculoskeletal Injuries

The use of stem cell therapy also extends into treating numerous musculoskeletal diseases and injuries. Stem cells have been used to aid in healing and functional restoration of bone regeneration in patients with impaired restoration [24]. Treatment of tibial nonunion with osteoprogenitor cells was found to stimulate osteogenesis in 18 of 20 patients [25]. Osteonecrosis is also thought to respond to cell-based therapies [24]. Additionally, stem cells have also demonstrated substantial utility in cartilage pathology. Autologous chondrocyte implantation has become an established treatment for focal articular cartilage defects larger than 4 cm^2, or as a secondary treatment following failure of initial treatments such as microfracture [26]. This technique has yielded good to very good long-term clinical results in the majority of patients [27, 28].

Intra-articular injections of MSC have been successfully used to treat osteoarthritis (OA). Initial pilot studies evaluating injection of BM-SC into patients with knee OA have demonstrated safety and feasibility of the procedure, and MRIs of injected knees 2 years later have demonstrated increased cartilage and meniscal thickness [29–31]. VAS and functional outcomes in 50 knee OA patients were significantly improved with MSC injection compared to arthroscopic debridement only [32]. MSCs were also found to improve physical therapy assessments [33] and have demonstrated efficacy in the prevention of posttraumatic arthritis [34]. A systematic review of a total of 844 procedures of local autologous MSC injections for OA revealed that the procedure was safe, with no reported major adverse effects of MSC implantation [35]. Another study evaluating 227 clinical cases of intra-articular MSC injection for OA reported three self-limiting cell-related complications as the only safety issues [31]. No malignant transformations were seen at two-year follow-up.

Furthermore, stem cells have been combined with surgical debridement of talar dome defects and found to improve function after 2 years [36]. Core decompression with local delivery of bone marrow auto grafts improved Harris Hip scores and significantly reduced the need for arthroplasty when performed prior to collapse of the joint surface [37].

Epicondylitis has also been a target of regenerative therapies. One study of 20 patients with ultrasound-confirmed, refractory medial epicondylitis received autologous blood injection to the site of maximum injury [38]. Eighty-five percent of patients reported statistically significant reduction in VAS and Nirschl pain score at both 4 weeks and 10 months without complications. A study of 35 patients with ultrasound-confirmed refractory lateral epicondylitis also demonstrated significant reductions in Nirschl and VAS scores [39]. Autologous dermal fibroblasts were also found to be safe and effective in treating both lateral epicondylitis and refractory patellar tendinopathy [40].

Growth Factors' Role in Regenerative Medicine

With the advancement of molecular technology, production of recombinant proteins, including growth factors (GFs), has increased to an industrial scale. Disk degeneration results from dyssynergy between anabolic and catabolic regulators. A central strategy to delay progression of DDD is to utilize GFs to strengthen disk integrity by shifting metabolic status from catabolic to anabolic. This is accomplished by stimulating cells in the disk with appropriate GFs to upregulate matrix metabolism [41]. In vitro investigations suggest that disks themselves are capable of expressing and producing numerous GFs. Thompson et al. first described the anabolic effects of growth factors including TGF-β, epidermal growth factor, and basic fibroblast growth factor on PG synthesis [42]. Others have demonstrated that IGF-1 stimulated PG synthesis in a dose-dependent manner [43] and that recombinant human bone morphogenetic proteins (BMP) like BMP-2 increased cell proliferation and mRNA expression of collagen in disk cells [44]. Other BMPs like BMP-7, also known as osteogenic protein-1 (OP-1), was found to strongly upregulate the production and formation of PG and collagen [45]. OP-1 was further found to enhance nucleus and annular repair [46] and cause PG and collagen synthesis in both early and advanced stages of DDD; however, synthesis was more effective early in degeneration [45, 47].

Clinical Use of Growth Factors

The successful induction of matrix synthesis has paved the way for clinical applications of GFs, especially in spinal fusion surgery. Spinal fusion depends largely upon bone grafting [48], and because of the morbidity associated with the gold standard of bone augmentation, autologous iliac crest bone graft (ICBG), bone graft substitutes were sought. Given BMPs successful osteoinductive properties, recombinant human BMP-2 has been used as an autologous bone graft substitute in single-level lumbar interbody fusion from L4-S1 with a proprietary cage [48, 49]. Clinical outcomes as well as fusion rates were comparable to ICBG [50, 51]. Though the risk of any adverse events was high, they were similar between the two groups [50, 51].

OP-1 was also approved for use after it demonstrated safety and efficacy both as an adjunct to ICBG for noninstrumented posterolateral fusions in patients with degenerative spondylolisthesis, and as an alternative to ICBG [52–54]. Numerous studies also support OP-1 as a safe and effective treatment of fractures and atrophic nonunions [52, 55, 56].

Another novel, minimally invasive regenerative strategy using GFs involves intradiscal injection of a fibrin sealant. Fibrin sealant has been developed to address physical findings associated with symptomatic internal disk disruption by sealing annular nociceptors from inflammatory compounds [57]. Additionally, fibrin's persistent presence may also promote cellular repair of annular fissures. One specific formulation of fibrin, known as BIOSTAT BIOLOGIX, significantly downregulated inflammatory cytokine synthesis and proteolytic enzymes [58, 59]. It also upregulated anabolic cytokines and maintained nuclear volume while mitigating negative mechanical consequences of surgical denucleation [57].

The Biostat® System is one system combining an intradiscal delivery of BIOSTAT BIOLOGIX fibrin sealant along with active ingredients including human fibrinogen, thrombin, calcium chloride, and synthetic aprotinin acetate [57, 59]. In a pilot study of 15 patients, 87% demonstrated at least a 30% reduction in low back VAS compared to baseline at 26-week end-point [56]; however, success criteria for primary analysis of the Biostat® System were not met in a subsequent Phase III study [60]. Additional clinical trials are necessary to confirm its efficacy.

Gene Therapy

Gene therapies may provide additional treatment options, especially at the most advanced stage of degeneration. In genetic therapy, new genes are inserted into diseased cells or tissues using viral vectors or naked deoxyribonucleic acid [61]. Nishida et al. demonstrated the feasibility of direct in vivo transduction of disk cells with an adenoviral vector [61, 62]. Zhang et al. successfully stimulated PG and collagen production by transducing adenovirus vectors carrying various BMP genes [63]. The delivery of gene combinations has also been investigated, as TGF-β, BMP-2, and IGF-1 were found to synergistically increase PG synthesis in vitro [64].

Cell-based gene delivery, or the injection of cells pretransduced with therapeutic genes, may also prove to be a therapeutic option, especially in severe DDD, where cell loss is a major contributor to pathogenesis [61]. It may also prove to be a safer option than gene transfer, because cells adjacent to the injection site, or "bystander" cells, will not be infected. Leo et al. demonstrated the feasibility of cell-based gene therapy in DDD by transfecting rodent intervertebral disks and tracking these cells with in vivo bioluminescent imaging [65]. Zhang et al. also demonstrated that articular chondrocytes transduced to overexpress BMPs can stimulate PG and collagen production when cocultured with NP cells in vitro [66].

Several in vitro studies have been conducted to apply gene therapy to human NP cells. One such study harvested lumbar and cervical disk tissue from 15 patients during surgical disk procedures including disk herniation, stenosis, and idiopathic

scoliosis [64, 67]. It concluded that cells from degenerated disks were no less susceptible to gene transfer than those from nondegenerated disks [64]. The study also demonstrated a minimum dose to be sufficient to achieve transduction of nearly 100% of disk cells regardless of patient age, sex, surgical indication, disk level, and disk degeneration grade [67]. In a subsequent study, cervical and lumbar disk tissue from 22 patients requiring surgical disk procedures was obtained [67]. These cells were separated into different groups including those treated with saline, exogenous GF TGF-β1, and those transfected with the gene responsible for synthesizing TGF-β1. TGF-β1 levels were higher in the transfected cells and exhibited an increase of approximately 200% in PG synthesis over other groups. These results demonstrate advantages of gene transfer over exogenous GF, including superior bioavailability of endogenous TGF-β1, and possible upregulation of TGF-β1 receptors [64].

Conclusions

As we have reviewed in this chapter, regenerative therapies, including stem cells, growth factors, and gene therapy, have demonstrated the capability to treat a diversity of conditions from DDD of the spine to peripheral musculoskeletal issues. Regenerative medicine also represents a unique approach to treating these conditions, focusing on reversing pathophysiology at the cellular and molecular level, while synergistically enhancing current treatment modalities. Despite regenerative medicine's enormous potential, widespread clinical translation and acceptance within the medical community has been slow to develop. An important reason for this is the lack of large-scale clinical trials. As we have seen in this chapter, clinical understandings of stem cell, growth factor, and gene therapy are mainly gleaned from studies with limited participating patients and with differing methods. For example, stem cell clinical trials published thus far have utilized different inclusion and exclusion criteria; different mechanisms for isolation, purification, expansion, and injection of MSCs; and different outcome measurements. Additional clinical trials are necessary to determine ideal candidates for regenerative therapy, standardize treatment protocols, and to optimize therapeutic outcomes [68]. Doing so will establish regenerative therapies as important treatment modalities and will facilitate clinical translation by demonstrating the role they can play in patient care.

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Chapter 72
Electro-analgesia for the Treatment of Pain in the Rehabilitation Patient: Calmare Pain Mitigation Therapy

Stephen J. D'Amato and Frank R. Sparadeo

The Problem of Chronic Pain

Chronic pain impacts the lives of millions of individuals and their families. The Institute of Medicine's recent report estimates that there are 116 million Americans burdened by chronic pain, at a cost of between $560 billion and $635 billion annually [1]. The Federal Medicare program bears fully one-fourth of US medical expenditures for pain; in 2008, this amounted to at least $65.3 billion, or 14% of all Medicare expenditures [1]. When considering Medicaid, the total estimated medical expenditures for chronic pain are at least $99 billion. Pain is associated with a wide range of injury and disease, and is frequently the disease itself. Some conditions may have pain and associated symptoms arising from a discrete cause, such as postoperative pain or pain associated with a malignancy, whereas in other conditions, pain constitutes the primary problem, such as neuropathic pain disorders or headaches. Recent research has indicated that the prevalence of chronic pain is on the rise for at least five reasons: (1) aging of the US population; (2) rising prevalence of obesity, which is associated with chronic conditions that have painful symptoms (e.g., diabetic peripheral neuropathy); (3) progress in saving the lives of people with catastrophic injuries, which include military injuries; (4) under-managed postsurgical pain and an increase in outpatient surgical procedures; (5) greater understanding

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of chronic pain syndromes and the development of some new treatments may cause many people to seek treatment that they would not have otherwise [1].

While acute pain is a normal sensation triggered in the nervous system to alert you to possible injury and the need to take care of yourself, chronic pain is different. Chronic pain persists. Pain signals keep firing in the nervous system for weeks, months, or even years. There may have been an initial mishap, such as a sprained back or serious infection, or there may be an ongoing cause of pain, such as arthritis, cancer, or ear infection. However, some people suffer chronic pain in the absence of any past injury or evidence of body damage. Many chronic pain conditions affect older adults. Common chronic pain complaints include headache, low back pain, cancer pain, arthritis pain, and neuropathic pain, which includes pain resulting from damage to the peripheral nerves or to the central nervous system itself.

Chronic pain becomes maladaptive and destroys the balance in every aspect of a person's life, including the following: mood, activities of daily living, interpersonal relationships, ability to work and be productive, enjoyment of hobbies and activities, and general social interactions.

The treatment of chronic pain has been much less than optimal. The treatment field is wrought with failure. Because of the desperation felt by people experiencing chronic pain, they often cycle through various pain clinics, pain specialists, and emergency departments on a frequent basis, driving up the cost of health care with little sustained impact.

Commonly Reported Pain Conditions

When asked about four common types of pain, respondents of a National Institute of Health Statistics survey indicated that low back pain was the most common (27%), followed by severe headache or migraine pain (15%), neck pain (15%), and facial ache or pain (4%) [2]. Other types of commonly seen pain conditions include peripheral neuropathy, complex regional pain syndrome, and postherpetic neuralgia.

Standard Chronic Pain Interventions

Currently, several treatment modalities exist for the management of chronic pain, including physical therapy, pharmacologic therapy, behavioral medicine, neuromodulation, minimally invasive interventions, and surgery. Given the heterogeneous nature of chronic pain syndromes, the appropriate management strategy relies heavily on patient-specific factors. Though not always indicated, pharmacologic measures are a commonly prescribed component of chronic pain management. While many medications are available in a practitioner's arsenal, including nonsteroidal anti-inflammatory agents, anticonvulsants, antidepressants, and opioids, it is exceedingly common for patients to use multiple agents to try to achieve reasonable pain control [3].

Recognizing the limitations and hazards of polypharmacy, an increasing emphasis has been placed on the non-pharmacologic options for management of persistent pain. It is well established that a strategy combining psychological and physical medicine approaches can provide significant benefit for these patients [4]. Neuromodulation techniques, particularly since the commercial availability of wearable transcutaneous electrical stimulation (TENS) units in the mid-1970s, have gained popularity as an adjunct to both pharmacological and non-pharmacologic pain managements. Unfortunately, the data on such methods remain limited and nebulous, underscoring the need for novel therapeutic options [5, 6].

Origins of Electro-analgesia

The concept of pain relief by application of an electrical device dates back to antiquity. Waters in ancient Greece inhabited by electric "Torpedo Fish" were known to have powers to numb the feet, while standing in these pools [7]. Over the centuries, "thinkers" like Benjamin Franklin and scientists like Melzack and Wall, [8] intrigued by such electro-analgesic effects, influenced the introduction of this type of therapy into clinical medical usage [8]. With their proposed "Gate Control Theory" (GCT) of pain, Melzack and Wall started the movement towards the research and refinement of electro-analgesic modalities for the relief of acute pain [9]. There were misgivings and stumbling blocks along the way, the greatest of which was the application of electro-analgesia for chronic pain. Chronic pain does not resolve with recovery of the nociceptive insult that elicited the alarm of tissue damage, requiring cerebral awareness and bodily repair.

Since the introduction of Transcutaneous Electrical Nerve Stimulation (TENS) as an outgrowth and attempted application of GCT, electrical analgesic modalities proliferated to today's "potpourri" of available devices. Along with the well-known TENS, now available are: Percutaneous Electrical Nerve Stimulation (PENS), also referred to as neuromodulation, transcranial electrostimulation, deep brain stimulation, transcutaneous acupoint electrical stimulation, H-wave therapy, interferential current therapy, piezoelectric therapy, and the ultimate electro-analgesic device to date, the implanted spinal cord stimulator. These methods' principle theoretical basis is in the notion that the applied stimulation "closes the gates," as expounded upon in the many scientific articles on gate control theory.

Melzack continued to expand his theories of chronic pain and he eventually proposed the neuromatrix theory [10], to explain chronic pain, which he believed to be a better theoretical framework than his original GCT. Neuromatrix theory basically postulates that the experience of chronic pain involves brain-based circuitry made up of key brain structures, otherwise known as the pain neuromatrix. He also speculated that for the person with chronic pain to improve, he/she must experience an intervention that returns the brain to homeostasis, which essentially alters or short-circuits the pain neuromatrix.

In contractual agreement with the University of Rome, Tor Vergata, Delta Research, Professor Giuseppe Marineo went to work in the early 1990s to create a new theory model for chronic pain and a device representing this theory was introduced. The result of this scientific research and development is called: Scrambler Therapy, which is also referred to in the USA as Calmare Pain Mitigation Therapy™. This therapy was created to address chronic neuropathic pain as a condition in which erroneous information (pain codes) is "scrambled" in favor of non-pain information.

The Calmare Pain Mitigation Therapy™(CPMT) system is a bioengineered system specifically designed to be consistent with the theoretical aspects developed in the basic research, which suggests that chronic pain is the result of erroneous information [11]. By offering the nervous system codes that reveals "non-pain" information, there will be a subjective experience of significantly reduced pain or even elimination of pain. It differs from the Transcutaneous Electrical Nerve Stimulation (TENS) system in its theoretical premises, its "intelligence," the emission of signals characterized by a high information content, and its capacity to build arbitrary waveforms controlled by real-time digital synthesis and associated with suitable control algorithms driving the proposed theoretical system.

Theory of Action

As highlighted above, the treatment of chronic pain has essentially followed the gate control theory, which postulates that a gating system exists in the dorsal horn of the spinal cord that can be influenced by various types of treatment (e.g., medication, electrical stimulation, physical therapy, descending tracts from the cortex). The effectiveness of the pain treatment depends on the degree to which the treatment "closes" the gates and reduces noxious stimulation carried by slow unmyelinated C-fibers to the ascending tracts and ultimately to the brain [9].

Calmare Pain Mitigation Therapy™ although developed independent of the neuromatrix theory, also approaches chronic pain from a central perspective, in which an initial sensory source enters the spinal cord from the periphery, activates neurochemical responses, and ultimately sends information (coded) to the brain that is decoded as pain. Despite surgical correction or natural healing, the information sent to the brain for decoding erroneously persists as pain well beyond the expected healing time frame. As this persists, entropy increases and the individual is now trapped in an inescapable pain experience that has little hope of improving since corrective information is not being produced by any treatment approach. By providing corrective information (bioelectrical codes) through the periphery (via dermatomes) to the dorsal horn of the spinal cord and CNS, the new code "tricks" the brain to read a discernable non-pain code as real and generated from self. Through plasticity, the brain will then learn to expect and to look for the non-pain signal and prefer it; thereby, there will be an improved state of homeostasis (perhaps deactivating the pain neuromatrix proposed by Melzack [10]).

In the development of CPMT™ a human like neuro-information conduction pathway was created to transmit, via surface electrodes, synthetic "non-pain" information to the CNS, which would be recognizable as "self" and "non-pain." This requires the substitution of endogenous pain information with synthetic "non-pain" information. This was accomplished by digitally synthesizing 16 different kinds of action potentials (with variable geometry), very similar to endogenous action potentials, which produce diverse perception effects depending on the "string sequence" they are assembled in over time, and how they are modulated.

The CPMT™ MC-5A device is able to transmit, through disposable surface electrodes, synthetic "non-pain information" to surface C-fiber receptors. The effect of this new information is immediate "zeroing out" of pain. In the typical treatment cycle of ten sessions, pain is progressively reduced in intensity until complete resolution. The pain relief effect is lasting. The treatment can be repeated when needed.

Figure 72.1 represents the process by which the MC-5A scrambler microprocessor device generates 16 diverse individual action potentials that are the physical representation of the chemical reactions leading to their formation. Each "symbol" is in its own rite a part of the individual coded message of "non-pain" that was once dynamically assembled by the patented algorithm into "string sequences." Purely by chance, just one sequence may be the patient-specific electrical "string sequence of non-pain" information that the CNS was expecting after tissue damage repair was completed in that specific patient. Much like our DNA, our "non-pain information" is species specific and individually unique.

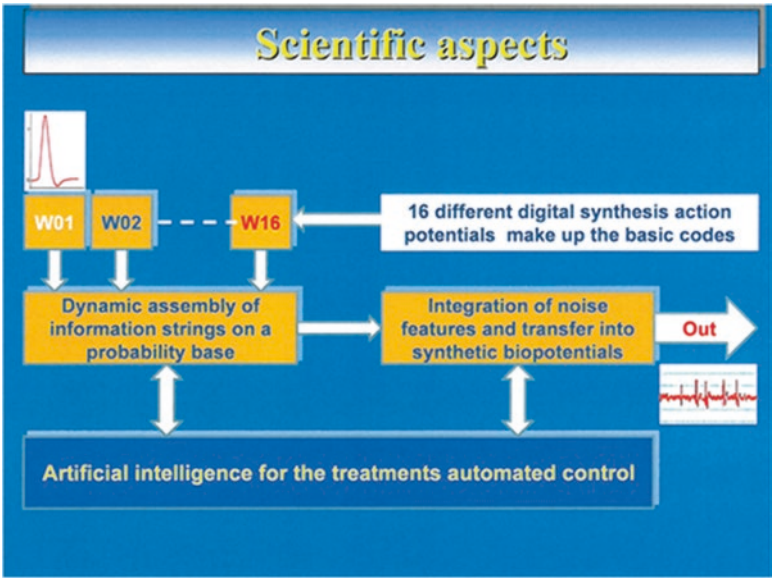

Fig. 72.1 A diagrammatic visualization of the process of scrambler therapy is represented on this slide from Professor Marineo's own teaching program in Rome, Italy and given to the author for teaching purposes in 2009

As stated in the basic concept above, the pain treatment response is immediate when properly performed by a skilled operator of the device. Due to the nature of the patient population being treated, it is imperative that the provider also has a firm understanding of the pathophysiology of neuropathic pain and an awareness of a guideline-based medical regimen, as well as possible interactions with the neuroplastic repair process being created by the device. The operator and assistant must constantly interact with the patient to establish the point at which the patient's perception of their pain is totally replaced by the "tingling" sensation of the devices' surface C-fiber transmission of the "non-pain string sequences." Once the patient's pain is "zeroed out," the device's timer is reset to a minimum of thirty (30) min (the author prefers 45 min) and the patient is placed in the position of most comfort and allowed to rest while "pain free" in an ambiance conducive to relaxation and learning. Calmare Pain Mitigation Therapy™ is a learning process of neuroplastic repair. Repetition is paramount to learning. Hence, CPMT™ is a process of learning, not a single event or treatment session.

Not all patients respond to this therapy, as is true of all modalities in use for every illness or injury. However, in the experience of the authors, the device has been highly effective in over 80% of the 1000 plus patients treated in the Rhode Island clinic that is devoted one hundred percent (100%) to the use of CPMT™ for chronic pain disorders.

The Normal Course of Calmare Pain Mitigation Therapy™

A patient treated with CPMT™ has the area of pain identified and then has electrodes placed on normal tissue around the area of pain, preferably one dermatomal level above that corresponding to the pain's epicenter and one below (i.e., along nerve distributions proximal and distal to the area of pain). The electrodes are not to be placed at the site of actual pain, and should be placed at a location of preserved sensation. The MC-5A CPMT™ device is turned on and increased signal is given until the patient feels a buzzing sensation underneath the electrodes. Dials that modulate intensity of stimulation are adjusted according to patient comfort and, if electrodes have been placed in the correct area, pain will usually be displaced by the device sensation, which is often described as "pleasant, vibratory, and/or humming." Up to five sets of electrodes can be used to treat the area of pain. However, the fewest number of electrodes to bring the patient's pain to zero is the intended goal. The machine is allowed to run for a total of 30–45 min, and the ending sensation is generally soothing for the patient.

Typically, when the scrambler machine is turned off, the patient notes that the pain has been markedly reduced or has disappeared entirely. The benefit from scrambler therapy, after just one treatment, typically will only last for a relatively short period of time (usually minutes to hours). When treatment is reinitiated the next day, the same process happens, but the benefit generally lasts longer (oftentimes, for a few hours). The duration of posttreatment relief classically lengthens

with continued iterations until, ideally, the benefit is maintained throughout the day. Usually, scrambler therapy is given for a total of ten treatment sessions on consecutive days, if feasible, although some patients need fewer and some patients need more treatments. The pain relief can be expected to persist for months after scrambler therapy is stopped. In many, the pain relief may be permanent. However, some patients do experience relapse; booster doses can be given in this situation. It may only require 1–2 booster sessions to reestablish the benefit that was seen previously and this benefit may last for a substantial period of time (oftentimes months or longer).

Evidence of the Validity and Efficacy of Calmare Pain Mitigation Therapy™ (Scrambler Therapy)

Literature

In one of the first published investigations of scrambler therapy, Marineo reported on the treatment of 11 terminal cancer patients suffering from drug-resistant neuropathic pain [11]. He applied ten treatment sessions of CPMT™ to these patients and reported that 81.8% of the patients were able to discontinue pain medications and 18.2% were able to reduce their dosage of pain medication. These results were felt to be encouraging and a second investigation was conducted and published in 2003, in which 33 patients suffering from drug-resistant chronic neuropathic pain were treated with ten sessions of ST [12]. The entire sample responded positively to the treatment, with significant declines in VAS (Visual Analog Scale) scores. Seventy-two percent of the patients suspended treatment with pain medications while the remaining 28% reduced their use of medications.

Sabato et al. [13] expanded their population to the treatment of 226 patients with various forms of neuropathic pain (e.g., sciatic and lumbar pain, postherpetic pain, postsurgical nerve injury pain, pudendal neuropathy, brachial plexus neuropathy, and others). They applied only five ST treatments of 30 min and were able to demonstrate significant improvement with 80% of the sample reporting a better than 50% relief from pain and only 9% with no positive response to the treatment.

More recently, several studies have continued to demonstrate efficacy of the MC-5A Calmare device. In a study of 40 cancer patients and 33 non-cancer pain patients, VAS scores were compared at the initiation of treatment, after the 10-session treatment, and again at 2 weeks following treatment [14]. In their sample, the average VAS score was 6.2 just prior to treatment. After ten treatment sessions, the average VAS was 1.6. Two weeks following treatment the average VAS score was 2.9.

Marineo et al. [15] conducted a clinical trial with patients randomized to either guideline-based pharmacological treatment or Scrambler Therapy (ST). Patients were matched by type of pain (i.e., postherpetic neuralgia, postsurgical neuropathic pain, and spinal canal stenosis). The VAS score was recorded prior to the initiation of the first treatment and after each of ten treatment sessions. The control group

VAS was 8.1 and the ST group 8.0. At 1 month following the last ST treatment session, the ST group VAS score was 0.7, while the control group was 5.8. At two and 3 months, the mean VAS scores in the control group were 5.7 and 5.9. The ST group scores were 1.4 and 2.0. These results clearly suggest that ST is far superior at relieving neuropathic pain than drug management. The mechanisms by which this treatment effect occurs were speculated to include raising the "gate" threshold for pain at the spinal cord, reducing "wind-up" (central sensitization of the spinal cord and brain that amplifies the abnormal feelings), reducing impulses from the damaged nerve, and reducing psychological maladaptation to pain [16]. A recent investigation (2012) has demonstrated similar levels of treatment efficacy in the treatment of postherpetic pain with CPMT™ [17].

A prospective pilot trial experience was published in 2014. The study involved the treatment of 37 patients with chemotherapy-induced peripheral neuropathy, noting about a 50% reduction in pain, tingling, and numbness [18]. The last 25% of patients entered on this clinical trial did substantially better than did the first 25% of patients, which likely implies a significant operator practice effect as further experience was obtained.

Recently a double-blind, sham-controlled, randomized clinical trial involving 30 patients with low back pain was also conducted using the MC-5A Calmare device [19]. These authors noted significant decreases in the Brief Pain Inventory back pain scores and pain interference scores ($P < 0.05$). They also noted improvements in pain sensitivity as well as the amount of painful stimulation required to actually cause pain in the initially painful areas. The sham arm appeared to be robust, in that 66% of subjects responded that they had definitely received CPMT™ Therapy, 20% were unsure, and 13% responded that they definitely had not received CPMT™ Therapy. For those who actually received the treatment (CPMT™), similar responses about perceived treatment thoughts were recorded.

No direct investigation comparing CPMT™ to implanted devices (i.e., intrathecal morphine pump, spinal cord stimulator) has been conducted to date. Spinal cord stimulation devices have made significant progress with regard to rates of sustained pain reduction with newer products such as HF-10 therapy and Dorsal Root Ganglion (DRG) stimulation techniques. However, it is important to note that all invasive modalities, including implanted devices, carry the inherent risks for infection and other surgical and technical problems [20–22].There is also a subset of patients that are successfully treated initially, only to request the implanted device be removed as the pain returns. The noninvasive Calmare Pain Mitigation Therapy™ device can now be considered as part of the protocol prior to the use of surgically implanted devices.

The authors of this publication conducted a pilot applied research program in 2011 using data generated by SD in his usual practice (a unique private practice using the CPMT™ device exclusively for chronic pain relief). This evaluation provided a "snapshot" of the efficacy of this innovative treatment in action. At the time of the evaluation, 153 chronic patients had been treated with varying etiologies (spinal stenosis, complex regional pain syndrome, peripheral neuropathy, failed back syndrome, failed surgery, postherpetic neuropathy, oncologic pain, and others).

When taking all 153 patients and comparing incoming pain levels using the Visual Analog Scale (0–10 scale with 10 highest level of pain and 0 no pain), the outcome VAS level for each session, and the final outcome level, there was a significant treatment effect with the average pretreatment VAS score of 7.5 and the average outgoing VAS score of 1.0. Follow-up studies were completed on a total of 36 patients with either complex regional pain syndrome (CRPS) or spine-based neuropathic pain. Follow-up VAS scores were significantly lower 3 months following treatment (1.7), as compared to their pretreatment level of 7.5. Patients with complex regional pain syndrome entered treatment with an average VAS of 7.5 and were at 2.1 three months following treatment. These patients were administered the Brief Pain Inventory and paired T-test comparisons were performed, which included the VAS. Tables 72.1 and 72.2 summarize these results for the spine pain group and the CRPS group:

Additional analyses were completed, including computation of odds ratios by diagnosis, trend analyses, and analyses of failure cases. These results clearly indicated that the CPMT™ approach was successful. Archival data was eventually collected across various diagnostic groups, analyzed and published in two separate manuscripts [23, 24].

The most recent co-authored publication in 2016, a review publication [25], presents 20 peer-reviewed studies on the effectiveness of the Calmare Pain Mitigation Therapy™ (Scrambler Therapy) device. This publication summarizes all the literature for the reader in a concise format.

Table 72.1 Chronic spine-based neuropathic pain group ($N = 17$)

Variable	Pretreatment mean	3-month follow-up mean
VAS	7.6	1.7*
General interference	8.0	2.2*
Mood	5.9	1.6*
Maneuverability	7.4	2.1*
Work/Household chores	8.1	2.8*
Interpersonal relations	5.3	1.8
Sleep difficulty	5.9	3.3
Level of joy	7.5	1.9*

*$p < 0.01$

Table 72.2 Complex regional pain syndrome ($N = 19$)

Variable	Pretreatment mean	3-month follow-up mean
VAS	7.6	1.7*
General interference	8.0	2.2*
Mood	5.9	1.6*
Maneuverability	7.4	2.1*
Work/Household chores	8.1	2.8*
Interpersonal relations	5.3	1.8
Sleep difficulty	5.9	3.3
Level of joy	7.5	1.9*

*$p < 0.01$

Cost-Effectiveness

Calmare Pain Mitigation Therapy™ (Scrambler Therapy) is very cost-effective. The application of Calmare Pain Mitigation Therapy™ (Scrambler Therapy) is non-invasive, non-painful, and there are no known side effects or adverse events. Each initial treatment series is generally less expensive than a series of three [3] or more epidural steroid injections (ESIs). The treatment requires 10 consecutive days, with applications lasting 1 h each time. Patients who are treated successfully with CPMT™ most often either significantly reduce or completely eliminate their use of expensive medications. The patient's commitment to the treatment is less encumbering than surgery and other forms of treatment that require extensive time commitments. Physical therapy/occupational therapy can be more effective once the patient's pain is reduced or eliminated by CPMT™. Therefore, the patient can return to work sooner when used as an adjunctive modality than with other therapies alone.

Conclusions

Calmare Pain Mitigation Therapy™ (Scrambler Therapy) is a cost-effective and efficacious treatment for chronic neuropathic pain. It is an additional and adjunctive therapy to such treatments as spinal cord stimulators, implanted medication pumps, steroid injections, and opioid analgesics. A growing list of controlled clinical trials, applied clinical research, and anecdotal reports have demonstrated significant improvement in patients with various forms of chronic neuropathic pain including such diagnoses as complex regional pain syndrome, failed back surgery syndrome, chemotherapy induced peripheral neuropathy, and various neuralgias. Calmare Pain Mitigation Therapy™ (Scrambler Therapy) is driven by "information theory" and seems to fit well with neuromatrix theory in which the non-pain code generated by the MC-5A device is learned by the brain and impacts the pain neuromatrix reducing or eliminating the chronic pain.

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Recommended Reading

For a basic understanding of the concepts of "Information Theory" and communication principles, the reader may want to read:

Pain, Its Anatomy, Physiology and Treatment Paperback—March 24, 2014 by Aage R. Moller PhD (Author)

The Mathematical Theory of Communication First Edition (US) First Printing Edition by Claude E Shannon (Author)

Information Theory: A Tutorial Introduction Paperback—February 1, 2015 by James V Stone (Author)

Elements of Information Theory 2nd Edition (Wiley Series in Telecommunications and Signal Processing) 2nd Edition, by Thomas M. Cover (Author), Joy A. Thomas (Author)

Part XIV
Business and Legal Perspectives

Chapter 73
The Business of Pain Medicine in the Rehabilitation Patient

Anish S. Patel

The Cost of Healthcare

It should come as no surprise that the cost of healthcare has risen in the United States (US) at a greater rate than that seen in all developed nations. The national healthcare expenditure in 2013 was $2.9 trillion or $9255 per person. Of that expenditure, chronic pain costs the US up to $635 billion each year, inclusive of the cost of medical treatments, as well as the loss of productivity. The United States is expected to see a population increase of over 72 million baby boomers by the year 2030, despite no proven mechanism, as of yet, to curtail costs [2]. The national healthcare expenditure is expected to increase without a drastic intervention in the US healthcare delivery system (Fig. 73.1).

The elements of cost can be divided into the cost of direct healthcare services as well as the cost of doing business. This may not necessarily correlate with the critical healthcare cost drivers outlined below that have become omnipresent today. Three important factors should be considered:

(a) Health Information technology (HIT), which is a considerable investment with elusive results, should be considered. Today's average cost of implementing an Electronic Health Records (EHR) system in a medical practice is approximately $32,000 per physician, through the first 60 days after system launch. One-time hardware costs can range from $25,000 to $60,000 per practice for internet switches, cables, and wireless internet connections, plus approximately $7000 per physician for computers, printers, and other hardware. Software and maintenance costs, which begin at implementation, can range from $12,000 to $19,000 per physician annually [3]. In addition, one must consider the

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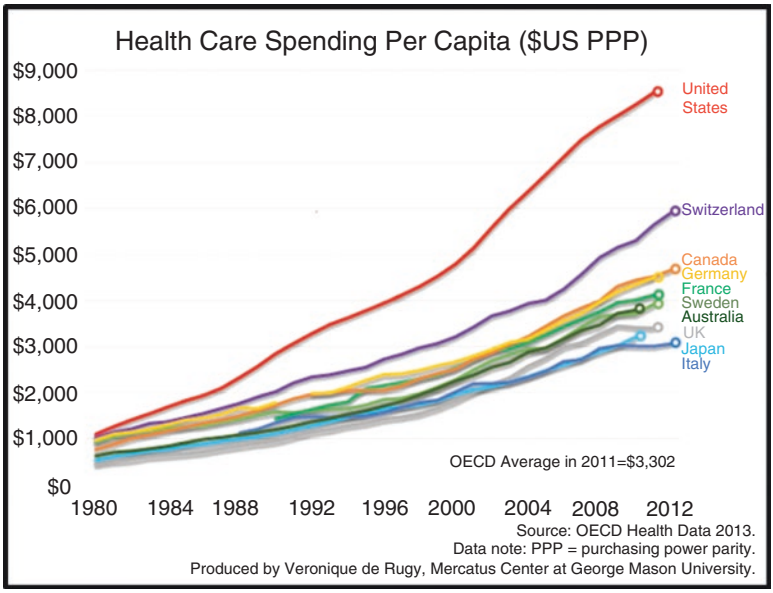

Fig. 73.1 Healthcare spending per capita [4]

nonfinancial costs, which include the monetary costs of salaries per physician as well as his or her support staff and implementation team. Despite the variability in region, practice size, and vendor, there is considerable cost associated with origination and implementation of any EHR system.

(b) Consolidation has been promoted by reform efforts seeking to reduce waste and to reward value instead of volume, but these monopolizing forces are contributing to a rise in costs and leading to lack of competition and extinction of independent medical practices. While independent practices struggle with payer pressures and management challenges, they can deliver a greater quality/value proposition overall. Through mergers and acquisitions, hospitals have grown larger in size and have thereby ensnared more physicians under their control in the last decade. Hospital acquisitions of physician practices tend to lead to higher prices, mostly because of added facility fees by the hospital systems and consolidation of practices, which has not led to either improved quality or reduced costs. It may be argued that the true role of consolidation is to enhance bargaining power with payers and not necessarily to produce integration nor to enhance performance. Advocates of healthcare consolidation, however, may continue to argue that economies of scale, in time, are likely to reduce waste in the system and to ultimately push prices down.

(c) Patient consumer movement towards social media and shared decision-making has forced medical practices to engage in newer strategies, which attract new patients and engage their existing clientele. The internet age has helped to ease the dissemination of information, but at a cost to the provider. Ninety percent of adults state that they rely on information gathered from peers through any

number of social networks and over seventy percent search online to address health concerns and referral sources. Digital healthcare marketing has seen a significant increase in the past 10 years by reaching consumers through various technologies and targeted campaigns. It has been proven to be highly measurable by allowing providers to focus on targeted populations. However, website development, paid searches, and reputation management all come at a direct cost to a medical practice and although these channels may help to improve traffic and ultimately direct patient flow, it can lead to misappropriation of funds at a cost to patient care. It is important to remember that the best and most cost-effective way to begin marketing efforts is by providing excellent care and service to existing patients. Facilitating potential patient movement, whether it's simply through word of mouth, marketing assistants, digital marketing, or print advertisements, should not cost a lot of money. Optimizing consumer movement by letting patients know that a practice is willing and able to care for them, and by providing payers an image of quality and professionalism both show how a practice can provide high-quality, cost-effective care.

ICD-10 and Beyond

October 1, 2015 ushered in a new era in the US healthcare system with the 10th revision of the International Statistical Classification of Diseases and Related Health Problems. Four nonphysician groups, or cooperating parties, were all tasked with the development of ICD-10: The Centers for Disease Control and Prevention, Centers for Medicare and Medicaid Services, American Hospital Association, as well as American Health Information Management Association. Along with the national Clinical Modifications (CM) of ICD, some 68,000 codes are available for use at present day [5]. The financial implications of ICD-10, as well as Meaningful Use (MU) and Physician Quality Reporting Systems (PQRS), can be significant, specifically for those that had remained unprepared and had not begun preparing well before that dreadful day in October.

The impact of ICD-10 spreads through all components of the practice of pain medicine. Billing services, EHR, payers, and documentation are but a few of the components of a medical practice to be affected. Survival in today's climate is dependent on a rapid and effective management strategy, which involves both practice management systems integration and staff education. CMS reports improvements in clinical care, operational enhancement, and professional advocacy as the goals of ICD-10, but the real question is at what cost to the nation?

Estimated costs over a 15-year period are potentially over $1 trillion [6]. Although this may have led to a significant growth in the Health Information Technology (HIT) and consulting industries, who is to say that the cost justification will ultimately help to achieve the goals set out by CMS over that period of time? Cash flow disruptions to any size medical practice will be significant, as over 50% of providers remain unaware of the cash crunch and over 75% report a lack of preparedness [7].

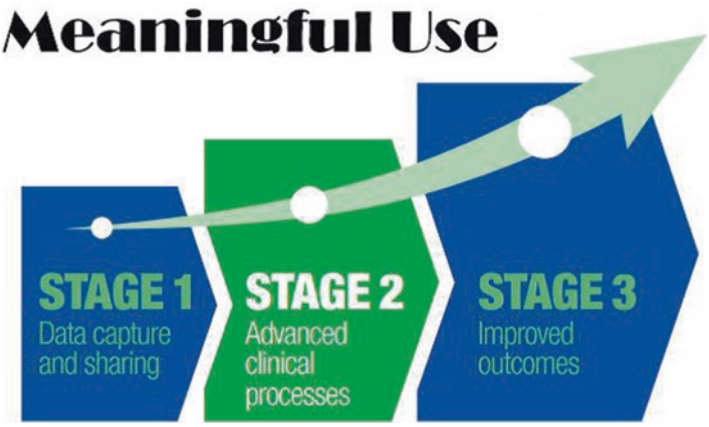

Fig. 73.2 Meaningful use

So, what is the bottom line? Transition and implementation seems to be complicated and time consuming. Furthermore, there does not seem to be any basis on evidence or medical necessity. Even though nonsignificant, improvements have been demonstrated; the system is used in over 200 countries and the US healthcare system must follow the lead if it is to survive [8]. ICD-10 will also impact other required programs. Meaningful Use (MU) is a set of proposed rules, which is designed to improve outcomes and measurement of those outcomes by following a three-stage process (Fig. 73.2).

Formerly known as the Physician Quality Reporting Initiative (PQRI), the Physician Quality Reporting System (PQRS) is a voluntary reporting program, which provides a financial incentive for medical and other healthcare professionals who participate in Medicare to submit data on 260 specified quality measures to CMS. The program shifted from voluntary to mandatory utilization in 2015, characterized by the assessment of penalties for a failure to participate as outlined in the table.

Current Financial Implications

The Value Based Modifier (VBM) program, which is based in part on participation (Fig. 73.3), assesses both quality of care furnished and the cost of that care under the Medicare Physician Fee Schedule. CMS began phase-in of the VBM in 2015, and is anticipated to be completed in 2017, when the VBM will be applied to solo practitioners and groups of two or more providers. The premise involves rating providers based on the PQRS measures. Providers undergo mandatory quality tiering to determine if performance is statistically better, the same, or worse than the national mean.

	2012	2013	2014	2015	2016	2017	2018	2019
Medicare MU Incentive	$44,000 over 5 years	$39,000 over 4 years	$24,000 over 3 years					
Medicaid MU Incentive	$63,750 over 5 years	$63,750 over 5 years	$63,750 over 5 years	$63,750 over 5 years	$63,750 over 5 years			
Medicare MU Payment				-1%	-2%	-3%	-3-5%	MIPS*
eRx Incentive	1%	0.5%						
eRx Penalty	-1%	-1.5%	-2%					
PQRS Incentive	0.5%	0.5%	0.5%					
PQRS Penalty				-1.5%	-2%	-2%	-2%	MIPS*

Fig. 73.3 Financial implications

Quality Tiering Protocol [9]

Beginning in 2019, Medicare will begin to issue payments based on the combination of MU, PQRS, and VBM (Fig. 73.4). This system has been designated as the Merit-Based Incentive Payment System (MIPS). A composite performance score of 1–100 will be assessed, which is based on performance in quality, resource utilization, clinical practice-improvement activities, and meaningful use of EHR. Providers, whose composite performance scores are above the set threshold, will receive positive payment adjustments. These adjustments can be up to 4% in 2019 and may grow over time to a maximum of 9% in 2022 and beyond [10]. A special additional "Incentive Payment," funded with $500 million per year, is applied for the top 75% of physicians above the performance threshold. The interpretation of pain management specialty outcomes measures is poorly understood, at best. Most carriers fail to understand measurable pain medicine outcomes, such as reduction of emergency room visits, surgery, missed work days, opioid burden, and increases in function, quality of life, and mood. Education will be the key to both the understanding and the legitimate assessment of such measures, as it relates to our specialty.

Accountable Care Organizations

An accountable care organization (ACO) is a type of payment and delivery reform model that ties reimbursements to providers, quality metrics, and reductions in cost of care for an assigned population of patients. An ACO is formed by groups of

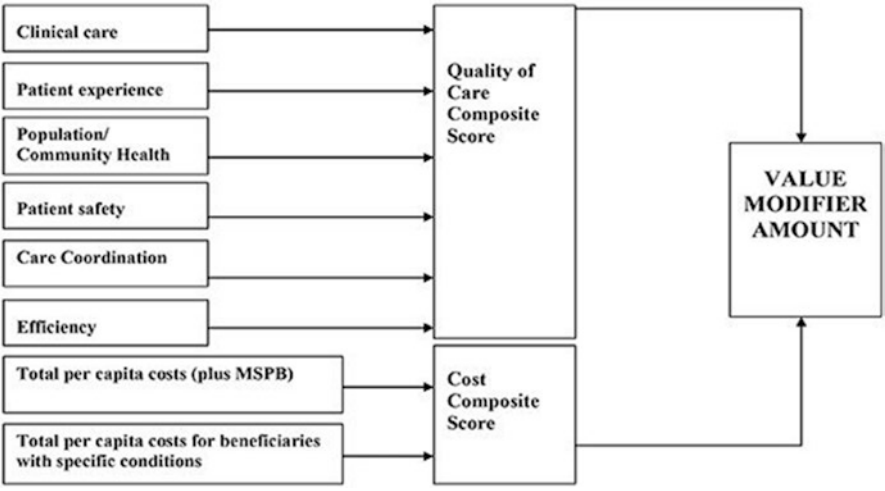

Fig. 73.4 Quality/tiering protocol

doctors, hospitals, and other healthcare providers, who come together voluntarily to provide coordinated quality care to their patients; it is accountable to patients and payers for the quality, appropriateness, and efficiency of the healthcare provided. The model is designed to be flexible with three core principles that have been defined for all ACOs: ACOs are provider-led organizations, collectively accountable for quality and costs across the full spectrum of care; ACO payments are linked to quality improvement metrics that also reduce overall costs; ACOs have reliable performance measurements to support improvement and savings achieved through improvements in care. ACOs can be subdivided into three types: (a) Medicare Shared Savings Program, which facilitates Medicare fee-for-service program providers becoming an ACO; (b) Advance Payment ACO Model, which is a supplementary incentive program for selected participants in the Shared Savings Program; (c) Pioneer ACO Model that was originally designed for early adopters of coordinated care [11].

These care models have been adopted by Medicare, state Medicaid plans, and commercial health insurers and their initiatives have led to an increase in the number of ACOs from fewer than 100, to well over 700 in the past 5 years. ACOs now exist in all 50 states and provide care for more than 23 million people [12]. The dynamic change in our healthcare system, whereby providers will increasingly be paid to effectively manage the health of populations rather than based on the volume of services they provide, has led to a change in the payment model. The financial risk from payers has now shifted toward providers and in doing so, providers are strongly incentivized to change how they are delivering care, with the goal of decreasing spending, while improving quality measures and patient satisfaction.

Interventional pain management and reimbursement reform is a murky area as it pertains to ACOs. The specialty of pain management provides cost-effective care using minimally invasive procedures instead of major surgery or excessive and

expensive drug prescriptions. Minimizing drug prescriptions reduces unnecessary admissions and the complications of accidental deaths and prescription drug abuse. Interventional pain management specialists, with direct communication between primary care providers and surgical specialists, also improve the continuum of care, which is one of the principal aspects of healthcare reform and foci of ACOs. This structure includes bundled payments, which compensate the hospital and the ACOs a pre-decided amount for a specific episode of care. Bundled payments will supposedly incentivize physicians to work together to reduce cost, but do not necessarily incentivize doctors to work together or lead to higher quality care, nor do they take into account the treatment of chronic conditions. There are some who may consider this methodology as an oversimplification of physicians' motives, reducing them to mere responders to economic incentives. In time, with societal and specialty organization support and lobbying, there will hopefully be a realization that interventional pain specialists care about providing high-quality care, while understanding the importance of cost-effectiveness. This will be a critical component of specialty reform and survival of interventional pain management under the ever-growing proliferation of ACOs.

Site of Service

Site of service implies the location at which a medical service or procedure is provided. In the realm of pain management, this can be accomplished at one of four settings: (a) an outpatient department in a hospital; (b) hospital-based inpatient care; (c) an ambulatory surgery center (ASC); (d) the physician office. All sites pose certain advantages and disadvantages as it pertains to regulations and reimbursement. A "Site of Service Differential" is the difference in the amount paid when the same service is performed in the different practice settings noted above. For example, an interventional procedure performed in a physician's office vs. hospital facility vs. ASC will lead to different payments. Choosing the appropriate setting for your practice will affect all aspects of the practice, from patient referral patterns to reimbursement for services provided to patients. In addition, equipment, supplies, and staffing will vary by location. It is critical to consider operational efficiencies, the availability of procedure time, staffing, and setup costs in each of the settings.

Comparison of Medicare fee schedule in three settings 1998–2005: [13].

(a) Hospital Outpatient Department: The advantage of the outpatient setting is that the cost and staffing is a direct cost to the hospital (Fig. 73.5). There is no financial burden placed on the physician, as the hospital can fund and staff the program. Depending on hospital policy, it may require physicians to join the medical staff and to maintain requirements deemed standard by the hospital system, such as privileges and board certification. In return, all policy and procedures, clinical, quality, and administrative management is provided by the hospital and the performance of a majority of procedures is permitted after

		Office			ASC			HOPD		
CPT	*Description*	*Physician*	*Overhead*	*Total*	*Physician*	*Facility*	*ASC total*	*Physician*	*Facility*	*Total*
62310	Cervical epidural	111.70	132.82	244.52	111.70	368.37	480.07	111.70	671.80	783.50
62311	Lumbar epidural	92.01	133.18	225.19	92.01	368.37	460.38	92.01	671.80	763.81
64483	L/S TF epidural injections	115.64	106.69	222.33	115.64	368.37	484.01	115.64	671.80	787.44
64490	C/T facet joint injections, 1st Level	109.55	83.42	192.97	109.55	368.37	477.92	109.55	671.80	781.35
64493	L/S facet joint injections, 1st Level	93.80	81.27	175.07	93.80	368.37	462.17	93.80	671.80	765.60
64510	Injection, Stellate ganglion	75.54	54.06	129.60	75.54	368.37	443.91	75.54	671.80	747.34
64520	Injection, lumbar sympathetic	83.06	106.33	189.39	83.06	368.37	451.43	83.06	671.80	754.86

Adapted from Source: Utilization data by Specialty from CMS shows percentage of procedures utilized in facility settings.

Fig. 73.5 In the outpatient setting the cost and staffing is a direct cost to the hospital

provider competence has been determined. Major disadvantages encompass a lack of control by the physician and dependence on the hospital, which can lead to difficulty in securing block time, C-arm availability, and inefficiencies inherent to a large organization. Most hospital-based outpatient facilities are multispecialty and may not be readily equipped to optimize efficiencies as it relates to pain management, often experienced by slow turnaround time performing procedures and a limited number of interventions that may be performed in a day. Of particular importance is the fact that reimbursement for the physician under Medicare part B is at a lower rate.

(b) Hospital-Based Inpatient Care: As a growing number of hospitals face negative profit margins, finance leaders are examining ways to expand revenue generating inpatient services. One often-overlooked option that can drive strong service line revenue is comprehensive pain management, which is able to transition from inpatient care to chronic outpatient care. Many hospital administrators consider pain management to be a poor source of revenue. However, the simple fact is that leading hospitals have found that comprehensive pain management programs that are strategically located, energetically developed, well run, and able to successfully transition to outpatient care, can attain strong profitability within a relatively short time. While these financial results are within reach for most organizations, creating a strong pain management center takes careful planning and effective execution. Key strategies will include understanding demographics of the center, creation of an active inpatient consultation service, leadership and staffing with board-certified pain specialists, comprehensive services for patients, marketing to referring physicians, optimizing efficiencies, and effective billing and collections.

(c) With regard to physician income, a private pain physician receives only modest reimbursement for evaluation and management (E&M), and facility reimbursement for E&M is nominal, unless the E&M is performed by a hospital-employed physician. Successful programs employing a pain physician in-house will likely

use a productivity-based compensation plan. A common model includes a guaranteed base salary during the first year, with compensation increasing via either a productivity bonus percentage or whole percentage of collections, which incrementally increases year after year. Focused sizable hospital revenue can also be generated from the referral of patients to support services that are an integral part of a comprehensive program, such as imaging, multidisciplinary specialty consultations, physical therapy, nutritional consultation, and behavioral counseling, which are but a few facets of integrated pain service. Tracking referrals to these services helps to validate the return on investment (ROI) of the pain program and allows analysis of key metrics for profitability and optimization of an inpatient pain service.

(d) Ambulatory Surgical Center: The ASC setting may be considered similar to the hospital facility, with regard to policy and procedures, clinical care, quality, and administrative management. Pain management procedures in ASCs generally have a quick turnaround, with only a short recovery time needed for this select group of patients. Further specialization of ASCs allows for improved efficiencies and streamlined operations. This is valuable to the pain management provider, who may be able to perform in excess of four to perhaps six procedures per hour, based on required support staff. Adding pain services to an existing multispecialty ASC includes the capital cost for the fluoroscopy services, which are often already on site for other specialties. If efficiently scheduled, adding pain management services can increase revenue and can provide ASC enhancement. The private practice sector also permits physicians to participate in ownership of the center. ASCs continue to be one of the most highly regulated healthcare entities and are subject to numerous regulatory issues based on licensure, certification, accreditation, as well as payer participation. They offer value today, and in the future, and can be significantly more profitable under the right circumstances. A disadvantage can be the inability to perform certain procedures based on their complexity, which in turn may not be reimbursed in this setting.

(e) Physician Office: When providing services in an office setting, the reimbursement rate is greater for the physician, with the site of service differential in place to aid the provider with funds for their practice expenses. Such funds can be used to supplement rent/mortgage, staffing, and acquisition/maintenance of equipment and supplies. Certain states have detailed regulations governing physician office-based procedures and it is the responsibility of the physician to provide the policies and procedures, as well as clinical, quality, and administrative management.

It is important to keep in mind that in all of the aforementioned locations, pain management physicians will have to bill andcollect for their services. Knowledge of reimbursement and minimization of costs are key in reaching and maintaining profitability. The ultimate decision is making the right choice for an individual practice. Having a facility of your own is likely to generate income, but at a cost, including capital expenditures, overhead, and time. There is more to facility ownership than

simply revenue potential, which should always be viewed in the context of risk. A common characteristic of all successful practices is the ability to foresee the future in terms of growth and development and to devise an adequate plan to reach created benchmarks. This can be achieved by the physician understanding what he/she is getting into and the economic climate in his/her local region. It is important for the physician to know what he/she doesn't know and it is always advisable to consult with professional healthcare consultants and trusted colleagues, who may understand the nuances of the local healthcare sector. Every state and municipality is different and requires knowledge of licensure and certification. Large amounts of money and time can be wasted with errors in understanding the regulatory processes and applications.

Private Equity and Medicine

Private equity is finance provided in return for an equity stake in potentially high growth companies. However, instead of going to the stock market and selling shares to raise capital, private equity firms raise funds from institutional investors, such as pension funds, insurance companies, endowments, and high net worth individuals. Private equity firms use these funds, along with borrowed money and their own commercial acumen, to help build and to invest in companies that have the potential for high growth. Reimbursement model changes and cost-cutting pressures imposed by the Patient Protection and Affordable Care Act (ACA), a lukewarm economy, and new regulatory challenges within healthcare have caused changes in the traditional business model of healthcare. This has led to private equity investment within the healthcare industry, with particular interest in the specialty of pain management. Nearly 100 million Americans suffer from acute and chronic pain and over $600 billion is spent each year on pain management, with a large amount of dollars spent each year on treatment [14]. A large proportion of pain management profits are also derived through ancillary services such as ASCs and laboratory testing.

There has been a tremendous increase in investment interest in the pain management sector during the last several years. Activity in this space since 2010 includes Chicago Growth Partners' acquisition of Advanced Pain Management, Sentinel Capital Partner's investment in National Spine & Pain Centers, and the 2012 formation of Prospira PainCare, which was created with the backing of three private equity firms and has acquired pain centers across the country.

In 2014, Pain Doctor, a leading pain management firm, accepted a significant capital investment by Catterton Partners, a consumer-focused private equity firm [15]. The intention was to expand Pain Doctor's network across the US to assist with the growth and expansion of its core business support and care services. This formed relationship has become the prototype model of successful collaboration between the healthcare industry and the financial sector and is likely to lead to further growth of the medico-economic relationship in years to come.

Entrepreneurship

Entrepreneurship can be defined as a process of identifying and starting a business venture or the addition of services in response to a revenue generating opportunity. Today's profit-driven, market-oriented healthcare industry may send mixed signals to physicians and patients. Many believe the doctor–patient relationship to be a social contract, not simply a business agreement. Some may argue that physicians have a conflict of interest when they have an obligation to act in their patients' best interest, but at the same time also have incentives to act in their own interest or to increase practice profitability. The traditional belief is that a physician earns their livelihood through professional efforts of healthcare delivery and that a physician's income should be derived from direct services or supervision of healthcare services and not entrepreneurial activities. An increasing number of physicians now have economic interests outside direct healthcare delivery such as additional healthcare services, ancillary goods, and facilities. It seems that business entities, insurers, hospitals, pharmaceutical companies, and the medical device industry are all making money, so why should the enterprising physician not be included? The legalities of healthcare such as Stark and anti-kickback policies help to keep overzealous providers from exploiting our patient population and regulating such ethically immoral activities. By contrast, the enterprising physician is now able to provide and coordinate services and goods on-site out of convenience to the patient and often at a discounted rate. The scope of services is vast with varying returns on investment.

Ancillary Revenue Streams

Self-employed physicians are entrepreneurs, in that they earn profits and bear the risk of loss from their practice (Fig. 73.6). They sell medical services, tests, drugs, medical devices, and may own or invest in hospitals, ASCs, or other medical facilities. There are rapid and innovative developments in the pain management market space, which continues to grow. However, it should be noted that the ancillary market opportunities come and go at a rapid rate, with a relatively short shelf life as it pertains to maximum profitability. It is much more beneficial to stratify risk across large physician groups with shared interests as opposed to aggregates of independent practitioners. There are opportunities to improve healthcare delivery as well as to generate income, if you look.

Conclusion

The important issues facing pain management are access and survival of the specialty.

Fig. 73.6 Some ancillary revenue streams

Unfortunately, access may become difficult because of the Affordable Care Act, which has empowered the private insurers. Patient access and the survival of interventional pain management practices continue to be jeopardized by reduced reimbursement, increased regulations, and escalating costs. Evidence-based medicine and its comparative effectiveness are being strongly encouraged, but there is no robust evidence supporting these regulations from the private healthcare industry, which follows and supports them. The costs of managing a practice are tremendous, with increasing inflation, increasing benefit package requirements, reducing reimbursement, mandatory requirements of EHR, various quality issues, and ICD-10. Interventional pain management has come under attack with expensive infection control measures, which have increased the cost of drugs, depleted the differential paid for procedures performed in offices, and has reduced available profits for surgery centers, while hospitals continue to receive reimbursement at higher rates. Advocacy is the key to maintaining the profitability of pain medicine. The modern-day pain physician cannot afford to sit idly on the periphery, without active involvement. In the end, we are fortunate to be part of a specialty that continues to experience adequate compensation for our services when compared to other specialties. Focus should always be on delivering optimal care to the patient. A successful ethical practice, with strong leadership and foresight, will always help to maintain patient volume and to generate revenue.

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Chapter 74
Medicolegal Issues of Pain Medicine in the Rehabilitation Patient

Segun Toyin Dawodu

Introduction

Medical errors have been noted to cause between 44,000 and 98,000 deaths per year in hospitalized patients, which makes it the eighth leading cause of death in the USA [1]. In the outpatient setting, such errors are also rampant in the field of pain medicine, where the inherent dangers from the use of opioid prescriptions are ever more apparent. In many states, unintentional overdose from prescription opioid analgesics is becoming one of the leading causes of death [2].

There is increasing regulation and enforcement of protocols in the prescription of opioid medications along with an increasing number of sanctions and licensure revocations of pain medicine physicians in the USA related to opioid prescriptions.

The increasing need for prevention of legal consequences related to prescribing opioids will require better awareness. In addition, checks and balances will need to be in place for prevention or mitigation of their occurrence.

This chapter will focus on common legal issues that can occur in the practice of pain medicine from a broad perspective. These issues are not specific to pain medical practices alone. Legal issues that could arise can be classified as either civil or criminal in nature.

	Civil case	Criminal case
Domain	Private	Public (Federal or State)
Outcome against defendant	Liable	Guilty
	Economic compensation or noneconomic damages	Misdemeanor or Felony with possible jail time
Jurisdiction	Federal or State Civil Court	Federal or State Criminal Court

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	Civil case	Criminal case
Who sues?	Plaintiff (e.g., patient)	Prosecutor (Federal or State)
Legal service for indigent client	Not available for most cases	Available for most cases

It is important not to confuse civil law, as practiced in most European countries except for Great Britain, with civil cases as stated above. Also, it is also important to understand the type of law that is practiced in Great Britain, as well as its former colonies, and to understand that such practice in the USA is referred to as the common law. Most of the following discussions are based on the common law.

The majority of legal issues that arise in the practice of pain medicine are mostly civil cases. Criminal cases are increasing in number, especially if death is involved or in case that deal with the prescription of opioid analgesics. Such cases can be classified as both criminal and civil from the same transaction and occurrence, and decision in the criminal case can be used as evidence in a later civil case.

There are other laws enacted by Congress or by the State, which provide strict liability, regardless of prior knowledge of that law or by intent in the act. An individual is strictly liable whenever the requirements of the law are not met. This is often classified as a misdemeanor and rarely a felony except as stated otherwise. Other legal issues may arise from contractual obligations and employments of others either directly or as independent contractors. While this topic will not address the totality of legal issues in pain medicine, the following discussions will focus on relevant legal terms.

Relevance to Clinical Practice

Civil cases tend to be assessed under Tort laws that may require intentional acts or voluntary acts, or those that do not require intentional acts. The most common area of litigation in medicine in general, and specifically to pain medicine, is negligence.

Medical Negligence: Generally, negligence requires some elements that have to be present, which include the following [3]:

Duty of Care

This is a duty owed to foreseeable plaintiffs in the zone of danger, defined as the amount of care that is expected from a reasonable prudent person under such circumstances. For physicians, this is based on a national standard. For a specialist in pain medicine, duty will be based on the national standard expected of a board-certified pain physician.

Duties of care are presumed where there is assumption of risk, such as with the treating physician, statutory obligation as based on statutory law or regulations, contractual obligation such as concierge medicine, existing relationship such as that between a patient and a physician even outside the hospital, and creation of a peril such as

when a physician tries to help and makes the situation worse. Overall, while there is no general obligation to come to the aid of another, trying to help and in so doing creating more problems leads to a duty to care under creation of a peril.

Breach of Duty

This is when the above duty is not met under the expected circumstance. For example, if the expected standard of care fell short of the national standard.

Causation

This is based on two parts, which include actual causation and proximate causation. Actual causation is based on the "but for" test, if there is a single defendant whereby but for the act of that defendant, there will not be harm that ensues. In a situation where there are possible multiple defendants, the "substantial factor" test is used in terms of effects leading to the harm. In a situation where this is unascertainable, there is a "shift of burden of proof" test, which shifts the burden of proof to the defendant. This shift of burden occurs where multiple physicians are caring for a patient and a mishap occurs in which there is difficulty in finding a substantial factor for the mishap. The burden shifts to each of the defendants to prove that each individually was not culpable.

Proximate causation is the direct or indirect cause of the harm that the patient experienced. A direct cause is a foreseeable cause when the expected duty is breached. An indirect cause is a consequence that is an intervening cause. For example, an indirect cause occurs if an epidural injection by a pain physician leads to an epidural abscess from negligent nonuse of an aseptic technique, which subsequently leads to the need for surgical decompression, which in turn leads to a spinal cord injury. The interventional pain physician may be liable for the spinal cord injury because the surgical decompression is an intervening action. The intervening cause test does not apply if such act is due to an intentional tort or a crime.

Damages: There has to be harm in the process of the breach of the duty of care for medical negligence to occur.

Res Ipsa Loquitur

Under the breach of duty of care, and the doctrine of Res Ipsa Loquitur, it is presumed that the very nature of a medical mishap which causes injury to a patient suggests negligent conduct, even if there are not enough facts to define breach. This is because of unknown circumstances of the events leading to the injury. This requires three elements:

- The harm will not normally occur without negligence.
- Such harm will normally be caused due to negligence on the part of the defendant, which in this case is the physician.
- The circumstances under which the harm occurred were in the exclusive control of the defendant (physician).

An example of Res Ipsa Loquitur includes a circumstance whereby a patient came in for an epidural injection under sedation, walks into the procedure room on that day, but after the procedure is found to be paraplegic. The above three elements would be applicable and this would avoid the need to try and prove that there is either a breach or non-breach of duty.

There are defenses to medical negligence that include an **assumption of risk,** such as when a patient is fully aware of all the risks through an informed consent process and still opts to proceed with the treatment plan. **Contributory negligence** is based on a patient contributing to the harm by his/her action, which may bar recovery in minority jurisdictions. **Comparative negligence** is based on the percentage of culpability in which a jury will assign a percentage of faults; **pure comparative fault** is based strictly on that percentage, whereby **partial/modified comparative fault** only allows the patient to recover his/her percentage if it is below 50% and none if it is above 50%. The tort cases requiring intentional acts include assault, battery, false imprisonment, and intentional infliction of emotional distress.

Assault

This is a voluntary/intentional act by a defendant, which causes reasonable apprehension of imminent harmful or offensive contact. The defense to this is appropriate consent, which could be expressed or implied. This situation could arise when a patient feels threatened by a physician's action, even if it is only perceived as imminently harmful or offensive contact.

Battery

This is a voluntary/intentional act by a defendant that causes harmful or offensive contact. In this instance, consent is also a defense. Both assault and battery could occur together, whereby touching a patient is termed offensive or causes harm. This could occur after a procedure is performed without consent, is performed on the wrong part of the body from that which was consented to, or when the scope of consent is exceeded.

False Imprisonment

This is an intentional act or omission that confines or restrains a plaintiff by the defendant to a bounded area, without alternative option of escape, and the plaintiff is aware or is harmed by such confinement. This could occur in an office setting when a patient wants to leave but is physically or chemically restrained from moving around or leaving.

Intentional Infliction of Emotional Distress (IIED)

This is an intentional or reckless extreme and outrageous conduct, which leads to severe emotional distress. This could occur when a patient is mistreated or mishandled. A bystander could sue for IIED if he/she was present when the injury occurred, if he/she is a close relative of the patient, and if the defendant is aware that the relative was present and closely related to the patient.

Each of the preceding examples could plead the defense of informed consent. Informed consent could be expressed when either written or when agreed upon orally; however, it is better to always have written consent in writing. Consent could also be implied, such as when a patient walks into an office to see a physician; however, implied consent has to remain within the reasonable scope of expectation. The reasonable standard is an objective standard based on the expectations of a prudent and reasonable member of the public.

The informed consent process requires both legal and mental capacity. Legal capacity is dependent on age; in the USA, patients must be 18 years or above to give consent. Mental capacity assumes that a patient has the mental faculties to understand and to make an informed consent, and if not, consent from a legal guardian or contact with official power of attorney is required.

There are other tortious acts that could lead to legal actions. In brief, these include the following

Misrepresentation

This includes both "intentional" and "negligent," in which there is misrepresentation of material fact that the defendant knows or believes is false, which induces the plaintiff to justifiably rely on such misrepresentation, which in turn causes harm.

Product Liability

This applies when a product used by a physician causes harm, such as when a tainted compounded medication is used for an epidural steroid injection and leads to an unintentional consequence. Such product liability actions will be analyzed under negligence as stated above.

Vicarious Liability

This is also termed the doctrine of Respondeat Superior and makes employers liable for torts committed by employees, within the scope of their employment. A **frolic** is a circumstance whereby the employee's actions were not within the scope of

employment; a **detour** is an action that is not within the scope of employment, but is done during the phase of scope of employment.

Intentional torts are generally not applicable, except when it occurs within the job description of the employee, such as when restraining a patient, if needed. As independent contractors are not employees, employers are generally not liable for their actions, except when the contractor is doing a job that is within the control of the employer, such as when a credentialed medical staff is moonlighting, or when there is negligence in hiring medical staff, whereby candidates are not properly vetted.

Under criminal law, **Assault and Battery** is also defined as above under torts, which means that a physician may be liable for assault and battery under both civil and criminal actions. Other criminal liabilities are the following:

Homicide

This is the killing of another human being with malice aforethought and without legal justification (i.e., unlawful killing). Malice aforethought could include the intent to kill or to cause serious bodily injury, wanton and reckless indifference to life, and felony murder, whereby death occurs during the commission of a felony of battery, arson, robbery, rape, or kidnapping. Murder under the intent to cause serious bodily injury can be claimed when a treatment is perceived to have the potential to cause severe bodily injury, or when the treatment is perceived to be tantamount to reckless and wanton action.

Under homicide, categories include the following: first-degree murder, second-degree murder, voluntary manslaughter, and involuntary manslaughter.

First-Degree Murder

This is deliberate, willful, and premeditated and enumerated murder, as stated above. This circumstance might arise in a rehabilitation/palliative medicine setting, as in the circumstance of a merciful killing (euthanasia) of a terminally ill person using opioid medications.

Second-Degree Murder

This includes everything other than murder as stated above under common law.

Voluntary Manslaughter

This arises in a murder with adequate provocation, which might occur in the heat of passion when there is no time to cool off and there was no cool off period.

Involuntary Manslaughter

This occurs when death is caused by criminal negligence, which is defined as reckless disregard for others [4], or after battery or misdemeanor. This could also occur after a negligent action leads to death, which could be the result of a prescription of opioid analgesics, or by failing in the duty of care as the treating physician.

Legal defense for the crime of homicide, applicable in medicine, will often be based on the lack of the necessary intent, which can change a case from first- or second-degree manslaughter to a lesser charge of involuntary manslaughter.

There are other laws and regulations that could make a pain physician liable if breached and include the following.

Civil False Claims Act

This involves knowingly presenting or causing to be presented, a false or fraudulent claim to the US government for payment. This could occur by sending a false claim to Medicare for a patient that was never treated, by up-coding, by falsifying certificates of medical necessity, and by unbundling. Most physicians who have been prosecuted were prosecuted based on their perceived reckless disregard for truth in conduct, whereby such conduct is out of line with normal business. The penalty for this includes a $10,000 fine for each false claim, exclusion from participation in a federal healthcare program such as Medicare and Medicaid, and triple damages in any civil suit.

Under the **Qui Tam Relator** doctrine, a whistleblower can bring an action under this act, as a private party, or on behalf of the US government. That party will be entitled to 15–30% of the amount recovered by the government, which may sometimes even include legal fees.

Criminal False Claims Act

This is an act of knowingly making a false claim, with the intent to defraud the government. The penalty for this is a felony, which is punishable by imprisonment for up to 5 years with a possible fine of $250,000 for individuals and $500,000 for institutions.

Anti-kickback Law

This was created in 1972 and administered by the office of the Inspector General (OIG). It includes knowingly or willfully inducing, soliciting, or accepting remuneration, offers, or payment, in return for the purchase order of items paid for through a federal program. Penalties include imprisonment of up to 5 years for each violation, a fine of up to $25,000 per violation, and exclusion from federal programs if criminal prosecution occurs through the OIG. Furthermore, it could lead to a civil penalty of up to $50,000 per violation, along with assessment of up to three times the amount of the illegal payment.

Stark Law

This is similar to the anti-kickback law and prohibits physician self-referral. Penalties include repayment of all claims made in self-referral, $15,000 per prohibited service, and exclusion from all federal programs. There is an exception to Electronic Medical Records (EMR) adoption and cooperation.

Obstruction of Criminal Investigation of Healthcare Offenses

This includes willfully obstructing, misleading, delaying, or engaging in any action that makes it difficult to have access to the records of a criminal investigator, who is in the process of investigating a violation of a federal healthcare offense. This can occur after requests for records are denied or when records are destroyed in the process of avoiding such criminal investigation.

HIPAA/HITECH

The Health Insurance Portability and Accountability Act (HIPAA) was passed in 1996 and states that a covered entity may not use or disclose protected health information (PHI) , except as permitted or required for treatment, payment, healthcare operations, operation of the law, patient authorization, or waiver of that patient's authorization. It does not cover PHI that has been de-identified.

The Health Information Technology for Economic and Clinical Health (HITECH) is part of the American Recovery & Reinvestment Act (ARRA), which is also called the "Stimulus Package." It provides expanded and strengthened enforcement for HIPAA, with increased penalties. It enhances security breach notification and extends HIPAA to business associates, among others. Penalties for HIPAA violations

include a minimum of $100 per violation and a maximum fine of $25,000 per calendar year, for cases in which offense was not unintentional. There is a minimum fine of $1000 per violation and a maximum fine of $50,000 per calendar year for violations due to reasonable cause, but not due to willful neglect; there is a minimum fine of $10,000 per violation and a maximum fine of $250,000 per calendar year for an infringement corrected by the organization once detected, and not due to willful neglect; there is a minimum fine of $50,000 per violation and a maximum fine of $1.5 million per calendar year for violations due to willful neglect, which are not corrected by the organization.

Cutting Edge/Unique Concepts/Emerging Issues

Risk management in a pain medicine setting involves taking steps to avert an actual or potential calamity through the provision of a safe and effective environment. This should include having a dedicated risk management department, which should be staffed with people experienced in taking appropriate steps in preventing or mitigating such risks. State and national regulatory bodies, such as Joint Commission for Accreditation of Healthcare Organization (JCAHO) and Commission on Accreditation of Rehabilitation Facilities (CARF), also require risk management, which is recognized by payors and the Center for Medical Services (CMS) as evidence of the set standard of care.

With increasing regulations in prescribing opioid medication in addition to the increasing abuse of such opioid medications, there is a need to follow all regulations, which include maintaining an opioid agreement, random drug testing, patient self-disclosure of opioid abuse, and excuse from liability for potential discharge from care, due to positive random drug tests. For these reasons, having a risk management team in place is essential. The responsibilities of risk management include identification, analysis, treatment, and evaluation of possible hazards. A dedicated risk manager has the responsibility to ensure prevention and reduction of loss, claims management, financial risk, risk regulation, and accreditation compliance [5].

Various protocols and steps should be in place as part of risk management, which include the following:

- Adequate documentation of every patient encounter. The EMR helps in this regard.
- Policies, procedures, and enforcement of treatment protocols, as these form part of the operational steps and standards of care.
- Incidence and occurrence reporting, especially at the time of the incident by those directly involved. This helps in preventing mishaps in the future by instituting new policies and training, and can also be the basis for evidence of events as part of the business record doctrine.
- Update on new rules and regulations affecting treatment of pain patients and the enforcement of such rules and regulations.

The increasing legal use of marijuana by the public is creating the potential for a new set of complications that could lead to litigation, especially if the patient is also using marijuana in addition to prescribed opioids.

Conclusion

This chapter covered the basic legal issues pertinent to pain medicine physicians, with a goal of providing a baseline level of knowledge to avoiding legal minefields and an awareness towards mitigation. This chapter does not provide any legal advice per se. It is always advisable to acquire the services of an attorney as early as possible when any legal issue should arise.

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