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Pain Medicine

An Essential Review

Springer

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Foreword

Pain Medicine is a young and growing field with continually evolving concepts, pathways, and procedures. Furthermore, with the multitude of specialties participating in this multidisciplinary field, the knowledge base required of pain practitioners is immense. While all pain fellowships now require exposure to psychiatry, neurology, anesthesiology, and physiatry, one year is a short amount of time to attempt a full mastery of all these disciplines that are needed to become a pain management expert.

This excellent resource was conceptualized by accomplished clinicians and educators at Harvard Medical School and beautifully encapsulates the practical information needed for pain practitioners. This comprehensive work covers all important clinical concepts in depth. I encourage all trainees, recent graduates as well as seasoned practitioners to use this resource as it covers all the disciplines of pain medicine in an easily digestible format with clinical pearls aimed at having pain practitioners learn from the experience and wisdom of the writers.

This evidence-based, up-to-date book should be a go-to reference for all, as there are many aspects of pain medicine, from basic to complex concepts, that we are all required to master and for which we sometimes need a little refresher. The editors have a passion for education as evidenced by their numerous teaching awards and their ability to distill complex topics into concise summaries and pearls. I highly recommend this book, and they should be very proud of their work.

Department of Anesthesia, Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, MA, USA

Edgar L. Ross

Preface

Written by residents, fellows, and attending staff, the book provides practical and concise information for pain medicine. The **inception of the idea** of the book came due to the limited references available that concisely summarize pertinent topics that are frequently encountered in the field of pain medicine. Pain medicine is a diverse field with an expansive breadth of knowledge required.

Pharmacology, physical examination, radiology, anatomy, neurology, and psychiatry all have to be incorporated seamlessly to be an effective pain physician. For new graduates, there are a multitude of materials available from many different sources to cover everything from imaging to pharmacology. Because there is not one concise textbook available, new graduates often find themselves resorting to Internet searches to answer simple questions as "what is the CPT code for a trigger point injection?"

Our purpose in writing this textbook is to create an easy to read yet comprehensive resource for new graduates, providing clinical pearls and practical information for the aforementioned variety of topics.

We are grateful for the support of all our contributors from many different institutions, as well as the house staff, fellows, and attendings at Vanderbilt, the US Navy, Albert Einstein College of Medicine, and Brigham and Women's Hospital. As physicians, we feel privileged to work with an incredible group of individuals who support our clinical activities each day. This includes our surgical colleagues, nursing, and support staff.

We are especially indebted to a number of individuals, whose unending support and encouragement made this work possible. These include Drs. Charles Vacanti, Edgar L. Ross, Tara Sheridan, and Karina Gritsenko. We would like to thank the Springer staff, including Michael Wilt and Shelley Reinhardt.

Finally, a very special thanks to our parents and families for their continued encouragement, love, and support.

We hope you find this book practical and please provide feedback so we can make this as useful as possible as you endeavor as a new pain physician.

Boston, MA, USA

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Part I

General

1 Anatomy and Physiology: Mechanisms of Nociceptive Transmission

Daniel Vardeh and Julian F. Naranjo

Nociception is the measurable physiological response of specialized sensory receptors (nociceptors) to overt or potential tissue damage and is perceived in the CNS—via the spinothalamic tract, the thalamus, and finally different areas in the neocortex—as pain. Initially, noxious chemical, mechanical, or thermal stimuli are detected at nerve endings of primary sensory neurons with their soma located in the dorsal root ganglion (DRG) for body sensation, and in the trigeminal ganglion (gasserian ganglion) for face sensation. Specialized receptors (**transducers**) located at the cell membrane of sensory nerve endings translate the intensity of a given stimulus into action potential frequency, which results in the emission of glutamate and peptides in the respective area in the spinal cord dorsal horn (mostly superficial laminae I and II with some projections to lamina V).

Nociceptors can be divided into different groups by means of their anatomical structure, their characteristic expression of various proteins or the distinct receptors at their terminals, as described below.

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Fibers Types of Nociceptors

Generally, A-δ and C-fibers are the major contributors to physiological nociception, with A-β fibers contributing in pathological states of central sensitization.

C-fibers are small in diameter; they are unmyelinated and conduct impulses at the slow rate of 0.5–2 m/s. C fibers have smaller receptive fields than the A-δ nociceptors and mostly terminate in lamina LII of the spinal dorsal horn. Their activation results in a more prolonged sensation of dull and burning pain. Most C-fibers are polymodal receptors and are activated by high-threshold mechanical and various chemical stimuli, as well as by heat (starting at 39–41 °C). These polymodal C-fibers are heavily influenced by both the phenomena of sensitization (enhanced response to a lasting/repetitive stimulus of same intensity) and fatigue (reduced response to a lasting/repetitive stimulus of same intensity).

A-δ fibers function as thermal and high-threshold mechanical receptors. Generally, they respond with higher discharge frequencies than C-fibers and the discriminable information supplied to the CNS is greater. Most of these fibers have polymodal properties (with high heat threshold at 40–50 °C), are thinly myelinated (conduction velocity between 5 and 35 m/s) and terminate in LI and LV of the dorsal horn. Activation of A-δ fibers generally results in a short sensation of sharp, pricking pain, in contrast to the dull sensation mediated by C-fibers.

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A-β fibers are myelinated fibers (conduction velocity 35–75 m/s) which play a major role in encoding muscle spindle information and vibration. They also conduct typically innocuous mechanical stimuli, but some also encode stimulus intensities in the noxious range and in some cases respond to noxious heating of the skin. A-β fibers are major players in mediating allodynia (a painful feeling upon gentle touch) in states of central sensitization.

Molecular Properties of Nociceptors

Under physiological conditions, nociceptors do not fire spontaneously. Their electrical action potential is triggered by transduction, which occurs when a noxious stimulus of sufficient strength depolarizes the nociceptor membrane. The specific receptive properties of nociceptors are determined by their membrane bound transducing ion-channel receptors. These ion channels are nonselective potassium or sodium channels gated by temperature, chemical stimuli, or mechanical shearing forces. Activation of these channels leads to depolarization of the membrane, which—if strong enough—results in activation of voltage-gated sodium channels, leading to further depolarization and burst of action potentials, which will finally result in glutamate release at central terminals in the spinal cord. The duration and frequency of this signal is determined by the duration and intensity of the noxious stimulus.

Heat

Several unselective cation channels have been described to transduce increased temperature into membrane depolarization. **TRPV1** is characterized by a moderate heat threshold around 43 °C and its activation by capsaicin (the pungent ingredient in chilli peppers). **TRPV2** does not respond to capsaicin and shows a high heat threshold of over 50 °C. Other TRPV channels, namely **TRPV3** and **TRPV4**, have been described with thermal activation thresholds between 31 and 39 °C and thus are probably responsible for the sensation of warmth. TRPV channels have been shown to be substantially expressed in keratocytes indicating an important role of the epidermis in heat detection. Moreover, TRPV1 plays a pivotal role in setting the heat threshold to lower levels in state of inflammation and is therefore substantially contributing to heat hyperalgesia.

Cold

Similar to the TRPV family, a closely related **TRPM8** receptor has been described, with a thermal activation threshold of 26 °C and chemical activation by Menthol. While TRPM8 with its moderate cold threshold is responsible for the perception of gentle cooling, the **TRPA1** receptor might be a sensor of "noxious cold" since it responds to temperatures below 17 °C. Other contributing and rather modulating mechanisms have been suggested, such as the inhibition of ubiquitously expressed K-channels by cool stimuli.

Mechanosensation

Evidence for mechanical transducer channels has been elusive and various theories exist to explain this mechanism. Whereas low pressure touch and muscle tension are generally detected by A-β and A-α fibers, high threshold mechanosensation is conducted by A-δ and C-fibers. Some studies suggest osmosensitive ion channels, which are directly gated by membrane stretch and distortion. Another hypothesis favors the model of ion channels being tethered to cytoskeletal or extracellular matrix molecules so that displacement relative to the cell surface can be detected.

Voltage-Gated Channels

Once transducing ion channels are activated by adequate stimuli, voltage-gated sodium channels are responsible for the rising phase of the action potential. They play a key role in determining

the excitability of the sensory neurons and in conduction currents from the periphery to the CNS. DRG neurons express several distinct types of sodium channels, including the **$Na_{v1.7}$, $Na_{v1.8}$, and $Na_{v1.9}$ channel**. The importance of these sodium channels in transmitting nociceptive stimuli is exemplified by the rare but dramatic human mutation of $Na_{v1.7}$, which results in loss of function and complete inability to sense pain. In contrast, autosomal dominant mutations leading to excessive channel activity of $Na_{v1.7}$ cause erythromelalgia, a condition characterized by episodes of burning pain in feet and hands, erythema and increased skin temperature in affected areas.

Central Projections

Once a stimulus has reached sufficient intensity and duration, transducers and subsequently voltage gated ion channels will produce robust action potentials which will travel from the nerve endings via the DRG into the **specific lamina of the dorsal horn** (LI, II, and V).

To transmit these incoming signals upon the central projection neuron, every central nociceptive terminal holds multiple neurotransmitters, usually an excitatory amino acid such as glutamate or aspartate, and modulating peptides such as substance P (SP), vasoactive intestinal peptide (VIP), somatostatin, and calcitonin gene-related peptide (CGRP). Incoming signals can be dampened or completely calmed by descending pathways originating in brain stem centers like the **periaqueductal grey (PEG)**, the serotoninergic **nucleus raphe,** and the norepinephrinergic **locus coeruleus**, which project mainly to superficial spinal laminae (LI and LII) and lead—via g-aminobutyric acid (GABA) and glycine—to inhibitory postsynaptic potentials (IPSPs) on central projection neurons. Further modulation of incoming signals is mediated by a complex network of inhibitory and excitatory **spinal interneurons**.

Projection neurons in the dorsal horn propagate the summation of this information via the **anterior and lateral spinothalamic tracts (STT)** to the thalamus. These tracts decussate within a few segments of the level of entry and terminate directly on central neurons of the **ventral posterior lateral (VPL) subnucleus** of the thalamus, conveying sensations of pain, temperature, and itch from the contralateral side of the body. **Trigeminothalamic axons** join the STT after decussating at the level of the medulla to convey equivalent sensation from the contralateral face. Other collaterals synapse on the **posterior Ventral Medial Nucleus (VMpo)**, which further projects to the posterior insula, where information is integrated with visceral afferent activity (e.g., vagal and gustatory afferents) to influence autonomic responses. Other projections run to the **medial dorsal nucleus (MDvc)**, which relies information to the anterior cingulate cortex and is important for the affective/motivational aspect of pain . Yet other projections reach **intralaminar thalamic nuclei** and have widespread cortical projections contributing to arousal and attention.

Suggested Reading

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Pharmacology of Pain Transmission and Modulation

2

Jürg Schliessbach and Konrad Maurer

Nociceptive Nerve Fibers

Pain is transmitted to the central nervous system via thinly myelinated Aδ and unmyelinated C-fibers. The former convey the sensation of sharp, lancinating "first" pain, whereas the latter conduct the dull, longer-lasting "second" pain. Aδ-fibers predominantly respond to mechanical stimuli (Type I or "high-threshold mechanoreceptor") or to noxious heat (Type II). Conversely, the C-fibers are polymodal, the same fiber responding to mechanical, thermal and chemical stimuli. Both Aδ- and C-fibers terminate in the superficial dorsal horn, mainly in Rexed Laminae I and II, although some Aδ-fibers also terminate in the deeper lamina V. In the periphery, the distal endings terminate freely in the tissues. These free nerve endings express a variety of signal transducing molecules, one of the most extensively investigated being the transient receptor potential ion channel TRPV1, also known as the capsaicin receptor [1].

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From Pain Transduction …

Apart from thermal or mechanical stimuli, several endogenous or exogenous compounds can activate the nociceptors. Examples for exogenous compounds include capsaicin or menthol, provoking heat and cold sensations via the TRPV1 and TRPM8 channel, respectively. Endogenous activators comprise histamine, serotonin, prostaglandins, bradykinin, substance P as well as H^+- and K^+-ions. They either directly activate the nociceptor or modulate its activation threshold—a process called peripheral sensitization. Neurogenic inflammation serves as an example for peripheral sensitization of nociceptors: noxious stimulation of a free nerve ending causes release of substance P and calcitonin-gene related peptide (CGRP) from adjacent nerve endings via axon reflex. These mediators in turn attract leukocytes that release cytokines and mast cells that release histamine. The cytokines (IL-1 and TNF-α) and histamine stimulate and sensitize the nociceptors, thus causing ongoing pain and hyperalgesia.

… to Pain Transmission

Upon activation by a noxious stimulus, the primary afferent neurons release excitatory neurotransmitters in the dorsal horn. Aδ-fibers mainly release glutamate while the so-called

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"peptidergic" C-fibers release neuropeptides, in particular substance P. Glutamate excites the second-order neuron in the dorsal horn primarily via the ionotropic AMPA-receptor, resulting in immediate propagation of a sharp, localized pain signal. Substance P, on the other hand, binds to the neurokinin-1 receptor, a member of the G-protein coupled receptor family. The ensuing intracellular signaling cascade is complex and involves activation of arachidonic acid pathways, nitric oxide synthesis and NMDA-Receptors (see below). Changes in gene expression, receptor upregulation or downregulation and dendritic spine formation may occur, ultimately leading to a state of sustained hyperexcitability. This so-called central sensitization is characterized by enhanced response to noxious stimuli, enlargement of receptive fields and painful response to usually non-noxious stimuli [2].

Selected Key Players in Pain Processing

- ***NMDA-Receptors*** are ion channels that are blocked by a Mg^{2+}-ion in the resting state. Binding of glutamate to the receptor does not cause activation unless the Mg^{2+}-ion has been removed by prior depolarization of the cell membrane. This may occur after sustained excitation of the cell, e.g., by AMPA-receptors or substance P. NMDA-receptors are therefore said to be both ligand- and voltage gated ion channels. Following opening of the channel, Ca^{2+}-ions enter the cell and initiate a signaling cascade that is thought to be responsible for long-term potentiation and wind-up. Ketamine, methadone, and dextromethorphan are examples of substances acting as (partial) antagonists at the NMDA-receptor.
- ***Voltage-gated calcium channels (VGCC):*** Several classes of VGCC exist throughout the body, of which the N-type and the T-type channel play a role in nociception. The N-type channels are found presynaptically and are involved in transmitter release (glutamate and substance P) upon arrival of an action potential. They can pharmacologically be inhibited by several medications (Gabapentin, Lamotrigine, Ziconotide), thereby reducing excitation of the postsynaptic neuron. The T-type channels are present on both first- and second-order neurons and have more a complex function. They take part in sensitization of neurons by co-activating NMDA-receptors or decreasing the threshold for action potential generation. No T-type-selective drugs are available to date, but anticonvulsants such as Pregabalin or Gabapentin may exert some of their effect by blocking a subunit of these channels.
- ***Opioid receptors*** belong to the family of G-protein coupled receptors. They are abundantly present all along the neuraxis and mediate both spinal and supraspinal analgesia. They are even expressed at peripheral nociceptive nerve endings in states of tissue injury and inflammation. According to their respective endogenous ligand, they are classified as μ-, δ-, and k-opioid receptors which differ in terms of localization and function. However, effects common to most subtypes are inhibition of VGCC (thereby reducing release of excitatory neurotransmitter) and opening of potassium channels leading to hyperpolarization (rendering neurons less sensitive to excitatory transmitters). Endogenous opioids (endorphins, enkephalins, dynorphin) are found in the CNS and in the periphery. In the CNS they are released by spinal interneurons or brainstem projection neurons, in the periphery they stem from opioid-secreting leukocytes. Morphine and its semi-synthetic analogues are among the most potent analgesics that are currently available.
- ***Gamma-aminobutyric acid (GABA)*** is the most abundant inhibitory neurotransmitter in the CNS. There are two types of GABA-receptors: the $GABA_A$-Receptor is a ligand-gated chloride channel causing hyperpolarization of the cell membrane when activated. The $GABA_B$-Receptor is a G-protein coupled receptor which stabilizes the membrane potential via opening of K^+-channels. GABAergic interneurons in the dorsal horn form axo-axonal synapses with first-order

nociceptive neurons, thereby causing presynaptic inhibition of excitatory neurotransmitter release. $GABA_A$-agonists have been shown to exert anti-hyperalgesic effects in animal and human experimental pain models. Benzodiazepines are allosteric modulators of the $GABA_A$-receptor, increasing its affinity for GABA. Baclofen is a $GABA_B$-agonist used to treat spasticity.

Descending Pain Modulation

Spinal processing of nociceptive signals is modulated by projection neurons descending from the brainstem to the dorsal horn. The most important brainstem sites include the periaqueductal gray (PAG) and the rostral ventral medulla (RVM) for serotonergic cells as well as the locus coeruleus for norepinephrinergic cells.

Serotonin is released in the spinal cord after simulation of the RVM and the PAG. However, its role in pain processing is less clear as it produces both pro- and anti-nociceptive effects, depending on the type of receptor activated. Currently, there is no pharmacologic means that specifically targets the serotonergic system. Although both tricyclic antidepressants and the newer serotonin-norepinephrine reuptake inhibitors (SNRI, e.g. duloxetine) act on the serotonergic system, norepinephrinergic mechanisms are more likely to explain their analgesic properties.

Norepinephrine binds to presynaptic α_2-adrenoceptors located on the primary afferent neuron, thus reducing the amount of glutamate and substance P released. The result is a strong antinociceptive effect at the level of the dorsal horn. This mechanism possibly explains the analgesic effect of the commercially available α_2-adrenergic agonists clonidine and dexmedetomidine.

Dysfunction or loss of descending pain modulation has been implicated in many chronic pain disorders. But despite considerable efforts, these endogenous modulatory systems are far from completely understood. Other inhibitory pathways are currently being investigated, including the neurotransmitters glycine and oxytocin. New receptors and transmitters continue to be discovered and pharmacologic modulation of inhibitory pathways might be a promising therapeutic target in the future.

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Development of Pain Systems

3

Ingrid A. Fitz-James Antoine, Karina Gritsenko, and Veronica Carullo

Physiologic and Behavioral Pain Assessment Measures in the Fetus and Newborn

The assessment of pain intensity traditionally relies on analgesic scoring methods that utilize self-reporting. This is not applicable in the preterm infant and newborn. In this vulnerable population, pain behavior guides assessment.

Behavioral parameters: facial grimace*, cry, body movement, sleep pattern

*Facial expression—most useful and specific in neonates (eyes tightly closed, furrowed eye brows, square mouth)

Physiologic parameters: heart rate/heart rate variability, respirations, oxygen saturation, blood pressure, vagal tone, palmar sweating, plasma cortisol, cortical hemodynamic assessment via near-infrared spectroscopy (NIRS)

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Neonatal Pain Scales

- typically combine behavioral observations with physiologic criteria
- useful for assessment of acute pain, but not prolonged pain states

Common scales utilized:

1. The Neonatal Infant Pain Scale **(NIPS)** facial expression, crying, breathing pattern, arm movement, leg movement, and state of arousal (6 indicators, maximum score: 7)
   - used to assess procedural pain in preterm and full term infants
   - popular due to practicality, ease of use
2. Premature Infant Pain Profile **(PIPP)** gestational age, behavioral state, change in heart rate, change in SpO2, brow bulge, eye squeeze, nasolabial furrow (7 indicators, maximum score: 21)
   - used to assess neonatal procedural and postoperative pain
3. Crying, Requires oxygen to obtain saturation > 95%, Increased vital signs, Expression and Sleepless Scale **(CRIES)** (5 indicators, maximum score: 10)
   - used to assess neonatal postoperative pain
   - primarily utilized in research setting
4. Neonatal Pain, Agitation and Sedation Scale **(NPASS)**

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crying/irritability, behavior state, facial expression, extremities/tone, vital signs (5 indicators, positive score indicates pain, negative score indicates sedation, range: −10 to 10)
- developed to assess both infant pain and sedation in the neonatal intensive care unit (NICU)

General: Development of Pain Systems, by Gestational Age (GA)

Cutaneous/peripheral nociception:

- By 7 weeks GA—cutaneous, perioral peripheral nociceptors
- By 11 weeks GA—spread to the face, palms of hands, and soles of feet
- By 15 weeks GA—spread to the trunk and proximal portions of arms & legs
- By 20 weeks GA—spread to all mucocutaneous surfaces

Development of central nociception:

- 8–12 weeks GA—Migration of cerebral cortical neurons from periventricular zone to cortical zone; extension of peripheral nociceptive fibers into the dorsal horn of the spinal cord (larger A fibers enter prior to C fibers)
- 12–16 weeks GA—Thalamocortical projections and laminar structure begin to form
- 20 weeks GA—All cortical neurons formed
- 23–25 weeks GA—Free nerve endings and spinal cord projections fully mature*
- B/w 22–30 weeks GA—Myelination of pain pathways in spine and brainstem complete
- By 30 weeks GA—Extension of myelination into thalamus
- By 37 weeks GA—Extension of myelination into cortex
- Post-term—Development of cortical descending inhibition

**Although thalamocortical connections are not fully developed until 30 weeks gestation, the 24-week fetus possesses all the sensory neural elements necessary to perceive noxious stimuli.*

Development of Pain Behavior in the Fetus and Newborn

The most common pain behavior studied in preterm and term infants (and in the rat model) is the flexor reflex response of the lower extremity in the setting of acute injury, acute inflammation, and acute reinjury [1].

Repetitive low-intensity skin stimulation provokes hyperexcitability at lower threshold and is visualized as movement of all limbs.

More robust response to noxious stimulus is documented in younger preterm infants (magnitude and duration).

- Flexor reflex thresholds is very low and the response is synchronized and long-lasting
- Repetitive noxious stimulation results in sensitization (i.e., wind-up)
- Cortical responses studied in infants through the application of real-time near-infrared spectroscopy (measures total hemoglobin concentration over the contralateral somatosensory cortex) [2].
- Robust response to noxious stimulation (heel lancing) was demonstrated under the influence of wakefulness with an increase in magnitude and decrease in latency with increasing age.
  - This response did not occur with mechanical stimulation, even when reflex withdrawal occurred.
- Response less exaggerated as maturation occurs
  - Maturation thought to be the consequence of growth and connectivity in primary afferent terminals in the spinal cord

Development of Peripheral and Dorsal Horn Mechanisms of Nociception and Nociceptive Connections in Higher Centers

Nociception must be distinguished from pain which implies central processing in the somatosensory cortex.
Nociceptors = free nerve endings which transmit the action potential generated by localized tissue

injury and mechanical stimulation to the dorsal horn of the spinal cord.

Classes of nociceptors:

1. C-fibers (unmyelinated)—largest group of nociceptors; slow conduction; transmit electrical impulses generated by thermal, mechanical, or chemical stimuli; responsible for sensing slow, diffuse pain.
2. Aδ fibers (thinly myelinated)—faster conduction; transmit noxious stimuli generated by tactile stimulation (discriminative touch and proprioception); responsible for sensing sharp, pricking pain.
3. Silent nociceptors—activated by endogenous inflammatory chemical mediators as a result of tissue injury and intense mechanical stimulation. Increased and spontaneous activation may occur in response to noxious and repetitive innocuous stimulation of these neurons, which become the basis for chronic pain states.
   - Neonates have a greater density of high threshold thinly myelinated mechanoreceptors per square centimeter than C fiber density or connectivity in the spinal cord.
   - Spinal cord develops ventral to dorsal → motor neurons followed by deep dorsal horn neurons followed by substantia gelatinosa neurons.

Nociception = sensation of painful stimuli and depends on the transmittal of action potential through ascending pathways to subcortical and cortical regions of the brain and is modulated by descending pathways originating in the rostroventral medulla which mature in the human neonate postnatally.

- Noxious stimulus is detected at the peripheral terminal of a nociceptive neuron (primary afferent neuron) where an action potential is generated
  - Cell body located in DRG
- Peripheral axon has two branches:
  - Distal process—attached to a terminal nerve ending which senses a stimulus
  - Proximal process—transmits the stimulus to the dorsal horn of the spinal cord where it synapses and sends ascending signals via the spinothalamic tract
- When the stimulus reaches a critical threshold, it is transmitted to the central nervous system.

Long-Term Consequences of Neonatal Pain

Long-term effects of neonatal pain are not well-defined, but there is some preliminary evidence that suggests that early pain experiences and responses can influence later pain behaviors and neurodevelopment.

- Long-term alterations in pain-related behaviors at 4–6 months of age in non-anesthetized circumcised infants in their response to immunization [3].
- Greater pain in preterm infants is associated with reduced white matter integrity and increased grey matter neuronal loss [4].

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Peripheral and Central Sensitization

4

Daniel Vardeh and Julian F. Naranjo

Neuronal excitation in nociception is not a static process of the kind "same stimulus–same response," but rather underlies dynamic plasticity to adapt to different situations. **Allodynia** (pain due to a stimulus that does not usually provoke pain) and **hyperalgesia** (increased pain from a stimulus that usually provokes pain) both exemplify these dynamic changes, and are the result of a leftward shift of the stimulus–response curve to a specific (e.g., a mechanical or temperature) stimulus. Hyperalgesia/allodynia is typically divided into two types. While hyperalgesia occurring at the site of injury is termed primary hyperalgesia, enhanced pain sensitivity in the sourrounding uninjured area is termed secondary hyperalgesia**. Primary hyperalgesia** is contributed to by sensitization of peripheral nerve endings (**peripheral sensitization**), whereas **secondary hyperalgesia** is due to changes in the spinal cord and higher brain areas (**central sensitization**). Depending on the provoking stimulus, hyperalgesia can be divided into **heat hyperalgesia** and **mechanical hyperalgesia**.

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Functional Changes

Altered sensitivity in response to mechanical or heat stimuli can be attributed to **different mechanisms**:

- Mechanically insensitive afferent A-δ and C-fibers show **lowered thresholds** after injury or inflammation and are therefore recruited to fire in response to nonhazardous stimuli;
- Other A-δ and C-fibers exhibit **enhanced responses** to suprathreshold mechanical stimuli;
- adjacent naïve receptive fields of A-δ and C-fibers start expanding into the injured area therefore **increasing innervation** and thus sensibility of the injured site;
- **recruitment of myelinated low-threshold A-β fibers**, usually mediating light touch, can under pathological circumstances convey painful stimuli (e.g., mechanical allodynia) due to changes in their central projection neurons in the spinal cord;
- Changes in the spinal cord mediated by altered neuronal gene expression, immune cell activation and modulation of descending inhibitory pathways results in **disinhibition** of pain pathways and secondary hyperalgesia

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Molecular Mechanisms of Sensitization

Peripheral Sensitization

Peripheral sensitization is a decrease in threshold, an increase in responsiveness and sometimes a spontaneous activity of peripheral ends of nociceptors. It occurs after **tissue damage and inflammation** and arises due to the action of inflammatory chemicals released at the affected site by both sensory nerve fibers and inflammatory cells. Some of these compounds can **directly activate peripheral nociceptors** (such as protons, ATP, serotonin) while others have a more **modulating role** leading to enhanced responsiveness of nerve endings. Two processes have been implicated in this increased sensitivity: (1) Early posttranslational changes in the peripheral terminals of nociceptors, e.g., phosphorylation of ion channels, and (2) altered gene expression.

Posttranslational Changes

Some inflammatory markers (e.g., bradykinin, histamine, prostaglandins, nerve growth factor) mediate their effects by activating **G-protein-coupled receptors** or receptor **tyrosine kinases** that initiate second-messenger pathways resulting in activation of **Protein kinases A and C**. Both protein kinases modulate activity of the sensory neuron-specific channels like $\mathbf{Na_{v1.8}}$ and $\mathbf{Na_{v1.9}}$ as well as transducer molecules like **TRPV1** by **phosphorylation**. This increases the excitability of nociceptors by lowering the threshold at which ion channels open and/or result in longer opening times, eventually resulting in prolonged depolarization and enhanced response.

Altered Gene Expression

In contrast to altered activity of ion channels, some responses to inflammatory stimuli travel back to the DRG cell body and **change transcription or translation** of certain proteins. Whereas local changes in terminal nerve fibers take minutes, transcriptional changes can take up to a day. A good example is upregulation of the TRPV1 channel by the release of nerve growth factor (NGF) triggered by local inflammation NGF.

Central Sensitization

Central sensitization differs fundamentally from peripheral sensitization. Peripheral sensitization is due to posttranslational and transcription changes in the terminal ends of high-threshold nociceptors resulting in primary hyperalgesia. Central sensitization in contrast typically manifests in **tactile allodynia** and **secondary hyperalgesia** (in tissue not affected by any harmful condition). Pain is generated as a consequence of changes within the CNS that lead to alterations of how to interpret sensory inputs, rather than reflecting the presence of peripheral noxious stimuli. The newly proposed **definition by the IASP** describes "central sensitization" as the "increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input."

This sensitization in the CNS, which ultimately results in enhanced synaptic transfer, is characterized by a number of distinct mechanisms:

Shorter lasting, activity triggered mechanisms include wind-up and heterosynaptic potentiation, whereas **long lasting effects** are due to alterations in microglia, astrocytes, gap junctions, membrane excitability, and gene transcription, all of which can contribute to the maintenance of central sensitization.

Wind-Up (Homosynaptic Potentiation)

Wind-up describes a phenomenon of increasing action potential output from dorsal horn neurons during a train of low frequency firing of C-fibers. By this repetitive C-fiber stimulus, higher calcium levels are achieved in the C-fiber central presynaptic terminal, which leads to release of increasing glutamate and peptides (like SP and CGRP), resulting in increasing postsynaptic depolarization. **This process results in progressively increasing output of the dorsal horn neuron during a train of identical incoming C-fiber stimuli**. The temporary plasticity created by wind-up is dependent on constant incoming activity and thus **does not outlast the stimulus**.

Heterosynaptic Potentiation

Heterosynaptic sensitization in the spinal cord differs in two ways from the wind-up phenome-

non: the increased responsiveness of the dorsal horn neuron outlasts the primary stimulus by hours; these changes affect not only the response triggered by the primary stimulus, but also the response to stimuli from other afferents converging on the same dorsal horn neuron. Ultimately, **subthreshold incoming stimuli from converging nociceptors as well as high threshold Aβ fibers are converted to suprathreshold action potentials due to the changes at the dorsal horn neuron**. This manifests clinically as hyperalgesia (stimuli originating from C and Aδ nociceptors), allodynia (stimuli originating from Aβ fibers) as well as secondary hyperalgesia due to recruitment of fibers supplying sensation to areas outside the primarily injured area.

Other Mechanisms

While the above changes can outlast the stimulus for hours, **longer lasting changes** in the CNS contribute to the maintenance of hyperalgesia, allodynia and secondary hyperalgesia for a much longer time. These changes are due to alterations in posttranslational processing (e.g., phosphorylation of ion channels) and gene transcription, immune cell/glial activation, and disinhibition at a spinal and supraspinal level.

Excitation of central synapses will eventually lead to activation of nuclear proteins like cyclic AMP response element-binding protein (CREB), resulting in **neuronal transcription** of early response genes like c-FOS and COX-2 and late response genes like NK1 and TrkB.

Neuron-immune cell interactions are increasingly recognized as playing a pivotal role in hyperalgesia elicited in states of inflammatory and neuropathic pain. Microglia at the affected level in the spinal dorsal horn respond to injury to peripheral nerves with a stereotypic response, including upregulation of the purinergic receptor $P2X_4$. In addition, there is evidence for T-lymphocyte recruitment into the spinal cord in experimental models for neuropathic pain. In this activated state, immune cells release cytokines which sensitize nociceptive signaling and disinhibit neurons in the spinal nociceptive network. Recent research has suggested that microglia activation might be closely linked to opioid induced hyperalgesia.

Inhibitory dorsal horn interneurons synapse with the central terminals of primary sensory neurons as well as postsynaptic projection neurons and thus are able to modulate nociceptive transmission (via release of GABA and glycine). On a higher level, **descending inhibitory pathways** originating in the anterior cingulate cortex (ACC), amygdala and hypothalamus reach the spinal cord via brain stem nuclei in the periaqueductal gray (PEG) and rostroventral medulla and exhibit a tonic inhibition of central projection neurons through release of norepinephrine, serotonin, and endogenous opioids. Impaired inhibition as a result of peripheral inflammation or spinal cord injury may unblock these pathways and lead to inappropriate spread of incoming afferents across modalities and somatotopic borders.

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Designing, Reporting, and Interpreting Clinical Research Studies

5

Steven Y. Chinn, Elizabeth Chuang, and Karina Gritsenko

Formulating Hypotheses

- Test a novel treatment
- Evaluate clinical practice variations
- Fill gaps in the literature

Determining Goals/Aims of Study

Precisely and narrowly define a goal to design the most rigorous study

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Minimizing Bias

1. *Sampling error*: deviation of the selected sample from the true characteristics of the population, limits generalizability.
2. *Validity:* the extent to which a measurement reflects the phenomenon it is intended to measure. Depends on subject's understanding of the question and ability to report an accurate answer. e.g., FACES scale is a more valid tool in pediatric populations who are unable to give a numeric rating for their pain
3. *Reliability:* the extent to which a measurement remains stable over repeated measures of the same phenomenon.
4. *Reporting bias*: subjects report answers they think the experimenter is expecting. Use computer or paper-based surveys or blinding subjects to the treatment group by using placebos. In pain, research using functional outcomes rather than self-report may minimize bias.
5. *Observer bias*: expectations of the researcher influences data collection/interpretation; minimized by blinding the examiner
6. *Confounding*: occurs when other variables could explain the observed relationship between the intervention and outcome.

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- happens when confounding variables co-occur with the predictor or intervention of interest
- minimized by randomization
- can be statistically controlled when confounders are known

Research Design

** Listed in order from strongest to weakest evidence of causality.*

Experimental:

1. Randomized Controlled Trial
   - Gold standard; can most confidently draw causal conclusions
   - Random assignment to intervention or placebo decreases likelihood that outcomes are due to a systematic difference between intervention and control groups

Observational:

2. Cohort studies group patients by exposure or nonexposure to risk factor and follow for development of outcome of interest
3. Case–control studies define patients by presence or absence of outcome and track back exposures to risk factors
4. Cross-sectional surveys "snapshot" in time to determine correlation between risk factor and outcome
5. Case series or case reports

Presenting Data

See Table 5.1.

Evaluating Statistical Significance

1. *p*-value: probability of obtaining the given data sets, assuming the null hypothesis is true (no real difference exists between data sets)
2. *alpha* (typically, 0.05): the probability at or below which the null hypothesis can be rejected. Must be set prior to data collection.
3. Confidence interval: likelihood that the population parameter is estimated by particular sample statistic
   - Typically 95% CI is calculated using the mean ± 1.96*standard deviation
4. Power: ability of a study to detect a true difference
   - *Power = (1 – beta)*, where *beta* (error) is the probability of falsely accepting the null hypothesis
5. Sample size: directly related to power, large studies will have a higher likelihood of detecting a difference.

Interpreting the Literature and Understanding Limitations

PICO Model: Determine relevance to your clinical practice

Table 5.1 Applying the Statistical Measures to the Data

Type of data		Statistics	Tests of association
Interval	Continuous (e.g., 1.23, 33.598)	Mean, median, mode	*t*-test, linear regression
	Discrete or integral (1,2,3, etc.)	Mean, Median, Mode	*t*-test, linear regression
Categorical	Ordinal—ordering or ranking (1st, 2nd, 3rd)	Frequencies	Mann–Whitney U, Wilcoxon test
	Binary—yes/no, alive/dead	Proportion or percent	Chi-square, logistic regression
	Nominal—different colors	Frequencies	ANOVA chi-square

Patient—what patients were included in the trial? Are they similar to my patients?

Intervention (or Exposure)—What was the intervention? Is it clearly defined?

Comparison—What was the comparison or control group? Were there potential biases?

Outcome—Is the outcome well-defined and measured correctly? Is the outcome important?

Baysean approach

Subjectivist approach that considers the *a priori* chances of a study finding being correct, based on previous literature and known medical facts. One study may shift thinking on a particular topic in the literature but a body of evidence is more convincing.

***Special Considerations for Pain Research** Many studies have a limited follow-up time due to financial and time constraints. Late adverse effects of treatments, e.g., long-term effects of chronic opioid treatment, may not be seen in short-term studies.

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The Oxford Centre for Evidence Based Medicine. http://www.cebm.net

Animal Models of Nociception and Pain

6

Kyle Silva, Karina Gritsenko, and Sayed E. Wahezi

Why Animal Research?

- Provides a foundation for understanding the neurobiology of nociception and pain.
- Test novel treatment options.
- Predict analgesic efficacy.

Ethics of Animal Experimentation

- Investigators must comply with federal, state, and local regulations when performing animal research.
- All who use animals for research, testing, or teaching must assume responsibility for their well-being.

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"*Three R's*" focus on minimizing pain experienced by animals

1. *Replacement*: use alternatives to animals when possible.
2. *Reduction*: minimize number of animals used.
3. *Refinement*: study design must minimize pain.

Study Design

1. *Mimic Human Pain*: Design should attempt to reproduce similar pain conditions to those experienced by humans.
2. *Subjects*: Invertebrates and/or vertebrates.
   - Commonly used subjects: fruit flies, nematode worms, waxworms, rodents.
   - Cats, dogs, and nonhuman primates.
   - Pigs share a similar distribution of nociceptive and non-nociceptive nerve fiber classes to that of humans.
3. *Stimuli*:
   - Nociceptive and/or non-nociceptive stimuli: Electrical, thermal, mechanical, chemical stimulation; Surgical destabilization of joints to induce arthritic changes.
   - Neuropathic stimuli: Chronic constriction injury, ligation, photochemical-induced, diabetes-induced, and drug-induced neuropathy.
4. *Endpoints*: Observable histologic, physiologic, and/or behavioral responses (see Table 6.1).

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Table 6.1 Common validated behavioral pain responses in rats

Common behavioral responses
Passive avoidance behaviors
Autotomy (i.e., self-attack)
Paw licking
Abdominal licking without grooming
Abdominal retractions
Writhing
Limping
Decreased feeding

Current Models Evaluate

1. Inflammatory Pain.
2. Visceral Pain.
3. Pain after Peripheral Nerve Injury.
4. Pain after Injury to the Spinal Ganglia and Dorsal Roots.
5. Central/Peripheral Neuropathic Pain.
6. Cancer Pain.
7. Postoperative Pain.

Commonly Used Tests for Pain/Nociception

Tail flick test: Evaluates acute pain in rodents after application of thermal nociceptive stimulus.

Thermal hyperalgesia: Hot plate test, measures latency of escape behaviors after application of noxious thermal stimulus. Tests heat hyperalgesia in various painful conditions.

Chemical stimuli: Injection of formalin into paw of a rodent followed by observed behavioral changes.

Allodynia test: Neuropathic pain model using von Frey filaments (monofilaments that provide an approximate logarithmic scale of force) to quantify changes in mechanical pain threshold.

Musculoskeletal pain models:

1. Arthritis model: surgical joint destabilization inducing arthritis.
2. Muscle pain model: ischemia and hypertonic saline induced.
3. Bone pain model: fracture induced.

Visceral pain: Mimic pain from heart, kidneys, pancreas, urinary bladder, and reproductive organs through induced ischemia, over distension, or chemical/mechanical irritation and stricture formation.

Neuropathic pain: injuries to peripheral or central nervous system via chronic constriction, ischemia, partial nerve ligation, as well as mechanical or chemical means.

Limitations

- Results have limited applicability to human pain that involves higher order processing.
- Animals may have different thresholds for pain intensity and react differently than humans.
- Quantifiable data may be biased by subjective interpretation of behavioral changes.

Future Research

Barring future advancements in research methodology, animal research currently serves as a means to better understand pain, so that we may better treat it.

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Ethical Standards in Pain Management and Research

7

Jessica M. Tsukanov, Karina Gritsenko, and Daniel Tsukanov

Fundamentals

- There are basic human rights for patients at the end of life.
- Guidelines are unclear with respect to chronic and postsurgical pain.
- Withholding pain management may lead to psychological consequences.
- Physicians have a moral responsibility to alleviate suffering.
- Research is governed on international, national, and professional levels.
- Fundamental ethical principles of autonomy, beneficence, nonmaleficence, and justice.

Autonomy

- Patients select their preferences in pain management and research enrollment, including informed consent.
- Research enrollees must do so free from coercion or implied coercion.
- Vulnerable populations include patients that lack capacity due to dementia or mental illness, socioeconomically disadvantaged or underinsured patients, prisoners, students, and children.
- Vulnerable populations are susceptible to coercion or implied coercion.
- Withholding information is an infringement of autonomy.

Beneficence

- Physician must do what is good for the patient (i.e., appropriate pain treatment).
- Pseudo-addiction is iatrogenically caused "drug seeking" behavior due to poorly controlled pain.
- Principle Investigator (PI) and Institutional Review Board (IRB) must complete adequate risk benefit analysis prior to initiating a study.

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Nonmaleficence

- "Do no harm."
- Includes withholding adequate pain management.
- Obligation to minimize pain and risk potential for research subjects.

Justice

- Equal treatment based on pain syndrome.
- Equal study enrollment regardless of gender, age, ethnicity, and preexisting conditions.
- Children and pregnant women are vulnerable groups and often are excluded from research.

Double Effect

- Death hastened by medications with a goal of relieving intractable symptoms—not to cause death.

Professionalism and Quality Assurance

- Necessitates interdisciplinary approach to treatment.
- Acknowledges physiological and psychological aspects of pain.
- Joint Commission sets standards of pain care and centers for excellence.
- Centers for Medicare and Medicaid Services (CMS) stress importance of this in nursing home populations.
- Requirement for continued education of pain management professionals.

Ethical Standards of Research Design, Review and Implementation, Informed Consent, Use of Animals

- Most human research to be approved by an IRB.
- IRB reviews prior to initiation for risk/benefit analysis or exemption if criteria are met.
- Requirement of accurate scientific data, a scientifically defensible hypotheses, and appropriate scientific methods.
- Need to maintain wellbeing of subjects by minimizing risks caused during their enrollment.

Informed Consent

- Attribute of autonomy.
- Properly documented discussion of benefits, risks, costs, and side effects as well as options for pain control.
- Capacity to consent includes the ability to comprehend, analyze, and express a consistent treatment choice.
- Patients that lack capacity (vulnerable populations) may be enrolled in a study by a surrogate acting in their best interest.
- Where possible, patient should assent and participate in shared decision making.
- Careful avoidance of coercion or implied coercion.

Use of Animals

- Should be avoided when possible.
- High scientific quality must be met.
- Pain should be avoided or minimized.
- Level of pain must match the potential benefit of the information obtained.
- Clear description of the anticipated pain or related symptoms as well as justification of why they cannot be avoided.

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Epidemiology

8

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Definitions

- Acute Pain—normal, predicted, physiological response to adverse chemical, thermal, or mechanical stimulus.
- Chronic Pain—lasting beyond 3 months, beyond normal tissue healing time.

Measurements of Burden of Disease in a Population

- Incidence–Number of new cases of pain (or recurring episodes) in patients at risk within a given time period, often expressed in person-years. Patients with pain at outset of study are not "at risk" and are not included.
- Prevalence—Proportion of study population with pain.
- Point prevalence at a discrete time.
- Period prevalence; e.g., during 1 year or over a lifetime; includes patients already with pain and patients developing pain within the period.

Of patients reporting pain at specific sites, 66–83 % reported chronic pain.

Methods of Evaluating Risk Factors for Pain

1. Cohort Studies: subjects are defined by exposure or non-exposure to a risk factor of interest and followed over time to determine the incidence of pain.

Strengths

- Can be prospective which limits recall bias.
- Efficient for rare exposures.
- Can obtain measures of frequency of outcome in population.

Limitations

- Differential loss to follow-up of exposed and unexposed patients may lead to bias.
- Inefficient for rare outcomes.

Measure of Strength of Association

- Relative risk.

2. Case Control Studies: subjects defined by outcome of interest (i.e., case patients have pain and control patients do not). Compare

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Table 8.1 Demography of Pain

Type		Prevalence (%)
Headache[a]		40.4
Back pain[a]		39.2
Neck pain[a]		30.8
Hip/knee[a]		28.3
Abdominal[a]		23.4
Chronic widespread pain[a]		9–14
Single site[a]		16.8
Multi-site[a]		53
Cancer[a]	Localized	36
	Metastatic	59–67
Pediatric[b]	Back	9.8–36
	Head	26–69
	Abdominal	3.8–41.2
	Multiple sites	12.1–35.7
Geriatric[c]		45–80

[a](Blyth, et al.)
[b](Henschke, et al.)
[c](Blyth, et al.)

proportions of cases and controls with exposure to risk factors.

Strengths

- Can be used to explore many different potential risk factors.
- Efficient for rare outcomes.

Limitations

- Risk of recall bias in retrospective study.
- No measures of disease frequency are obtainable.

Measures of strength of association

- Odds ratio.

Both Cohort and Case–Control studies are observational; differences may not be causal but may be due to uncontrolled differences between exposed and unexposed.

Risk Factors for Development of Chronic Pain

1. Age
   - increased prevalence in older populations
   - increased incidence of specific conditions such as low back pain
2. Gender
   - females, both adults and pediatric, report pain of increased intensity and frequency leading to more pain related disability
3. Socioeconomic
   - low education level, low income, housing status, and unemployment associated with increased pain prevalence and increased pain severity
4. Comorbid conditions
   - obesity
   - depression

Risk Stratification to Guide Treatment

1. Screening tools such as questionnaires and prediction tools can help to identify and target subgroups at increased risk for chronic pain.
2. Interventions more effective earlier in course.
3. Stepped-care approach: delineating different intensity levels of treatment. Patients enter at different levels depending on specific risk factors.

Impact of Pain

1. Psychosocial.

   Negative effects on general health perception, relationships and social interaction, increased depressive symptoms.
2. Economic
   - Direct medical care—physical therapy, inpatient services, pharmacy.
   - Additional ancillary services (i.e.-housekeeping).
   - Lost work productivity.
   - Costs dispersed among patients, employers, health care systems, caretakers.
   - In the USA during 2010, total costs ranged $560–635 billion.

Interpreting Diagnostic and Predictive Tests

- True Positive (TP): patient does have disease and the test is positive.
- True Negative (TN): patient does NOT have disease and test is negative.
- False Positive (FP): patient does NOT have disease and test is positive.
- False Negative (FN): patient does have disease and test is negative.

Sensitivity = TP/(TP+FN); high sensitivity helps rule out disease with negative result (snout).

Specificity = TN/(TN+FP); high specificity helps rule in disease with positive result (spin).

Positive Predictive Value (PPV) = TP/(TP+FP).

Negative Predictive Value (NPV) = TN/(TN+FN).

PPV and NPV depend on the prevalence of disease in the population, whereas sensitivity and specificity are independent of the population prevalence.

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Part II

Assessment and Psychology of Pain

Pain Assessment

9

Michael P. Zaccagnino and Srdjan S. Nedeljkovic

Introduction

Pain is a subjective, multidimensional experience. A widely recognized pain assessment model is from Melzack and Casey (1968) that consists of three dimensions:

1. Sensory-discriminative.
2. Affective-motivational.
3. Cognitive-evaluative.

Today, these three dimensions have been further categorized into additional *domains* such as:

- Pain intensity
- Pain quality
- Personality
- Psychosocial impact
- Physical/social functioning
- Emotional functioning
- Patient beliefs and coping
- Quality of care

Goals of Pain Assessment

1. Determine pain characteristics
2. Aid in diagnosis
3. Formulate choice of therapy
4. Evaluate effectiveness of therapy

Measuring Pain

To measure pain, a number of assessment tools are utilized. *Measurement* tools often assign a numerical unit to an aspect of pain in a single dimension, such as a pain scale to assess pain intensity. *Assessment* tools are broader, include one or more pain measurements, and attempt to evaluate the importance of pain across one or more dimensions. One example is the McGill Pain Questionnaire (MPQ).

Pain assessment strategies may be *direct* (self-report) or *indirect* (behavioral and biological). Because pain perception is a subjective experience, self-report metshodologies are most common and represent the standard; however, they are subject to a variety of biases and interpretations. A great deal of research has been done in testing and refining pain assessment methods, although work still needs to be done to continue establishing quality assessment tools to ensure clinically meaningful outcomes.

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Self-Report **Measures Include**
- The clinical interview
- Pain scales and questionnaires
- Diaries

Behavioral **Measures Include**
- The clinical interview
- Behavioral observation

Biological **Measures Include**
- Experimental pain assessment
- Psychophysiological assessment

Outcome Measures in Pain Studies

Basic Requirements

To measure outcomes in research and clinical care, pain measurement and assessment tools must meet high quality psychometric properties of reliability, validity, and utility.

- *Reliability* ensures that a test's results are consistent, and is expressed numerically as a correlation coefficient, with 0.0 signifying total unreliability and 1.0 indicating perfect reliability. Reliability coefficients above 0.85 are generally regarded as high and those between 0.65 and 0.85 as moderate.
- *Validity* ensures that the test measures what it is supposed to measure. It is generally seen as the most important consideration in the evaluation of a pain measure.
- *Utility* ensures that the test is easy to use and versatile, and often comes as a sacrifice to reliability and validity.

Current Issues

Current issues in research and clinical trials include:

- Determining the number of pain problems and pain domains to assess and treat.
- Determining clinically important differences in measured outcomes.
- Reducing variability in outcome measures to improve the efficacy and effectiveness of treatments.

For more information, the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) group has provided recommendations for interpreting the clinical importance of treatment outcomes in clinical trials.

- Four domains of pain assessment were proposed:
  1. Pain intensity.
  2. Physical functioning.
  3. Emotional functioning.
  4. Global ratings of improvement.
- Among these, *physical* and *emotional* outcome domains are recommended as core components of overall *health-related quality of life* (HRQoL).

Future Development

Systematic collecting and reporting of clinically important differences need to be achieved to further validate assessment methods and provide more meaningful comparisons between clinical trials. In addition, future development of *patient-reported outcomes* (PROs) may provide more sensitive and efficient assessment of patients' pain.

Methods of Pain Assessment

- Clinical interview.
- Pain scales and questionnaires.
- Diaries.
- Experimental pain assessment.
- Behavioral observation.
- Psychophysiologic assessment.
- Assessment from family members and significant others.

Clinical Interview

The interview is a rich source of information about a patient's pain. It also provides an opportunity to interact with the patient, establish rapport, and make observations.

Pain's Characteristics
- Pain location
- Radiation
- Intensity
- Characteristics/quality
- Temporal aspects
  - Onset
  - Duration
  - Changes since onset
- Constancy or intermittency
- Characteristics of any breakthrough pain
- Exacerbating/triggering factors
- Palliative/relieving factors

Pain's Associated Symptoms/Global Functioning
- Restriction of range of motion, stiffness, or swelling
- Muscle aches, cramps, or spasms
- Color or temperature changes
- Changes in sweating
- Changes in skin, hair, or nail growth
- Changes in muscle strength
- Changes in sensation
  - Positive—dysesthesias, itching
  - Negative—numbness

Pain's Impact on Life
- Social and recreational functioning
- Emotional functioning
- Mood and anxiety
- Relationships
- Occupation
- Sleep
- Exercise
- Activities of daily living

Previous Pain Evaluations and Treatments
- Obtain all prior pain records
  - Clinician offices
  - Hospitals
  - Imaging centers/laboratories
  - Pharmacies

Patient Perceptions and Psychological Factors
- Specific beliefs and understanding of pain
- Expectations
- Maladaptive behavior patterns
  - Depression
  - Anxiety
  - Substance abuse
- Support systems

General History
- Past medical, surgical, psychiatric history
- Medications
- Family history
- Social history
- Socioeconomic considerations
- Gender-related differences
  - Pregnancy/menstruation

Pain Scales and Questionnaires

Pain scales and questionnaires are fundamental methods in determining patients' pain characteristics. They provide focused assessment and quantification of patients' pain in single (pain intensity scales) or multiple (pain questionnaires) dimensions in a timely and cost-effective manner. Because published scales and questionnaires have met standards for reliability and validity, greater confidence can be placed in the information provided by these measures (see Chap. 21).

Single Domain Scales:
- *Pain intensity*
  - Numerical Rating Scale (NRS)
  - Verbal Rating Scale (VRS)
  - Visual Analog Scale (VAS)
  - Faces Pain Scale Revised (FPS-R)

Multiple Domain Questionnaires (grouped according to major domain being evaluated):
- *Pain quality*
  - McGill Pain Questionnaire (MPQ)
  - Pain Quality Assessment Scale (PQAS)
- *Pain-Related Physical Functioning*
  - Multidimensional Pain Inventory (MPI)
  - Brief Pain Inventory (BPI)
  - Pain Disability Index (PDI)

- Oswestry Disability Index (ODI)
- Roland-Morris Disability Questionnaire (RDQ)

- *Psychological Functioning*
  - Minnesota Multiphasic Personality Inventory (MMPI)
  - Millon Behavioral Health Inventory (MBHI)
- *Pain-Related Emotional Functioning*
  - Beck Depression Inventory (BDI)
  - Profile of Mood States (POMS)
  - Center for Epidemiologic Studies–Depression Scale (CES-D)
  - Hospital Anxiety and Depression Scale (HADS)
  - Patient Health Questionnaire Depression Scale (PHQ-8, 4 and 9)
- *Patient Beliefs and Coping*
  - Survey of Pain Attitudes (SOPA)
  - Pain Stages of Change Questionnaire (PSOCQ)
  - Chronic Pain Coping Inventory (CPCI)
  - Pain Catastrophizing Scale (PCS)
  - Chronic Pain Acceptance Questionnaire (CPAQ)
- *Global Rating of Quality and Improvement*
  - Patient Global Impression of Change (PGIC)
  - Patient Outcome Questionnaire (POQ)
  - Treatment Outcomes of Pain Systems (TOPS)

Diaries

Diaries allow the recording of prospective, real-time pain information and its associated temporal factors. This method is unique in that it helps to eliminate the distortion associated with memory and recall.

Experimental Pain Assessment

This method of pain assessment is gradually being established. It consists of administering standardized noxious stimuli and measuring patients' responses (see Chap. 21).

Behavioral Observation

Patients can communicate pain through body postures, facial expressions, vocalizations (i.e., crying, moaning), and actions (i.e., limping, guarding, and rubbing the affected area). Behavioral observation is a valuable method of gathering adjunct pain information, especially in populations with cognitive or physical limitations that interfere with verbal and written communication. Studies using the Facial Action Coding System suggested that a universal set of "pain expressions" exists across all age groups, and could prove beneficial in populations where verbal report is unavailable. In general however, the use of behavioral observation methods is commonly limited to the clinical research setting because of the time-intensive and costly nature of these methods (see Chap. 21).

Psychophysiologic Evaluation

Psychophysiologic assessment is a biological method of measuring pain. It helps determines if psychological factors are influencing physical responses to pain, and can provide behavioral feedback strategies for coping. Biofeedback is the most common psychophysical measure applied (see Chap. 21).

Assessment of Family Members and Significant Others

Information gathered from family may provide additional insight into patients' pain, and can be especially beneficial in nonverbal/cognitively impaired populations. Also, assessment of family members is important to evaluate pain-relevant communication and the impact that pain has on significant others. Lately, interest has been placed on hypothesized roles of social contingencies in the perpetuation of persistent pain and disability, as well as the negative impact that caring for patients with pain has on significant others.

Specific Patient Populations

Elderly Patients

Pain is highly prevalent in the elderly population. Older patients may have difficulty communicating their pain, and studies have shown their pain is often undertreated. This may be due to older patients reporting less pain, as seen in studies utilizing the original MPQ. However, the short form of the MPQ correlates highly with the original and seems to be easier for older patients to use. Deficits in sensory function (i.e., hearing and vision) must be considered and adjusted for, as well as consideration of cognitive status. In the cognitively intact older patient, self-report assessment methods are still the most reliable and valid pain measurement tool. Among these, the VRS produces the least failure responses while the VAS produces the most, with the NRS falling in the middle. Lastly, special consideration needs to be given to assessment of this population's medication use, functional and psychosocial status, beliefs and attitudes about pain, and the implications of living in long-term care facilities.

Nonverbal/Cognitively Impaired

The prevalence and severity of pain in cognitively impaired individuals is the same as cognitively intact individuals. However, older people with dementia are at greater risk than those who are cognitively intact for under-treatment of pain. It is important to investigate the possible pathologies that could produce pain in this population. Preliminary evidence supports the use of self-report by patients with mild–moderate cognitive impairment. However, in severe dementia, self-report becomes impossible and indirect assessment methods such as behavioral observation and information from significant others becomes necessary. A variety of behavioral tools have been developed for pain assessment in cognitively impaired/nonverbal older adults, but none has been found to have sufficient reliability and validity to support broad adoption in clinical practice.

Pediatric Patients

The assessment of pain in pediatric patients presents a number of challenges, though major advances in the measurement of pain, particularly in the reliability and validity of assessment methods, have occurred. Self-report methods of assessment are well validated in children. Behavioral and biological measures can be used for all ages of children, but are requisite in neonates, preverbal children, and children with significant handicaps (see Chap. 21). Depending on the child's age, certain pain measures are appropriate. For instance, in children less than 6 years old, behavioral scales are routinely applied, whereas children over 6 years old can use the self-report "faces" scale. Around age 8 and above, children can rate their pain on a 0–10 scale and can indicate descriptors of pain.

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Physical Exam of the Cranial Nerves

10

Daniel Vardeh

The cranial nerve exam can give important diagnostic clues to painful disorders of the head and neck, systemic toxicity for both opioids and adjuvant medications as well as raise "red flags" for potentially dangerous conditions. New deficits in cranial nerve function should always prompt specialist referral and in most cases require advanced brain imaging. As either headache or facial pain can be the first signs of intracranial pathology, the pain physician should be familiar with the basic examination of cranial nerves.

The Cranial Nerves Can Be Divided in Five Functional Major Systems: Smell (I), Vision and Eye Movements (II, III, IV, VI, VIII), Face Function (V, VII), Oropharyngeal Function (IX, X, XII), and Head/Neck Movement (XI)

Olfactory Nerve (I) [Smell]

How?

Ask patient to smell coffee or soap with each nostril

Why?

Rarely tested, unless specific pathology suspected, e.g., basal subfrontal tumor or early Parkinson disease. Disruption of the olfactory nerves as they run through the cribriform plate can be the result of head trauma.

Optic Nerve (II) [Eye Vision]

How?

1. **Ophthalmoscopic exam**: look for papilloedema, optic nerve atrophy, retinal process.
2. **Acuity**: best tested with eye chart (e.g., Snellen chart) with one eye covered at a time. Refraction errors of the cornea/lens have to be eliminated before testing acuity, so patient should keep glasses on.
3. **Color vision**: tested usually by presenting a bright red object and comparing the perception of "redness" from one eye to the other.
4. **Peripheral visual fields**: ask patient to fixate straight ahead, one eye at a time, and present finger(s) in each of the four quadrants of each eye. Note that the nasal quadrants of each eye are more restricted than the temporal quadrants because of the nose.
5. **Visual extinction**: ask patients which finger moves while presenting fingers in both temporal fields simultaneously.

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Why?
Direct injury anywhere between the retina and the visual cortex can affect **acuity and vision**. Alternatively, increased intracranial pressure, either idiopathic or symptomatic from an intracranial expansive process, can cause optic disc edema and result in blurred vision, scotoma or visual field deficits. **Desaturation** of for example the color red in one eye compared to the other is indicative of more subtle, central optic nerve damage, as in optic neuritis. **Monocular vision deficits** are localized before the optic chiasm, **binocular congruent deficits** behind. True **visual extinction** in the absence of visual deficits is localized outside the primary visual pathway, often in the parietal lobe.

Pupils

How?
Look for difference in pupil size (**anisocoria**), which can be exaggerated in dim light (failure of one pupil to dilate) or bright light (failure of one pupil to constrict). Next, constriction of the illuminated pupil (**direct light response**) and contralateral pupil (**consensual or indirect light response**) is noted.

Why?
The **direct light response** is impaired in lesions of the afferent reflex arch (optic nerve, pretectal area) or efferent arch (parasympathetic fibers originating from the Edinger-Westphal nucleus and traveling with CN III). The **consensual light response** is impaired in lesions of the illuminated optic nerve or the contralateral parasympathetic fiber tract. **Anisocoria** can be caused by disruption of either the sympathetic (e.g., carotid dissection) or parasympathetic (e.g., compression of the CN III by aneurysm) supply of the iris, or local drug effects (e.g., anticholinergic eye drops). Systemic drug side effects, e.g., miosis from opiate use, should never cause anisocoria. Painful stimuli will cause a transient bilateral pupillary dilatation due to increased sympathetic drive.

Occulomotor (III), Trochlear (IV), Abducens (VI) and Vestibulocochlear (VIII) Nerve [Eye Movements/Hearing]

How?
Note **ptosis and gaze preference** in neutral position. Then have patient follow one finger with eyes only in all directions, note **full range of motion** and ask for **double vision** in any position. True double vision will always stop after covering one eye; the peripheral/outer picture will disappear by covering the misaligned/faulty eye. Also, observe eyes for **smooth pursuit** in both horizontal and vertical direction. Note **nystagmus** to evaluate for vestibular function in either horizontal or vertical plane (slow deviation phase with quick correction phase) or rotatory nystagmus. Voluntary eye movements in either the horizontal or vertical plane (**saccades**) can be tested by asking the patient to switch fixation from on target to another (e.g., by holding up 2 widely spaced fingers).

Test **hearing** function by rubbing fingers close to the ear or whispering into each ear. A tuning folk can be used to distinguish conductive hearing problems from neurosensory/cochlear pathology (Rinne and Weber test).

The **vestibular function** can be further tested by the vestibulo-occular reflex (VOR). This can be done by asking the patient to fixate on the examiner's nose, while the patient's head is turned rapidly side to side and up and down. In patients who are unable to participate (e.g., coma), VOR can be tested either turning the head while keeping eyes open or by caloric testing (infusing ice cold water into the ear canal resulting in asymmetric stimulation of the vestibular system and tonic deviation of the eyes towards the infused ear within about 30 s).

Why?
Ptosis can be either due to CN III dysfunction (innervating the levator palpebrae muscle) or disruption of the sympathetic innervation to the tarsalis superior (Mueller's) muscle as in Horner's syndrome. **Conjugated eye deviation**

or deficits in conjugated eye movements point to a lesion (either structural or functional) in the eye coordination centers of the pons, midbrain or cortex (frontal eye field). In contrast to conjugated eye movement deficits, **dysconjugated eye movement** deficits will result in misalignment of the optical axis and therefore always cause double vision in the acute phase. This can be a result of a local orbital process, eye muscle or neuromuscular junction disease, or damage to cranial nerves III, IV, VI or their nuclei in the brainstem. CN VI is particularly vulnerable to changes in intracranial pressure due to its long course in the subarachnoidal space and its course ascending the clivus and being tethered inside Dorello's canal. Cerebellar damage of various etiologies (structural, toxic for example due to alcohol abuse, degenerative) typically causes disruption of **smooth pursuit** as well as inaccurate **saccades** (overshooting or undershooting the target) in addition to more widespread ataxia. **Jerk nystagmus** (direction is defined by the quick phase of the eye movement) is most often caused by imbalance in the vestibular system of either peripheral (e.g., damage to vestibular nerve or vestibular organ) or central (lesion in brainstem or vestibulocerebellum) origin. It is crucial but not always easy to distinguish central from peripheral causes. **Peripheral vestibular dysfunction** usually has a violent onset with associated vertigo and nausea/vomiting, but often presents a transient and more benign condition (e.g., BPPV, vestibular neuritis). Looking for other brainstem or cerebellar deficits to identify a **central etiology** is crucial. Intoxications (e.g., alcohol, amphetamines), metabolic derangements, and medication side effects (typically anticonvulsants, including phenytoin, carbamazepine, lamotrigen) are all common causes of acute onset nystagmus.

Mass lesions like vestibular schwannomas causing sensorineural hearing loss can often affect adjacent nerves like CN VII in the cerebellopontine angle or CN V causing trigeminal neuralgia.

Trigeminal (V) and Facial (VII) Nerve [Facial Sensation and Movements]

How?

All three areas supplied by each of the three branches of the trigeminal nerve (ophthalmic nerve V1, maxillary nerve V2, mandibular nerve V3) are tested by **light touch in the corresponding areas**, and **pressure** is applied to their respective exit points on the face. Other modalities like **temperature and pinprick nociception** can be tested in selected cases. **Vibration** using a tuning folk applied to the forehead is sometimes tested and its absence on one side usually points to a psychological etiology of the patient's symptom (vibration is transmitted through the bony structures of the skull and therefore cannot be confined to one side only). The **chewing muscles** are innervated by the motor portion of CN V and are palpable during jaw clench (masseter and temporal muscle) or tested during horizontal and vertical movement of the jaw against resistance (pterygoid muscles). The **jaw jerk** (CN V reflex) is tested by lightly tapping the chin while the patient's jaw is relaxed. The **corneal reflex** (afferent arch V1, efferent arch bilateral CN VII) is tested by touching the cornea gently with a cotton wisp or applying eye drops, and the reflex blink response is observed in both eyes.

Muscles of facial expression (innervated by CN VII) are tested by observing for asymmetry of face folds while having the patient rise eyebrows, forcefully shut eyes, and forcefully smile. The inability to whistle or blow up cheeks can also indicate perioral weakness. The exact location of a peripheral facial nerve lesion can be determined by assessing the function of the **intermediate nerve**, which runs along CNVII and (from proximal to distal) innervates the **tear gland** (disruption causing dry eye), **stapedius muscle** (disruption causing ipsilateral hyperacusis), and—via the **chorda tympani**—taste of the ipsilateral 2/3rd of the tongue.

Why?

To look for alterations in sensation (**hypo/hyperaesthesia**) along the course of CN V can be

helpful in determining the cause of facial pain in conditions such as trigeminal neuralgia, supraorbital neuralgia, or zoster ophthalmicus (due to reactivation of VZV in the gasserian ganglion, causing typically rash in the V1 distribution and potentially eyesight threatening keratitis). **Tactile sensations** are transmitted to the principle nucleus of CN V in the pons, while **nociceptive and temperature stimuli** are transmitted to the spinal nucleus in the medulla and high cervical spinal cord. Selective loss of one of these qualities has therefore localizing value.

Unilateral facial weakness can be divided into peripheral and central facial palsy. **Peripheral facial palsy** (caused by for example HIV, Lyme, Bell's palsy) will involve the entire side of the face and depending on the exact location of the lesion, can involve dry eyes, hyperaccusis, and loss of taste. **Central facial palsy** (caused by for example Stroke, Tumor, MS, post-ictal) spare muscle weakness of the forehead due to the bilateral motor cortex supply to the facial subnucleus innervating the forehead.

Glossopharyngeal (IX), Vagal (X), and Hypoglossal (XII) Nerve [Speech and Swallowing]

How?

Listen for slurred speech **(dysarthria)**, ask for trouble swallowing (**dysphagia**) and have the patient say "**G**" (guttural, CN IX), "**L**" (lingual, CN XII), "**M**" (buccal, CN VII)). If pathology is suspected, evaluate symmetric **palate elevation** by having the patient say "ahh" (CN IX). Have the patient **stick out the tongue** straight and notice any side deviation. Have the patient then wiggle tongue from one side to the other or have patient press tongue into cheek against resistance to either side (CN XII).

The **gag reflex** (CN IX, X) can be elicited by touch of the posterior pharynx, and can be tested in patients with suspected brainstem pathology, dysphagia, or impaired consciousness.

Why?

Generally, functional trouble (**dysarthria, dysphagia**) will often predate detectable clinical signs of asymmetric palate elevation or tongue deviation/atrophy. Isolated glossopharyngeal pathology is rare, and is typically part of a more extensive cranial neuropathy or brain stem process. **Glossopharyngeal neuralgia** causes intermittent shooting pain to the posterior tongue or walls of the pharynx and can be caused by vessel or mass compression. Lesion of CN XII will cause **ipsilateral tongue deviation** and weakness on this side

Accessory Nerve (XI) [Head/Neck Movement]

How?

Have the patient **turn the head** to either side and do **head flexion** against resistance (sternocleidomastoid muscle). Have the patient **shrug shoulders** and **extend the head** against resistance (trapezius muscle).

Why?

Lesions in the cervical cord can affect the spinal (main) division of the accessory nerve, which arises from the ventral horn of C1–C6. This will typically cause more extensive symptoms of spinal cord origin.

Neck

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Aaron Jay Yang and Nitin B. Jain

Introduction

- Careful examination of the neck begins with a thorough history and physical examination including strength and sensory testing as well as observation of gait to exclude neurologic involvement. Obtaining a history of aggravating factors is helpful in narrowing down the etiology of pain. For example, pain worse with prolonged neck flexion may signify a disc issue as opposed to pain worse with neck extension, which may suggest facet-mediated pain. Pain worse with lateral flexion causing ipsilateral neck pain may indicate neural compression due to narrowing of the ipsilateral neuroforamen.

Physical Examination

- ***Inspection*** should include the positioning of the neck in the sagittal plane and should note whether there is loss of normal cervical lordosis. The forward head position may point to a source of neck pain as there is increased work requirements of the cervical musculature due to the weight of the head by this posture [1].
- ***Palpation*** is important for evaluation of myofascial pain. Fibers that compose the upper trapezius muscles may particularly be tender in those with poor neck posturing in the head forward position. The sternal and clavicular heads of the sternocleidomastoid muscles should be palpated as well as the posterior cervical muscles which can cause referred pain to the head. Segmental evaluation of the facet joints can be performed by translating each segment from right to left or vice versa in a flexed, extended, or neutral position of the neck as well as direct palpation over the facet joints [2].
- ***Range of motion*** of the neck should be assessed in flexion, extension, lateral bending, and rotation. The atlantoaxial (C1–C2) joint accounts for 50 % of the rotation of the cervical spine while 50 % of neck flexion and extension occurs at the occiput and C1 vertebral body. Distal to C2, flexion and extension of the cervical spine is greatest at C5–C6 and C6–C7 while lateral bending and rotation occurs mostly at C3–C4 and C4–C5 [2].
- Although there remains great variability in measurement of range of motion of the cervical spine as well as varying ranges due to age of the subject, below is a sample range of degrees seen with motion of the cervical spine
  - Normal Range of Motion [3]
    - Cervical flexion: 54–69°
    - Cervical extension: 73–93°

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- Lateral bending: 30–66°
- Lateral rotation: 50–94°

- The following are ***special tests*** of the cervical spine that may individually provoke or alleviate the patient's symptoms

  Spurling's Test

  This test is performed by extending the neck and tilting the head toward the painful side while applying downward pressure to the top of the patient's head. This test is considered positive if pain radiates into the ipsilateral limb at which the head is rotated potentially indicating a cervical radiculopathy. Prior studies have demonstrated a sensitivity of 30 % and specificity of 93 % when evaluating cervical radiculopathy [4].

  Caution must be used during this test as axial pressure may worsen the radiculopathy. The test may be done initially with no axial pressure, followed by gentle pressure to carefully elicit radicular symptoms.

  Shoulder Abduction test

  This test is based on the principle that by raising the arm above the head, there is relief of ipsilateral radicular symptoms caused by nerve root compression. A positive test is signified by a reduction or relief of radicular arm symptoms by active or passive abduction of the ipsilateral shoulder. This test may also be helpful to distinguish shoulder pathology such as a rotator cuff related pain in which shoulder abduction may aggravate the patient's pain.

  Neck distraction test

  This test is performed with the patient laying supine with the examiner placing one hand under the chin of the patient and the other hand around the occiput and slowly lifting the patient's head. Pain relief with this maneuver is considered to be a positive test, indicating relief of pressure on the cervical nerve root.

  Hoffman's Sign

  The origin and clinical significance remains disputed, however it is postulated that a positive sign indicates an upper motor lesion or damage to the spinal cord due to conditions such as a cervical myelopathy. This test is traditionally described as follows: Support the subject's hand so it is relaxed and the middle finger is grasped in partial extension. The nail of the middle finger is snapped by the examiner's thumb nail and the sign is considered positive if there is flexion of the thumb or index finger. There is disagreement on whether the sign is positive if only the thumb flexes.

- Neck pain can be nonspecific, but commonly recognized syndromes of neck pain include cervical postural syndrome, acute nerve root pain, whiplash injury, and acute wry neck. Cervical postural syndrome is characterized by head forward and rounded shoulder position which is commonly seen in sedentary occupations. These patients may present with aching pain across the shoulders and neck that is relieved by movement. Patients subsequently develop tightness in the upper trapezius and pectoralis muscles while presenting with weak and inhibited deep neck flexor and lower trapezius muscles. Physical therapy aimed at adjusting posture and strengthening the weakened muscles often improves pain associated with this syndrome.

Question

1. Where is the most cervical flexion and extension range of motion seen? What about for cervical rotation? Atlantoaxial (C1-C2) joint and atlanto-occipital joint, respectively.
2. What is the significance of the Hoffman's sign? May signify an upper motor neuron process.

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Shoulder

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Aaron Jay Yang and Nitin B. Jain

Introduction

- The glenohumeral joint is the most mobile joint in the body with a large degree of range of motion. Along with this increased mobility comes a higher degree of instability due to a shallow and smaller glenoid as compared with the humeral head, which can lead to subsequent shoulder injuries. Pathology related to the rotator cuff is the leading cause of shoulder pain and can often present with pain, weakness, and loss of range of motion. However, the differential diagnosis of shoulder pain can be broad and includes labral tears, glenohumeral ligament tears or sprains, acromioclavicular ligament tears, osteoarthritis, adhesive capsulitis, peripheral neuropathy, and cervical radiculopathy. As a result, a thorough examination should include the cervical spine and the contralateral shoulder.

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Physical Examination

- ***Inspection*** should include the muscle bulk, position of the scapula, and the position of the neck in relation to the shoulders. Patients may commonly present with rounded shoulders and a forward head posture which can subsequently lead to humeral internal rotation and scapular protraction. In cases of chronic massive rotator cuff tears, the humeral head can be superiorly displaced and abut the acromion.
- ***Scapula:*** Important anatomical landmarks include the superior angle of the scapula which corresponds to the 2nd rib, the spine of the scapula to the third thoracic vertebrae (T3) and the inferior border of the scapula to T7.
  - The scapula can be tilted or "winged" depending on the etiology of weakness. As the patient resists forward flexion of the shoulder or does a wall push-up, weakness of the serratus anterior secondary to a long thoracic nerve injury may cause the scapula to wing medially. However, when there is weakness of the upper trapezius secondary to spinal accessory nerve injury, the scapula may wing laterally with resisted arm abduction. This can be measured by the distance from the spinous processes to the medial border of the scapula with side to side comparison

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- ***Palpation***
  - Biceps tendon: palpation of the long head of the biceps tendon is performed in the bicipital groove between the lesser and greater tuberosity of the humeral head. Pain with internal and external rotation during palpation indicates potential tendinosis of the biceps tendon.
  - The acromioclavicular (AC) joint: is palpated for tenderness by following the distal end of the clavicle to the AC joint, palpating for tenderness along the joint, which indicates potential AC joint sprain or osteoarthritis.
- ***Range of motion*** of the shoulder includes forward flexion, extension, internal/external rotation, abduction, and adduction. Active range of motion (AROM) should be performed first in order to observe which particular movements are painful for the patient. The Apley Scratch test is a functional way to assess internal range of motion. The patient is asked to reach behind their back in internal rotation and the examiner assesses the highest level the patient can reach with their thumb. This degree of internal rotation can be correlated with the level of the spinous process that can be reached based on the landmarks mentioned above. Pain with decreased ROM may indicate rotator cuff pathology, glenohumeral joint osteoarthritis, and adhesive capsulitis.
- ***Strength testing*** can be performed by the examiner exerting resistance to a particular movement.
  - External rotation is predominantly exerted by the infraspinatus muscle
  - Internal rotation is predominantly exerted by the subscapularis muscle
  - Abduction is predominantly exerted by the supraspinatus muscle
- There are over 25 ***special tests*** described for examination of the rotator cuff, the discussion of which is beyond the scope of this text [1]. Please refer to the suggested reading section below for discussion on how to perform these individual tests.
  - Subscapularis
    - Lift-off test, belly press test, bear hug test
  - Supraspinatus
    - Empty Can test (Jobe test), Drop Arm test, Full can test
  - Teres Minor
    - Hornblower sign
  - Biceps tendon
    - Speed's test, Yergason's test
  - Impingement Tests
    - Neer's sign, Hawkin's test
  - Shoulder instability
    - Apprehension test, Load and shift test, Jerk test
  - Labral pathology
    - O'Brien's test (Active compression test), Crank test, Anterior slide test
  - AC joint
    - Cross arm adduction test, Active compression test

Questions

1. What are the two different types of scapular winging and what peripheral nerve is involved? Medial and lateral winging secondary to Long Thoracic and Spinal Accessory nerve palsy respectively.
2. The spine of the scapula and inferior border of the scapula correspond to which spinous process? T3 and T7 respectively.
3. What causes loss of active and passive range of motion? Adhesive capsulitis and glenohumeral joint osteoarthritis

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Elbow

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Aaron Jay Yang and Nitin B. Jain

Introduction

- Examination of the elbow joint requires careful examination of the shoulder and neck as well as the wrist joint as pain can be referred to the elbow from both of these locations. The elbow joint is a synovial joint that allows flexion and extension. There are no intra-articular ligaments that stabilize the elbow joint and the majority of stability of the elbow joint arises from surrounding ligaments, muscles, joint capsule, and bony articulation. The elbow articulations are made up of the ulnohumeral and radiohumeral joint. The most common musculoskeletal condition that is encountered around the elbow is an overuse syndrome related to excessive wrist extension known as lateral epicondylosis.

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Physical Examination

- ***Inspection***
  - Should include the carrying angle of the arm, which is formed by the long axis of the humerus and ulna when the elbow is straight and forearm is supinated.
  - In adults, there is a slight valgus deviation of the carrying angle with a normal angle of 5–10° in males and 10–15° in females [1].
  - Medial epicondyle is the origin of the flexor muscle mass or the common flexor tendon.
  - Lateral epicondyle is the origin of the common extensor tendon.
  - Posterior elbow is the location of the olecranon bursa, which overlies the bony protuberance of the ulna and can become inflamed due to prolonged pressure or trauma.
- ***Palpation*** of the elbow may begin with the medial epicondyle, which is easily palpable and is the site of origin of the common flexor tendon. Just posterior to this is the ulnar groove in which Tinel's test can be performed to reproduce paresthesias along the distribution of the ulnar nerve. Posteriorly, the olecranon process is palpable as well as the distal insertion of the triceps tendon into the olecranon. Superficial to the lateral epicondyle is the muscles that compose the common

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extensor tendon and the anconeus muscle can be palpated between the olecranon and lateral epicondyle. A radial head fracture should be considered if a patient presents with a history of trauma and pain located along the radial head while pronating or supinating the forearm.

- Passive and active ***range of motion*** should be observed and compared side to side. Normal range of motion of the elbow is as follows: flexion (140–160°), extension (0–10°), pronation (80–90°), and supination (90°) [2].
- The following are ***special tests*** performed around the elbow with a particular focus on lateral epicondylosis which is more commonly encountered in the office setting.
  - Lateral Epicondylosis (Tennis Elbow)
    - Cozen's test, also known as the resisted wrist extension test, is performed by extending the wrist against resistance with the forearm pronated causing increased pain along the lateral epicondyle. The more extended the elbow while performing this test, the more likely wrist extension with resistance is to cause pain.
    - Mill's test is performed by the examiner palpating the patient's lateral epicondyle while passively pronating the forearm, flexing the wrist, and extending the elbow. The test is considered positive if there is reproduction of pain near the lateral epicondyle.
    - Maudsley's test, also known as the resisted middle finger extension test, is performed by the patient trying to extend the 3rd digit of the hand against resistance, stressing the extensor digitorum brevis muscle and tendon while palpating the patient's lateral epicondyle. The test is considered positive if there is reproduction of pain near the lateral epicondyle.
    - Chair lift test is performed and considered positive by having pain that is reproduced along the lateral epicondyle while lifting the back of a chair with the elbow fully extended.
  - Medial Epicondylosis (Golfer's Elbow)
    - There are few tests that can be performed for this condition but symptoms may be reproduced with resisted wrist flexion and pronation. This test is performed by flexing the elbow to 90° and with the forearm supinated; the patient makes a fist and flexes the wrist while the examiner attempts to extend the wrist. The test is considered positive if resisted wrist flexion causes pain along the medial epicondyle.
  - Elbow Instability
    - Varus stress testing stresses the lateral collateral ligament of the elbow. This test is performed by placing the arm in 20° of flexion and slight supination. The examiner places their hand over the medial aspect of the distal humerus while placing the other hand lateral to the distal forearm. Varus stress is applied to the forearm while counter force is applied to the humerus. Excess gapping of the lateral elbow joint compared to the contralateral side may signify injury to the ligament. Valgus testing stresses the medial collateral ligament and applies pressure to the medial joint line of the elbow.
  - Ulnar Neuropathy at the Elbow
    - Tinel's can be performed at the elbow by tapping the ulnar nerve within the ulnar groove that is formed by the olecranon process and medial epicondyle. A positive sign is indicated by tingling along the ulnar distribution of the forearm and hand.
    - Wartenberg's sign may be observed by placing the patient's hand resting on the table while the examiner passively spreads the fingers apart and then asks the patient to bring them together. A positive test would be the inability to squeeze the little finger to the remainder of the hand.
    - Froment's sign is observed by having the patient hold a piece of paper between their thumb and index finger. The examiner then tries to pull the paper out of the patient's hand. With a ulnar neuropathy, the patient will flex their thumb by using

their flexor pollicis longus muscle to compensate for their weak pinch grip due to weakness of the adductor pollicis muscle, which is innervated by the ulnar nerve.

Question

1. Lateral epicondylosis occurs secondary to what type of repetitive motion causing tendinosis of which tendon? Repeated wrist extension causing tendinosis of the extensor carpi radialis brevis (ECRB) tendon.

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Abdomen

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Aaron Jay Yang and Nitin B. Jain

Introduction

- The abdominal examination in patients with chronic pain may often prove to be difficult. Pain can be referred from another organ system such as the gastrointestinal, genitourinary, as well as the gynecologic tracts in addition to presenting with visceral, somatic, or neuropathic pain. While the etiology of abdominal pain can be overwhelming, a careful history and systematic physical examination may aid in narrowing down the diagnosis. Red flags that should raise particular concern include fever, weight loss or anorexia, jaundice, edema, blood in urine or stool, abdominal mass, or pain that awakens the patient at night.

Physical Examination

- Examination should start with assessment of the patient's vital signs as well as examination of the eyes and skin for signs of jaundice. This is followed by auscultation and percussion of the chest and abdomen for bowel sounds. Careful palpation of the abdomen should be done for any signs of masses, tenderness, and peritoneal signs. Rectal and pelvic examination by appropriate personnel should be included if suspicion arises for presence of occult blood or involvement of the gynecologic tract.
- Another potential cause of abdominal pain may include thoracic radiculopathy or radiculitis. The physical examination is not a reliable way to make this diagnosis although patients may present with localized paraspinal tenderness and sensory disturbance in a dermatomal pattern. The thoracic region does not lend itself to isolated muscle testing and physical examination is more helpful to rule out myelopathy secondary to a thoracic disc herniation [1].

Potential Sources of Abdominal Pain Due to Nerve Entrapments

Abdominal pain can be difficult to diagnosis and treat and by the time most patients end up in a pain clinic they have often undergone exhausting tests, imaging, treatments, and sometimes diagnostic abdominal surgeries. Between 10 and 30 % of patients with chronic abdominal pain will have chronic abdominal wall pain [2].

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- *Anterior abdominal cutaneous nerves (AACN)* arise from the nerve trunks of T7–T12. They pass anteriorly and inferiorly between the transversus abdominis and internal oblique muscles. These nerves give rise to the lateral and anterior cutaneous branches which can be affected in entrapment neuropathies. Typically the entrapment occurs at the level of the muscular foramen of the rectus abdominis muscle. Carnett's test is a maneuver that can help differentiate abdominal wall pain from visceral pain and indicates AACN entrapment. The test is performed with the patient supine and the patient is then asked to lift their head and shoulders off of the table and tense the abdominal wall muscles. Typically, intra-abdominal pain improves with this movement and abdominal wall pain worsens. Further, palpation of the abdomen during this maneuver with the location of a point of maximal tenderness indicates the level at which the nerve is affected. The treatment for such neuropathies includes transversus abdominis plane blocks or AACN nerve injections (see Chap. 87).
- *Ilioinguinal and iliohypogastric nerves* arise from the L1 and T12-L1 nerve roots respectively. These nerves arise from the lateral border of the psoas major muscle while coursing around the abdominal wall and penetrating the transverse abdominal and internal oblique muscles to innervate the hypogastric and inguinal region. The iliohypogastric nerve supplies sensation to the posterolateral gluteal skin and suprapubic skin while the ilioinguinal nerve supplies sensation over the penile root and upper scrotum in males and the skin covering the mons pubis and labia majora in females.
- *Genitofemoral nerve* is formed by the L1 and L2 nerve roots and often penetrates the psoas major muscle in which it then divides into the genital and femoral branch. The genital branch is partially responsible for the cremasteric reflex and also supplies sensation to the skin of the scrotum in males and mons pubis and labia majora in females. The femoral branch supplies sensation to the anterior aspect of the femoral triangle. Groin pain in the genitofemoral distribution with neuropathic pain may be an indication for nerve blockade.
- The ilioinguinal, iliohypogastric, and genitofemoral nerves are collectively known as the "border" nerves because these nerves supply the skin between the abdomen and thigh. These nerves are at risk of injury from lower abdominal incisions due to appendectomy, inguinal herniorrhaphy, or laparoscopic surgery. Patients may present with neuropathic pain in addition to groin pain that may extend to the scrotum or testes in men and to the labia in women.

Questions

1. Which nerve roots supply the genitofemoral nerve? L1 and L2 nerve roots
2. A patient is planning to undergo an inguinal herniorrhaphy, which nerve blocks would be most beneficial? Ilioinguinal and iliohypogastric nerve blocks
3. The ilioinguinal nerve can be found between which muscle planes? Internal oblique and transversus abdominus muscles

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Low Back

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Aaron Jay Yang and Nitin B. Jain

Introduction

- Evaluation of low back pain can prove difficult at times and a nonspecific diagnosis may lead to poor treatment outcomes. Aside from detailed history and physical examination, neurologic and vascular examination are important components that may help to rule out more serious causes of low back pain such as myelopathy or abdominal aortic aneurysm. Low back pain with leg pain may be secondary to a herniated intervertebral disc compressing on a nerve root. Careful examination will allow for an accurate diagnosis and a focused treatment plan including a specific approach with interventional procedures.

Physical Examination

- ***Inspection*** should occur during history taking as the patient may exhibit avoidance of certain postures such as bending, twisting, or standing during the examination. The iliac crests typically correlates with the level of the 4th lumbar vertebrae and the iliac crests should be equal in height as asymmetry may signify pelvic obliquity. The patient may demonstrate a spine shift in which they shift their lumbar spine away from an irritated nerve root due to a disc herniation. This may potentially draw the nerve root away from the herniated disc. Scoliosis should be noted along with the apex of the curvature as well as any associated muscle asymmetry. When examining the patient in the sagittal plane, the patient should demonstrate a certain degree of lumbar lordosis. Exaggerated lordosis may signify spondylolisthesis, hip flexion contracture, or weak hip extensor muscles.
- ***Palpation*** usually begins with the patient standing and the examiner palpating the top of the iliac crest which corresponds with the L4–L5 disc space. The spinous processes should be palpated for any step off deformity which may indicate spondylolisthesis. The paraspinal muscles may demonstrate spasm or trigger points upon palpation which may indicate presence of underlying pathology. Other structures that should be palpated for any tenderness include the greater trochanters, sacroiliac joints, and ischial tuberosities, on which the proximal hamstring tendons insert.
- ***Range of motion*** should be assessed actively in all planes including flexion, extension, side bending, and rotation. Particular attention

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should be pain to symmetry with lateral flexion and rotation. Mean degrees of normal lumbar range of motion are as follows: flexion (59°), extension (19°), lateral flexion (30–31°), and rotation (32–33°) [1]. Schobers test is another way to assess range of motion of the lumbar spine. A positive test is indicative of a restriction of the lumbar spine, most commonly caused by ankylosing spondylitis. This test is performed by marking the level of the L5 vertebral body with a mark 10 cm above this as well as another mark 5 cm below the original mark. The patient then flexes forward and the distance between the two marks is measured. Normal range of motion should increase the distance between the two marks, but when there is a restriction in lumbar flexion, the distance increases less than 4–5 cm indicating a positive test, signifying restriction.

- ***Neurologic examination*** should include manual muscle testing, sensory testing along the appropriate dermatomes from L2–S1, and reflex examination in the bilateral lower extremities. Radicular pain may be present along a lumbar nerve root pattern while a radiculopathy is technically considered when there is an objective finding such as weakness, sensory, or reflex loss. Common muscles to test include hip flexors (L1–L3 nerve roots), quadriceps (L2–L4), tibialis anterior (L4–L5), extensor halluces longus (L5–S1), and gastrocnemius-soleus muscles (S1–S2). Functional testing is often helpful and can include repeated heel raises (testing S1–S2 nerve roots), single legged sit to stand (L3–L4), and single leg stance (Trendelenburg test) to assess hip abduction weakness (L5 nerve root). It should be noted that dermatomes may vary from patient to patient, with the least variation in distal extremity testing. Common reflexes tested in the lower extremities include the patellar reflex (L2–L4) and Achilles reflex (S1). The L5 reflex can be elicited by tapping the medial hamstring tendon.
- ***Special tests*** of the lumbar spine include provocative tests that may reproduce the patient's radicular leg pain. The examiner should take note if the provoked pain radiates along a dermatomal pattern, which may be correlated with imaging if available and can guide a potential intervention. These tests should not be performed in isolation and used in combination with the remainder of the physical examination.
  - The straight leg raise (SLR), or Lasegue sign, is performed by laying the patient supine and passively lifting the affected leg with knee extended. The test is considered positive if radicular pain is reproduced in the leg between 30 and 70°. Any pain beyond 70° is thought to be secondary to hamstring or gluteal muscle tightness. Sensitivity of this test can be increased by adding foot dorsiflexion and is most helpful for radicular pain that arises from the lower lumbosacral roots.
  - The slump test has been shown to have even greater sensitivity than the SLR test. This test is performed with the patient seated with arms behind their back, legs together and knees against the examining table. The patient slumps forward as much as possible and the patient is asked to flex their head while the examiner applies further light pressure to flex the neck. While maintaining full spine and neck flexion, the affected knee is extended and the patient is asked whether their pain is concordant to their symptoms. Again, increased sensitivity can be added by adding foot dorsiflexion. The patient is then asked to extend their neck and relief of their symptoms with neck extension indicates a positive test. As with the SLR test, this test is more useful when the lower lumbosacral nerve roots are involved.

The femoral stretch test is more useful for upper lumbar nerve root irritation from the L2, L3, or L4 levels. This test is performed by having the patient lay prone with the examiner putting the knee into flexion and assessing whether pain is reproduced in the anterior part of the thigh. Increased sensitivity can be added by also applying hip extension while flexing the knee. This

test is not pathognomonic for an upper lumbar disc herniation and other etiologies can give a false positive test such as a femoral neuropathy, quadriceps or hip flexor tightness, or hip pathology.

- Evaluation of the facet joints can be done to evaluate for axial back pain to due zygapophyseal or facet arthropathy. Typically, pain is worse with hyperextension and the pain can be reproduced in the patient with the passive extension rotation test. In this test, the patient is in the seated position with their arms across their chest. The patient is then brought into extension with full rotation to either side. This increases loading on the facet joints and if pain is elicited during this maneuver, it is considered positive, indicating facet arthropathy or facet mediated pain. However, due to poor sensitivity and specificity of physical examination manuevers for diagnosing facet mediated pain, diagnostic medial branch blocks may be the preferred confirmatory method.

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Hip

16

Aaron Jay Yang and Nitin B. Jain

Introduction

- Unlike the shoulder joint, the hip joint is one of the most stable joints as the femoral head fits within the acetabulum like a ball in a socket. A complete examination should include the lumbar spine and knee as pain can often be referred from these areas to the hip.

Physical Examination

- ***Inspection*** should include any skin changes, swelling, or asymmetry of the muscle or bony contour surrounding the hip region. Foot position while standing may indicate femoral retroversion if there is excess external rotation of the foot while excess internal rotation of the foot may indicate femoral anteversion. Gait should be assessed with attention to abnormal gait patterns which may manifest as leg circumduction, trunk extension, or hip hiking. This may indicate leg length discrepancy, pain, or weakness of the hip extensors. Patients with antalgic gait may demonstrate pain with weight bearing and a shortened weight bearing stance on the affected leg. Single leg stance should be assessed to observe the presence of a "Tredelenbug sign" which would indicate weakness of the gluteus medius muscle. Patients may compensate for this by shifting their upper body over the affected lower extremity.
- ***Palpation*** of the hip region varies by location. Anteriorly, the rectus femoris, iliopsoas, sartorius, and adductor muscles may be palpated as well as the femoral artery. Posteriorly, the posterior superior iliac spine and ischial tuberosities may be palpated. The piriformis muscle is a flat and pyramid shaped muscle which originates anterior to the sacrum and attaches on the greater trochanter of the femur. This muscle can occasionally be palpated for presence of a muscle spasm or trigger point. Laterally, the iliac crest and greater trochanter should be palpated as the presence of bursitis may manifest by point tenderness over the trochanter. The tensor fascia lata and the gluteus medius and minimus muscles may cause tenderness laterally in which they insert into the greater trochanter.
- ***Range of motion*** *of* the hip is often assessed with the patient in supine position. While stabilizing the pelvis, internal and external range of motion can be assessed while prone positioning is preferred to assess hip extension. Symmetry along the hips may be the most

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useful indicator of abnormal pathology as the normal range of motion can vary widely in the literature. The average range of motion needed for common daily activities include sitting (112° of flexion) and ascending stairs (67° of flexion). Functionally, the patient should have ranges of motion of 120° of hip flexion, 20° of abduction, and 20° of lateral rotation [1].

- The following are ***special tests*** that can be used to assess muscle tightness along the hip and lumbopelvic region.
  - Thomas test is useful for determining hip flexion contractures or tightness. The patient lies supine while the examiner assesses for excessive lumbar lordosis. The examiner passively flexes one of the patient's hips and brings the knee to the chest to flatten out the lumbar spine and holds the hip against the chest. If contracture or tightness is present, the patient's straightened leg rises off the table.
  - Ely test is used to identify tightness of the rectus femoris muscle. The patient lies prone while the examiner passively flexes the patient's knee. Upon knee flexion, the patient's hip on the same side may also flex, signifying a positive test and that the rectus femoris muscle is tight.
  - Ober's test is used to assess tightness of the iliotibial band and tensor fascia lata. The patient lies on their side with the affected thigh facing towards the examiner. The leg closest to the table is flexed to remove any lumbar lordosis and the upper leg is flexed at the knee while the examiner holds the ankle lightly with one hand and stabilizes the hip with the other. The upper leg is abducted and extended so that the thigh is in line with the body. If there is tightness of the muscles mentioned above, the leg will remain passively abducted and the test is considered positive.
- The following are ***special tests*** that can be used to assess for any periarticular or intra-articular hip pathology.
  - Stinchfield's test, also known as resisted active straight leg raise test, is performed with the patient lying supine with knee extended. The patient flexes their hip to 20–30° while the examiner provides resistance. Reproduction of groin pain is considered positive indicating potential for an intra-articular hip pathology.
  - FABERE test (Flexion, abduction, external rotation, and extension) is performed by laying the patient in supine position. The examiner then flexes, abducts, and externally rotates the hip being testing with the ankle resting on the contralateral knee. Pressure is applied in a posterior direction to the knee causing further external rotation of the hip. The test is considered positive if it provokes anterior groin pain while pain along the back on the contralateral side may indicate sacroiliac joint pathology.
  - Hip scouring, also known as the hip quadrant test, is performed by laying the patient supine and examiner flexing and adducting the hip to end range until resistance is felt. The examiner than moves the hip in a circular arc while applying compression into the hip joint while maintaining a flexed position of the hip. This attempts to load as much of the acetabular surface with the femoral head and any reproduction of pain, clicking, or locking is considered a positive test. Patients with femoroacetabular impingement may often present with pain with adduction and internal rotation of the hip.
  - Axial hip distraction is performed by laying the patient in supine position and the examiner abducting the hip to 30° and applying traction to the leg by holding the ankle. Relief of the patient's symptoms indicates potential intra-articular process due to compressive forces at the hip.

Questions

1. Trendelenburg sign is indicative of weakness of which muscle? Ipsilateral gluteus medius muscle
2. Thomas test is useful for determining tightness of which structure? Hip flexors (Iliopsoas muscle)

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Knee

17

Aaron Jay Yang and Nitin B. Jain

Introduction

- A thorough examination of the knee should include the hip and ankle joints as knee pain can be secondary to pathology from the surrounding joints. The knee contains two joints: the tibiofemoral joint and patellofemoral joint. The knee joint relies on the surrounding ligaments for stability and it is important to test the ligaments during examination. While the most common diagnosis encountered in the outpatient setting may be patellofemoral pain syndrome, any acute knee injury associated with a "pop" that is felt followed by immediate swelling should be considered to be an anterior cruciate ligament (ACL) tear until proven otherwise and require immediate medical attention.

Physical Examination

- ***Inspection*** of the knee should begin with the patient standing and varus and valgus alignment of the knee should be noted. Patellar position should be observed including whether it is rotated or tilted compared to the contralateral knee as tightness in the quadriceps may change the positioning of the patella on the knee. Swelling of the knee associated with trauma may point to a ligamentous injury, fracture, or meniscal tear. Recurrent swelling without acute trauma may indicate an underling arthritic process. Gait should be observed keeping in mind that knee hyperextension at heel strike may indicate weak hamstring muscles or weak quadriceps may cause excessive hip extension leading to knee hyperextension on heel strike to prevent knee buckling.
- ***Range of motion*** of the knee can be assessed in the neutral position which occurs when the femur and tibia are in a fully extended position. Symmetry of the knee during range of motion should be assessed while normal knee flexion ranges around 135° and extension of 5–10° [1]. Decreased range of motion of the knee can be due to an effusion within the knee joint, a meniscal tear that may limit or block end range knee flexion or extension, or osteoarthritis that typically limits full extension of the knee.
- ***Palpation*** of the knee can be divided into four sections based on their location. The presence of tenderness should be compared side to side and the presence of a knee effusion is best determined by palpation.
  - Medial structures that are palpated on examination include the medial tibial plateau and the medial femoral condyle. Joint line tenderness may lead to suspicion for

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osteoarthritis or medial meniscal tear. Tears of the posteromedial portion of the medial meniscus are the most common type of meniscal tear. Medial meniscal tears are more commonly encountered due to its firm attachment to the medial collateral ligament and joint capsule. The medial collateral ligament as well as the tendons of the sartorius, gracilis, and semitendinosus cross the knee joint and insert on the lower tibial plateau. The pes anserine bursa is located near the common insertion of these muscle tendons and may cause pain when it is inflamed.

- Lateral structures that are palpated on examination include the lateral tibial plateau and lateral femoral condyle, fibular head, and Gerdy's tubercle. The iliotibial band attaches at Gerdy's tubercle distally and is commonly painful along the lateral femoral condyle in which the band can cause friction over this bone. The peroneal nerve courses around the fibular head and is a common location of injury that can subsequently cause a foot drop. The lateral collateral ligament runs between the lateral femoral condyle and attaches at the fibular head distally. The lateral joint line may be a source of tenderness if there is injury to the lateral meniscus.
- Anterior structures that are palpated on examination include the patella and the trochlear groove of the femur which is located above the level of the patella. The patellar tendon should be palpated as it is a continuation of the quadriceps tendon.
- Posterior structures that should be palpated on examination include the posterior fossa which is the common location of Baker's cysts as this often communicates directly with the joint space of the knee. The fossa is bordered by the hamstring tendons superiomedially (semimembranosus tendon) and laterally (biceps femoris) while the medial and lateral heads of the gastrocnemius muscle borders it inferiorly. The popliteal artery passes through the fossa and palpation of this artery is best performed with the knee in flexion as this relaxes the calf and hamstring muscles.

- There are multiple ***special tests*** of the knee that vary depending on the structure that is being tested. Only select tests will be specifically described here, while we recommend you refer to the suggested reading section below for discussion on how to perform these individual tests.
  - Ligaments
    - Anterior Cruciate Ligament: Anterior drawer test, Pivot shift test, Lachman test.
      - The Lachman test is performed with the patient supine while the knee is held at 15° of flexion. The femur is stabilized with one hand while the other hand applies pressure to the proximal tibia in attempt it to translate it anteriorly. Side-to-side comparison should be performed and a firm endpoint indicates an intact ligament.
    - Posterior Cruciate Ligament: Posterior drawer test, Posterior sag sign.
    - Medial Collateral Ligament: Valgus stress testing.
    - Lateral Collateral Ligament: Varus stress testing.
  - Meniscus
    - Joint line tenderness, McMurray test, Apley grind test, Bounce home test, Thessaly test.
      - McMurray test is performed with the patient lying supine with the knee flexed. One hand is placed along the joint line while the other hand cups the sole of the foot. The examiner stabilizes the lateral side of the knee while applying a valgus stress with the other hand as it rotates the leg externally while extending the knee. If there is pain or a click with knee extension, this indicates a positive test for a medial meniscal tear. The opposite motion of varus stress and internally rotating the leg while extending the knee tests the integrity of the lateral meniscus.

- Patella
  - Patellofemoral grind test, Apprehension test.

Questions

- What is the most common location for a meniscus tear? Posteromedial corner of the medial meniscus.
- What tendons insert at the pes anserine? Gracilis, Sartorius, Semitendinosus.
- What is the most common cause of anterior knee pain? Patellofemoral pain syndrome.

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Ankle

18

Aaron Jay Yang and Nitin B. Jain

Introduction

- Complete examination of the ankle should also include the foot and knee. Lateral ankle sprains are one of the most common sports injuries encountered and the anterior talofibular ligament (ATFL) is the most common ligament injured. Ankle inversion injuries are much more common than eversion injuries due to weakness of the lateral ligaments compared to the medial deltoid ligaments. Ankle sprains can be graded based on the presence or extent of a ligament tear. Grade 1 includes a stretch or partial ATFL tear, Grade 2 includes a complete ATFL tear with stretch or partial tear of the calcaneofibular ligament (CFL), and Grade 3 includes complete tears of the ATFL and CFL. Appropriate physical examination and knowledge of special tests can help diagnose and allow proper grading of ankle injuries. Although ankle sprains are mostly thought of as a benign injury, inadequate healing time and rehabilitation can lead to prolonged symptoms and can mask other injuries around the ankle joint such as fractures and tendinopathies.

Physical Examination

- ***Inspection*** of the ankle begins by examining the patient's gait, standing posture, and shoe wear pattern. Any gross deformity, atrophy, or malalignment should be noted with side to side comparison. Hallux valgus (bunion), hammertoes, skin, and nail deformities should also be noted. Weight bearing posture of the foot and ankle should be observed with shoes and socks removed. This may reveal a high longitudinal arch (pes cavus) or flat foot (pes planus) as well as varus or valgus deformities of the hindfoot.
- ***Palpation*** of the foot can be divided into three sections: hindfoot (talus and calcaneus), midfoot (navicular, cuboid, and cuneiforms), and forefoot (metatarsals and phalanges).
  - Proximally, the shaft of the tibia and fibula should be palpated as syndesmotic injuries can occur in association with ankle injuries and can even cause fractures of the proximal fibula. The ankle mortise should be palpated along the tibiofibular and tibiotalar articulation. The medial and lateral malleolus should be palpated noting that the lateral malleolus extends more distally, thus limiting eversion of the ankle.

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- Posteriorly, the Achilles tendon should be palpated into the insertion point near the calcaneal tuberosity. Pain may be present at this location due to tendonitis or bursitis at the retrocalcaneal bursa.
- Careful palpation of the navicular and the base of the 5th metatarsal should be performed as chronic injuries can be seen at these locations. Metatarsal shafts should be individually palpated as tenderness along the dorsum of the foot may indicate a fracture. Pain along the plantar aspect of the first metatarsophalangeal joint may indicate inflammation of the joint capsule, which is also known as "Turf toe."
- The ATFL originates along the anterior border of the lateral malleolus and inserts along the body of the talus while the CFL also originates along the lateral malleolus and inserts on the calcaneus. This ligament is most taut with the ankle in a slightly dorsiflexed position. The posterior talofibular ligament originates from the posterior border of the lateral malleolus and inserts on the posterior talus and is the strongest of the lateral ligaments. Medially, the deltoid ligament originates from the medial malleolus and is composed of four different ligaments.

- ***Range of motion*** of the ankle should evaluate passive and active range of motion. Passive range of motion should be assessed with the foot off the ground and resting on the examining table. Motions can be complex based on the multiplanar joint movements and interactions. The tibiotalar joint is primarily responsible for foot dorsiflexion and plantarflexion while the talocalcaneal (subtalar) joint allows foot inversion and eversion. Internal and external rotation of the ankle refers to the combined tibiotalar and talocalcaneal motion while pronation and supination of the foot involve movements of the midfoot and forefoot.
- ***Special tests*** of the ankle may not only provoke the patient's pain or demonstrate increased laxity of the ankle joint, but may also help narrow down the etiology of pain and also allow for grading of ankle sprains.
  - **Anterior draw test** is used to examine the ATFL and the integrity of the ligament. The patient is sitting and relaxed while the examiner stabilizes the distal part of the leg with one hand while the other hand is used to cup the calcaneus. Anterior force is applied to the heel in attempt to sublux the talus anteriorly from beneath the tibia. Side to side comparison should be performed to assess degree of subluxation.
  - **Talar tilt test** is used to primarily examine the lateral ligaments and the CFL in particular. The patient is in a seated position with the ankle and foot unsupported to 10–20° of plantarflexion. The examiner stabilizes the medial aspect of the distal part of the leg just proximal to the medial malleolus while the other hand is used to supinate the hindfoot. The degree of tilt should be compared side to side and pain may be experienced over either the CFL or ATFL.
  - **Syndesmosis squeeze test** examines the distal tibiofibular joint. This test is performed by manually compressing the fibular to the tibia above the midpoint of the calf. A positive test would produce pain over the area of the syndesmotic ligaments.
  - External rotation or **Kleiger's test** is also used to identify syndesmotic injuries. The patient is seated and the distal tibia is stabilized while externally rotating the foot. External rotation of the foot causes widening of the tibiofibular joint and the patient may have pain anterolaterally. A positive test would be indicated by increased external rotation of the foot when compared bilaterally or pain along the anterolateral ankle joint.
  - **Thompson's test** is used to confirm an Achilles tendon rupture. The patient is placed in prone position with their foot hanging off the edge of the bed. The calf muscle is squeezed slightly distal to the widest girth of the muscle belly. A positive test would be when there is no plantar movement of the foot when the calf is squeezed indicating rupture of the Achilles tendon.

Questions

1. The most common ligament affected with lateral ankle injuries is? Anterior talofibular ligament
2. Which joint primarily allows dorsiflexion and plantarflexion of the foot? Tibiotalar joint

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Vascular

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Aaron Jay Yang and Nitin B. Jain

Introduction

- Patients with predominantly lower extremity limb pain may have underlying vascular disease from thrombosis or vascular claudication. The axillary, calf, and femoral veins are common sites of thrombosis and it is important to take into consideration a history of clotting disorders such as Factor V Leiden, antiphospholipid syndrome, protein C or S deficiencies, and antithrombin III deficiency. Symptoms related to vascular claudication may first be noticed with exercise or prolonged walking and may mimic musculoskeletal diseases or symptoms closely resembling neurogenic claudication from spinal stenosis. The goals of the physical examination should be to establish quality and presence of pulses and to identify the presence of bruits, venous disease, signs of ischemia, or presence of an aneurysm.

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Physical Examination

- Examination should follow this sequence: observation, auscultation, and palpation.
- ***Observation*** should include any signs of gangrene, blackening of the extremities, and presence of ulcers. Careful observation should be performed in the legs and feet including behind the ankle and between the toes. Each limb should be observed for ischemic signs including color, capillary refill, temperature, and ulceration. Capillary refill should be checked at the nail bed with normal refill occurring less than 2 s.
  - Venous signs include brawny coloration, ulceration, varicose veins, and edema.
  - The 5 "P's" for signs of acute ischemia include pulseless, pallor, paresthesia, paralysis, and poikilothermia. Nerves are most susceptible to acute ischemic injury followed by muscle and tendon and bone.
  - Chronic ischemia can lead to skin changes which can include loss of hair, abnormal nail growth or fungus formation, and thin, dry skin.
- Ulcers can also signify poor blood supply and can be arterial or venous in nature.
  - Arterial ulcers are distal in location with sharp margins and often associated with no pulse and can be painful.
  - Venous ulcers are often located around the malleolus with irregular margins and associated with normal pulses and can vary in terms of pain presentation.

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- ***Auscultation*** should be performed over areas in which bruits might be present. Bruits are caused by turbulent arterial blood flow through a narrowed portion of the artery. Locations to auscultate for bruits include the carotid, aorta, and femoral arteries.
- ***Palpation*** should include checking for pulses. Pulses should be palpated at the dorsalis pedis, posterior tibialis, femoral, popliteal, and carotid arteries. Abdominal examination should also include careful palpation to rule out an aortic aneurysm.
- The following are ***special tests*** that can be used to assess for patients with peripheral vascular disease and arterial insufficiency.
  - Ankle brachial index assesses for presence of peripheral vascular disease. This test can be unreliable in patients with calcified arteries or in those with edema. This index is calculated by dividing the systolic blood pressure of the ankle by the pressure in the arm. Normally, the pressure at the ankle is slightly higher than at the elbow with normal values ranging between 0.9 and 1.2. Any value less than 0.4–0.5 requires urgent referral to a vascular specialist.
  - Buerger's test for arterial insufficiency. The patient is placed in the supine position and the color of the feet and soles is noted (should typically be pink). The legs are elevated to 45° or more for 1 min and then the color of the soles should be reassessed. If there is marked pallor then ischemia should be suspected. The angle in which pallor is first noted is also known as the vascular angle and an angle of less than 20° indicates severe ischemia. The patient can then be sat upright and it can be noted how quickly the soles of the feet regain their pink color.

Questions

- What are the 5 "P's" of acute ischemia? Pulseless, pain, pallor, paresthesia, paralysis, and poikilothermia.
- What would an ABI of >1.2 signify? Abnormal blood vessels due to severe peripheral vascular disease or significant calcification.
- What type of ulcers is more commonly painful? Arterial ulcers which are also more sharply demarcated and distal in location.

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Dystonia

20

Aaron Jay Yang and Nitin B. Jain

Introduction

- Dystonia is a movement disorder characterized by involuntary, sustained muscle contractions causing posturing, twisting, and repetitive movements that can change in severity depending on activity and posture. This can be further classified as focal, segmental, or generalized [1].
- Dystonic movements can be triggered or exacerbated by voluntary movements or intentional movement of body parts and can last up to hours to weeks, when severe, leading to bony deformities and contractures with subsequent loss of function.
- Treatment often depends on the focality of symptoms. General dystonias may respond to medications affecting GABA transmission while techniques such as stretching, massage, and interventional modalities may be useful for focal dystonias.

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Physical Examination

- This section will focus on a more common dystonic symptom known as cervical dystonia or torticollis.
- The goal of physical examination should be to identify the presence of cervical dystonia as the primary process, as opposed to a generalized dystonia, which may suggest other forms of dystonia such as those with a genetic etiology.
- Although abnormal head position is enough for the diagnosis, physical examination in patients with cervical dystonia must be focused on detection of "pseudodystonia" secondary to structural abnormalities. A complete neurologic examination should be performed, including strength testing, sensory deficits, and gait evaluation to exclude secondary dystonia. The presence of corticospinal, sensory, cerebellar, oculomotor, or cortical signs with cervical or extracervical dystonia suggests secondary dystonia [2].
- ***Inspection*** of head and neck posturing as well as neck range of motion in passive and active planes should be characterized and noted.
- Documentation should include tone of the neck muscles as symmetric, assymetric, or absent and a description of the muscle bulk on palpation should also be noted.
- ***Findings seen on physical examination***
  - Rotational torticollis is characterized by a slightly rotated head with nose and chin towards the shoulder on the affected side, which is the most common head and neck

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deviation. With simple torticollis, no head tilt is present.

- Torticollis may further be characterized by the direction of rotation defined by the chin:
  - Laterocollis—head tilts to one side with ear toward the shoulder in coronal plane while there is asymmetric tone and muscle bulk.
  - Anterocollis—head tilts forward with chin toward the chest with increased tone and bulk of the anterior cervical muscles.
  - Retrocollis—head tilts in hyperextension with increased tone and bulk of the posterior cervical muscles.
- 66–80 % of patients present with a combination of these movements [2].
- Phasic head components include:
  - Spasmodic jerks—rapid, clonic, irregular jerks with less rapid recover toward the neutral position.
  - High frequency oscillations—horizontal, vertical, mixed, or irregular tremors.
  - Of note, the terms spasmodic and spastic are misleading when describing torticollis because there is no evidence that cervical dystonia is a spastic disorder or caused by dysfunction of the pyramidal tracts [2].

Other conditions that should be considered in the evaluation of a patient with torticollis include:

- Acquired dystonia of childhood—hematoma or tumor of sternocleidomastoid muscle.
- Anterior horn disease.
- Radiculopathy.
- Cervical facet syndrome.
- C1 and C2 fractures.
- Cerebral palsy.
- Multiple sclerosis.
- Parkinson disease.
- Peritonsillar abscess.
- Retropharyngeal abscess.
- Spinal hematoma.
- Tardive dyskinesia.

Questions

- What is the most common deviation seen with cervical dystonia? Rotational torticollis, followed by head tilt, retrocollis, and anterocollis. There is no statistically significant preponderance of right or left deviation.

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Pain Assessment Tools

21

Michael P. Zaccagnino and Srdjan S. Nedeljkovic

Methods of Pain Assessment

- **Self-report**
  - Pain scales
  - Pain questionnaires
- **Behavioral**
  - Observation methods
- **Biological**
  - Experimental pain assessment
  - Psychophysiological assessment

Self-Report Pain Measurement

Because pain perception is considered a subjective experience, self-report methodologies are most commonly used and represent the standard of care in determining patients' pain characteristics. They provide focused assessments and quantifications of patients' pain in single (pain intensity scales) or multiple (pain questionnaires) dimensions in a timely and cost-effective manner. Because published pain scales and questionnaires have met standards for reliability and validity, greater confidence can be placed in the information provided by these measures.

Pain Scales

Pain scales are simple, single-dimensional methods of pain measurement, and *only assess the domain of pain intensity*. They provide valuable, efficient, minimally intrusive numerical measures of pain intensity and have been widely used in clinical and research settings. The main disadvantage of pain scales is that they fail to account for the complex, multidimensional experience associated with pain. The most commonly used pain scales in research and clinical practice include:

Pain Intensity

Numerical Rating Scale (NRS)

- Description: Consists of a scale 1–10 with "no pain" (0) and "worst possible pain" (10) endpoints. Patients are asked to choose the number that best corresponds to their pain intensity.
- Pros/Cons: Simple to administer with high completion rates. Demonstrates reliability and validity, though single item assessment hin-

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ders reliability. Additionally, NRS does not have ratio qualities, and the choice of endpoint descriptors can significantly affect results. Recommended by IMMPACT as a core outcome measure of pain intensity in chronic pain clinical trials.

Verbal Rating Scale (VRS)

- Description: Consist of verbal pain descriptors from least to most intense, and patients are asked to choose the word that best describes their pain intensity over some time interval.
- Pros/Cons: Simple to administer with high completion rates. Demonstrated reliability and validity. May be difficult for persons with poor English language skills, and descriptors may not accurately represent the pain experienced. Also, VRS does not have ratio qualities, and compared to NRS and VAS, lacks sensitivity to detect changes.

Visual Analog Scale (VAS)

- Description: Consist of a 10-cm line with "no pain" and "worst possible pain" endpoints, and patients are asked to place a mark on the line that corresponds to their pain intensity over some time interval.
- Pros/Cons: Simple to administer, however, more likely to be incomplete (vs. NRS or VRS). Demonstrates reliability and validity, though single item assessment hinders reliability. This tool uses *ratio* properties that allow more meaningful comparison over time and between independent individuals. Additional limitations in this scale are in patients with perceptual-motor issues (commonly seen in elderly and cognitively impaired populations) and the inability to use in telephone surveys.

Faces Pain Scale Revised

- Description: Comes with verbal administration instructions, and was originally developed for children older than 6 years of age. Consist of a series of faces with "no pain" and "very much pain" endpoints, and the patients are asked to choose the face that best corresponds to their pain intensity.
- Pros/Cons: Simple to administer with high completion rates. Demonstrates reliability and validity. It can be converted to a 0–10 rating scale. And because the faces were shown to represent equal intervals, thus having ratio qualities, it shares a close relationship to VAS. Also proves useful in elderly patients with cognitive impairment.

Pain Questionnaires

Pain questionnaires are more complex, multidimensional methods of pain assessment. These were created to further assess and encompass the full experience of pain as well as to aid in diagnosis and better measure treatment outcomes. There are a variety of questionnaires that assess various numbers of different domains, and they are often grouped according to the major domain being evaluated. This review will focus on the more broadly used questionnaires.

Pain Quality

McGill Pain Questionnaire (MPQ)

- Description: The original MPQ was designed to correlate with Melzack and Casey's threedimensional model of pain assessment (sensorydiscriminative, affective-motivational, and cognitive-evaluative). It is among the most widely studied tools for measuring pain. The MPQ consists of 20 sets of verbal descriptors used to assess the sensory (10 sets), affective (5 sets), evaluative (1 set), and miscellaneous (4 sets) dimensions of pain. Patients select the words that describe their pain and a VRS to assess present pain intensity (PPI). This information is grouped into three major indices: (1) pain rating index (PRI), (2) total word count, and (3) PPI.
- Pros/Cons: Correlates highly with sensory, affective, and evaluative domains, demonstrating reliability, validity, and utility. Translated into at least 20 languages and takes 5 min to complete. Contains a large number of descriptors that may prove difficult for cognitively impaired individuals to benefit from, and may not be needed to adequately assess validity—one reason the short-form MPQ was developed.

By using a composite PRI, this limits investigators ability to detect the impact of specific pain qualities. As a result, this reduces the test's sensitivity and responsiveness to treatment effects. Also, high anxiety levels and other psychological disturbances generate high affective scores thereby offsetting its discriminative capacity.

Short-Form McGill Pain Questionnaire 2 (SF-MPQ 2)

- Description: The original SF-MPQ was developed to provide additional discriminatory information and minimize assessment burden. However, recent advances in research and pain measurement techniques prompted the development of the more frequently used SF-MPQ 2 to include additional descriptors associated with neuropathic pain conditions. The SF-MPQ 2 consists of 22 descriptors grouped into four subscales—continuous pain (6), intermittent pain (6), neuropathic pain (6), and affective descriptors (4). Each descriptor is rated by the patient on a NRS between 0 and 11, with "no pain" and "worst possible pain" endpoints, and the mean is computed from each subscale and total score.
- Pros/Cons: Demonstrates reliability, validity, and utility, with adequate discriminating capacity for neuropathic and non-neuropathic pain qualities, as well as sensitivity to change. It is also easy to administer with a low assessment burden. SF-MPQ 2 web-based questionnaires produced significantly higher neuropathic pain scores; therefore, additional research is needed to address this potential shortcoming.

Pain Quality Assessment Scale (PQAS)

- Description: The PQAS is a modification of the original, highly utilized Neuropathic Pain Scale (NPS) questionnaire, with ten additional neuropathic and non-neuropathic pain descriptors incorporated to assess more pain qualities across chronic pain conditions. The PQAS consists of 21 items total, with 18 quality and spatial descriptors, and three temporal items. Like the SF-MPQ 2, each of the 18 descriptors is rated on a NRS between 0 and 11, with "not tender" and "the most tender sensation imaginable" endpoints.
- Pros/Cons: Demonstrates reliability and validity, and sensitivity to change. It has also been shown to be more useful than the NPS for identifying specific effects of pain treatments on different qualities of pain. More research is accumulating regarding its potential and may prove to be the most useful measure of pain's effects on specific pain qualities.

Psychological Functioning

Minnesota Multiphasic Personality Inventory 2 (MMPI 2)

- Description: The original MMPI is an objective measurement tool of personality and psychological functioning of patients. The more recent version, MMPI 2, was developed in light of advances in psychopathology, as well as contains fewer items to reduce patient burden. The MMPI 2 consists of 338 T/F items grouped into scales of higher-order, clinical, validity, somatic/cognitive, internalizing, externalizing, interpersonal, interest, and personality psychopathology.
- Pros/Cons: The original MMPI was normalized to psychiatric patients, and has significant concerns regarding utility in patients with chronic pain—clinical differences between pain and non-pain samples have demonstrated to more likely reflect disease status than psychological functioning. Regarding the MMPI 2, no information is available to indicate whether this issue has been elucidated, and should be used with caution in chronic pain patients until further studies are available to validate its use.

Global Rating of Quality and Improvement

Patient Global Impression of Change (PGIC)

- Description: Consist of a single item question on a 7-point Likert scale with "very much worse" and "very much improved" endpoints.
- Pros/Cons: Easy to administer with widespread use in recent chronic pain trials as an anchor in determining the clinical importance of improvement in pain ratings. Provides a responsive and readily interpretable assessment of patients' viewpoint on the importance of their pain treat-

ment. Recommended by IMMPACT as a core outcome measure of global improvement with treatment in chronic pain clinical trials.

Pain-Related Physical and Emotional Functioning

Please see Chap. 22.

Behavioral Pain Measurement

Behavioral Observation

Research in the objective assessment of pain behavior has produced a wide array of sophisticated observational techniques and rating scales, though many are specific to particular pain conditions. Such techniques have demonstrated reliability and validity, and have shown to be especially useful for measuring pain in newborns, infants, and preverbal children. Additional utility has been shown in patients who lack language skills and the cognitively impaired. The best evidence of the reliability and validity of behavioral measures is based on studies of short, painful stimuli. To ensure psychometric qualities are met, often considerable technological sophistication and expense is required. Accordingly, behavioral observation methods are commonly limited to the research setting and clinical utility is limited.

Patients may communicate pain through body postures, facial expressions, vocalizations (i.e., crying, moaning), and actions (i.e., limping, guarding, and rubbing the affected area); these verbal and nonverbal behaviors are termed pain behaviors. In addition to measuring pain, pain behavior assessment can be valuable in evaluating physical functioning and analyzing factors that may reinforce pain (i.e., solicitous responses from others).

Biases in behavioral observation are important to consider. Healthcare providers have been shown to systematically underestimate pain measurement. Moreover, when discordance exists between nonverbal pain behavior and patients' verbal report of pain, the discrepancy is often resolved by disregarding patients' self-report. Correspondence between self-report and behavioral observation are modest at best, and behavioral measures of pain should not replace the gold standard of self-report when feasible.

There is a lack of consensus regarding which one of the available measures is the most valid and reliable in most populations. Please refer to published reviews for the most up-to-date information regarding behavioral observation measurements. Below are a few of the more commonly used assessment tools.

Facial Action Coding System

- Has been developed for measuring pain in infants, children, and adults. Consists of facial actions that trained coders can identify, accordingly, they often require video recording and are time consuming. Also, patients' faces that are obstructed because of medical/surgical interventions make facial actions difficult to assess.

Dementia in Elderly

Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC)

- Appears valid for use in elderly individuals with dementia, but more research is needed.

Pediatric Postoperative Pain Assessment

Face, Legs, Activity, Cry, and Consolability (FLACC)

- PedIMMPACT recommended the FLACC scale for postoperative pain in pediatric patients aged 3–18. Behavior is rated by a trained observer using a 0–2 scale. It has extensive reliability and validity data.

Children's Hospital of Eastern Ontario Pain Scale (CHEOPS)

- PedIMMPACT also recommended CHEOPS for postoperative pain in pediatric patients aged 3–18. It consists of six types of behavior (crying, facial expression, verbal expression, torso position, touch position, and leg position), with demonstrated interrater reliability

and validity, as well as sensitivity after intravenous opioids administration.

Pediatric Critical Care Pain Assessment

COMFORT Scale

- PedIMMPACT recommended the COMFORT scale pain measurement in pediatric critical care settings. It reports on alertness, calmness or agitation, respiration, physical movement, change in blood pressure, change in heart rate, muscle tone, and facial tension. Extensive validity data exists.

Biological Pain Measurement

Experimental Pain Assessment

This method of pain assessment consists of administering standardized noxious stimuli under controlled conditions and measuring patients' responses. Noxious stimuli commonly used to induce pain consist of: thermal, mechanical, electrical, chemical, and ischemic. Typical pain parameters measured include: pain threshold, pain tolerance, and ratings of suprathreshold noxious stimuli using an NRS, VAS, or VRS. Experimental pain assessment can be used to subtype patients with chronically painful conditions, to identify mechanisms of chronic pain, and to prospectively predict postoperative pain.

Psychophysiologic Evaluation

Psychophysiologic measures can provide a number of important functions in assessment of acute and chronic pain. It helps determine if psychological factors are influencing biological responses to pain and can provide behavioral feedback strategies for coping. Biofeedback is the most common psychophysical measure applied. Clinicians can use this data to determine the utility of certain pain treatments, and patients can receive direct feedback regarding the success of behavioral strategies. Psychophysiologic data serve as a prerequisite for performing biofeedback as well as serve to elucidate concomitants of pain not easily measured by self-report.

Techniques to Gather Psychophysical Data Include

- Surface electromyography (EMG)
- Electroencephalography (EEG)
- Measures of blood flow
- Skin temperature
- Heart rate variability
- Skin conductance

EMG is the most widely used technique for psychophysiologic evaluation since muscle tension is implicated in the majority of musculoskeletal pain disorders. EEG has been used in studies to assess brain responses to pain, and studies have shown the EEG measured cortical responses to standardized noxious stimuli are enhanced in patients with chronic pain. Blood flow and skin temperature measurement can provide feedback in pain syndromes such as headaches and Reynaud's disease.

Despite high initial correlations between pain onset and changes in physiological responses, many physiological responses habituate with time despite the persistence of pain. Furthermore, these responses are not entirely specific to the experience of pain and occur under other conditions, such as general arousal and stress. Overall, psychophysiologic measures can provide unique information about pain response; however, they cannot serve as surrogate measures for the experience of pain.

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Functional Assessment Tools

22

Michael P. Zaccagnino and Srdjan S. Nedeljkovic

Introduction

Assessment of patients' pain-related physical and emotional functioning is one of the most important measures in pain evaluation, and are two of the four key domains recommended by IMMPACT for interpreting the significance of treatment outcomes in clinical trials.

Because functional assessment is a multidimensional experience, multiple domains are concomitantly evaluated; these include the impact of pain on daily activities and the level of function in emotional, occupational, and social settings. In general, functional assessment largely involves self-report questionnaires that attempt to measure patients' perception of how pain interferes with specific activities and behavior.

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Functional Assessment Questionnaires

This review will focus on the more well-known functional assessment tools.

Global Pain Related Physical Functioning

Multidimensional Pain Inventory (MPI)

- Description: The MPI (formerly known as the West Haven-Yale Multidimensional Pain Inventory—WHYMPI) consists of 64 items composed of 3 parts and 12 subscales. Part 1 includes 6 scales measuring pain-related interference across several domains, including a pain severity scale. Parts 2 and 3 assess spouse responses to patient pain behaviors and participation in various life activities, respectively. The interference domain assesses the degree to which pain affects daily activities, satisfaction with activities, and social relationships.
- Pros/Cons: Takes 10–15 min to complete and is written at a 5th grade reading level. Demonstrates reliability, validity, and utility in many medical conditions including chronic back pain, temporomandibular disorders, and headaches. Has a strong association with pain severity and is responsive to change associated with

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pain treatments. Is particularly useful for assessing spousal predictors of patients' severity of pain and pain-related disability and distress. Appreciably, IMMPACT has recommended use of the MPI interference scale as a functional outcome measure in pain clinical trials.

Brief Pain Inventory (BPI)

- Description: Originally developed for cancer patients, however, is widely used in all pain conditions. The original BPI consists of 32 items used to assess seven domains of pain interference: general activity, mood, walking ability, relations with other people, work, sleep, and enjoyment of life. Patients rate their pain interference on a NRS between 0 and 10, with "no interference" and "completely interferes" endpoints, and responses from each of the seven domains are averaged to form the pain interference scale score.
- Pros/Cons: Takes 10 min to administer, and demonstrates reliability, validity, and utility in all pain patients. It also shows strong associations with measures of pain intensity. The BPI was modified to reflect patients with physical disability (by changing the wording from "walking" to "mobility" interference), and increased its validity by including 5 additional domains of pain interference: self-care, recreational activities, social activities, communication, and learning. However, this modification sacrificed brevity, which is why the short-form BPI (SF-BPI) was developed.

Short-Form Brief Pain Inventory (SF-BPI) and PEG

- Description: The SF-BPI consists of 15 items. The PEG is an ultra-brief version of the BPI that consists of 3 items: (P) pain intensity, (E) enjoyment of life, and (G) general activity.
- Pros/Cons: The SF-BPI maintains the original's psychometric qualities, is available in many languages, and is appreciably recommended by IMMPACT for use as a measure of physical functioning in pain clinical trials. The PEG also demonstrates reliability and validity, although some sources say PEG warrants further validity evaluation.

Pain Disability Index (PDI)

- Description: Consists of 7 items that assess perceived disability within family and home responsibilities, recreation, social activity, sexual behavior, self-care, and life support activity. Each item is rated on a 10-point Likert scale with "no disability" and "worst disability" endpoints.
- Pros/Cons: Brief assessment with excellent reliability. Validity has been demonstrated through its association with the Oswestry Disability Index. Proven useful in tracking responses to treatment in a broad range of painful conditions across a variety of different treatment modalities.

Back Pain Related Physical Functioning

Oswestry Disability Index (ODI)

- Description: Specific questionnaire for back pain research. Consists of 10 sections that include pain intensity, personal care, lifting, walking, sitting, standing, sleeping, sex, social life, and travelling. Each section is scored on a 0–5 NRS, with "no limitation" and "maximal limitation" endpoints, and are added up for a total of 50 points, then doubled and interpreted as a percentage of the patient's perceived disability (the higher the score, the greater the disability).
- Pros/Cons: Excellent reliability and clinical face validity. Considered by many to be the gold standard for measuring degree of disability and estimating quality of life in a person with low back pain.

Roland-Morris Disability Questionnaire (RDQ)

- Description: Originally derived from the Sickness Impact Profile (SIP) questionnaire and modified by adding "because of my back

pain" to each item; thus, specific to assessment of back pain. Consist of 24 items involving physical function that are potentially affected by low back pain, and patients simply answer "yes" or "no," for a total possible score of 24.

- Pros/Cons: Strong psychometric properties of reliability and validity, and sensitive to change over time. Used in a variety of studies and translated into many different languages.

Global Pain Related Emotional Functioning

Beck Depression Inventory II (BDI-II)

- Description: Probably a well known measurement of depressive symptoms, and used commonly in pain assessment. This questionnaire consists of 21 items with each containing 4 answer statements designed to assess severity of depressive disorders for a total score ranging from 0 to 63.
- Pros/Cons: Demonstrates excellent reliability and validity, as well as sensitive to change especially in pain treatments (pharmacological and non-pharmacological). Recommended by IMMPACT for assessment of emotional functioning, one of the core outcome measures, in pain clinical trials. Chronic pain patients have demonstrated that somatic items may be associated with pain rather than mood. Also, bias may exist in certain populations (i.e., women, adolescents, and elderly persons).

Profile of Mood States (POMS)

- Description: Used extensively as per the pain treatment literature. Consists of a 65 item adjective checklist that provides a total mood disturbance score and 6 subscale scores (tension, depression, anger, vigor, fatigue, and confusion). Patients are report the degree to which each mood state has applied to them over the past week via a 0 (not at all) to 4 (extremely) Likert scale.
- Pros/Cons: Strong psychometric properties and sensitive to change (especially in analgesic medication trials) in a variety of painful conditions. Has the ability to capture negative and positive dimensions of emotional function, takes 5 min to administer, and available in multiple languages. Recommended by IMMPACT for assessment of emotional functioning, one of the core outcome measures, in pain clinical trials.

Hospital Anxiety and Depression Scale (HADS)

- Description: Originally developed in 1983 for patients with physical health problems in a general medicine clinic. This questionnaire consists of 14 items that generate ordinal data for the two most common mood disturbances – depression and anxiety. Seven items relate to anxiety and seven to depression, each of which is scored 0–3, providing a 0–21 severity score for either condition.
- Pros/Cons: Shows great psychometric properties in a wide variety of settings, including chronic pain with responsiveness to change as a result of pain treatment. Easy to complete in only a few minutes and available in multiple languages. Importantly, avoids the use of somatic symptoms to reduce false positives, as well as adequately distinguishes between the two mood states. Does not over-report the incidence of depression.

Patient Health Questionnaire 8 (PHQ-8)

- Description: The original, self-report questionnaire developed by Pfizer in the 1990s to assess anxiety, depression, and somatoform disorders (known as the Primary Care Evaluation of Mental Disorders (PRIME-MD)) was modified for more efficient administration into the Patient Health Questionnaire. Today, there exists a few different versions of the PHQ, including the full and brief PHQ, as well as, the PHQ-2, -8,-9 (evaluates depression only), and -15 (evaluates somatoform disorders). We will focus on the PHQ-8, which omits the 9th item (self-harm) on the PHQ-9 for reasons of

redundancy and lack of added clinical value in non-depression research studies and clinical settings. The PHQ-8 consists of eight items, each of which is scored 0–3, providing a 0–24 severity score (mild, moderate, and severe).

- Pros/Cons: Shows great psychometric properties in a variety of different settings, including the elderly, patients with mild cognitive impairment, adolescents, and peripartum women. Demonstrates sensitivity to change over time periods and with treatment, is easy to administer, and available in multiple languages.

Functional Capacity Evaluation (FCE)

Introduction

A FCE is a systematic, comprehensive, and "objective" set of tests, practices, and observations that are combined to determine a person's maximum safe functional ability relative to a variety of circumstances, most often for employment. There are a number of different types of functional capacity evaluations, with recent interest from insurance companies and governmental agencies (i.e., United States Social Security Administration (SSA)) for their utility. Typically, a physical or occupational therapist provides recommendations on which FCE to use, as well as, administers the evaluation. The United States SSA has its own FCE, called the Assessment of Disability. Also, the World Health Organization (WHO) recently designed a new FCE called the International Classification of Functioning, Disability and Health (ICF).

Physician Role

Clinicians provide the best evidence of medical impairments and their implications. As a result, their role is to define and document such findings from all available sources and integrate the information into a coherent picture of the patient's overall medical-related ability.

General Functions of FCEs

- Determine fitness to work following a period of medical leave
- Provide information on prognosis and potential occupational rehabilitation treatment measures, as well as evaluate the effectiveness of such rehabilitation
- Identify changes in the workplace that an employer might be able to undertake to accommodate an employee
- In some instances, required by insurers before payments can be made
- Determine eligibility for disability or pension insurance in the event that an person is unable to return to work

Limitations of FCEs

- Performance testing by a trained therapist, vs. self-report, is considered more useful; however, such testing is time-consuming, requires specialized equipment, and expensive.
- Self-report measures have been found to systematically underestimate functional ability when compared to performance testing.
- Less than maximal effort on the patient's part will severely limit the results.
- Measure functional ability at a single point of time, so issues of fatigue and endurance are minimized.
- Patients' performance appears to be influenced by psychological and social factors.
- Overall, FCE results are not predictive of outcome following multidisciplinary rehabilitation and are only modestly predictive of future return-to-work.

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Placebo and Pain

23

William Caldwell and Karina Gritsenko

Introduction and History

- Placebos and their effects have been described in medical literature for at least two centuries, but the complex neurological mechanisms responsible for it are still unknown.
- The word "placebo" comes from Latin origins meaning, "I shall please."
- Beginning in the 1960s, the placebo effect became widely recognized and placebo controlled trials became the norm in the approval of new medications.

Definitions

- A placebo is an intervention designed to simulate medical therapy, but not believed to be a specific therapy for the target condition.
- A placebo effect is a change in a patient's illness attributable to the symbolic import of a treatment rather than a specific pharmacologic or physiologic property.
- A placebo response refers to any change in patient behavior or condition following the administration of a placebo.
- Nonspecific influences of treatments may produce adverse effects or "nocebo effects" [1].

Mechanism of Placebo

- The mechanism of the "placebo effect" is still unknown, but is thought to be due to complex interactions between the perception of pain and the interaction of the brain and body.
- Current thinking is that placebos reduce pain by initiating the release of endorphins and by changing the patient's perception of pain.

Placebo in the Literature

- The placebo effect is particularly important in studies of pain, where many painful conditions exhibit varied temporal patterns of intensity, and a reduction in pain following administration of a placebo, which may be either a placebo effect or something that would have happened regardless of the intervention.
- This gradual improvement over time is a statistical phenomenon known as regression to the mean that assumes that in a given population, extremes in reported pain intensity will

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change over time toward the average of that population.

- The open-hidden paradigm represents a way of studying placebo mechanisms and the specific effects of a treatment where the treatment is given by the clinician and in full view of the patient or alternatively, the treatment can be received in a "hidden" manner where the clinician is not present and the patient is unaware that the treatment is being administered [2].
- Several analgesia studies have used the open-hidden paradigm, demonstrating that open administration of a drug is significantly more effective than hidden administration [3–5].

Incidence of the Placebo Effect

- Beecher's widely cited study of clinical analgesic trials concluded that an average of 30 % of patients respond to placebo treatments for pain.
- Levine et al. found that 39 % of patients had an analgesic response to placebo treatment [6].
- A study of normal volunteers using ischemic arm pain performed by Benedetti found that 26.9 % of the subjects responded to a placebo analgesic, as compared with a no-treatment control group.

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24 Cervical Spine Imaging: Normal Anatomy and Degenerative Disease

Nehal A. Shah and Glenn C. Gaviola

Anatomy

- Seven cervical vertebrae: Craniocervical junction formed by skull base, C1 and C2, remainder of C3–C7 vertebrae.
- Intervertebral disc: thinnest in cervical spine, increases in size throughout the spine with largest disc at L4–L5.
- Uncovertebral joint: from C3 to C7 formed by uncinate process on lateral margin of superior endplate and opposing surface of the inferior aspect of vertebral body above.
- Facet joint: formed by superior and inferior articular processes.
- Anterior longitudinal ligament, posterior longitudinal ligament, ligamentum flavum, interspinous ligament and nuchal ligament provide stability by limiting hyper- flexion and extension of cervical spine.
- Eight cervical nerves: nerve roots exit above their respective vertebrae and course inferiorly in their respective neuroforamen. For example, at C4-C5, the C5 nerve root will be in the neuroforamen.

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Imaging

- Radiographs
  - AP view demonstrates C3–C7 bodies, uncovertebral joints and intervertebral disc spaces, on end spinous processes which appear ovoid in midline (Fig. 24.1a).
  - Lateral view visualizes the C2–C7 vertebral bodies and spinous processes, facet joints, atlantodens interval (<3 mm in adults), intervertebral disc spaces, and prevertebral soft tissues. The prevertebral soft tissues should be: Nasopharynx <10 mm, retropharynx ≤7 mm, retrotracheal ≤22 mm in adults (Fig. 24.1b).
  - Oblique view visualizes the neuroforamina, uncovertebral, and facet joints (Fig. 24.1c).
- Flexion and Extension: lateral projection with neck in flexion and extension to evaluate for instability in traumatic and atraumatic spine disease. The flexion/extension radiographs are useful in evaluating ligamentous stability in patients with trauma, and in atraumatic cases, it is useful for evaluation of dynamic changes in degree of spondylolisthesis in patients with sensory/motor deficits, for assessing mobility & for preoperative planning.
- Computed Tomography (CT)
  - Non-contrast CT examination

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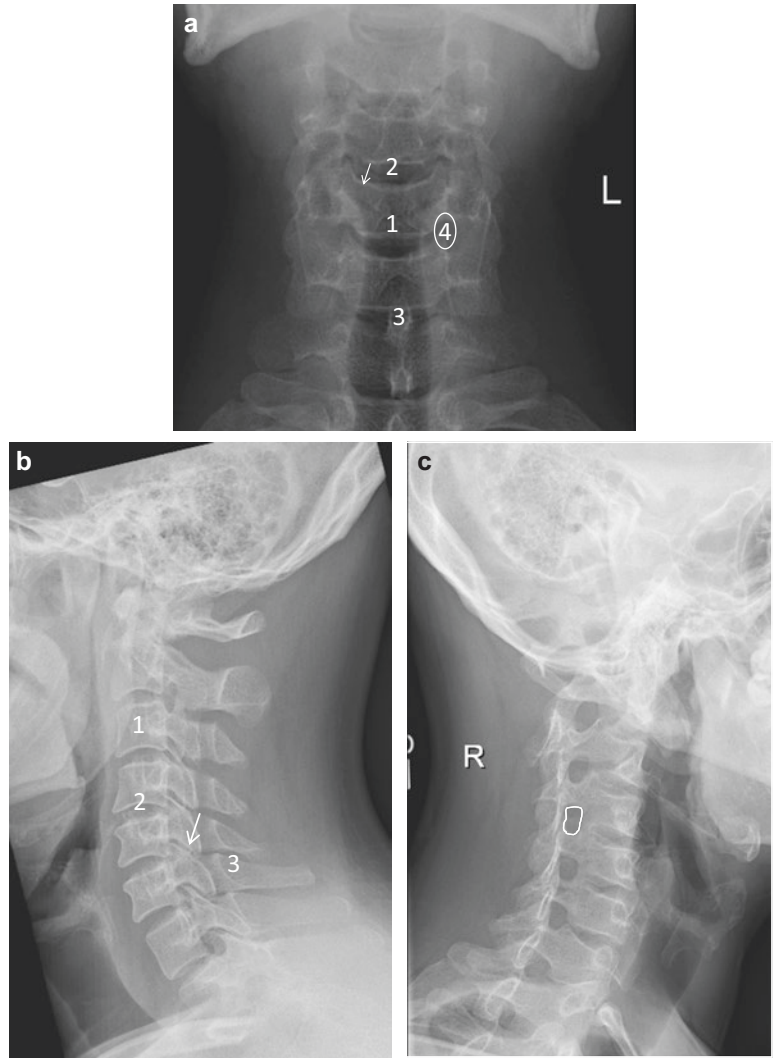

Fig. 24.1 (**a**) AP view. (**b**) Lateral view. (**c**) Left Oblique view demonstrates the ovoid right sided neuroforamina. The C4–C5 neuroforamen is outlined. (1) Vertebral body; (2) Intervertebral disc space; (3) Spinous process; (4) Uncovertebral joint (outlined); (5) Facet joint (*arrow*)

- Axial acquisition with bone and soft tissue windows, coronal and sagittal bone window reformations (Fig. 24.2).
- Excellent for bony anatomy but there is limited contrast resolution between spinal cord and surrounding CSF within the spinal canal.

- Magnetic Resonance Imaging (MRI)
  Provides the best contrast resolution in evaluation of the spinal contents.
  Sagittal T1, T2, STIR, axial T2, and axial T2*-weighted (MPGR—multiplanar gradient recalled) sequences are recommended for cervical spine evaluation
  Sagittal T1W: The osseous structures demonstrate high signal intensity compared to adjacent intermediate signal intensity intervertebral discs. The spinal cord is also intermediate in signal intensity surrounded by low signal intensity cerebrospinal fluid (CSF) Fig. 24.3a.
  Sagittal and axial T2W: On fast spin echo (FSE) T2-weighted images, the osseous structures are low in signal intensity compared to adjacent high signal intensity intervertebral discs. High signal intensity CSF surrounds intermediate signal intensity spinal cord Fig. 24.3b, d.

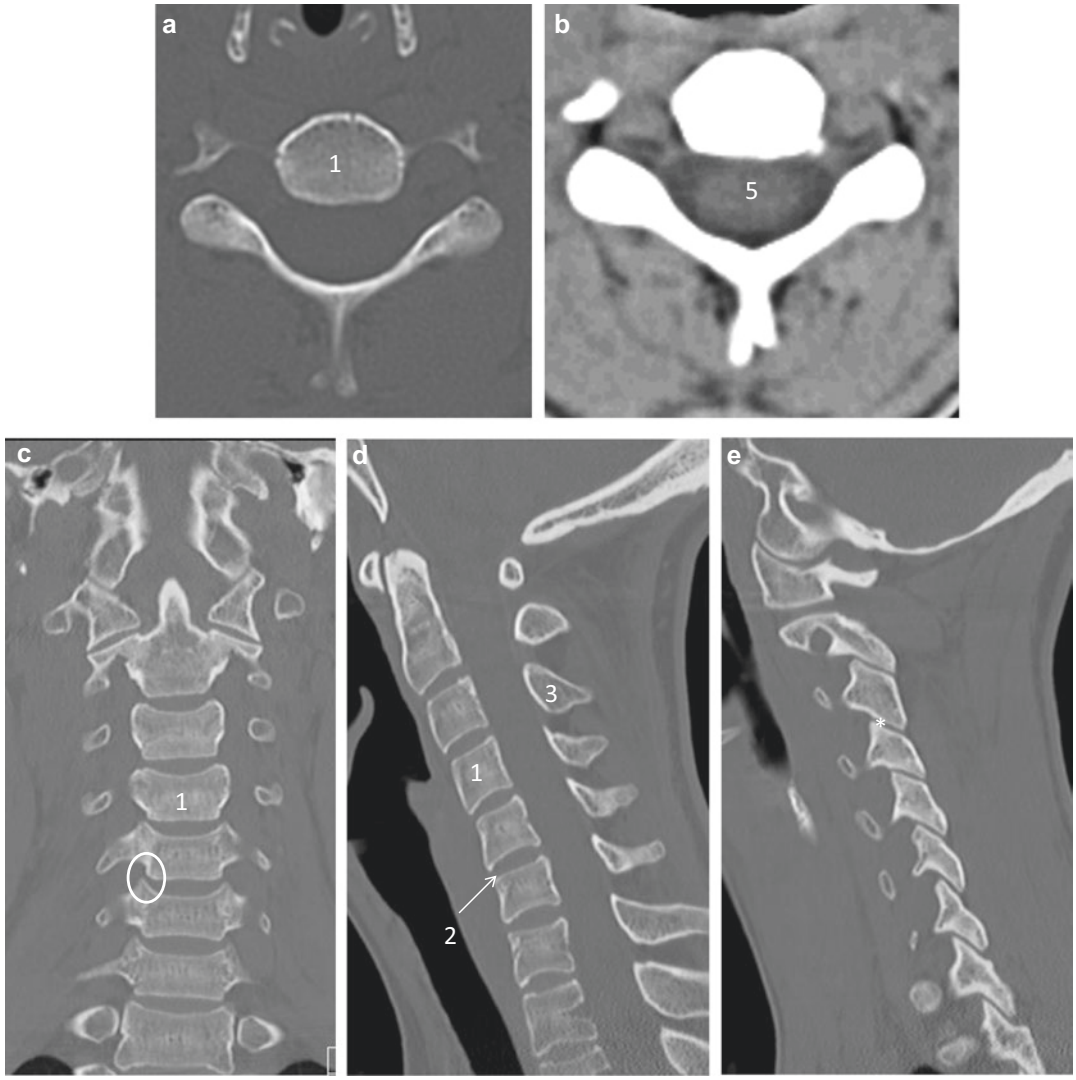

Fig. 24.2 Representative CT images of cervical spine. (**a**) Axial bone. (**b**) Axial soft tissue. (**c**) Coronal. (**d**) Midline Sagittal. (**e**) Parasagittal. (1) Vertebral body; (2) Intervertebral disc (*straight arrow*); (3) Spinous process; (4) Uncovertebral joint (*white oval*); (5) Facet joint (*asterisk*)

Sagittal STIR: The osseous structures demonstrate low signal intensity compared to adjacent high signal intensity intervertebral discs. The CSF is high in signal intensity compared to intermediate signal intensity spinal cord Fig. 24.3c.

Axial T2*W MPGR: High signal intensity CSF surrounds an intermediate signal intensity spinal cord. The intervertebral disc is high in signal intensity while the osseous structures demonstrate low signal intensity Fig. 24.3e.

Degenerative Disease of the Cervical Spine

Imaging Indications

- Symptoms of neck pain, radiculopathy, or cervical myelopathy warrant imaging workup to localize the cause of symptoms.
- For most patients with chronic neck pain and neurologic signs, radiographs and MRI are recommended.

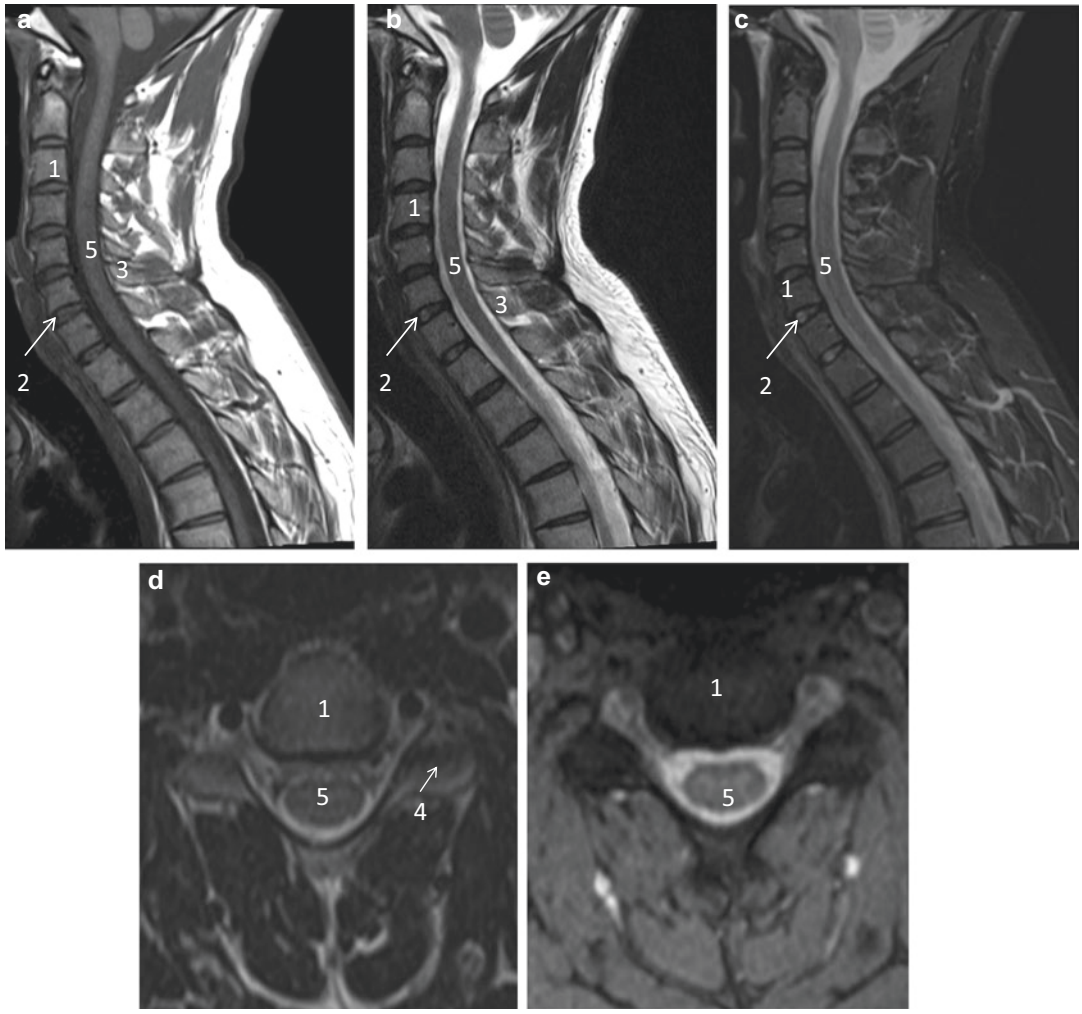

Fig. 24.3 Representative MR images of cervical spine. (**a**) Sagittal T1, (**b**) Sagittal T2, (**c**) Sagittal STIR, (**d**) Axial T2, and (**e**) Axial T2* sequences. (1) Vertebral body; (2) Intervertebral disc (arrow); (3) Spinous process; (4) Facet joint; (5) Spinal cord

- When there is contraindication to MRI, CT, or CT myelography is recommended.
- Flexion and extension lateral radiographs are suggested in patients with suspected instability or prior history of cervical spine surgery.

Imaging Evaluation

Disc and Osseous Degenerative Changes

- Disc and Vertebral body
  In the cervical spine, posterior vertebral body osteophytes and disc disease occur concurrently and is termed disc osteophyte complex which can be diffuse or focal.
  Similar to lumbar spine, the disc osteophyte complex is described by its location: central, right/left central, subarticular, foraminal, and extraforaminal.
  Evaluate on frontal and lateral radiographs (Fig. 24.4a), Sagittal and axial CT (Fig. 24.5), Sagittal T1, T2, and axial T2 and T2* sequences (Fig. 24.6).
- Associated vertebral body endplate changes of bone marrow edema (Modic Type I), endplate sclerosis (Modic Type II), and fatty replacement (Modic Type III).

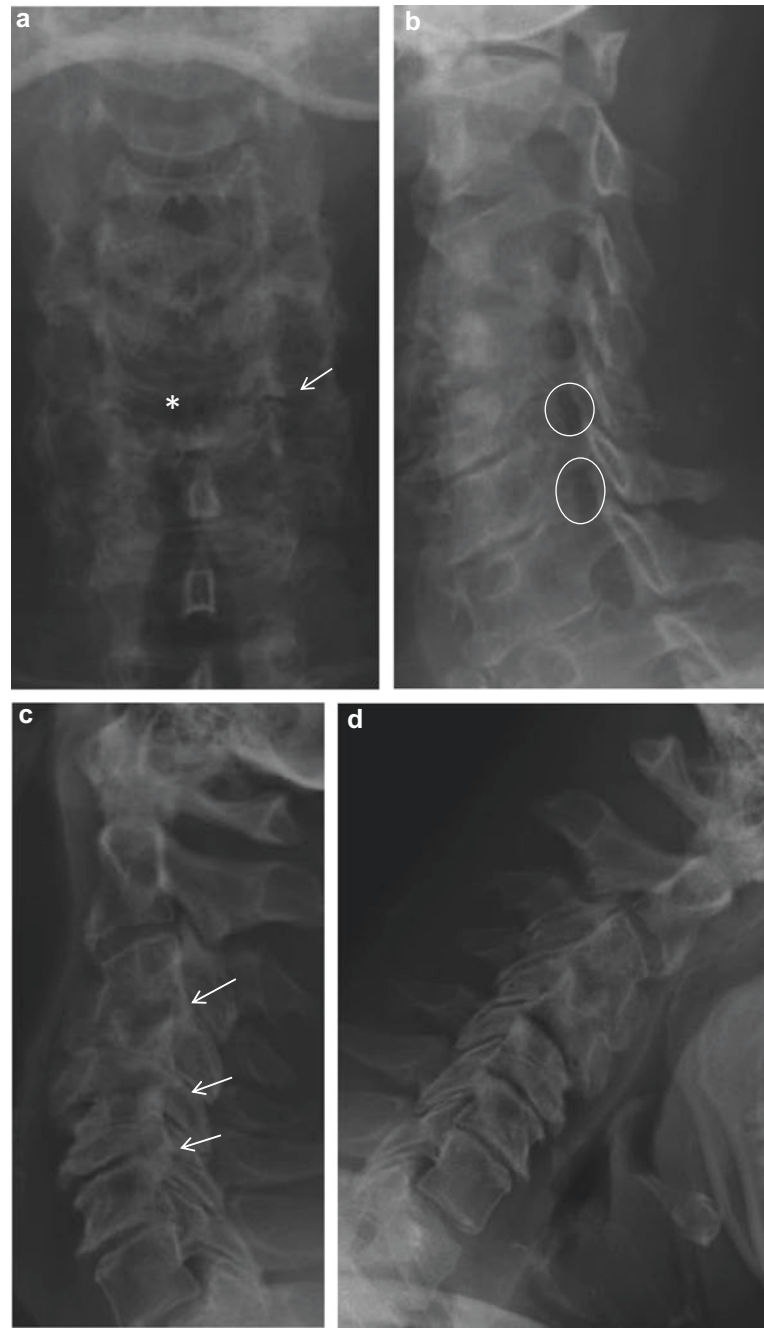

Fig. 24.4 (**a**) AP view shows multilevel disc space narrowing (*) and uncovertebral hypertrophy (*arrow*). (**b**) Oblique view showing multilevel osseous neuroforaminal narrowing. (**c**) Lateral extension view shows multilevel retrolisthesis (*arrows*). (**d**) Lateral Flexion view demonstrates reduction of retrolisthesis

Evaluate on Sagittal T1, T2, and STIR sequences.

- Uncovertebral osteophytes are common and contribute to neuroforaminal narrowing.
  Evaluate on frontal and oblique radiographs (Fig. 24.4a, b), Coronal, Sagittal, and Axial CT (Fig. 24.5), Axial T2 and T2* sequences (Fig. 24.6).
- Facet degeneration with osteophyte formation and ligamentum flavum infolding contribute to both central canal stenosis and neuroforaminal narrowing.

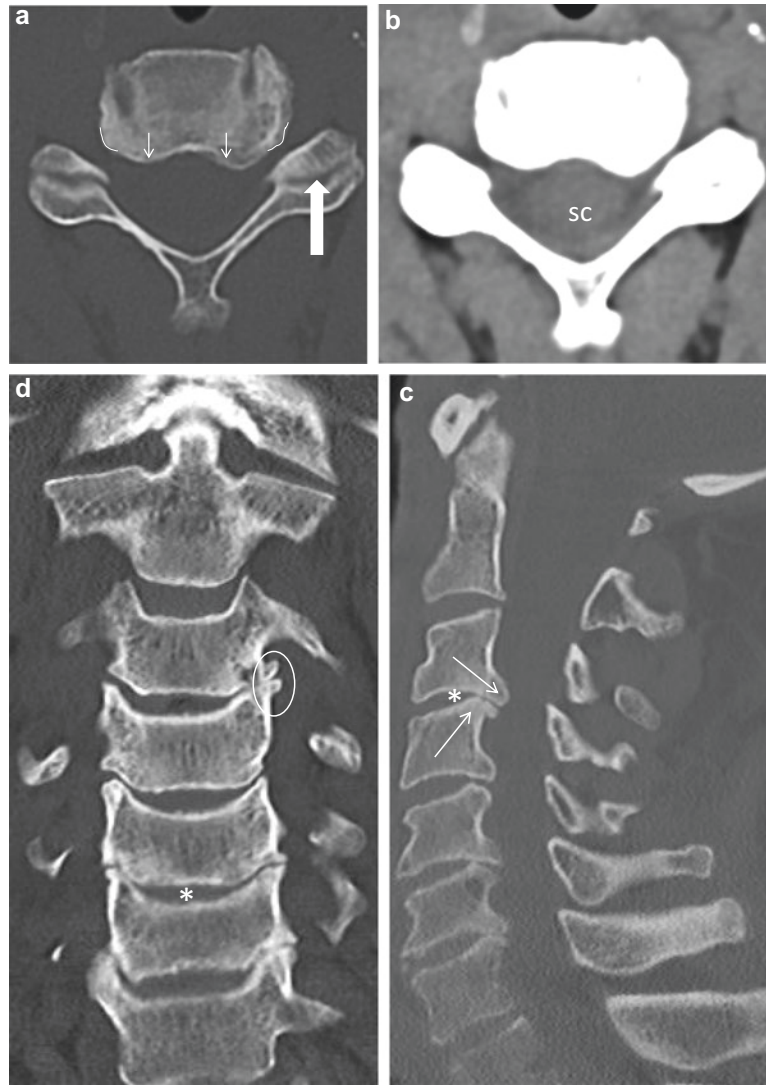

Fig. 24.5 Representative CT images showing uncovertebral hypertrophy (*curved line*), disc osteophyte complex (*arrows*) resulting in severe central canal stenosis and moderate right and severe left neuroforaminal narrowing as well as minimal CSF around the spinal cord (sc) due to central stenosis on axial bone and soft tissue windows (**a, b**), intervertebral disc height loss (*asterisks*) and disc osteophyte complex (*arrows*) on sagittal bone window (**c**), and uncovertebral hypertrophic change on coronal bone reformats (**d**)

Evaluate on frontal and lateral radiographs, Sagittal and axial CT, Sagittal T1, T2, and axial T2 sequences.

Spinal Stenosis

- Refers to central canal stenosis, lateral recess narrowing, and neuroforaminal narrowing.
- Degree of Central Stenosis, edema within the spinal cord or affected nerve roots and loss of spinal cord volume (myelomalacia) is best evaluated on Sagittal and axial T2-weighted sequences (Fig. 24.6b, d).
- Lateral recess narrowing is evaluated on axial CT, Axial T2 and T2* sequences.
- Neuroforaminal narrowing can be assessed on oblique radiographs, axial CT, Axial T2 and T2* sequences.

Instability

- Lateral flexion/extension views (Fig. 24.4c, d).
- No consensus for degenerative cervical spondylolisthesis.
- 3.5 mm of lateral displacement of adjacent vertebral bodies or >1 mm of change between flexion and extension views.
- Segmental kyphosis of >11° between the inferior and superior endplate of adjacent vertebral bodies.

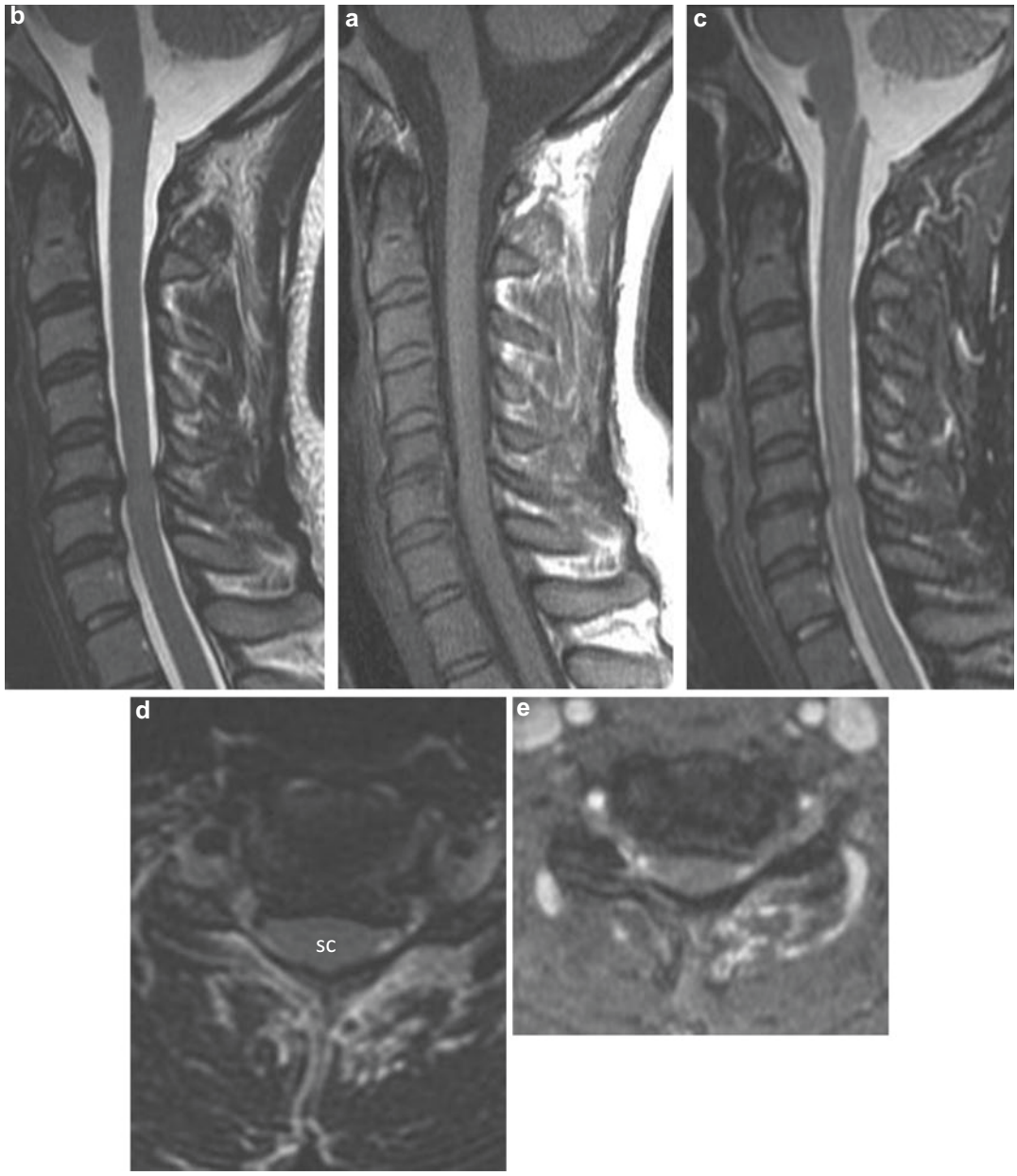

Fig. 24.6 Representative MR images show disc osteophyte complex at C5-C6 causing moderate bilateral neuroforaminal narrowing and severe central canal stenosis (lack of hyperintense CSF around spinal cord). (**a, b, c**) Sagittal T1W, Sag T2W and SAG STIR images show C5-C6 disc space narrowing without spinal cord signal abnormality on the STIR or T2W sequences. (**d**) Axial T2W image shows severe central canal stenosis as noted by lack of hyperintense CSF around the spinal cord. (**e**) Axial T2 GRE image demonstrates moderate bilateral neuroforaminal narrowing

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Electrical Nerve Stimulation

25

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Electromyography (EMG)

Uses needle electrodes to evaluate the electrical activity of muscle fibers. It can provide information on the integrity, function, and innervation of motor units and muscle fibers. It can help differentiate between radiculopathy, neuropathy, myopathy, and neuromuscular junction disease.

Indications

Primarily used for evaluation of suspected polyneuropathy, radiculopathy, plexopathy, myopathy, neuromuscular junction (NMJ) disease, peripheral nerve injury, or motor neuron disease (i.e., ALS).

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Contraindications

Anticoagulation therapy (relative), coagulopathy, implanted hardware near desired site, target muscle is desired for biopsy.

General Technique

Surface landmarks are used to identify the target. Using clean technique, needle electrodes are advanced in the muscle belly. Muscle potentials are monitored during insertion and graded. Placement is performed with small incremental movements and any spontaneous muscle activity is noted as it suggests abnormalities. The patient then voluntarily contracts the muscle at submaximal and maximal levels. Morphology, number, and recruitment of motor unit action potentials (MUAP) are assessed.

Spontaneous Activity

Normal muscle produce short bursts of insertional activity with electrical silence between insertions. Denervated or injured muscle fibers produces spontaneous activity that persists after the needle is moved. The amount, size, and frequency indicate the severity of the disease process.

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Spontaneous Activity Grade

0: No activity
1+: Transient but reproducible discharged with needle movement
2: Occasional discharges at rest at >2 different sites
3: Spontaneous activity at rest
4: Abundant continuous spontaneous activity

Analysis of EMG

Normal MUAP have characteristic amplitude, duration, and number of phases. Abnormalities in the characteristics allow trained providers to diagnose the type and chronicity of disease.

Clinical Pearls

EMG is useful when the source of pain or dysfunction is believed to be due to neurologic, intrinsic muscle, or NMJ disorder. To maximize benefit of the EMG, the leading diagnosis should be clearly elucidated by history physical and other studies.

EMG can be helpful in differentiating fibromyalgia from generalized neuromuscular disorders as EMG will be normal in the former.

EMG can be suggestive of the time course of a disease process.

Nerve Conduction Velocities (NCS)

Permit noninvasive assessment of nerve function and physiology. Slow conduction velocity or delay in latency denotes injury to myelin. Diminished amplitude suggests axon injury or loss. The distribution of these deficits across several nerves can differentiate focal vs. diffuse disease process.

Indications

Suspected peripheral nerve entrapments, polyneuropathies, radiculopathy (motor studies as sensory studies are usually normal), plexopathy, or NMJ disease.

Contraindications

Pacemakers, implantable cardioveter/defibrillators (ICD), spinal cord stimulator other electrosensitive implant. If implant is remote from site may not be contraindicated. Marked edema or skin damage at site of test.

General Technique

Pickup electrode is placed over the desired target nerve which is localized based on anatomical placement. A reference electrode is placed in proximity to the desired target and a ground electrode is placed on the patient. The nerve is then stimulated at a specific measured distance. In general sensory nerves are stimulated at 14 cm and motor nerves at 8 cm away from pickup electrode. An action potential (AP) is generated which propagates down the nerve and is detected by the pickup electrode. The AP is recoded and analyzed specifically assessing the Peak latency for sensory nerves, and Onset latency for motor nerves. Additionally, the amplitude and shape are recorded of the action potential. Conduction velocities are calculated using the measured distance and latency. Stimulation can be repeated at different points on the nerve to evaluate different segment of the nerve, which is useful in identifying focal (i.e., peripheral) lesions.

Study Types

Conduction studies can evaluate sensory, motor, and mixed sensory/motor nerves.

Limitations

Nerve conduction studies (NCS) can only measure the fastest conducting nerve fiber specifically the nerves that are myelinated, i.e., A fibers. Mainly A-alpha for motor and A-beta and A-delta for sensory. Injury to associated smaller nerves (i.e., unmyelinated C-fibers) will go undetected (i.e., small fiber peripheral neuropathy). NCS particularly sensory are sensitive to temperature

changes and required normalization (32C upper and 30C lower extremities) of the patient's temperature for accurate results. Cold extremity temperatures can prolong peak and onset latencies; however, amplitudes are increased.

Clinical Pearls

As sensory NCS assess nerves distal to the dorsal root ganglion, it is characteristic that the majority of radiculopathies have normal sensory NCS.

Somatosensory Evoked Potentials (SSEPs)

Evaluates time-locked responses of the nervous system to an external stimulus. They represent the function of the ascending sensory pathways using an afferent potential which travels from peripheral nerve to the plexus, root, spinal cord (posterior column), contralateral medial lemniscus, thalamus, to somatosensory cortex.

Indications

Primarily used to monitor the nervous system during spine surgery. This modality can measure nerve output and assess if there is any injury occurring to the sensory nerves immediately intraoperatively. Other utilities include: peripheral nerve injury, CNS lesions (i.e., MS showing increased interpeak latency), brachial neuropathies, assessment of complete versus incomplete spinal cord injury, and it is helpful in identifying spinal shock.

Limitations

Anesthesia such as halothane and isoflurane will affect both the upper and lower limbs; however, this can be avoided by using nitrous oxide and low dose isoflurane. Intraoperatively, SSEP can miss the development of Anterior Cord Syndrome as it only monitors the posterior column pathway. Specificity for localizing focal lesions may be difficult due to evaluating such a long neural pathway.

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Quantitative Sensory Testing: QST

26

Sivan Schipper and Konrad Maurer

Definition of QST

- Quantitative Sensory Testing is a psychophysical method used to quantify the functional status of the somatosensory system. QST evaluates all types of afferent nerve fibers by applying quantitative and graded stimuli (graded von Frey hairs, several pinprick stimuli, pressure algometer, quantitative thermotesting, tuning fork etc) using specific testing algorithms [1].

Indications for QST for Clinical Practice

- QST may aid to detect and monitor sensory neuropathies.
- When standard electrophysiological testing appears normal, and suspicion for small fiber neuropathy persists, QST may reveal small fiber function deficits.
- QST may be a helpful, but not a specific diagnostic tool, to differentiate between neuropathic and non-neuropathic pain states.
- QST may detect important pain related phenomena, i.e., hyperalgesia, allodynia, wind-up phenomenon, and paradoxical heat sensations in different pain states.
- By establishing an individual somatosensory profile ("Sensory Phenotyping") for pain patients, QST may help reveal the underlying mechanism [2] and may, in the future, help in therapeutic decision-making based on a mechanism-oriented antineuropathic pain therapy [3].
- QST may monitor quantitative somatosensory deficits over time. For example, the determination of vibration or tactile deficits may identify patients at high risk for developing further sensory loss and thus help avoid complications such as diabetic foot ulcer formation.
- QST may be used in clinical research for patients with fibromyalgia, painful neuropathies, lumbar radiculopathy, complex regional pain syndrome (CRPS), central nervous system impairment states, and many others.

How to Perform QST

- QST is mostly performed at the site of maximal sensory symptoms (negative or positive symptoms).
- QST is performed by applying quantitative and graded stimuli using well defined testing algorithms. A standardized QST protocol was proposed by the German Network on Neuropathic Pain (DFNS) [4, 5].

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Responses from the symptomatic site are compared either with the asymptomatic side or with reference data gathered by a healthy population. Reference data are available for hands, feet, face, mouth, as well as for the back.

Diagnostic Value of QST

- QST assesses the entire somatosensory system (Aβ, Aδ, and C fibers, lemniscal and spinothalamic tracts), whereas standard electrophysiological recordings measure large fiber function (Aβ) and lemniscal function only.
- QST assesses minus symptoms (e.g., hypoesthesia to cold, warmth or touch, hypoalgesia to cold, heat, or mechanical stimuli) as well as plus symptoms (e.g., pin prick hyperalgesia, mechanical dynamic allodynia, cold and heat allodynia), whereas standard electrophysiological measurements assess minus symptoms only.
- Measurement of enhanced temporal summation (increased perception of pain to repetitive painful stimuli), which can be a sign of central sensitization.

Limitations of QST

- Because of its subjective nature, QST is prone to subjective bias such as attention, motivation, malingering, language deficits and cognitive deficits.
- QST does not have a diagnostic value by itself and should be used as a supplemental diagnostic tool. It has to be set in a wide context and interpreted together with results of bedside clinical examination, pain questionnaires, sensory nerve conduction velocity studies (electroneurography), and somatosensory evoked potentials (Table 26.1).

Table 26.1 QST parameters measured and their possible clinical interpretations

QST parameter	Type of stimulus	Physiological sensation elicited	Testing device	Fibre type	Central pathway	Taxonomy and possible clinical Interpretation: minus symptom	Taxonomy and possible clinical interpretation: plus symptom
MDT	Mechanical static punctuate	Touch	Calibrated von Frey filaments	Aβ	Lemniscal	Hypoesthesia: e.g., Sensory neuropathy	n.a.
VDT	Vibration	Vibration	Vibrometer, graduated tuning Forg	Aβ	Lemniscal	Pallhypesthesia: e.g., Diabetic polyneuropathy	n.a.
ALL	Brushing	Touch	Brush	Aβ, (C)	Lemniscal	Hypoesthesia: e.g., Sensory neuropathy	Mechanical dynamic allodynia: central sensitization in dorsal horn
MPT	Pinprick	Sharp pain	Calibrated needles	Aδ	Spinothalamic	Hypoalgesia: small- or large-fibre neuropathy	Mechanical hyperalgesia: primary and/or secondary hyperalgesia
PPT	Blunt pressure	Sharp pain	Pressure algometer	Aδ, C	Spinothalamic	n.a.	Deep tissue hyperalgesia
WDT	Warm	Warmth	Thermotest	Aδ, C	Spinothalamic	Thermhypesthesia: small fibre neuropathy	n.a.
CDT	Cold	Cold	Thermotest	Aδ	Spinothalamic	Thermhypesthesia: small fibre neuropathy	n.a.
HPT	Heat pain	Painful heat	Thermotest	Aδ, C	Spinothalamic	Small fibre neuropathy	Heat allodynia: primary hyperalgesia
CPT	Cold pain	Painful cold	Thermotest	Aδ, C	Spinothalamic	n.a.	Cold allodynia: peripheral sensitization and/or central disinhibition
MPS	PinPrick and touch			Aδ, Aβ, C	Lemniscal spinothalamic	Hypoesthesia	Mechanical statical hyperalgesia
WUR	Repetetive noxious stimuli	Sharp pain	PinPrickNeedle	Aδ, C	Spinothalamic	n.a.	Temporal summation: central sensitization
PHS	Paradoxical heat sensors	Heat sensation on cold stimulus	Thermotest	Aδ, C	Spinothalamic	n.a.	Small fibre damage or central disinhibition
TSL	Thermal sensory limen	Warmth/cold	Thermotest	Aδ, C	Spinothalamic	n.a.	Small fibre damage or central disinhibition

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Lumbar Spine Imaging: MRI

27

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MR Imaging

Indications

As per the American College of Radiology (ACR) Appropriateness Criteria:

- *Low back pain* complicated by radiculopathy or sciatica, cauda equina syndrome, neurogenic claudication, spinal stenosis or in patients with risk factors including osteoporosis, focal/progressive neurological deficit, >6 weeks symptom duration; age >70; suspected cancer, infection or immunosuppression; or history prior lumbar surgery;
- *Myelopathy,* in particular, non-traumatic myelopathy, whereas CT is best for evaluating traumatic myelopathy;
- **IV contrast** is preferred in suspected cases of cancer, infection, inflammation, or vascular causes of myelopathy; and in ***postoperative evaluation for recurrent disc herniations and scar***;

Technique

- *T1-weighted sequences:* best for evaluation of epidural fat and differentiation from cerebrospinal fluid (CSF), and for evaluation of optimal targets for epidural steroid injections (On T1, fat is bright and hyperintense in signal intensity and CSF is dark and hypointense in signal intensity) (Fig. 27.1a);
- *T2-weighted sequences:* best for evaluation of cord signal changes and surrounding soft tissue pathology; best for evaluation of the conus medullaris and cauda equina nerve roots given optimal contrast resolution between the CSF and the nerve roots, unlike T1-weighted images (Fig. 27.1b).
- *Fluid sensitive sequences (e.g., STIR or T2-weighted fat-suppressed):* best for marrow edema and fractures; disc extrusions and hydration of the nucleus pulposus (Fig. 27.2);

Evaluation

- Degenerative disc disease (Fig. 27.3) which includes annular fissures, loss of disc hydration and disc height, disc bulging, Modic endplate changes of edema (type 1), fatty replacement (type 2) and sclerosis (type 3) and for evaluation of disc migration:
  - *Disc herniation* defined as localized or focal displacement of disc material beyond

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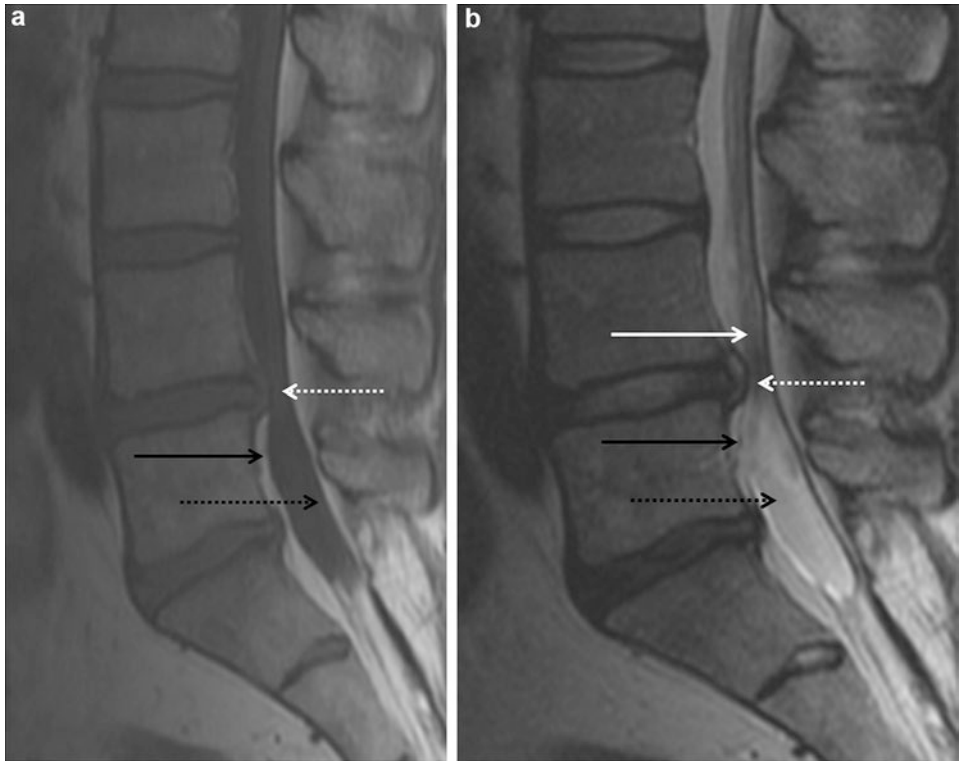

Fig. 27.1 (**a**) Sagittal T1-weighted MR image of the lower lumbar spine demonstrates the utility of T1-weighting in differentiating epidural fat (*solid black arrow*), which is hyperintense in signal intensity, versus cerebrospinal fluid in the thecal sac (*dashed black arrow*) which is hypointense in signal intensity. Note the L4–L5 disc bulge which effaces the epidural fat and makes a ventral impression upon the thecal sac resulting in focal spinal canal stenosis at this level (*dashed white arrow*). The cauda equina nerve roots are not well seen because they are of similar signal intensity relative to the CSF due to suboptimal contrast resolution. (**b**) Sagittal T2-weighted MR image of the lower lumbar spine at the same level demonstrates the utility of how epidural fat (*solid black arrow*) and cerebrospinal fluid (*dashed black arrow*) have the same signal intensity on T2-weighting and thus make it difficult to differentiate the two. The L4–L5 disc bulge is again seen effacing the ventral thecal sac resulting in focal spinal canal stenosis at this level (*dashed white arrow*). Note that because of the bright signal of the CSF, there is improved contrast resolution with the cauda equina nerve roots (*solid white arrow*) and they are best depicted on these sequences

the intervertebral disc space and is categorized by:

- *Protrusion:* disc migration involving disc material less than 25% of circumference of disc margin on axial imaging;
- *Extrusion:* displaced disc material measuring greater than the base of the displaced material at its origin in any one plane;
- *Sequestration:* form of disc extrusion with loss of continuity from parent disc;
- *Volume and location* of displaced disc material including:
  - Degree of spinal canal stenosis and neural foraminal narrowing;
  - Proximity to, compression of, or distortion of nerve roots and cord;

- Facet arthropathy (Fig. 27.3)
  - Cartilage thinning, subchondral sclerosis, osteophyte formation, synovial inflammation and ligamentous laxity; helpful for evaluation of subchondral bone marrow edema.

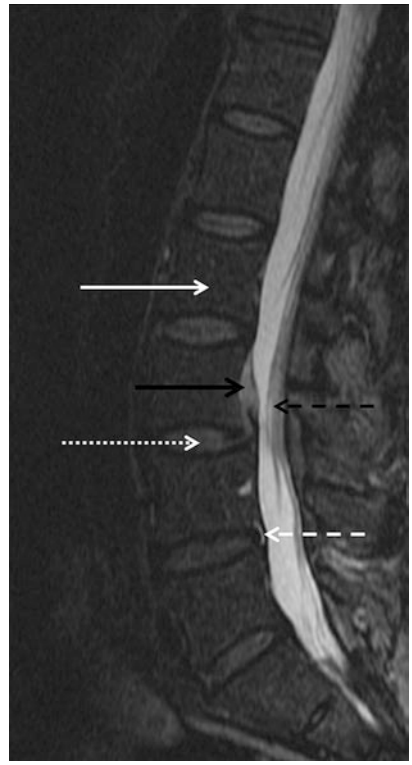

Fig. 27.2 Sagittal fluid-sensitive sequence (STIR, *short tau inversion recovery*) MR image of the lumbar spine demonstrates the utility of fluid sensitive sequences in depicting disc pathology. The bright signal intensity of fat is nulled, such as in the marrow (*solid white arrow*) resulting in only fluid signal to be hyperintense, as in the cerebrospinal fluid and nucleus pulposus of the intervertebral disc (*dotted white arrow*). Note the hyperintense disc extrusion at the L3–L4 level (*solid black arrow*) migrating cranially and posterior to the L3 vertebral body resulting in anterolisthesis, focal spinal canal stenosis and narrowing of the CSF space for the cauda equina nerve roots at this level (*dashed black arrow*). Note also the hyperintense curvilinear signal (*dashed white arrow*) within the dark annulus fibrosis of the L4–L5 intervertebral disc in keeping with an annular fissure

  - Fluid and vacuum phenomenon suggest spondylolisthesis, and possibly dynamic instability.
- Intradural pathology
  - Evaluate for masses, such as mengiomas, nerve sheath tumors, and epidural lesions including hematoma and lipomatosis;
- Intramedullary pathology
  - Intrinsic spinal cord abnormalities, including:
    - Masses such as syrinx formation or tumors;
    - Medullary signal changes in demyelinating disease, infection or inflammatory conditions;
    - Volume loss from myelomalacia;
    - IV contrast helpful for vascular lesions of the cord or active disease processes such as active demyelination in multiple sclerosis;

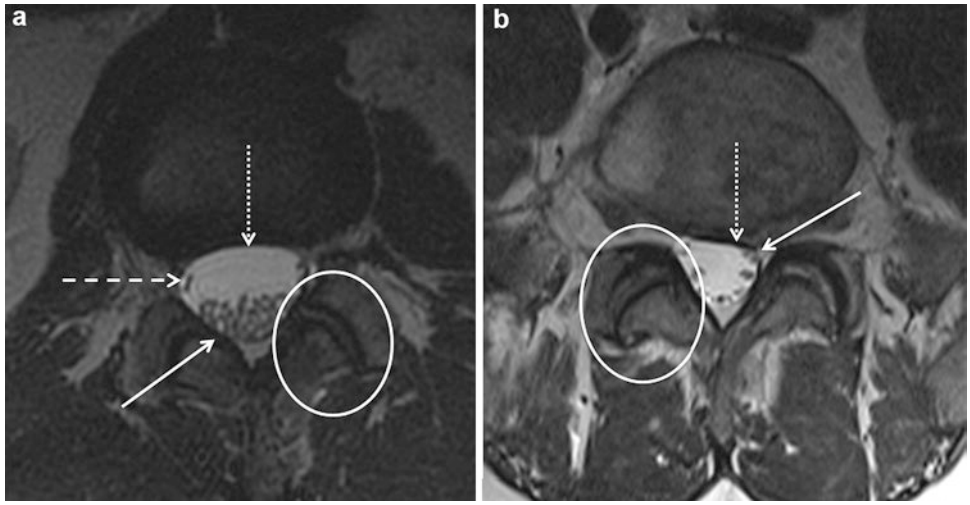

Fig. 27.3 (**a**) Axial T2-weighted MR image of a normal intervertebral disc level shows the normal convex margin of the ventral thecal sac due to the posterior contour of the disc annulus fibrosus (*dotted white arrow*) in the absence of disc pathology. Note the cauda equina nerve roots layering dependently in the spinal canal surrounded by hyperintense CSF and the traversing nerve roots about to exit near the neural foramen (*dashed white arrow*). The facet joints (*white oval*) are synovial lined joints bounded ventrally by the ligamentum flavum (*solid white arrow*). (**b**) Axial T2-weighted MR image of an abnormal intervertebral disc level shows flattening of the convex margin of the ventral thecal sac due to a left paracentral disc herniation (*dotted white arrow*) and encroachment upon the traversing left sided cauda equina nerve roots (*solid white arrow*). In addition, there is arthropathy of the facet joints (*white oval*) with osteophyte formation and thickening of the ligamentum flavum. Both facet arthropathy and degenerative disc disease with migration of disc material can result in loss of the normal shape and volume of thecal sac, spinal canal stenosis, and compression of the nerve roots

Suggested Reading

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Trigeminal Nerve Imaging

28

Sami H. Erbay and Juan E. Small

ANATOMY: The trigeminal nerve (TN) is a mixed (motor and sensory) nerve. The TN arises from the mid-lateral surface of the pons. There are four segments of the TN (see Figs. 28.1 and 28.2):

1. Intra-axial segment: located within the brainstem, with four brainstem nuclei (three sensory and one motor).
2. Cisternal segment: emerges from the ventrolateral pons at the root entry zone, and courses anteriorly through the prepontine cistern, piercing the dura at the porus trigeminus and thus entering Meckel's cave.
3. Interdural (Meckel's cave) segment: houses the Gasserian ganglion.
4. Extracranial segment: composed of the ophthalmic (V1), maxillary (V2) and mandibular (V3) nerve divisions.

The root entry zone is the proximal most 5–10 mm segment adjacent to the brainstem, a dense, converging point of all TN fibers. The longer cisternal segment courses through the ambient cistern in close proximity to adjacent vessels and is the most commonly affected part of the nerve in cases of neurovascular compression. The porus trigeminus is the entrance to Meckel's cave, which houses the trigeminal (Gasserian) ganglion.

Beyond the Gasserian ganglion, the TN has three major divisions easily visualized on imaging: ophthalmic (V1), maxillary (V2), and mandibular (V3). Although there are multiple branches arising from these three principal divisions, they are beyond the scope of a basic and succinct imaging overview.

(a) The ophthalmic (V1) division is purely sensory, courses in the lateral wall of the cavernous sinus inferior to cranial nerve IV, and enters the orbit through the superior orbital fissure.
(b) The maxillary (V2) division is purely sensory. Directly after its Gasserian ganglion origin, it gives off the maxillary nerve, which travels adjacent to the middle meningeal artery. The predominant portion of V2 courses along the inferolateral wall of the cavernous sinus inferior to cranial nerve V1. V2 then exits the skull base via the foramen rotundum and enters the pterygopalatine fossa.
(c) The mandibular (V3) is the most prominent of the divisions with sensory and motor divisions. V3 is the only division that does not course through the cavernous sinus, exiting the skull base instead through foramen ovale.

IMAGING: The trigeminal nerve can be best studied with MRI. Despite being the largest cranial nerve, it remains challenging to visualize the

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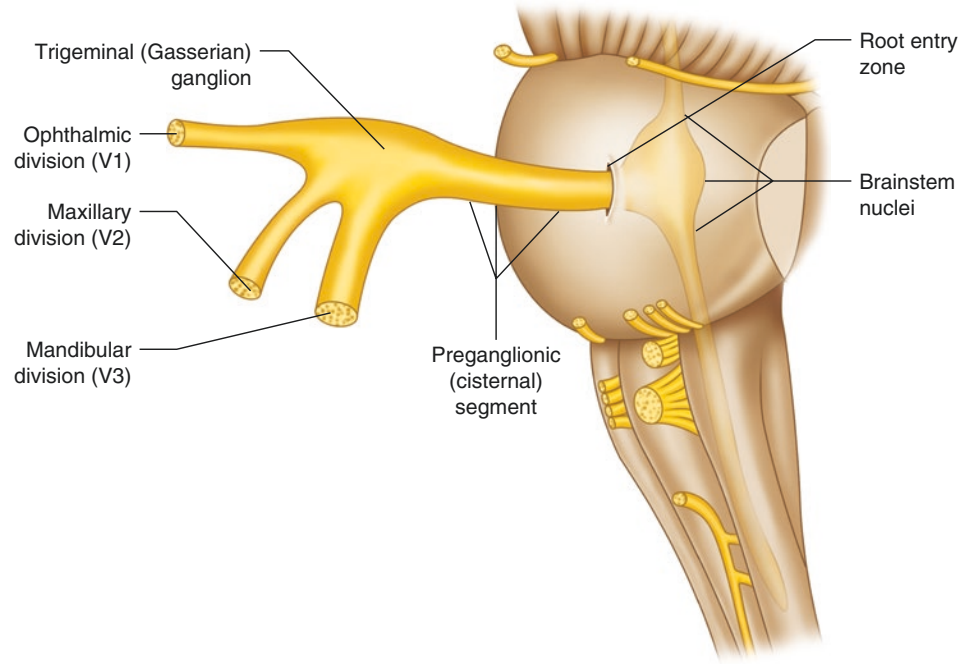

Fig. 28.1 The trigeminal nerve (TN) is a mixed (motor and sensory) nerve. The TN arises from the mid-lateral surface of the pons

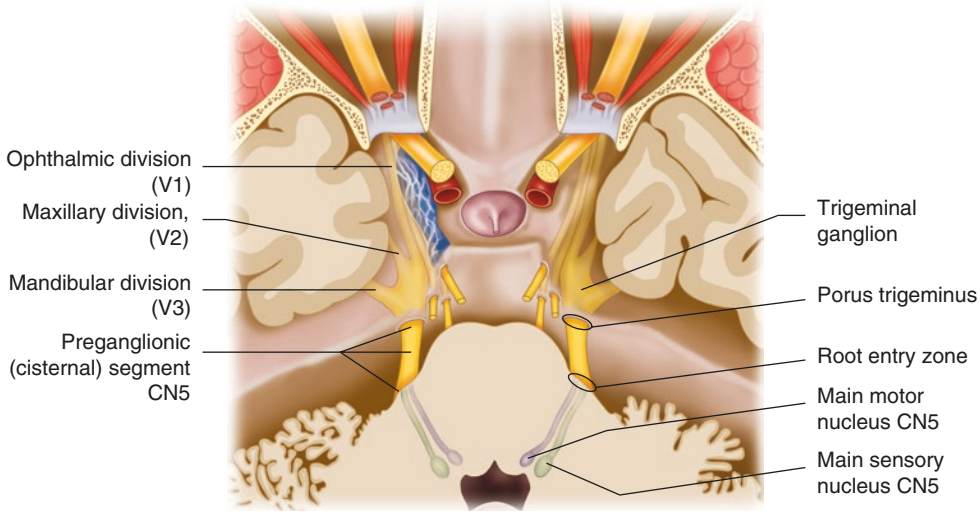

Fig. 28.2 The trigeminal nerve (TN) is a mixed (motor and sensory) nerve. The TN arises from the mid-lateral surface of the pons

TN with other imaging modalities. Thin cuts, multiplanar capability, excellent soft tissue detail, and volumetric acquisition makes MRI ideal for TN evaluation. MRI is the study of choice for the evaluation of the brainstem, cisternal and intradural segments. High resolution T2 weighted, balanced gradient echo sequences (FIESTA, CISS, etc.) can further enhance visualization of the TN. These sequences may afford excellent delineation of the nerve fibers, vessels, and their relation with each

other. If MRI is contraindicated (pacemaker, etc.), CT cisternogram may be performed although delineation of subtle pathology may be obscured in these studies. CT is the study of choice for evaluation of the skull base and skull base foramina.

PATHOLOGY/PATHOPHYSIOLOGY: A variety of conditions may affect the TN [1], including pathology intrinsic and extrinsic to the nerve. Lesions may occur anywhere along the course of the nerve (see Figs. 28.3, 28.4, 28.5, 28.6, 28.7, 28.8, 28.9, 28.10, and 28.11). Inflammatory, infectious, neoplastic and even post-treatment conditions may need to be carefully evaluated to explain imaging findings and clinical presentations. Extrinsic lesions located in the brain stem, subarachnoid spaces, Meckel's cave, cavernous sinus, and skull base may affect the TN or its nerve bundles.

In addition to these secondary etiologies of TN pathology, intrinsic processes may affect the TN fibers with resultant neuropathy. This has been the presumed pathophysiology for essential trigeminal neuralgia. This age-old disease may present with debilitating symptoms. Multiple theories have been proposed to explain underlying pathology. Nerve fiber degeneration, atrophy, and demyelination have been observed in the autopsy samples of the deceased who had suffered from trigeminal neuralgia. Underlying demyelination in the brainstem and/or the nerve fibers has been the leading theory for trigeminal neuralgia based on these postmortem findings. More recent information obtained by direct visualization of the TN during microsurgical techniques and with increasing utilization of MRI has revealed that neurovascular compression of the TN is the likely cause of neuralgia. Nerve degeneration and atrophy appear to be the result rather than the cause of nerve damage. TN atrophy as demonstrated with MRI may serve as an addi-

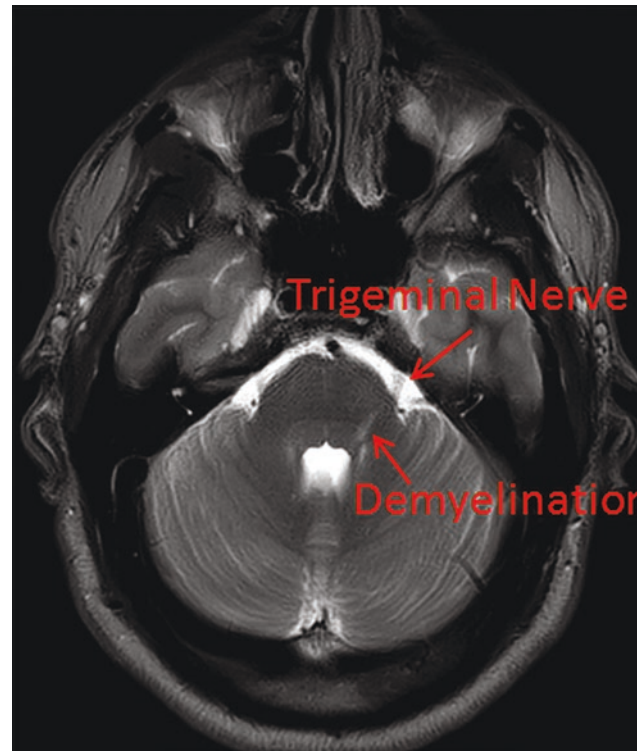

Fig. 28.3 Brainstem involvement of the trigeminal nerve: an axial T2 weighted image demonstrates a T2 hyperintense demyelinative plaque along the intra-axial course of the left trigeminal nerve

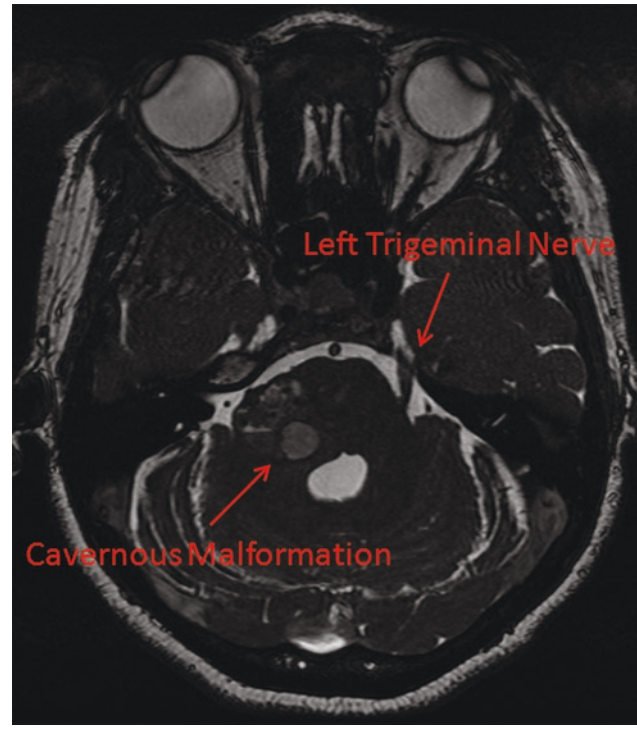

Fig. 28.4 Brainstem involvement of the trigeminal nerve: an axial thin section T2 image demonstrates a right sided cavernous malformation along the course of the right trigeminal nerve nuclei markedly distorting and displacing a severely atrophied right sided trigeminal nerve (not visible). A normal sized nerve is evident on the left

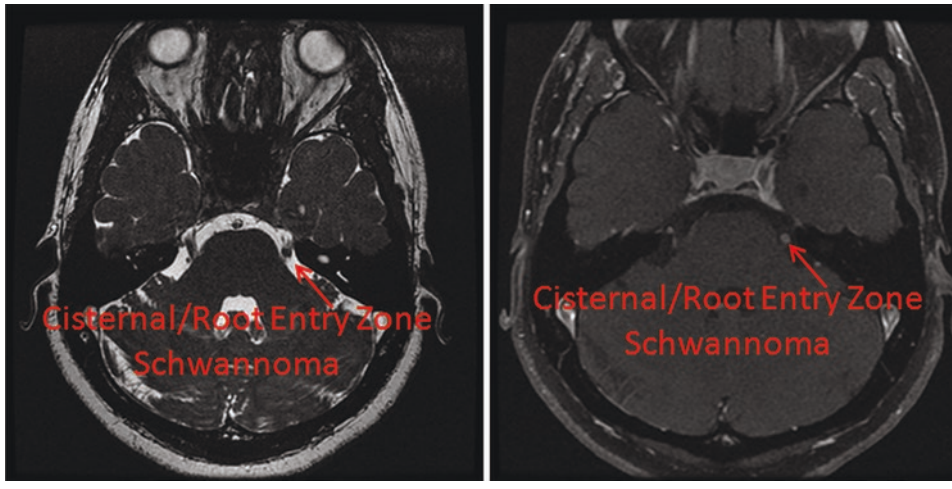

Fig. 28.5 Nerve entry zone lesion: high resolution axial T2 and T1 fat sat post-contrast images demonstrate an oval shaped enhancing schwannoma centered in the region of the root entry zone of the left trigeminal nerve (*arrows*)

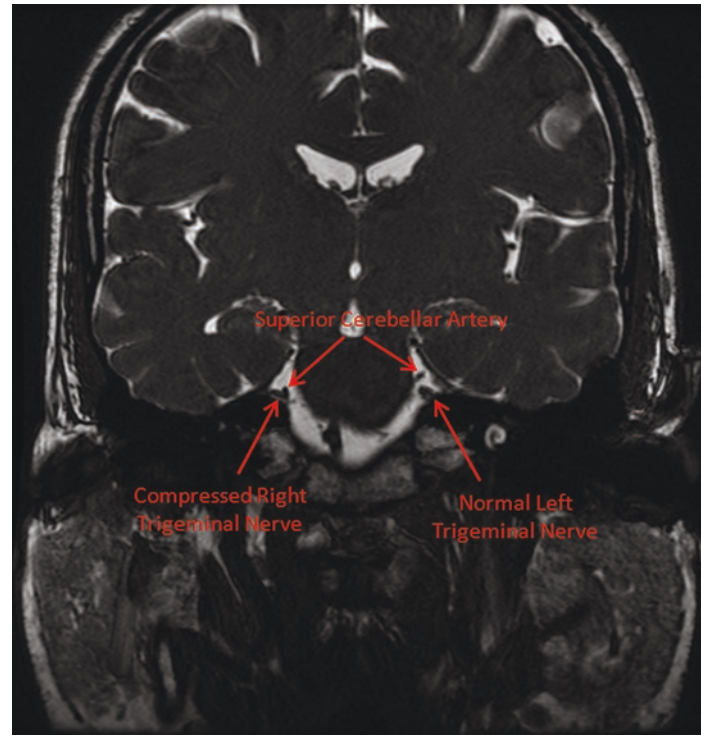

Fig. 28.6 Neurovascular compression: a coronal high resolution T2 image demonstrates neurovascular compression of the cisternal portion of the right trigeminal nerve by the right superior cerebellar artery

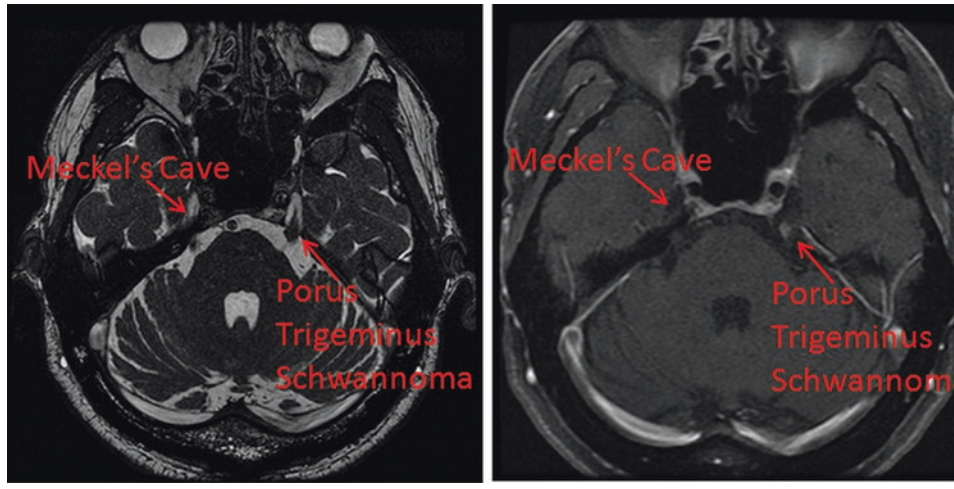

Fig. 28.7 Porus trigeminus lesion: high resolution axial T2 and T1 fat sat post-contrast images demonstrate an oval shaped enhancing left trigeminal nerve schwannoma centered in the region of the porus trigeminus

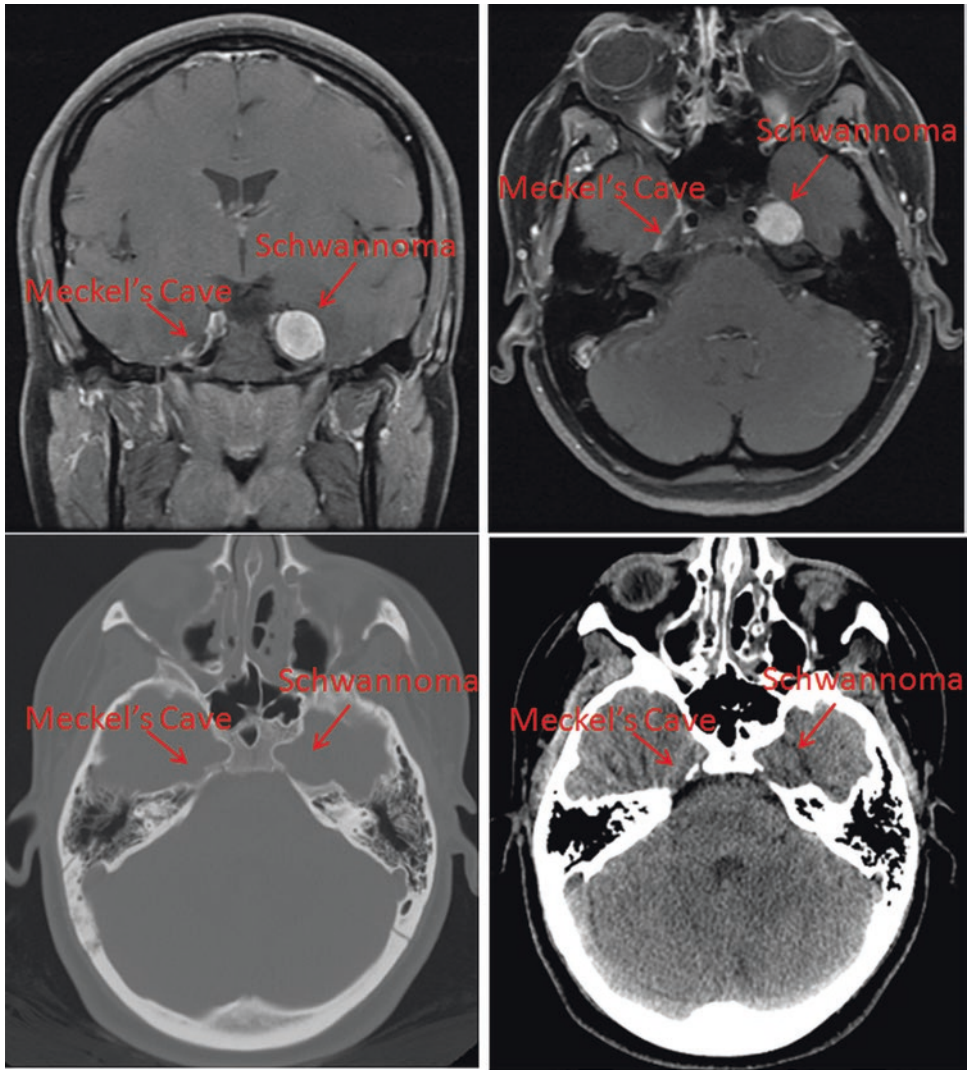

Fig. 28.8 Meckel's cave lesion: coronal and axial T1 fat sat post-contrast images demonstrate an oval shaped enhancing schwannoma markedly expanding Meckel's cave on the left. Note asymmetric expansion and bony erosion evident on bone window and soft tissue window CT images

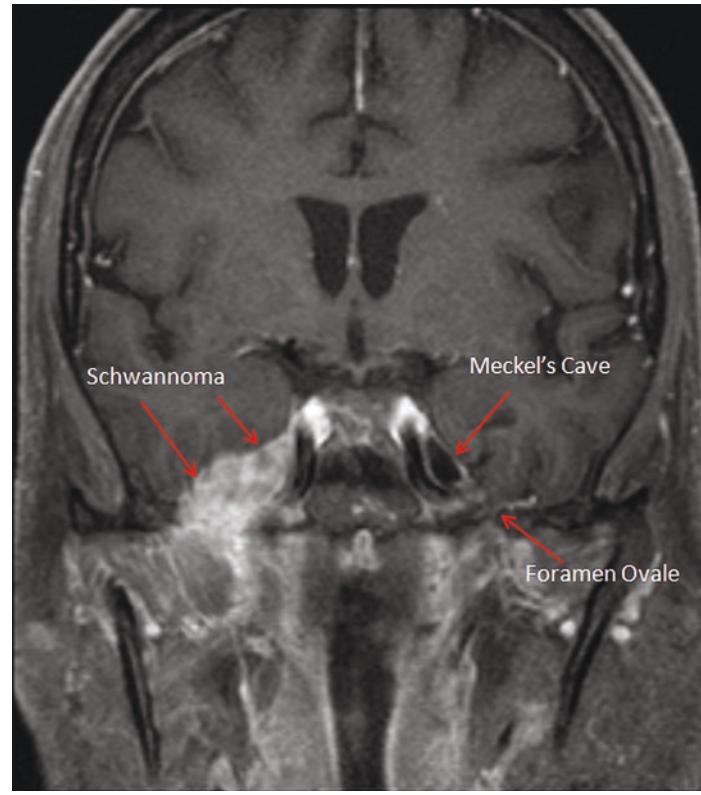

Fig. 28.9 Extracranial extension: coronal T1 fat sat post-contrast image demonstrate a heterogenously enhancing right sided schwannoma involving Meckel's cave and the mandibular V2 division, with inferior extracranial extension through foramen ovale

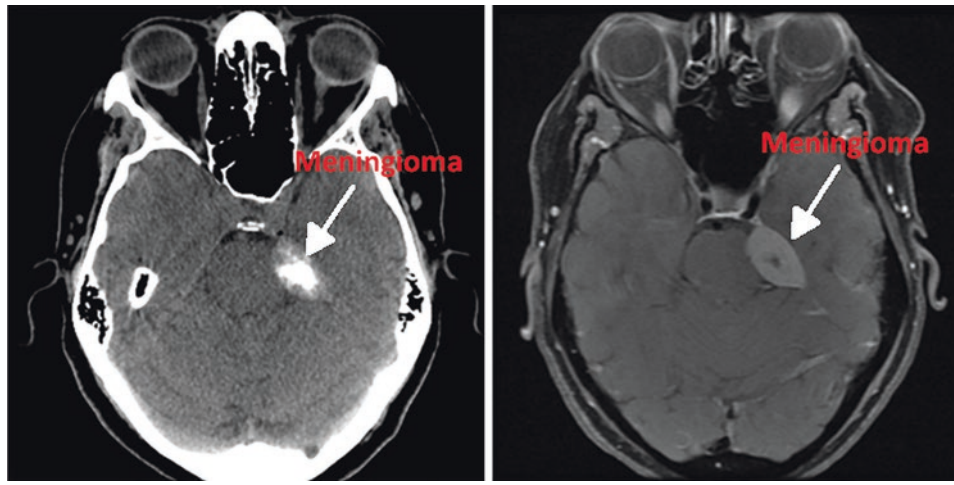

Fig. 28.10 Extrinsic compression: axial CT and T1 fat sat post-contrast images demonstrate a partially calcified meningioma extrinsically compresses the pons, root entry zone and cisternal portions of the left trigeminal nerve. The trigeminal nerve is not visible due to compression

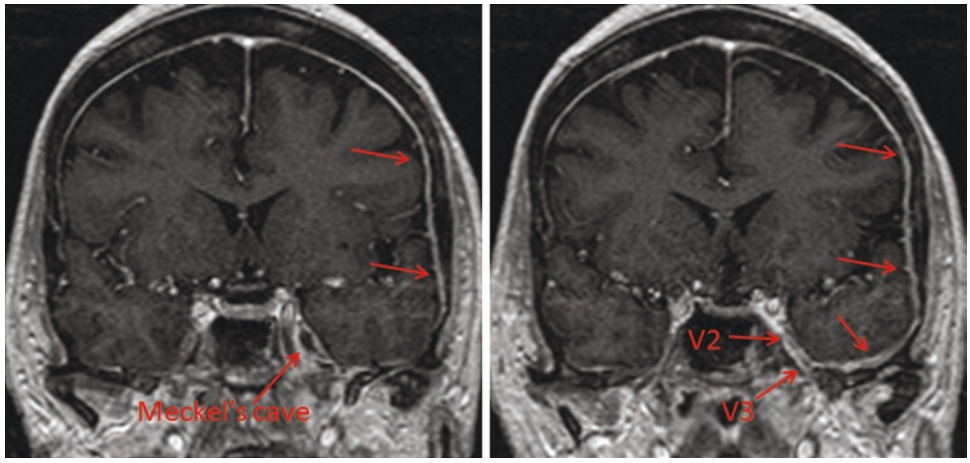

Fig. 28.11 Carcinomatous involvement: coronal T1 post-contrast images in a patient with dural carcinomatosis demonstrate asymmetric left sided dural enhancement with left sided Meckel's cave involvement as well as perineural spread to the second and third divisions of the left trigeminal nerve (*arrows*)

tional proof for and underlying pathologic process [2, 3].

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Lumbar Spine Imaging: X-Ray and CT

29

Glenn C. Gaviola and Nehal A. Shah

Anatomy: 33 normal vertebra with 24 presacral segments: 7 cervical, 12 thoracic rib-bearing and 5 lumbar non-rib-bearing. Approximately 5 % of population with variant transitional anatomy with lumbarization of S1 or sacralization of L5 due to partial fusion of transverse process with sacrum, which may predispose to Bertolotti's syndrome, which can be a source of back pain caused by the transitional lumbosacral anatomy (Fig. 29.1).

X-Ray Imaging

Indications

- Trauma to evaluate for fracture/dislocations;
- Instability to evaluate for spondylolisthesis and spondylolysis;
- Low back pain with "red flags" as per American College of Radiology Appropriateness Criteria, including osteoporosis, focal/progressive neurological deficit; >6 weeks symptom duration; age >70; suspected cancer, infection or immunosupression; pain with radiculopathy and surgical or interventional candidate; prior lumbar surgery; cauda equina syndrome.

Technique

- Standard images include anteroposterior (AP), lateral, and coned-down lateral projections of lumbosacral junction.
- Bilateral oblique ("Scotty dog") views helpful to evaluate for facet arthropathy and for pars interarticularis defects and spondylolysis.
- Lateral views with patient in flexion and extension helpful for evaluating instability and spondylolisthesis (Fig. 29.2).

Evaluation

- Designate number of lumbar vertebra for proper anatomy, evaluate for transitional anatomy;
- Assess bony mineralization and vertebral body heights, evaluate for osteoporosis and fracture;
- Assess vertebral body alignment for spondylolisthesis as measured by incongruence of the posterior cortices:

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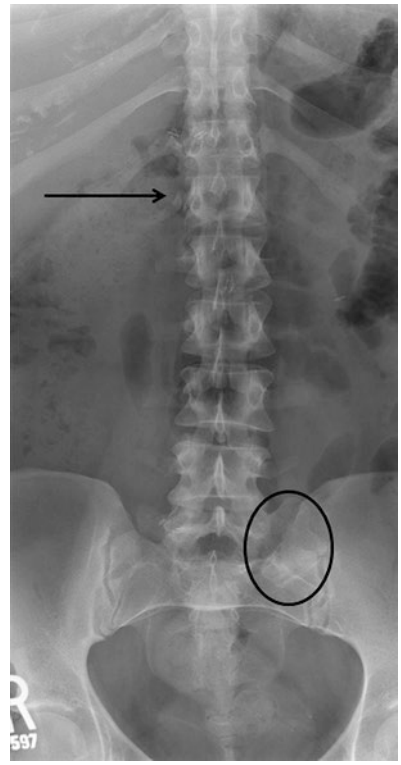

Fig. 29.1 Frontal radiograph of the lumbar spine shows transitional lumbosacral anatomy with prominent left transverse process of the L5 vertebral body which is partially articulating with the left hemisacrum with resultant sclerosis (*oval circle*) as can be seen with Bertolotti's syndrome. Note that 5 non-rib bearing vertebral bodies are presumed with a right-sided small rib denoted at the T12 level (*solid black arrow*)

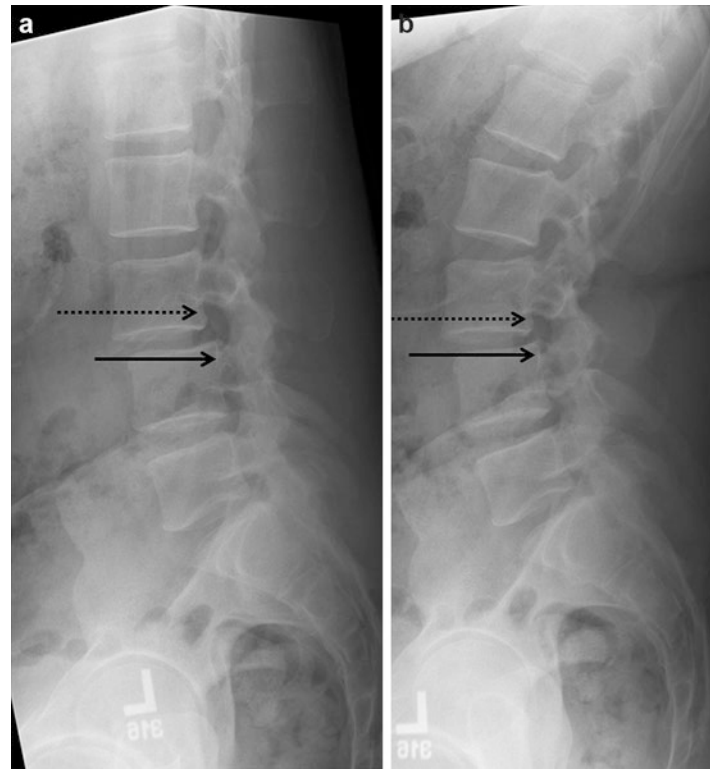

Fig. 29.2 (**a**) Lateral flexion view of the lumbar spine shows anterior translation of the L3 vertebral body (*dashed black arrow*) over the L4 vertebral body (*solid black arrow*), by less than 25 % of the vertebral body width, or grade 1 anterolisthesis (anterior spondylolisthesis), as measured by the differences between the posterior cortices. (**b**) Lateral extension view of the lumbar spine shows minimal interval decrease in the degree of anterior translation of the L3 vertebral body (*dashed black arrow*) over the L4 vertebral body (*solid black arrow*). The differences in anterolisthesis between flexion and extension views can be used to evaluate for the degree in dynamic instability

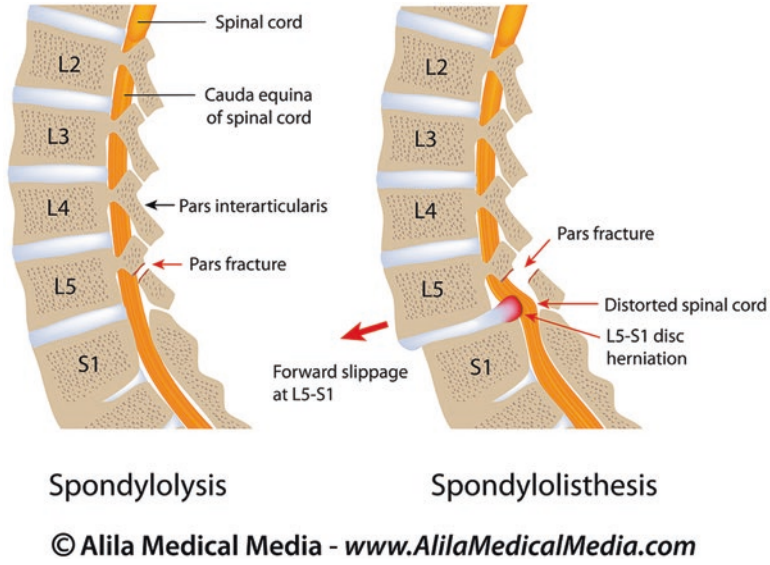

Fig. 29.3 Sagittal schematic images of the lumbar spine show the difference between spondylolysis, which alone is defined as a bony defect or fracture of the pars interarticularis (also known as a pars fracture), versus "true" spondylolisthesis, which is malalignment and incongruence of the posterior cortices of the vertebrae with anterior translation secondary to a pars fracture. In contrast, pseudospondylolisthesis (not shown) is translation in the absence of a pars fracture, usually the result of degenerative disc disease or facet arthropathy. (Used with permission from Alila Medical Media)

  - *True spondylolisthesis* results from a pars interarticularis fracture and spondylolysis (Fig. 29.3);
  - *Pseudospondylolisthesis*, or degenerative spondylolisthesis, results from degenerative disc disease and facet arthropathy without spondylolysis;
- Spondylolisthesis and instability based on measurable changes of horizontal displacements or translation and angular changes between adjacent vertebral bodies between flexion and extension;
- Curvature for normal lumbar lordosis (on lateral view) and degree of scoliosis (on frontal view);
- Intervertebral disc space heights for disc space narrowing and degenerative disc disease and the vertebral endplates for osteophytes and subchondral sclerosis;
- Facet joints to evaluate for osteophytes, subchondral sclerosis, and joint space narrowing in facet arthropathy

CT Imaging

- Provides greater sensitivity with superior bony detailed evaluation of the trabecular and cortical bone as compared to X-rays, particularly in evaluation of fracture healing and characterization of bone tumors;
- Multiplanar reformations allow cross-sectional imaging in coronal, sagittal, and axial planes for evaluation of fractures, spondylolysis, pseudoarthrosis, and spinal canal and neural foraminal bony stenosis, particularly in preoperative evaluation (Fig. 29.4);

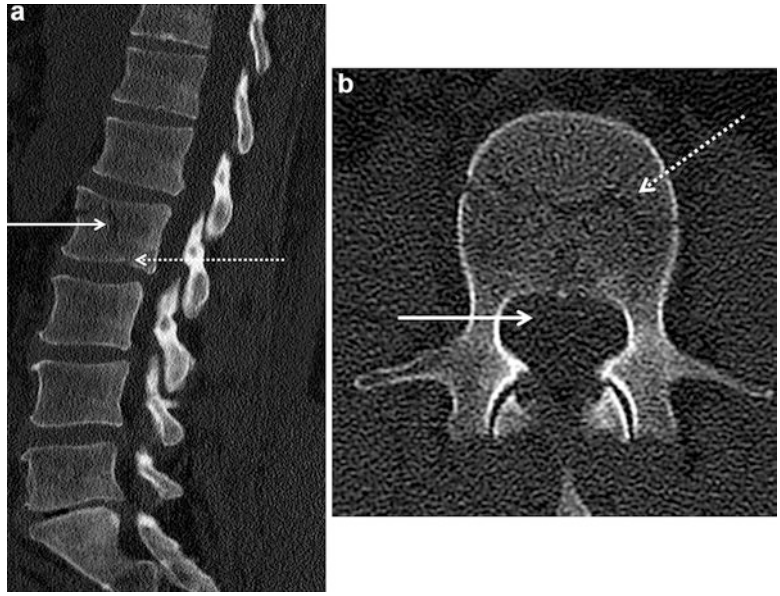

Fig. 29.4 (**a**) Sagittal-reformatted CT image of the lumbar spine shows a minimally displaced comminuted fracture of the L2 vertebral body (*solid white arrow*) extending to the inferior endplate (*dashed white arrow*) which was occult on radiography (not shown). Compared with radiographs, CT demonstrates superior bony detailed evaluation of the cortex and trabeculae due to the lack of overlapping densities from soft tissue structures and abdominal contents. (**b**) Axial CT image of the lumbar spine again shows a minimally displaced comminuted fracture of the L2 vertebral body (*dotted white arrow*) which however, does not show extension to the pedicles or posterior elements. The posterior cortex is intact and no retropulsed bony fragments are seen encroaching on the spinal canal (*solid white arrow*)

- In the setting of multiple trauma, routine multidetector CT with sagittal and coronal reconstructions is supplanting the role of radiographs;
- Less useful for soft tissue pathologies such as spinal cord or nerve pathology;
  - IV contrast can be useful for soft tissue pathology
  - Useful if MRI is contraindicated or unavailable;
- Used in conjunction with fluoroscopic-guided myelography for evaluation of disc herniations
- Helpful in evaluation of postoperative bony graft healing and hardware complications
- Static acquisition in supine or prone positioning precludes dynamic or weight-bearing evaluation of lumbar spine.

Suggested Reading

Davis PC, Wippold 2nd FJ, Brunberg JA, et al. ACR appropriateness criteria on low back pain. J Am Coll Radiol. 2009;6(6):401–7.

Leone A, Guglielmi G, Cassar-Pullicino VN, et al. Lumbar intervertebral instability: a review. Radiology. 2007;245(1):62–77.

Lumbar Spine Imaging: Myelography

30

Glenn C. Gaviola and Nehal A. Shah

Myelography

Indications

- Served as the primary diagnostic imaging evaluation and gold standard for disc herniations and spinal stenosis, but has now been replaced by the advent of MRI and CT imaging;
- Helpful in patients with contraindications to MRI;
- Now used in combination with post-myelography CT scanning for surgical planning and trouble-shooting;
- Commonly used to evaluate for site of cerebrospinal fluid (CSF) leak or patients with signs and symptoms of spontaneous intracranial hypotension;
- Relative contraindications include intracranial lesions with increased intracranial pressure; allergic reaction to iodinated contrast media; history of seizures; and inaccessibility to puncture site, to name a few;

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Technique and Evaluation

- Invasive procedure performed by qualified physician with appropriate training and demonstrated competence at a certified institution;
- Requires dural puncture under fluoroscopic-guidance with access into the CSF and thecal sac, usually at L2–L3 or L3–L4 levels using interlaminar approach to avoid the conus medullaris, and subsequent injection of approved water-soluble contrast agent resulting in opacification of the thecal sac with the patient in prone position;
- Unlike MRI or CT scan, use of real-time fluoroscopy allows for dynamic imaging evaluation:
  - With rotation and Trendelenberg maneuvers, the column of contrast is distributed uniformly across the thecal sac, usually extended to the lower thoracic level to visualize the conus;
  - Used to visualize the thecal sac and nerve roots seen as filling defects, and impressions of the CSF from herniated discs and endplate and facet osteophytes;
  - Helpful for identifying lesions and masses of CSF origin, such as arachnoid and perineural cysts, as these will opacify with contrast; and for identifying CSF leaks by

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dynamic visualization of the leading edge of contrast flow into the leak;

- Flexion/extension maneuvers can be performed to evaluate for instability (spondylolisthesis) and dynamic compression of the CSF;

- Most institutions utilize post-myelography CT scanning for detailed evaluation of disc herniations and degree of spinal canal stenosis by looking for compression of the opacified thecal sac (Figs. 30.1 and 30.2).

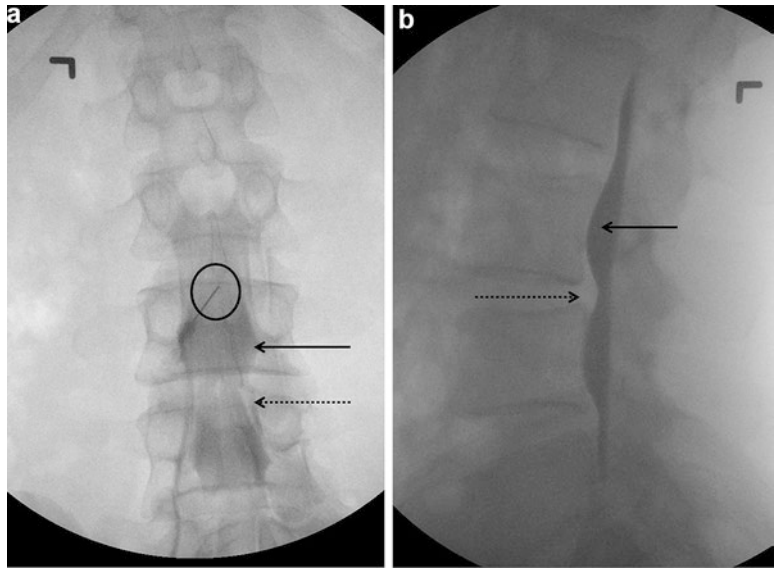

Fig. 30.1 (**a**) Frontal projection obtained during a fluoroscopic-guided lumbar myelogram shows intrathecal needle puncture via an L2–L3 interlaminar approach (*oval circle*) and contrast opacification of thecal sac (*solid black arrow*). The nerve roots of the cauda equina are represented as the white filling defects (*dotted black arrow*) in the background of contrast within the thecal sac. (**b**) Lateral fluoroscopic projection obtained during a lumbar myelogram shows contrast opacification of the thecal sac (*solid black arrow*). Posterior impressions from intervertebral disc bulging (*dotted black arrow*) are represented as ventral indentations of the contrast-opacified thecal sac

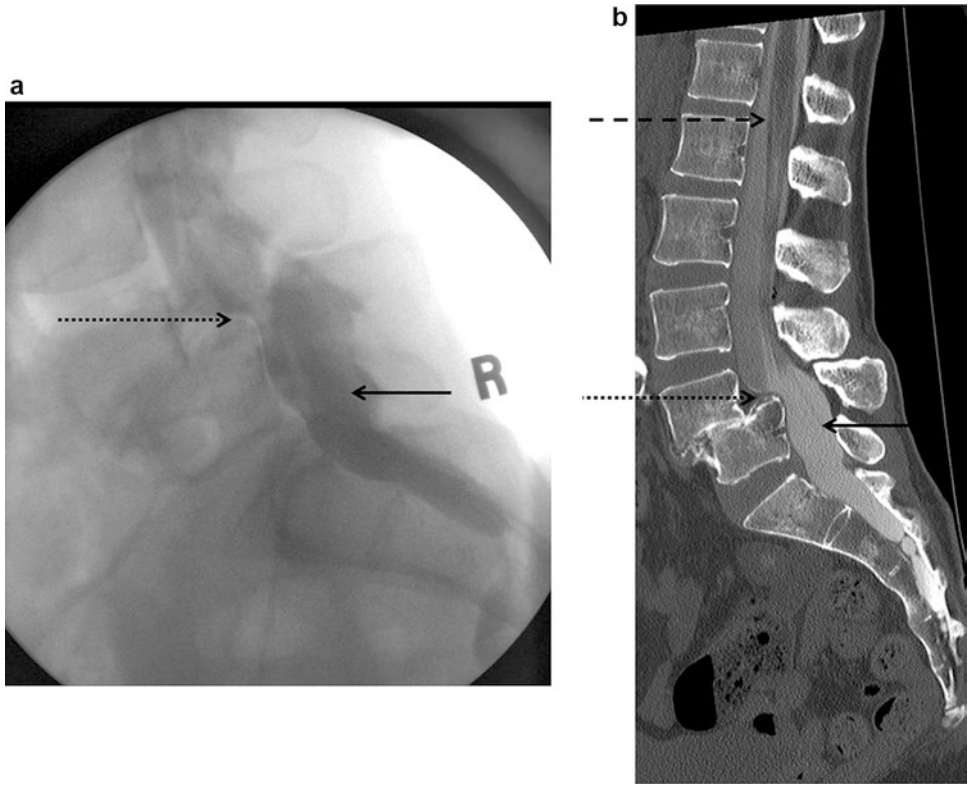

Fig. 30.2 (**a**) Fluoroscopic images obtained during a myelogram shows contrast opacification of the thecal sac (*solid black arrow*) and ventral indentation from a disc-osteophyte complex (*dotted black arrow*) from marked intervertebral disc space narrowing and anterolisthesis (anterior spondylolisthesis) at the L4–L5 level. (**b**) Post-myelography, sagittal reformatted CT images of the lumbar spine shows again contrast opacification of the thecal sac (*solid black arrow*) and better depicts the ventral indentation from a disc-osteophyte complex (*dotted black arrow*) from marked disc space narrowing and anterolisthesis at the L4–L5 level. Notice that despite the spondylolisthesis, the spinal canal remains patent at this level as demonstrated by contrast opacification of the CSF space. The conus medullaris and cauda equina nerve roots are seen as filling defects in this background of contrast (*dashed black arrow*)

Suggested Reading

ACR Guidelines and Standards Committee and ASNR Guidelines Committee: Practice Guideline for the Performance of Myelography and Cisternography (amended 2014), http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/Myelography.pdf

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Part III

Psychology

Psychosocial and Cultural Aspects of Pain

31

Kathleen A. McChesney and Genelle Weits

Pain Is a Biopsychosocial Experience

To best conceptualize pain, the traditional biomedical model is insufficient. The model does not take into account psychosocial, cultural, and environmental influences on the pain experience. The biopsychosocial model more accurately accounts for the individual's complex interactive systemic experience of pain. Unlike the unilateral and deterministic biomedical model, this approach emphasizes that pain is more than a physical symptom resulting from a disease process, tissue injury or pathology. Rather, pain is "...a subjective perception that results from the transduction, transmission, and modulation of sensory input filtered through a person's genetic composition and prior learning history and modulated further by the person's current physiological status, ideosyncratic appraisals, expectations, current mood state, and sociocultural environment" (Turk & Monarch, 2002). This comprehensive model as illustrated in Fig. 31.1 integrates pathophysiology (biological), mental health status (psychological), and environment (social). Etiology is multifaceted, and moderating variables influence perception, interpretation, presentation, and prognosis.

Biology, psychology, social and cultural factors influence how pain ins manifested and whether psychological symptoms reflect pain neurophysiology alone, independent psychiatric disorders, or a functional interaction together. paPsychological symptoms do not necessarily constitute pathology. sRather, many psychological symptoms are diretly associated with pain neurophysiology.

NOTE: Once pain becomes chronic (> 6 months) sensory input plays a dimished role and affective and cognitive pathways play a more prominent role in the creation of painful perceptions (Apkarian, et. al. 2005 in Williams, 2013).

Therefore, physical pathology does not always predict severity of pain or level of disability and pain severity does not adequately determine psychological distress or extent of disability observed. Cognitive appraisals, interpretations, understanding of one's status and prognosis play a crucial part in the differential versus co-morbid diagnoses and treatment of the individual.

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The Commission on Accreditation Rehabilitation Facilities (CARF) only accredits chronic pain programs that are interdisciplinary in evaluation and treatment and have a psychologist/psychiatrist as part of the core team. Objectives of the psychosocial assessment of a pain patient are to include:

1. Understanding of the patient's subjective 'story' of the development of the pain experience.
2. Determination of location, distribution, intensity, and quality.
3. Observations of verbal and non-verbal pain behaviors and their function.
4. Patient's socio-cultural, developmental, educational, relationship, and family history.
5. Co-morbid symptoms associated with the pain experience, including sleep, energy, cognition, insight, function, versus dysfunction.
6. Assess mood, anxiety, personality and characterological vulnerabilities.
7. Determine the patient's engagement in relationships, employment, recreation, hobbies, social engagements.

Clinically significant Psychiatric disorders can be assessed according to the guidelines of the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 5th Ed.).

Individual Differences in Affective, Cognitive, and Behavioral Responses to Pain

Objectives of psychological evaluations:

1. Pain quality: intensity, location, distribution.
2. Co-morbid symptoms: sleep, fatigue, focus, memory, and function (physical, recreational, sexual).
3. Mood and affect: dysphoria, depression, personality disorders, anxiety, anger.
4. Beliefs and attitudes: self-efficacy, locus of control, coping resources, catastrophizing, kinesiophobia, resilience.
5. Responses to pain: based on beliefs, expectations, attitudes about the meaning of pain.
6. Environment/social influences (past and present): communication with family, friends, peers; culture, medical, employment.

Coping Styles: Definition and Effect on Pain Experience and Response to Treatment

Cognitive: Distortions: Catastrophizing, magnifying, ruminating. ("No-one cares about my pain") Locus of control: Internal "I can handle this" vs. External "You need to fix me, you're the expert."

Affective: Emotional reactions to pain sensations (hopelessness, fear, anger, kinesiophobia).

Behavioral: moaning, limping, clenching teeth, wincing, experiential and behavioral avoidance and withdrawal, etc. Not all patients will show how they feel and think (due to pride, minimizing, alexithymia).

Effects of Active vs. Passive Toward Biopsychosocial Treatment Model

Passive-Cognitive: ("I Need a Cure")

Belief pain indicates something needs repair/removal; once resolved, the pain will cease. Driven to "fix" the problem. Inability to consider any alternative treatment methods that do not have the goal of pain resolution. Person needs to feel in control of the pain; cannot see that this may not be within his control.

Passive-Cognitive: ("There Is No Cure Possible")

Lack of coping often occurs with the belief that pain signals mean ongoing damage or injury. Rather than searching for the cure, he feels completely helpless to change the pain. He avoids any actions that increase pain, leading to further disability.

Unexplained Pain

Pain considered unexplainable or "more than expected" gives the message that there is no known way to decrease the pain. Can lead to hopelessness and passive coping. Conversely, may become more resolute on finding the specific reason for the pain by continually seeking a provider who can determine the cause. Previous providers may be labeled as inadequately trained or lacking understanding or empathy (otherwise they would have "worked harder" to find the cause and ultimately take the pain away).

Active-Cognitive/Behavioral: ("Pain Will Remain, Suffering Is Optional")

When it's understandood that the absence of pain may not be possible, this coping goal is to change the reactions to the pain. Not considered until it is clear there is no long-term relief, realizing the pain may not change, but the impact of the pain and suffering can drastically change.

Cultural and Environmental Factors: Effect on Expectations, Disability, Treatment Outcomes, and Maintenance of Treatment Effects

Success of treatment is based on patient beliefs and expectations.

Biomedical model = medical provider is an expert with the power to resolve the pain condition He/she has the answer and ability to give (medications), conduct a procedure or otherwise alter the physical source of the pain locality (surgery, injections) to relieve pain. When not met, trust in providers and belief of future treatment success is decreased.

Biopsychosocial model = The experience of pain is an OUTPUT of the brain, influenced by neurophysiological developments from plasticity, learning history, biogenetic templates, psychological perceptions, cognitions, interpretations, and sociocultural moderators. The patient is a pro-active participant in his/her recovery and works with a comprehensive staff to address all relevant biopsychosocial aspects of his/her pain experience with intrusive biomedical methods being only one of several forms of treatment.

Pain behaviors (overt expressions of pain, distress, suffering) are acquired through observing models in early life or currently. Strategies are uniquely developed to help one avoid pain and learn "appropriate" (acceptable) ways to react within the context (not necessarily healthy coping).

Through external contingencies or reinforcements, acute pain behaviors can evolve into chronic pain problems via operant learning principles. Behaviors may be positively reinforced by others or maintained by escaping noxious stimuli (via drugs, rest, or avoidance of undesirable activities— i.e., work).

Healthy, adaptive behaviors may not be sufficiently reinforced and can be extinguished. The behaviors in response to pain can be shaped based by what is positively and negatively reinforcing for the individual. All members of a patient's social system are affected dynamically if the sufferer gradually loses functionality. *The more difficulties in the patient's social systems, the more likelihood of further disability.*

Cultural, Environmental, Racial Variations, and Family Influence in Experience and Expression of Pain

Cultural, environmental, psychological, and social factors act indirectly on pain and disability by reducing physical activity (leading to reduced muscle flexibility, tone, strength, physical endurance). Fear of re-injury, loss of disability compensation, job dissatisfaction can influence return to functionality. This impacts how others see the patient and the patient's self-image (changes in roles, responsibilities, communication). Ethnic and cultural groups may respond differently to painful stimuli. Ethnic expectations and gender and age stereotypes may influence the practitioner–patient relationship and may result in premature diagnosis.

Ethnic, gender, social, occupational, and familial group membership influence how one perceives, labels, responds to, and communicates various symptoms, and may determine from whom one elects to obtain care when sought.

Obtain longitudinal information about the patient's learning history during early developmental and current functional environments to understand current presentation of patient.

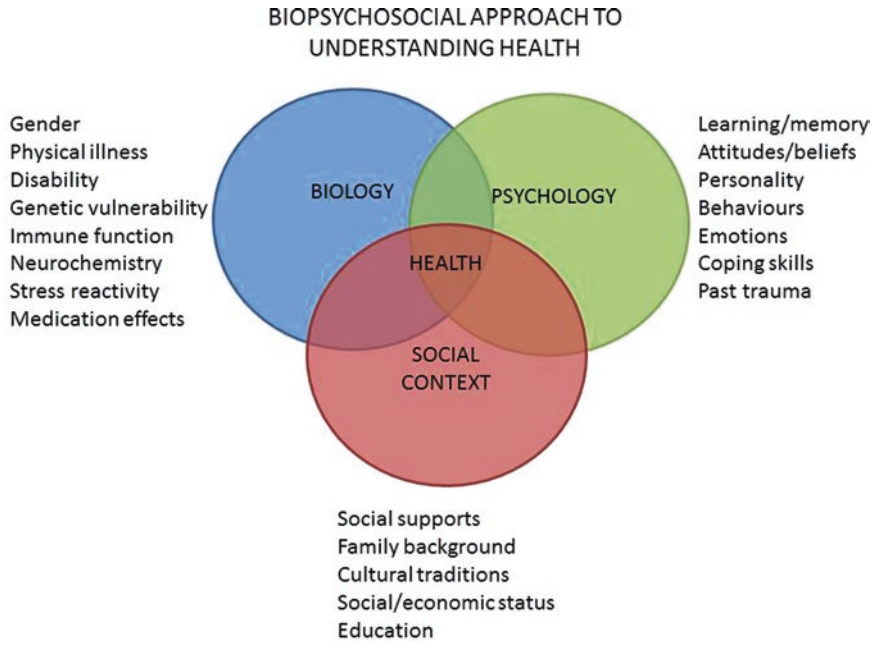

Fig. 31.1

Common Emotional Problems and Psychiatric Disorders Associated with Pain

Depression: (Major Depressive Disorder vs. Adjustment Disorder) due to loss, identity change.

Anxiety: fears regarding pain and future consequences of pain (no work options, death from pain).

Post-Traumatic Stress Disorder (PTSD): Trauma may be recent/related (accident with fear of death, harm that led to pain) or past (current state of vulnerability due to pain triggers past trauma).

Somatic Symptom Disorder (formerly Somatoform Disorder).

Suggested Reading

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Sex and Gender in Pain

32

Priya Pinto, Devina Persaud, and Karina Gritsenko

Sex: It is the genetic, hormonal, and anatomic characteristics that determine whether a person is a biological female or male; typically defined by physical assessment of genitalia.

Gender: It is an individual's innate sense of being male, female, or somewhere in between.

- Gender role—society's expectations of attitudes, behaviors, and personality traits typically based on biologic sex. Masculinity vs. femininity.
- Gender expression—how gender is presented to the outside world.

Epidemiology of Pain

- Men and women report different symptoms associated with the same disease process.
- There are also differences in pain incidence and prevalence (see Table 32.1).
- Females are more likely to experience pain (>2×), report higher levels of pain, and are more likely to use analgesics than males [1].
- Females also tend to have more persistent pain as well as pain that leads to disability [2].

Gender and Opioids

- In a meta-analysis of 18 studies that enrolled 1014 males and 1014 females using opioid agonists; in 10/18 studies, males consumed significantly more opioid analgesics in the immediate post-operative period when compared to females [3].

Gender Differences in Pain Perception

- There have been several studies looking at sex and gender in pain over the last few decades (Fig. 32.1).
- Females have a lower pain threshold than males.

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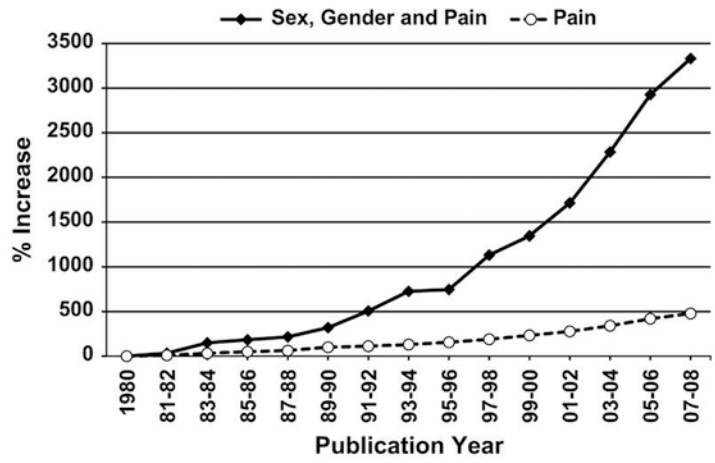

Fig. 32.1 Demonstrates the annual percentage increase in publications about sex and gender in pain since 1980. Reprinted from The Journal of Pain, Vol 10, Issue 5, Fillingim RB, King CD, Ribeiro-Dasilva MC, Rahim-Williams B, Riley JL 3rd, Sex, gender and Pain: A Review of Recent Clinical and Experimental Findings, 447–48, Copyright (2008), with permission from Elsevier

Table 32.1 Disease prevalence based on sex

Female	Male
Multiple sclerosis	Pancreatic disease
Rheumatoid arthritis	Duodenal ulcer
Raynaud disease	Ankylosing spondylitis
Fibromyalgia	

- 70 % of women ages 18–65 reported at least 1+ pain condition as compared to 60 % of men in the same age group.
- 15 % of women ages 18–65 years reported 3+ pain conditions, whereas <10 % of men reported 3+ pain conditions [4].

1993, Bandelow study [5]

- Research about sex and gender differences in pain has increased significantly in the past 30 years (Fig. 32.1).
- Females believed their own ideas about fear and anxiety affected their perception of pain. Males focus on the physiological aspect of pain rather than the psychological.
- Majority believed females were better able to cope with pain than were males.
- Males more likely to refrain from emotion associated with pain.

Substance Abuse and Treatment

- More men than women die from overdoses from prescription pain medications.
- Among adults discharged from a substance abuse program men were more likely than females to complete outpatient treatment (39 vs. 32 %) with similar rates for dropouts and termination of program [6].

Summary

It is imperative for the provider to individualize the plan of care for pain management to suit the specific needs of each patient. Increased awareness among providers is essential in preventing undertreatment and avoiding negative physiological and psychological problems.

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6. http://wwwdasis.samhsa.gov/teds07/TEDSHigh2k7.pdf

Part IV

Addiction

Addiction

33

Claudia P. Rodriguez, Tyler Dodds, and Joji Suzuki

Defining Addiction

Addiction is a primary, chronic disease of brain reward, motivation, memory, and related circuitry. The dysfunction in these circuits leads to characteristic biological, psychological, social, and spiritual manifestations. The core features of addiction are defined by the "4 C's of addiction": loss of control, compulsive use, cravings, and ongoing use despite negative consequences. Patients with addiction display an inability to consistently abstain from using the drug, impairment in behavioral control, cravings for the drug with negative affective states when access to drug is denied, and diminished recognition of significant problems with one's behaviors and interpersonal relationships.

While physiological dependence (tolerance and withdrawal) is included as criteria in the DSM 5 for diagnosing a substance use disorder, it is neither sufficient nor necessary for the diagnosis of addiction. Tolerance, or the need for increased amounts of the drug to achieve the desired effect or a markedly diminished effect with continued use of the same amount of drug, can exist for both positive and negative effects of a drug. Withdrawal, manifested by psychologic and/or physiological responses to abrupt discontinuation of a drug, can be experienced following discontinuation of many prescription medications and substances of abuse.

A number of prescription medications have considerable abuse liability, and can lead to addiction in some individuals. These include opioid medications, benzodiazepines, and stimulants.

Opioids

Intoxication

Opioids are compounds that activate the mu opioid receptor, leading to analgesia and other effects. Opiates refer to opioids derived from the poppy plant, namely morphine and codeine. Commonly used opioids today are derived from opiates, such as oxycodone, and are semisynthetic opioids. Activation of the mu opioid receptor results in analgesia, euphoria, constipation, nausea, sedation, respiratory depression, miosis, and impairment in attention. Respiratory depression is the most specific sign of overdose. Administration of naloxone, an opioid antagonist, can rapidly reverse opioid overdose.

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Withdrawal

Signs and symptoms of opioid withdrawal include dilated pupils, anxiety or irritability, tachycardia, diaphoresis, gastrointestinal symptoms including diarrhea, stomach cramping, nausea/vomiting, tremors and physical restlessness, rhinorrhea, lacrimation, piloerection, yawning, insomnia, and bone or joint aches. Opioid withdrawal can be managed with methadone, buprenorphine, or a symptomatic non-opioid regimen. Both methadone and buprenorphine are titrated to the severity of symptoms of withdrawal, and tapered over the course of several days. The symptomatic regimen includes medications such as clonidine for anxiety and restlessness, diphenhydramine for rhinorrhea, loperamide for diarrhea, dicyclomine for abdominal cramping, and ibuprofen/acetaminophen for pain. Sleeping agents, such as trazodone, can be used for insomnia in the acute phase of opioid detoxification.

Unlike other substances of abuse, there are several treatments that have been shown to be beneficial in management of opioid use disorder. Methadone maintenance can only be provided from federally licensed methadone clinics. Buprenorphine can be prescribed from the office settings, and requires the prescribers to obtain a DEA waiver. Naltrexone, an opioid antagonist, can be prescribed for the treatment of both alcohol and opioid use disorder, and is available in a daily oral formulation or long acting monthly intramuscular injection.

Implications in Pain Treatment

Opioids are used in the management of acute and chronic pain. In the late 1990s, several factors led to an increase in the number of opioid prescriptions written and dispensed. These included encouragement of clinicians to treat pain more proactively and effectively, aggressive marketing by pharmaceutical companies, and greater social acceptability for using medications to manage pain. With an increasing number of opioid prescriptions available, there has been a notable increase in opioid related unintentional overdose deaths. As a result, efforts have been made to institute safer prescribing of opioid medications—the use of prescription monitoring programs, routine urine testing, risk stratification, treatment agreements, minimizing the dose, and maximizing non-opioid management strategies. Greater emphasis has been placed on improving social and physical functioning, instead of focusing exclusively on ameliorating pain.

Alcohol

Intoxication

Alcohol affects almost all neurotransmitter systems in the brain, with most prominent effects through activation of the GABA system. Blood alcohol concentration after ingestion of alcohol is affected by factors such as body weight, body composition, and rate of absorption from the gastrointestinal tract. Alcohol intoxication is associated with euphoria, muscle relaxation, slurred speech, and impaired coordination, attention, and judgment. At higher doses, individuals may have significant cognitive deficits, mood lability, aggressiveness, impulsivity, and anterograde amnesia. Blood alcohol levels above 300–400 mg/dL can be associated with autonomic dysfunction, respiratory depression, coma, and death. Effects of alcohol are enhanced when combined with any other CNS depressants, such as benzodiazepines. Treatment is based on severity of CNS depression.

Withdrawal

Alcohol withdrawal may require medical intervention. Signs and symptoms include tachycardia, nausea/vomiting, diaphoresis, tremors, headache, auditory, tactile, or visual disturbances, anxiety and agitation, and confusion/disorientation. Without appropriate management, seizures, delirium tremens, and death may ensue. Delirium tremens typically manifests within 48–72 h of alcohol cessation, and is identified by severe autonomic dysfunction, delirium, and tremors.

Management of alcohol withdrawal typically involves use of benzodiazepines which are slowly tapered over time. Anticonvulsants, such as valproic acid, may be incorporated, especially in patients

who have a recent history of alcohol withdrawal seizures. In cases of delirium tremens, admission to an intensive care unit is typically required due to need for aggressive sedation and vital sign monitoring. In addition to benzodiazepines, monitoring and correction of electrolyte imbalances is important. With prolonged alcohol use, thiamine deficiency and potentially Wernicke's encephalopathy may develop. As a preventative measure, patients are provided with thiamine supplementation during treatment of alcohol withdrawal. Wernicke's should be suspected in an individual presenting with evidence of malnutrition, ocular signs, mental status change, and/or cerebellar signs.

FDA approved treatments for alcohol use disorder include naltrexone, acamprosate, and disulfiram. Naltrexone is an mu opioid receptor antagonist and has been shown to decrease number of heavy drinking days, drinks per drinking day, and cravings. Acamprosate, a GABA-glutamate system modulator, can be helpful in decreasing cravings, though studies have been mixed with regards to its effectiveness in the USA. Disulfiram inhibits aldehyde dehydrogenase, leading to an accumulation of acetaldehyde when alcohol is consumed. This results in uncomfortable symptoms of nausea and vomiting, flushing, and palpitations with alcohol intake.

Implications in Pain Management

Due to the significantly elevated risk of overdose, the concurrent use of alcohol with opioids should be avoided.

Cannabis

Intoxication

Cannabis is derived from the hemp plant, cannabis sativa, whose various parts have different potencies. Intoxication is indicated by behavioral or psychological changes such as impaired motor coordination, euphoria, anxiety, altered time perception, impaired judgment, increased appetite, dry mouth, or social withdrawal. Additional signs that are associated with intoxication include conjunctival injection and tachycardia. Some patients may also experience perceptual disturbances, including auditory hallucinations and intense paranoia.

Withdrawal

Cannabis withdrawal is indicated by three or more of the following signs or symptoms develop within approximately one week following cessation of prolonged, heavy use (daily or almost daily over at least a few months): irritability/aggression, anxiety, sleep difficulty (insomnia or disturbing dreams), decreased appetite, restlessness, and depressed mood. Individuals may also experience physical symptoms including abdominal pain, tremors, sweating, chills, and/or headache.

Implications in Pain Treatment

Use of cannabis in pain management is controversial. Research has evaluated the benefits of using cannabinoids, smoked cannabis, cannabis extracts, and medications such as dronabinol, in pain management. Studies to date point a possible role for cannabinoids in managing chronic nonmalignant pain, but further well-controlled studies are needed.

Stimulants

Intoxication

Stimulants are substances that exert their effects primarily through enhancing the effects of dopamine and norepinephrine. Examples include methamphetamine, cocaine, and methylphenidate. Intoxication is associated with euphoria, increased alertness and attention, tachycardia, hypertension, elevated temperature, diaphoresis, psychomotor agitation, and dilated pupils. Individuals also experience insomnia, hyperactivity, irritability or anxiety, and anorexia. At higher doses, stimulant use can lead to cardiac arrhythmia and myocardial infarction, seizures, stroke, rhabdomyolysis, and other end organ damage. On examination, depending on the route of administration, nasal septum perforation or track marks, indicative of intravenous drug use, can be seen. In addition, stimulant intoxication can lead to psychosis, delusions of parasitosis, paranoia, persecutory delusions, and aggressive behaviors. These symptoms can present

in the emergency department as a psychiatric emergency, and generally respond to sedation and fluid resuscitation.

Withdrawal

The clinical syndrome associated with stimulant withdrawal includes depressed mood, sleep disturbances, and hyperphagia that can last for several days to weeks.

Implications in Pain Management

Patients receiving pain medications are often required to agree to abstain from all illicit substance use, and stimulant users should be referred to substance abuse treatment. Because many over-the-counter and prescription medications result in positive amphetamine result in urine toxicology tests, clinicians need to understand how to interpret such results appropriately.

Sedatives/Tranquilizers

Intoxication

Sedatives and tranquilizers are for the treatment of insomnia, anxiety, muscle spams, migraines, and seizures. They are typically indicated for short term use. The signs and symptoms of intoxication include sedation, disinhibition, nystagmus, slurred speech, ataxia, and confusion. With higher use, individuals can have paradoxical agitation and anterograde amnesia. When combined with other CNS depressants, notably alcohol or opioids, the risk of respiratory depression, hypotension, and overdose increases significantly. Overdose is a medical emergency and requires intervention with flumazenil, a benzodiazepine antagonist, in addition to supportive measures.

Withdrawal

Common withdrawal symptoms of sedatives/tranquilizers include tremor, nausea, insomnia, irritability and anxiety, poor concentration, delirium, and seizures. Autonomic changes, including tachycardia, can also be seen with acute withdrawal.

Implications in Pain Management

Due to the significantly elevated risk of overdose, the concurrent use of sedatives/tranquilizers with opioids should be avoided if possible.

Assessing Risk of Addiction

Prior to initiating opioid therapy for chronic pain, the patient's medical and psychiatric history should be assessed, including obtaining a urine drug screen, reviewing prior medical records and state prescription monitoring program.

The risk that a patient may use the medication for nonmedical purposes or become addicted can be assessed using such tools as the Opioid Risk Tool (ORT, see Table 33.1 below) or The Screener and Opioid Assessment for Patients with Pain (SOAPP, available online). Both are brief self-report measures. The SOAPP incorporates additional risk factors such as mood swings, history of legal problems, and having close friends who have had problems with drugs or alcohol.

Table 33.1 Opioid risk tool (ORT)

Sex	Female	Male
Family history of substance abuse		
Alcohol	1	3
Illegal drugs	2	3
Prescription drugs	4	4
Personal history of substance abuse		
Alcohol	3	3
Illegal drugs	4	4
Prescription drugs	5	5
Personal history of psychiatric illness		
ADD, OCD, bipolar disorder, schizophrenia	2	2
Depression	1	1
Other risk factors		
Age between 16 and 45 years	1	1
History of preadolescent sexual abuse	3	0
Total score		
Scoring guide	0–3: Low 4–7: Moderate ≥8: High	

Managing Risk

If a patient presents a high risk, consideration is given to avoiding opioids altogether and utilizing non-opioid pharmacotherapies, or implementing more rigorous monitoring strategies—such as shorter prescriptions, or more frequent urine drug screens.

For "safe opioid prescribing" providers should routinely assess the "4 A's" including analgesia, activities of daily living, aberrant behaviors, and adverse effects.

Assessing for Nonmedical Use and Addiction

Once opioid pain medications are started, patients need to be monitored closely for signs of nonmedical use or addition, such as unexpected urine toxicology results, requests for early prescriptions, apparent intoxication during visits, or prescriptions from other providers discovered in review of the state prescription monitoring program.

Self-report surveys such as the Current Opiate Misuse Measure (COMM, available online) can also be used to look for possible indications of nonmedical use: signs and symptoms of intoxication, emotional volatility, aberrant use of health care services, excessive amount of time spent thinking about the medication, use of the medication in ways that are not prescribed or for symptoms other than pain (e.g., to help with sleep or mood), or taking others' pain medications.

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Addiction: Substance Abuse

34

Brian Lockhart and Michael Nguyen

Traditionally, substance abuse and addiction are closely related, yet have different meanings. Substance abuse occurs when a drug or medication is used in any way other than as prescribed or designed for medical purposes. Addiction is the pattern of behavior associated with the psychologic and physiologic compulsive desire to use a drug or medication, particularly the continued use of the medication even in the setting of it negatively affecting one's life [1]. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V), however, essentially defines substance use disorders as traditional addiction. Criteria include requiring more of a substance, "cravings," inability to control use, spending time thinking about and obtaining a given substance, withdrawal, tolerance, and persistent use despite negative consequences [2].

Important associated terms are tolerance and dependence. Tolerance occurs with long-term use of a medication and simply means that more of the drug is required to produce the same physiologic effect. Dependence refers to the change in one's physiology as a result of long-term exposure to a drug or medication, such that upon cessation or antagonism of the chemical, withdrawal symptoms will occur. There can be a fair amount of confusion distinguishing dependence from addiction. In fact, the DSM-V combined the two into one disorder. However, it is key to remember that dependence is the body's physiologic response to the drug or medication, while the addiction component of substance abuse is the pattern of behavior that results from an individual's cravings for the substance.

As an example, an individual who requires escalating doses of oxycodone in the setting of an unchanged stimulus is developing tolerance. Over time this chronic use leads to withdrawal should the oxycodone be abruptly halted (dependence).

If this individual were to crush and snort the medication or take it in excessive quantities not to treat the pain but rather for the euphoric effects, this would be crossing over into substance abuse. If this use of the drug leads to poor performance at work or negligent in duties to family because of the medication misuse and being unable to stop, then this would be considered addiction.

Some signs that an individual may be addicted:

- Taking the drug more often or in a form not prescribed (i.e., crushing pills)
- Going to multiple physicians to obtain the same medication
- Using medication prescribed for others
- Avoiding disclosure of all medications being taken
- Continuation of a drug after it is no longer needed for a medical condition
- Mixing medications with alcohol

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Prevalence: It is important to note that addiction is one of the most prevalent diseases that exists. Nearly one in ten Americans (~23 million people) is addicted to a substance. Alcohol is by far the most commonly abused substance (more than two-thirds of those 23 million). The most common nonalcohol substance use disorders are marijuana, opioids, and cocaine [3].

Addiction to opioids can be as high as 50 % in patients who suffer from chronic, nonmalignant pain. While in patients with pain related to cancer, opioid addiction is much lower, around 7.7 % [4].

The most commonly abused medications include pain medication (primarily opioids), stimulants (i.e., methylphenidate), sleeping medication (i.e., zolpidem), and benzodiazepines (i.e., diazepam). Rates of prescription medication abuse have been on the rise, so much so that the CDC has labeled it an "epidemic" [5]. The top four most common prescription medications involved in overdose deaths are hydrocodone (Vicodin), oxycodone (OxyContin), oxymorphone (Opana), and methadone.

Mechanism: The physiology leading to addiction lies in the pleasure principle—the human brain rewards itself with pleasure. A substance (or behavior) bathes the nucleus accumbens with dopamine. The hippocampus forms memories of the instant pleasure, and the amygdala patterns the stimuli's conditioned response. A larger surge of dopamine has a greater propensity to form addictive behavior, which is why faster onset routes (i.e., intravenous) have greater abuse potential. As neuroscience progresses, evidence points to an evermore complex web of neuroconnectivity. The mesolimbic dopamine reward pathway implicates other regions of the brain as well, including the ventral striatum, hypothalamus, frontal regions of the cerebral cortex, locus coeruleus, and dorsal raphe.

Treatment: Addiction is very difficult to treat. Relapse rates of opioids are typically 40–60 % [6]. Treatment is typically initiated with detoxification. Depending on the substance, this may need to occur as medically supervised withdrawal. Psychosocial support is required to effectively treat addiction, as it is considered a lifelong disease. Treatment programs include long-term and short-term residential centers, outpatient treatment clinics, as well as individual and group counseling. As a long-acting opiate, methadone can be used in select patients. In addition, Suboxone, a combination of an opioid agonist (buprenorphine) and antagonist (naloxone), aims to activate opioid receptors to decrease cravings while preventing abuse by combining it with an antagonist.

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Part V

Treatment of Pain

Pharmacology of Pain Transmission and Modulation

35

Brian Lockhart and R. Jason Yong

Pain transmission is extraordinarily complex and still not fully understood. Different varieties of pain exist (i.e., somatic, visceral, neuropathic); however, this chapter will follow the pain pathway from peripheral activation to the brain and focus on the different sites along the route that can be used as molecular targets for pain relief.

Transduction

Local inflammation leads to the release of a number of substances that both activate and sensitize nociceptive peripheral nerve endings. These pro-inflammatory factors include bradykinin, prostaglandin, nerve growth factor, tumor necrosis factor, leukotriene, histamine, adenosine, glutamate, substance P, H+ ions, capsaicin, nitric oxide, and serotonin. This chemical swarm promotes the initial *transduction* of pain from the periphery. Thus, agents aimed at preventing peripheral nerve transduction include NSAIDs, antihistamines, membrane-stabilizing agents, local anesthetics, capsaicin, and bradykinin and serotonin antagonists.

Transmission

From the peripheral nerve, pain is transmitted to the dorsal horn of the spinal cord. Along this path, action potentials are propagated along neural axons. Local anesthetics block sodium channels to prevent membranes from achieving action potentials, thus preventing the *transmission* of pain to the dorsal horn. Membrane-stabilizing agents, which include gabapentin, pregabalin, carbamazepine, oxcarbazepine, lamotrigine, and topiramate, modulate transmission by decreasing action potential propagation, often via Na+ channels.

Modulation

At the dorsal horn of the spinal cord, pain is modulated via the following molecules: glutamate and aspartate (excitatory amino acids), substance P and neurokinin A (excitatory neuropeptides), and glycine and GABA (inhibitory amino acids). At this point in the pathway, the main receptors involved are NMDA, AMPA, kainate, and metabotropic (i.e., G-coupled receptors). Mu-opioid receptors are abundant in the spinal cord.

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Norepinephrine, serotonin, and dopamine are monoaminergic neurotransmitters also involved in neuromodulation. Descending pathways that further influence pain transmission add another layer of complexity. Making matters more convoluted, serotonin and dopamine can be either pro- or antinociceptive depending on the receptor and pathway involved.

Norepinephrine is an antinociceptive substance that acts via alpha-receptors, promoting GABA and glycine release (neural inhibition). Serotonin, on the other hand, can be antinociceptive via 5-HT1 receptor activation, however, contributes to nociceptive transmission via 5-HT2/5-HT3 receptors. Similarly, D1 spinothalamic projections enhance nociception, while D2 and D3 receptors inhibit pro-nociceptive neurotransmitter release.

At this point in the pain pathway, there are a number of targets for the *modulation* of pain. At the dorsal horn, these include spinal opioids, alpha agonists, NMDA antagonists, anticholinesterases, CCK antagonists, and NO inhibitors. SNRIs and TCAs can also help modulate the descending pathway input.

Perception

Pain then ascends to the brain primarily through the spinothalamic tract. The cortex is the main center for nociceptive *perception*; however, there is a convoluted web in the human brain that couples pain to emotion, and neuroscience continues to discover new cerebral links. Medications that blunt the perception of pain are opioids (targeting central mu-opioid receptors), NMDA antagonists (decrease responsiveness to glutamate to deter central sensitization), and central alpha agonists.

In short, pain processing is comprised of transduction, transmission, modulation, and perception. Pharmacologic therapy to target each of these elements is summarized below.

Transduction: NSAIDs, antihistamines, membrane-stabilizing agents, local anesthetics, opioids, bradykinin antagonists, serotonin antagonists, capsaicin, and SNRIs

Transmission: Local anesthetics, gabapentin, pregabalin, carbamazepine, oxcarbazepine, lamotrigine, and topiramate

Modulation: Spinal opioids, alpha agonists, NMDA antagonists, anticholinesterases, NO inhibitors, CCK antagonists, SNRIs, SSRIs, TCAs, and Tylenol

Perception: Opioids, alpha agonists, and NMDA antagonists

Future research: Given the potential for abuse of opioid medication and the plethora of receptors involved in the pain pathway, there is significant potential for the development of new medications with novel mechanisms, particularly in the modulation stage of pain transmission.

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Short-Acting Opioids

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Jessica S. Hellums and Edgar L. Ross

Opioids

Opioids are used for the treatment of both acute and chronic pain with analgesia primarily obtained through μ-receptor activation. Morphine is the prototypical opioid in clinical use.

Mechanism of Action

Opioids bind to membrane-bound G-protein-coupled receptors. Different opioids have different affinities for the receptor subtypes (μ, δ, κ). Their analgesic effect is mediated by inhibition of nociceptive transmission from primary afferent neurons at the dorsal horn of the spinal cord and to activate central descending inhibitory pathways.

G_i receptor activation → ↓ adenylyl cyclase → ↓ cAMP → ↓ Ca^{2+} and ↓ K^+ conductance → neuronal hyperpolarization → decreased neuronal excitability

Sites of opioid receptors include the cortex, thalamus, hippocampus, amygdala, medulla, dorsal horn, and periaqueductal gray matter.

Receptor Classification

- μ1: supraspinal analgesia, euphoria (or dysphoria), miosis, and urinary retention
- μ2: spinal analgesia, respiratory depression, bradycardia, decreased GI motility, and dependence
- δ: analgesia, respiratory depression, urinary retention, and dependence
- κ: dysphoria, analgesia, miosis, sedation, and diuresis

Short-Acting Opioids

Endogenous: B-endorphin, dynorphin, and enkephalin

Exogenous Short-Acting Opioids

- IV: alfentanil, fentanyl, remifentanil, and sufentanil
- Oral: morphine IR, hydromorphone, oxycodone IR, hydrocodone, and codeine

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Table 36.1 Side effects

Common	Rare
Sedation	Seizures
Constipation	Muscle rigidity
Nausea	Dysphoria
Pruritus	
Respiratory depression	
Urinary retention	
Miosis	
Bradycardia (exception: meperidine)	
Hypotension	
Histamine release (morphine, meperidine, codeine)	
Hyperalgesia	
Smooth muscle spasm (biliary colic)	
Vasodilatation	
Decreased cellular immunity	

Short-Acting Opioid Antagonist

Naloxone IV or IM competitively binds μ, δ, and κ receptors reversing effects of endogenous and exogenous opioids.

Relative Properties

Hepatic Extraction Ratio

- Opioids can be classified as having low (<0.3), intermediate (0.3–0.7), or high (>0.7) hepatic extraction ratios. Drugs with high hepatic ERs metabolism is directly proportional to hepatic blood flow. Those with low hepatic ERs metabolism is largely dependent on the liver's intrinsic metabolism by the cytochrome P450 system. Intermediate extraction ratio drugs depend on a combination of both intrinsic hepatic metabolism and hepatic blood flow.
- Intermediate hepatic ER: alfentanil and codeine.
- High hepatic ER: sufentanil and fentanyl.

Potency

- Potency is directly proportional to receptor affinity.
- Alfentanil < fentanyl < remifentanil < sufentanil.
- Alfentanil is 5–10× less potent than fentanyl. Sufentanil is 5–10× more potent than fentanyl.
- Fentanyl and remifentanil are 100× more potent than morphine.

Lipid Solubility

- Fentanyl and sufentanil are highly lipophilic giving them fast entry and exit from the blood-brain barrier and rapid onset and offset.
- Sufentanil's onset is immediate and fentanyl's onset is 3–5 min after injection.

pKA

- Opioids are weak bases. At physiologic pH, the higher pKA opioids have a greater fraction of unionized drug capable of crossing the blood-brain barrier quickly and exiting quickly.
  - Alfentanil: 6.5
  - Remifentanil: 7.1
  - Sufentanil: 8
  - Fentanyl: 8.4
- Alfentanil and remifentanil have a rapid onset of action (1–2 min) despite lesser lipid solubility because of their low pKa.

Drug Interactions

- Metabolism of oxycodone, hydrocodone, and codeine by CYP2D6 is inhibited by SSRIs leading to higher plasma levels of these opioids.
- CYP3A4 inhibitors (grapefruit juice, midazolam, protease inhibitors, antifungal agents, macrolide antibiotics, cimetidine, omeprazole, valproic acid, diltiazem, isoniazid, and SSRIs) prolong the effects of fentanyl, alfentanil, and sufentanil.
- CYP3A4 inducers (barbiturates, St. John's wort, glucocorticoids, progesterone, carbamazepine, tamoxifen, rifampin) reduce effect time of fentanyl, alfentanil, and sufentanil.
- Volatile anesthetic MAC is reduced when opioids are administered concurrently.

Clinical

Clinical Indications

- Cough: Morphine IR, codeine, hydrocodone, and dextromethorphan are useful short-acting opioids that act at the cough center in the medulla providing antitussive effects.
- PCA: Fentanyl is commonly utilized for patient-controlled analgesia because of its rapid onset (5 min) and short duration of action (45 min).
- Short-acting IV opioids are useful for induction of anesthesia because of their rapid onset, ability to blunt airway reflexes, and cardiovascular stability.

Special Considerations

- Potency and clearance are decreased in the elderly necessitating dose reductions.
- Obese patients should be dosed for opioids based on lean body weight, not total body weight.
- Context-sensitive halftime is the time it takes for plasma concentration to decrease by 50 % after stopping a continuous infusion. After discontinuing fentanyl, alfentanil, and sufentanil, drug will continue to redistribute from peripheral compartments to plasma despite no longer administering the infusion. Remifentanil is unique in that it has a constant elimination halftime regardless of infusion duration.
- Remifentanil is metabolized by plasma and tissue esterases and is rapidly hydrolyzed to nonspecific esterases. Its clearance is unaffected by inhibiting acetylcholinesterase (neostigmine), hepatic dysfunction or renal insufficiency.
- Incomplete cross-tolerance requires dose decrements by 30–50 % when changing from one opioid to another. A patient can become tolerant to one opioid and when introduced to a new opioid at an equianalgesic dose exhibit sensitivity which could result in respiratory depression.
- Oxycodone has an increased half-life in uremic patients, and women clear oxycodone 25 % slower than men.

Clinical Pearls

- Despite continued opioid use, tolerance does not develop to constipation or miosis.
- Respiratory depression is dose dependent. Tolerance develops to respiratory depression with continued opioid use. Other respiratory depressant drugs, like benzodiazepines, enhance opioid-induced respiratory depression.
- Intrathecal opioids are more likely to cause pruritus than intravenous opioids.
- Codeine is converted to morphine by CYP2D6 in the liver. Genetic polymorphisms of this enzyme can prevent this conversion, and patients will have no analgesia with codeine administration.
- High-fat meals increase the bioavailability of oxycodone and oxymorphone but delay their absorption.
- Opioid-induced hyperalgesia is the paradoxical hypersensitivity to nociceptive stimuli after exposure to opioids.
- Abrupt reversal of opioids with naloxone can result in sympathetic stimulation, acute pain, and withdrawal symptoms in opioid-dependent patients.

Literature Review

A systematic review of 157 articles on opioid-induced hyperalgesia implies it is both dose and duration dependent of the potent opioid used. It is also partially NMDA dependent and can be blunted by preadministration of ketamine, an NMDA antagonist. Once established, opioid antagonists do not reverse hyperalgesia.

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Long-Acting Opioids

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Jessica S. Hellums and Edgar L. Ross

Long-Acting Opioids

Long-acting opioids, like morphine, have a prolonged duration of action compared to fentanyl. This is not because of greater receptor affinity, but because of lesser lipid solubility and prolonged duration at receptor sites.

IV: morphine, hydromorphone, methadone, meperidine, oxymorphone

Oral: methadone, morphine sustained release (*MS Contin, Oramorph, Kapalon, MXL*), oxycodone sustained release (*OxyContin*)

Long-acting opioid antagonist: Naltrexone PO is used as maintenance therapy for opioid and alcohol abuse.

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Relative Properties

Hepatic Extraction Ratio

- High extraction ratio opioids have poor oral bioavailability secondary to high hepatic first pass metabolism through the P450 system prior to reaching the systemic circulation.
- Low hepatic ER: methadone.
- Intermediate hepatic ER: hydromorphone.
- High hepatic ER: morphine, meperidine.
- Morphine PO is significantly less bioavailable than IV or neuraxial secondary to its high first pass hepatic metabolism.

Potency

- Meperidine is 10× less potent than morphine.
- Hydromorphone is 5× more potent than morphine.
- Oxymorphone 10× more potent than morphine.

Lipid Solubility

Least → greatest

Morphine → hydromorphone → meperidine → methadone

Methadone's high lipid solubility gives it a long elimination half-life and great interpatient variability.

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pKA

- Morphine: 8
- Methadone: 8.25
- Meperidine: 8.7
- Hydromorphone: 8.9

Side effects: (see common and rare opioid side effects in Chap. 36, Short-acting opioids)

- Histamine release: Morphine, meperidine, and codeine cause histamine release that can result in flushing, urticaria, and pruritus.
- Meperidine:
  Seizures from accumulation of normeperidine, an active metabolite that causes CNS excitation
  Tachycardia secondary to structural similarity to atropine.
  Dysphoria or euphoria.

Drug Interactions

- Meperidine and MAOIs both inhibit reuptake of serotonin. This can lead to serotonin syndrome causing hyperthermia, blood pressure lability, muscle rigidity, seizures, coma, and potentially death.
- Methadone is highly protein bound to alpha-1-acid glycoprotein and can be displaced by other medications including propranolol, chlorpromazine, prochlorperazine, thioridazine, and TCAs leading to higher plasma methadone levels.

Clinical

Clinical Indications

- Chronic pain: Common regimens include oral methadone every 12 h, sustained-release oral morphine or sustained-release oral oxycodone dosed every 12 h or every 24 h depending on the formulation.
- Acute pain: Morphine and hydromorphone are commonly used IV for acute pain. They are also common medications used with patient-controlled analgesia.
- Shivering: Meperidine can be used for postoperative shivering.
- Diarrhea: Loperamide PO can be used to treat diarrhea.
- Acute coronary syndrome: Morphine causes decreased preload, bradycardia, and decreased afterload. In acute myocardial infarction, it decreases myocardial oxygen consumption and chest pain.

Special Considerations

- Renal insufficiency: Hydromorphone has no active metabolites and is the preferred long-acting opioid in patients with renal disease. Morphine's metabolite M6G is excreted by the kidneys and has a high affinity for μ receptors. In renal insufficiency, M6G can accumulate causing respiratory depression. Meperidine's active metabolites can also accumulate in renal insufficiency.
- Severe liver disease places patients at a higher risk of opioid-induced sedation.

Clinical Pearls

- Morphine metabolites, morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G), are capable of crossing the blood-brain barrier. M6G crosses the BBB less than morphine, but M6G has greater analgesic and respiratory depressing effects at opioid receptors than morphine. M3G has a low affinity at μ receptors and actually antagonizes morphine and M6G-induced analgesia and respiratory depression.
- Pruritus: Histamine-induced pruritus from morphine, codeine, and meperidine is not reversible with naloxone. Pruritus from activation of opioid receptors, commonly from neuraxial opioid, is reversible by naloxone.
- Intrathecal morphine causes delayed respiratory depression 12–18 h after administration from rostral spread.
- IV/PO conversions:
  Methadone 1:2
  Morphine 1:3
  Hydromorphone 1:5

Literature Review

Opioids impair immune function and morphine may have a pro-angiogenic effect promoting tumor growth. This raises concern for the use of opioids in oncologic surgery. A Cochrane review of four trials (either RCT or CCT) involving 746 patients undergoing primary tumor resection (abdominal, prostate, or colon) followed for 9–17 years compared general anesthesia versus general plus epidural anesthesia (EA). They examined overall survival, progression-free survival, and time to tumor progression and found no significant benefit of EA over general anesthesia alone. More RCTs are ongoing and necessary because of the current paucity of prospective data.

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Methadone

38

Robert M. Chow and Mohammed Issa

Methadone is commonly used for treatment of chronic pain and opioid addiction (only by specially licensed facilities). Its unique pharmacokinetic and pharmacodynamic properties (half-life of 24–60 h), high oral bioavailability (40–99 %), absence of active metabolites, and its relatively low cost make it an attractive alternative to other opioids in special circumstances.

Mechanism of Action

Methadone is primarily an agonist at the μ- and δ-opioid receptors. Uniquely, methadone is also an NMDA antagonist and a reuptake inhibitor of both serotonin and norepinephrine.

Example:

Generic	Brand name	Starting dose
Methadone	Dolophine	2.5–5 mg TID

Side effects:

Common	Rare
Sedation	Arrhythmia
Nausea	Hallucination
Dizziness	Itching
Sweating	Seizures
Constipation	Glossitis

Drug Interactions

The cytochrome P450 enzymes, particularly 2D6 and 3A4 subtypes, are responsible for the metabolism of methadone in the liver. As such, medications that alter the activity of the CYP450 enzymes can alter the metabolism and elimination of methadone.

Clinical

Clinical Indications

Chronic pain and opioid addiction

Initiation

In opioid naïve patients, the recommended starting dose is 2.5 mg every 8–12 h. Dose can be increased by 2.5–5 mg increments every 5–7

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days. For opioid-tolerant patients, an appropriate methadone-to-morphine conversion ratio ranges from 1:5 to 1:20. It is not recommended to start beyond 30 mg of methadone per day in any patient.

Weaning

Abrupt discontinuation can lead to significant opioid withdrawal symptoms. Methadone should be gradually weaned over weeks by slowly decreasing the dose every 2–4 days.

Special Considerations

- If QTc > 450 ms, discuss risks of treatment with patient.
- If QTc > 500 ms, consider alternative therapy.

Clinical Pearls

- Methadone has become the most common opioid related to unintentional deaths in the USA. Thus, it should be used with extreme caution.
- Quick up-titration of methadone dose (< every 5 days) can be fatal due to its cumulative effects.
- For opioid addiction, methadone is dosed only once daily to prevent withdrawals, but its analgesic half-life is only 6–8 h.
- Other medications that prolong QT interval, such as TCAs, should be used with caution when co-administered with methadone.
- An EKG should be done prior to starting methadone and repeated annually or sooner if the dose exceeds 100 mg/day due to concerns for QT prolongation.
- Methadone, unlike other LAOs, is intrinsically long-acting and is therefore beneficial in patients with impaired GI absorption.

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Buprenorphine

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Robert M. Chow and Mohammed Issa

Sublingual (S/L) buprenorphine is FDA approved only for treatment of opioid addiction (opioid detoxification and maintenance). Buprenorphine in patch form is approved only for analgesia. However, buprenorphine is present at a significantly lower dose in the patch form as compared to the S/L forms.

Mechanism of Action

Buprenorphine acts as a partial agonist at the μ-opioid receptor with unusually high affinity. It has weak partial antagonist effect on the κ-opioid receptor (has antidepressant effects). It has a ceiling effect on respiration and CNS depression, which provides a considerable margin of safety in a high-risk population.

Example:

Generic	Brand name	Starting dose
Buprenorphine patch	Butrans	5 μg/h
Buprenorphine/naloxone	Suboxone	4–8/1–2 mg

Sublingual

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Side effects:

Common	Rare
Sedation	Weight gain
Headache	Hepatotoxicity
Constipation	Oral hypoesthesia (film)
Nausea	Glossodynia (film)

Drug Interactions

Buprenorphine is metabolized by CYP450 3A4. Thus, one can see fluctuations in blood levels of buprenorphine if there is concomitant administration of medications that either induce or inhibit the CYP450 3A4 enzyme such as several anticonvulsants and protease inhibitors.

Clinical

Clinical Indications

Treatment of chronic pain and opioid addiction

Initiation

S/L buprenorphine (for treatment of addiction) should be initiated only when the patient is in mild-moderate withdrawals (W/Ds) to prevent

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precipitated W/Ds. The typical starting dose for S/L buprenorphine is 4 mg, titrating up every 1/2 h by 2–4 mg increments until W/D symptoms improve. The dose can be increased every week by 4–8 mg increments to stop cravings and/or improve pain until a maximum daily dose of 32 mg (however, not recommended beyond 24 mg/day).

Butrans should be started at 5 μg/h in the opioid naïve patient and titrated up by 5 μg every week to a maximum dose of 20 μg/h (possible QT prolongation with doses >20 μg/h). If the patient is opioid-tolerant with an oral morphine equivalent of 30–80 mg/day, the starting patch dose is 10 μg/h.

Weaning

Abrupt discontinuation can lead to opioid withdrawal symptoms; however, the withdrawal symptoms are usually milder when compared to full agonist opioids.

Special Considerations

- Buprenorphine may precipitate withdrawal symptoms in patients currently on opioid therapy.

Clinical Pearls

- A special physician waiver is needed to prescribe Suboxone (X-number).
- S/L buprenorphine can be used to treat both addiction and pain in high-risk patients.
- Liver function tests should be obtained prior to and during treatment with Suboxone.
- If patients maintained on Suboxone develop acute pain, four options are available to treat their pain:
  - Divide buprenorphine dose to Q6H.
  - Increase buprenorphine dose.
  - Stop buprenorphine and start full opioid agonist.
  - Continue buprenorphine and add full opioid agonist (this can cover remaining 5–15% of opioid receptors, providing notable analgesia).
- In options 3 and 4 (above), naloxone should be available at bedside since patient can easily develop respiratory/CNS depression.

Suggested Reading

1. Stahl SM. Buprenorphine. In: Stahl's essential psychopharmacology. New York, NY: Cambridge University Press; 2014. p. 87–90.

Nonsteroidal Anti-Inflammatory Medications

40

David J. Kim and Srdjan S. Nedeljkovic

Nonsteroidal Anti-Inflammatory Medications

Nonsteroidal anti-inflammatory drugs (NSAIDs) have analgesic, antipyretic, and anti-inflammatory effects.

Mechanism of Action

NSAIDs inhibit cyclooxygenase (COX) enzymes to decrease the production of inflammatory mediators (e.g., prostaglandins). The inhibition of COX-2 leads to its analgesic, antipyretic, and anti-inflammatory effects. The inhibition of COX-1 may result in gastrointestinal (GI) bleeding and ulcers.

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Examples of nonselective COX inhibitors:

Generic	Brand name	Starting dose (mg)
Ibuprofen	Advil	200–400
Naproxen	Aleve	250
Diclofenac	Voltaren	25
Acetylsalicylic acid	Aspirin	325–650

Examples of selective COX-2 inhibitors:

Generic	Brand name	Starting dose
Celecoxib	Celebrex	200 mg

Side effects:

Common	Rare
Dizziness	Acute renal failure
Rash	GI bleed
Heartburn	Platelet dysfunction
Tinnitus	Fluid retention
	Increased risk of MI, CVA

Drug Interactions

Caution should be exercised using high doses when combined with ACE inhibitors, loop diuretics, lithium, methotrexate, and SSRIs. NSAIDs are highly protein-bound and can displace other highly protein-bound drugs (e.g., warfarin), which may lead to supratherapeutic levels of these other drugs.

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Clinical

Clinical Indications

Mild to moderate pain, particularly musculoskeletal, headache, osteoarthritis, muscle sprains/strains, cancer-related pain, inflammatory disease, and fever.

Initiation (Using Ibuprofen as an Example)

Typical starting dose is 200–400 mg every 6–8 h. Max daily dose 3200 mg. Approximately 2 weeks are required for an adequate trial.

Weaning

No need to wean. Try to use lowest effective dose for shortest duration.

Special Considerations

- Reduce dose in hepatic or renal impairment.
- Can exacerbate bronchospasm in patients presenting with asthma, rhinitis, and nasal polyps.

Clinical Pearls

Analgesia from NSAIDs has a ceiling effect. Selective COX-2 inhibitors may have lower risk of GI bleeding vs. nonselective COX inhibitors. Consider switching NSAID classes if one class of NSAID does not provide sufficient analgesia after an adequate trial (e.g., salicylate vs. proprionic vs. indole classes). If analgesia is effective with a specific NSAID but has intolerable side effects, consider switching to NSAID from the same class first.

Literature Review

A meta-analysis of 754 trials showed that the risk of major vascular events (nonfatal MI, nonfatal stroke, vascular death) is increased with the use of diclofenac, coxibs, and possibly ibuprofen, but not by naproxen. Heart failure risk and GI complications were increased by the use of all of these NSAIDs.

Suggested Reading

1. Coxib and traditional NSAID Trialists' (CNT) Collaboration. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. Lancet. 2013;382(9894):769–79.

Acetaminophen

41

David J. Kim and Srdjan S. Nedeljkovic

Acetaminophen

Acetaminophen is used in the treatment of mild to moderate pain. It is an analgesic and antipyretic but with minimal anti-inflammatory effects.

Mechanism of Action

Unknown mechanism. Initially considered to be a nonspecific cyclooxygenase (COX) enzyme inhibitor leading to decreased production of prostaglandins. Other studies suggest it may inhibit COX-3 and have serotonergic properties.

Examples:

Generic	Brand name	Starting dose
Acetaminophen	Tylenol	325–1000 mg

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Side effects:

Common	Rare
Nausea	Hepatotoxicity
Vomiting	Severe skin reactions (e.g., Stevens-Johnson syndrome)
Abdominal pain	
Constipation	
Headache	
Atelectasis	
Pruritus	

Drug Interactions

Caution should be exercised when using high doses and when combined with barbiturates, isoniazid, phenytoin, carbamazepine, zidovudine, warfarin, and NSAIDs.

Clinical

Clinical Indications

Mild to moderate pain, osteoarthritis, headache, cancer pain, fever.

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Initiation

Typical starting dose is 325–1000 mg every 4–6 h. Recently, manufacturers have suggested limiting maximum daily dose to 3000 mg/day, particularly with "extra strength" formulations. However, current FDA guidelines are 4000 mg/day for the adult daily maximum dose. Recent FDA recommendations state that combination drug products should not contain more than 325 mg of acetaminophen per dosage.

Weaning

No need to wean.

Special Considerations

- Use with caution in patients with alcoholism, preexisting liver dysfunction, G6PD deficiency.
- Risk of analgesic nephropathy in long-term use when combined with NSAIDs.

Clinical Pearls

Analgesia from acetaminophen has a ceiling effect. It is the most common drug-related cause of acute liver failure. It appears to have a better side effect profile vs. NSAIDs (i.e., acetaminophen has minimal GI bleeding and platelet dysfunction). While used commonly for mild to moderate pain, it can be used as an adjunct to opioids for severe pain. In the perioperative period, acetaminophen has an opioid-sparing effect.

Literature Review

A US multicenter, prospective study of 662 patients with acute liver failure showed 275 cases (42 %) were due to acetaminophen liver injury. Of these 275, 38 % took ≥2 acetaminophen preparations simultaneously and 63 % used narcotic-containing compounds. In this cohort, almost half of the overdoses (48 %) were unintentional, while 44 % were intentional (suicide attempts).

Suggested Readings

1. Chandrasekharan NV, Dai H, Roos KLT, et al. COX-3, a cyclooxygenase-1 variant inhibited by acetaminophen and other analgesic/antipyretic drugs: cloning, structure, and expression. Proc Natl Acad Sci USA. 2002;99:13926–31.
2. Larson AM, et al. Acetaminophen-induced acute liver failure: results of a United States multicenter, prospective study. Hepatology. 2005;42(6):1364–72.

Tricyclic Antidepressants

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R. Jason Yong and Mohammed Issa

Tricyclic Antidepressants

Tricyclic antidepressants (TCAs) are used in low doses to treat chronic pain conditions and in high doses to treat mood disorders such as depression. TCAs may also be used as migraine and chronic tension headache prophylaxis.

Mechanism of Action

Tricyclics primary work as serotonin-norepinephrine reuptake inhibitors (SNRIs) by blocking serotonin and norepinephrine transporters. TCAs do not block dopamine reuptake.

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Examples:

Generic	Brand name	Starting dose
Amitriptyline	Elavil	10–25 mg
Desipramine	Norpramin	10 mg
Nortriptyline	Pamelor	25 mg

Side effects:

Common	Rare
Dry mouth	Disorientation
Blurred vision	Tremor
Constipation	Arrhythmia
Urinary retention	Seizures
Drowsiness	
Orthostasis	
Weight gain	

Drug Interactions

Caution with high doses and when combined with other serotonergic agents such as SNRIs, SSRIs, MAOIs, lithium, triptans, St. John's wort, and illicit substances.

Clinical

Clinical Indications

Neuropathic pain, fibromyalgia, generalized pain with comorbid depression/anxiety.

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Initiation (Using Amitriptyline as an Example)

Typical starting dose is 10–25 mg at bedtime. Every 2 weeks, the dose can be increased by 10–25 mg with a usual maximum dose of 150 mg. Approximately 6–8 weeks are required for an adequate trial.

Weaning

Abrupt discontinuation can lead to withdrawal symptoms such as anxiety, insomnia, headaches, nausea, and motor disturbances. TCAs should be gradually weaned over weeks to months.

Special Considerations

- Avoid in elderly secondary to exacerbation of cognitive impairment and increased falls.
- Most TCAs are also beneficial for insomnia.

Clinical Pearls

In general practice, TCAs are a second-line treatment after neuroleptics such as gabapentin/pregabalin for neuropathic pain. Nortriptyline has a better side-effect profile than amitriptyline and has equal efficacy. If patients can tolerate the TCAs, I will increase to maximum effective dose before considering lack of effect a failure. If limited by side effects, I will consider splitting doses. Nortriptyline has been found to be the most weight neutral when comparing antidepressants for pain.

Literature Review

A Cochrane review of 13 placebo-controlled trials showed TCAs were significantly more efficacious than placebo for neuropathic pain conditions. Additionally, studies comparing one TCA to another showed no difference among the TCAs.

Suggested Reading

Saarto T, Wiffen PJ. Antidepressants for neuropathic pain. Cochrane Database Syst Rev. 2007;4:CD005454.

Selective Serotonin Reuptake Inhibitors

43

Robert M. Chow and Mohammed Issa

Selective serotonin reuptake inhibitors (SSRIs) are used primarily for treatment of depression and anxiety. Their effectiveness in pain management is limited and inconsistent.

Mechanism of Action

The mechanism of SSRIs is self-explanatory as they work to block serotonin reuptake, effectively increasing the amount of serotonin at the neural synapses, which in turn increases cell signaling.

Examples:

Generic	Brand name	Starting dose
Paroxetine	Paxil	10 mg
Fluvoxamine	Luvox	50 mg
Fluoxetine	Prozac	20 mg

Side effects:

Common	Rare
Drowsiness	Agranulocytosis
Insomnia	Angina
Headache	Glaucoma
Decreased libido	Angioedema
Dizziness	Tinnitus
Nausea	Dysmenorrhea
Weakness	

Drug Interactions

Caution should be used when combined with other serotonergic agents such as SNRIs, TCAs, MAOIs, lithium, triptans, St. John's wort, yohimbe, and MDMA. NSAIDs should also be used with caution as their antiplatelet effects are enhanced by SSRIs. NSAIDs also reduce the efficacy of SSRIs. Caution should be utilized with medications that are metabolized by CYP450 2D6 as the enzyme is inhibited by SSRIs.

Clinical

Clinical Indications

Depression, anxiety, neuropathic pain, and fibromyalgia (limited efficacy)

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Initiation (Using Paroxetine as an Example)

Typical starting dose is 10 mg a day. Reassess in 2 weeks. Afterward, the dose can be increased by 10 mg/day every 2–4 weeks up to a maximum dose of 60 mg/day.

Weaning

A simple regimen to follow is to reduce the dose by 50 % for 3 days, followed by another 50 % reduction for 3 days, and finally stopped. If any withdrawal symptoms occur, the medication can be titrated back up and then weaned even slower.

Special Considerations

- Although TCAs in general have better analgesic qualities compared to SSRIs, they have a more problematic side-effect profile especially in elderly patients.

Clinical Pearls

- Escitalopram (Lexapro), although widely prescribed as an antidepressant, has failed to show any analgesic effect.
- The antinociceptive effects of paroxetine were found to be inhibited by naloxone, indicating either direct or indirect action at the opioid receptors.
- Use of SSRIs vs. SNRIs in patients with comorbid depression/anxiety and pain depends on whether such psychiatric symptoms prevail (in which case SSRIs are preferred) or if pain symptoms are the primary complaint (SNRIs should be tried first in this case).
- Analgesic effects of SSRIs are somewhat better with higher doses, especially in fibromyalgia, possibly due to inhibition of norepinephrine reuptake at such doses.

Suggested Reading

1. Smith AJ. The analgesic effects of selective serotonin reuptake inhibitors. J Psychopharmacol. 1998;12(4): 407–13.
2. Duman EN, et al. Possible involvement of opioidergic and serotonergic mechanisms in antinociceptive effect of paroxetine in acute pain. J Pharmacol Sci. 2004; 91(2):161–5.
3. Benzon H, et al. Antidepressants as analgesics. In: Practical management of pain. Maryland Heights, MO: Mosby; 2013. p. 530–42.

Serotonin-Norepinephrine Reuptake Inhibitors

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Robert M. Chow and Mohammed Issa

Serotonin-norepinephrine reuptake inhibitors (SNRIs) are used to treat chronic pain conditions as neuropathy and fibromyalgia and mood disorders such as depression and anxiety. They generally have a more favorable side-effect profile than TCAs.

Mechanism of Action

SNRIs work by blocking serotonin and norepinephrine transporters, thus increasing the presence of serotonin and norepinephrine at neural synapses. Different SNRIs have differing affinities for 5-HT (serotonin) and NE (norepinephrine) systems, with resultant variable efficacy in chronic pain conditions.

- Venlafaxine 30:1 (5-HT/NE)
- Desvenlafaxine 14:1
- Duloxetine 5–10:1
- Milnacipran 1:1

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Examples:

Generic	Brand name	Starting dose
Duloxetine	Cymbalta	30 mg
Venlafaxine	Effexor	37.5–75 mg

Side effects:

Common	Rare
Headache	SIADH
Nausea	Abnormal healing
Weakness	Alopecia
Weight loss	Dyslipidemia
Insomnia	Seizure
Xerostomia	Impotence

Drug Interactions

As serotonin syndrome is a potential risk, caution should be exercised when utilizing high doses and when combining with other serotonergic agents such as SSRIs, TCAs, MAOIs, lithium, triptans, St. John's wort, and illicit substances.

Clinical

Clinical Indications

Painful diabetic neuropathy (PDN), fibromyalgia (FM), polyneuropathy, musculoskeletal pain, osteoarthritis, depression, and anxiety

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Initiation (Using Duloxetine as an Example)

The typical starting dose is 30 mg daily for 1 week and then increased to 60 mg daily if tolerated.

Weaning

Abrupt discontinuation can precipitate serotonin withdrawal symptoms such as anxiety, nausea, and motor disturbances; this is most notably seen with venlafaxine. Although there is paucity for the ideal rate, SNRIs should be gradually tapered over several weeks.

Special Considerations

- Venlafaxine should be used with caution in patients with a history of cardiac disease.
- Patients with untreated angle-closure glaucoma should not be started on SNRIs.
- Duloxetine is preferably avoided in patients with hepatic insufficiency.

Clinical Pearls

- Cymbalta is more effective than venlafaxine for peripheral neuropathies.
- Higher doses of Cymbalta (>60 mg QD) have similar efficacy to lower doses but greater side effects.
- Nausea is the most common side effect encountered with SNRIs. It usually resolves with continued use.
- For venlafaxine, pain relief occurs with doses >150 mg QD.
- Milnacipran is eliminated primarily by renal excretion.

Literature Review

A Cochrane review of 18 trials showed duloxetine was significantly more efficacious than placebo for PDN, FM, and painful physical symptoms of depression.

Suggested Reading

1. Lunn MPT, et al. Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia. Cochrane Database Syst Rev. 2014;1:CD007115.

Atypical Antipsychotics

45

Sean J. Nabar and Ehren Nelson

Atypical Antipsychotics

Antipsychotics (also called neuroleptics) have an established role in the treatment and management of acute and chronic psychotic disorders. The role of antipsychotics in chronic pain is less defined; however, there is increasing literature supporting their utility.

Atypical antipsychotics, also known as second-generation antipsychotics, generally have a lower risk of extrapyramidal side effects (EPS) compared with first-generation antipsychotics.

Mechanism of Action

The mechanism by which antipsychotics work to relieve pain is still under debate and may differ between agents. In addition to dopamine D2 antagonism (the predominant target of first-generation antipsychotics), atypical antipsychotics address other neurotransmitter systems.

Antidopaminergic properties of most antipsychotics may mediate analgesic effects for some pain syndromes (i.e., migraines). Serotonin antagonism of some antipsychotic agents is also believed to mediate analgesic effects. Olanzapine has been shown to have agonistic activity at alpha2-adrenoreceptors. In animal models, risperidone has been shown to have potent antinociceptive effects with involvement of μ1-, μ2-, and kappa1-opioid and, to a lesser extent, delta-opioid mechanisms.

Side Effects

Atypical antipsychotics are generally considered far safer than first-generation antipsychotics; however, side effects may include:

Common	Rare/severe
Weight gain	Agranulocytosis (clozapine)
Sedation	Extrapyramidal side effects
QT prolongation	Tardive dyskinesia
Anticholinergic effect	Neuroleptic malignant syndrome (NMS)
Seizures	

Examples:

Generic	Brand name	Starting dose (mg)
Olanzapine	Zyprexa	5–10
Risperidone	Risperdal	2–3
Quetiapine	Seroquel	50
Ziprasidone	Geodon	20

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Clinical

Atypical antipsychotics are usually second or third line in the treatment of chronic pain conditions (headaches, fibromyalgia, low back pain, diabetic neuropathy, etc.) after neuropathic pain medications (gabapentin/pregabalin) and tricyclic antidepressants. For chronic pain patients, atypical antipsychotics are most useful for treating psychiatric comorbidities such as anxiety, depression, mood disorders, or insomnia.

Special Considerations

- Avoid (especially ziprasidone) in patients with history of arrhythmias or taking other QT prolongers.
- Side effects of certain medications can be used as secondary outcomes (olanzapine—weight gain; quetiapine—sedation).

Literature Review

A Cochrane review [1] of five randomized double-blind studies showed beneficial effects of antipsychotics (first and second generation) in the treatment of acute and chronic pain. The authors concluded that results for antipsychotics in the treatment of different painful conditions are mixed, and most sample sizes in the reviewed RCTs are small. Further studies on atypical antipsychotics in larger double-blind placebo-controlled studies that include standardized pain assessment and documentation are warranted.

Suggested Reading

1. Seidel S, Aigner M, et al. Antipsychotics for acute and chronic pain. Cochrane Database Syst Rev. 2013;8:CD004844.

Benzodiazepines

46

David J. Kim and Srdjan S. Nedeljkovic

Benzodiazepines

Benzodiazepines are typically used to treat anxiety, and it is best to leave their prescribing to psychiatrists. They are rarely indicated to treat pain.

Mechanism of Action

Benzodiazepines work via $GABA_A$ activation, which enhances GABA-mediated chloride currents and leads to neuronal hyperpolarization and decreased excitability (Tables 46.1 and 46.2).

Drug Interactions

Caution should be exercised in using high doses and when combined with opioids, which could lead to fatal outcomes. Current guidelines from the Centers for Disease Control (CDC) advise against any coadministration of benzodiazepines and opioids. Benzodiazepines also interact with phenytoin, barbiturates, St. John's wort, amitriptyline, erythromycin, digoxin, and grapefruit juice.

Clinical

Clinical Indications

There are no clinical indications for using benzodiazepines for chronic pain, including neuropathic pain or muscle spasms.

Treatment of Anxiety (by psychiatrists)

Clonazepam: typical dose is 0.5 mg at bedtime. Can titrate up to 4 mg daily.

Diazepam: typical dose is 2–5 mg given 3–4 times per day. Can titrate up to 10 mg per dose.

Lorazepam: typical dose is 2–3 mg per day divided into 2–3 daily doses (e.g., 0.5–1 mg per dose). All of these drugs can lead to rapid habituation and to the development of tolerance.

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Table 46.1 Examples

Generic	Brand name	Starting dose (mg)
Clonazepam	Klonopin	0.5
Diazepam	Valium	2–5
Lorazepam	Ativan	0.5

Table 46.2 Side effects

Common	Rare
Sedation	Neutropenia
Somnolence	Delirium
Ataxia	Depression
Hypotension	
Respiratory depression	

Weaning

Abrupt discontinuation can lead to a withdrawal syndrome that can be life threatening. Symptoms can include anxiety, restlessness, tremor, diaphoresis, delirium, insomnia, psychosis, seizures, and death. Therefore, benzodiazepines should be tapered gradually (e.g., a 25 % dose reduction every 1–2 weeks until completely tapered). The schedule for tapering should be adjusted as necessary based on patient response. The use of benzodiazepines for pain is not recommended due to lack of analgesic efficacy as well as the development of tolerance and habituation.

Special Considerations

- Typically prescribed by psychiatrists for anxiety disorders.
- Avoid alcohol.
- Caution in elderly and patients with renal, hepatic, and pulmonary disease.
- Contraindicated in acute narrow-angle glaucoma.
- Pregnancy category D.
- Using benzodiazepines and opioids together has been associated with a greater risk of overdose and fatality.

Clinical Pearls

- Benzodiazepines are not recommended for the use for chronic pain as they have no primary analgesic effect.
- Diazepam has active metabolites that can accumulate especially in renal disease.
- Diazepam also has decreased clearance with increasing age.
- Lorazepam metabolism and excretion is not affected by renal disease or age.
- Flumazenil is a competitive antagonist at the benzodiazepine receptor for the treatment of benzodiazepine overdose. Doses of 0.2–0.5 mg IV up to 3 mg can be given.

Literature Review

There is a lack of evidence to support the use of benzodiazepines in terms of their efficacy for the management of pain. Central nervous system adverse effects such as sedation and dizziness are significant. Muscle relaxants must be used with caution. The risks of dependence, withdrawal, and tolerance are high.

Suggested Reading

1. Paquin AM, Zimmerman K, Rudolph JL. Risk versus risk: a review of benzodiazepine reduction in older adults. Expert Opin Drug Saf. 2014;13(7):919–34.
2. Donoghue J, Lader M. Usage of benzodiazepines: a review. Int J Psychiatry Clin Pract. 2010;14(2):78–87.
3. Kim PM, Weinstein SL. Johns Hopkins Psychiatry Guide: Benzodiazepines. Website: http://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_Psychiatry_Guide/787140/all/Benzodiazepines. May 8, 2015. Accessed Oct 2016.

Anticonvulsants

47

Robert M. Chow and Mohammed Issa

Anticonvulsants

Anticonvulsants were initially developed to treat seizure disorders; however, they have been used with reasonable efficacy to treat neuropathic pain and in some cases fibromyalgia.

Mechanism of Action

Anticonvulsants are a diverse group of medications that have various mechanisms of action. Carbamazepine (C) exerts its actions by stabilizing inactivated voltage-gated sodium channels as well as by acting as a GABA receptor agonist. Gabapentin (G) and pregabalin (P) on the other hand works by reducing the activity through voltage-gated calcium channels. Topiramate (T) is thought to act on voltage-gated sodium and voltage-gated calcium channels as well as at GABA-A receptors.

Examples:

Generic	Brand name	Starting dose
Carbamazepine	Tegretol	50–100 mg BID
Gabapentin	Neurontin	100–300 mg TID
Pregabalin	Lyrica	75 mg BID
Topiramate	Topamax	25 mg daily

Side effects:

Common	Rare
Dizziness	Bone marrow suppression (C, T)
Drowsiness	Suicidal thoughts (C, P, T)
Headache	Stevens-Johnson syndrome (C, T)
Nausea	Loss of libido (G, P)
Vomiting	Rhabdomyolysis (P)
Ataxia	

Drug Interactions

Carbamazepine is a CYP 450 inducer, which decreases the level of many drugs, most notably warfarin. Carbamazepine can also decrease the efficacy of oral contraceptives. Topamax has weak action on the CYP 450 enzymes.

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Clinical

Clinical Indications

Neuropathic pain, fibromyalgia

Initiation: Using Gabapentin as an Example

Typical starting dose is 300 mg at bedtime. After the first week, the dose can be increased to 300 mg BID, and after the second week, the dose can be increased to 300 mg TID.

Weaning

Abrupt discontinuation can lead to withdrawal symptoms such as seizure, irritability, anxiety, confusion, and tachycardia. Anticonvulsants should be weaned appropriately over the course of weeks.

Special Considerations

- Topiramate is a sulfamate-substituted monosaccharide and should be avoided in patients with sulfa allergies.
- Gabapentin doses should be adjusted for renal failure.

Clinical Pearls

- Gabapentin and pregabalin should be started at doses one third of typical in renal failure patients and titrated up more slowly.
- With gabapentin and pregabalin, moving daytime doses to the nighttime dose can help with sleep and prevent daytime somnolence.
- Long-acting formulations of gabapentin (Gralise or Horizant) can be a reliable alternative if daytime somnolence or TID dosing affects compliance.

Suggested Reading

Tremont-Lukats IW, et al. Anticonvulsants for neuropathic pain syndromes. Drugs. 2000;60(5):1029–52.

Muscle Relaxants

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Robert M. Chow and Mohammed Issa

Muscle Relaxants

Muscle relaxants are comprised of a group of heterogeneous medications that work through various mechanisms to act as antispasmodics.

Mechanism of Action

As previously stated, muscle relaxants have varied mechanisms of action. Cyclobenzaprine (C), though heavily studied in terms of its use for muscle spasms, does not have a clear mechanism of action. In addition, metaxalone (M) also has not had its mechanism of action elucidated. Tizanidine (T) is an α2 adrenergic agonist, and baclofen (B) is a $GABA_B$ receptor agonist.

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Examples

Generic	Brand name	Dose
Cyclobenzaprine	Flexeril	5 mg TID
Metaxalone	Skelaxin	800 mg TID
Tizanidine	Zanaflex	2 mg daily
Baclofen	Gablofen	5 mg TID

Side effects:

Common	Rare
Dizziness (C,M,T)	Hepatotoxicity (T)
Drowsiness (B,C,M,T)	NMS (C)
Tachycardia (C)	Arrhythmia (C)
Weakness (B,T)	Seizures (C,M)
Hypotension (T)	Impotence (B)
Xerostomia (T)	Angioneurotic edema (M)

Drug Interactions

Cyclobenzaprine has TCA-like qualities and antagonizes serotonin, histamine and muscarinic receptors. Therefore, cyclobenzaprine should be used with caution with other CNS depressants as well as with TCAs. In addition cyclobenzaprine should not be taken concomitantly with MAOIs or serotonergic drugs. Metaxalone is metabolized by the CYP 450 system, and caution is advised

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when co-administering medications for liver metabolism.

Clinical

Clinical Indications

Spasticity, musculoskeletal conditions

Initiation: Using Cyclobenzaprine

Typical starting dose is 5 mg TID. Muscle relaxants are recommended only for short-term therapy when treating musculoskeletal conditions.

Weaning

When using cyclobenzaprine 5 mg TID, no weaning is needed.

Special Considerations

- Baclofen should be avoided or reduced in renal failure patients, and with ESRD, baclofen-induced encephalopathies have been reported.
- Tizanidine is potentially hepatotoxic and should be used cautiously in patients with impaired hepatic function.

Clinical Pearls

- Cyclobenzaprine 5 mg TID is as effective as cyclobenzaprine 10 mg TID, but with fewer side effects.
- Baclofen should not be abruptly discontinued as this can lead to baclofen withdrawal.
- Tizanidine can be used to decrease withdrawal symptoms from patients weaning off opioids.

Suggested Reading

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Local Anesthetics

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Robert M. Chow and Mohammed Issa

Local Anesthetics

Local anesthetics can be used in various formulations for the treatment of pain. They are commonly used to anesthetize the skin prior to interventional therapy and are often used in the injections themselves. In addition, lidocaine can be applied topically as well as intra venously.

Mechanism of Action

Local anesthetics work at the voltage-gated sodium channels, blocking their activity. This prevents the formation of an action potential and subsequent propagation of electrical signaling.

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Examples

Generic	Brand name	Starting dose
Lidocaine	Lidoderm	1 patch q day
Lidocaine	Topicaine	Thin layer TID
Bupivacaine	Marcaine	Not for home use
Mepivacaine	Carbocaine	Not for home use

Side effects

Common	Rare
Erythema	CNS depression
Dermatitis	Bradycardia
Urticaria	Methemoglobinemia
Paresthesia	Anaphylactoid
	Seizure
	Arrhythmia

Drug Interactions

Lidocaine is a major substrate for CYP1A2 and CYP3A4. Medications that affect these enzymes can drastically alter the blood levels of lidocaine and thus should be used with caution. This includes β-blockers, St. John's wort, and amiodarone.

Clinical

Clinical Indications

Neuropathic pain, musculoskeletal pain

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Initiation: Up to three lidocaine patches can be applied to a patient's skin for up to 12 h in a 24 h period.

Lidocaine gel can be applied up to three times daily in a thin layer over the affected area. The dose should not exceed 4.5 mg/kg or 300 mg.

Though there is no standard for the dosing of intravenous lidocaine in the treatment of chronic pain, it has been shown to be a useful adjunct in the treatment of chronic pain. One possible dose is 500 mg in 250 mL of normal saline infused over 30 min. However, of note no difference in efficacy was noted when comparing lidocaine doses of 5–7.5 mg/kg.

Weaning

No weaning is needed.

Special Considerations

- Safe in renal failure patients.
- Elimination half-life is 90–120 min but may be prolonged with hepatic impairment.

Clinical Pearls

- When using lidocaine patches, the 12 h on and 12 h off concept is used to prevent tachyphylaxis.
- While amide local anesthetic allergies are extremely rare, often patients will report allergic reactions to the adhesive or binding agents.
- Intralipid can be used to treat local anesthetic toxicity. A bolus of 1.5 to 4mL/kg can be used followed by an infusion of 0.25 to 0.5mL/kg/min.

Suggested Readings

Ferrera de Souza M, et al. The analgesic effect of intravenous lidocaine infusion in the treatment of chronic pain: a literature review. Rev Bras Reumatol. 2014;54(5):386–92.

Derry S, et al. Topical lidocaine for neuropathic pain in adults. Cochrane Database Syst Rev. 2014;7:CD010958.

Corticosteroids

50

Mona Patel and R. Jason Yong

Glucocorticoids are commonly used agents in epidural injections (caudal, interlaminar, transforaminal) for the treatment of radicular pain emerging from cervical, thoracic, or lumbar spine with the intention to deliver highesr concentrations in close proximity to the area of greatest inflammation.

Mechanism of Action

Immune Modulating

Corticosteroids bind to a cytosolic receptor, and the complex is translocated into the nucleus to inhibit the transcription factors for genes that code for cytokines and adhesive proteins that mount an immune response. Decrease in the cytokines leads to reduced leukocyte adhesion, macrophage accumulation, and capillary permeability.

Anti-inflammatory

Their anti-inflammatory features arise from inhibiting phospholipase A2 thereby decreasing prostaglandin and leukotriene synthesis.

Other

In addition to their anti-inflammatory and immunosuppression effects, they act as direct membrane stabilizers.

Individual Agents

Long-acting steroid preparations approved for intramuscular use are available for administration in the epidural space for treatment of radicular pain. Some of the most commonly utilized agents are listed below (Table 50.1).

They are available in solutions that are equipotent; these equipotent doses are shown in Table 50.2 below. They exhibit varying properties of anti-inflammatory potency and duration of action. The duration of anti-inflammatory activity of glucocorticoids is approximately equal to the duration of suppression of the hypothalamic-pituitary adrenal axis.

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Table 50.1 Commercially available steroids

Steroid	Particulate	Dose (IM; mg)	Duration of action/HPA suppression
Betamethasone sodium phosphate	Yes	9	1 week
Methylprednisolone acetate	Yes	40–80	4–8 weeks
Triamcinolone acetonide	Yes	40–80	2–4 weeks
Dexamethasone sodium phosphate	No	4	3–4 weeks

Table 50.2 Equivalent corticosteroid oral dosages

Cortisone	25 mg
Hydrocortisone	20 mg
Prednisolone	5 mg
Prednisone	5 mg
Methylprednisolone	4 mg
Triamcinolone	4 mg
Dexamethasone	0.75 mg
Betamethasone	0.6 mg

Indications

The use of corticosteroids is widespread in pain management. Patients with central stenosis, neuroforaminal stenosis, nerve impingement from disc herniation, and peripheral nerve irritation can benefit from epidural steroid injections. Joint injections and soft tissue injections also utilize corticosteroids for their anti-inflammatory properties. Though these agents are widely used for radiculopathy, it should be noted none are approved by the FDA for this indication.

Adverse Reactions

- Hyperglycemia (increased insulin requirements in diabetics)
- Hypertension
- Peripheral edema from fluid retention
- Myopathy
- Adrenocortical insufficiency
- Osteoporosis
- Avascular necrosis
- Psychoses
- Subcutaneous fat atrophy
- Anaphylactoid reaction

Clinical Pearls

- Anatomical studies have demonstrated that critical arteries are found in the posterior aspect of the intervertebral foramen that can potentially be injured during transforaminal injections. Hence, the use of live fluoroscopy with contrast and non-particulate steroids decreases the risk of serious central nervous system damage. Dexamethasone is a non-particulate steroid, which significantly decreases the risk of vascular embolism with inadvertent intra-arterial injection.
- Corticosteroids injected in the scalp can cause localized muscle wasting or alopecia.
- Corticosteroids repeatedly injected into certain muscles can cause atrophy and muscle wasting and must be weighed against potential benefit.

Literature Review

A systematic review of 39 studies showed a significant amount of patients with lumbar radicular pain secondary to disc herniation experienced pain relief and improved function with avoidance of surgery leading to reduced health care requirements in patients with lumbar radicular pain after lumbar transformanial steroid injection [1].

Reference

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Engel A, King W, MacVicar J. The effectiveness and risks of fluoroscopically guided cervical transforaminal injections of steroids: a systematic review with comprehensive analysis of the published data. Pain Med. 2014;15(3):386–402.

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Immunoglobulin G

51

Yury Khelemsky, Karina Gritsenko, and Jason Litt

Immunoglobulin G

Immunoglobulin G (IgG) concentrates are immune-modulating, anti-inflammatory human blood plasma-derived products that can be used for the treatment of some peripheral neuropathies and a range of other pain disorders. While evidence is still emerging, IgG is a relatively safe but expensive, therapeutic strategy for chronic pain conditions.

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Mechanism of Action

In most neuropathic chronic pain conditions, there is evidence of local and/or systemic cytokine production. Evidence shows that the degree of central immune activation is connected with the development of chronic pain. Blocking the central immune response using IgG can be adequate to interrupt chronic pain. That is, the analgesic effect of IgG in chronic pain conditions is thought to be secondary to the modulation of cytokine expression and function and immunosuppression. In particular, pathological autoantibodies to components of the voltage-gated potassium channel complex (VGKC complex) are thought to be involved in chronic pain.

Side effects

Common	Rare
Headache	Thrombosis
Hypertension	Anaphylaxis
Skin rash	Renal failure
Fatigue	

Drug Interactions

IgG might reduce the therapeutic effects of live vaccines; therefore, live vaccination administration should be delayed 6 months after receiving IgG. Caution is also advised when using IgG with other thrombogenic drugs, like estrogen derivatives, as the combination might lead to thrombosis.

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Clinical

Clinical Indications

CRPS, diabetic lumbosacral radiculoplexus neuropathy, diabetic neuropathic pain, Sjögren's syndrome-associated neuropathy, fibromyalgia, postpolio syndrome, and pain secondary to pathological autoantibodies

Initiation: Administered intravenously (intravenous immunoglobulin [IVIg]) or subcutaneously (subcutaneous immunoglobulin [SCIg])

Doses vary by what condition is being treated, but generally:

IVIg 0.5–2 g/kg

SCIg 0.5 g/kg/mo

Duration

Onset of action ranges from 2 days to 2 weeks, while the peak effect is typically 1–2 months. The half-life of IVIg varies from 18 to 32 days, which is the same range for native IgG. Remission may be achieved through continuous IgG treatment.

Special Considerations

- Expensive
- Limited RCTs currently only in CRPS and postpolio syndrome

Clinical Pearls

In general practice IgG is a relatively novel treatment for chronic pain conditions, but there is emerging evidence that is convincing for its use in many neuropathic conditions. In reality, the guidelines for its use mostly are derived from an expert panel discussion in Liverpool, UK, in 2012, and as such, there is currently no published evidence suggesting a better efficacy for high-dose as compared with low-dose IgG treatment. Therefore, the use of a "Liverpool protocol" for IgG treatments is suggested where patients should initially be treated with a lower dose of 0.5 g/kg, and if greater than 40 % pain relief is achieved, patients should then, 2 weeks later, be offered a trial of 6–12 months of low-dose maintenance treatment.

Literature Review

At a workshop in Liverpool, UK (October 2012), experts discussed IgG and its benefit of reducing pain in a number of neuropathic chronic pain conditions. While the initial evidence is encouraging, more RCTs are needed to better support the use of IgG.

Suggested Reading

1. Tamburin S, Borg K, et al. Immunoglobulin G for the treatment of chronic pain: report of an expert workshop. Pain Med. 2014;7:1072–82.

NMDA Antagonists

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Karina Gritsenko, Adam Bromberg,
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Background

Mechanism

Excitatory amino acid-mediated neurotransmission occurs via activation of ionotropic and metabotropic glutamate receptor families:

- *Ionotropic* glutamate receptors are directly coupled to specific ion channels.
- *Metabotropic* glutamate receptors are coupled to signal transduction cascades which alter intracellular second messengers.

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Three main types of ionotropic, or ligand-gated, receptors have been identified:

- α-Amino-3-hydroxy-5-methyl-4-isoxazole proprionic acid (AMPA) receptors
- *N*-methyl-D-aspartate (NMDA) receptors
- Kainate (KA) receptors

When Activated

AMPA receptor channel opens quickly allowing a rapid influx of cations, mediating fast synaptic transmission in the central nervous system. The subunit composition of these receptor channels determines their ion permeability and affects the way the receptor is modulated.

NMDA receptors are both voltage and ligand gated and allow permeability to both sodium (Na+) and calcium ions (Ca++). Magnesium ions (Mg++) block the channels of NMDA receptors. These receptors can only become unblocked following a sustained depolarization of the extracellular membrane, which allows the magnesium ion to disengage intracellularly. The opening and activation of the NMDA receptor-channel complex results in a sustained depolarization.

Two phenomena have been linked to NMDA receptor activation*

(1) "Wind-up," which is increasing responses to repeated stimuli of equal intensity

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(2) "Central sensitization," which is decreased thresholds for response and/or increased vigor of response due to a sensitizing event

*NMDA antagonists are thought to mitigate both of the above. These phenomena can also be stopped prior to their development by pharmacological antagonists that block the initial event leading to the sustained depolarization and NMDA receptor activation. As a consequence, the antagonism of other excitatory systems (i.e., AMPA receptors, etc.) or the activation of endogenous inhibitory systems may also blunt or block mechanism thought to result in hyperalgesia.

Hyperalgesia and the Role of the NMDA Receptor

Hyperalgesia and neuropathic pain result from the sensitization of spinal neurons. Subsequent treatment with opioids leads to decreased sensitivity of the opioid receptor and tolerance thus necessitating higher doses to achieve the same analgesic effect. The clinical utility of NMDA antagonists is in resensitizing the opioid receptor and allowing for enhanced analgesia with a reduction in opioid-related side effects.

NMDA Antagonists

- *Strong NMDA antagonists:* ketamine
- *Weak NMDA antagonists:* methadone, memantine, amantadine, and dextromethorphan

Ketamine

- *Complex regional pain syndrome:* Multi-day infusions of ketamine or so-called ketamine comas have been used to treat the most severe form of neuropathic pain, complex regional pain syndrome. Sub-anesthetic doses ("ketamine boosters") are used to treat early CRPS, whereas anesthetic dosages of greater than 2 mg/kg are used for refractory cases as the analgesic effects of ketamine are dose dependent. Complete remission of CRPS has been observed shortly after ketamine therapy. In patients who relapse, significant pain relief may still be achieved at 6 months. Overall, the use of ketamine in CRPS still remains controversial.
- *Opioid sparing:* Ketamine can be used in the perioperative setting for its dose-dependent analgesic effects. For example, the addition of low-dose ketamine to opioids versus opioids alone in postoperative patients who had undergone major abdominal surgery produced better analgesia with less sedation. Ketamine is particularly useful for analgesia in patients with malignancy-related pain who have diminishing analgesic benefits from increasing doses of opioids with mixed neuropathic pain complaints.
- *Side effects:* Significant CNS adverse effects, most notably hallucinations, which can be distressing for patients and limit clinical utility. Other side effects include dizziness, fatigue, nightmares, and an out-of-body sensation. Hallucinations and dysphoria can be decreased through the addition of benzodiazepines.

Methadone

- The L-enantiomer of methadone (levomethadone) is a μ-opioid receptor agonist and the R-enantiomer (dextromethadone) is an NMDA antagonist. Methadone has been used as a replacement for stand-alone opioid therapy in patients with neuropathic pain resulting in better analgesia and a decrease in opioid-related adverse effects. Cancer patients received a similar benefit when switching from morphine to methadone.
- Methadone adverse effects: Much like ketamine, methadone has significant adverse effects. Methadone causes a dose-dependent QT prolongation, which may result in torsades de pointes. Drug interactions: Methadone is extensively metabolized by cytochromes CYP3A4 and CYP2D. Conversion from morphine to methadone can also be challenging as methadone is more potent at increasing doses of morphine necessitating special conversion ratios.

Suggested Readings

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Antihistamines

53

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Antihistamines

Antihistamines are a broad class of drugs, which can be further subdivided by their receptor specificity (H_1 vs H_2) and whether they cross the blood–brain barrier (first generation) or remain in the periphery (second generation). *This chapter will focus on the first-generation H_1 antagonists commonly used in clinical practice for purposes of sedation, nausea and vomiting prophylaxis, and roles in* pain management.

Mechanism of Action

H1 receptor is a G_q-type G-protein receptor with clinically relevant activity in the CNS, vascular smooth muscle, and the heart. Antihistamines act as inverse agonists, stabilizing the H_1 receptor in the inactive conformation (Table 53.1).

Side effects:

Common	Rare
Sedation	Tachycardia
Sleepiness	Diplopia
Dizziness	Constipation
Incoordination	Urinary Retention
Thickened secretions	Thrombocytopenia
Epigastric distress	Anemia
Dry mouth	Agranulocytosis

Drug Interactions

Increased sedation when used with alcohol and CNS depressants (such as opioids). MAO inhibitors will prolong anticholinergic effects of antihistamines.

Clinical

Clinical Indications

Sedation, treatment and prevention of postoperative and opioid-induced nausea and vomiting, and treatment of opioid-related urticarial reactions.

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Table 53.1 Examples of dosing:

Name	Starting dose (mg)	Onset (oral) (h)
Diphenhydramine	25–50	2
Hydroxyzine	25–100	2
Promethazine	12.5–50	2

Initiation: (Using Promethazine as an Example)

For postoperative nausea and vomiting prophylaxis, a dose of 12.5–25 mg IV can be given near the end of surgery with follow-up q4h dosing.

Special Considerations

- Avoid in elderly patients due to increased incidence of worsened cognitive impairment and delirium.
- Promethazine should be avoided in patients with Parkinsonian symptoms due to increased incidence of extrapyramidal side effects.
- Promethazine carries a black box warning for increased incidence of respiratory depression in children <2 years old and for severe tissue injury associated with IV infiltration.

Clinical Pearls

Systemic reviews have demonstrated that diphenhydramine's use has been associated with decreased incidence of postoperative vomiting and postoperative nausea and vomiting.

Diphenhydramine has been used in a 4.8:1 (diphenhydramine/morphine) ratio in PCA pumps with 30 mg of diphenhydramine IV at initiation of therapy and has been found to reduce morphine-related emesis without additional sedative effects.

Dosing of 0.1 mg/kg IV promethazine preoperatively can reduce morphine consumption by 30 % in the first 24 h.

Suggested Reading

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Sympatholytic Agents

54

Yury Khelemsky, Karina Gritsenko,
and Christopher Curatolo

Overview of Sympatholytic Agents

Sympatholytic drugs are agents that decrease the activity of the sympathetic nervous system (SNS). This is accomplished via a variety of mechanisms that most commonly include adrenergic receptor blockade (e.g., α and β adrenergic receptor antagonism) as well as specific receptor agonism (i.e., α_2 adrenergic receptor agonism) (1). The SNS signal, however, may be blocked in other ways (e.g., peripheral ganglionic blockade) (2).

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Adrenergic Receptor Antagonists

Description and Mechanism of Action

The most common sympatholytic agents block adrenergic receptors via competitive antagonism at peripheral α and β adrenergic receptors.

Examples

- β Adrenergic receptor (βAR) antagonists—metoprolol, propranolol
- α Adrenergic receptor (αAR) antagonists—prazosin, terazosin, doxazosin, phenoxybenzamine

Clinical Indications

Migraine headache prophylaxis—propranolol and metoprolol. Not useful in acute migraine attacks.

Complex regional pain syndrome (CRPS)—recommended in SNS-mediated pain syndromes. α_1AR antagonists (esp. terazosin and phenoxybenzamine) are recommended.

Acute panic symptoms/performance anxiety (e.g., public speaking)—βAR antagonists (esp. propranolol) are effective in controlling SNS-mediated symptoms (e.g., sweating, tachycardia, etc.).

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Post-traumatic stress disorder (PTSD)—prazosin (αAR antagonist) is effective for PTSD-related nightmares.

Side Effects

αAR antagonists: orthostatic hypotension, dizziness, weakness, tachycardia
βAR antagonists: bronchospasm (esp. nonselective βAR antagonists), bradycardia, fatigue, sleep disturbance, hypoglycemia

Interactions

Caution in patients with cardiac conduction defects.
Caution in patients on medications that slow cardiac conduction (e.g., calcium channel blockers).
Beta receptor antagonists can interfere with the clearance of lidocaine.

Weaning

Avoid abrupt discontinuation (esp. βAR antagonists)

Alpha-2 Adrenergic Receptor Agonists

Description and Mechanism of Action

α_2AR agonists cause sedation, analgesia, and hypotension in a dose-dependent fashion. The effects of these agents are predominantly centrally mediated. These agents decrease sympathetic discharge via preganglionic fibers in the splanchnic nerves and postganglionic fibers of cardiac nerves. Additionally, these agents stimulate parasympathetic outflow. The agents' hypotensive effects may result from activation of preganglionic α_2ARs causing a decrease in catecholamine release from postganglionic sympathetic nerves (1).

Examples

Clonidine (oral, transdermal, IV, intrathecal, epidural), dexmedetomidine (Precedex), tizanidine (Zanaflex), and epinephrine

Clinical Indications

Adjunctive analgesia, especially perioperative—clonidine, dexmedetomidine, epinephrine

- Clonidine is a potent adjuvant when added to regional and intrathecal techniques.
  - Enhances the effects of epidural opioids
  - Prolongs and enhances the activity of intrathecal local anesthetics
- Clonidine may be an important adjuvant for acute pain management.
- Dexmedetomidine reduces opioid requirements and reduces postoperative nausea and vomiting without increasing recovery time.
- Epinephrine enhances and prolongs the effects of epidural local anesthetics.

Adjunctive anesthesia—reliably reduces the minimum dosage of other anesthetics needed to produce sedation and general anesthesia (esp. IV dexmedetomidine)

Refractory CRPS—epidural clonidine

Restless leg syndrome—clonidine (esp. refractory cases)

Spasticity (cerebral and spinal cord disorders)—tizanidine

Side Effects

Sedation, hypotension, bradycardia, fatigue, dry mouth

Interactions

Caution with other drugs that may lower blood pressure or heart rate

Weaning

Abrupt discontinuation of long-term therapy may cause rebound hypertension

Other Sympatholytics

Description and Mechanism of Action

A reduction in SNS activity may occur via other mechanisms such as the blockade of ganglionic transmission (e.g., trimethaphan), the reduction of neurotransmitter release (e.g., guanethidine), or the depletion of neurotransmitters (e.g., reserpine) (2). These agents are rarely employed today and are listed for historical purposes only.

Other agents that contain some amount of sympatholytic activity include ergot alkaloids (e.g., dihydroergotamine), which are primarily used for acute migraine treatment, and neuroleptics (e.g., chlorpromazine, haloperidol) that in addition to their primary action as antidopaminergic agents produce significant αAR antagonist (1).

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1. Blaudszun G, Lysakowski C, Elia N, Tramer MR. Effect of perioperative systemic alpha2 agonists on postoperative morphine consumption and pain intensity: systematic review and meta-analysis of randomized controlled trials. Anesthesiology. 2012;116(6):1312–22.
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Miscellaneous Adjuvant Analgesics

55

Yury Khelemsky, Karina Gritsenko, and Shahbaz Farnad

Acetaminophen

Acetaminophen is the most commonly used adjuvant analgesic. Commonly combined with opioid formulations for enhanced analgesia and decreased likelihood of abuse.

Mechanism of action: analgesic MOA unknown. May cause weak central inhibition of prostaglandin synthetase.

Indications: first line for osteoarthritis pain.

Dosing: children >12 and adults: 325–650 mg every 4–6 h.

Side effects: nausea, headaches, rash

Special considerations: risk of intentional or accidental fatal overdose. Caution in patients using OTC preparations which may contain acetaminophen.

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

Mechanism of action: inhibits cyclooxygenase, reducing prostaglandin and thromboxane synthesis (Table 55.1).

Side Effects

Common: dyspepsia, nausea, abdominal pain, constipation, headache, rash, fluid retention, mild elevation of hepatic enzymes, tinnitus

Serious: GI bleed/ulcer/perforation, MI, stroke, CHF, thromboembolism, HTN, hemolytic anemia, pancytopenia, and inhibition of PLT aggregation

Special considerations: Cox-2-specific inhibitors (e.g., rofecoxib (Vioxx) 50 mg/day), although associated with significantly less risk of GI events and platelet dysfunction, have been associated with a significantly higher risk of CV events including MI and stroke.

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Table 55.1 Examples

Generic	Brand name	Starting dose
Celecoxib	Celebrex	100 mg daily
Diclofenac	Voltaren	50 mg BID
Ibuprofen	Advil, Motrin	200 mg QID
Ketorolac	Toradol	10 mg BID
Meloxicam	Mobic	7.5 mg daily
Nabumetone	Relafen	1000 mg daily
Naproxen	Naprosyn, Aleve	250 mg BID

Table 55.2 Commonly used antidepressants

Generic (brand name)	Daily dose (mg)	MOA
TCAs		
Amitriptyline (Elavil)	25–100	NE and 5HT reuptake inhibition
Nortriptyline (Pamelor)	25–150	NE>5HT reuptake inhibition
SSRIs		
Sertraline (Zoloft)	50–200	5HT>>NE reuptake inhibition
Paroxetine (Paxil)	10–40	
Citalopram (Celexa)	10–40	
Atypicals		
Venlafaxine (Effexor)	25–225	5-HT>NE>DE reuptake inhibition

Antidepressants

Antidepressants of varying classes, including tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and norepinephrine and dopamine reuptake inhibitors, are commonly prescribed in the treatment of many chronic pain syndromes, particularly in neuropathic-mediated pain. Doses used for analgesia are typically significantly lower than those used for antidepressant therapy (Table 55.2).

Side Effects

TCAs: drowsiness, dizziness, constipation, blurred vision, palpitations, diaphoresis, orthostatic hypotension, syncope, QT prolongation, extrapyramidal symptoms

SSRIs/atypicals: nausea, headache, insomnia, diarrhea, sexual dysfunction, suicidality, mania, serotonin syndrome, hyponatremia, SIADH

Special considerations: Caution must be observed for signs and symptoms of serotonin syndrome when prescribing this class of medications.

Anticonvulsants

Several anticonvulsants have proven very effective in the modulation of chronic neuropathic pain syndromes. Many consider anticonvulsants as first-line therapy for neuropathic conditions including trigeminal neuralgia (TN), postherpetic neuralgia (PHN), diabetic peripheral neuropathy (DPN), HIV neuropathy, and central poststroke syndrome (CPPS) (Table 55.3).

Side Effects

Carbamazepine: rash, Stevens-Johnson syndrome*, dizziness, drowsiness, n/v, ataxia

Oxcarbazepine: dizziness, headache, n/v, somnolence, diplopia, hyponatremia, anaphylaxis, angioedema

Gabapentin/pregabalin: dizziness, somnolence, peripheral edema, blurred vision, weight gain, angioedema, exfoliative dermatitis

Lamotrigine: dizziness, vertigo, diplopia, ataxia, n/v, blurred vision, somnolence, rash, angioedema

Special considerations: evidence of a rash with the use of any of these medications should warrant

Table 55.3 Commonly used anticonvulsants

Generic (MOA)	Daily dose	Indication
Carbamazepine (Na+ Ch blocker)	100–400 mg BID	TN
Oxcarbazepine (Na+ Ch Blocker)	300–1200 mg BID	TN
Gabapentin (voltage-gated calcium Ch blocker)	300–1200 mg TID	PHN, DPN
Pregabalin (voltage-gated calcium Ch blocker)	50–100 mg TID	PHN, DPN
Lamotrigine (voltage-gated Na+ Ch blocker)	24–400 mg daily	TN, CPPS

extreme caution/consideration for discontinuation of medication for risk of Stevens-Johnson syndrome or toxic epidermal necrolysis. Discontinuation of these medications should not be abrupt, and doses should be titrated down 25% weekly.

Suggested Reading

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Serotonin Syndrome

56

Nantthasorn Zinboonyahgoon
and Mohammed Issa

Pharmacology

Serotonin syndrome involves stimulation of the postsynaptic 5-HT1A and 5-HT2A receptors. It results from any combination of drugs that has the net effect of increasing serotonergic neurotransmission, most commonly serotonergic antidepressants (SSRIs, SNRIs, TCAs, MAOIs). Other drugs may include analgesics (tramadol), antiemetics (metoclopramide, ondansetron), triptans, and drugs of abuse (MDMA, LSD).

Clinical

Clinical Manifestations

Classic serotonin syndrome is described as a triad of mental status changes (agitation, disorientation, delirium), autonomic hyperactivity (tachycardia, hypertension, hyperthermia, diaphoresis), and neuromuscular abnormalities (tremors, myoclonus, hyperreflexia, muscle rigidity). The onset is acute, usually starting within 6–24 h.

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Diagnostic Criteria

Diagnosis is based on clinical findings using the Hunter toxicity criteria. The patient must have taken a serotonergic agent and meets ONE of the following conditions:

- Spontaneous clonus
- Inducible clonus PLUS agitation or diaphoresis
- Ocular clonus PLUS agitation or diaphoresis
- Tremor PLUS hyperreflexia
- Hypertonia PLUS hyperpyrexia (>38 C) PLUS ocular clonus or inducible clonus

Special Considerations

In severe serotonin syndrome, patients can develop hypotension, hyperthermia, rigidity, and rhabdomyolysis, which may be difficult to distinguish from neuroleptic malignant syndrome (NMS). NMS is slower in onset (develops over days to weeks), takes longer to resolve (9 days as compared to less than 24 h for serotonin syndrome), and involves sluggish neuromuscular responses, unlike neuromuscular hyperactivity seen in serotonin syndrome.

Treatment

- Discontinue all serotonergic agents.
- Supportive care to normalize vital signs.
- Sedation with benzodiazepines to control agitation and vital signs. If this fails, consider using serotonin antagonists such as cyproheptadine.

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- For severe cases, patients may need to be admitted to the ICU for hemodynamic control or intubation and paralysis.

Clinical Pearls

- Serotonin syndrome involving MAOIs may be more severe and can be lethal.
- Serotonin syndrome may result from therapeutic medication use, inadvertent interactions between drugs, and/or intentional self-poisoning.
- If tramadol is to be prescribed with a serotonergic drug, do not exceed a daily dose of 300 mg.

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Boyer EW, Shannon M. The serotonin syndrome. N Engl J Med. 2005;352:1112–20.

Lerner BA. A life-changing case for doctors in training. New York Times, August 14, 2011.

Part VI

Psychological Treatments

Cognitive-Behavioral Therapy

57

Syed Hazique Mahmood

Cognitive-behavioral therapy (CBT) has been shown to be valuable in treating chronic pain.

CBT emphasizes techniques that substitute negative thoughts leading to the modification of pain perception and associated symptoms like depression.

There are three main approaches in CBT:

1. Reconceptualization
2. Skills acquisition
3. Maintenance and Post-treatment follow-up

Reconceptualization

Often the muscle tension and distress caused by negative thoughts and emotions during pain flares leads to more pain. Reconceptualization is a method that involves reinterpreting these thoughts and emotions associated with pain positively. It is a valuable tool with the goals of creating greater self-awareness, identification and modification of stress-associated thoughts and emotions, and ameliorating the sense of being overwhelmed. The technique also involves educating patients on positive thoughts to facilitate coping better during painful periods.

Skills Acquisition

This method involves learning specific techniques that help in modifying the patient's affect and experience of pain. This is primarily accomplished by incorporating techniques that help in reducing muscle tension, diverting focus from the feeling of pain, fostering relaxation, and minimizing stress. Examples of specific techniques are breathing exercises, distracting methods like counting or relaxing imagery, and physical exercise such as walking. After educating patients on these coping skills, patients are also guided to practice these skills for effectively integrating in their daily routines and especially during painful flares.

Maintenance and Post-treatment Follow-up

As the name suggests, this method involves guiding patients to negotiate problems that may come up during the posttreatment period. Patients are encouraged to discuss their expected difficulties in the posttreatment period and then plan to deal with obstacles during this period. Education regarding treatment relapses and impediments is

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meted out to patients. Patients are also counseled not to view setbacks as discouraging but to remember that they can utilize the skills learned previously.

In order to monitor progress, tools such as maintaining diaries for pain and maintaining before or after treatment visual records are beneficial. This method seeks to give a greater sense of awareness for patients about their painful periods and progress. Patients are educated and encouraged on confidently coping with problems like relapses and painful episodes independently.

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Behavioral Interventions

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Syed Hazique Mahmood

Pain is a multifaceted experience. It is not only influenced by the pathophysiologic response but also by the patient's mood, behavior, and emotions.

Behavioral intervention is an important method that alters the mood or psychology which in turn influences sensitivity to pain beneficially.

Examples of behavioral interventions include operant behavioral therapy and respondent behavioral therapy which are discussed below.

Operant Behavior Therapy (OBT)

This method is based on the model that sensitivity to pain is influenced by pain behaviors and its consequences. Pain behaviors such as verbalizations, facial expressions, or avoidance of activity can lead to functional limitations, depression, or deconditioning. Furthermore, the patient can be conditioned to pain behaviors as it leads to preferred consequences such as increased attention or avoidance of activity. Accordingly, OBT focuses on achieving reduced perception of pain by minimizing pain behaviors and promoting "well behaviors." Examples of well behavior would be improved sleep hygiene and activity, exercise routine based on previously determined realistic schedule rather than on pain tolerance, and pain medication based on timed schedule rather than on feeling of pain. OBT also recognizes the potential role of family in reinforcing or conditioning of pain behaviors. In this regard, the family is also educated on not encouraging pain behaviors and instead reinforcing well behavior.

OBT has been shown to be an effective mode of pain management in adults with low back pain and myofascial pain.

Additionally, OBT in conjunction with biofeedback has been shown to be especially beneficial for phantom limb and temporomandibular joint pain.

Biofeedback is self-monitoring of physiological functions such as heart rate, respiratory rate, blood pressure, or perspiration via sensors attached to monitoring devices. This serves to give greater sense of awareness and control over sympathetic responses such as tachycardia, increased respiratory rate, and muscle tension especially in response to pain periods. Biofeedback has also been shown to be helpful for several chronic pain disorders such as fibromyalgia and headaches.

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Respondent Therapy

Like operant therapy, respondent therapy also seeks to eliminate pain behaviors. The main difference between the two is that in respondent therapy, the pain perception is recognized to be associated with an external stimulus, whereas in operant, the focus is on the consequences. For instance, the patient may become conditioned to having increased pain after occupational therapy, and thus, just the presence of a therapist might invoke an increased pain sensation and muscle tension. Respondent therapy emphasizes desensitization to stimuli, progressively tolerated exercise regimen, and patient education about the link between anxiety, fear, and pain.

Desensitization often begins with learning relaxation techniques which seek to replace the feelings of anxiety and fear.

Relaxation techniques reduce physical and mental tension primarily via activation of the parasympathetic nervous system. The following are descriptions of relaxation techniques used:

Deep Breathing Exercises Deep or diaphragmatic breathing is achieved by utilizing the muscles in the diaphragm during respiration. The contraction of the diaphragm serves to increase the volume of available oxygen within the lungs. In addition, it is associated with reduction of heart rate and blood pressure. Deep breathing techniques are often utilized to help patients with anxiety disorders as well.

Progressive Muscle Relaxation (PMR) This is characterized by the sequential tensing and relaxing of major muscle groups for several seconds and passively focusing on how the tensed muscle feels. It enables the greater focus on the difference between the sensation of tension and relaxed muscle leading to greater self-awareness and control.

Autogenic Training (AT) Autogenic refers to regulating one's self. In the setting of AT, it refers to regulating the physical state by the mind. This method involves envisioning a tranquil environment and soothing bodily positioning. The patient also uses verbal cues for facilitating comfortable bodily positions combined with visualization to induce a state of relaxation.

Suggested Readings

Roditi D, Robinson ME. The role of psychological interventions in the management of patients with chronic pain. Psychol Res Behav Manag. 2011;4:41–9.

Springhouse Corporation. Expert pain management (Springhouse guide). Foreword by Carol A. Warfield, MD. Springhouse Corporation, 1997.

Psychiatric Comorbidities and Treatments

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Syed Hazique Mahmood

There are multiple psychiatric comorbidities that mediate the pain perception and merit medical attention. Below are the prominent comorbidities that require medical attention for optimal treatment of pain.

Somatization Disorder

According to DSM-V, the disorder has been renamed to somatic symptom disorder (SSD). The DSM-IV disorders of somatization disorder, pain disorder found especially in chronic pain patients, and undifferentiated somatoform disorder have been replaced and now fall under the category of SSD.

SSD, as applied to chronic pain patients, is defined by somatic symptoms for at least 6 months of duration that are stressful or result in significant functional impairment, as well as disruptive feelings and behaviors. Depressions often coexist in patients with SSD. Cognitive behavioral therapy is the primary treatment.

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Depression

Depression is commonly found in patients with chronic pain. Patients with concomitant chronic pain and depression tend to have characteristics such as greater avoidant behavior, less compliant with treatment, and reduced response to treatment unless depression is addressed.

When evaluating for depression, it's preferable to focus on the psychological symptoms of depression such as anhedonia, decreased concentration, guilt, worthlessness, suicide, and despair. This is because symptoms like fatigue, sleep disturbances, or loss of appetite can be secondary to other medical conditions causing pain.

Depression is treated both pharmaceutically and with the help of psychotherapy. Transcranial magnetic stimulation has also been FDA approved for treatment of depression.

Medications such as SSRI (selective serotonin inhibitors) and serotonin norepinephrine reuptake inhibitors such as Cymbalta have been shown to be effective.

Psychotherapeutic treatment is carried out in a variety of settings as described below.

One to One This therapy takes place in a one-to-one setting and uses cognitive behavioral therapy and behavioral interventions as previously discussed.

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Group This therapy takes place in a setting with more than two people. Through this arrangement, patients are able to exchange their experiences and ideas while receiving mutual support from peers. This exercise tends to alleviate the sense of isolation for the patients.

Family/Couples Patients in pain can have wide-ranging effects on the family unit. The pain-afflicted patient may not be able to fulfill his previous responsibilities and function in the household. Such changes can strain relations and create complications within the family dynamics. This strain can also instead have a negative effect on the underlying depression. The primary aim of family therapy is to foster greater understanding about the patient's depression and pain symptoms and ways to mitigate the effects on the family unit.

It is also expected that family therapy can also prevent from the worsening of depression symptoms as well as related disability

Anxiety

Anxiety is common among patients with chronic pain. Anxiety has been found to cause higher pain levels due to its activation of the limbic system. This is due to the limbic system suppressing the pain-inhibiting signals from the midbrain. Pain and anxiety can lead to increased muscle tension. The increased tension on the muscle can predispose to damage of muscle cells that results in release of pain-mediating substances and, thereby, leads to increased perception of pain.

Below are the various ways to treat anxiety in the setting of pain.

Medications Interestingly treatment for anxiety has also been found to ameliorate pain symptoms as well. Examples of optimal medications used are selective serotonin reuptake inhibitor (SSRI), serotonin and norepinephrine reuptake inhibitor (SNRI) such as duloxetine and venlafaxine (FDA approved for generalized anxiety disorder), tricyclic antidepressants, and several anticonvulsants such as pregabalin (for generalized anxiety disorder) and valproic acid (for panic disorder.)

Cognitive Behavioral Therapy (CBT) CBT is used to treat anxiety disorders in the setting of chronic pain. Relaxation techniques such as progressive muscle relaxation, as previously described, is beneficial in treatment of anxiety and pain.

Sleep Disorders

Sleep disturbances frequently coexist with pain especially with fibromyalgia. These are characterized by longer sleep onset latencies, frequent awakenings, and shorter duration of sleep. The diagnosis involves a thorough history and physical exam, sleep diaries, and finally confirmatory tests such as polysomnography.

Prolonged sleep disturbances can worsen perception of pain. For example, the deficiency in Stage IV sleep has been associated with increased muscle tenderness and stiffness that increases sensitivity to pain.

Other comorbidities such as depression may also contribute to sleep disturbances among patients with pain. Restless leg syndrome can also cause sleep disturbances due to the feeling of paresthesia and the impulse to move the extremity.

Accordingly, evaluating for the potential etiology for sleep disturbance in setting of pain is important because treatment will be determined by the cause. For example, if depression is suspected as the cause, then an antidepressant will be appropriate. On the other hand, for restless leg syndrome, anticonvulsant would be appropriate.

Substance-Related Disorders

Substance dependence has been found to be associated with chronic pain patients especially ones with somatic system disorders.

Substance dependence is distinguished by the patient trying to acquire medications such as opiates for reasons such as psychological respite rather than pain alleviation. These patients also demonstrate drug-seeking behavior from multiple caregivers and also can indulge in illegal activities for acquiring pain medications. Examples of drug seeking behavior include inquiring for specific brand name pain medications and asking for dosages to be increased.

However, caution must be exercised to differentiate between substance dependence and pseudoaddiction. Pseudoaddiction is distinguished by an aim of the patient for acquiring pain relief. Patients with chronic pain can be predisposed to pseudoaddiction if they receive insufficient dosing or excessive time spacing between dosing. Patients with pseudoaddiction may also manifest behaviors similar to substance dependence such as Examples of drug seeking behavior include inquiring for specific brand name pain medications and asking for dosages to be increased. But unlike substance dependence patients, acquiring more medications will minimize drug-seeking behaviors and improve function as well as drug compliance.

Personality Disorders

Personality disorders such as histrionic, dependent, and borderline have been found to be commonly associated with chronic pain patients. Diagnosing personality disorders in pain patients can better prepare the physician for planning treatment. It will also enable the physician to understand the perspective of patient with regard to his illness and the respective coping mechanism.

Treatment is based on dialectical behavioral therapy and cognitive behavioral therapy.

Schizophrenia

Studies have shown that patients with schizophrenia demonstrate higher pain thresholds as well as decreased sensitivity to pain (pain insensitivity in schizophrenia, Robert H. Dworkin 1994). There have been some theories postulated for this finding. Primary among these theories is the higher levels of endogenous opioids found in the cerebrospinal fluids of schizophrenic patients that may alleviate pain. Additionally, it is also believed that the abnormal activity in the limbic system of schizophrenic patients might be disrupting the perception of pain signal. Treatment of schizophrenia is based on atypical antipsychotics. Interestingly, studies have shown antipsychotics do not alter pain thresholds (Jochum et al. 2006).

Transcranial Magnetic Stimulation (TMS) Treatment Modality

Studies have shown TMS to be beneficial in treating neuropsychiatric diseases such as depression and seizures. Accordingly, TMS was approved by the FDA for treatment of depression in 2008.

TMS is a novel therapy that involves passing an electrical current through a circular insulated coil. The passage of current through the coil produces a magnetic field. Thus, when the TMS coil is applied to the head, this leads to a magnetic pulse permeating the cranium to the brain cortex. When repetitive pulses at specific regular frequencies are applied, this can lead to modification of cortical and subcortical activity.

Recent literature has shown that TMS may be greatly beneficial in the treatment of neuropathic pain. TMS is also recognized to have an important advantage over pain medication with regard to localized site of action and reduced potential for side effects. While pain medications have to be absorbed into the bloodstream and have potential of acting on unintended parts of the body, TMS acts only over the brain. This has potential for fewer side effects. In addition, TMS is noninvasive and does not require sedation.

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Stimulation-Produced Analgesia

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Narayana Varhabhatla and Ehren Nelson

Introduction

Stimulation-produced analgesia is a concept that has been in use for many years, from the use of acupuncture by the Chinese thousands of years ago to the modern implantable spinal cord stimulators that are common in pain practice today. Described in this chapter are the current methods in pain management that employ this useful tool in providing analgesia to our patients.

Acupuncture

Acupuncture is a system of health care developed in China over 3000 years ago, based on the concept that good health comes from harmony among bodily functions. The vital energy of the body, *qi* (pronounced "Chee"), flows through the body in patterns (called meridians) and free flow of these energies ensures good health. *Qi* flows in 12 major meridians and eight minor meridians. Change in free flow is believed to lead to pain and disease conditions. Insertion of acupuncture needles, which are fine metallic needles, along specific meridians restores the proper flow of *qi*. Traditional Chinese medicine holds that there are 2000 acupuncture points.

Mechanism of Action

The exact mechanism of action of acupuncture is unknown. Stimulation of A-delta fibers by needling is thought to release endorphins, enkephalins, dynorphins in the brain and spinal cord, and elevated ACTH in the hypothalamic-pituitary axis. Local anesthesia at the site of acupuncture needle insertion sites negates the therapeutic effect of acupuncture. Therefore, part of the mechanism is through stimulating the areas of innervation. Naloxone reverses low-frequency electroacupuncture-induced analgesia. However, recent systematic reviews have demonstrated that the placebo effect itself is mediated by release of endogenous opioids. Therefore, further studies are needed to determine the exact mechanism of action of acupuncture.

Efficacy

Studies have shown efficacy for migraine and tension headaches, chronic neck pain, low back pain, and soft-tissue injuries of peripheral joints.

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Meta-analysis done by Furlan evaluated 35 RCTs and 2861 patients with nonspecific chronic LBP and found small improvements in pain relief and functional status. They recommend acupuncture as part of a multidisciplinary approach to low back pain.

Contraindications

Bleeding disorders, warfarin use, severe psychiatric disease, and local skin infections. It is not contraindicated in pregnancy, but caution must be used in pregnant patients.

Side Effects

Side effects are reported in a wide range in the literature and include needle pain (1–45 %), tiredness (2–41 %), bruising (0.03–38 %), and faintness (0–0.3 %).

TENS

TENS is short for transcutaneous electrical nerve stimulation. It is an electrical stimulus applied to the skin for control of pain and is thought to work via a combination of gate theory and via the upregulation of endorphins and enkephalins. The apparatus consists of a battery-powered pulse generator, leads, and electrodes that produce different pulse characteristics and stimulation frequencies. The voltage on the device is increased until the patient feels a pleasant tingling sensation without any motor contraction and can be classified as high intensity or low intensity. Frequencies are classified as low (<10 Hz), high (>50 Hz), or burst (bursts of high frequency applied at varying intervals). Lower frequencies (<30 Hz) have an effect similar to acupuncture. Most people use low-intensity voltage and high-frequency pulses, between 30 and 100 Hz.

It is recommended to be applied in the painful area with both electrodes in the same dermatome as the pain. After placing the electrodes, the pulse generator is slowly increased until the patient feels a threshold stimulation without any motor symptoms.

Most TENS units have a conventional mode, burst mode, and modulation mode. Conventional mode is between 50 and 200 Hz with a pulse width of 200 μs and gives rapid pain relief. Burst mode uses lower frequencies and is similar to acupuncture and gives longer-lasting pain relief. Modulation mode is similar to burst mode but with a continuously cycled pulse width, which gives it a massage-like sensation.

Contraindications to TENS unit include the presence of a pacemaker, spinal cord stimulator, impaired sensation such as with quadriplegics, pregnant patients, and skin breakdown as with eczema or psoriasis. It is also not recommended to use the TENS unit while sleeping or in the anterior cervical spine, as this may trigger a vasovagal response.

Spinal Cord Stimulation

Background

Spinal cord stimulators are minimally invasive devices used to achieve analgesia. They were first implanted by the neurosurgeon, Dr. Norman Shealy, in 1967 based on the gate control theory proposed by Wall and Melzack. He implanted his devices via cutdown and laminotomy, which was bulky and prone to technical problems with cumbersome, unreliable equipment. Since then, improved hardware, battery technology, lead placement techniques, and programmability have made it simple and efficient to use this technology.

The epidurally placed leads electrically stimulate the dorsal column of the spinal cord. Painful sensations, most often the back and legs, are replaced with a more tolerable tingling sensation. The leads are now placed via percutaneous epidural access, whereas before a laminotomy was required. The tip of the lead is typically placed between T8 and T10, with programming done during placement to assure adequate coverage of the painful area. The position is critical to get good coverage as even small changes in placement can lead to drastic decrease in coverage.

Further, the anatomic midline does not correspond to physiologic midline. In fact, only 27 % of patients with perfectly midline leads on imaging feel symmetric coverage.

Because the device is an implanted one, the patient needs to be psychologically stable and understand the implications of having a foreign body implanted. Further, the risk of infection requires that patients are compliant with post-procedural care and antibiotic use.

The implantation process can be thought of in three phases: prescreen, trial, and implantation. The prescreening phase involves a clinic visit to assess candidacy and discuss the details of trialing and implantation and psychology evaluation. The trial phase involves placement of temporary epidural stimulator leads, after which the patient goes home with the implanted epidural leads for 1 week to determine if the coverage is satisfactory to them. If the trial is a success, the patient may go ahead with a permanent implantation procedure of the device.

Mechanism of Action

The mechanism of SCS was initially thought to work via the gate control theory, which postulated that activating A-beta motor fibers modulates dorsal horn "gate" and reduces nociceptive input from the periphery. Now it is known that other mechanisms play a more significant role. There are increased extracellular GABA and adenosine levels within the spinal cord. Within the brain, there is an increase in descending analgesic pathways from the periaqueductal gray and an increase in serotonin. SCS also activates areas corresponding to pain pathways within the cortex as found on functional MRI, including the somatosensory and affective components of pain.

Efficacy

A large RCT by North showed that SCS is more efficacious than reoperation in patients with failed back surgery syndrome (FBSS) or postlaminectomy syndrome. Success in FBSS varies from 12 to 88 %, and a systematic review by Turner showed that 59 % of patients had >50 % relief of pain with SCS. There was a 25 % return to work rate and 61 % improvement in activities of daily living. These studies also show a 40–80 % reduction in opioid consumption after placement of SCS.

Complications

Lead migration (24 %), lead failure (7 %), IPG failure (2 %), and infection (5 %)

Contraindications

Unstable psychiatric disorder, sepsis, anticoagulation, bleeding disorders, and local skin infection

Suggested Readings

Berman BM, Langevin HM, Witt CM, Dubner R. Acupuncture for chronic low back pain. N Engl J Med. 2010;363(5):454–61.

Lewis K, Abdi S. Acupuncture for lower back pain: a review. Clin J Pain. 2010;26(1):60–9.

Stojanovic MP, Abdi S. Spinal cord stimulation. Pain Physician. 2002;5(2):156–66.

Part VII

Interventional Pain Management

Interlaminar Epidural Steroid Injection: Cervical and Lumbar

61

R. Jason Yong and Ehren Nelson

CPT: Epidural single shot lumbar / caudal : Without imaging 62322 and With imaging 62323
Epidural single shot cervical / thoracic: Without imaging 62320 and With imaging 62321
Professional component 26

Indications

Current insurance guidelines do not cover LESIs for spinal stenosis. Primarily used for lumbar radiculopathy or lumbar degenerative disk disease. CESI's should also be performed primarily for cervical radiculopathy (Fig. 61.1).

Equipment/Materials

Fluoroscopy, 20 g/17 g Tuohy, loss of resistance syringe, +/− contrast, local anesthetic, and +/− corticosteroid

Procedure

Position: prone
IV: not required unless previous vagal episodes
Antibiotics: not required
Steps:

1. Start with AP view and center spinous process between pedicles. Not necessary to adjust caudal/cephalad tilt.
2. Isolate insertion point in between spinous process and pedicle of the affected side. Ideally, aim for the superior aspect of the inferior lamina of the desired interspace.
3. After local anesthetic infiltration, insert the Tuohy needle coaxially between spinous process and pedicle. See Fig. 61.2.
4. Once trajectory is verified to be coaxial in between spinous process and pedicle, switch to contralateral oblique (45–55°) view.
5. Without adjusting lateral/medial orientation of the needle, advance in the contralateral oblique view to the anterior laminar line. Adjustment of the caudal/cranial angle of the needle may be required to navigate in between lamina. See Fig. 61.3.

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R.J. Yong et al. (eds.), *Pain Medicine*, DOI 10.1007/978-3-319-43133-8_61

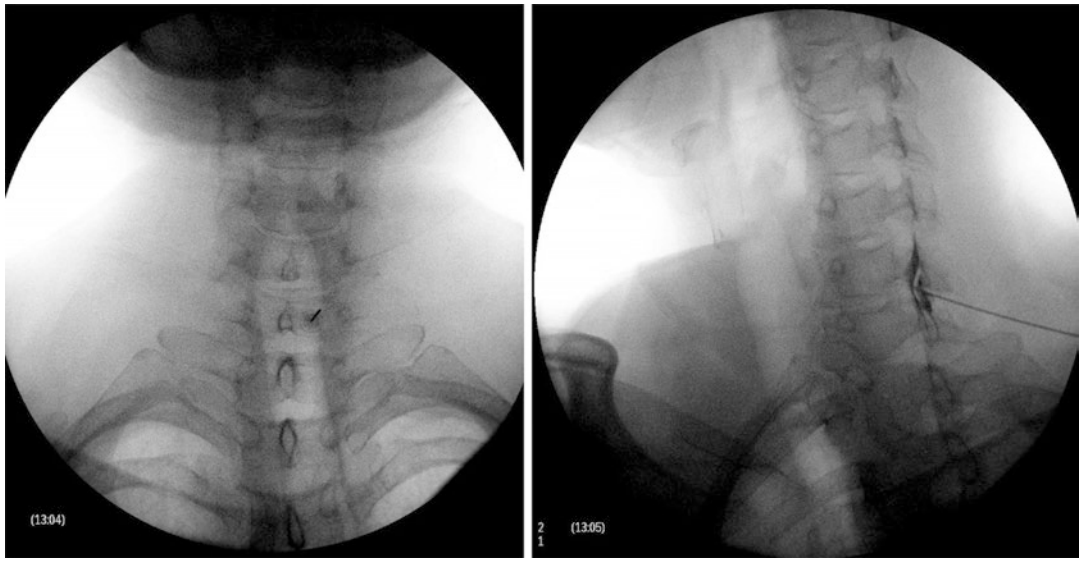

Fig. 61.1 Cervical epidural steroid injection under contralateral oblique fluoroscopy views. Left image is the AP view and the right image represents the contralateral oblique view

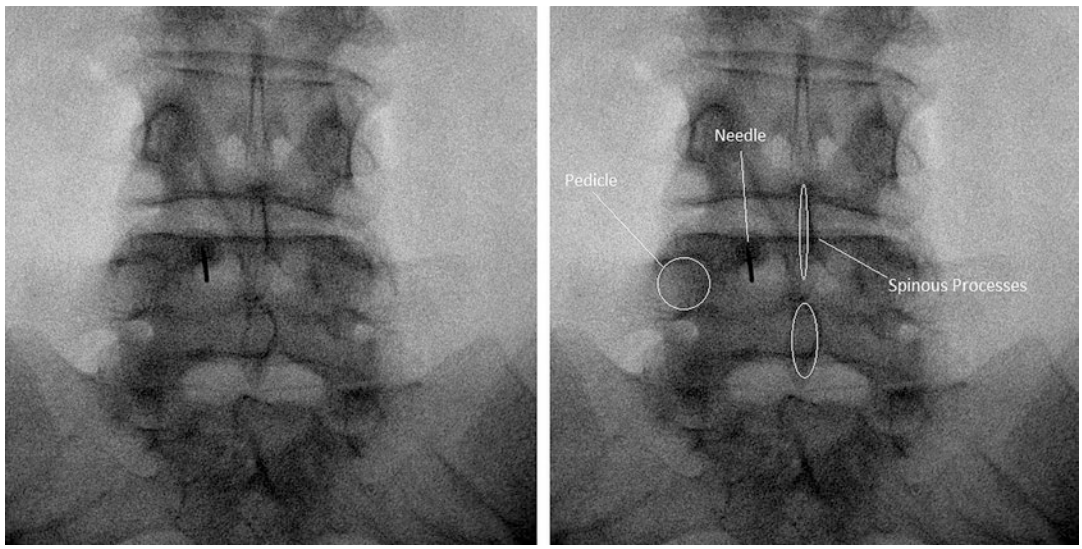

Fig. 61.2 AP view—note how the needle is inserted coaxially between the spinous processes and the pedicle

6. Once at the anterior laminar line, remove the stylet and check for loss of resistance.
7. When loss of resistance is achieved, contrast can be injected for verification of epidural spread (optional).
8. Save final image and administer injectate.

Complications

Epidural bleeding, epidural abscess, and direct spinal cord trauma are some of the potential complications. Good aseptic technique and adherence to ASRA guidelines on neuraxial procedures limit

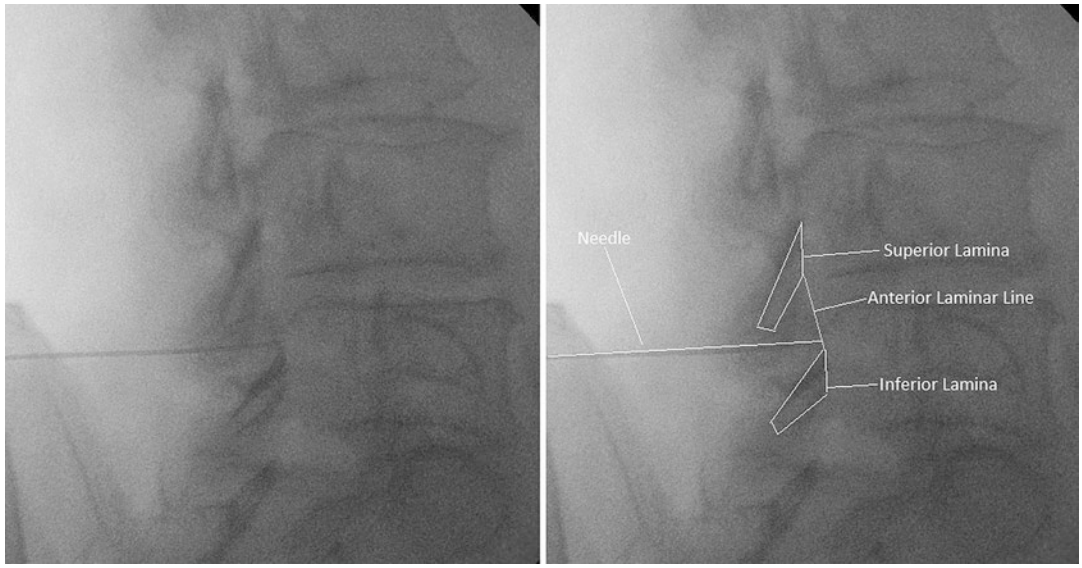

Fig. 61.3 Contralateral oblique view—note how the needle is advanced between the laminae to the anterior laminar line

the first two. Direct cord puncture has varying degrees of injury from transient to permanent symptoms, but injection of material into the cord is catastrophic. Avoid heavy sedation to allow identification of cord contact. Always review the MRI, if available, prior to the procedure.

Clinical Pearls

For lumbar radiculopathy, we mentally prepare patients to expect a series of three injections typically 4 weeks apart. If patients receive >50 % response, we will continue with the series. We will limit yearly injections to 4–6 per year.

There is no consensus on injectate. Volumes vary from 2 to 10 cc and choice and dosage of corticosteroid vary widely as well. We typically use 80 mg of methylprednisolone mixed with 0.5 % lidocaine and 4–6 cc of total volume based on levels affected, fall risk, and degree of stenosis.

Evidence

Lidocaine Only vs with Steroid

In a prospective, randomized controlled trial from multiple sites, the treatment of lumbar spinal stenosis had equivocal results from injection of lidocaine only versus lidocaine with glucocorticoid. Both groups responded positively, thus justifying the use of epidural injections for spinal stenosis with lumbar radiculopathy.

Interlaminar vs Transforaminal

While there are few studies comparing the two approaches, a 2014 systematic review revealed that both approaches were effective at reducing pain and improving functional status in patients with unilateral radiculopathy. There were no clinically significant differences between the two approaches.

Suggested Readings

Friedly JL, Comstock BA, et al. A randomized trial of epidural glucocorticoid injections for spinal stenosis. N Engl J Med. 2014;371(1):11–21.

Chang-Chien GC, Knezevic NN, et al. Transforaminal versus interlaminar approaches to epidural steroid injections: a systematic review of comparative studies for lumbosacral radicular pain. Pain Physician. 2014;17(4):E509–24.

Lumbar Transforaminal Epidural Steroid Injection

62

Yi Cai Isaac Tong and R. Jason Yong

CPT Codes

64483: injection, anesthetic agent and/or steroid, transforaminal epidural; lumbar or sacral, single level
64484: injection, anesthetic agent and/or steroid, transforaminal epidural; lumbar or sacral, each additional level (list separately in addition to code for primary procedure)
77003: fluoroscopic guidance—not required as this is bundled with the above codes

Indications

- Radiculopathy
- Lumbar disk displacement without myelopathy
- Axial pain
- Postlaminectomy with recurrent pain
- Spinal or foraminal stenosis

Equipment/materials: fluoroscopy, 22- or 25-gauge Quincke needle, contrast, local anesthetic, and +/− corticosteroid (non-particulate)

Procedure

Position: prone
IV: not required unless previous vagal episodes
Antibiotics: not required

Steps

1. Prep area with chlorohexanol or Betadine and drape in the usual sterile fashion.
2. Square off superior end plate of desired level.
3. Oblique ipsilaterally, usually 15–30°.
4. Needle should be coaxial with the C-arm and directed just under the pedicle and lateral to the pars interarticularis, above the superior articular process inferiorly.
5. Once the needle tip is just under the pedicle medially, the fluoroscopy is rotated to the lateral view, and the needle is advanced slowly into the upper 1/3 of the foramen.
6. The tip of the needle should be placed in the area of the "safe triangle." The safe triangle is bounded superiorly by the pedicle and by the

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outer margin of the exiting nerve root and the border of the vertebral body.
7. After negative aspiration of blood, ~1 cc of radiographic contrast is injected under live fluoroscopy +/− digital subtraction.
8. Save final image and administer injectate.

Fluoroscopy Image (Fig. 62.1)

Clinical Pearls

- Reports of catastrophic neurologic injury following transforaminal epidural steroid injections used particulate steroid, so the use of non-particulate steroid such as dexamethasone is advised.
- The technique described above is the traditional supraneural (above the nerve root) technique. Some physicians prefer the infraneural technique citing a lower likelihood for vascular injection.

Evidence

Ghahreman et al. evaluated the efficacy of transforaminal injection of steroids for the treatment of lumbar radicular pain in 2010 in a prospective, randomized study. The authors compared the outcomes of transforaminal injection of steroid and local anesthetic, local anesthetic alone, or normal saline and intramuscular injection of steroid or normal saline. The authors found a significantly greater proportion of patients treated with transforaminal injection of steroid (54 %) achieved relief of pain than did patients treated with transforaminal injection of local anesthetic (7 %) or transforaminal injection of saline (19 %), intramuscular steroids (21 %), or intramuscular saline (13 %) [1].

In Buenaventura et al., the authors performed a systematic review of TFESI for the management of low back and lower extremity pain. Studies were compiled from 1966 to November 2008 and the primary outcome measure was pain relief (short-term relief = up to 6 months and long term > 6 months). Secondary outcome measures were improvement in functional status, psychological status, return to work, and reduction in opioid intake. The systematic review concluded that there is Level II evidence for TFESI for short-term relief of lower back pain and Level II-2 for long-term improvement in the management of lumbar nerve root and low back pain [2].

In 2014, Chang-Chien et al. conducted a systematic review of transforaminal versus interlaminar epidural steroid injections in the management of lumbosacral radicular pain. Five prospective and three retrospective studies were included assessing 506 patients. The findings show that both TFESI and ILESI are effective in reducing pain and improving functional scores in unilateral LSRP. In the treatment of pain, TFESI demonstrated non-clinically significant superiority to ILESI only at the 2-week follow-up [3].

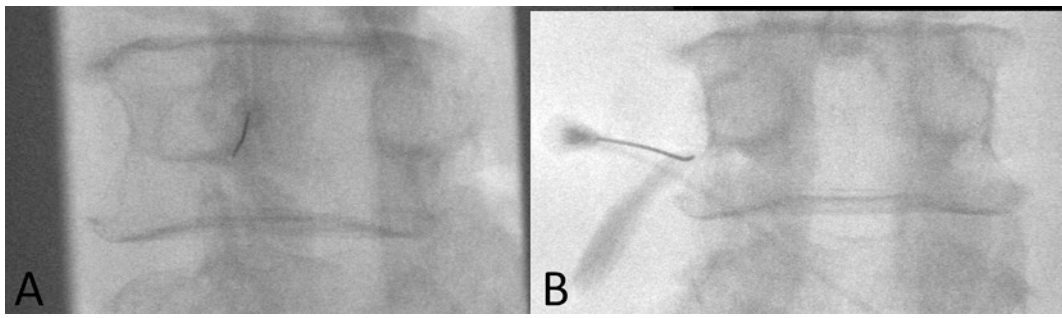

Fig. 62.1 (**a**) Oblique view and (**b**) AP confirmatory view with contrast injection

References

1. Ghahreman A, Ferch R, Bogduk N. The efficacy of transforaminal injection of steroids for the treatment of lumbar radicular pain. Pain Med. 2010;11(8):1149–68. doi:10.1111/j.1526-4637.2010.00908.
2. Buenaventura RM, Datta S, Abdi S, Smith HS. Systematic review of therapeutic lumbar transforaminal epidural steroid injections. Pain Physician. 2009;12(1):233–51.
3. Chang-Chien GC, Knezevic NN, McCormick Z, Chu SK, Trescot AM, Candido KD. Transforaminal versus interlaminar approaches to epidural steroid injections: a systematic review of comparative studies for lumbosacral radicular pain. Pain Physician. 2014;17(4):E509–24.

Cervical Facet Injection/Medial Branch Block

63

Yi Cai Isaac Tong and R. Jason Yong

CPT Codes

64490: Zygapophyseal joint (or nerves innervating that joint) with image guidance, cervical or thoracic; single level
64491: Zygapophyseal joint, second level
64492: Zygapophyseal joint, third and any additional level

Background

Many people will experience neck pain in their lifetimes, and the lifetime prevalence estimates are as high as 67%. In the cervical spine, the shape and orientation of the joints are very different from those in the lumbar region. The C2–C3 joint is the most frequent pain source. The area of the greatest mobility in the cervical spine is at C5–C6, which is the second most affected cervical facet joint. The innervation of the cervical facets is varied. There are eight cervical nerve roots, which exist above the corresponding vertebral body. The C3–C4 through C7–T1 joints receive innervation from the medial branches at the same level and the level above. The majority of the innervation of the C2–C3 joint comes from the dorsal ramus of C3. The C3 dorsal ramus divides into two separate medial branches, the larger of which is known as the third occipital nerve. Pathology involving the branches of C2 and C3 dorsal rami is a common source of occipital headaches.

Indications

- Cervical spondylosis
- Postlaminectomy syndrome, cervical region
- Cervicalgia
- Cervicocranial syndrome
- Neck sprain and strain

Equipment/materials: fluoroscopy, 22- or 25-gauge 2.5–3.5 in. spinal needle, +/− contrast, local anesthetic, +/− corticosteroid

Procedure

Position: prone or lateral
IV: not required unless previous vagal episodes
Antibiotics: not required

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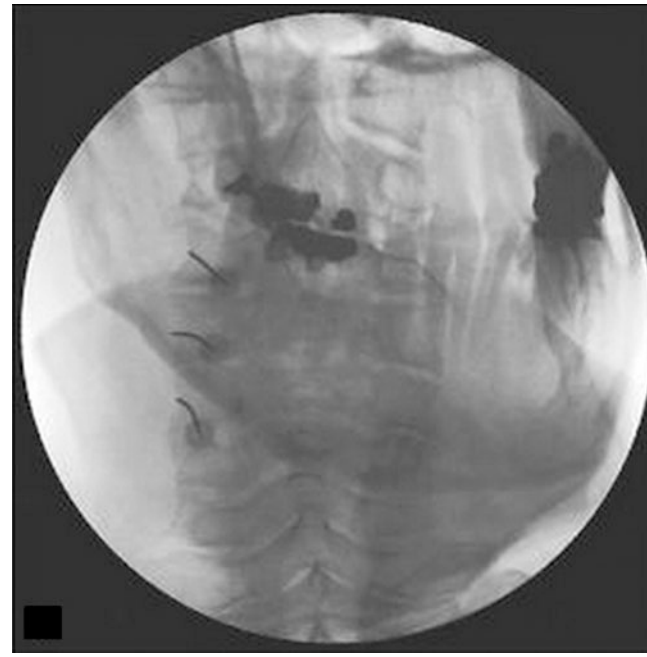

Fig. 63.1 Posterior approach

Steps

- The patient may be placed in a prone or lateral position.
- In both positions, the needle is inserted in the coaxial plane and advanced toward the facet target in the middle of the articular pillar, midway between superior and inferior articular surfaces of the vertebra.
- In the posterior approach, the needle is placed on the lateral margin of the facet column in the middle of the "scalloped waist" (Fig. 63.1).
- On the lateral position, the target is the trapezoid and the needle is advanced in the middle of the trapezoid (Fig. 63.2).
- The needle position is confirmed with both AP and lateral images.
- Once the needle is confirmed, 0.1–0.2 ml of contrast should be injected. 0.3–0.5 ml of local anesthetic (1 % lidocaine or 0.25 % bupivacaine) should be injected for diagnostic purposes.
- If steroid is used, consideration should be given for the use of non-particulate steroids due to the proximity to the vertebral artery in this technique.

Clinical Pearls

- The triad of axial neck pain, muscle spasms, and posterior headaches often points to cervical facet arthropathy as a major generator of pain.
- Diagnostic cervical medial branch blocks as a determination for candidacy of radiofrequency ablation should use low volumes (0.3 cc) to reduce confounding spread to adjacent structures.

Evidence

There is some literature to support the basis of cervical zygapophysial joint injections for chronic neck pain. In patients with chronic neck pain after whiplash, the prevalence of zygapophysial joint pain has been estimated to be over 50 %. Cervical medial branch blocks (MBB) have established utility. They are a great tool for diagnosing a common cause of chronic neck pain. Patients who are correctly diagnosed can benefit from percutaneous radiofrequency ablation of the affected nerves. McDonald et al. have

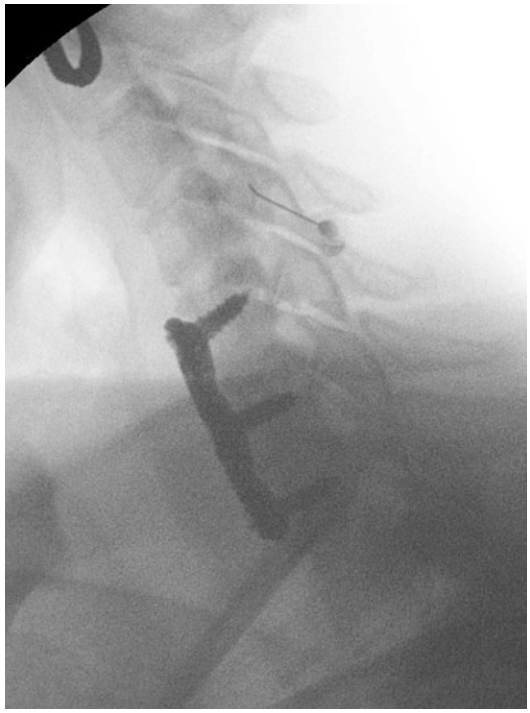

Fig. 63.2 Lateral approach

shown that patients who obtain complete relief from cervical medial branch blocks can expect a 70 % chance of achieving complete relief of their pain after cervical medial branch neurotomy [1]. Falco et al. performed a systematic review to evaluate the efficacy of cervical facet joint interventions in the relief of short-term and long-term pain, improvement in functional status, psychological status, return to work, and reduction in opioid intake. The authors found that the evidence for cervical radiofrequency neurotomy and cervical medial branch blocks is fair. The evidence for radiofrequency neurotomy is mostly based on one high-quality randomized trial (Lord et al.) and multiple moderate-quality observational studies [2, 3].

There are new studies that have evaluated the efficacy of ultrasound in cervical medial branch blocks. Finlayson et al. performed a randomized controlled trial in 50 patients undergoing C7 medial branch blocks. The patients were randomized to either fluoroscopy or ultrasound and the primary outcome was time of procedure. The authors found that US-guided C7 cervical MBBB resulted in significantly shorter performance time and fewer needle passes. While the preliminary data is encouraging, the safety and efficacy of US-guided cervical MBBs need to be further elucidated [4].

References

1. McDonald GJ, Lord SM, Bogduk N. Long-term follow-up of patients treated with cervical radiofrequency neurotomy for chronic neck pain. Neurosurgery. 1999;45(1):61–7. discussion 67–8.
2. Lord S, Barnsley L, Wallis B, McDonald G, Bogduk N. Percutaneous radio-frequency neurotomy for chronic cervical zygapophyseal-joint pain. N Engl J Med. 1996;335:1721–6.
3. Falco FJ, Manchikanti L, Datta S, Wargo BW, Geffert S, Bryce DA, Atluri S, Singh V, Benyamin RM, Sehgal N, Ward SP, Helm 2nd S, Gupta S, Boswell MV. Systematic review of the therapeutic effectiveness of cervical facet joint interventions: an update. Pain Physician. 2012;15(6):E839–68.
4. Finlayson RJ, Etheridge JP, Tiyaprasertkul W, Nelems B, de Tran QH. A randomized comparison between ultrasound- and fluoroscopy-guided c7 medial branch block. Reg Anesth Pain Med. 2015;40(1):52–7.

Thoracic Facet Pain/Medial Branch Blocks

64

Yi Cai Isaac Tong and R. Jason Yong

CPT Codes

64490: zygapophyseal joint (or nerves innervating that joint) with image guidance, cervical or thoracic; single level
64491: zygapophyseal joint, second level
64492: zygapophyseal joint, third and any additional level

Background

The prevalence of chronic upper or mid back pain secondary to thoracic disorders is relatively small. While the lifetime prevalence of spinal pain has been reported as occurring in 54–80 % of the general population, thoracic lower back pain may only account for 3–22 % [1]. The prevalence of mid back and upper back pain secondary to involvement of the facet joints has been reported in controlled studies in as many as 34–48 % of patients [2].

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Indications

- Thoracic spondylosis
- Degeneration of thoracic or thoracolumbar intervertebral disk
- Postlaminectomy syndrome, thoracic region
- Pain in thoracic spine

Equipment/materials: fluoroscopy, 22- or 25-gauge 3.5 inch spinal needle, +/− contrast, local anesthetic, +/− corticosteroid

Procedure

Position: prone
IV: not required unless previous vagal episodes
Antibiotics: not required

Steps

- The patient is placed in the prone position and prepped in the usual sterile fashion.
- A true AP view of the thoracic spine should be obtained with fluoroscopy.
- The needle tip should be placed at the superior

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lateral edge of the transverse process, where each medial branch is located as it travels around the inter-transverse ligament before it continues medially toward the cephalad neuroforamina.

- The medial branch nerves are not labeled for the transverse process they transverse, but from the originating somatic nerves. For example, T9 medial branch crosses the superior lateral edge of the T10 transverse process.
- The T1–T10 levels are injected in the manner described above.
- T11–T12 are injected with the use of the landmarks for lumbar medial branch nerves.
- Once the needle approaches the superior lateral edge of the transverse process in the AP view, a lateral image should be obtained to assess depth.
- Contrast is injected with continuous fluoroscopy in the AP and lateral view to assess of vascular uptake.
- Once the physician is satisfied with the position of the needle, the injectate can be administered.

See Fig. 64.1.

Clinical Pearls

- Progressing down from T1 to T10, the medial branches lay in an increasingly medial along the transverse process.
- Small volumes should be used if the block is used to assess candidacy for radiofrequency ablation.

Evidence

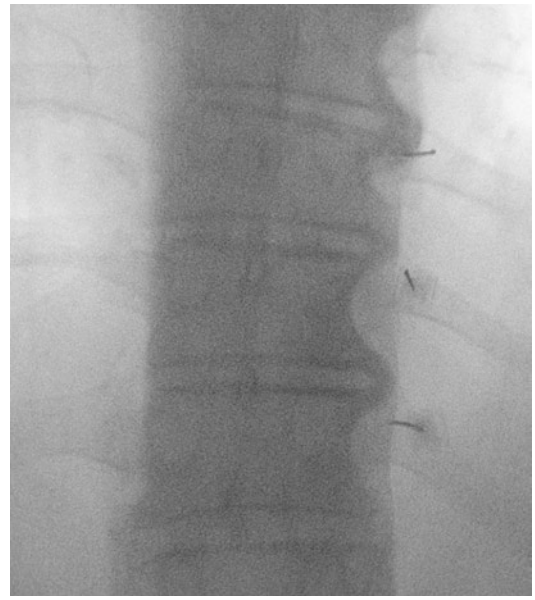

Fig. 64.1 AP view of thoracic facet injection

Manchikanti et al. conducted a systematic review of all articles published from 1966 to March 2012 [1]. The review noted that there was fair evidence for therapeutic thoracic facet joint nerve blocks and limited for thoracic radiofrequency neurotomy.

References

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2. Manchikanti L, Boswell MV, Singh V, Pampati VS, Damron KS, Beyer CD. Prevalence of facet joint pain in chronic spinal pain of cervical, thoracic, and lumbar regions. BMC Musculoskelet Disord. 2004;5:15.

Lumbar Facet Block

65

M. Alice Vijjeswarapu and Edgar L. Ross

CPT: *Facet Joint L-S Single Level with X-ray guidance (Left, Right, Bilateral)*: *64493*
Facet Joint L-S Single 2nd Level (Left, Right, Bilateral): *64494*
Facet Joint Joint, L-S 3+ Levels (Left, Right, Bilateral): *64495*

Indications

Facet arthropathy, traumatic or nontraumatic non-radicular low back pain, and pain worsened by facet joint loading on exam (extension and rotation). Injections can be diagnostic or therapeutic.

Contraindications

Unable to consent patient, allergies to drugs used, ongoing local or systemic infection, pregnancy, and anticoagulation

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Anatomy

Synovial joints are formed by the inferior and superior articular processes of the superior and inferior lumbar vertebra, respectively. A facet joint receives dual innervation from the dorsal rami of the vertebral body above and below it via medial branches.

Equipment/Materials

Fluoroscopy, 22–25-gauge 3.5 in. spinal needle (adjusted for body habitus), +/− radioopaque contrast, local anesthetic, +/− corticosteroid

Procedure

Position: most commonly prone +/− towel roll under belly. Alternatively, slightly obliquely by ~45° with the side to be injected up
IV: not required unless previous vagal episodes
Antibiotics: not required

Steps

1. Start with AP view and center the spinous processes between the pedicles. You can locate the appropriate level by counting up from the sacrum.

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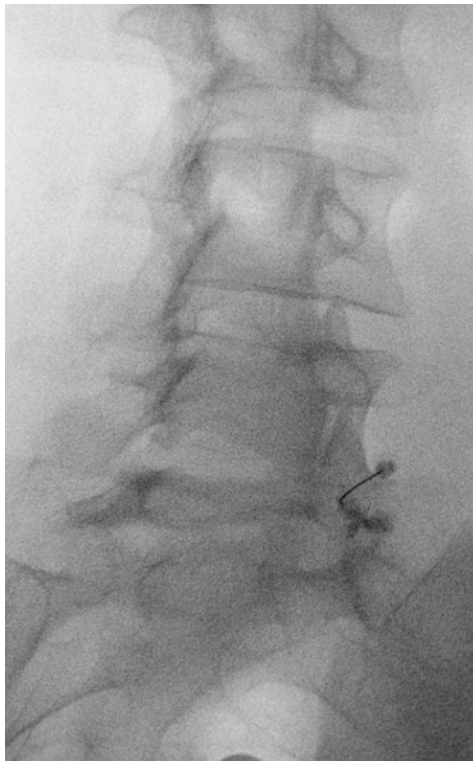

Fig. 65.1 Image of needle at the pedicle

2. Rotate to obtain the oblique view with target facet joint fully visible. Adjust your angle until you can appreciate the "scotty dog" view (about 20–30°).
3. Once the target joint is located, mark its corresponding point on the skin and sterilize the area. Administer superficial local anesthetic infiltration to the target area.
4. Insert the spinal needle downward in line with the fluoroscopy beam (coaxially) under direct visualization.
5. Under continued visualization, slowly maneuver the spinal needle until it contacts the bony "eye of the scotty dog" landmark at the target joint. The needle is now at the pedicle of the desired joint level. Do not advance further (Fig. 65.1).
6. Confirm depth in the lateral fluoroscopic view to ensure that the needle tip does not extend into the vertebral foramen at the corresponding vertebral body.
7. Confirm location in the anterior-posterior fluoroscopic view to ensure that the needle tip is medial to the lateral aspect of the superior articular process at the corresponding vertebrae.
8. After confirmation, local anesthetic +/− steroid component is injected into the correctly identified area.
9. Since each joint has dual innervation, steps 3–7 are repeated at a level above and below the desired level to ensure adequate block of the affected joint. For the L5–S1 facet joint, the lower block should be placed at the superior articular process of the sacrum and the sacral ala (Fig. 65.2).

Complications

Complications with this procedure are largely uncommon. Minor complications include, but are not limited to, lightheadedness, nausea, syncope, flushing, headache, local swelling, and pain. More serious complications include dural puncture, spinal cord trauma, subdural or epidural injection, and intravertebral foramen injection. There is also a risk of intravascular injection, epidural hematoma, epidural abscess, and bacterial meningitis. Good aseptic technique and adherence to ASRA guidelines on neuraxial procedures should be always practiced. Complications can also result from systemic effects of corticosteroids including pituitary-adrenal axis depression, hyperglycemia, osteoporosis, myopathy, weight gain, and Cushing syndrome, among others.

Clinical Pearls

When optimizing the fluoroscopic view of the target facet joint, the upper lumbar regions may be visible on AP view due to the orientation of these joints. However, the lower facet joints can usually only be visualized in the oblique view.

Some practitioners choose to use 0.2–0.25 mL of radioopaque contrast under low pressure to

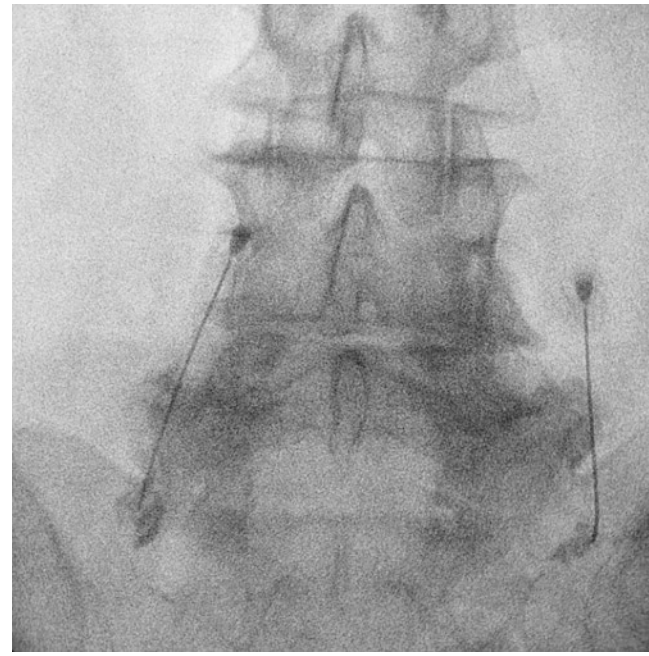

Fig. 65.2 L5–S1 lower level block at the superior articular process of the sacrum and the sacral ala

confirm that the needle has not punctured epidural, intrathecal, or intravascular space.

There is no consensus on injectate. Volumes and choice of local anesthetics and corticosteroid vary widely. We typically use 0.25–0.50 mL of local anesthetic (0.25 % bupivacaine) mixed with 0.25–0.50 mL of corticosteroid (total 80 mg of methylprednisolone divided equally) for each joint and adjusting for patient variability.

Evidence

Lumbar Facet Joint Injection vs. Lumbar Medial Branch Block

Lumbar medial branch blocks are largely preferred by clinicians over lumbar facet joint injections for diagnostic purposes given technical simplicity and correlation with long-term relief from lumbar medial branch radiofrequency ablation. Lumbar medial branch blocks are also preferred over lumbar facet injections because of improved therapeutic value. However, evidence comparing the two techniques is lacking.

Pre-procedural SPECT imaging has been shown to identify patients that would benefit from facet joint injections.

Suggested Readings

Patel VB, Data S. Chapter 23: Facet Joint Interventions: intraarticular injections, medial branch blocks, and radio frequency ablations. In: Atlas of Pain Medicine Procedures. McGraw-Hill Education. 2015.

Lamer TJ. Chapter 67: Intra-articular injections and facet blocks. In: Principles & practice of pain medicine, 2nd ed.

Pneumaticos SG, et al. Low back prediction of short-term outcome of facet joint injection with bone scintigraphy. Radiology. 2006;238(2):693–8.

Lumbar Medial Branch Radiofrequency Lesioning

66

Yi Cai Isaac Tong and R. Jason Yong

CPT Code

Destruction by neurolytic agent. The term neurolytic agent includes chemical, thermal, electrical, or RF methods. CPT assignments for paravertebral facet RF ablations are the following:
64635: destruction by neurolytic agent paravertebral facet joint nerve(s) with imaging guidance, lumbar or sacral, single facet joint
64636: additional facet joint: lumbar or sacral

Indications

- Significant pain relief documented after either an intra-articular zygapophysial joint or a medial branch block injection.

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Equipment/materials: fluoroscopy, radiofrequency (RF) generator, RF electrodes, RF needles, grounding pad with cable, +/− contrast, local anesthetic.

Steps

1. Prep area with chlorohexanol or Betadine and drape in sterile fashion.
2. Place the grounding pad on the patient. Ensure good contract with patient's skin.
3. Maneuver the C-arm image intensifier to square off the superior end plate and then tilt the C arm 15–20° caudally.
4. Oblique the C-arm image intensifier 15° toward the procedural side
5. The RF needle tip be placed at the junction of the transverse process and the lateral border of the SAP.
6. Tip: At L5, the iliac crest may impede proper needle positioning. The tilt angle should be adjusted accordingly.
7. Once the RF needle is in the correct position, an ipsilateral oblique, lateral, and anteroposterior view (with superior endplate squared off) should be obtained.
8. The ipsilateral oblique view should be used to confirm that the probe is not beyond the superolateral edge of the SAP to avoid lesioning the dorsal root or ventral roots. See Fig. 66.1.

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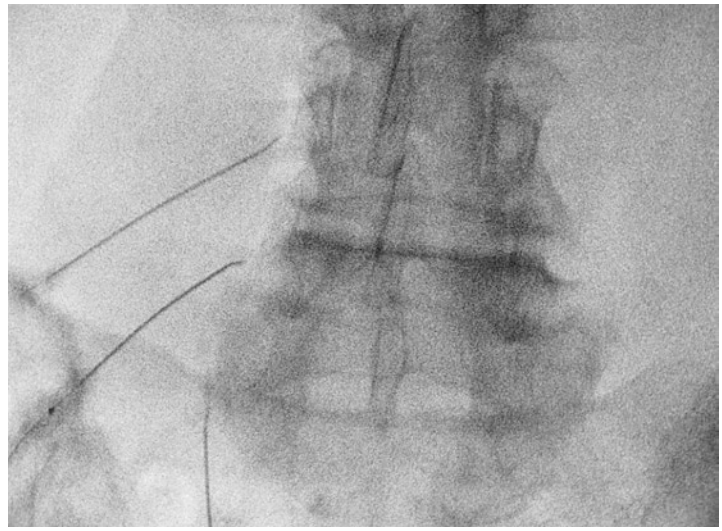

Fig. 66.1 Example of unilateral lumbar radiofrequency lesioning

9. One should always reposition the RF electrode if the patient reports paresthesia or pain into the lower limb during the placement, stimulation, or neurotomy.
10. Sensory stimulation is usually performed prior to denervation. Most recommend a threshold of no more than 0.6 V.
11. Motor stimulation is considered a safety measure to ensure adequate distance from motor fibers. Motor stimulator can elicit the contraction of the multifidus muscles.
12. Approximately 1 cc of local anesthetic (Lidocaine 1.5 % or 2 %) should be injected prior to RF denervation.
13. Commonly 80 °C for 1.5–2 min is used for ablation.
14. In some studies, patient has been noted to receive significant pain relief for 6 months–1 year.

Clinical Pearls

- Prior to ablation, at least two rounds of medial branch blocks with low volumes (0.3 cc) should be performed to determine likelihood of response to ablation.
- Tilting the fluoroscopy image intensifier 15° caudal from the angle where the superior end plate of the targeted level is squared off ensures a caudal to cephalad approach to lie within the SAP-transverse process groove.

Evidence

There is good data to support the use of RF in the management of chronic lower back pain. MacVicar et al. published a prospective outcome study to determine the effectiveness of lumbar medial branch radiofrequency neurotomy in a community setting. A total of 106 patients were selected to receive RFN after complete relief of pain following diagnostic medial branch blocks. Successful outcome was defined as complete relief of pain for at least 6 months. The study found that over 53–58 % of patients achieved a successful outcome. The study found that after repeated treatment, patient maintained relief for a median duration of 17–33 months. The study concluded that lumbar RFN could be very effective in the treatment of chronic lower back pain [1].

In 2012, Smuck and colleagues addressed the question of effectiveness of repeated RFN for zygapophysial joint pain. In their systematic review, 17 articles were reviewed. There were nine cervical studies, of which six were prospective and three were retrospective. There were eight lumbar studies, of which four were

prospective and four were retrospective. The authors found that the average duration of greater than 50 % pain relief for cervical RFN was 77.3–8.6 months. Repeated cervical RFN was successfully 67–97 % of the time. The average duration of >50 % relief of lumbar RFN was 9 months. The average duration of pain relief after successful repeated lumbar RFN was 11.6 months [2].

Falco et al. performed a systemic review of therapeutic lumbar facet joint interventions in managing chronic lower back pain. The review looked at 112 studies and found seven lumbar facet joint RFN RCTs. RCTs were assessed using a version of the Cochrane risk of bias tool. Six out the seven RCTs showed positive results. The reviewers concluded that the evidence for radiofrequency neurotomy is good for lumbar facet joint pain for short and long-term improvement [3].

References

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2. Schofferman J, Kine G. Effectiveness of repeated radiofrequency neurotomy for lumbar facet pain. Spine (Phila Pa 1976). 2004;29(21):2471–3.
3. Falco FJ, Manchikanti L, Datta S, Sehgal N, Geffert S, Onyewu O, et al. An update of the effectiveness of therapeutic lumbar facet joint interventions. Pain Physician. 2012;15(6):E909–53.

Sacroiliac Joint Injection

67

Yi Cai Isaac Tong and R. Jason Yong

CPT Codes

27096: injection procedure for sacroiliac joint, arthrography, and/or anesthetic/steroid

Background

The sacroiliac joint is a large diarthrodial synovial joint supported by many muscles and fascial layers. These structures include the gluteus maximus and medius, biceps femoris, piriformis, and the latissimus dorsi via the thoracolumbar fascia. The joint's primary role is to provide stability and weight bearing. The SI joint is innervated by many sources. The posterior joint and surrounding ligaments appear to receive innervation from the S1–S3 dorsal rami and contribution from L5. One recent study suggests that the SI joint also receives afferent input from S4 [1]. There are many etiologies for SI joint pain. The causes can be divided into intra- and extra-articular sources. Arthritis and infections are two common causes of intra-articular pain. Extra-articular causes may include fracture, enthesopathy, ligamentous injury, and myofascial pain. Numerous factors can contribute to SI joint pain. Risk factors include obesity, leg length discrepancy, gait abnormalities, persistent strain or low grad trauma, scoliosis, and pregnancy. Spine surgery may also increase load bearing and resulting SI joint pain.

Pain Distribution

There are several provocative tests that have been advocated as screening tools for SI joint pain, but several studies have shown that these tests lack both specificity and high sensitivity. There are no pathognomonic radiation patterns for pain from the SI joint. The pain may radiate from the buttock to the ipsilateral thigh, groin, lumbar region, or posterior thigh and leg.

Equipment/materials: fluoroscopy, 22 or 25 gauge 3.5 in. spinal needle, +/− contrast, local anesthetic, +/− corticosteroid

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Procedure

- Position: prone
- IV: not required unless previous vagal episodes
- Antibiotics: not required

Steps

- The patient is placed in the prone position and care is taken to pad all pressure points.
- The lumbosacral area is prepped in the usual sterile fashion.
- The fluoroscope is used to image the SI joint in the AP view. Consider tilting the fluoroscopy cephalad approximately 10–15° to improve the lucency of the posterior plane of the joint.
- Obliquing the C arm may also aid in the optimal view of the posterior SIJ opening.
- A 22-gauge, 3½- or 5-in. (depending on patient size) straight or 10°-curved-tip spinal needle is advanced toward the posterior SI joint.
- As the needle contacts firm tissue on the posterior aspect of the joint, the needle is maneuvered through the ligaments and capsule into the joint by advancing it about 5–10 mm.
- A lateral image should be obtained to ensure that the needle has not been advanced too far ventrally.
- Intra-articular position is confirmed by injecting 0.2–0.5 mL of contrast material.
- Contrast should be visualized outlining the medial and lateral aspects of the SIJ.
- If resistance to injection is encountered, rotation of the needle and withdrawing or advancing the needle 1–2 mm should be considered.
- 2 ml of local anesthetic and steroid should be injected after confirmation of the joint space with contrast.

See Fig. 67.1.

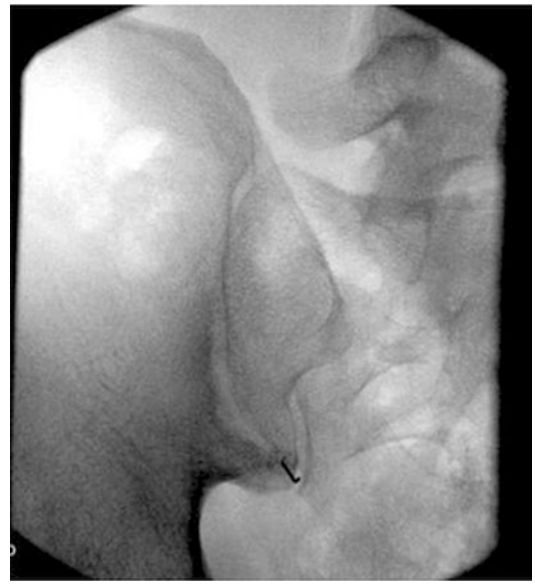

Fig. 67.1 SI joint injection

Evidence

In a systematic review of literature, Rupert et al. looked at all articles related to diagnostic and therapeutic sacroiliac joint interventions between 1966 and 2008. The authors' objective was to evaluate the accuracy of diagnostic sacroiliac joint interventions and the utility of therapeutic sacroiliac joint interventions, and their primary outcome was at least 50 % pain relief coupled with a patient's ability to perform previously painful maneuvers with sustained relief. Based on this systematic review, five studies supported the diagnostic accuracy of sacroiliac joint injections with level II evidence [2]. Simopoulos et al. confirmed this finding again in 2012 in a systematic review. The authors found good evidence supporting the use of diagnostic SI joint injections [3].

There is some debate on whether intra-articular injections are more advantageous than periarticular injections. Patients may exhibit either intra- or extra-articular SI pathology, but no reliable physical exam or tests are available to distinguish between the two. Murakami et al. performed a prospective study comparing intra-articular vs. periarticular injections. The authors found that the periarticular injections effectively relieved pain in all 25 patients, but intra-articular injection was effective in only nine of 25 patients. All 16 patients in the intra-articular group who failed to respond to the initial injection

experienced significant relief after they received an injection using the periarticular approach. Overall, the 96 % improvement rate after the periarticular injection was significantly higher than the 62 % [4].

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2. Rupert MP, Lee M, Manchikanti L, Datta S, Cohen SP. Evaluation of sacroiliac joint interventions: a systematic appraisal of the literature. Pain Physician. 2009;12(2):399–418.
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Sacroiliac Joint Pain/ L5 Dorsal Ramus and S1–S3 Lateral Branch Radiofrequency Ablation

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CPT Code

Radiofrequency ablation (RFA) of the sacroiliac joint
64635: RF of L5 dorsal primary ramus
64640: RF of S1 lateral branches
64640: RF of S2 lateral branches
64640: RF of S3 lateral branches

Background

Radiofrequency ablation of the L5 dorsal primary ramus and lateral branches of the posterior primary rami of the sacral nerve roots S1–S3 should be considered for patients who receive only temporary relief from intra-articular SI joint injections.

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Procedure

- Position: prone
- IV: not required unless previous vagal episodes
- Antibiotics: not required

Equipment/materials: fluoroscopy, radiofrequency (RF) generator, RF electrodes, RF needles, grounding pad with cable, +/− contrast, local anesthetic.

Steps for L5 dorsal ramus and S1–S3 lateral branch radiofrequency ablation

- The patient is placed in the prone position and care is taken to pad all pressure points.
- The lumbosacral area is prepped in the usual sterile fashion.
- The targets are dorsal ramus of L5 and lateral branches of S1–S3.
- Tip: avoid lesioning dorsal ramus at the foramen to minimize the risk of cutaneous dysesthesias.
- Obtain an anterior-posterior fluoroscopic image by aligning the L5-S1 vertebral end plates.
- The S1–S3 posterior sacral foramina should be identifiable. If not, the image can be rotated 10–15° in the ipsilateral direction to better

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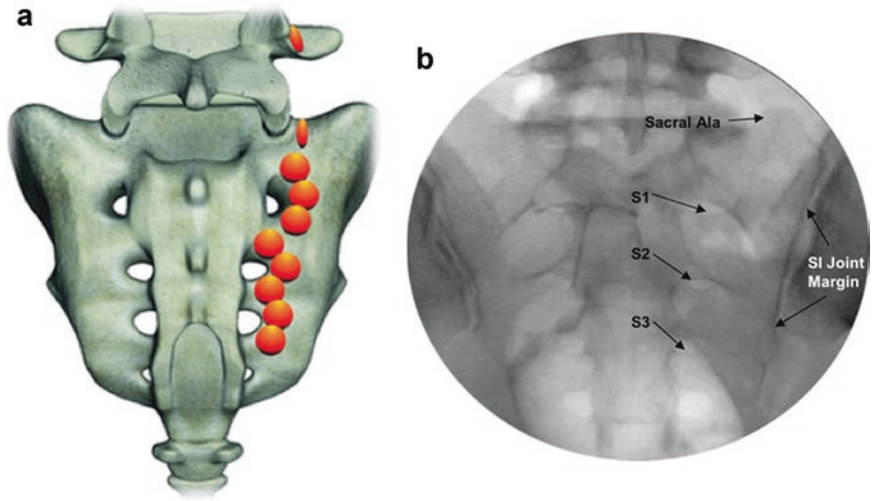

Fig. 68.1 (**a**) and (**b**) Targets

visualize the posterior sacral foramina.

- RF needles should be positioned in the lateral arc around each dorsal sacral aperture.
- Temperatures used for ablation vary from 60 to 80 °C and times vary from 2 to 3 min per lesion.
- Remove RF probe, replace stylet, redirect to next target, and repeat. Only one skin entry site for each sacral level.

See Fig. 68.1a, b.

Evidence

The first literature supporting the use of cooled radiofrequency system is in 2008 by Kapural et al. In a case series 27 patients with chronic low back pain who underwent cooled RF of S1–S3 lateral branches and of dorsal ramus L5 following two diagnostic SI joint blocks (>50 % of pain relief) were followed. The case report showed that after cooled RF, the majority of patients with chronic SI joint pain experienced a clinically relevant degree of pain relief and improved function at 3–4-month follow-up. The VAS pain scores fell from 7.1 to 4.2 3–4-months post procedure [1].

In 2008, Cohen et al. conducted a randomized placebo-controlled study conducted in 28 patients with sacroiliac joint pain. Fourteen patients received L4-L5 primary dorsal rami and S1–S3 lateral branch radiofrequency denervation using cooling-probe technology after a local anesthetic block, and 14 patients received the local anesthetic block followed by placebo denervation. The results were very promising. One month post procedure, 79 % of patients who received radiofrequency treatments had over 50 % relief in their pain. Only 14 % of patient who received the placebo received relief after the first month. 57 % of patient had sustained relief at 6 months after receiving L4-L5 primary dorsal rami and S1 -S3 lateral branch radiofrequency denervation [2].

In 2013, Stelzer et al. confirmed prior reports of the efficacy of cooled RF to treat SIJ-mediated lower back pain. The authors preformed a retrospective case series of 126 patients with chronic low back pain who underwent treatment with cooled RF. Cooled RF LBN involved lesioning the L5 dorsal ramus and lateral to the S1–S3 posterior sacral foraminal apertures. Visual analog scale (VAS) pain scores, quality of life, medication usage, and satisfaction were collected, recorded, and analyzed before the procedure, at

3–4 weeks post procedure, and once again between 4 and 20 months post procedure. The authors found that 86 % of patients reported over 50 % pain relief on the VAS pain score 4–6 months post procedure. The study also noted that 100 % of patients stopped or decreased their opioids 4–6 months after the procedure [3].

The evidence supporting SIJ radiofrequency ablation is good, and this technique should be considered for patients who receive only temporary relief from intra-articular or Dreyfuss SI joint injections.

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Lumbar, Thoracic, and Cervical Discography

69

Michael P. Zaccagnino and Srdjan S. Nedeljkovic

CPT

- **62290:** Injection procedure for discography, each level, *lumbar*
- **62291:** Injection procedure for discography, each level, *cervical or thoracic*
- **72285:** Radiological supervision and interpretation of discography, each level, *cervical or thoracic*
- **72295:** Radiological supervision and interpretation of discography, each level, *lumbar*

Note: Bill for *each discogram* level and *each radiological interpretation* level (make sure to add the −51 modifier to each). Also, make sure to bill for the radiopaque contrast (J-codes) and for sedation if given.

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Indication

1. To evaluate a diagnosis for patients with persistent (>3 months) neuraxial or cervical, thoracic, lumbar radicular pain when diagnostic imaging modalities are inconclusive
2. To evaluate if a patient's pain complaints are concordant with diagnostic image findings
3. To identify which vertebral levels might benefit from further intervention

Contraindications

- Patient is unwilling or unable to consent for procedure.
- Patient is unable to communicate appropriate responses to the procedure.
- Localized or systemic infection.
- Pregnancy.
- Anticoagulant therapy or bleeding diathesis.
- Allergy to radiographic contrast or local anesthetic.
- Anatomic derangements that would compromise a safe and effective procedure.

Complications

- Discitis
- Disc damage and progression of disc degeneration

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- Worsening back pain
- Meningitis
- Spinal headache
- Subdural or epidural abscess
- Intrathecal or retroperitoneal hemorrhage
- Arachnoiditis
- Nerve root injury
- Paravertebral muscle contusion
- Vasovagal reactions
- Allergic reactions

Equipment/Materials

General

Fluoroscopy with compatible procedural table; 8- to 12-inch radiopaque pointer and marking pen; contrast dye; local anesthetics; +/− antibiotics; +/− procedural sedation (midazolam, +/− small doses of fentanyl)

Lumbar Discography

180 or 240 mg/ml iohexol contrast dye; 5-ml syringe fitted with extension tubing

Dual-needle technique: 18-gauge 1.5-inch skin puncture needle; 18-gauge 1.5-inch introducer needle; 22-gauge 5- or 7-inch disc puncture needle

S*ingle-needle technique*: 22-gauge 5- or 7-inch disc puncture needle

Thoracic Discography

180 or 240 mg/ml iohexol contrast dye; 3-ml syringe fitted with extension tubing; 22-gauge 3.5- or 5-inch disc puncture needle

Cervical Discography

240 mg/ml iohexol contrast dye (preferred for better contrast visualization); 3-ml syringe fitted with extension tubing; 22-gauge 3.5-inch disc puncture needle

Procedure

Position: prone (lumbar/thoracic); supine (cervical)
IV Access: +/−

- Recommended for discography
- Necessary for IV antibiotics or sedation

Antibiotics: +/−

- Intravenous (IV) antibiotics—cefazolin 1 g 15–30 min prior to needle insertion
- Intradiscal (ID) antibiotics—cefazolin (1 mg/ml of contrast) or clindamycin (6–7.5 mg/ml of contrast)

Steps for Lumbar Discography

General

(1) Identify the targeted disc(s) in AP view, and then using cephalocaudal motion, square the superior subchondral end plate of the vertebral body caudal to the chosen disc.
(2) Rotate the C-arm oblique to the contralateral side of the patient's predominant pain until the superior articular process (SAP) of the level below appears to transect the midpoint of the inferior end plate of the level above.
(3) Once the contralateral oblique view is obtained, locate the disc entry site—just lateral to the SAP and over the midportion of the cranial-caudal aspect of the targeted disc (Fig. 69.1a).

Dual Needle Technique

(a) After local anesthetic infiltration, the introducer needle is advanced using tunnel vision through the anesthetic track toward the disc entry site (just lateral to the SAP).
(b) Position the C-arm in lateral view with end plates squared (Fig. 69.1b), and using active lateral fluoroscopy, advance the disc puncture needle through the introducer needle toward the intervertebral disc (slight increased resistance is felt at the disc annulus), penetrate the annulus, maneuver into the center of the

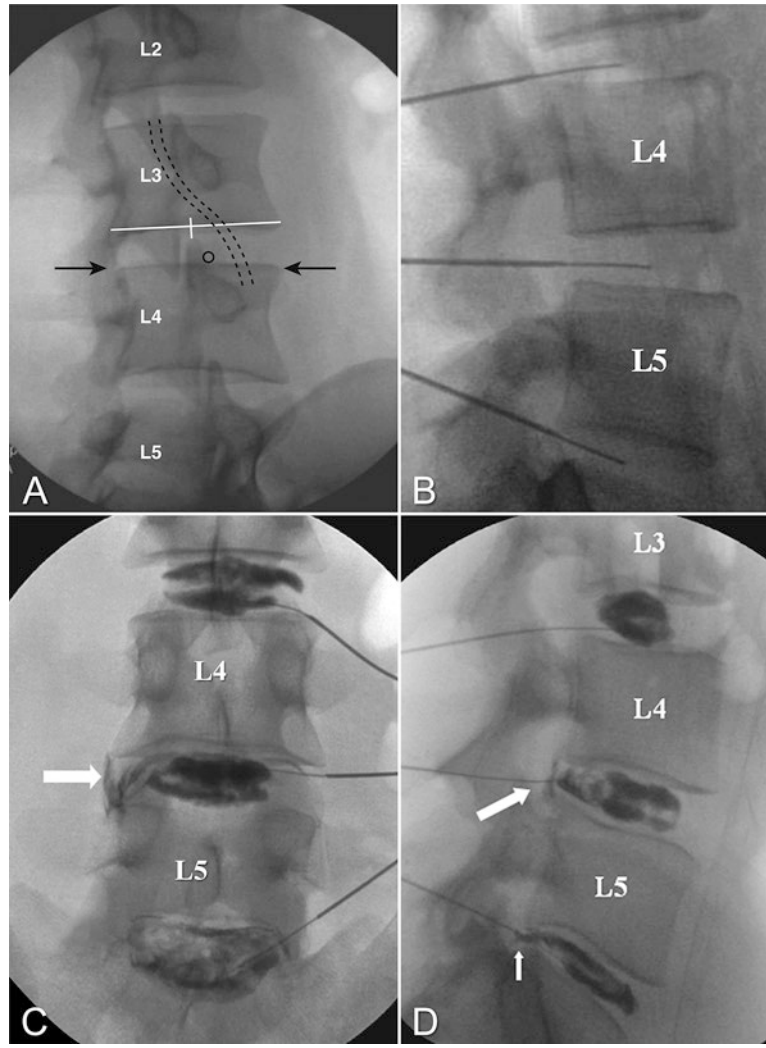

Fig. 69.1 (**a**) Lumbar spine right oblique view. The superior end plate of L4 is parallel to x-ray beam (*arrows*). The SAP of L4 appears under the midpoint of the L3 inferior end plate. (*Circle* indicates target. *Dashed black lines* represent the L3 ventral ramus.) (**b**) Lateral view of lumbar spine. Using active lateral fluoroscopy, needles are advanced into the center of each disc pulposus. (**c** and **d**) Postinjection AP and lateral views, respectively. L3–L4 shows no evidence of annular disruption; however, L4–L5 and L5–S1 reveal significant disruption of disc architecture (*arrows*). Image A reprinted from *Pain Procedures in Clinical Practice.* 3rd Edition, Lennard TA, Walkowski S, Singla AK, Vivian DG (Eds). Discography, Vivian DG, Landers MH, pp 407–440, 2011, with permission from Elsevier. Images B-D used with permission from [1]

intervertebral disc (i.e., nucleus pulposus), and then verify position in AP view.

Single-Needle Technique

(a) After local anesthetic infiltration, the disc puncture needle is advanced using tunnel vision with intermittent fluoroscopy toward the disc entry site (just lateral to the SAP); advancement is halted once the disc annulus is contacted (slight increased resistance).

(b) Position the C-arm in lateral view (Fig. 69.1b) with end plates squared, and under active lateral fluoroscopy, maneuver the disc puncture needle through the annulus and into the center of the disc pulposus, and then verify position in AP view.

(4) Once the disc puncture needle is within the disc pulposus, disc stimulation can proceed (Fig. 69.1c, d)—depending on preference, choose AP or lateral view and square the end plates, and then using active fluoroscopy, inject contrast in 0.5-ml aliquots and observe disc architecture; injection proceeds until one of the following endpoints is reached (for positive discogenic pain criteria, see section below):

(a) Significant pain is produced (≥5/10).

(b) Volume of contrast injected is >3.5 ml.

(c) Significant extradiscal extravasation of contrast is noted.

(5) Save final images in both AP and lateral views and document data—at a minimum, the pain level, concordance of stimulated pain with usual pain, volume of injectate, the estimated pressure endpoint generated (soft or firm) with the syringe, and description of contrast pattern (disc architecture and extravasation of contrast).

Steps for Thoracic Discography

(1) Identify the targeted disc(s) in AP view, and then using cephalocaudal motion, square the end plates surrounding the chosen disc.

(2) Rotate the C-arm obliquely to the contralateral side of the patient's predominant pain, while following the infrasegmental pedicle and rib head, cross the vertebral body until the hyperlucent "magic box," or disc entry site, appears—bordered cephalocaudally by the superior and inferior end plates, respectively, bordered medially by the pedicle, and bordered laterally by the rib head (Fig. 69.2a).

(3) After local anesthetic infiltration, the disc puncture needle is advanced using tunnel vision with intermittent fluoroscopy toward the disc entry site; advancement is halted once the disc annulus is contacted (slight increased resistance).

(4) Now position the C-arm in lateral view with end plates squared, and using active lateral

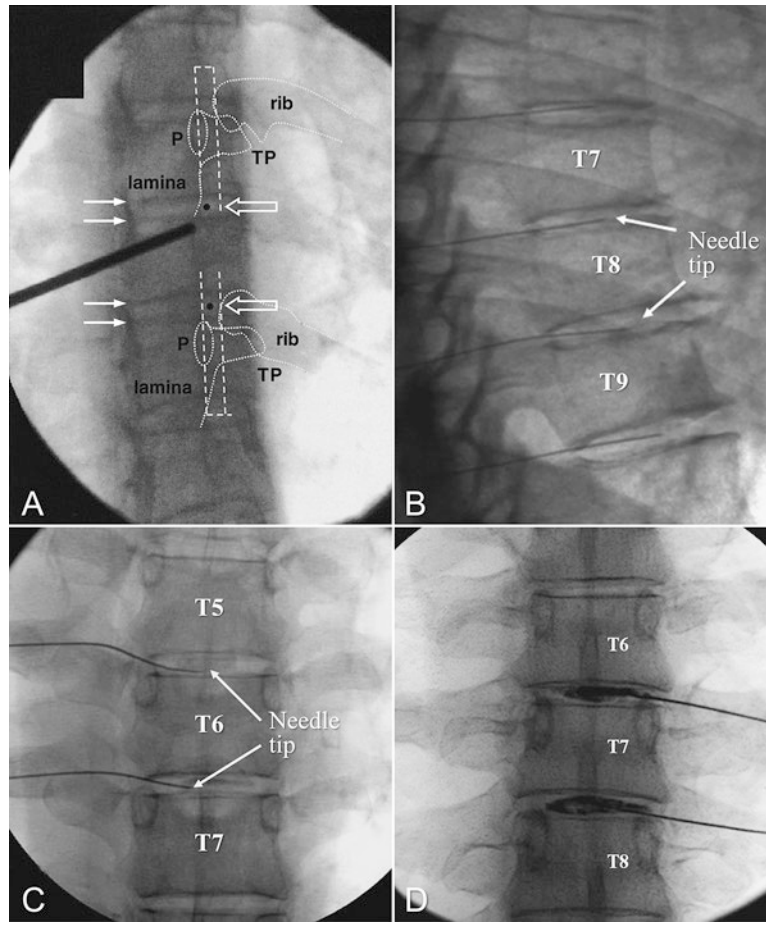

Fig. 69.2 (**a**) Right oblique view midthoracic spine. Disc end plates are squared (*solid arrows*). *Open arrow* points to target "box." (*P* pedicle, *TP* transverse process). (**b** and **c**) Lateral and AP views of thoracic spine, respectively. Needles have been advanced into the center of each disc pulposus. (**d**) Postinjection AP view of thoracic spine. Image A used with permission from [2]. Images **b**–**d** used with permission from [1]

fluoroscopy, maneuver the disc puncture needle through the annulus and into the center of the disc pulposus, and then verify position in AP view (Fig. 69.2b, c).

(5) Once the disc puncture needle is within the disc pulposus, disc stimulation can proceed—using active lateral fluoroscopy, inject contrast in 0.5-ml aliquots and observe disc architecture (Fig. 69.2d); injection proceeds until one of the following endpoints is reached (for positive discogenic pain criteria, see section below):
   a. Significant pain is produced (≥5/10).
   b. Volume of contrast injected ranges from 0.5 to 2.5 ml, depending on location (more rostral discs accept less volume).
   c. Significant extradiscal extravasation of contrast is noted.

(6) Save final images in both AP and lateral views, and document data as described above in the lumbar discography section.

Steps for Cervical Discography

(1) Place the patient in supine position with a pillow under the shoulders for neck extension, and rotate the head slightly to the left (needle insertion is always from the right as to avoid the esophagus).

(2) Identify the targeted disc(s) in foraminal view—fluoroscopy is obliqued until the foramina are seen at their widest extent in both the cephalocaudal and ventral-dorsal dimensions—and then using cephalocaudal motion, square the end plates surrounding the chosen disc (Fig. 69.3a).

(3) Identify the disc entry site—approximately one third the distance between the uncinate process and the ventral disc margin (Fig. 69.3a, b).

(4) Apply pressure over the skin insertion site (along medial border of sternocleidomastoid) to decrease the distance between the skin and disc and remove vulnerable soft tissue structures away from the needle track.

(5) After local anesthetic infiltration, ask the patient to refrain from vocalization, swallowing, or coughing, and then using active fluoroscopy, carefully maneuver the disc puncture needle toward the disc entry site, and advancement is halted once contact is made within the disc annulus (Fig. 69.3b).

(6) Now position the C-arm in lateral view with end plates squared, and using active lateral fluoroscopy, maneuver the disc puncture needle through the annulus and into the center of the disc pulposus, and then verify position in AP view.

(7) Once the disc puncture needle is within the disc pulposus, disc stimulation can proceed—using active lateral fluoroscopy, inject contrast and observe disc architecture (Fig. 69.3c, d), often as little as 0.2 ml may produce pain; injection proceeds until one of the following endpoints are reached (for positive discogenic pain criteria, see section below):
   a. Significant pain is produced (≥5/10).
   b. Neurologic symptoms experienced.
   c. Significant extradiscal extravasation of contrast is noted.
   d. Firm resistance to injection.

(8) Save final images in both AP and lateral views and document data as described above in the lumbar discography section.

Positive Discogenic Pain Criteria

Lumbar Discography

- Concordance of pain at a VAS of ≥5/10.
- Negative anatomic internal control level.
- Pain is noted at minimal pressure upon the syringe during injection.
- Pain occurs with a volume of contrast <1.5 ml.
- Internal disc disruption may be confirmed by a post-procedure CT scan, with a radial fissure to the outer third of the annulus (i.e., a grade 3 or higher lesion).

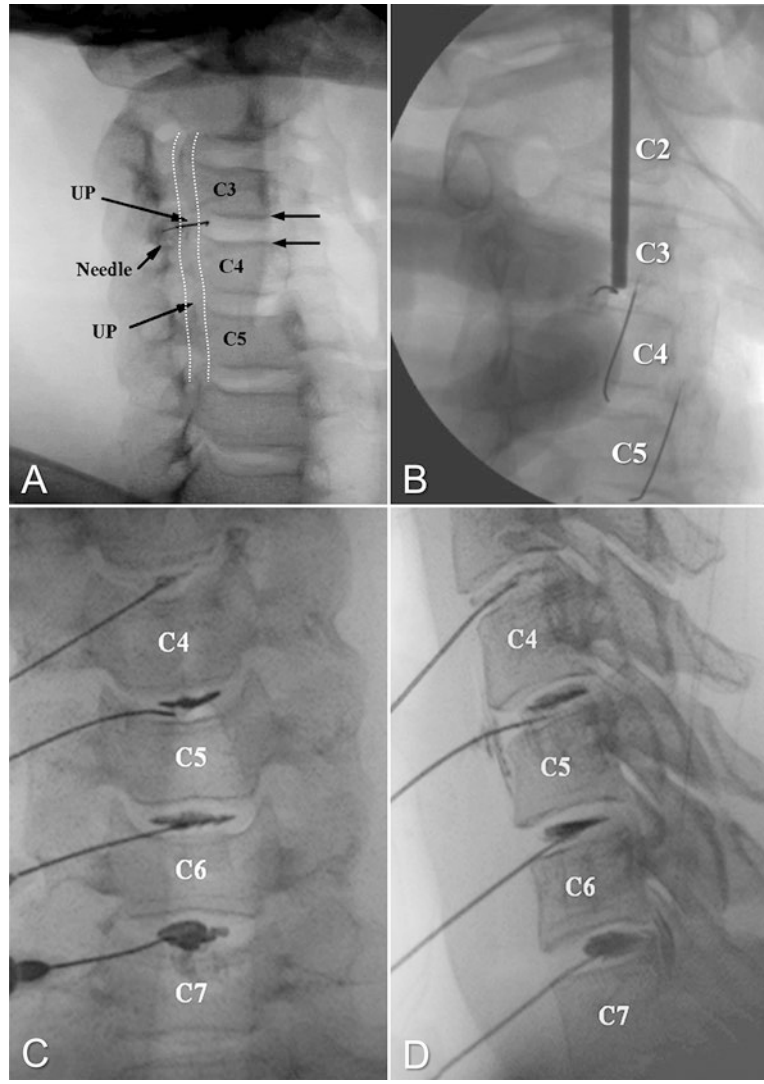

Fig. 69.3 (**a**) Foraminal view of the cervical spine. Note inferior end plate of C3 and superior end plate of C4 are squared. *Light dashed lines* represent the position of the vertebral artery. (*UP* uncinate process). (**b**) Foraminal view of the cervical spine with needles already placed in the C4, C5 and C5, C6 disc pulposus. Blunt instrument tip is marking the skin entry site for the C3 and C4 disc. While applying pressure, and using active fluoroscopy, the needle is carefully advanced into the disc. (**c** and **d**) Postinjection AP and lateral views of the cervical spine, respectively. Images **a**, **c**, and **d** used with permission from [1]. Image B reprinted from *Pain Procedures in Clinical Practice.* 3rd Edition, Lennard TA, Walkowski S, Singla AK, Vivian DG (Eds). Discography, Vivian DG, Landers MH, pp 407–440, 2011, with permission from Elsevier

Thoracic Discography

- Information is limited regarding criteria for a positive thoracic discogram; at this time use of lumbar standards is acceptable.

Cervical Discography

- Concordance of pain on injection at a VAS of ≥5/10
- Negative anatomic internal control level

Clinical Pearls

General

- It is advised to prepare the patient with a detailed account of what to expect during the procedure.
- Regarding sedation, midazolam is adequate; however, many clinicians advocate for no sedation during the procedure. Additionally, opioids should not be used, or used with cau-

tion, as they may increase the pain threshold and obscure disc provocation results.
- Contact with the disc annulus may cause mild axial discomfort (secondary to innervations of the posterior annulus)—discs that produce such pain are often positive for discogenic pain upon injection of the disc pulposus. However, annular irritation is a frequent cause for false-positive results.

Lumbar Discography

- To avoid the ventral ramus that lies in the intervertebral foramen, lateral and cephalad to the disc entry site, some advocate for bending the tip of the disc puncture needle opposite the bevel to facilitate maneuverability.
- The L5–S1 disc access may be difficult due to a high ilium preventing visualization of the disc entry point when using true oblique view. Consequently, the SAP is positioned more laterally (Fig. 69.4a), and a bent and dual-needle technique may facilitate maneuverability of the disc puncture needle around the SAP and medially into the center of the disc pulposus (Fig. 69.4b).

Thoracic Discography

- The lung lies just lateral to the medial rib head—it is recommended to stay medial to this to avoid a pneumothorax.
- If contact with bone is made during needle advancement, withdrawing 1–2 mm, rotating, and reinserting the needle tip help facilitate passage through this narrow space between the rib head and superior articular process.

Cervical Discography

- The course of the vertebral artery runs in a cephalocaudal orientation over the uncinate line—it is recommended to stay anterior to this structure.
- Almost all cervical discs when stimulated with sufficient pressure can produce pain whether pathologic or not.
- The zygapophysial joint must be avoided during provocation discography to eliminate false-positive results.
- It is recommended that at least three levels be studied to prevent omitting a painful disc.

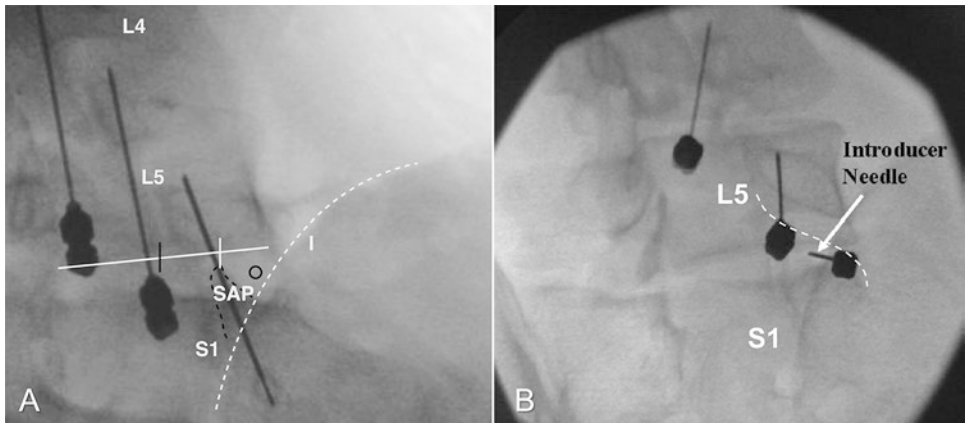

Fig. 69.4 (**a**) Right oblique view of L5–S1 intervertebral disc with a high ilium (I) (*white broken line*). The tip of the SAP (*short white line*) is seen to lie in a lateral position in relation to the inferior end plate of L5 (*long white line*) rather than at the midpoint (*short black line*). Consequently, the skin entry site (*small circle*) is more medial; therefore, the disc puncture needle has to be maneuvered medially to enter the disc pulposus (otherwise will end up in the disc annulus). (**b**) Introducer needle is now in position (*white arrow*). (*Dashed white line* represents the L5 ventral ramus.) Image (**a**) reprinted from *Pain Procedures in Clinical Practice*. 3rd Edition, Lennard TA, Walkowski S, Singla AK, Vivian DG (Eds). Discography, Vivian DG, Landers MH, pp 407–440, 2011, with permission from Elsevier. Image (**b**) used with permission from [1]

Evidence

Dual- vs Single-Needle Techniques

Proponents of both techniques exist. The incidence of complications is similar between the two techniques; however, many clinicians favor the dual technique as the introducer needle tends to stabilize the disc puncture needle, making it easier to maneuver. The single-needle technique may create less scatter radiation. Use of longer disc puncture needles creates less space to maneuver between the image intensifier and the patient, so careful attention to sterile technique must be followed. By using a shorter introducer needle first, the operator may be better able to stabilize the longer disc puncture needle. This technique may be more time efficient, leading to faster placement of the disc puncture needle into the disc and reducing overall fluoroscopy time. Additionally, the dual-needle technique offers the advantage of producing a sharper angle that is sometimes needed to access the L5–S1 disc in patients with a high ilium. The International Spine Intervention Society (ISIS) and the North American Spine Society (NASS) recommend the two-needle approach.

Antibiotics

The administration of prophylactic antibiotics for prevention of discitis is controversial. Studies have not proven that neither intravenous nor intradiscal antibiotics reduce the incidence of discitis over sterile technique alone. However, considering the difficulties in treating discitis and because complications from administering IV antibiotics are rare, many clinicians administer IV antibiotics prior to proceeding with discography.

Analgesic Discography

The rationale behind evaluating discography by its analgesic benefits centers on using pain relief with local anesthetic as the reference standard for a positive test (as seen with facet and sacroiliac joints) rather than pain provocation. Proponents believe that using analgesia as an endpoint reduces false-positive rates associated with discography. Additionally, intradiscal steroid injection might prove to be a beneficial treatment for reducing discogenic pain. Overall, studies involving analgesic discography show mixed results and further research is needed.

References

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2. Calodney A, Griffith D. Discography. In: Mathis JM, Golovac S, editors. Image-guided spine interventions. New York: ©Springer Science+Business Media, LLC; 2010. doi:10.1007/978-1-4419-0352-5_6.

Suggested Readings

Bottros MM, Cohen SP. Lumbar discogenic pain and diskography. In: Benzon HT, Rathmell JP, Wu CL, Turk DC, Argoff CE, Hurley RW, editors. Practical management of pain, 5th ed. Pennsylvania: Mosby, an imprint of Elsevier Inc.; 2014. p. 885–914.

Derby R, Landers MH, Wolfer LR, Kim P. Provocation discography. In: Kapural L, Kim P, Deer TR, editors. Diagnosis, management, and treatment of discogenic pain. Pennsylvania: Saunders, an imprint of Elsevier Ltd; 2012. p. 48–64

Vivian DG, Landers MH. Discography. In: Lennard TA, Walkowski S, Singla AK, Vivian DG, editors. Pain Procedures in clinical practice. 3rd ed. Philadelphia, PA: Elsevier Inc.; 2011. p. 407–40.

Epidural Blood Patch

70

Manuel Coradi, Sean J. Nabar, and Konrad Maurer

CPT

(1) Injection epidural blood/clot patch 62273
(2) Collection of venous blood by venipuncture 36415

Indications

The epidural blood patch (EBP) is regarded as the most efficient measure in the treatment of moderate-to-severe post-dural puncture headache (PDPH). In the PDPH treatment algorithm, it is recommended to first exhaust conservative therapeutic options (lying flat, prone position, abdominal binder, caffeine, sumatriptan, fluid) prior to the performance of an EBP. The EBP may also be used in the treatment of low-pressure headaches from spontaneous or chronic CSF leaks.

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Contraindications

In general, the contraindications include those that also apply to a standard epidural injection, including the presence of fever, raised white cell count, elevated CRP, or local skin infection over the epidural site.

Equipment/Materials

Basic monitoring (ECG, NIBP, SpO2), Tuohy needle, loss of resistance syringe, local anesthetic, IV and/or blood draw setup (sterile), fluoroscopy setup, and +/− second provider

Procedure: Fluoroscopic-Guided Epidural Blood Patch

IV: Single blood draw kit or IV placement for blood draw. Second IV placement recommended if history of vagal episodes
Antibiotics: not required

Steps (See Epidural Steroid Injection Procedure Chapter for Sample Images)

- The EBP can be done using either the standard "blind technique" or with the use of fluoroscopy.

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- If using the standard "blind technique," the patient may be placed in the lateral position or sitting position if the patient can tolerate this. It is recommended to tap at the level of the supposed dural puncture or a level below the known puncture.
- Once the epidural space is found using the loss of resistance technique, the autologous blood may then be injected (see below for details).
- For an EBP using fluoroscopy, start with AP view and center spinous process between pedicles. Not necessary to adjust caudal/cephalad tilt.
- Isolate insertion point in between spinous process and pedicle at or near the site of prior dural puncture. Ideally, aim for the superior aspect of the inferior lamina of the desired interspace.
- After local anesthetic infiltration in the skin, insert the Tuohy needle coaxially between spinous process and pedicle.
- Once the trajectory is verified in between spinous process and pedicle, switch to contralateral oblique (45–55°) view (Fig. 70.1).
- Without adjusting lateral/medial orientation of the needle, advance in the contralateral oblique view to the anterior laminar line. Adjustment of the caudal/cranial angle of the needle may be required to navigate in between lamina.
- Once at the anterior laminar line and ligamentum is engaged, remove the stylet and check for loss of resistance.
- When loss of resistance is achieved, contrast can be injected for verification of epidural spread.
- Save final image.
- At this point, have another provider, if available, draw 10–30 ccs of autologous venous blood via the pre-placed IV or from direct blood draw. Care should be taken to guarantee that the blood draw and the administration of the autologous blood into the epidural space are done in a sterile fashion.
- 20–30 ml of autologous blood is then slowly injected into the epidural space. However, the patient may not tolerate this volume and less can be given. As little as 10 ml can provide relief from PDPHs, but 20 ml is typically the goal volume.
- Epidural access in the lumbar spine is preferred when treating known CSF leaks or dural punctures in the lumbar region. Lumbar

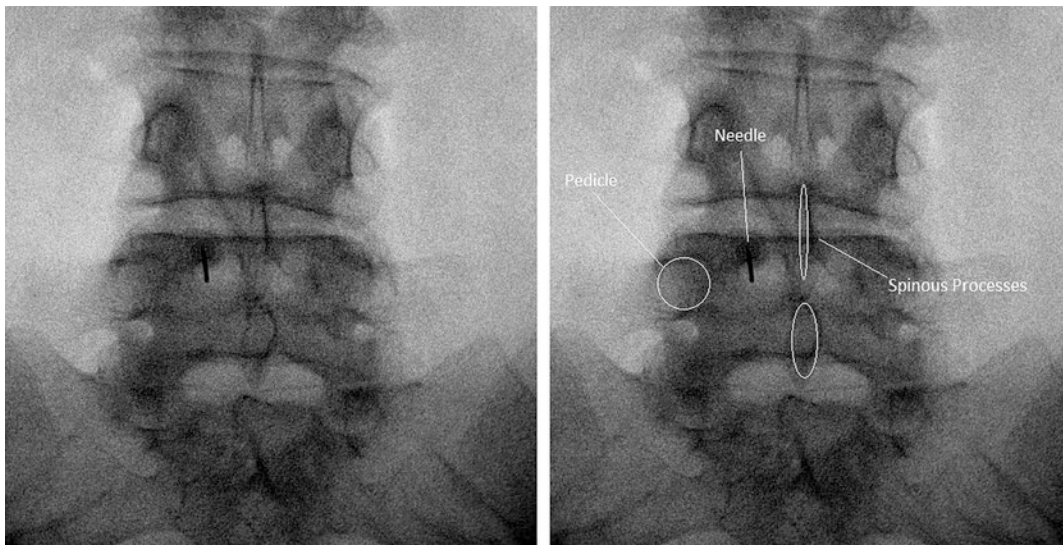

Fig. 70.1 Contralateral oblique view—note how the needle is advanced between the laminae and the anterior laminar line

epidural blood patch of 20 ml may also be sufficient for known or suspected CSF leaks in the thoracic or cervical spine.

Complications

Complications associated with EBP include those associated with a standard epidural injection, which include infection, epidural abscess, epidural hematoma, and nerve injury. The added step of autologous blood draw with injection into the epidural space adds a potential infection risk. Strict care must be taken to maintain proper sterile technique during the blood draw and subsequent epidural injection.

Clinical Pearls

For the treatment of PDPH with EBP, different success rates were reported. In the past, high achievement ratios (permanent relief of headache) as high as 95 % were reported. More recent investigations suggest lower success rates of EBP around 65 %. If an EBP fails to terminate the PDPH, repeating the procedure has a similar effectiveness. After failure of the second EBP, many clinicians tend to repeat it for a third and sometimes also for a fourth time. Nevertheless, in the presence of a persisting severe headache, an alternative cause should be sought after.

Evidence

15, 20, or 30 cc of Blood?

Multinational, multicenter, randomized trial compares three different volumes of autologous blood for an epidural blood patch on obstetric patients with PDPH. The incidence of permanent or partial relief of headache was highest in the 20 cc group at 73 % compared to 61 % and 67 % in the 15 cc and 30 cc groups, respectively. Complete relief in the 20 cc group was 32 % compared to 10 % and 26 % in the 15 cc and 30 cc group, respectively.

Suggested Readings

Paech MJ, Doherty DA, Christmas T, Wong CA. The volume of blood for epidural blood patch in obstetrics. Surv Anesthesiol. 2011;55(6):285. Print.

Turnbull DK, Shepherd DB. Post-dural puncture headache: pathogenesis, prevention and treatment. Br J Anaesth. 2003;91:718–29.

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Sudlow C, Warlow C. Epidural blood patching for preventing and treating post-dural puncture headache. Cochrane Database Syst Rev. 2002;2, CD001791.

OnabotulinumtoxinA Injections for Chronic Migraine

71

Paul Rizzoli

CPT

64615. Buy and bill: J0585 (drug) + 64615 (procedure)

Indications

Prophylaxis of headache in adult patients with chronic migraine (≥15 days per month with headache lasting 4 h a day or longer).

Equipment/materials

One 200 Units of onabotulinumtoxinA; one 21-gauge, 2-inch needle for reconstitution; one 50-mL syringe; four 1-mL tuberculin syringes for injection; four 30-gauge, 0.5–1-inch needles for injection; one 10-mL single-use vial of preservative-free; 0.9 % sodium chloride; alcohol swabs; gauze pads; one pair of gloves; and hazardous medical waste container.

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Procedure

1. A 200-Unit single-use vial of powder is reconstituted with sterile, non-preserved 0.9 % sodium chloride injection USP as a diluent. Mix by rotating the vial. Keep refrigerated and use within 24 h. Four millilitre of diluent added to the 200-Unit vial will produce a dose of 5 Units per 0.1-mL injection.
2. An injection is prepared by drawing into an appropriately sized sterile syringe an amount of reconstituted toxin slightly greater than the intended dose. Air bubbles are expelled and the appropriate-sized needle is attached.
3. The recommended dose is 155 Units IM, 5 Units (0.1 mL) in each site. Sites are divided among seven head/neck muscle areas. With the exception of the procerus which is one midline site, all other muscles are injected bilaterally (Table 71.1). The recommended retreatment schedule is every 12 weeks.

Clinical Pearls

Not for use in episodic migraine.

The clinical effect tends to wane, necessitating repeat injections for continued symptom control.

Clinical benefit is reported at times when injections are moved to locations where the patient is experiencing more headache, so-called

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Table 71.1 OnabotulinumtoxinA dosing by the muscle for chronic migraine

Head/neck area	Recommended dose (number of sites)
Frontalis	20 Units divided into four sites
Corrugator	10 Units divided into two sites
Procerus	5 Units in one site
Occipitalis	30 Units divided into six sites
Temporalis	40 Units divided into eight sites
Trapezius	30 Units divided into six sites
Cervical paraspinal muscles	20 Units divided into four sites

Source: Package insert from Allergan Pharmaceuticals

chase the pain, and this approach is appropriate in some patients.

Symptoms including asthenia, weakness, diplopia, ptosis, dysarthria, and breathing difficulties have been reported beyond the site of local injection in the hours and initial weeks after injection with the use of onabotulinumtoxinA injections for multiple indications; however, no such definitive serious adverse events have been reported with toxin use in the prevention of chronic migraine.

The level of immunogenicity to the protein appears to be low and antibody levels are not routinely obtained.

The potency units of onabotulinumtoxinA (Botox) are specific to the preparation and *are not* interchangeable with other botulinum toxin preparations.

Pregnancy: There are no well-controlled studies in pregnant women. OnabotulinumA toxin should only be used in pregnancy when the potential benefit outweighs the potential risk.

Safety and efficacy have not been established in patients under 18 years of age.

Evidence

OnabotulinumA toxin blocks acetylcholine release from motor and sympathetic nerve terminals. The mechanism of action in the prevention of headache in chronic migraine is unknown.

Two randomized multicenter placebo-controlled double-blind studies in patients with chronic migraine demonstrated statistically significant and clinically meaningful improvement from baseline compared to placebo for frequency of headache days and total cumulative hours of headache on headache days.

Suggested Readings

Aurora SK, et al. OnabotulinumtoxinA for treatment of chronic migraine: results from the PREEMPT 1 trial. Cephalalgia. 2010;30(7):793–803.

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Spasmodic Torticollis/Cervical Dystonia (CD)

72

Daniel Vardeh

CPT

64616 (chemodenervation cervical spinal muscle(s))
95874 (needle electromyography for guidance in conjunction with chemodenervation)

Indications

Botulinum toxin is considered the first-line treatment for the majority of focal dystonias, including Cervical Dystonia (CD).

Only types A (onabotulinumtoxinA, commercially available as Botox®, Dysport®, or Xeomin®) and B (rimabotulinumB, commercially available as Myobloc® or NeuroBloc®) are FDA approved for cervical dystonia.

Equipment/Materials

1 cc tuberculin syringe with 25 ga×5/8 in. needle

Botulinum toxin

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Procedure

Position: usually sitting
IV: not required unless previous vaso-vagal episodes
Antibiotics: not required

Steps

- Observation of abnormal head position or movement both at rest and during provoking maneuvers to identify target muscle(s). Distraction can help to prevent the patient from activating compensatory muscles.
- Muscles should be palpated for hypertrophy or asymmetry.
- Supplementary techniques like EMG can help to confirm clinically identified muscle groups. Compensatory muscle activation is sometimes hard to distinguish from primary dystonic muscle groups on electrophysiological grounds alone, and clinical observation of the primary dystonic movement is paramount. If muscles are superficial and hence readily accessible, EMG guidance might not be needed.
- Based on severity of symptoms, muscle bulk, clinical response and activity on EMG, and injection doses can vary considerably. Typical range per single injection is 10–100 U (onabotulinumtoxinA) and 750–5000 U (rimabotulinumB).

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Complications

[US Boxed Warning]: Distant spread of botulinum toxin beyond the site of injection has been reported; dysphagia and breathing difficulties have occurred and may be life threatening; other symptoms reported include blurred vision, diplopia, dysarthria, dysphonia, generalized muscle weakness, ptosis, and urinary incontinence which may develop within hours or weeks following injection. The risk is likely greatest in children treated for the unapproved use of spasticity. Systemic effects have occurred following use in approved and unapproved uses, including low doses.

Specific Complications

- Neutralizing antibody formation, often caused by higher and/or more frequent dosing, which can result in decreased efficacy.
- Dysphagia (common) due to weakness of pharyngeal muscles. Risk factors include small neck muscle mass, bilateral injections into the sternocleidomastoid muscle, or levator scapulae.
- Patients with neuromuscular junction disorders (e.g., myasthenia gravis, Lambert–Eaton syndrome) are at increased risk for developing dysphagia and respiratory compromise.
- Patients on medications interfering with neuromuscular junction transmission (e.g., aminoglycosides) are at increased risk for complications.
- Patients with preexisting respiratory disease are at increased risk for respiratory failure due to induced weakness of accessory respiratory muscles.

Clinical Pearls

- Ultrasound can also be used in lieu of EMG to correctly identify muscle groups and ensure intramuscular injection.

Evidence

- Two Cochrane analyses of 13 (677 participants for onabotulinumtoxinA) and three (308 participants for rimabotulinumB) high-quality RCTs for botulinum toxin treatment in cervical dystonia showed that single injection is effective (objective and subjective rating scales), with mean benefit duration of at least 16 weeks, and is safe and effective on repeat injections.
- Meta-analysis of 18 high-quality studies (over 1900 patients) found that mean duration of effect of onabotulinumtoxinA in the treatment of CD was 93–95 days. For doses ≥180 Units, the mean duration was 15.3 weeks, while the mean duration of doses <180 Units was 12.5 weeks.
- Botulinum toxin can prevent secondary degenerative changes of the cervical spine and associated radiculopathy due to CD.

Suggested Readings

An evidence-based review of botulinum toxin applications in non-cosmetic head and neck. JRSM Short Rep. 2013;4(2):10.

Botulinum toxins in the treatment of primary focal dystonias. J Neurol Sci. 2012;316(1–2):9–14.

Occipital Nerve Block

73

Daniel Vardeh

CPT

64405 (greater occipital nerve block)
64450 (minor or third occipital nerve block)

Indications

1. Occipital neuralgia
2. Cluster headache
3. Cervicogenic headache
4. Migraine
5. As an adjuvant to medication-overuse headache

Equipment/Materials

25-gauge, 1.5-in. needle and 5-ml syringe
0.25–0.5 % bupivacaine (5 ml)
10–20 mg of methylprednisolone

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Procedure

Position: sitting
IV: not required unless previous vaso-vagal episodes
Antibiotics: not required

Steps

- Identification of the injection point varies between providers. We typically draw an imaginary line between the mastoid process and the midpoint between the occipital protuberance and the top of the head. The injection point is at the midpoint of that connection line. If possible, it is helpful to palpate the occipital artery in order to avoid excessive bleeding or intravascular injection.
- The injection point (see Fig. 73.1) is cleaned in the typical fashion with disinfectant.
- A 25-gauge, 1.5-inch needle is advanced until the periosteum is touched slightly, then the angle is lowed, and the needle advanced further just above the periosteum for 0.5–1 cm. After negative aspiration, three injections are performed in a fan-shaped distribution.
- The lesser occipital nerve may be blocked as well by injection of 2–3 ml about 1 cm lateral to the inferior aspect of the mastoid process.
- After completing either of the injections, it is important to gently massage the injection side to spread the injectate equally.

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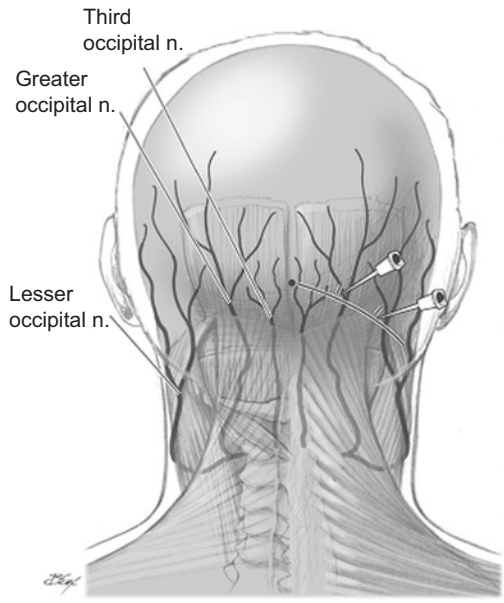

Fig. 73.1 Locations for major and minor occipital nerve block. Used with permission from Blumenfeld A et al. Expert Consensus Recommendations for the Performance of Peripheral Nerve Blocks for Headaches—A Narrative Review. Headache. 2013 Mar;53(3):437–46

Complications

Injections are generally well tolerated, but carry the usual risk of infection, bleeding, and a vasovagal reaction/syncope.

Specific risks include:

- Small area of alopecia with cutaneous atrophy at steroid injection sites. This is typically a self-resolving condition, but can last up to 24 months.
- Puncture of the occipital artery resulting in hematoma.
- Peripheral facial nerve palsy due to spread of the anesthetic solution along tissue planes.
- There is no research demonstrating the safety or effectiveness of ONB in minors.

Clinical Pearls

- Given tremendous anatomical variability of the GON in relation to palpable landmarks, several authors suggest to inject at the area of maximal tenderness in that region or to use ultrasound or electric nerve stimulation for better localization.
- In patients with occipital neuralgia and clear but short-lasting response to GON blocks, botulinum toxin injection, occipital nerve subcutaneous neurostimulation, and occipital nerve radiofrequency ablation are options for longer-term relief.
- Response to ONB in patients with chronic migraine and chronic cluster headache does not reliably predict occipital nerve stimulator response.
- For refractory cervicogenic headache, a subcompartmental injection of 5 ml of the same injectate (under fluoroscopic guidance) can result in significantly longer benefit compared to classic GON block (2 weeks vs 24 weeks of relief in one study).
- It is common to combine a local anesthetic with a steroid injectate, although the evidence is unclear regarding additional benefit from the steroid. If the injection has an abortive purpose, local anesthetics should suffice. If preventive/long-term control is desired, the addition of a steroid is reasonable. If the patient only gets therapeutic benefit for a few days from local anesthetic injection, the addition of a steroid is reasonable.

Evidence

- Several RTCs with patient numbers 20–50 and multiple observational studies show various levels of evidence for the benefit of GON block in the following conditions (evidence grade): cluster headache (B), cervicogenic headache (B), migraine headache (C), tension-type headache (insufficient evidence), hemicrania continua (insufficient evidence), and chronic daily headache (C). In general, significant headache relief was reported in about 50–80 % of patients, lasting from one to several weeks on average.
- There is insufficient evidence for the use of GONB in the acute setting as abortive therapy.
- No consensus exist regarding the choice of injectate. Most studies use lidocaine (1 % at 3–5 ml, 2 % at 0.5–5 ml) or bupivacaine

(0.25 %, 0.325 %, or 0.5 % at 0.5–5 ml), and a minority of studies a combination of both.
- Common steroids used are triamcinolone (5–40 mg), methylprednisolone (40–80 mg), dexamethasone (4 mg), and betamethasone (2–12 ml). One dose comparison case report using only methylprednisolone showed that 40 mg was ineffective, 50–60 mg was effective, and an increase in headache symptoms was noted at 80 mg in a patient with chronic migraine.
- Evidence to support the routine addition of corticosteroids to local anesthetics when performing GON block for headache is strongest for cluster headache patients.
- Common frequency of anesthetic injections is every 2–4 weeks, and steroid injection about every 3 months, depending on therapeutic benefit. More frequent injections up to every second day for a total of ten blocks have been described without any long-term complications.

Suggested Readings

Occipital nerve blocks in the treatment of headaches: safety and efficacy. J Emerg Med. 2015; 48(1): 115–29.

Expert consensus recommendations for the performance of peripheral nerve blocks for headaches—a narrative review. Headache. 2013;53(3):437–46.

Peripheral nerve blocks and trigger point injections in headache management—a systematic review and suggestions for future research. Headache. 2010;50: 943–52.

Supraorbital Nerve Block

74

Daniel Vardeh

CPT 64400 (injection, anesthetic agent trigeminal nerve, any division or branch)

Indications

Supraorbital neuralgia

Equipment/Materials

25-gauge, 1.5-inch needle and 5-ml syringe
0.25–0.5 % bupivacaine or 1 % lidocaine (3–5 ml)
10–20 mg of methylprednisolone

Procedure

Position: supine or sitting
IV: not required unless previous vaso-vagal episodes
Antibiotics: not required

Steps

- The supraorbital foramen is palpated along the upper boarder of the orbital bone, just below the eyebrow (see Fig. 74.1).
- Sterile skin preparation is performed.
- A 25-gauge, 1.5-inch-long needle is inserted about 1 cm above the foramen, and 1–2 ml of lidocaine 1 % and/or bupivacaine 0.5 % are injected across the supraorbital notch.
- To block the supratrochlear branch of the ophthalmic nerve, the needle is directed medially parallel to the eyebrow, and 1–2 ml is injected.
- Pressure is held for 1 min to stop bleeding and spread the injectate equally.

Complications

- Generally rare. Most often hematoma from injury to the supraorbital or supratrochlear artery.
- Infections can rarely spread along the venous drainage of the superior ophthalmic vein to the cavernous sinus and intracranially.

Clinical Pearls

- If using steroid, localized subcutaneous fat wasting at the injection site can occur and can take many months to resolve.

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R.J. Yong et al. (eds.), *Pain Medicine*, DOI 10.1007/978-3-319-43133-8_74

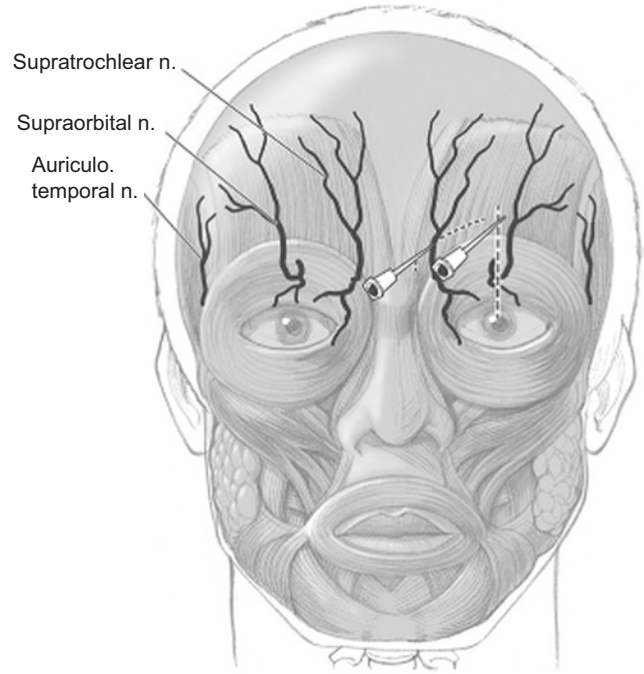

Fig. 74.1 Locations for supratrochlear and supraorbital nerve block. Used with permission from Blumenfeld A et al. Expert Consensus Recommendations for the Performance of Peripheral Nerve Blocks for Headaches—A Narrative Review. Headache. 2013 Mar;53(3):437–46

- As one of the terminal branches of the ophthalmic nerve (V1), the supraorbital nerve provides the sensory innervation to the ipsilateral forehead. It runs with the supraorbital artery through the supraorbital foramen, where it can be injured by impact trauma or tight-fitting goggles.
- Diagnostic criteria for supraorbital neuralgia according to the International Headache Society are the triad of:
  a. Paroxysmal or constant pain in the region of the supraorbital notch and medial aspects of the forehead in the area supplied by the supraorbital nerve.
  b. Tenderness over the nerve in the supraorbital notch.
  c. Pain is abolished by local anesthetic blockade or ablation of the supraorbital nerve.
- The disorder can sometimes be confused with migraine, cluster headache, or sinusitis given the unilateral forehead location and occasional involvement of the eye (blurred vision, redness).
- If a nerve block does not result in long-lasting pain relief, RFL of the supraorbital nerve, surgical decompression at the foramen, and implantation of a peripheral nerve stimulator are possible options, although no trials exist to prove their efficacy or safety (see below).

Evidence

There are no randomized controlled trials showing long-term benefit from supraorbital nerve block/lesioning. Supraorbital nerve blocks in patients with refractory migraine located to the forehead distribution have been described to result in long-lasting (>6 months) benefit. Similarly, surgical release and peripheral nerve stimulation can sometimes be effective in patients with neuralgia.

Suggested Readings

Supraorbital neuralgia. Vågå study of headache epidemiology. Cephalalgia. 2005; 25(4):296–304.
Review supraorbital neuralgia: supraorbital neuralgia. Curr Pain Headache Rep. 2006; 10(4):302–5.
Expert opinion. Supraorbital neuralgia. Headache. 2009; 49(2):278–81.
Supraorbital neuralgia: a clinical study of 18 patients over 7 years. Cephalalgia. 2001;21(3):216–23.

Auriculotemporal Nerve Block

75

Syed Irfan Qasim Ali and Srdjan S. Nedeljkovic

CPT

Auriculotemporal nerve block 64400
Injection, anesthetic agent; trigeminal nerve, any division or branch 64400

Indications

The auriculotemporal nerve originates from the mandibular division of trigeminal nerve and provides somatosensory innervation to the TMJ capsule, temporal and preauricular skin, pinna and external auditory meatus partially, and external part of tympanic membrane and also provides secretomotor supply to the parotid gland. Indications for performing an auriculotemporal nerve block include posttraumatic neuralgia, certain variations of atypical facial pain, acute herpes zoster involving the external auditory meatus, and pain due to malignancy. This block may also provide relief in the alleviation of pain due to involvement of geniculate ganglion causing Ramsay Hunt or Frey's syndrome.

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Equipment/Materials

25/27 G 1.5-inch needle, +/− Ultrasound

Procedure

Position: Supine
Antibiotics: Not required

Steps: The Procedure Can Be Performed with or Without Ultrasound

1. The patient is placed supine with the head turned away from side of block.
2. The origins of the zygomatic arch and temporomandibular joint are identified by palpation.
3. The temporal artery is palpated and identified just above the TMJ. After all landmarks are identified, the area is pepped and draped in usual sterile fashion.
4. If using ultrasound guidance, a linear probe is placed over temporal artery in transverse plan.

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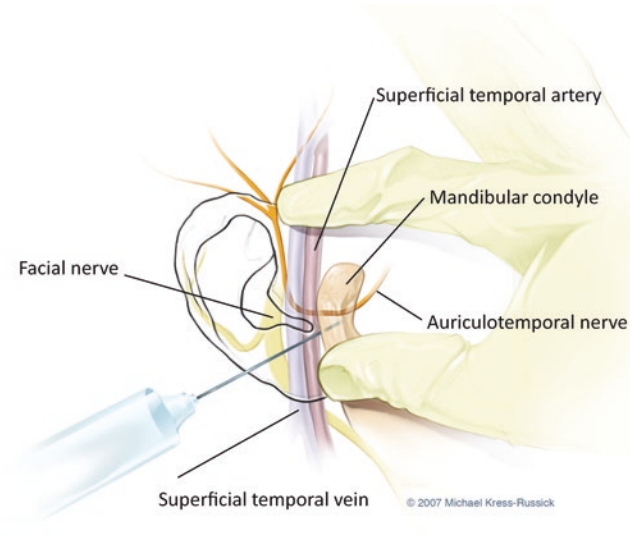

Fig. 75.1 Auriculotemporal nerve block. Illustration © Michael Kress-Russick. Used by permission

5. The auriculotemporal nerve lies adjacent to temporal artery. Once identified using an out-of-plane ultrasound approach, a 22 G needle is advanced perpendicular to probe.
6. If using a technique based on surface anatomy, a 25 or 27 G needle is advanced perpendicular and just below the temporal artery until the periosteum is reached.
7. Once a paresthesia is felt by patient, gentle aspiration is followed by injection of 3 ml of local anesthetic. After initial injection, the needle is redirected in a cephalad direction, and an additional 2 ml of anesthetic is injected.
8. Depending on the clinical indication for the block, only local anesthetic, local anesthetic with steroid or neurolytic block with phenol (for intractable pain due to malignancy), may be injected.

See Fig. 75.1.

Complications

Bleeding, infection, intravascular injection due to close proximity to major vessels, transient facial nerve palsy, vasovagal syncope, ecchymosis, and hematoma at the site of injection. In view of these possible complications, using US guidance may help clarify the location of needle placement.

Clinical Pearls

Using US guidance may help identify adjacent anatomical structures. To avoid facial nerve paralysis and reduce the risk of systemic local anesthetic toxicity, an alternate approach by Bebawy et al. is recommended using only 3 ml of local anesthetic instead of 5 ml and blocking the nerve 1 cm above the tragus to be even far-

ther away from facial nerve. Lidocaine, ropivacaine, or bupivacaine may be used along with 40–80 mg of methylprednisolone. Phenol injection may be a consideration if pain is caused by malignancy.

Evidence

A recent review by Ahmad Alshadwi et al. presented evidence that botulinum neurotoxin therapy may have benefit for treating various head and neck disorders, including auriculotemporal syndrome in adults.

Suggested Readings

Atlas of interventional pain management, 4th ed. By Steven D. Waldman, MD, JD.

Alshadwi A, et al. Therapeutic applications of botulinum neurotoxins in head and neck disorders. Saudi Dent J. 2015;27(1):3–11.

Bebawy JF, et al. A modified technique for auriculotemporal nerve blockade when performing selective scalp nerve block for craniotomy. J Neurosurg Anesthesiol. 2014;26(3):271–2.

Trigeminal Nerve Block

76

Maureen F. McClenahan and M. Gabriel Hillegass, III

CPT

Injection, anesthetic agent; trigeminal nerve, any division or branch 64400

Fluoroscopic guidance 77003

Destruction by neurolytic, trigeminal nerve; second and third division branches at foramen ovale 64605

Indications

Trigeminal neuralgia, palliation of cancer pain, acute herpes zoster, postherpetic neuralgia, acute facial pain emergencies, differential neural blockade, prognostic block prior to neurolysis

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Equipment/Materials

Fluoroscopy machine, 25/27 gauge needle (for skin infiltration), 5 mL syringe (for local anesthetic solution), connection tubing, 22 gauge 3.5 in. styleted needle (for injection of local anesthetic or neurolytic agent), contrast agent, local anesthetic (1–2 % lidocaine, 0.25–0.5 % bupivacaine, or 0.2–0.5 % ropivacaine), or neurolytic agent (6–10 % phenol in glycerin, 95–97 % alcohol, or 40–50 % glycerol)

Procedure

Position: supine with cervical spine in neutral position

IV: required for moderate sedation; however, level of sedation should allow for ongoing patient communication.

Steps

1. The coronoid notch is identified either fluoroscopically using a lateral view or by landmarks and palpation. This is facilitated by asking the patient to open and close their mouth while palpating the temporomandibular region just anterior and inferior to the external auditory meatus.

R.J. Yong et al. (eds.), *Pain Medicine*, DOI 10.1007/978-3-319-43133-8_76

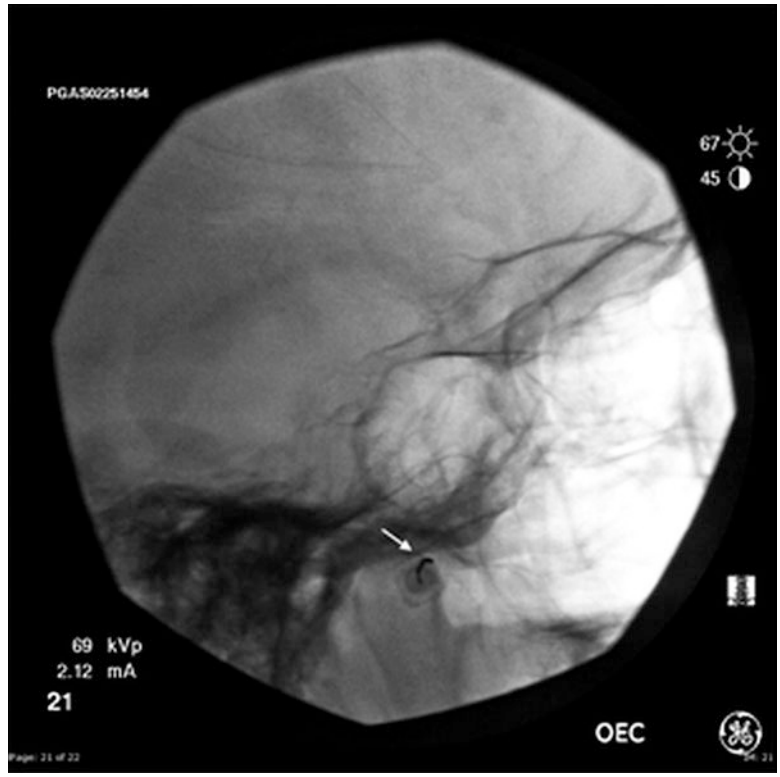

Fig. 76.1 Lateral view: the needle (*white arrow*) is inserted coaxially in the coronoid notch

2. Using sterile technique, after local anesthesia and employing a lateral fluoroscopic view, a 22 gauge 3.5 in. styleted needle is inserted lateral to medial using coaxial technique in the middle of the coronoid notch just below the zygomatic arch (Fig. 76.1). The needle is advanced 1.5–2 in. perpendicular to the skull until the lateral pterygoid plate is contacted which is verified on PA view (Fig. 76.2). After contact, the needle is withdrawn slightly. Injection of a small amount of contrast will detect vascular uptake and elucidate the extent of injectate spread. If blockade of both V2 and V3 is desired, 7 mL of solution can be injected using incremental aliquots after negative aspiration each time.
3. For *selective blockade of the maxillary nerve (V2)*, after contact with the lateral pterygoid plate, the needle is redirected anterosuperiorly to advance past the anterior margin of the lateral pterygoid plate. Elicitation of a paresthesia in the maxillary nerve distribution is commonly encountered approximately 1 cm beyond the depth at which the lateral pterygoid plate was contacted.
4. For *selective blockade of the mandibular nerve (V3)*, after contact with the lateral pterygoid plate, the needle is redirected posteroinferiorly to advance past the inferior margin of the lateral pterygoid plate. Elicitation of a paresthesia in the mandibular nerve distribution is commonly encountered approximately 1 cm beyond the depth at which the lateral pterygoid plate was contacted.
5. Injection of a small amount of contrast will detect vascular uptake and elucidate the extent of injectate spread. Use an incremental injection technique to administer 3–5 mL of solution for selective blockade of the maxillary or mandibular nerve.

Complications

Dysesthesias, anesthesia dolorosa, weakness of the muscles of mastication, facial hematoma, secondary facial asymmetry, meningitis, intracranial hemorrhage with inadvertent intracra-

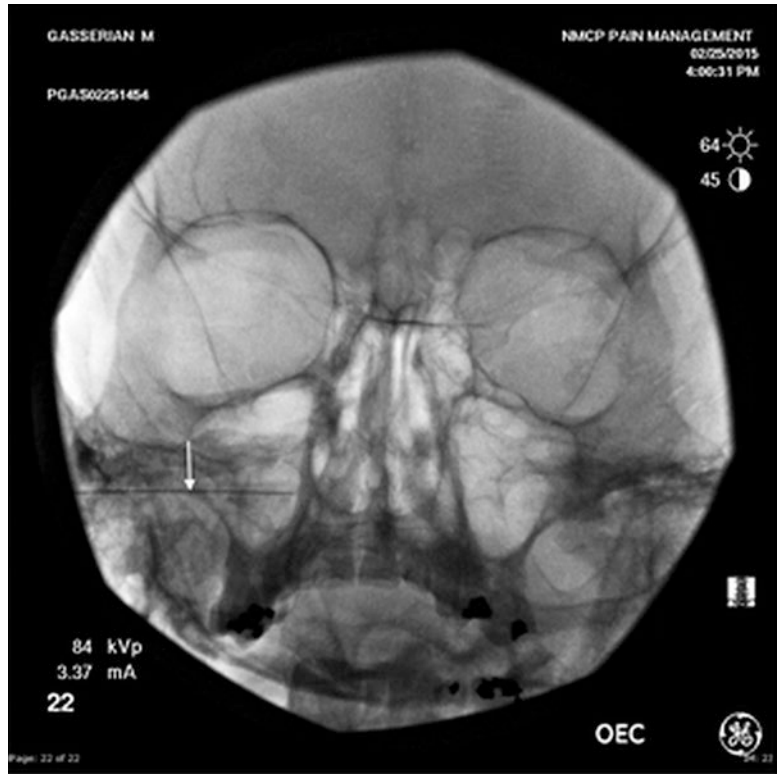

Fig. 76.2 PA view—the needle (*white arrow*) is advanced medially until it contacts the lateral pterygoid plate

nial needle placement, and total spinal anesthesia

Clinical Pearls

Due to the proximity of the highly vascular pterygopalatine fossa, both hematoma formation and local anesthetic toxicity are the major side effects of this procedure. Regardless, this technique can safely be performed in anticoagulated patients by using a 25 or 27 gauge needle.

Evidence

For additional reading discussing various peripheral and ganglion-level procedures available for treating trigeminal neuralgia including success and complication rates for each technique:

Peters G, Nurmikko T. Peripheral and gasserian ganglion-level procedures for the treatment of trigeminal neuralgia. Clin J Pain 2002; 18: 28–34.

Acknowledgments We would like to express appreciation for the efforts of Bill Douglas, RN and the support of the Bio Skills Training Center staff at the Naval Medical Center Portsmouth, VA both of whom were instrumental with the acquisition of the above images.

Disclaimer The views expressed in this article are those of the author(s) and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

Suggested Readings

For additional reading on radiofrequency lesioning, neurodestructive techniques, or trigeminal nerve blockade using the coronoid approach:

Raj P, et al., editors. Interventional pain management: image-guided procedures. 2nd ed. Philadelphia: Saunders Elsevier; 2008.

Waldman S, editor. Atlas of interventional pain management. 4th ed. Philadelphia: Saunders Elsevier; 2015.

Gasserian Ganglion Block

77

Maureen F. McClenahan and M. Gabriel Hillegass, III

CPT

Injection, anesthetic agent; trigeminal nerve 64400

Fluoroscopic guidance 77003

Destruction by neurolytic, trigeminal nerve; second and third division branches at foramen ovale 64605

Indications

Local anesthetic block	Neurolytic block
Surgical anesthesia	Palliation of cancer pain
Prognostic block prior to neurolytic procedures	Trigeminal neuralgia
Acute pain emergencies	Cluster headache
Differential neural blockade	Intractable ocular pain

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Equipment/Materials

Fluoroscopy machine, 25/27 gauge needle (for skin infiltration), 5 mL syringes (for local anesthetic solution), connection tubing, 22 gauge B-bevel 8–10 cm needle (for injection of local anesthetic or neurodestructive agent), contrast agent, 1–2 % lidocaine, 0.25–0.5 % bupivacaine, 0.2–0.5 % ropivacaine, 6–10 % phenol in glycerin, 95–97 % alcohol, 40–50 % glycerol

Procedure

Position: supine with the cervical spine extended (use a shoulder roll if needed).

IV: required for moderate sedation; however, level of sedation should allow for ongoing patient communication.

Steps

1. Identify landmarks: The needle entry point is 2.5–3 cm lateral to the angle of the mouth with the needle directed 3 cm anterior to the external auditory meatus when viewed laterally, or directed to the pupil when viewed anteriorly. A 22 gauge, B-bevel, 8–10 cm needle is advanced coaxially in the submental view until contact is made with the base of the

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skull at which point it is slightly withdrawn and walked posteriorly into the foramen ovale.

2. Radiographic confirmation of needle trajectory should be verified in the submental oblique, lateral, and PA views.
   a. **Submental oblique view** (Fig. 77.1): The C-arm is moved approximately 30° ipsilaterally with a slight caudal tilt to 30°. This will bring into view the mentonian arch, with the foramen ovale located in the upper-internal quadrant. The foramen ovale appears medial to the medial edge of the mandible. The needle is directed toward the foramen ovale using coaxial technique. Walk into the foramen if bone contacted. With this view, the ophthalmic and maxillary branches are located medially, and the mandibular division is located laterally.
   b. **Lateral view** (Fig. 77.2): Obtain a lateral view once the needle has been placed into the foramen ovale. This view should verify that the needle is directed toward the vertex of the clivus and the petrous ridge of the temporal bone. The tip should not exceed 2 mm in distance from the plane of the clivus (V3 just before the clivus, V2 at the clivus, V1 just beyond the clivus).
   c. **PA view** (Fig. 77.3): The petrous ridge is visualized through the orbits. Target is 1 cm medial to the lateral rim of the internal auditory meatus, which usually approximates the medial aspect of a dip in the petrous ridge.
3. Once needle placement is confirmed in all three views, careful aspiration for blood and CSF should be performed. CSF flow is usually encountered. Negative aspiration of CSF indicates that the needle tip likely does not rest within the trigeminal cistern but more anteriorly, within Meckel's cave. Incremental injection of 0.5 ml of contrast agent will aid in determining presence or absence of a dural puncture.
4. After radiographic confirmation of needle placement has been performed, 0.1 mL aliquots of preservative-free local anesthetic or

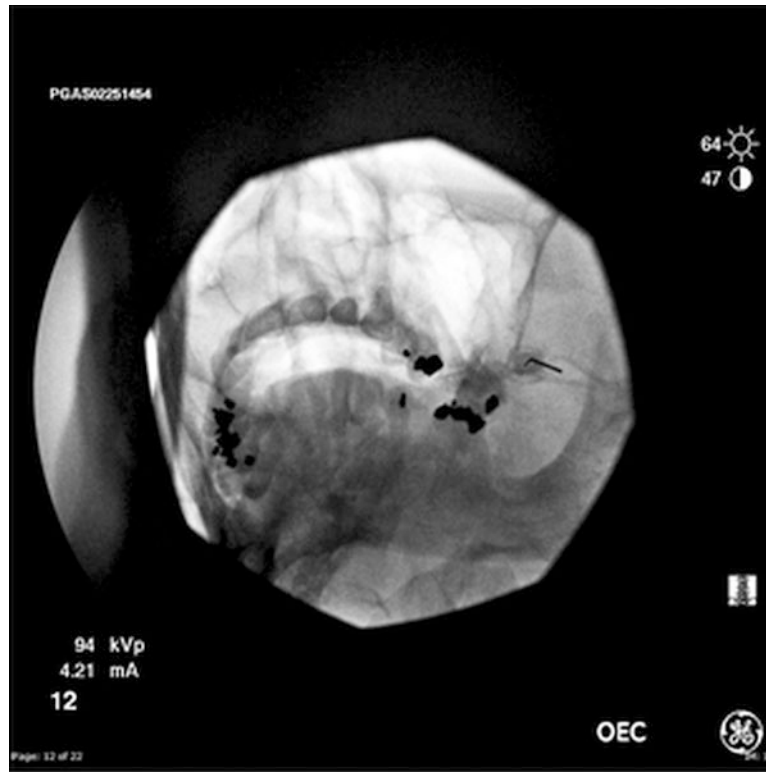

Fig. 77.1 Submental oblique view: note how the needle is advanced coaxially targeting the foramen ovale just medial to the mandible

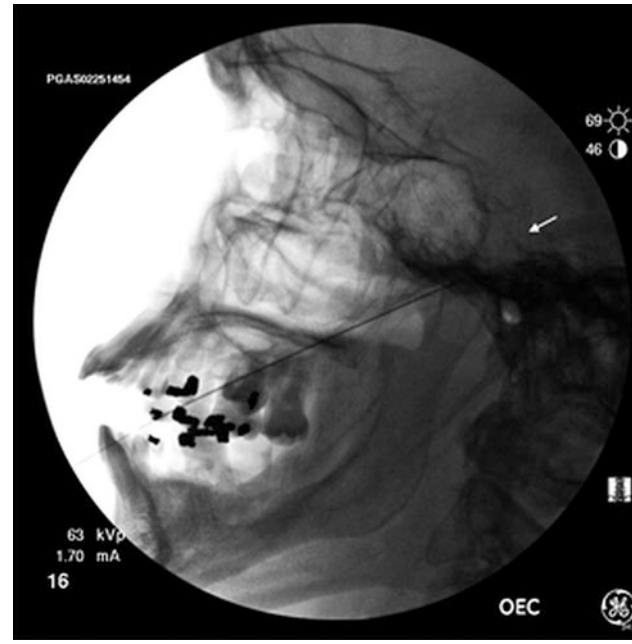

Fig. 77.2 Lateral view: the needle is advanced toward the vertex (*white arrow*) between the clivus and the petrous ridge

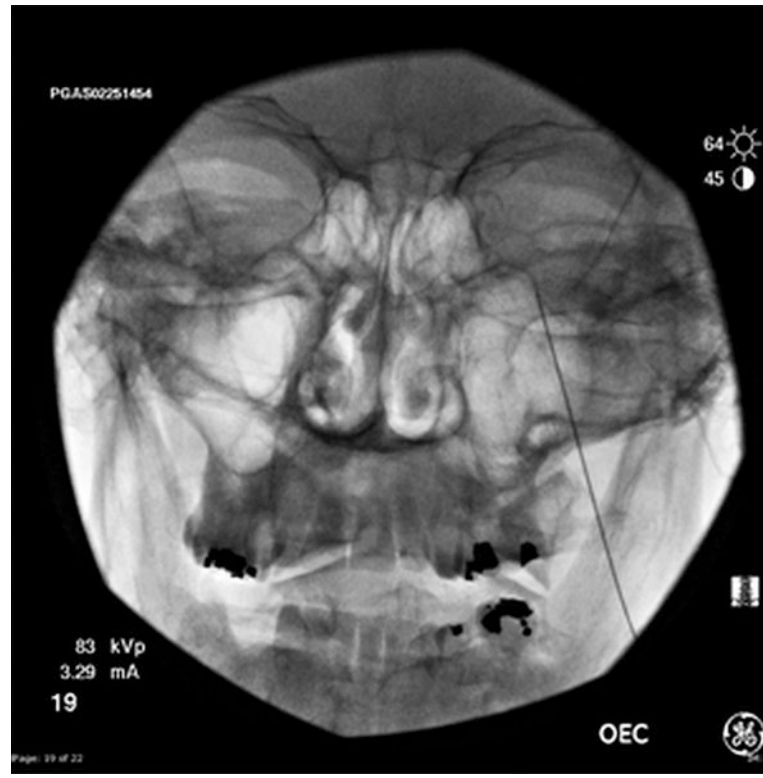

Fig. 77.3 PA view: the needle trajectory should target the medial aspect of a dip in the petrous ridge under which the foramen ovale is located

neurolytic agent may be injected. Due to patient variability in the size of Meckel's cave, careful titration of total volume is mandatory. Because the gasserian ganglion lies within the CSF, even small volumes of local anesthetic can lead to total spinal anesthesia. Consequently, small doses should be administered in an incremental fashion with time given to observe the effect of each aliquot administered. 0.4 ml is typically an adequate volume.

5. If hyperbaric neurolytic agents are used, the patient must be moved to a sitting position with the neck in a flexed position to avoid ophthalmic division or proximal brainstem structure involvement.
6. This approach may also be used for the placement of radio-frequency needles or cryoprobes.

Complications

Dysesthesias, anesthesia dolorosa, loss of corneal reflex, neurogenic keratitis, visual loss, retrobulbar hematoma, hematoma in the cheek, motor root deficit causing masticatory weakness, carotid puncture, carotid-cavernous fistula, meningitis, intracranial hemorrhage with inadvertent intracranial needle placement, monocular blindness, sixth cranial nerve palsy.

Clinical Pearls

The gasserian ganglion lies within Meckel's cave, close to the petrous part of the temporal bone in the middle cranial fossa. It is bordered medially by the cavernous sinus, superiorly by the temporal bone, and posteriorly by the brainstem. A dural pouch containing CSF lies at the posterior aspect of the ganglion.

The ophthalmic (V1) and maxillary (V2) nerves are purely sensory, whereas the mandibular (V3) nerve is mixed and contributes some motor innervation to the muscles of mastication.

The lateral view is necessary to ensure needle depth. Too deep of a placement can result in penetration of the brainstem and secondary hemorrhage.

Paresthesias in the mandibular nerve distribution are frequently encountered upon entry into the foramen ovale.

Due to the high vascularity of the pterygopalatine space as well as the proximity of the middle meningeal artery, facial hematoma and subscleral hematoma of the eye are not uncommon. If blood is aspirated, the needle should be adjusted. If bleeding continues, the procedure should be aborted.

In older or edentulous patients, the skin entry point should be slightly more posterior (3–4 cm from the angle of the mouth) in order to enter the foramen ovale at a proper angle.

Dural irritation may cause persistent headache, nausea, and vomiting that can last for days.

The pain specialist should monitor for and treat corneal anesthesia. If persistent anesthesia is discovered, prompt consultation with ophthalmology is necessary to prevent vision loss and other related ophthalmologic injuries.

Evidence

For additional reading discussing various peripheral and ganglion-level procedures available for treating trigeminal neuralgia including success and complication rates for each technique:

Peters G, Nurmikko T. Peripheral and gasserian ganglion-level procedures for the treatment of trigeminal neuralgia. Clin J Pain 2002; 18: 28–34.

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Suggested Readings

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Raj P, et al., editors. Interventional pain management: image-guided procedures. 2nd ed. Philadelphia: Saunders Elsevier; 2008.

Waldman S, editor. Atlas of interventional pain management. 4th ed. Philadelphia: Saunders Elsevier; 2015.

Stellate Ganglion Block

78

Ross Gliniecki

CPT code: 64510

Stellate Ganglion Block

The stellate ganglion is a bilateral sympathetic ganglion located in the sympathetic chain at the level of the C6 or C7 vertebrae. The sympathetic nervous system is thought to play a role in neuropathic, vascular, and visceral pain. While the underlying pathophysiological mechanisms are unclear, there is likely an abnormal interaction between the sympathetic and the somatosensory nervous system in the peripheral nerve or in the dorsal root ganglion. Injection of local anesthetic at the stellate ganglion is frequently used in the diagnosis and treatment of vascular and painful conditions involving the face and upper extremity.

Anatomy

The stellate ganglion is a sympathetic ganglion located on either side of the base of the neck. It is normally formed by the fusion of the inferior cervical and the first thoracic ganglion, but may have contributions from the second thoracic ganglion is occasionally part of the ganglion. The stellate ganglion is supplied by efferent sympathetic fibers from the ipsilateral sympathetic chain along with the first and second thoracic segmental anterior rami.

The stellate ganglion is commonly located just anterior to the longus colli muscle, which is just anterior to the transverse process of the C7 and T1 but has been described lateral and posterior to the longus colli muscle.

Surrounding Anatomy

Anterior: Sternocleidomastoid muscle, carotid sheath
Anteromedial: Trachea, esophagus, thyroid
Posterior: Longus colli muscle, transverse process/vertebral body (C6, C7)
Posterolateral: Vertebral artery, brachial plexus

Indications

The stellate ganglion block is used to inhibit both efferent sympathetic fibers as well as visceral pain fibers in the upper extremity and face for a variety of sympathetically mediated pain conditions as well as for vascular disorders.

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Painful Conditions

CRPS 1 and 2
Herpes zoster
Postherpetic neuralgia
Peripheral nerve lesions
Phantom limb pain
Post-myocardial sympathetically mediated pain
Malignant sympathetically mediated pain

Vascular Conditions

Angina
Obliterative vascular disease
Raynaud's disease
Vasospastic disorders
Embolic phenomenon
Scleroderma
Ergotism
Frostbite

Other Conditions

Hyperhidrosis
Sudden idiopathic sensorineural hearing loss

Contraindications

Recent myocardial infarction, anticoagulant medications, coagulopathy, glaucoma, contralateral phrenic nerve dysfunction.

Techniques

Landmark Technique Patient in supine position with head turned to opposite side. Needle is inserted between the trachea and carotid sheath at the level of the cricoid cartilage and Chassaignac's tubercle (C6) to avoid potential damage to pleura. Although the stellate ganglion is typically located at the level of C7 and T1, the block is commonly performed at the level of C6 to reduce the likelihood of pneumothorax. The sternocleidomastoid muscle and carotid artery are pushed laterally while palpating Chassaignac's tubercle. The skin and subcutaneous tissue are pressed firmly onto the tubercle, and the needle is directed medially and inferiorly toward the body of C6. After making contact with the C6, the needle is withdrawn 1–2 mm so that it is just outside the longus colli muscle. Typical volumes of local anesthetic used range between 5 and 15 mL.

Fluoroscopy Assisted The same approach is used as with the landmark technique, and then fluoroscopy is used to confirm its position. Radiopaque contrast is injected, and the spread is visualized using anteroposterior and lateral views. Injection into the longus colli muscle is indicated by inability of the contrast medium to spread in between the tissue planes, while instantaneous disappearance indicates the presence of the needle in a vessel.

CT Guided Patient is positioned supine with the head turned away from injection site. The head of the first rib, vertebral artery, and vein are identified. A 25-gauge spinal needle is directed onto the head of the first rib, as close to the vertebral body as possible.

Ultrasound Guided Patient is positioned supine with the head turned away from the side of the block. A high-frequency linear transducer is placed on the neck at the level of cricoid notch, which should be at the C6 level. The block can also be performed at the level of C7. The carotid artery, internal jugular vein, thyroid gland, trachea, longus colli muscle, C6 nerve root, and transverse process of C6 are identified. If the carotid artery blocks the path to the cervical sympathetic chain, the transducer can be moved laterally for a more lateral needle trajectory to avoid the carotid artery. Doppler is used to evaluate whether or not the inferior thyroid artery is in the intended path of the needle; a lateral approach can be used if it is. Using an in-plane approach, a 25-gauge, 1-inch needle is inserted. The target is just anterior to the fascia surrounding the longus

colli muscle, which is where the sympathetic nerves and ganglion are located. Recommended local anesthetic volume ranges between 2–7 mL.

Side Effects

- Horner's syndrome (superior cervical ganglion)
- Hoarseness (recurrent laryngeal nerve)
- Phrenic nerve block (ipsilateral diaphragmatic paralysis)
- Brachial plexus block (partial block → arm weakness)

Complications

Vascular injury/hematoma
- Carotid artery, internal jugular vein, inferior thyroid artery
- Ascending cervical artery
- Retropharyngeal hematoma

Neurological injury
- Vagus nerve, brachial plexus root (C6,C7) injury
- Locked-in syndrome, stroke
- Neuraxial injection

Local anesthetic toxicity
Pneumothorax, chylothorax
Infection

Suggested Readings

Waldman SD. Ultrasound-guided stellate ganglion block. In: Ultrasound-guided pain management injection techniques, 1st ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2014. p. 156–62.

Day M. Sympathetic blocks: the evidence. Pain Pract. 2008;8:98–109.

Celiac Plexus Block

79

Srdjan S. Nedeljkovic and Syed Irfan Qasim Ali

CPT

Celiac plexus: 64530
Fluoroscopic needle guidance (nonspinal): 77002

Indications

Acute or chronic abdominal pain due to pancreatitis and pancreatic, gastric, esophageal, and biliary malignancies. Also used in mesenteric vascular occlusive disease-related pain and acute pain after liver embolization.

Equipment/Materials

20-G or 22-G 15 cm stylet needle, local anesthetic, contrast, phenol or alcohol, and fluoroscopy.

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Procedure

Anesthesia: MAC
Position: Prone

Steps

There are multiple approaches to this block, but transcrural and retrocrural approaches are most common. Other approaches include anterior, transaortic, transintervertebral disk, CT-guided, and endoscopic US-guided approaches.

Retrocrural Approach

1. A pillow is placed beneath the abdomen to decrease lordosis.
2. Anatomical landmarks include T12 and L1 and 12th rib. The needle insertion site is caudal to the 12th rib 5–7 cm away from the midline.
3. After infiltrating local anesthetic in the skin and subcutaneous tissue, a 22-G 15 cm needle is inserted on the left side at an angle of 45° from horizontal, toward the body of L1.
4. After making bony contact with L1 at a depth of approximately 6–9 cm, the needle depth is noted and is withdrawn and redirected at an increased angle to allow the needle tip to slide off the body of the vertebra anterolaterally.

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5. Advancement is stopped either at a point 1–2 cm beyond the anterior margin of the vertebral body or until aortic pulsation is felt.
6. The same procedure is repeated on the R side.
7. Contrast medium is injected after negative aspiration for CSF, blood, and urine.
8. Once correct needle placement is confirmed, 5–10 ml of local anesthetic is injected (0.25 % ropivacaine, 0.25 % bupivacaine, or 2 % lidocaine).
9. If the initial test dose leads to pain relief, then neurolysis can be performed using alcohol 50–95 % 10–20 ml on each side or phenol 5–10 % 10–15 ml on each side.
10. The needle should be flushed with saline before removal to prevent tracking of the neurolytic solution through the muscles and subcutaneous tissue.

See Figs. 79.1 and 79.2.

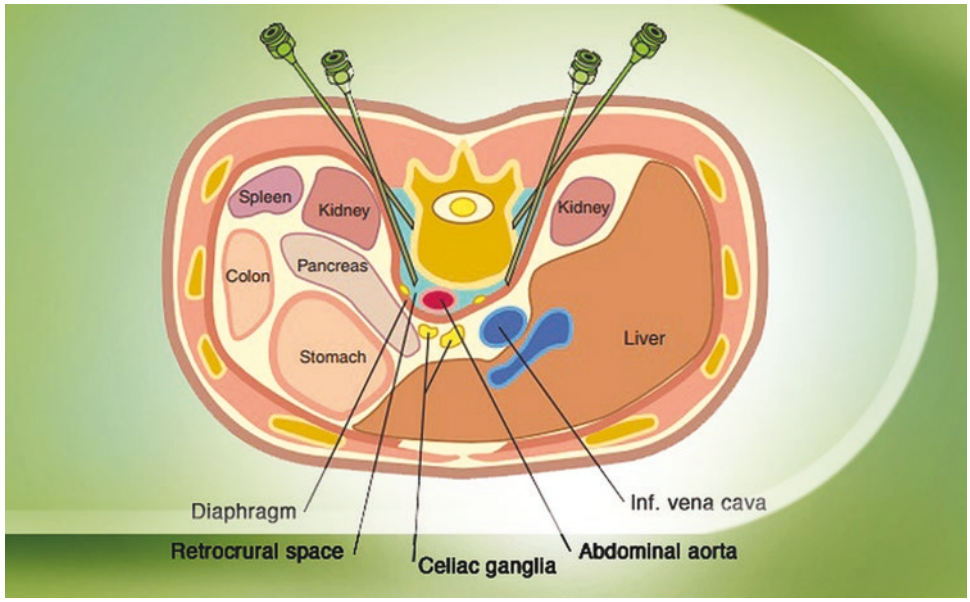

Fig. 79.1 Retrocrural approach for celiac plexus. Image courtesy of Dr Kambiz Bagherzadi @ begharzadi.com

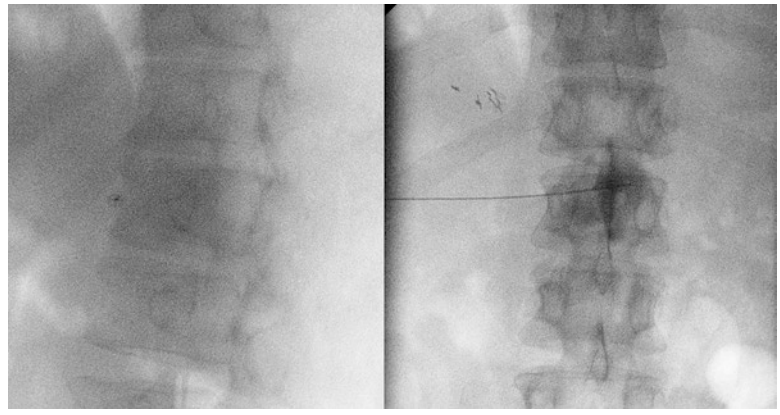

Fig. 79.2 *Left* shows coaxial placement of needle lateral to L1 transverse process. *Right* shows contrast spread in the AP view

Complications

Procedure-specific complications include orthostatic hypotension, diarrhea, and backache. More serious but less common complications include retroperitoneal hemorrhage, paraplegia, transient cord damage, aortic dissection, sexual dysfunction due to sympathetic chain neurolysis, and fistula formation. In a review of complications from celiac plexus block performed in 2730 patients, the overall incidence of serious complications was one in 683 patients.

Clinical Pearls

- Using imaging is mandatory in performing this nerve block.
- Alcohol injection itself may be painful, while phenol has local anesthetic type properties.
- An alternative to fixed distances and angles, fluoroscopy can guide the path of the needle by obliquing the image intensifier to the patient's left until the transverse process of L1 is in line with the anterior border of the L1 vertebral body and inserting the needle coaxially just lateral to the transverse process.

Evidence

A meta-analysis of celiac plexus block for cancer pain showed that at 3 months and beyond 3 months or until death, the reported pain relief was 90 % and 70–90 %, respectively. The most common adverse effects include local pain, diarrhea, and hypotension, all of which were transient. Complications occurred in 2 % of the patients. Performing a celiac plexus block may provide excellent pain relief with a relatively low risk of mostly transient side effects, regardless of the technique and agent used.

Additional Reading

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Lumbar Sympathetic Block

80

M. Gabriel Hillegass, III, John Damon Allen, and Thomas J. Moran

CPT

Injection, anesthetic agent; lumbar or thoracic paravertebral sympathetic 64520

Fluoroscopic guidance 77003

Destruction by neurolytic agent; other peripheral nerves or branch 64640 vs. unlisted procedure, nervous system 64999 (Recommend submitting 64999 with a procedure report and supporting explanatory documentation linking the procedure to similar sympathetic neurolytic techniques, e.g., 64680 or 64681.) [1].

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Indications

Complex regional pain syndrome (CRPS) and other sympathetically mediated neuropathic pain phenomena affecting the lower limb, acute herpes zoster, early postherpetic neuralgia, early phantom limb pain, vascular insufficiency affecting the lower extremities

Equipment/Materials

Fluoroscopy machine, 22 gauge bent-tip spinal needle (5–7 in.), syringes, connection tubing, contrast agent, local anesthetic for needle path, local anesthetic with epinephrine (5 mcg/mL) +/− corticosteroid for the block, phenol/alcohol for neurolysis, ASA standard monitors, skin temperature probe

Procedure

Position: prone, obtain baseline skin temperature distally on the affected side.

IV: strongly consider use for access in case of an adverse event and for moderate sedation if needed (for patient comfort, severe anxiety or needle phobia, or history of vagal events).

Antibiotics: not required

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Steps

1. When using a one-needle technique, start with an AP view, and center the L2 or L3 spinous process between its pedicles. Adjust caudal/cranial tilt to square the inferior L2 end plate or the superior L3 end plate, respectively, depending on the target level (Fig. 80.1a).
2. Oblique ipsilaterally toward the symptomatic side until the tip of the transverse process is even with the anterolateral margin of the target vertebral body (about 25°).
3. After local anesthetic infiltration, insert the spinal needle coaxially, aiming for the inferior anterolateral corner of the L2 vertebral body (Fig. 80.1b) or the superior, anterolateral corner of the L3 vertebral body, respectively.
4. Once the trajectory is verified to be coaxial, advance the needle incrementally under fluoroscopic guidance until contact with the vertebral body periosteum.
5. Walk the needle off of the vertebral body, rotate C-arm to a lateral view, and continue to advance it anteromedially. The needle tip should be placed within the anterior one-third of the vertebral body, but preferably as close to the anterior margin of the vertebral body as possible.
6. Rotate the C-arm back to an AP view, and confirm if the needle tip is medial to the lateral vertebral body margin. The tip will generally be beneath the shadow of the pedicle.
7. Remove the stylet, and after negative aspiration, inject a small volume of contrast using continuous fluoroscopy (or digital subtraction if available) in both the AP and lateral views to assess for vascular uptake. Verify expected contrast spread, which should extend in a cranial-caudal direction to cover the L2, L3, and possibly L4 vertebral levels along the anterolateral vertebral margin (Fig. 80.2).
8. Administer test dose (3 mL) of local anesthetic with epinephrine (5 mcg/mL) while monitoring vital signs to assess for increased heart rate due to vascular uptake. Adjust the needle position if needed, and reimage/retest.
9. Inject incrementally a total of 10–20 mL if a one-needle technique is used. If more than one needle is used due to inadequate contrast spread, divide the final injectate volume between each needle.
10. *Assess for the efficacy* of the block post-procedurally, and adjust the approach as

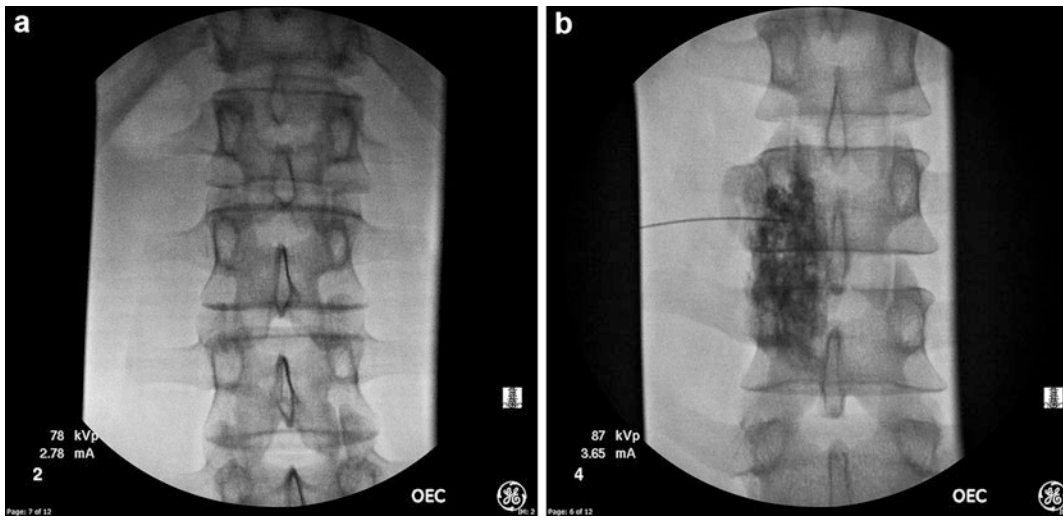

Fig. 80.1 (**a**) AP view of the lumbar spine with L2 centered and its inferior end plate squared off. (**b**) Oblique view to the left with a needle positioned to contact the anterolateral inferior corner of L2

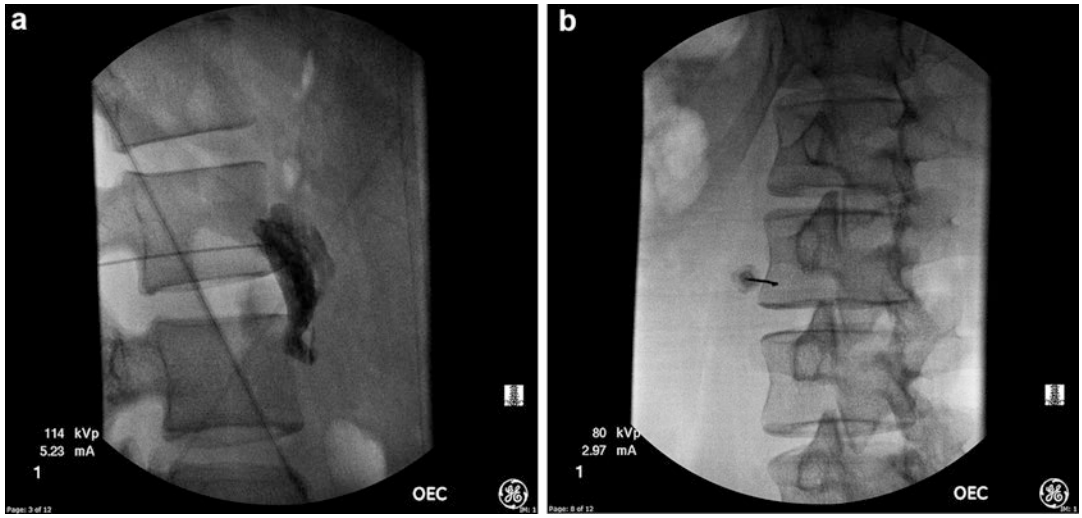

Fig. 80.2 (**a**) Lateral view of the L2–L3 junction depicting contrast spread along the anterior margin of the vertebral bodies. (**b**) AP view demonstrating desired contrast spread covering left anterolateral L2 and L3

needed for future procedures (e.g., change target level, or use multiple needles for inadequate sympathectomy and/or pain reduction):

a. Pre-/post-procedure symptoms at rest and with provocation.
b. Skin surface temperature—should increase by 2°C in the target limb only (although it's possible to have some spread contralaterally via the prevertebral space).
c. Sweat test—involved limb should be anhidrotic.
d. Functional improvement following block.
e. Pre-/post-procedure pain medication requirement.

Complications

Bleeding, infection, intravascular injection, local anesthetic systemic toxicity if iatrogenic overdose combined with intravascular injection, disk puncture and possible diskitis, genitofemoral neuritis, renal/ureter puncture, transient neural blockade from posterior spread of local anesthetic to epidural or subarachnoid spaces (rare), post-procedure back pain, retrograde ejaculation if bilateral sympathectomy

Clinical Pearls

If the desired extent of contrast spread is not observed, consider repeating the one-needle technique at a different level, or use multiple needles. The two-needle approach is often done at L2 and L4 concurrently instead of just a single injection at L2 or L3.

For neurolysis with phenol or alcohol, multiple needles are often used from L1 to L5 with small volumes (3–5 mL) of the neurolytic agent injected via each one.

Skin surface temperature monitoring can be fraught with error. Uncover both legs, and allow them to be exposed to the ambient environment for at least 10 min prior to recording the baseline skin temperatures. Record pre- and post-procedure temperatures for both legs. We typically use the dorsum of the foot, but measuring in multiple areas (anterior thigh, medial calf, etc.) can increase the sensitivity of this outcome.

Evidence

Although case reports and small case series have shown positive response to lumbar sympathetic block (LSB) and neurolytic sympathectomy,

there is little high-quality evidence to support this technique in the management of neuropathic pain and CRPS. Reported incidence of significant adverse events related to LSB is small; however, potential serious complications of sympathectomy are well documented [1].

A systematic review reported that 44 % of 66 patients received short-term meaningful relief (>2 weeks) of their cutaneous allodynia with neurolytic chemical sympathectomy for their neuropathic pain [2]. Manjunath et al. (2008) [3] compared percutaneous radiofrequency (RF) thermal lumbar sympathectomy to phenol lumbar sympathetic neurolysis in a double-blinded, randomized controlled trial [4]. They reported significant pain reduction out to 4 months in both groups with no significant difference between groups. Of note, the RF group had more postprocedure pain, and 10% of the phenol group had postsympathectomy neuralgia.

Disclaimer The views expressed in this article are those of the author(s) and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the US Government.

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Superior Hypogastric Plexus Block

81

Ryan H. Nobles and M. Gabriel Hillegass, III

CPT

Injection, anesthetic agent; superior hypogastric plexus 64517

Fluoroscopic guidance 77003

Destruction by neurolytic agent, with or without radiologic monitoring; superior hypogastric plexus 64681

Indications

Visceral pelvic pain of malignant and nonmalignant origin

Equipment/Materials

Fluoroscopy machine, 22 or 25 gauge bent-tip spinal needle (5 or 7 in. length), 5 and 10 mL syringes, connection tubing, contrast agent, local anesthetic +/− corticosteroid, phenol/alcohol for neurolysis, ASA standard monitors, supplemental oxygen

Procedure

Position: prone

IV: strongly consider use for access in case of an adverse event and for moderate sedation if needed (for patient comfort, severe anxiety or needle phobia, or history of vagal events)

Antibiotics: not required unless using a L5–S1 transdiscal approach (not described here)

Steps

1. Start with an AP view, and center the L5 spinous process between its pedicles. Angle the C-arm cephalad to square the inferior end plate of the L5 vertebral body or to alternately open up the L5–S1 intervertebral disk space.
2. Oblique the C-arm ipsilaterally until the tip of the transverse process of L5 just overlaps the lateral border of the vertebral body. Note: consider the locations of the iliac crest, sacral superior articulating process, and transverse process as C-arm adjustments may be necessary to create a clear path to the inferior aspect of the L5 vertebral body.

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3. Isolate the skin insertion point overlying the most inferior aspect of the anterolateral L5 vertebral body but superior to the L5–S1 disk.
4. Using sterile technique and after local anesthetic infiltration, insert the needle coaxially toward the target (Fig. 81.1a).
5. Advance the needle in a coaxial plane until contact with the vertebral body. Walk off of the lateral vertebral body, and reposition the C-arm to a lateral view to continue needle advancement.
6. Continue to advance the needle anteromedially until the needle tip is within the anterior one-third of the vertebral body on the lateral view (Fig. 81.1b).
7. Once at the anterior margin of the vertebra, gently aspirate, and if negative, inject a few milliliters of contrast under continuous fluoroscopy (or using digital subtraction if available). There should be no vascular uptake or posterior contrast spread, and it should distribute caudally along the anterior margin of the L5–S1 interspace (Fig. 81.2a).
8. Return to an AP view to confirm needle placement, and ensure appropriate medial and caudal spread of injectate (Fig. 81.2b). After negative aspiration, an additional contrast injection under continuous fluoroscopy (or digital subtraction) should be performed to confirm no vascular uptake or muscular spread pattern.
9. Repeat the technique for the contralateral side if there is inadequate contralateral contrast spread across the prevertebral space. Most procedures require bilateral needle placements for adequate coverage of the lumbosacral nerve plexus.
10. Inject incrementally for a total of 10 mL of injectate per side or 15–20 mL if a one-needle technique is used.

Complications

Neurologic deficit from posterior spread of injectate to the L5 nerve roots and intravascular injection of the iliac vessels are some of the potential complications. Use an adequate volume of contrast to predict injectate spread, and place the needle as close to the anterior margin of the vertebra as possible to decrease the likelihood of posterior spread. Injection of contrast under real-time fluoroscopy and use of digital subtraction should decrease risk of intravascular injection. Puncture of the L5–S1 disk is possible with diskitis as a potential complication. Also of concern are injury to the ureters, neuraxial injection or trauma, bleeding, hematoma formation, and infection (particularly in the immunocompromised).

Clinical Pearls

A transdiscal approach has also been described [1]. It is recommended that strict aseptic technique and pre-procedure antibiotics be utilized if

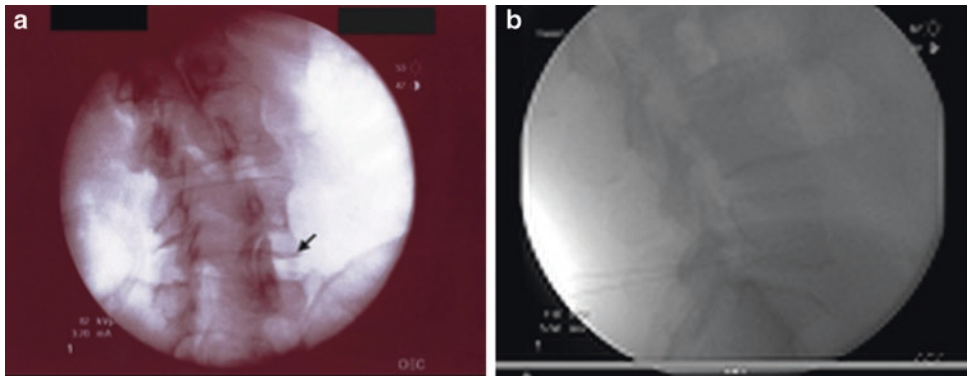

Fig. 81.1 (**a**) Right-sided oblique view of L5 depicting the needle target (*arrow*) at the inferior margin of the anterolateral vertebral body. (**b**) Lateral view depicting appropriate needle depth along the anterior one-third of the vertebral body width

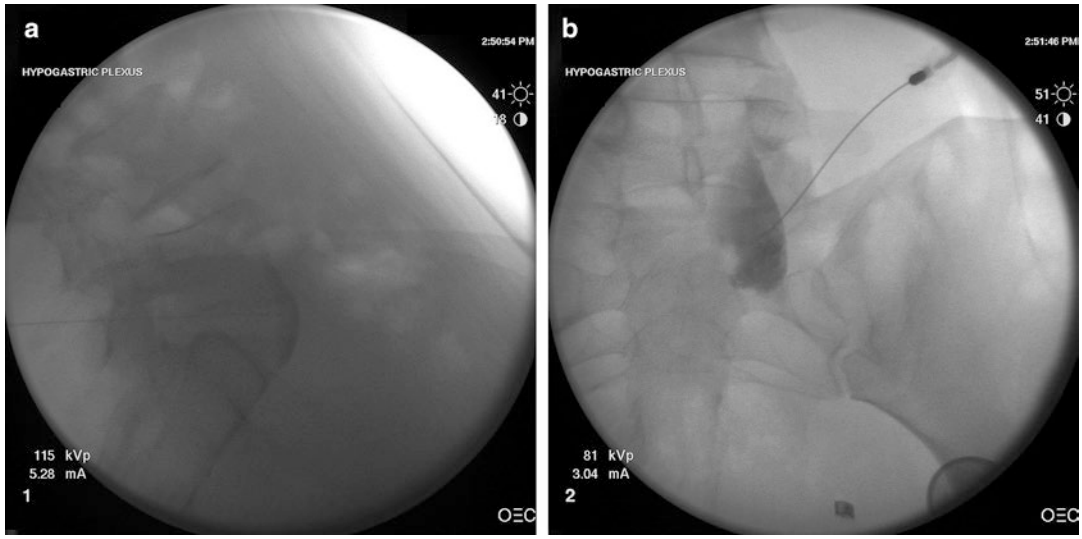

Fig. 81.2 (**a**) Lateral view of contrast spread along the anterior margin of the L5–S1 interspace. (**b**) AP view after contrast injection. Note the contrast is along the anterolateral vertebral body and spreading caudally

this approach were to be attempted due to risk of diskitis. An ultrasound-guided approach has also recently been described [2].

There is no consensus on injectate mixture or volume. We typically use 0.2–0.5 % ropivacaine or 0.25–0.5 % bupivacaine (+/− epinephrine 5 mcg/mL) with 10 mg of dexamethasone and 20 mL of total volume (10 mL per side). Similarly, there are practice variations on how neurolysis is performed with varying concentrations of phenol and ethanol and in varying volumes according to patient anatomic considerations.

Evidence

Neurolytic Blocks and Opiate Consumption

In a large cohort study, superior hypogastric neurolytic blocks for malignant pain in patients who responded favorably (>65 % relief) to diagnostic blockade resulted in a decrease in consumption of opioids from 40 to 60 % with about 70 % of patients reporting significantly improved pain [3, 4]. In a retrospective case series, older patients (mean age of 60) and patients with bladder cancer responded more favorably to neurolytic blockade. Lower baseline narcotic usage also predicted positive results [5]. Despite favorable response to diagnostic blockade, neurolysis for nonmalignant pain has shown short-term results in a retrospective case series (less than 1 month) [4].

Local Anesthetic +/− Steroid for Nonmalignant Pain

Case reports have reported successful relief of pelvic pain for varying periods of time (days to weeks) following local anesthetic blockade [4].

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Ganglion of Impar Injection/ Neurolysis

82

Erik P. Voogd

CPT: Unlisted Procedure
Nervous system 64999
Fluoroscopy 77003

Indications

Helpful for the treatment of rectal and coccygeal pain and can help differentiate pelvic from rectal pain if sympathetically mediated. Most insurance carriers do not automatically cover CPT 64999. When reporting an unlisted code, it will be necessary to submit supporting documentation such as a procedure report with the claim to provide a description of the extent, nature, and need for the procedure along with the time, effort, and equipment that was necessary.

Equipment/Materials

Fluoroscopy, 22G B-bevel or 18–20G needle depending on width and calcification of the rudimentary sacrococcygeal disk, +/− contrast, local anesthetic, +/− corticosteroid. For neurolysis, 3 ml of phenol and 6–10 % or 100 % ethanol are acceptable. Note: The ethanol causes a severe inflammatory reaction and is very painful. Concomitant use of local anesthetic prior to neurolysis and post-procedure pain medications are highly recommended.

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Procedure

Position: prone
IV: not required unless previous vagal episodes
Antibiotics: not required

Steps

1. Start with AP view, and center spinous process between pedicles. Adjust caudal/cephalad tilt to open the sacrococcygeal space maximally.
2. Identify the skin entry point midline directly coaxial to the sacrococcygeal space.
3. After local anesthetic infiltration, insert the needle of choice coaxially, and advance to the point of resistance. See Fig. 82.1.
4. Advance the needle just slightly to engage the fibroligamentous material.
5. Rotate C-arm to the lateral position, and advance the needle until the tip just begins to reach the ventral aspect of the sacrococcygeal space (additionally a decrease in resistance may be noted). See Fig. 82.1.
6. After attempted aspiration, inject radiocontrast dye, and note the caudal and cephalad

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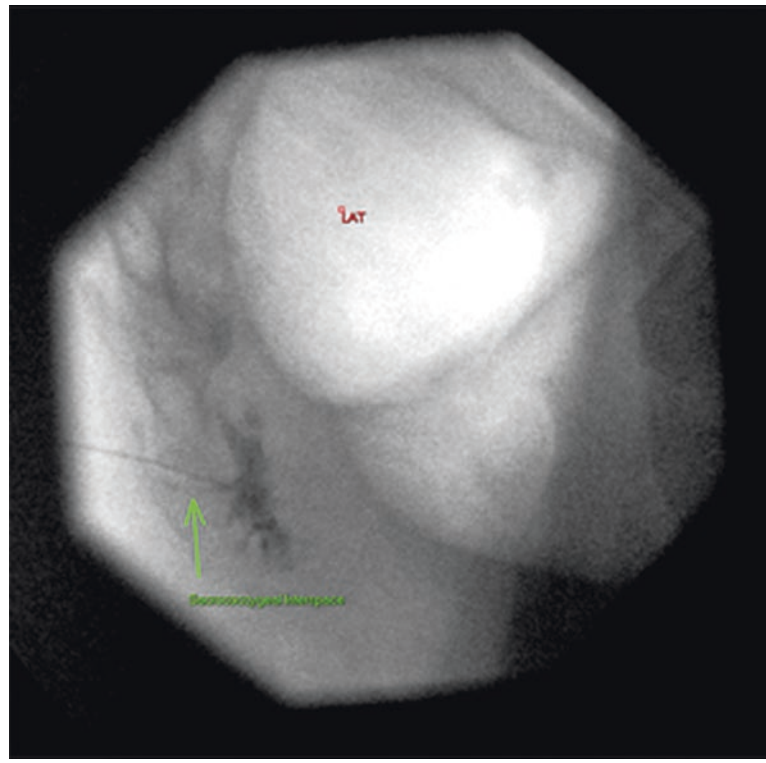

Fig. 82.1 Lateral view—note how the needle is inserted through the rudimentary disk space between the sacrum and the coccyx

spread in a lenticular shape along the ventral surface of the sacrum and coccyx.
7. Administer injectate.
8. Take and save final image.

Complications

Perforation of the rectum and tracking of contaminants are a concern. Infection in fistula formation, especially in immunocompromised patients or patients who have received radiation, can be potentially life-threatening.

Clinical Pearls

There is little consensus on injectate for the block. Volumes vary from 2 to 8 mm with choice and dosage of corticosteroid varying widely as well. We typically use 40 mg of triamcinolone mixed with 0.5% lidocaine and 4–6 cc of total volume. For neurolysis, 3 ml of phenol 6% with iohexol 240 mg/ml is typically used.

Evidence

Transsacrococcygeal Approach to GanglionImpar Block: In a prospective, observational study, the mean VAS for pain at presentation in neurolytic block and therapeutic block groups was 9.2 ± 0.98 and 8 ± 0.81, respectively. At 2 months, the average VAS for both groups was 2.

Additional Readings

Toshniwal GR, Dureja GP, Prashanth SM. Transsacroc occygeal approach to ganglion impar block for management of chronic perineal pain: a prospective observational study. Pain Physician. 2007;10:661–6.
Waldman SD. Atlas of interventional pain management, 4th ed. Chapters 115 & 116. 3 December. Saunders; 2014.

Brachial Plexus Blocks

83

David Ende and Jose Luis Zeballos

Indications: Typically used as a primary anesthetic or for postoperative pain control for procedures on the upper extremity, with block site dependent on location of procedure. May also be performed for acute pain control associated with trauma or chronic pain (CPRS, Raynaud's, peripheral neuropathy).

Equipment/Materials

Ultrasound machine with sterile probe cover and gel, emergency airway equipment/drugs, local anesthetic (choice dependent on indication for block and block goals), sedatives (midazolam and fentanyl).

Single-Shot Block

50 or 100 mm, 21 or 22 gauge echogenic block needle, skin antiseptic, sterile gloves, sterile drape, and 25G needle with syringe for lidocaine local skin anesthetic (1 % lidocaine).

Continuous Catheter Placement

Add standard sterile nerve block tray, 50 or 100 mm echogenic needle with Tuohy tip, and catheter system.

Procedures: Four Locations for Blockade

Interscalene Block

Very effective for: Shoulder surgery and orthopedic surgery involving the upper humerus and upper arm trauma or chronic pain.

Less effective for: Distal forearm/hand surgery due to common ulnar sparing and inconsistent lower trunk blockade.

Position: Supine, back at 30° incline, and arm at side.

IV: Required for risk of local anesthetic toxicity/intravascular injection.

Antibiotics: Not required.

Steps

1. With patient in supine position, expose neck and ipsilateral shoulder. Position patient's head facing away from the proceduralist to further expose the neck.

CPT:Single shot:
Interscalene/supraclavicular/infraclavicular: 64415
Axillary block: 64417
Continuous catheter block: 64416
Ultrasound guidance: 76942
Professional service component, modifier—26

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2. Using skin antiseptic, prep neck from mandible to clavicle extending from midline to where patient's neck contacts the bed.
3. Identify patient's external anatomy, including the clavicle, sternocleidomastoid (SCM) and cricoid cartilage, and carotid artery pulse.
4. Place ultrasound probe, with depth set to 2.5–3 cm, in transverse orientation on patient's neck at level of cricoid cartilage directly over carotid pulse with goal of visualizing carotid artery.
5. Slide probe posterolaterally keeping level with cricoid cartilage until anterior scalene (AS) and middle scalene (MS) muscles are visualized just lateral and deep to the posterior border of the SCM.
6. Brachial plexus will appear as 3–5 hypoechoic "stacked bubbles" positioned between the AS and MS (see Fig. 83.1).
7. Insert needle in lateral to medial trajectory into the skin with shallow angle under the ultrasound probe using an in-plane technique. While keeping full needle in view, advance tip through middle scalene muscle with goal placing tip between "bubbles" in fascial plane between AS and MS.
8. After aspirating, inject 15–25 cc of chosen local anesthetic in incremental doses and observe spread on ultrasound, with goal of achieving local anesthetic spread around all trunks of brachial plexus on both medial and lateral sides.

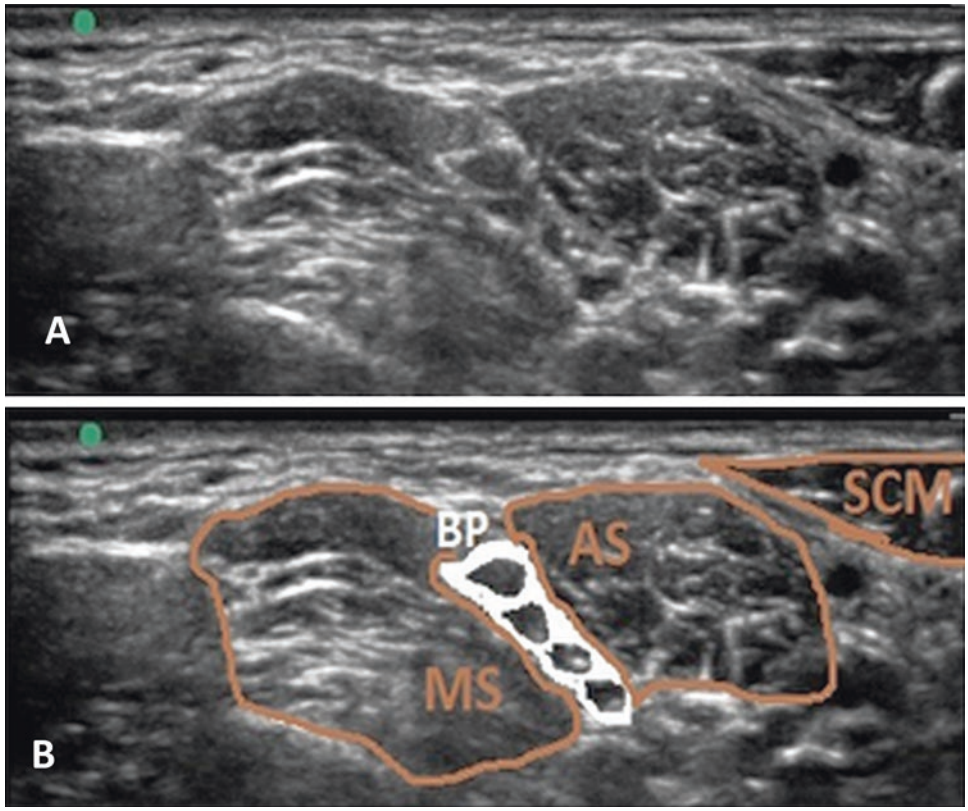

Fig. 83.1 Interscalene anatomy and target, unlabeled (**a**) and labeled (**b**). *BP* brachial plexus, *SCM* sternocleidomastoid, *AS* anterior scalene, *MS* middle scalene

9. If planning on continuous catheter placement, under ultrasound guidance, deploy catheter so that the tip is 3–5 cm beyond needle tip.
10. Withdraw needle with continuous catheter threading motion to ensure catheter tip remains close to brachial plexus.
11. Secure catheter with adhesive skin prep, clear sterile dressing, and tape.

Complications

This block can additionally anesthetize other non-brachial plexus nerves in the immediate area. It is important to prepare the patient for this and reassure them as it does happen relatively frequently.

- Phrenic nerve blockade and hemidiaphragm paralysis occurs with nearly 100 % of interscalene blocks; therefore, they are not typically performed on patients with severe pulmonary disease. In patients with normal pulmonary function, it is often not noticed or only noticed with a mild increase in dyspnea on exertion.
- Horner's syndrome (miosis, anhidrosis, and ptosis) can also occur due to blockade of the ipsilateral sympathetic chain.
- Recurrent laryngeal nerve blockade can cause a hoarse voice secondary to ipsilateral vocal cord medialization.
- Pneumothorax, vertebral/carotid arterial injury, and neuraxial injury are possible. These outcomes are extremely rare with good ultrasound visualization of the anatomy, careful needle technique, and aspiration prior to all injections. Prior to needle insertion, use color Doppler over brachial plexus and anticipated needle trajectory to help avoid inadvertent vascular puncture. The vertebral artery can occasionally resemble a nerve trunk of the brachial plexus.
- As with all other blocks, injection site infection, hematoma, local anesthetic toxicity/intravascular injection, and nerve injury are all very rare but possible risks best avoided with good technique. Ensure availability of lipid emulsion prior to beginning procedure.

Clinical Pearls

Troubleshooting ultrasound visualization:

Place probe in supraclavicular fossa and visualize the brachial plexus as it should be immediately adjacent and lateral to subclavian artery. Once visualized, the plexus can be traced superiorly up the neck to where it courses between AS and MS and targeted. Other anatomic clues to likely location are looking lateral to carotid artery and just lateral and deep to posterior border of SCM (see Fig. 83.1).

Often initial visualization of interscalene brachial plexus will inadvertently drift into a "high supraclavicular" view while placing needle due to propensity to drive needle tip inferiorly while coordinating needle-ultrasound movement. This can be somewhat avoided by holding block needle with overhand grip and constant vigilance to move needle into ultrasound field view, as opposed to moving ultrasound onto needle.

Upper roots/trunks are most important to anesthetize for shoulder surgery and upper arm surgery. For better distal coverage, ensure spread around lower trunks. Their blockade is typically unreliable, which is why an interscalene block is not an ideal choice for more distal procedures or pain.

Supraclavicular Block

Very effective for: Procedures of /trauma to midhumerus to distal forearm, elbow surgery.

Less effective for: Shoulder surgery and hand surgery due to sparing of the cervical plexus which innervates the skin over the shoulder and occasional ulnar sparing (although much less sparing than interscalene block and with good technique is typically covered).

Position: Supine, back at 30° incline, and arm at side.

IV: Required for risk of local anesthetic toxicity/intravascular injection.

Antibiotics: Not required.

Steps

1. With patient in supine position, expose neck and ipsilateral shoulder. Position patient's head facing away from the proceduralist to further expose the neck.
2. Using skin antiseptic, prep neck from cricoid cartilage past the clavicle onto the upper chest extending from midline to where patient's neck contacts the bed.
3. Place ultrasound probe in supraclavicular fossa, with depth set to 3–4 cm, in transverse orientation immediately superior to the clavicle just medial to its midpoint with goal of visualizing the subclavian artery (SC) in cross section as it dives underneath the clavicle and over the first rib. Visualizing the pleura as it resides just deep to the first rib is also important for orientation.
4. Once SC is visualized, the brachial plexus should be immediately superolateral and will appear as a bunch of hypoechoic bubbles grouped together (see Fig. 83.2).
5. Insert needle with lateral to medial orientation under ultrasound probe with in-plane technique at a shallow angle. Advance toward brachial plexus aiming at inferior aspect.
6. Needle tip target should be angle where SC meets the first rib, sometimes referred to as the "corner pocket." This location is where lower trunk nerves C8-T1 commonly reside, and

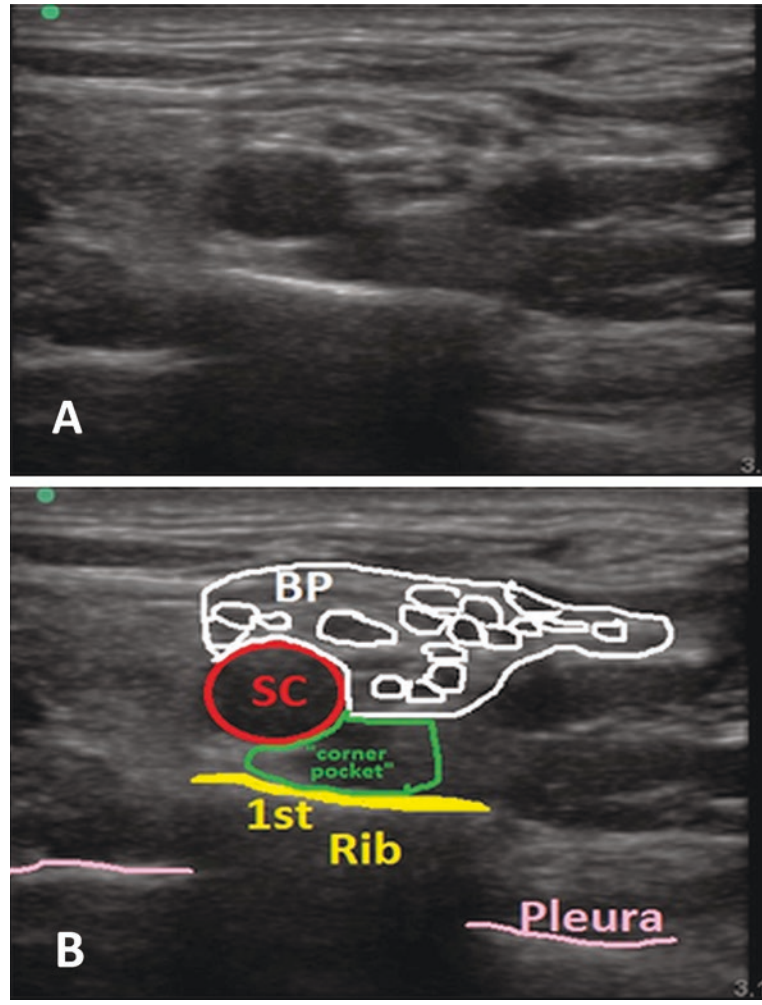

Fig. 83.2 Supraclavicular block anatomy and target unlabeled (**a**) and labeled (**b**). *SC* subclavian artery, *BP* brachial plexus

ensuring local anesthetic spread in this location will minimize risk for ulnar distribution sparing. Hydro-dissection of tissues may be helpful during needle advancement to avoid direct puncture of brachial plexus and "lift up" brachial plexus allowing for advancement of needle tip to target.

7. Once needle tip is immediately lateral to SC-first rib contact point (very carefully avoiding SC puncture and needle tip moving deeper behind the first rib and close to the pleura), aspirate and inject 20–30 cc local anesthetic with goal of local anesthetic spread "lifting" the brachial plexus anteriorly away from the first rib and ideally completely filling the "corner pocket" with local anesthetic.
8. Optionally a second injection deposit of 10 cc superiorly or on top of brachial plexus may speed onset/ensure adequate spread.
9. If planning on continuous catheter placement, under ultrasound guidance, deploy catheter so that the tip is 5–6 cm beyond needle tip. The best location of catheter is into hydro-dissected space under newly lifted brachial plexus.
10. Withdraw needle with continuous catheter threading motion to ensure catheter tip remains close to brachial plexus.
11. Secure catheter with adhesive skin prep, clear sterile dressing, and tape.

Complications

- Pneumothorax is the most concerning complication with supraclavicular block given the proximity of the block target to the apical pleura. The literature indicates it is a rare complication; however, with good ultrasound visualization of the anatomy and careful needle technique, ensuring the tip of the needle does not pass beyond the first rib should keep this complication quite rare.
- Intravascular injection can also occur given the proximity of block target to subclavian artery and otherwise vascular nature of the area. Prior to needle insertion, use color doppler over brachial plexus and anticipated needle trajectory (uncompressed) to help avoid inadvertent vascular puncture. Careful needle tip control while at block target is crucial to the avoidance of vascular puncture, as well as intermittent aspiration prior to and during injection.
- This technique can infrequently block other nerves in the immediate area and therefore will have a few side effects that should be self-limited.
- Horner's syndrome (miosis, anhidrosis, and ptosis) has been described after this block, again much less frequently than interscalene block.
- As with all other blocks, injection site infection, hematoma, and nerve injury are all very rare but possible risks best avoided with good technique. Ensure availability of lipid emulsion prior to beginning procedure.

Clinical Pearls

While good brachial plexus visualization is considered key to an effective block, there is some evidence that even without direct visualization, if local deposition is in the typical areas in reference to the subclavian artery, an effective block is still frequently achieved.

The supraclavicular block is frequently referred to as the "spinal" of the arm for its ability to frequently achieve total anesthesia of the upper extremity, including (usually) the hand.

Infraclavicular Block (Fig. 83.3)

Very effective for: Procedures of/trauma to distal humerus, elbow, wrist, and hand. Excellent for continuous blockade as catheter tip is easily fixed at target with less risk of inadvertent dislodgement.

Ineffective for: Shoulder surgery, proximal humerus trauma/procedures.

Position: Supine, back at 30° incline, and arm at side.

IV: Required for risk of local anesthetic toxicity/intravascular injection.

Antibiotics: Not required.

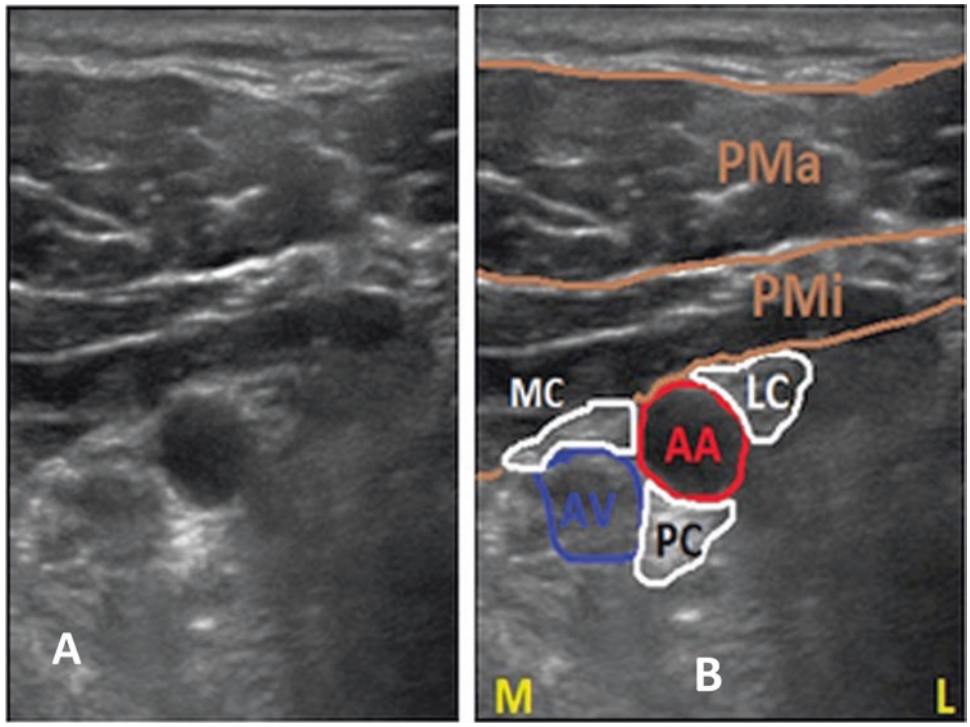

Fig. 83.3 Infraclavicular block anatomy unlabeled (**a**) and labeled (**b**). *AA* axillary artery, *AV* axillary vein, *MC* medial cord of brachial plexus, *LC* lateral cord, *PC* posterior cord, *PMa* pectoralis major, *PMi* pectoralis minor

Steps

1. With patient in supine position, expose neck and ipsilateral shoulder. Position patient's head facing away from the proceduralist.
2. Using skin antiseptic, prep from just above the clavicle extending down to ipsilateral nipple, from the mid-clavicle laterally to the axilla.
3. Place ultrasound probe longitudinally in deltopectoral groove, just below the clavicle and against the medial aspect of the coracoid process. Scan medially and laterally with goal to best visualize the Axillary Artery (AA) as lateral as possible on the chest. Depth depends on the patient's pectoral thickness; however, 3–4 cm should be a good starting point.
4. Once AA is visualized beneath the pectoralis major and minor, lateral, posterior, and medial cords of the brachial plexus may also be visible appearing as hyperechoic structures positioned typically at 3, 6, and 9 o'clock (lateral to medial, L→R) in reference to AA. Typically, also visible is the subclavian vein, medial to SCA. Scanning medially will reveal the pleura, which is to be avoided during needle advancement.
5. With AA visualized as far lateral as possible, insert needle with in-plane technique between superior aspect of ultrasound probe and inferior border of the clavicle and advance under ultrasound probe with inferior/posterior trajectory. Goal is to place needle tip immediately posterior to AA. Advance toward target keeping needle tip in view.
6. Goal of local anesthetic spread is to cover a U-shaped area posterior to AA which would encircle all three cords of the brachial plexus. This can be typically achieved by injecting a large volume directly at the 6 o'clock position; however, supplemental/incremental

injections at the 3 and 9 o'clock positions may help to ensure spread covering all three cords.
7. Typical injectate amount is 25–30 cc local anesthetic. Always inject after aspiration to avoid intravascular injection.
8. If planning on continuous catheter placement, under ultrasound guidance, deploy catheter so that the tip is 5–6 cm beyond needle tip when needle is in 6 o'clock position. The best location of catheter is into hydro-dissected space under newly lifted brachial plexus/AA.
9. Withdraw needle with continuous catheter threading motion to ensure catheter tip remains close to brachial plexus.
10. Secure catheter with adhesive skin prep, clear sterile dressing, and tape.

Complications

- Pneumothorax is also a concerning complication with infraclavicular block given the proximity of the block target to the pleura. It occurs quite rarely with good ultrasound visualization of the anatomy, careful needle technique, and ensuring the ultrasound probe is as lateral as possible prior to starting the block while still visualizing the AA.
- Intravascular injection can also occur given the proximity of block target to AA and otherwise vascular nature of the area. Prior to needle insertion, use color doppler over brachial plexus and anticipated needle trajectory (uncompressed) to help avoid inadvertent vascular puncture, while advancing toward target will help minimize risk. Careful needle tip control while at block target is crucial to the avoidance of vascular puncture, as well as intermittent aspiration prior to and during injection.
- As with all other blocks, injection site infection, hematoma, and nerve injury are all very rare but possible risks best avoided with good technique. Ensure availability of lipid emulsion prior to beginning procedure.

Clinical Pearls

While there is mixed evidence in the literature, in our practice, we find infraclavicular blocks typically take longer to onset than the other brachial plexus blocks, often taking full 20 min to set up if only using long-acting anesthetic (bupivacaine/ropivacaine).

Ultrasound visualization of brachial plexus can be challenging in this block due to depth of target and overlying pectoralis muscles. Fortunately, definitive visualization of the cords, while helpful, is not required for effective blockade. In this case, the best predictor of block success is achieving local anesthetic spread around the axillary artery as described.

Ultrasound visualization of the needle during placement of the block can also be challenging as the target depth and clavicle location make the angle of needle to ultrasound probe quite steep. Intermittent "wiggling" of the needle and small hydro-dissection injections may assist with needle tip localization under ultrasound.

Another technique of "retroclavicular" needle insertion has been described which greatly improves needle visualization. Essentially, with same ultrasound view as classic technique, needle insertion begins superior to the clavicle, and needle is passed into view under ultrasound immediately behind the clavicle. This significantly improves needle visualization as the angle of needle to probe optimally approaches 90°.

This technique also allows for easy needle tip placement in area of medial cord without risk of subclavian vein puncture.

Axillary Block (Fig. 83.4)

Very effective for: Procedures for/trauma to the forearm and hand.

Less effective for: Procedures for/trauma to the humerus and elbow.

Position: Supine, back at 30° incline, arm abducted at 90°, and hand supinated and flexed at the elbow. It is may be helpful to have a sling device around the patient's wrist fixed on top of stretcher to support the arm or place the hand behind the patient's head.

IV: Required for risk of local anesthetic toxicity/intravascular injection.

Antibiotics: Not required.

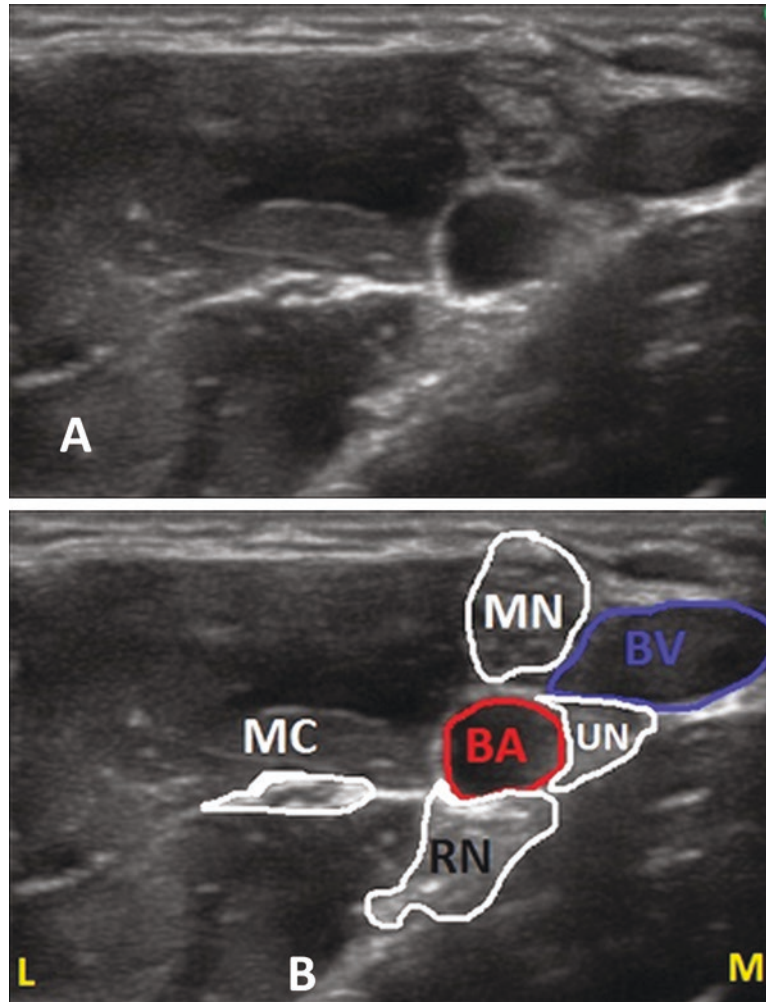

Fig. 83.4 Unlabeled (**a**) and labeled (**b**). Axillary block anatomy. Note how MC is easily identifiable as it is typically quite hyperechoic. *BA* brachial artery, *BV* brachial vein, *MN* median nerve, *RN* radial nerve, *UN* ulnar nerve, *MC* musculocutaneous nerve

Steps

1. With patient in above position, expose patient's axilla.
2. Using skin antiseptic, prep from coracoid process into the axilla and distally to the elbow, covering the entire exposed arm to this point. Ensure good axillary prep.
3. Place ultrasound probe longitudinally to the trunk (transverse to the upper arm) in axillary groove, just lateral to the pectoralis muscle prominence/insertion onto the humerus. Scan medially and laterally with goal to best visualize brachial artery (BA). Target is typically quite shallow; 1–2 cm depth on ultrasound is a good starting point.
4. Once BA is visualized, the brachial plexus as divided into ulnar nerve (UN), median nerve (MN), radial nerve (RN), and musculocutaneous nerve (MC) should be visible in immediate proximity, often as hyperechoic structures. Typical locations, in reference to BA, are MN at 3 o'clock, RN at 6 o'clock, and UN at 9 o'clock (lateral to medial, L → R).
5. MC is typically visualized as hyperechoic structure either within the coracobrachialis, biceps brachii, or between the two structures. Oftentimes, the best visualization technique involves scanning proximally and distally looking for a hyperechoic structure separating and joining from the median nerve.

6. It is important to note that visualizing these nerves definitively is often difficult as they are not always in their classical locations. Often the best confirmatory maneuver is to image each nerve distally at the elbow and trace back to the brachial plexus.
7. Prior to needle insertion, release pressure of ultrasound probe to take note of any veins in the area, and plan needle trajectory accordingly, as this is a particularly vascular area.
8. With BA and nerves visualized, insert needle with in-plane technique, at shallow angle under ultrasound probe with inferior/posterior trajectory. Goal is to place needle tip immediately posterior to BA. Advance toward target keeping needle tip in view, carefully avoiding vascular structures.
9. Goal of local anesthetic spread is to encircle BA covering UN, MN, and RN as well as cover MC nerve. In absence of direct visualization of all four nerves, ensuring local anesthetic spread around BA will typically provide effective blockade. This can be typically achieved by injecting 10–15 cc directly at the 6 o'clock position (RN) with supplemental injections at the sites of the other three nerves.
10. Typical injectate amount is 25–35 cc local anesthetic. Always inject after aspiration to avoid intravascular injection.
11. If planning on continuous catheter placement, under ultrasound guidance, deploy catheter so that the tip is 5–6 cm beyond needle tip when needle is in 6 o'clock position. Best location of catheter is into hydrodissected space under newly lifted brachial plexus/BA.
12. Withdraw needle with continuous catheter threading motion to ensure catheter tip remains close to brachial plexus.
13. Secure catheter with adhesive skin prep, clear sterile dressing, and tape.
14. If planning on use of the block as a primary anesthetic and a tourniquet will be used on the limb, this block will not cover the typical upper arm tourniquet site. To block this area (skin of medial upper arm), innervated by the intercostobrachial nerve, make a skin wheal of local anesthetic 5–10 cc that spans the entire width of the upper medial aspect, just distal to the axillary fossa.

Complications

- The axillary block is considered to be the safest of the brachial plexus blocks as there is no risk of pneumothorax or phrenic nerve blockade.
- Intravascular injection can also occur given the proximity of block target to BA and otherwise highly vascular nature of the area. Prior to needle insertion, use color doppler over brachial plexus and anticipated needle trajectory (uncompressed) to help avoid inadvertent vascular puncture while, advancing toward target will help minimize risk. Careful needle tip control while at block target is crucial to the avoidance of vascular puncture, as well as intermittent aspiration prior to and during injection.
- As with all other blocks, injection site infection, hematoma, and nerve injury are all very rare but possible risks best avoided with good technique. Ensure availability of lipid emulsion prior to beginning procedure.

Clinical Pearls

Positive identification of each nerve on ultrasound at this level can be challenging; typically local anesthetic infiltration around the brachial artery will provide an effective block. The nerve commonly spared with this technique is the musculocutaneous, leading to a sparing of the skin on the lateral side of the forearm and wrist. However, it is the nerve that is most easily identified as it dives through the musculature of the upper arm, looking like a bright, hyperechoic structure that travels to and away from the brachial plexus with movement of the ultrasound probe proximal and distal.

Onset of this block should be quite fast, within 15 min of local anesthetic injection, depending on local anesthetic choice.

Evidence

Interscalene Nerve Block and GA Versus GA Alone in Shoulder Surgery

In a prospective, blinded RCT 50 patients receiving rotator cuff surgery randomized to interscalene block and general anesthesia versus general anesthesia alone. An impressive 76% of patients

receiving interscalene block were able to skip stage I of PACU. They also reported less pain, ambulated earlier, were ready for home discharge sooner, had no unplanned hospital admissions, and were more satisfied with their care. No complications were reported in either treatment group.

Perineural Injections Versus Perivascular Injection in Axillary Block

Prospective, blinded RCT 50 patients receiving upper extremity surgery randomized to perivascular injection (at 6 o'clock position to brachial artery) versus perineural injection where each nerve was individually located and anesthetized showed no significant difference in block success. It is important to note that the musculoskeletal nerve was blocked specifically in both groups.

Additional Reading

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Thoracic Paravertebral Block

84

David Ende and Jose Luis Zeballos

Indications: Primarily used for postoperative pain control for procedures at level of thoracic vertebrae, such as mastectomy, open cholecystectomy, or thoracotomy. May also be performed for acute pain control associated with trauma (rib fractures) or chronic pain (herpetic neuralgia, chronic postsurgical pain).

Equipment/Materials

Emergency airway equipment/drugs, local anesthetic (ropivacaine/bupivacaine 0.25–0.5 % is commonly used), sedatives (midazolam and fentanyl), +/− ultrasound machine with sterile probe cover, and gel.

Single-Shot Block

21G 50 mm block needle, skin antiseptic, sterile gloves, sterile drape, 25G needle with syringe for lidocaine local skin anesthetic (1 % lidocaine), and +/− steroid (usually methylprednisolone 40 mg).

Continuous Catheter Placement

Add standard sterile nerve block tray, 50 mm block needle with Tuohy tip, and catheter system.

Procedure: Traditional Technique

Position: Sitting

IV: Required for risk of local anesthetic toxicity/intravascular injection.

Antibiotics: Not required.

Steps:

1. Place patient in a sitting position, facing away from the proceduralist in flexed position with relaxed shoulders, similar to optimal positioning for neuraxial block.
2. Identify and mark spinous processes and orient to specific levels using anatomic landmarks. (C7 is the most prominent cervical spine process; T7 is aligned with the caudal tip of the scapula.)
3. Measure and mark 2.5 cm lateral to each spinous process on targeted levels to estimate needle insertion point to contact associated transverse process (TP). For example, to cover breast surgery, target T2, T4, and T6.

CPT:Paravertebral sympathetic block: 64,461
Any additional levels: 64,462
Catheter placed for continuous infusion: 64,463
Ultrasound guidance: 76,942 (if applicable)
Professional component: 26

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4. After antiseptic skin prep, inject lidocaine subcutaneously at marked injection sites.
5. Prime block needle and attached tubing with local anesthetic and insert needle perpendicular to the skin at first marked injection site. Focus on needle depth and avoid medial/lateral tilt to needle while advancing parallel to spinous process until contact with TP is made, typically at 3–6 cm depth.
6. Now oriented to depth and location of TP, regrip needle 1 cm away from the skin. Withdraw needle most of the way back to the skin and "walk off" TP angling needle gradually cephalad or caudad until able to advance beyond the original noted depth of TP having reached superior/inferior edge of TP.
7. Advance 1 cm beyond noted TP depth with newly gripped fingers flush against the skin. Aspirate and inject 5–10 cc of local anesthetic (depending on concentration and number levels planned).
8. If planning on continuous infusion, thread catheter through needle until catheter tip is 3–5 cm beyond needle tip and withdraw needle with simultaneous catheter advancement to maintain catheter depth. Secure catheter in typical sterile fashion with adhesive tape/adhesive skin prep and clear adhesive dressing. Make sure to aspirate through catheter (to identify intrathecal/intravascular placement) prior to starting continuous infusion.
9. Repeat process at other planned levels.

Laminar Technique

Follow similar steps of traditional technique with a few differences:

1. When marking out estimated needle insertion points, mark 1.5 cm lateral to each targeted spinous process as the targeted needle contact point will be the lamina of each vertebra, not the transverse process as in traditional technique.
2. After antiseptic skin prep and infiltrating lidocaine subcutaneously at each injection point, insert block needle perpendicular to the skin and parallel with spinous process at first targeted injection site.
3. Advance needle until contact is made with the lamina, typically at 3–6 cm depth.
4. Withdraw 1–2 mm; aspirate and inject 5–10 cc (amount dependent on concentration and number of targeted levels) of chosen long-acting local anesthetic.
5. Withdraw needle and repeat process at each targeted level.

See Figs. 84.1 and 84.2.

Ultrasound-Guided Technique

Ultrasound guidance can offer some advantages with this block, as it allows for definitive visualization of both the transverse process and pleura. The downsides of ultrasound guidance are as follows it make the block take longer to perform, no evidence it is safer, and it may actually offer a false sense of safety if needle visualization is difficult.

Additional Equipment Required

– Linear high-frequency ultrasound probe, sterile cover, and a 50–100 mm echogenic block needle.

Steps:

1. Position and prep patient for block in similar fashion to traditional technique.
2. Instead of marking patient, place ultrasound in longitudinal axis immediately lateral to spinous processes, on side and at level of target block.
3. Goal of imaging is to visualize transverse processes with paravertbral space (PVTS) in between and hyperechoic pleura deep to PVTS.
4. Optimal image is obtained while sliding ultrasound probe lateral and medial noting surrounding structures. Transverse process will appear as flat-surfaced, superficial hyperechoic structures which when scanning lateral will turn into ribs which appear as more round-surfaced, deeper hyperechoic structures. Medial scanning will reveal lamina.

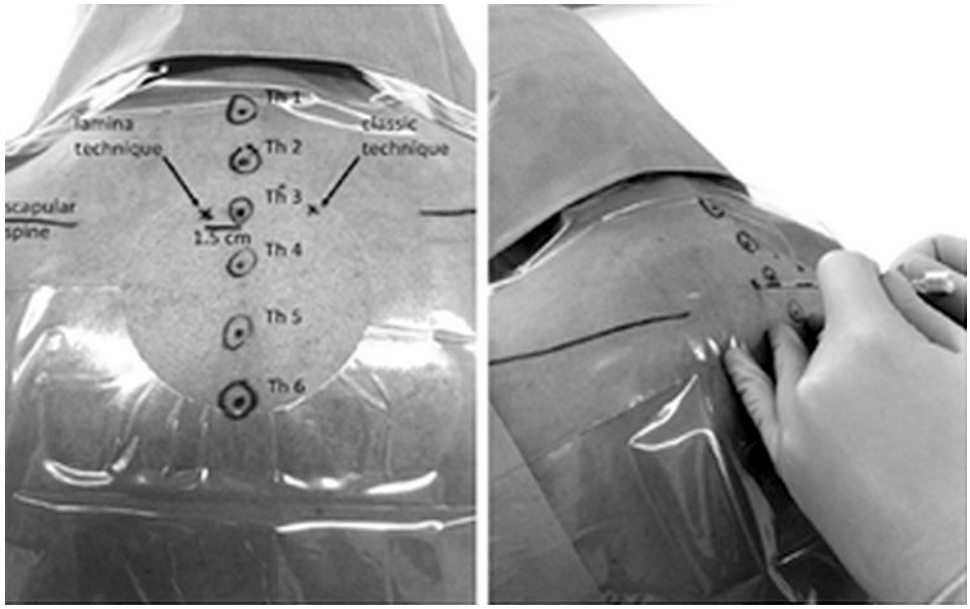

Fig. 84.1 Injection sites—note the difference between classic (traditional) technique and lamina technique, as well as the needle trajectory used in the right photograph

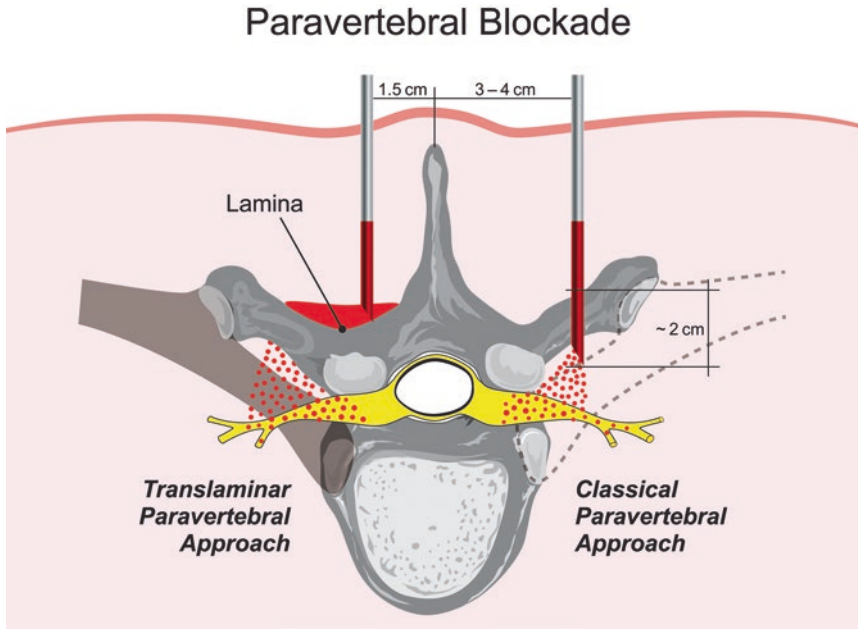

Fig. 84.2 Anatomy schematic—note differences between needle tip and local anesthetic location between laminar and traditional techniques. Credit: Brigham and Women's Hospital

5. When target PVTS is optimally imaged in plane with transverse processes, insert needle right at superior border of ultrasound probe with in-plane technique directed inferiorly under the probe and toward PVTS.
6. Target is to place tip of needle between transverse process in PVTS just deep superior costotransverse ligament while importantly avoiding pleural puncture. Pay close attention to needle depth externally as well as on ultrasound image.
7. Once the tip is in target area, aspirate and inject local anesthetic. Ideal image of local anesthetic spread "pushes" the pleura deep and away from PVTS.
8. If continuous blockade is planned, thread the catheter at this point.

Complications

Infection, neuraxial hematoma, and local anesthetic toxicity are the most serious complications. Good aseptic technique and adherence to ASRA guidelines on neuraxial procedures minimize these risks. While specific anticoagulation guidelines for paravertebral blocks are controversial, we feel this procedure should be treated as a neuraxial technique as needle passes very close to epidural/intrathecal space and local anesthetic often will spread to epidural space. Ensuring lipid emulsion availability prior to block and limiting local anesthetic to subtoxic dosing will help minimize local anesthetic-related complications. Other potential complications are nerve root injury, intrathecal puncture, and pneumothorax. Strict needle-advancing technique with avoidance of medial/lateral tilt and abortion of injection with patient complaint of sharp pain and aspiration prior to all injections will help decrease these risks. Avoidance of pneumothorax is best accomplished with focused attention on needle depth and ensuring the tip does not pass further than 1 cm beyond TP on traditional technique. Low threshold of suspicion for these complications will minimize time to diagnosis in the immediate post-procedure period.

Clinical Pearls

- When advancing the needle toward the paravertebral space during traditional technique, a "pop" may be felt which typically demarcates movement of the needle tip through the superior costotransverse ligament. The "pop" may also not be felt, particularly depending on type/size of the needle used, and should not be sought at additional depth for risk of pleural puncture.
- Laminar technique may be safer and easier to perform as needle "backstop" target is larger and easier to contact. Further, there is no blind passage of needle tip toward pleural space. Block is more reliable and dense with traditional technique when compared with laminar technique; however, this may be overcome with additional dosing at each level with laminar technique.
- Ultrasound imaging of needle can be difficult given an angle necessary to reach PVTS may be quite steep. In this scenario, particular attention must be made to externally noted depth of needle (as marked on needle) to avoid pleural puncture, as advancing beyond 1.5–2 cm beyond transverse process should be avoided.
- Evidence suggests local anesthetic will spread at least one level above and one below injection site in paravertebral space; therefore, when planning injection sites, it makes sense to inject every other level in targeted range. For example, for breast surgery levels, T1–T6 should be covered by block so injection at T2, T4, and T6 with total local anesthetic amount limited by calculated toxic dose. This will also avoid additional needle passes which should help to minimize all risks.

Evidence

Paravertebral Block Efficacy and Safety for Breast Surgery

A 2010 meta-analysis of 15 RCTs and 877 patients revealed that paravertebral block reduces postoperative pain scores, total opioid consumption, and time to rescue analgesics

when compared to general anesthesia alone. Reported complication rates were low; however, of the 248 patients for which complication rates were listed, there was only one transient Horner's syndrome episode reported and one episode of apparent intravascular injection resulting in local anesthetic toxicity and convulsions, which were quickly treated. There were no pneumothoraces reported.

Laminar Technique Efficacy

While there are no studies comparing traditional technique vs newly described laminar technique, the technique does appear to be very effective. In the original paper describing the technique, 25 patients received laminar catheters prior to breast surgery, and zero required opioids as rescue medication postoperatively or during the rest of the hospital stay. Postoperative analgesia provided with paravertebral catheters was rated very high by patients, staff nurses, and anesthesiologists involved in postoperative care.

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Intercostal Nerve Block

85

Daniel V.X. Friis and Konrad Maurer

Indications: The intercostal nerve block (ICN) is used in acute and chronic pain conditions of the thorax and the upper abdomen. It can be performed for analgesia in cases of rib fractures or in chronic pain conditions such as postmastectomy and post-thoracotomy pain.

Possible Techniques: Landmark technique and ultrasound guidance.

Equipment/Materials: Ultrasound with a linear transducer 6–13 MHz, 22G/25G/27G echogenic needle, local anesthetic (lidocaine 1 or 2 %, bupivacaine 0.25 %/0.5 %), and +/− corticosteroid.

Ultrasound-Guided Procedure

Position: Prone, other positions possible (lateral decubitus, sitting).

Site of Injection: Angle of the rib (6–7 cm from the vertebral spinous process) and midaxillary line.

Antibiotics: Not required.

Steps

1. Position the transducer in the short axis, perpendicular to the ribs, and identify two consecutive ribs with their typical dorsal shadowing. Note: identify the target rib and the rib below the target level (Fig. 85.1).
2. Identify structures such as internal and external intercostal muscles and especially the pleura, a prominent hypoechogenic line moving with respiration (Fig. 85.1).
3. Focus the needle target in the middle of the screen before beginning the procedure. The needle starting point is the superior border of the rib below the target rib, as the needle will be advanced in a cephalad trajectory to the inferior border of the target rib.
4. The needle is carefully inserted in plane. Slowly advance under direct visualization along the upper margin of the rib. While advancing the needle tip into the external intercostal muscle, the injection of a small amount of local anesthetic (typically lidocaine) is recommended for hydrodissection in order to verify tip position. Maintain visualization of the pleura at all times.
5. After entering the external intercostal muscle, the internal intercostal muscle layer is only a few millimeters deeper. Optimal needle tip position for the injection is approximately 2–3 mm from the pleura.
6. The injection of the local anesthetic (LA) is visualized in real time via the ultrasound. 2–5 ml of LA is sufficient for one level of blockade. The injection gives pain relief for several hours depending on the local anesthetic chosen.

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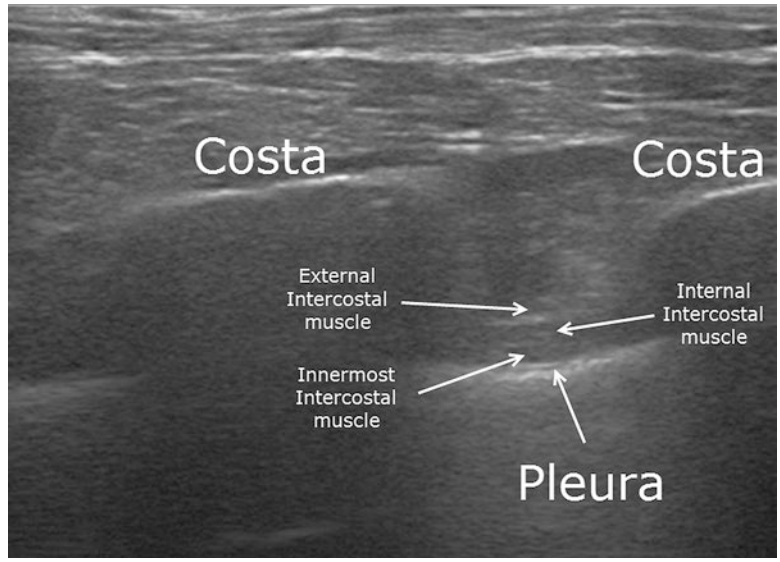

Fig. 85.1 Representation of the intercostal space with ultrasound

7. Before ending the procedure or continuing with the next intercostal block, check that there is no pneumothorax. The best way is to look for the pleura movement with the respiration.

Landmark Technique

Location: Angle of the rib or in the midaxillary line.
Material: 20G/22G/25/27G spinal needle.

1. Palpate the rib over the targeted level before the needle puncture and mark this point approximately 6–7 cm lateral to the spinous process.
2. Introduce the needle in the direction of the lower edge of the rib using a slight cephalad tilt.
3. When bone contact occurs (typically at 1 cm, although this varies depending on body habitus), retract the needle slightly and angle the needle inferiorly and walk off the rib to advance the needle under the inferior edge. Advance the needle about 3–4 mm deeper.
4. Because of the nerve location near the vascular bundle, intravenous needle placement should always be ruled out by aspirating prior to injection. If this is positive, retract the needle slowly 1–2 mm. If there is no blood return, then inject the local anesthetic, usually 2–5 ml at each level.

Complications

Pneumothorax; bleeding after unintended vessel puncture; infection; local anesthetic toxicity, especially when using larger volumes in cases of multiple blocks; and allergic reactions. Remember that intercostal nerve blocks are associated with the highest amount of systemic LA absorption for regional blocks.

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Transversus Abdominis Plane (TAP) Block

86

David Ende and Jose Luis Zeballos

Indications: Primarily used for acute postoperative abdominal pain with bilateral blocks covering midline surgical site. Best for incisional pain with unilateral coverage of the abdominal wall from dermatome T7 to L1 (most consistently T10 to L1) with each block. Can be single shot or with catheter deployment for continuous pain control. May also be used as both treatment modality and diagnostic maneuver for anterior cutaneous nerve entrapment syndrome (ACNES).

Equipment/Materials: Ultrasound with long linear high-frequency probe and sterile cover, skin antiseptic, sterile drape, 50 or 100 mm needle, 20 cc syringe, 25–30 cc local anesthetic (bupivacaine/ropivacaine) (0.25–0.5 % is a typical choice), +/− catheter, +/− Tegaderm, +/− tape (to secure catheter), and +/− steroid (methylprednisolone 40 mg).

CPT
TAP block unilateral: 64486
TAP block unilateral with catheter: 64487
TAP block bilateral: 64488
TAP block bilateral with catheter: 64489
Ultrasound guidance: 76942
Professional service component modifier: 26

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Procedure

Position: Supine
IV: Required for risk of local anesthetic toxicity
Antibiotics: Not required

Steps

1. With the patient in supine position, expose the abdomen, and using skin antiseptic prep abdominal area from costal margin to the iliac crest extending all the way posteriorly to where patient's flank meets the bed.
2. Place long linear ultrasound probe-oriented transverse to rectus muscles on the flank of the patient just above where patient's flank meets the bed between the iliac crest and costal margin.
3. Identify the three typically well-defined muscular layers of the abdominal wall from superficial to deep: external oblique (EO), internal oblique (IO), and transversus abdominis (TA). Below the TA is the peritoneum and loops of bowel may be visualized. If having difficulty identifying all three layers, scan medially to the rectus muscle or posterolaterally to the quadratus lumborum to visualize origin of three layers as they separate and track back to injection site.
4. Once muscular layers are identified, identify target injection site. We find the best injection site is just medial to muscle layer origin coming off and separating from the quadratus lumborum.

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5. Insert needle medially but in plane with ultrasound probe, and direct the tip posteriorly under probe and into the field of view, keeping the tip visualized throughout. Advance the tip to plane between the IO and TA (second and third muscle layers).
6. Aspirate from needle and if negative for blood, slowly inject total volume of chosen local anesthetic, watching spread on ultrasound. Ideal spread is to see TA "peel" off the IO. Since this is a high-volume block, 20–30 cc is a good starting point for total volume injected for single-shot block.
7. If continuous block is planned, after establishing a good space between the TA and IO, under ultrasound guidance deploy catheter so that the tip is 5–6 cm beyond needle tip.
8. Withdraw needle with continuous catheter threading motion to ensure catheter tip remains in TAP plane.
9. Secure catheter with adhesive skin prep, clear sterile dressing, and tape.

Complications

Complications with this block are very rare. Specific for this block is the concern for local anesthetic toxicity given this best effectiveness with high volume of local anesthetic and unclear rates of systemic absorption. Ensuring total dose is below calculated toxic level and careful aspiration prior to injection are the best ways to avoid complication. Peritoneal and bowel perforation are theoretically possible but exceedingly rare complications that should be easily avoided with ultrasound visualization of the needle tip throughout the block. As with most other blocks, injection site infection, hematoma, and nerve injury are all very rare but possible risks (Fig. 86.1).

Clinical Pearls

This is typically a fairly superficial block; make sure to optimize depth of ultrasound to allow abdominal wall to take up most of the screen.

In the obese patient, placing the patient in a semi-lateral position with a wedge under the block side can improve needle/block site visualization. This works to flatten the block site and push the subcutaneous fat medially, thereby reducing the depth of the target and allowing a shallower needle trajectory for better needle-probe alignment.

We feel the best location to inject is as far posterior as is possible to clearly visualize separate muscle layers under ultrasound. Effective spread should be easier to achieve more posteriorly. The closer to the quadratus lumborum, the better.

Evidence

Spread with Single Injection

There is some controversy regarding anesthetic coverage and local anesthetic spread with single-shot TAP blocks. While early cadaveric and imaging studies indicated coverage from T7 to L1 can be achieved, more recent clinical trials indicate obtaining coverage T7–T9 is more challenging and requires a second subcostal injection to reliably block. The clinical evidence repeatedly shows T10–L1 to be the reliable territory covered by single-shot injections, and this should be taken into account when planning a postoperative pain control regimen.

Efficacy of TAP Block as Postoperative Pain Control Adjuvant

There have been several small studies evaluating the efficacy of TAP blocks. One of the more recent trials is a RCT published in 2011: 40 patients undergoing colorectal surgery comparing a standard pain control regimen and bilateral intraoperative TAP block with either 0.25 % bupivacaine or saline. The bupivacaine TAP block arm had a significant decrease in 24-h morphine requirements as well as a significant reduction in early postoperative pain scores; sedation increased satisfaction scores.

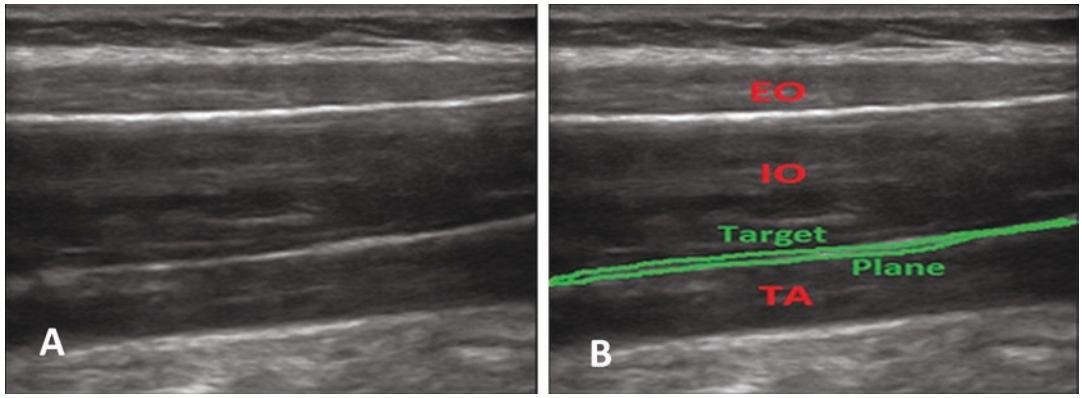

Fig. 86.1 TAP ultrasound anatomy and target, unlabeled (**a**) and labeled (**b**). The goal is to place needle tip into target plane and "peel" fascial layers apart with local anesthetic. *EO* external oblique, *IO* internal oblique, *TA* transversus abdominis

Additional Readings

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Anterior (Abdominal) Cutaneous Nerve Block

87

M. Gabriel Hillegass, III and Ryan H. Nobles

Indications

Anterior (abdominal) cutaneous nerve entrapment syndrome (ACNES) is a chronic focal abdominal wall pain along the lateral border of the rectus abdominis muscle where the anterior cutaneous branches of the intercostal nerves perforate the deep fascial layer and traverse it vertically in muscular foramina. ACNES occurs in up to 30 % of patients with chronic abdominal wall pain [1, 2].

Equipment/Materials

Ultrasound machine with high-frequency linear transducer (optional), sterile sleeve and coupling gel, 21–25-gauge needle of appropriate length (preferably echogenic if using ultrasound), 5 or 10 mL syringe, connection tubing, local anesthetic, and +/− corticosteroid

Procedure

Position: supine
IV: not required unless there are previous vagal episodes, severe anxiety, or needle phobia
Antibiotics: not required

Steps:

1. Identify and mark the site(s) of maximal tenderness with palpation. A positive Carnett sign (increased pain or no change in pain with abdominal muscle contraction, e.g., supine torso or leg lifts) increases the likelihood of ACNES.
2. If not using ultrasound, perform skin antisepsis, introduce the needle at a 90° angle to the skin, and advance to the target until the patient alerts you that their pain is reproduced (similar technique as a trigger point injection).
3. After negative aspiration, inject incrementally (typically 1–3 mL per level). Note: exacerbation of the patient's pain is expected with proper needle placement.
4. If using ultrasound, start with your transducer in a transverse (axial) position at the anatomic midline. Identify the linea alba and rectus abdominis muscles (Fig. 87.1). Slide the transducer laterally to the affected side to

CPT:Injection, anesthetic agent; intercostal, single 64420
Injection, anesthetic agent; intercostal, multiple 64421
Ultrasound guidance 76942

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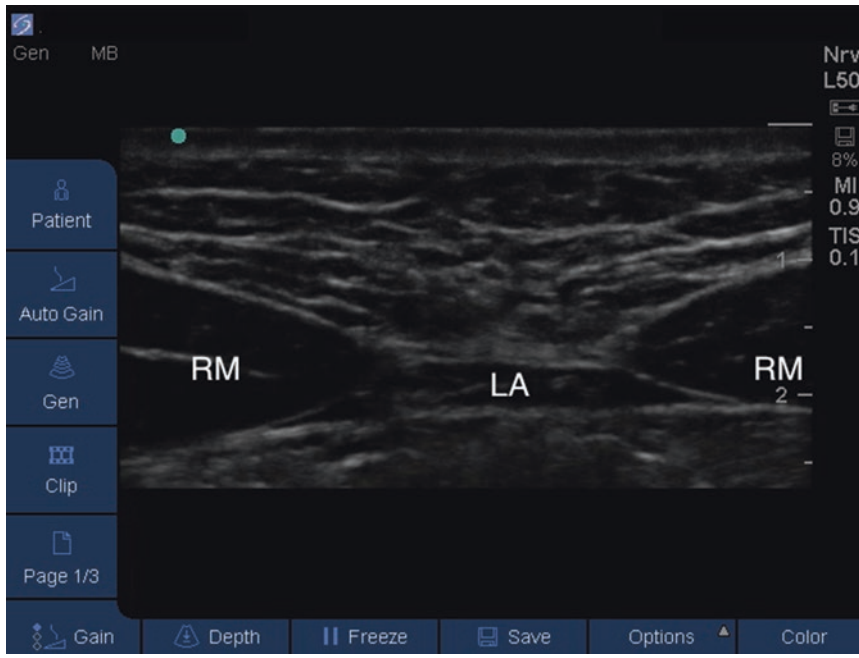

Fig. 87.1 Transverse (axial) view of midline of the abdominal wall using a high-frequency linear probe to depict the linea alba (LA) and bilateral rectus muscles (RMs)

identify the linea semilunaris, which is the transitional aponeurosis from the rectus sheath to the lateral abdominal wall muscle layers (Fig. 87.2). Identify the external and internal oblique and transversus abdominis muscles.

5. Using sterile technique and after local anesthesia is achieved, employ an in-plane lateral-to-medial approach to position the needle tip at the posterior lateral border of the rectus muscle. The nerve (and its associated vessels) typically travels in the lateral rectus muscle in a vertical channel 0.5–1 cm medial to the linea semilunaris. It may be visualized as a hyperechoic area within the muscle [3]. The patient should alert you when their pain is reproduced as the needle approaches the target.
6. After negative aspiration, inject incrementally (typically 1–3 mL per level). Larger volumes may be used for therapeutic purposes, but would decrease diagnostic specificity. Note: exacerbation of the patient's pain is expected with proper needle placement.

Complications

Bleeding and hematoma formation could result from trauma to the abdominal wall vasculature. Anticipate pain and possibly paresthesias in the terminal distribution of the target nerve when the needle approximates the muscular foramina. Direct needle trauma or intraneural injection could cause or worsen nerve injury. Infection is a low risk if strict aseptic technique is used. Should the needle penetrate the peritoneum, there is risk for trauma to the abdominal viscera, but this would be minimized with good ultrasonographic technique. Local anesthetic toxicity would be unlikely because of the small volume of injectate and resultant subtoxic dose. Ensure the total dose is well below maximal local anesthetic thresholds.

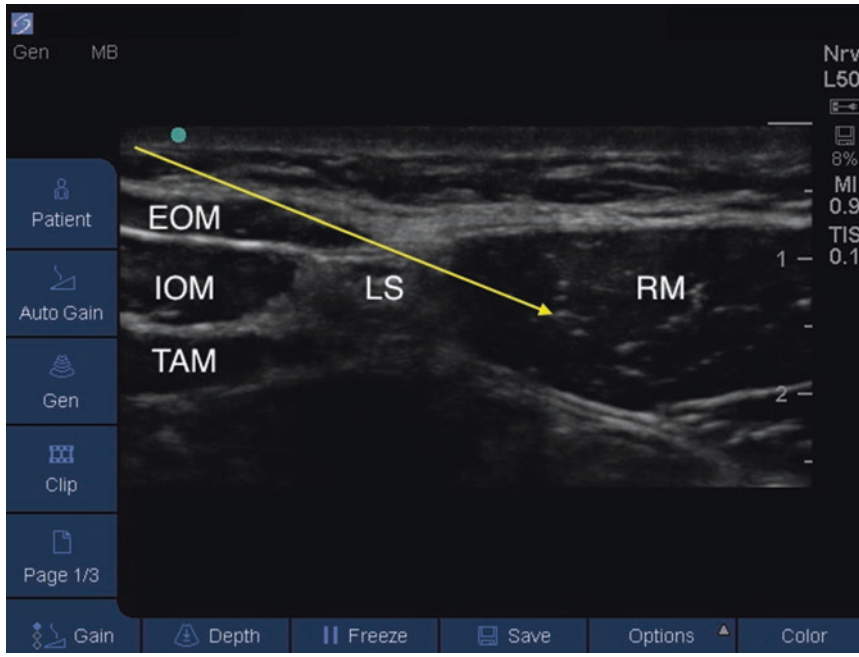

Fig. 87.2 Transverse (axial) view of the junction of the lateral border of the rectus muscle (RM) and the medial borders of the external oblique (EOM), internal oblique (IOM), and transversus abdominis muscles (TAM). The linea semilunaris (LS) aponeurosis adjoins the rectus sheath and the lateral abdominal wall muscle layers. The *solid line* represents the needle trajectory

Clinical Pearls

Patients should be counseled that their pain will be precipitated and possibly exacerbated by the procedure. They are expected to alert the physician when their typical abdominal pain is being reproduced to ensure the injectate is on target.

A variation of this procedure that should be performed if the neurovascular bundle is not identified or the patient's pain is unable to be directly reproduced with needle placement is a *rectus sheath block*. This technique requires the needle to be advanced to the posterior aspect of the rectus muscle just above the hyperechoic rectus sheath. The muscle should lift away from the rectus sheath as the injectate is incrementally administered. A total volume of 5–10 mL should be adequate for blockade.

Approximately one-third of patients have abdominal cutaneous nerve paths that are anterior to the rectus sheath. If there is a poor response with the techniques described above and a high suspicion of abdominal wall pain persists, consider performing a targeted *transversus abdominis plane (TAP) block* at the painful segmental level. This would anesthetize the terminal intercostal nerve segments more proximally [4].

Evidence

Management of ACNES in a Large Cohort [5]

Consecutive local trigger point injections were effective in one-third of patients. Surgical anterior neurectomy was effective in about two-thirds of the patients who did not respond to injections. Eighty percent of the entire ACNES cohort reported total or substantial long-term pain relief.

Disclaimer The views expressed in this article are those of the author(s) and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

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Ilioinguinal Nerve Block

88

Anthony A. Tucker, M. Gabriel Hillegass, III, and Robert J. Mendez

Indications

Pain in the inguinal region, most commonly postoperative neuralgia after herniorrhaphy or lower abdominal surgery in the region of the ilioinguinal nerve.

Equipment/Materials

Ultrasound machine with a high-frequency linear transducer, sterile sleeve and coupling gel, 21–22 gauge short-bevel echogenic needle (5–10 cm), 10 mL syringe, connection tubing, and local anesthetic +/− steroid.

CPT:Injection, anesthetic agent; ilioinguinal or iliohypogastric nerves 64425
Ultrasound guidance 76942

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Procedure

Position: supine
IV: not required unless previous vagal episodes, severe anxiety, or needle phobia
Antibiotics: not required

Steps:

1. Start with anatomic scanning along a line between the anterior superior iliac spine (ASIS) and the umbilicus using a transverse (axial) transducer orientation. Identify the ASIS, external oblique muscle, internal oblique muscle, transversus abdominis muscle, peritoneum, and bowel and neurovascular bundle.
2. The ilioinguinal nerve arises from T12 and L1. Above the inguinal ligament, the nerve emerges from the psoas muscle and lies in the plane between internal oblique and transversus abdominis muscles (Fig. 88.1). As the nerve courses caudally, below the inguinal ligament, the nerve travels superficially and is found in the plane between the external and internal oblique muscles.
3. The ilioinguinal nerve appears hyperechoic and typically lies within 2 cm medial to the ASIS. Typically a branch of the inferior epigastric artery and the iliohypogastric nerve lie medial to the ilioinguinal nerve.
4. Using sterile technique and after local anesthesia is achieved, the needle is advanced in a medial-to-lateral direction using an in-plane technique.

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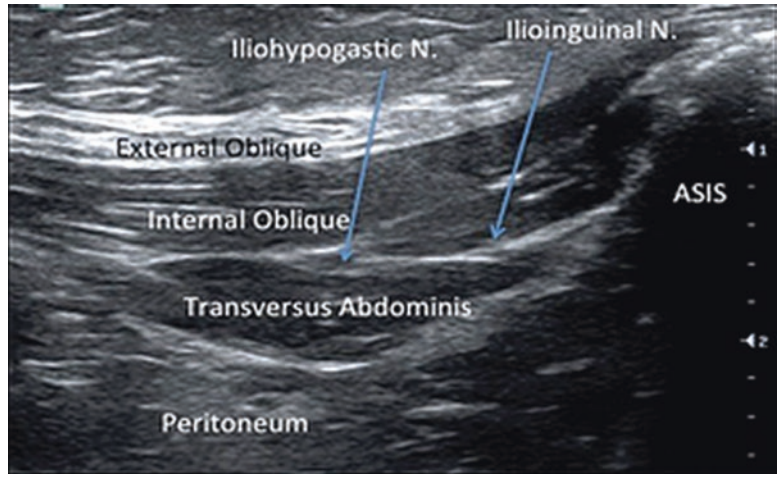

Fig. 88.1 Transverse (axial) view of the abdominal wall muscle layers medial to the anterior superior iliac spine (ASIS). Note the distinct fascial plane between the internal oblique and transversus abdominis muscles. The ilioinguinal nerve is lateral and closest to the ASIS

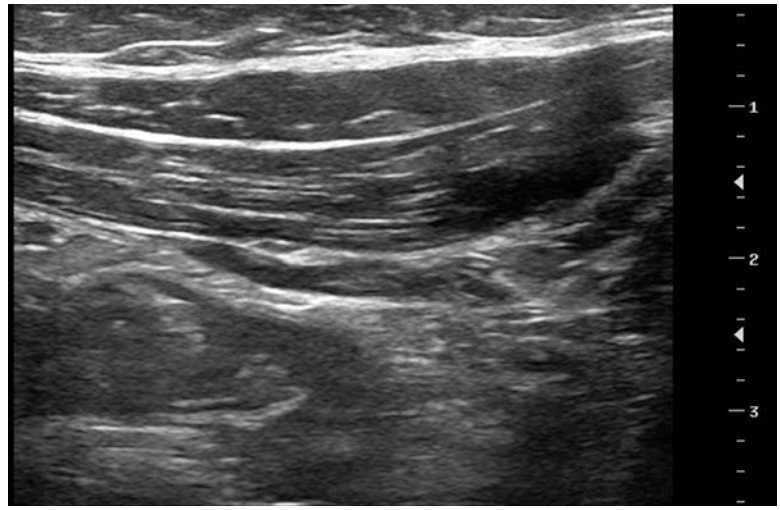

Fig. 88.2 In-plane medial-to-lateral needle trajectory directed at the target fascial layer between the internal oblique and transversus abdominis muscles

The needle tip is advanced under direct visualization into the plane between the internal oblique and transversus abdominis muscles (Fig. 88.2). Hydrodissection (1–5 mL of normal saline) can be used to aid needle tip visualization and confirm the correct tissue plane. 5–10 mL of injectate (local anesthetic +/− steroid) is injected around the nerve within the target tissue plane.

Complications

Overall this procedure has low-to-moderate risk. Moderate risk is attributable to the potential for bowel perforation if the needle inadvertently pierces the peritoneum. Avoidance of the peritoneum should be an advantage of using ultrasound, but the risk nevertheless exists. Bleeding and hematoma are also possible from vascular trauma, but the area is easily compressible. Anticipate pain and possibly paresthesias in the terminal distribution of the nerve when the needle enters the target fascial plane. Paresthesias can occur from mechanical or chemical irritation of neural structures. Post-procedure neuritis and nerve injury from direct needle trauma are other potential complications. Aseptic technique should minimize the risk of infection, and local anesthetic toxicity is unlikely given the low volume of local anesthetic required for neural blockade.

Clinical Pearls

This interventional technique can be helpful to diagnose ilioinguinal neuralgia as well as to provide a prognosis for the effectiveness of neuroablative (e.g., RFA) or neurolytic therapies.

In an adult patient, usually 5–10 mL of local anesthetic is adequate for successful blockade. High concentrations of local anesthetic are not required as the ilioinguinal nerve is primarily sensory. There is some motor innervation of the internal oblique and transversus abdominis muscles, which should not be of clinical significance following blockade.

If it is difficult to isolate the three lateral abdominal wall muscle layers, it can be helpful to start from anatomic midline and scan from medial to lateral. With this approach the three muscle layers can be identified medially as they arise from the aponeurosis just lateral to the rectus abdominis muscle.

Evidence

The management of chronic inguinal neuralgia can be difficult as there is no consensus on treatment. A cohort study published by Zacest et al. [1] reported that two-thirds of their chronic post-herniorrhaphy pain patients had complete (28 %) or partial (39 %) long-term relief (mean follow-up was 35 months) after undergoing selective ilioinguinal neurectomy. Most of these patients underwent a successful diagnostic nerve block prior to the surgery. Eppstein and colleagues [2] published a case series in which preoperative ultrasound-guided and nerve stimulator ilioinguinal nerve identification with methylene blue tattooing reduced operative time and morbidity, allowing for proximal neurectomy and retainment of mesh. Three of four patients had complete or near-complete pain relief.

Disclaimer The views expressed in this article are those of the author(s) and do not necessarily reflect the official policy or position of the Department of the Navy, the Department of Defense, or the US Government.

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Genitofemoral Nerve Block

89

James Slotto and Robert Jeremy Hackworth

Indications: Used for diagnosis and treatment of testicular, labial, or groin pain that is likely neuropathic in origin. Frequently the etiology of this pain is postsurgical.

Equipment/materials: Three methods include landmark or fluoroscopic guided, ultrasound guided, and CT guided. Injectate is generally local anesthetic +/− corticosteroid. +/− Stimulating needle. +/− Radio-frequency needle.

Pertinent anatomy: The description of the genital branch of the genitofemoral nerve (GFN) is highly variable. However, a majority of sources agree that the nerve originates from L1 and L2 nerve roots, passes anteriorly to lie on the psoas muscle belly, and travels lateral to medial joining the spermatic cord at or near the deep inguinal ring. The nerve can be medial, within, or lateral to the cord with most sources agreeing that the nerve is lateral and posterior to the spermatic cord. Here it follows the cord as it terminates and innervates the testicle. The spermatic cord passes directly over the pubic tubercle.

Clinical presentation: Distinguishing genitofemoral neuralgia from other similar appearing pain syndromes like ilioinguinal or pudendal neuralgia can be difficult. It is important to consider other nerve sources for testicular or groin pain. Clinical symptoms usually consist of pain along the path of the genitofemoral nerve.

CPT:Ilioinguinal nerve block: 64425
Ultrasound guidance: 76942
CT guidance: 77012
Fluoroscopic guidance: 77003

Procedure

Position: supine
IV: generally not required
Antibiotics: not required

Landmark/Fluoroscopic Guidance Approach

1. Either with palpation or with fluoroscopy, locate the pubic tubercle on the side to be blocked. The skin overlying the pubic tubercle is marked for skin entry.

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2. After sterile prep and local anesthetic infiltration, the needle is directed to touch down on the pubic tubercle and then withdrawn 3–7 mm. After negative aspiration, the treatment is rendered (injection, radio frequency, etc.). For a diagnostic block, a typical volume of injectate is 5–10 ml. If using a radiofrequency or stimulating needle, stimulation at 0.5 V can be used for a more targeted treatment. Small adjustments of the needle in a systematic approach should be used until the patient experiences symptoms in a similar pattern and area of their typical pain. This nerve targeting should be used regardless of the method used (landmark, ultrasound, CT).

Step Ultrasound Approach

1. The GFN is difficult to visualize with ultrasound so identifying the spermatic cord (or round ligament in females) is key. Using a high-frequency linear array ultrasound transducer, the femoral artery near the inguinal ligament is identified. The artery is then visualized long axis and followed proximal. The artery quickly dives deep (posterior). At this point, the probe is turned so the artery is viewed in short axis. With this view, a round, often not well defined, structure can be seen medial to the artery. This vessel inside this structure can often be visualized and confirms identification. Using an in-plane approach, a treatment needle is passed lateral to medial (after assuring that femoral vessels are missed) such that the tip will lie just posterolateral to the cord. Here, treatment is rendered as described in the landmark section. Some authors recommend injecting some of the medication inside the cord as the GFN can travel within the spermatic cord.

CT-Guided Approach

Scout images locate the pubic tubercle. The spermatic cord/round ligament and femoral vessels are easily identified lateral to the tubercle (Fig. 89.1).

Under CT guidance, the needle is advance lateral to medial such that the tip lies just posterior and lateral to the cord. Care should be taken to avoid femoral vessels. Treatment delivered is as described in the landmark and ultrasound technique.

Complications

Bleeding, soft tissue infection, and nerve injury. Specific complications such as damage to spermatic cord or testicular artery are unlikely.

Clinical Pearls

For testicular or labial majora pain, this block can be both diagnostic and therapeutic. A positive response with local anesthetic can be repeated with pulsed radio-frequency ablation, cryotherapy, or steroid additives for long-lasting pain relief.

Stimulating needles can be used and should reproduce a patient's painful symptom at low voltages for confirmation.

Volumes of injectate vary by technique. A range between 10–30 ml is used, with the landmark technique general requiring more volume than image-guided techniques.

Evidence

No studies have directly compared the efficacy of various imaging modalities for this block. Familiarity with US and CT guidance likely will impact success rates. In our experience, finding the spermatic cord/round ligament using ultrasound can be challenging, and as such, our imaging modality of choice is CT as the pertinent structures are extremely easy to identify in all comers.

Additional Reading

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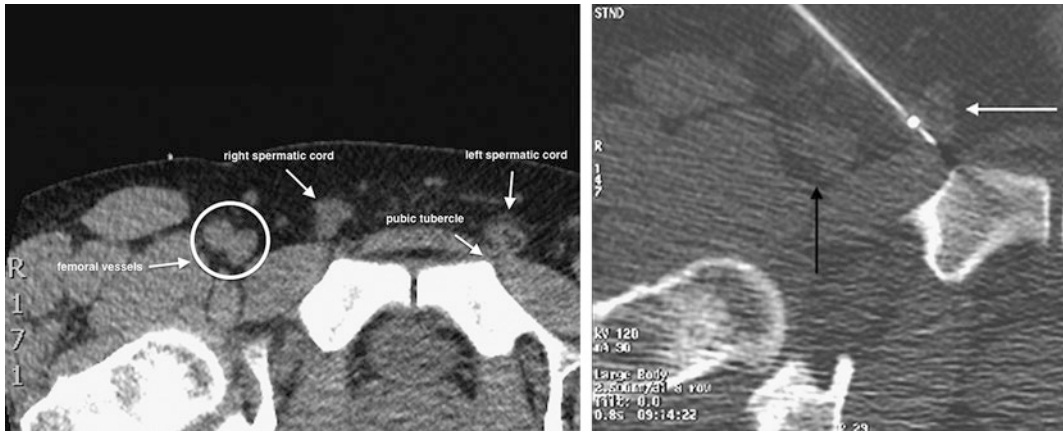

Fig. 89.1 CT images showing the spermatic cord in relation to the pubic tubercle and femoral vessels. *White arrow* on right image is needle tip placement posterior and lateral to spermatic cord. *Black arrow* is femoral vessels

Hackworth RJ, Nagel EJ, Slotto JG. Computed tomographic–guided genitofemoral nerve block: a simple anterior approach. J Comput Assist Tomogr. 2014;39(2):295–7.

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Lateral Femoral Cutaneous Nerve Block

90

Ian M. Fowler and Paul G. Maliakel

Indications: Useful in the diagnosis and treatment of the entrapment neuropathy of the lateral femoral cutaneous nerve (LFCN) known as meralgia paresthetica. Also can be used for surgical anesthesia and/or postoperative pain control for procedures on the anterolateral thigh such as skin graft harvesting and to alleviate tourniquet pain from lower extremity orthopedic procedures.

Equipment/materials: Ultrasound with high-frequency linear transducer, 22 gauge 3.5" spinal needle, local anesthetic, and +/− corticosteroid.

Procedure

Position: supine
IV: recommended

CPT:Injection, anesthetic agent; other peripheral nerve or branch: 64450
Ultrasound guidance 76942

Antibiotics: not required

Steps:

1. Locate the anterior superior iliac spine (ASIS) and inguinal ligament.
2. Place the ultrasound transducer parallel to the long axis of the inguinal ligament (Fig. 90.1).
3. Move the transducer 1.5 cm distally until the sartorius and iliacus muscles are identified.
4. The LFCN can be identified as a hyperechoic structure lying anterior to the sartorius muscle and posterior to the fascia lata (FL), between the fascia lata and the fascia iliaca (FI) (Fig. 90.2).
5. Anesthetize the skin, and then advance a 22 gauge 3.5" spinal needle in plane with the transducer through the FI until it is adjacent to the nerve.
6. After careful aspiration, inject 5–10 cc of local anesthetic incrementally while visualizing spread of the local anesthetic circumferentially around the nerve.

Complications

Ecchymosis/hematoma at the injection site, concomitant femoral nerve blockade, or trauma to the LFCN or femoral nerve. These complications can be mitigated with the use of ultrasound and small volumes of local anesthetic. Additionally, cold packs applied to the injection site may be beneficial after the procedure.

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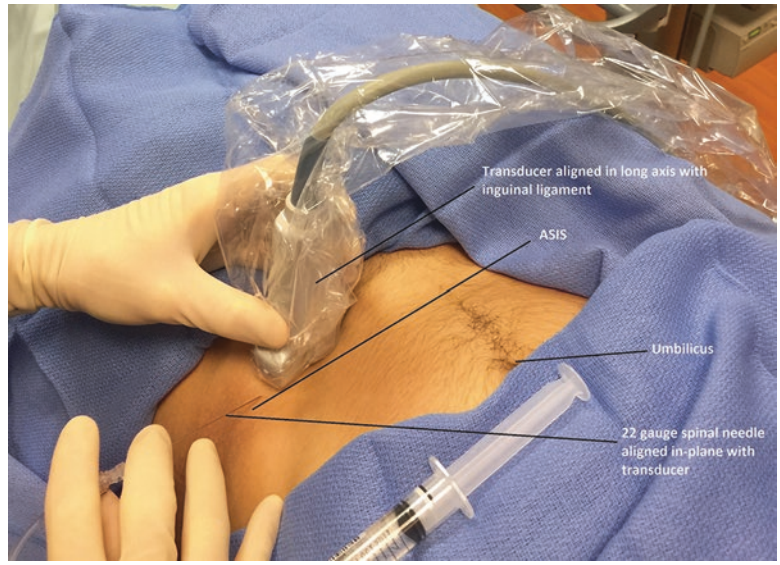

Fig. 90.1 Anatomic landmarks—anterior superior iliac spine (ASIS) and ultrasound transducer and needle locations

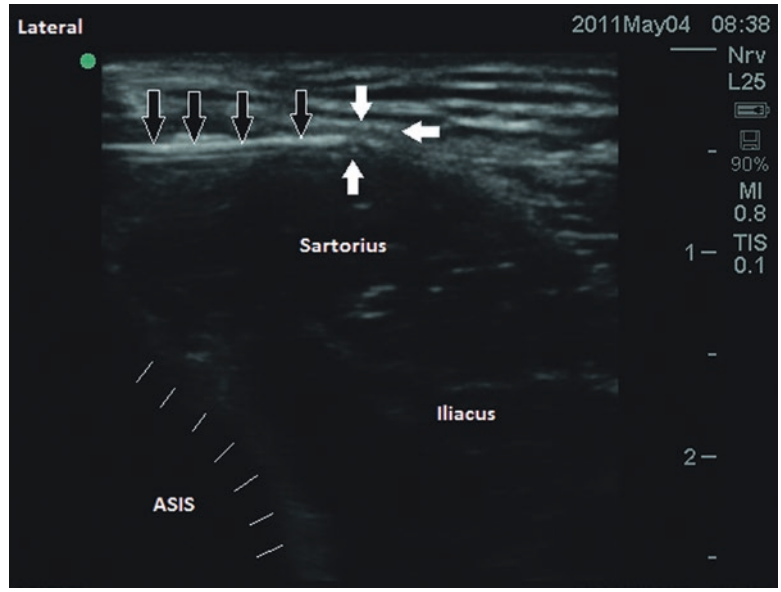

Fig. 90.2 Ultrasound image showing needle (*black arrows*) in contact with LFCN (*white arrows*). The anterior superior iliac spine (ASIS) is outlined by *solid white lines*

Clinical Pearls

- Moving proximal or distal to ASIS helps avoid contact of needle with ASIS.
- Using hydrodissection of FI and FL often causes LFCN to be visualized better.
- Place transducer over the sartorius muscle, and locate as it traverses superficially.
- Given the superior efficacy of the ultrasound-guided LFCN block, if a patient with symptoms consistent with meralgia paresthetica does not respond to blockade of the nerve,

lesions in the lumbar plexus or L2–3 radiculopathy should be considered.

Evidence

Anatomic Landmarks Versus Ultrasound Guidance

In a cadaveric study, 16/19 needles (84.2 %) were placed adjacent to the LFCN using ultrasound guidance as identified by indocyanine green staining as compared to only 1/19 (5.3 %) needles advanced using the landmark technique due to the highly variable anatomic course of the LFCN. In the same study, 16/20 marked positions (80 %) of the LFCN located using ultrasound in healthy volunteers corresponded to the location of the LFCN as identified using a percutaneous nerve stimulator compared to 0/20 marked positions identified using the landmark technique.

Efficacy

In a case series of ten patients, investigators used ultrasound guidance to achieve sensory blockade of the LFCN in all patients without inadvertent blockade of the femoral or obturator nerves.

In another series of 20 consecutive patients, ultrasound-guided blockade of the LFCN achieved symptom relief of meralgia paresthetica in 100 % of patients with symptoms disappearing 2 months after injection of a mixture of local anesthetic and corticosteroid.

A case report describes the use of ultrasound guidance for pulsed radio-frequency ablation of the LFCN to provide prolonged pain relief of recalcitrant meralgia paresthetica.

Additional Reading

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Piriformis Muscle Injection (Fluoroscopically Guided)

91

David V. Dent

Indications: Primarily used for piriformis muscle spasm/pain +/− piriformis syndrome.

Equipment/materials: Fluoroscopy, 25G spinal needle 3.5"+length, extension tubing, syringe for contrast, syringe for local anesthetic, syringe for corticosteroid, local anesthetic, contrast, and +/− corticosteroid.

Procedure

Position: prone
IV: usually not required
Antibiotics: not required

Steps:

1. Identify the patient, and confirm the planned procedure with the patient. Mark the side and area to be injected. Perform a time-out.
2. Prone position. Set the c-arm in an AP view with the greater trochanter and inferior aspect of the ipsilateral sacrum visible.
3. Prepare the entire ipsilateral buttock with an antiseptic/antimicrobial skin cleaner using sterile technique.
4. The target is midway between the greater trochanter and the lateral edge of the ipsilateral sacrum. This will be over the body of the ischium and medial to the acetabular margin (Fig. 91.1). Mark the skin entry point with a sterile marking pen.
5. Thoroughly anesthetize the skin at the entry point.
6. Next insert the spinal needle and advance the needle using a coaxial technique. One will most likely achieve a piriformis muscle twitch at some point prior to bony contact. The piriformis muscle twitch will let one know that the correct position has been achieved.
7. Once the needle is in correct positioning, place the extension tubing, which is connected to your syringe with contrast, onto the needle hub (make sure that your extension tubing is fully primed (all air is out of the extension tubing)). Use the length of your extension tubing to remove yourself as far as possible from the X-ray beam. Once aspiration is negative for blood, inject a small amount of contrast under a short burst of live fluoroscopy. There should be very little resistance to flow. If resistance is encountered, slightly redirect the needle. Ideal contrast flow will begin to outline the piriformis muscle (Fig. 91.2). Once ideal contrast flow is

CPT:Trigger point injection 1–2 muscles: 20552
Fluoroscopy (outside the spine) 77002
Professional component 26

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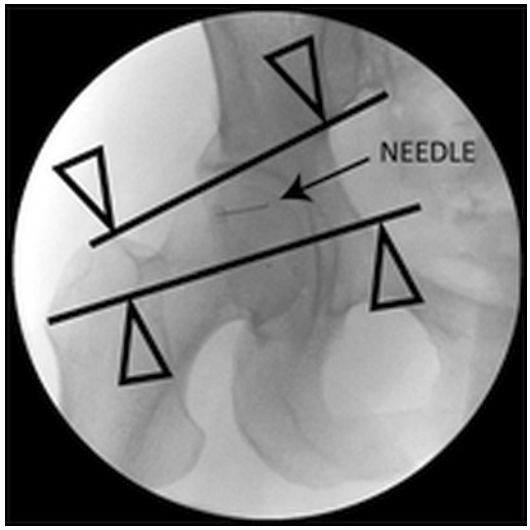

Fig. 91.1 AP view with the needle midway between the ipsilateral sacrum and greater trochanter. The needle is also medial to the acetabular margin. The lines and open arrowheads outline the typical location of the piriformis muscle

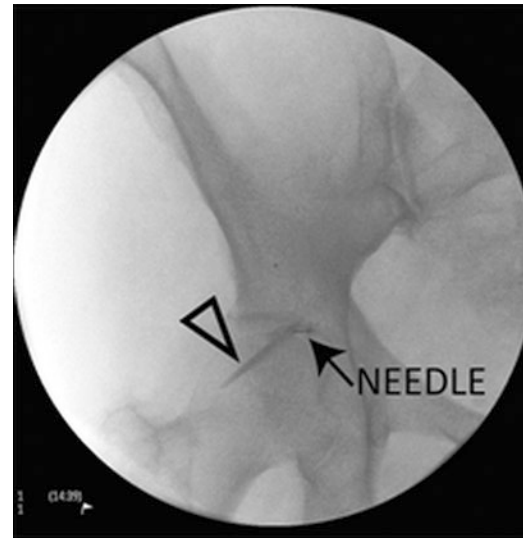

Fig. 91.2 AP view with the needle in the piriformis and contrast (open arrowhead) beginning to outline the piriformis

seen, no further contrast is needed. Save this AP image (some like to rotate to a lateral fluoroscopic position and save an image in this trajectory as well).

8. Remove the extension tubing from the contrast syringe, and place it on the syringe with your injectate. (A common injectate is 2 cc of 1 % lidocaine, and some will add 40 mg of methylprednisolone.) Make sure the extension tubing is primed and injected into the piriformis muscle. There should be very little resistance to injection. After half of the injectate is injected, take an AP image to make sure that the contrast is being diluted by the local anesthetic +/− corticosteroid mixture (saving this image is optional). If dilution is occurring, inject the remainder of the injectate. Remove the extension tubing and flush the needle with 1 cc of 1 % lidocaine and remove the needle.

Complications

Bleeding, infection, sciatic nerve damage/block, and intra-articular hip entry are some of the potential complications.

Good aseptic technique and adherence to proper setup will limit the chance for complications. Always review the imaging, if available, prior to the procedure.

Clinical Pearls

Staying over the body of the ischium at all times will allow one to avoid contact with important adjacent structures.

If the contrast pools at the end of the needle, the needle tip is not within the piriformis muscle and should be redirected.

Removing a needle through the skin with particulate steroid inside it can result in skin depigmentation and skin fat atrophy.

Evidence

A large prospective study revealed improved pain and function when proper diagnosis of piriformis syndrome is combined with trigger point injection(s) of this muscle.

A recent cadaveric study revealed the consistent anatomic position of the piriformis muscle.

A recent study confirmed similar success rates for injection into the piriformis muscle by means of fluoroscopic guidance as compared to ultrasound guidance.

Additional Reading

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Fowler IM, Tucker AA, Weimerskirch BP, Moran TJ, Mendez RJ. A randomized comparison of the efficacy of 2 techniques for piriformis muscle injection: ultrasound-guided versus nerve stimulator with fluoroscopic guidance. Reg Anesth Pain Med. 2014;39(2):126–32. doi:10.1097/AAP.0000000000000056.

Sonographically Guided Iliopsoas Injection

92

David V. Dent and Jason Dauffenbach

Indications

Diagnostic or therapeutic injection/aspiration of iliopsoas (IP) bursa, anterior hip pain syndromes, snapping hip syndrome, and post-arthroplasty hip pain.

Equipment/Materials

Sonographically guided: 22 g 3.5 in. spinal needle, local anesthetic, +/− corticosteroid, and low-frequency curvilinear ultrasound transducer.

Procedure

Position: supine
IV: not required
Antibiotics: not required

CPT:20610 bursa injection/aspiration (large)
76942 ultrasonic guidance for needle placement

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Steps:

1. Preinjection scanning in short- and long-axis views to visualize anatomy and neurovascular structures and determine optimal needle path (Fig. 92.1a, b).
2. Transducer placed in the axial oblique plane at the level of the acetabular rim, cephalad to the femoral head, approximately parallel to the inguinal ligament (Fig. 92.1a).
3. After appropriate sterile preparation, the IP tendon is viewed in short axis. Skin and subcutaneous anesthetic is infiltrated. The spinal needle is advanced under live sonographic guidance, in-plane, lateral to medial, targeting the deep lateral aspect of the IP tendon. (Fig. 92.2).
4. Hydrodissection with local anesthetic or saline can be used to isolate and partially distend the IP bursa.
5. Injection of local anesthetic +/− corticosteroid up to a volume of 5–7 mL.
6. Injectate should cause anterior displacement of the IP tendon with flow seen deep and/or medial to IP tendon.

Complications

The femoral neurovascular bundle lies anterior and medial to the iliopsoas tendon complex. Generous use of local anesthetic for pain control or hydrodissection prior to IP bursa injection

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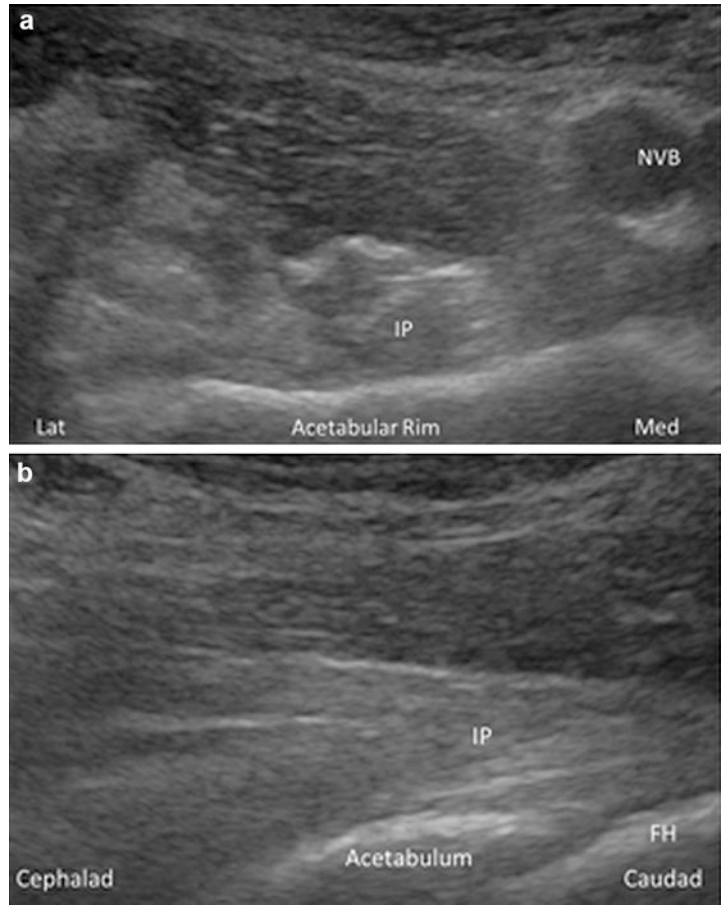

Fig. 92.1 (**a**) Right iliopsoas (IP) tendon in short axis. *Top*, superficial; *bottom*, deep; *left*, lateral; *right*, medial. Curvilinear 6–2 MHz transducer, Analogic BK Medical. (**b**) Right iliopsoas (IP) tendon in long axis. *FH* femoral head. *Left*, cephalad; *right*, caudad; *top*, superficial; *bottom*, deep. Curvilinear 6–2 MHz transducer, Analogic BK Medical

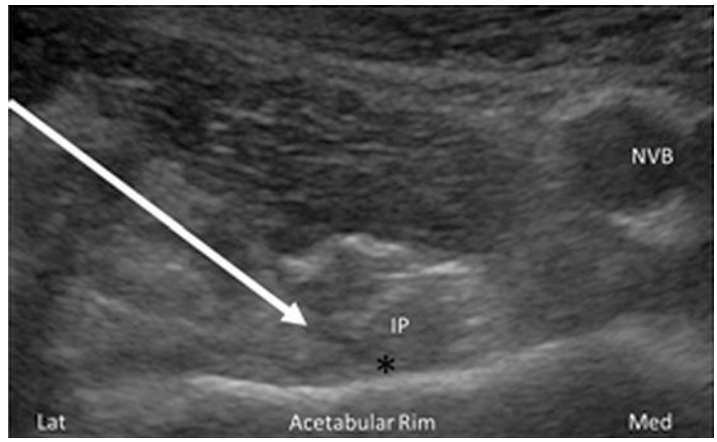

Fig. 92.2 Needle trajectory (*white arrow*) for injection of the IP bursa, with target needle placement at the deep lateral aspect of the IP tendon (*asterisk*). *Top*, superficial; *bottom*, deep; *left*, lateral; *right*, medial. Curvilinear 6–2 MHz transducer, Analogic BK Medical

could produce femoral block. Damage to neurovascular structures is possible if needle placed on superficial aspect of tendon.

Clinical Pearls

Intra-articular communication between the iliopsoas bursa and the hip joint has been described

in various clinical conditions (e.g., rheumatoid arthritis, osteoarthritis, etc.).

Dynamic imaging of the hip during flexion and abduction may aid in diagnosis of external snapping hip syndrome.

Evidence

Consult the Following Articles

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Dauffenbach J et al. Distribution pattern of sonographically guided iliopsoas injections: cadaveric investigation using coned beam computed tomography. J Ultrasound Med 2014;33:405–14.

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Saphenous Nerve Block

93

Thomas F. Olson and M. Gabriel Hillegass, III

Indications

Neuralgia in the saphenous nerve distribution and postoperative pain from surgery involving the medial lower leg and foot (e.g., saphenous vein harvesting or stripping, foot/ankle orthopedic or podiatric procedures, etc.)

Equipment/Materials

Ultrasound machine with a high-frequency linear transducer, sterile sleeve and coupling gel, 21–22 gauge short-bevel echogenic needle (5–10 cm), 10 mL syringe, connection tubing, and local anesthetic +/− steroid.

CPTInjection, anesthetic agent; other peripheral nerve 64450
Ultrasound guidance 76942

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Procedure

Position: supine, thigh abducted and externally rotated.
IV: not required unless previous vagal episodes, severe anxiety, or needle phobia.
Antibiotics: not required

Steps:

1. Start with anatomic scanning along the proximal anteromedial thigh using a transverse transducer orientation. Identify the sartorius, vastus medialis and adductor longus/adductor magnus muscles, and possibly the hyperechoic nerve adjacent to the femoral artery. The nerve traverses from deep (subsartorial) proximally to superficial distally. It can be found in the fascial plane between the sartorius and vastus medialis muscles with the superficial femoral artery in the distal third of the thigh (Fig. 93.1) or subcutaneously in association with the saphenous vein at the medial knee and below (Fig. 93.2).
2. Identify the point of optimal visualization of the femoral artery beneath the sartorius muscle in the distal anteromedial thigh. Color Doppler may be helpful if visualization of the artery is difficult.
3. Using sterile technique and after local anesthesia is achieved, use an in-plane approach from lateral to medial to position the needle tip medial to the femoral artery in the subsartorial compartment.

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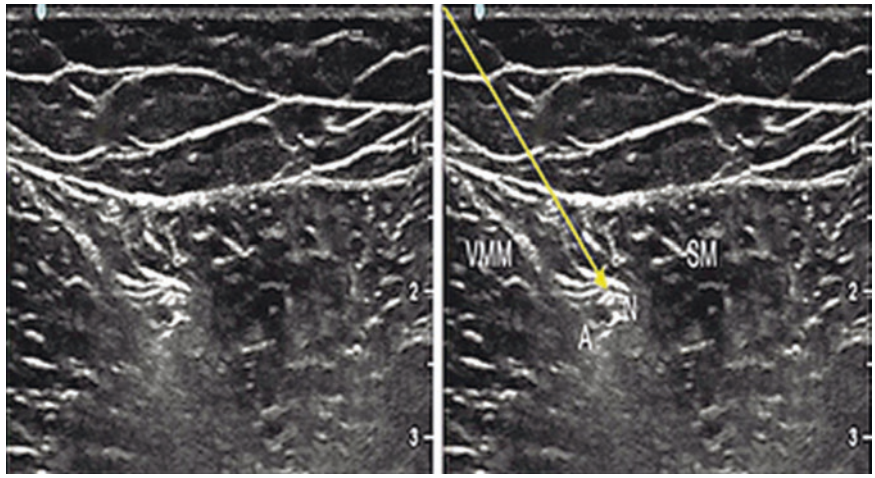

Fig. 93.1 Subsartorial technique: US image depicting fascial plane between the vastus medialis muscle (VMM) and sartorius muscle (SM), where the saphenous nerve (N) is seen adjacent to the femoral artery (A). Note the lateral to medial trajectory of the needle (*solid line*)

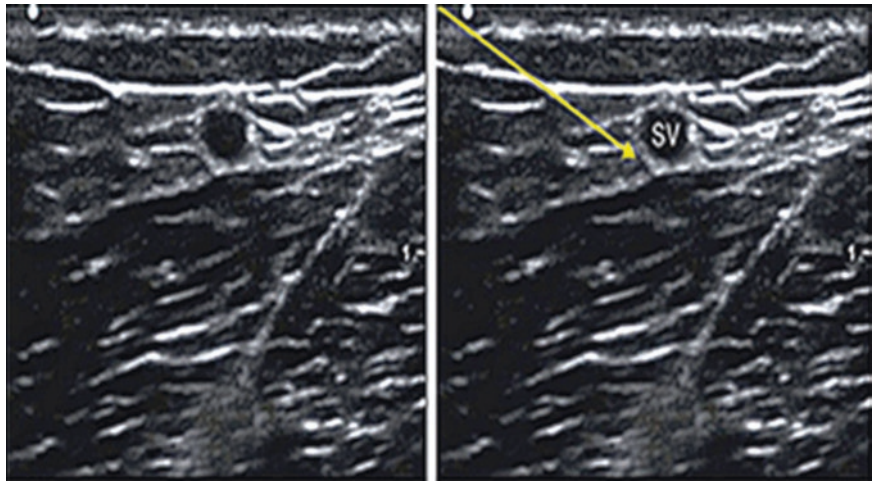

Fig. 93.2 Below-the-knee technique: US image depicting the saphenous vein (SV). Note the lateral to medial trajectory of the needle (*solid line*)

4. Inject 1–2 mL of local anesthetic to confirm proper injectate spread around the artery. The total injectate volume should be 5–10 mL.
5. The needle should be repositioned if poor injectate spread around the artery or with high resistance to injection (>15 psi).

Note: The adductor canal block is performed subsartorially in the middle third of the anteromedial thigh using a similar technique. Ensure that the needle penetrates both the sartorial and vastoadductor fascial layers and that the injectate surrounds the femoral vessels. Total injectate volumes are typically higher (20 mL) when seeking surgical anesthesia. Motor blockade of the nerve to the vastus medialis and the posterior division of the obturator nerve is expected, but the common femoral nerve is usually spared.

Complications

Bleeding and hematoma formation could result from trauma to the vasculature. Anticipate paresthesias in the saphenous distribution when entering its fascial plane. Direct needle trauma or intraneural injection could cause or worsen nerve injury. Infection is a low risk if strict aseptic technique is used. Local anesthetic toxicity would be unlikely because of the small volumes of injectate and resultant subtoxic dose; however, the risk increases when combined with other regional techniques or with the high volume used in an adductor canal block. Ensure the total dose is well below maximal local anesthetic thresholds.

Clinical Pearls

This interventional technique can be helpful to diagnose saphenous neuralgia as well as to provide a prognosis for the effectiveness of neuroablative (e.g., RFA) or neurolytic therapies.

In an adult patient, usually 5–10 mL of local anesthetic is adequate for successful blockade. High concentrations of local anesthetic are not required because the saphenous nerve is rather small in diameter and a purely sensory nerve.

An alternative to the subsartorial approach described above is to identify the subcutaneous saphenous vein using ultrasound and inject around this vessel (Fig. 93.2). The nerve is typically too small to be visualized in the lower leg. If the saphenous vein is not easily found, a tourniquet can be used to create venous engorgement.

Evidence

Above-the-Knee Versus Below-the-Knee Versus At-the-Knee?

Multiple studies have been conducted comparing these different approaches. A 2005 study by Benzon et al. suggested that the trans-sartorial above-the-knee approach is more effective in providing sensory blockade in the medial aspects of the leg and foot [1]. A more recent investigation by Kent et al. (2013) demonstrated that higher success rates are achieved with above-the-knee ultrasound-guided saphenous blocks [2].

Saphenous Nerve Block During TKA?

Two recent studies [3, 4] suggest that for knee surgery, adductor canal blocks reduce morphine consumption and promote early ambulation. Although strong evidence supporting its use in knee surgery is limited, saphenous blockade has the theoretical advantage of avoiding quadriceps weakness.

Disclaimer The views expressed in this article are those of the author(s) and do not necessarily reflect the official policy or position of the Department of the Navy, the Department of Defense, or the US Government.

References

1. Benzon HT et al. Comparison of different approaches to saphenous nerve block. Anesthesiology. 2005; 102(3):633–8.
2. Kent ML, Hackworth RJ, Riffenburgh RH, et al. A comparison of ultrasound-guided and landmark-based approaches to saphenous nerve blockade: a prospective, controlled, blinded, crossover trial. Anesth Analg. 2013;117(1):265–70.
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Pudendal Nerve Block

94

Nantthasorn Zinboonyahgoon
and Assia T. Valovska

Indications: Pudendal nerve block is indicated for diagnostic, as a part of essential diagnostic criteria (Nantes criteria), and for treatment of pudendal neuralgia.

Anatomy: Pudendal nerve arises from S2 to S4 sacral nerve roots and travels inferiorly to exit the pelvic through the greater sciatic foramina, just inferior to the piriformis muscle. The nerve passes posterior to the ischial spine, along with internal pudendal artery, between sacrospinous ligament (anterior) and sacrotuberous ligament (posterior). It reenters pelvic through lesser sciatic foramen then pass through Alcock's canal. Finally, it terminates into three branches: inferior rectal nerve (perianal sensation), peroneal nerve (perineum and posterior surface of scrotum/labia sensation), and dorsal nerve of the penis/clitoris (penis/clitoris sensation).

Procedure: Pudendal nerve block can be attained by transvaginal/transrectal approach, fluoroscopic or ultrasound-guided transgluteal approach, or fluoroscopic-guided transsacral S2–S4 block. No need for IV or antibiotic for the procedure.

Transvaginal/Transrectal Approach

Patient is in lithotomy position, and the ischial spine is palpated through the vaginal wall (female) or rectal wall (male). Needle is advance through the vaginal wall or perianal area along with the guided finger. Ten to fifteen ml of local anesthetics is injected just posterior to ischial spine. However, this conventional technique inherits risk of accidental puncture of needle to physician and patient discomfort.

Fluoroscopic-Guided Transgluteal Approach

1. Patient is in prone position, C-arm is set in AP view until pelvic inlet is visualized, and then highlight the ischial spine by 5–15° ipsilateral angulation of the C-arm (Fig. 94.1).
2. A 22 G spinal needle advances perpendicularly to C-arm aim at the tip of ischial spine.
3. Remove the stylet and check for negative aspiration for blood; inject 0.5 ml of contrast media to check the spread.

CPT64430

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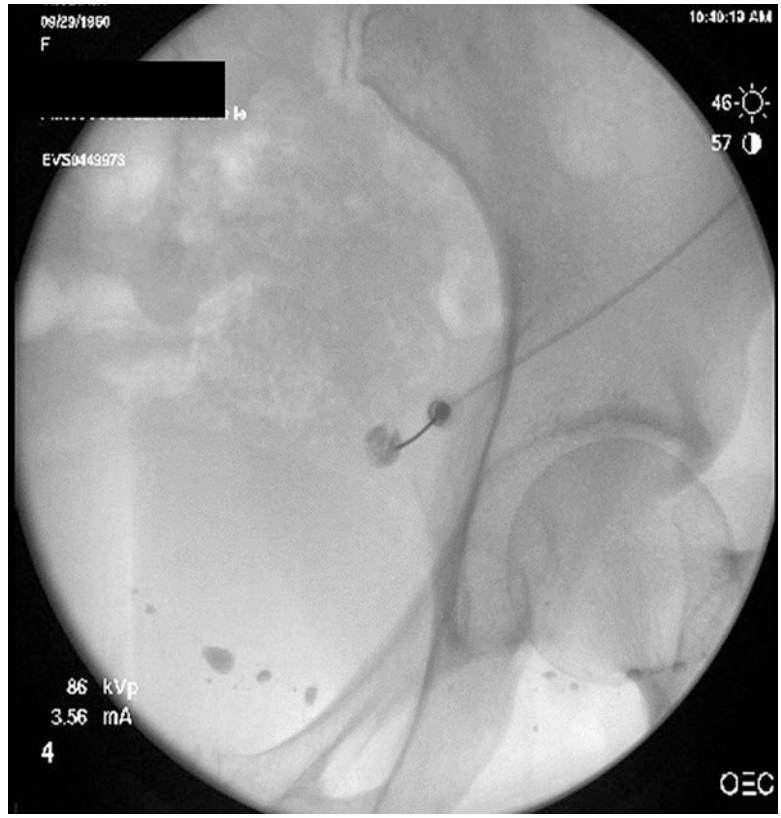

Fig. 94.1 Oblique view of pelvis—the needle tip points at ischial spine

4. After satisfied with needle position and spread, inject 3–4 ml of local anesthetics + − steroid as a final step.

Ultrasound-Guided Transgluteal Approach

1. Patient is in prone position; curvilinear low-frequency (2–5 MHz) probe is applied transversely at PSIS to visualize SI joint.
2. Scan caudally; the piriformis muscle will appear (Fig. 94.2) and will disappear when scan further caudally. At this level (level A in Fig. 94.1), hyper echoic process of ischial spine will appear on the medial side of the screen.
3. Sacrospinous ligament (Sp) is identified as hyperechoic line extending from the ischial spine. Sacrotuberous ligament (St) can be identified as thin parallel line superficial to Sp, but deep to gluteus maximus. Pudendal nerve and artery lie in plane between the two ligaments (Fig. 94.3).
4. Insert 100 mm echogenic needle, in plane, aims at the plane between the ligaments. Inject some local anesthetic until you visualize a good spread, and then inject total 3–4 ml of local anesthetic + − steroid as a final step.

Fluoroscopic-Guided Transsacral S2–S4 Block

1. Patient is in prone position; C-arm is set in AP view; adjust until S2, S3, and S4 sacral foramens are identified (Fig. 94.4).
2. A 25 G spinal needle advances perpendicularly to C-arm aim at each foramen.

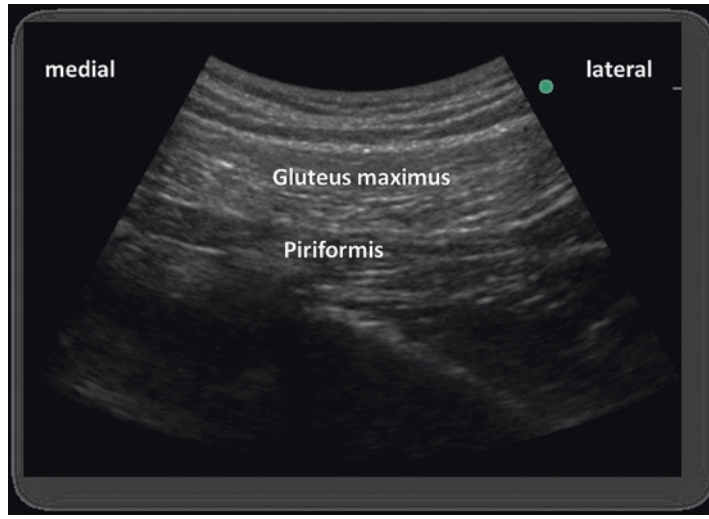

Fig. 94.2 Ultrasound image of structure cephalad to ischial spine level

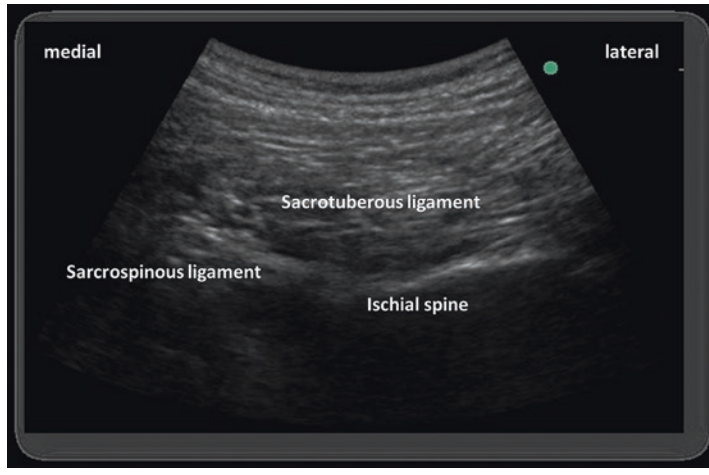

Fig. 94.3 Ultrasound image of structure at ischial spine level

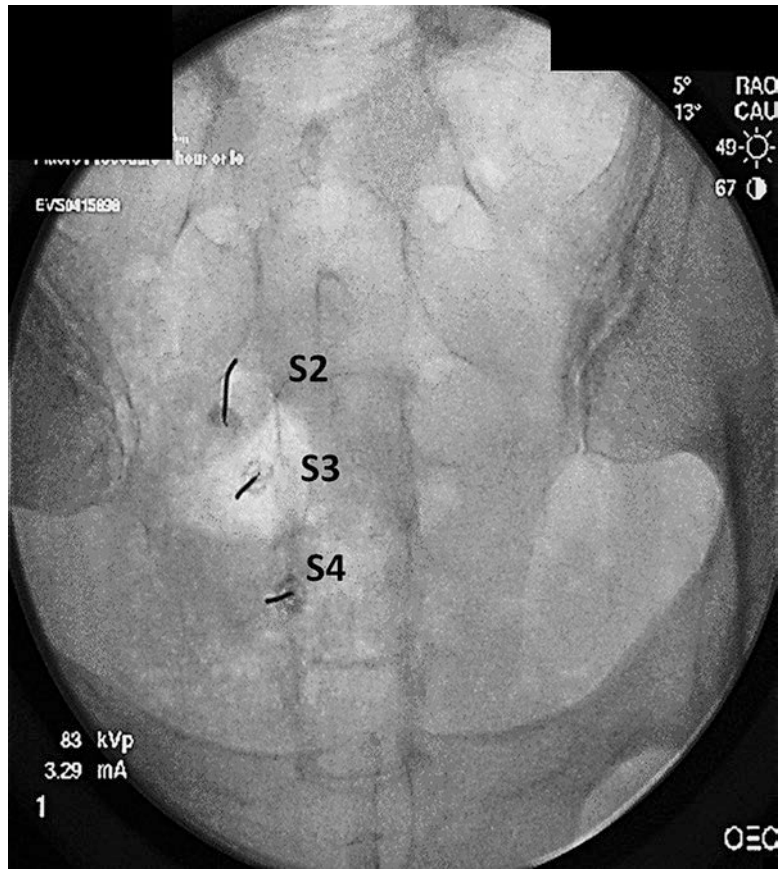

Fig. 94.4 AP view of sacrum—needles tip are at S2, S3, and S4 foramens

3. Remove the stylet and check for negative aspiration for blood. After satisfied with needle position, inject local anesthetics + −steroid 3–4 ml for each foramen.

Complications: intravascular injection, sciatic nerve injury, hematoma, and perforated rectum (infection, fistula).

Evidence: A comparison study showed ultrasound-guided transgluteal injection is as effective as fluoroscopic guided; however ultrasound allows visualization of the sciatic nerve and pudendal artery which potentially minimizes the risk of damages to both structures.

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Trochanteric Bursa Injection

95

David V. Dent

Indications: History and physical examination evidence of trochanteric bursitis.

Equipment/Materials: 22 or 25 g spinal needle 2" or longer, local anesthetic, and +/− corticosteroid; fluoroscopy or ultrasound may be needed in more difficult cases (such as morbid obesity).

Procedure

Position: Lateral recumbent
IV: usually not required
Antibiotics: not required

Steps:

1. Identify the patient and confirm the planned procedure with the patient. Mark the side and area to be injected. Perform a time out.
2. Lateral recumbent position with the affected hip up and a pillow between the knees.
3. Prepare the area to be injected with an antiseptic/antimicrobial cleaning solution using sterile technique.
4. Palpate the greater trochanter and ask the patient to let you know the point of maximal tenderness. Mark the entry point on the skin and anesthetize the skin. Once appropriate local anesthesia is obtained, insert the spinal needle and advance using a coaxial technique toward the underlying greater trochanter. Once bony contact is made on the greater trochanter, remove the needle slightly and aspirate. If negative aspiration and no resistance of injection, inject 50 % of the injectate (a common injectate is 40 mg of methylprednisolone and 3 cc of 1 % lidocaine). Reposition the needle slightly around the point of maximal tenderness (superior, inferior, anterior, and posterior), and inject equal amounts of the remaining injectate at each of these four points, after negative aspiration and no resistance to injection. If resistance to injection occurs, reposition the needle (Fig. 95.1).
5. Flush the needle with 1 cc of 1 % lidocaine and remove the needle.

CPT20610 arthrocentesis, aspiration, and/or injection; major joint or bursa

Complications

Infection and bleeding. Good aseptic technique and adherence to proper setup will limit the chance for complications. Avoid movement of the leg during the procedure.

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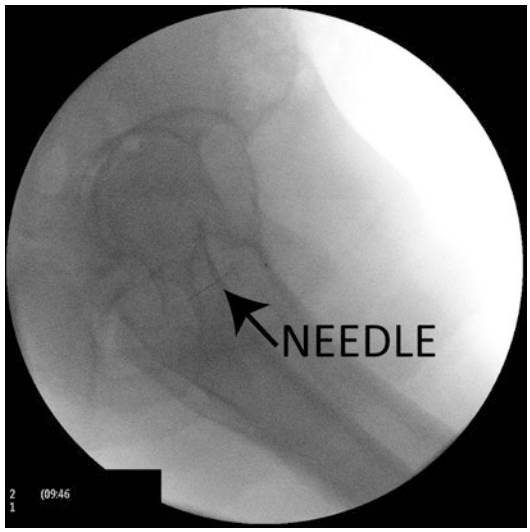

Fig. 95.1 Lateral fluoroscopic view. Note the needle at the trochanteric bursa. No contrast needed. Fluoroscopic guidance is optional

Clinical Pearls

Removing a needle through the skin with particulate steroid inside it can result in skin depigmentation and skin fat atrophy.

Obtain a pain score (lateral thigh pain) before and a few minutes after the procedure. This will allow you to determine if, and to what extent, the trochanteric bursa is the pain generator.

Evidence

Intra-Bursal Steroid Use

Prospective studies have suggested that corticosteroid and lidocaine injection for trochanteric bursitis is an effective treatment option with prolonged benefit.

"Blind" Injection

A recent randomized controlled trial revealed limited utilization of fluoroscopy for trochanteric bursa injections.

Additional Reading

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Ischial Bursa Injection

96

David E. Gutierrez, Hana Azizi, Soo Yeon Kim, and Karina Gritsenko

Indications: The ischial bursa can become inflamed (ischial bursitis or ischiogluteal bursitis aka "Weaver's bottom") due to minor trauma and overuse and from prolonged sitting. Patients typically complain of buttocks pain or pain worsened by the seated position.

Equipment/Materials: Fluoroscopy or ultrasound, 3–3.5 in. 22 gauge needle, loss of resistance syringe, +/− contrast, local anesthetic, and +/− corticosteroid.

CPTInjection of major joint or bursa: 20610
Professional component 26

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Procedure

Position: prone
IV: not required
Antibiotics: not required

Steps:

Blind

1. Sterile preparation and aseptic technique should be performed to the area.
2. The ischial bursa can be palpated along the inferior buttocks just proximal to the ischial tuberosity. This area should also correspond with the area of maximal point tenderness.
3. Insert the injection directly at this point into the bursa at a perpendicular angle to the buttocks. See Fig. 96.1.

Ultrasound Guided

1. Sterile preparation and aseptic technique should be performed to the area.
2. The ischial tuberosity should be palpated as a landmark for the ultrasound transducer. With the transducer in axial plane, one should be able to visualize the ischial tuberosity, gluteus maximus, hamstring tendons, and the sciatic nerve. Lateral movement of the transducer can better visualize the sciatic nerve if not in optimal view prior to injection.

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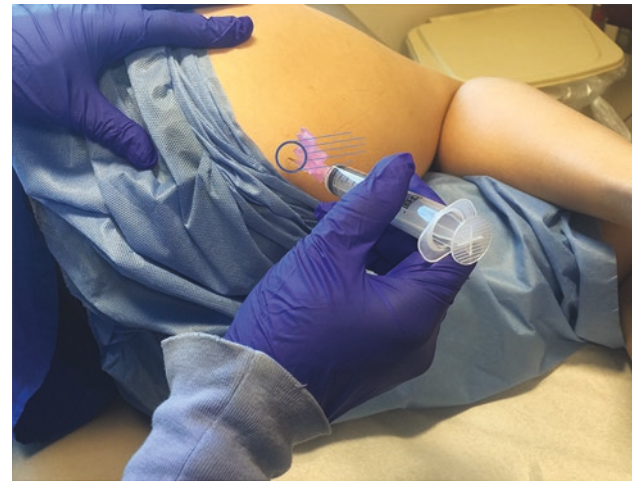

Fig. 96.1 Image of blind technique`

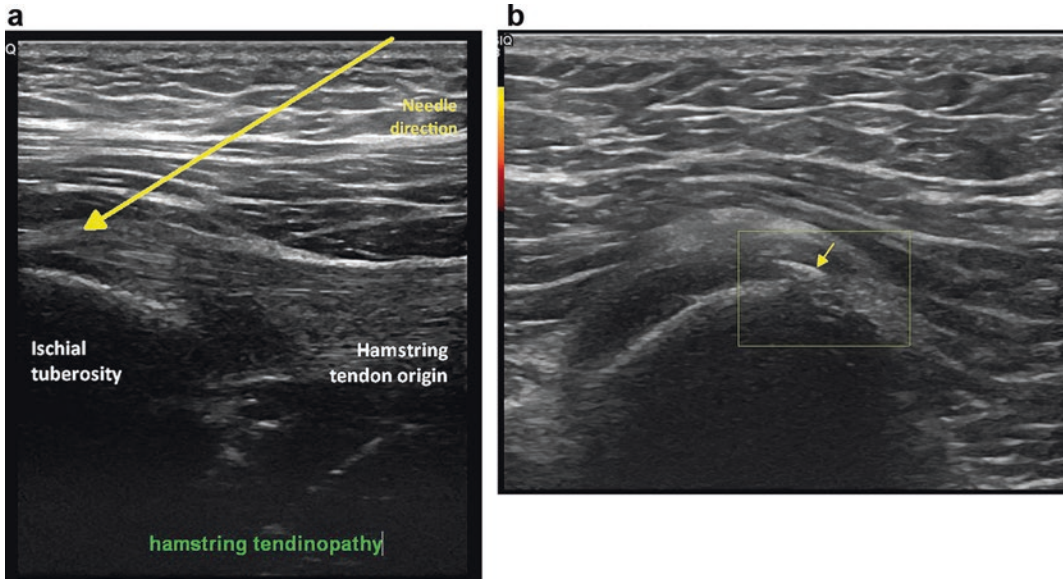

Fig. 96.2 (**a**) Image of ultrasound guidance. *Yellow arrow*: calcific tendinopathy. (**b**) Transverse view of ischial tuberosity

3. Insert the needle via an in-plane approach and visualize going into the ischial bursa just superficial to the hamstring tendons and deep to the gluteus maximus muscle. See Fig. 96.2.

Fluoroscopy Guided

1. Sterile preparation and aseptic technique should be performed to the area.
2. The beam should be centered over the obturator foramen and injection area which is the inferior aspect of the ischial tuberosity. The needle is advanced to the proximity of the ischial tuberosity.
3. Hip extension or knee flexion helps to show the needle movement. Injection of a small amount of radio opaque contrast will confirm the correct placement. See Fig. 96.3.

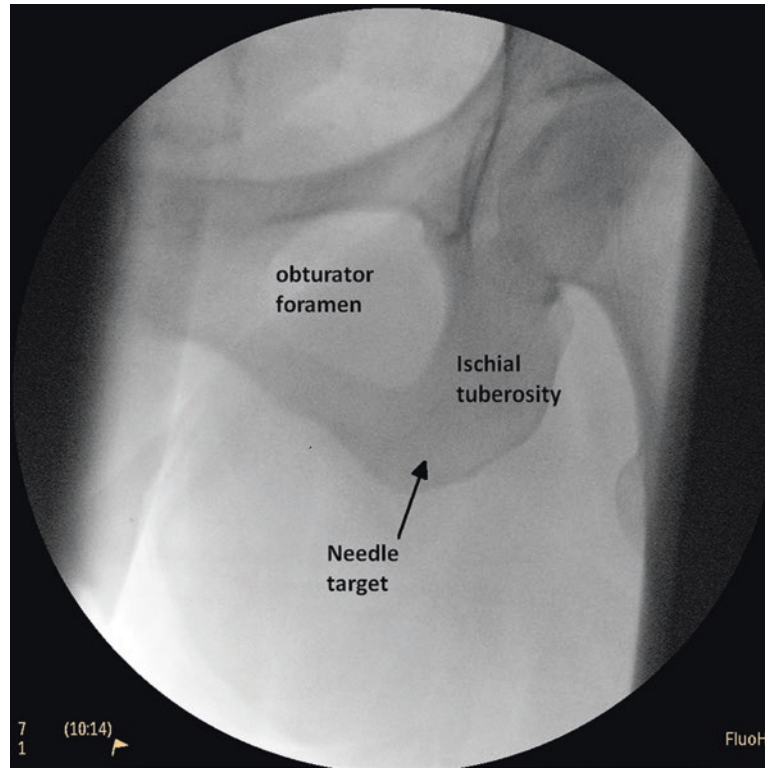

Fig. 96.3 Image of fluoroscopic guidance

Complications

If the patient complains of paresthesia, it is possible that your needle has contacted the sciatic nerve and will require repositioning. Aspirate before injecting any solution to ensure no entry into vasculature. If there is resistance, reposition the needle, as there should be little, if any, with successful penetration of the bursa.

Clinical Pearls

The ischial bursa is a deep bursa over the bony prominence of the ischium and is located between the ischial tuberosity and the gluteus maximus muscle. The sciatic nerve is one of the larger neurovascular anatomical structures in this area, just lateral to the ischial bursa. Anatomical landmarks are essential to this procedure.

It is important to note that ischial bursitis can often mimic hamstring insertional tendon injury. The practitioner should ensure that active hamstring range of motion does **not** cause pain before considering a diagnosis of ischial bursa inflammation.

Evidence

Blind Versus Ultrasound Versus Fluoroscopy

While there are few, if any, studies comparing the various approaches, one study revealed that the ultrasound approach was effective and technically feasible at targeting the ischial bursa in cadaver studies. Another study suggested that under fluoroscopic guidance, one may avoid or decrease the risk of causing paresthesias by avoiding contact with the sciatic nerve. There are benefits and cons of both techniques.

Additional Reading

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97 Intra-articular Shoulder Joint Injection (Fluoroscopically Guided)

David V. Dent

Indications: Primarily used for documented glenohumeral joint osteoarthritis/labral tear/adhesive capsulitis.

Equipment/Materials: Fluoroscopy, 22 or 25 g spinal needle 2" or longer, contrast dye, local anesthetic, +/− corticosteroid, and +/− saline.

Procedure

Position: supine
IV: Usually not required
Antibiotics: not required

Steps:

1. Identify the patient and confirm the planned procedure with the patient. Mark the side and area to be injected. Perform a time out.
2. Start with AP view and adjust the C-arm so that the entire anterior aspect of the humeral head is visible. This usually requires a slight contralateral oblique position.
3. After the entire anterior shoulder is prepared using an antiseptic/antimicrobial cleaning solution, mark the point of insertion. Think about the humeral head as a clock with 12 and 6 o'clock lined up with the shaft of the humerus. The insertion zone is between 11 and 2 o'clock.
4. After local anesthetic infiltration, insert the needle coaxially into the *insertion zone* (see Fig. 97.1).
5. Once the trajectory is verified to be coaxial, continue advancing until bone is contacted. Inject 0.5 cc of 1% lidocaine to make sure there is easy flow. If there is any resistance to flow, adjust the needle slightly.
6. At this point, remove the stylet from the spinal needle. After negative aspiration, inject a small amount of contrast. There should be no resistance to flow. If resistance is encountered, slightly redirect the needle—resistance could mean that the needle is in the joint capsule itself, a ligament or in a tendon. If the contrast does not rapidly spread and only stays at the end of the needle, adjust the needle position by repositioning medially or laterally a few mm. Ideal contrast flow will be throughout the capsule and into the glenohumeral joint (Fig. 97.1). Save this image.
7. After adequate spread of contrast is verified, the injectate medication is then injected. A common injectate volume is 4 mL and includes 40 mg of methylpred-

CPTIntra-articular injection (major joint): 20610
Fluoroscopy (outside the spine) 77002
Professional component 26

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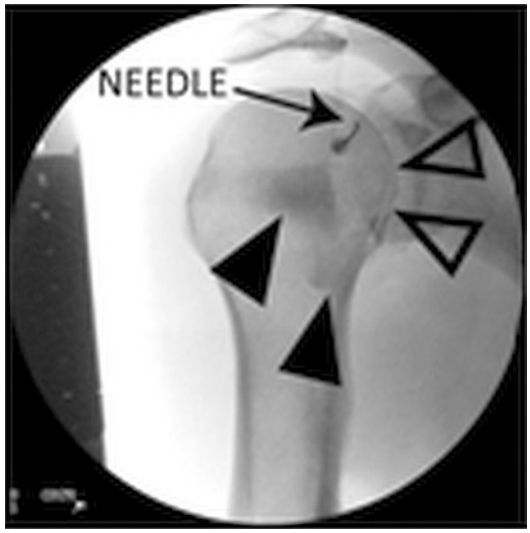

Fig. 97.1 AP view with slight contralateral oblique—note how the needle is inserted to the 1 o'clock position. The *open arrowheads* demonstrate contrast in the glenohumeral joint. The *solid arrowheads* demonstrate contrast filling up the joint capsule

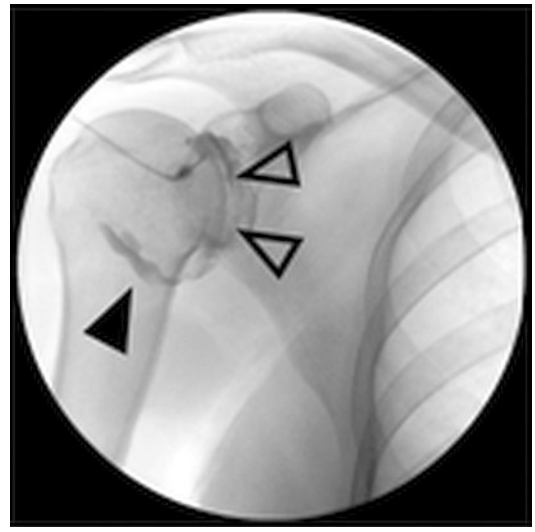

Fig. 97.2 AP view. Notice how the contrast is filling up the shoulder joint capsule. The *open arrowheads* demonstrate contrast in the glenohumeral joint. The *solid arrowhead* demonstrates contrast filling up the joint capsule

nisolone and 1 % lidocaine or 0.25 % bupivacaine. There should be no resistance to injection. After half of the injectate is injected, take an AP image to make sure that the contrast is being diluted by the local injectate (saving this image is optional). If dilution is occurring, inject the remainder of the injectate. Then take and save an AP post-injectate image showing that the injectate was placed intra-articular (the contrast will be diluted—Fig. 97.2). Flush the needle with 1 cc of 1 % lidocaine and remove the needle.

Complications

Bleeding, infection, trauma to the glenohumeral cartilage, and trauma to the glenoid labrum are some of the potential complications. Good aseptic technique and adherence to proper setup will limit the chance for complications. Avoid movement of the arm during the procedure. Always review the imaging, if available, prior to the procedure.

Clinical Pearls

Be sure the patient is in comfortable position as they will be lying on the table for about 5–10 min without moving. Position the affected arm with contact to the side of the patient with the thumb pointed toward the ceiling.

There is no consensus on injectate content or volume. Volumes vary from 2 to 25 cc, and choice and dosage of corticosteroid vary widely, although a typical volume is around 5 mL. There are some recent studies showing improvement with adhesive capsulitis when using high volume (20–25 ccs) into the glenohumeral joint to expand (but not rupture) the capsule.

Evidence

Intra-articular Steroid Use

In a prospective, randomized controlled trial, the treatment of partial rotator cuff tears with an intra-articular steroid injection resulted in improved night pain and improved activity.

In another prospective, randomized controlled trial, an intra-articular steroid injection

was associated with a more rapid improvement and improved ability to complete physical therapy in patients diagnosed with adhesive capsulitis.

Additional Reading

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Intra-articular Hip Joint Injection (Fluoroscopically Guided)

98

David V. Dent

Indications: Primarily used for documented hip joint osteoarthritis and/or labral tears.

Equipment/materials: Fluoroscopy, 22G spinal/skin needle 3.5" or longer, extension tubing, contrast, local anesthetic, +/− corticosteroid, +/− saline.

Procedure

Position: lateral recumbent (affected side up)
IV: usually not required
Antibiotics: not required

Steps:

1. Identify the patient and confirm the planned procedure with the patient. Mark the side and area to be injected. Perform a time-out.
2. Lateral recumbent position with the affected hip joint up and a pillow between the knees. Set the c-arm in a lateral view with femoral heads superimposed on each other (coronal plane).
3. Apply 45° of cephalad tilt to the image intensifier. The affected hip joint will be the lower one on the fluoroscopic image.
4. Prepare the area to be injected using an antiseptic/antimicrobial cleaning solution and sterile technique.
5. The initial target is the midline at the superior edge of the greater trochanter. Mark the entry point on the skin and anesthetize the skin. Once appropriate local anesthesia is obtained, insert the spinal needle and advance using a coaxial technique. Once bony contact is made on the superior edge of the middle of the greater trochanter, redirect the needle slightly superior to direct the needle superior to the greater trochanter.
6. At this point switch to an AP view. The target now is the neck of the femur. Advance the needle in an inferomedial direction to the neck of the femur in the AP view. Use caution not to come in contact with the head of the femur as this can disrupt the articular surface +/− acetabular labrum of the hip joint.
7. The needle should contact the bone as soon as the needle tip is over the neck of the femur on the AP view. If the bone is not contacted, but the needle appears to be over the neck of the femur, the needle is either too anterior or too posterior. Further medial advancement could risk coming into contact with neurovascular structures. If the bone is not contacted, go back to a lateral view with the C-arm and redirect the needle at the midline of the neck

CPT
Intra-articular injection (major joint): 20610
Fluoroscopy (outside the spine) 77002

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of the femur (make sure the two femoral heads are lined up so that you have a true coronal image).

8. Once the neck of the femur is contacted, remove the stylet from the spinal needle. Make sure that your extension tubing, which is connected to your syringe with contrast, is fully primed (all air is out of the extension tubing). Place the extension tubing onto the needle hub. Use your extension tubing to remove yourself as far as possible from the x-ray beam. After negative aspiration, inject a small amount of contrast under a short burst of live fluoroscopy. There should be no resistance to flow. If resistance is encountered, slightly redirect the needle (resistance could mean that the needle is in the joint capsule itself, in a ligament, or in a tendon). Ideal contrast flow will be down the neck of the femur and will collect at the inferior aspect of the hip joint (see Fig. 98.1). Once ideal contrast flow is seen, no further contrast is needed. Save this AP image (some like to rotate to a lateral fluoroscopic position and save an image in this trajectory as well).
9. Remove the extension tubing from the contrast syringe and place it on the syringe with your injectate. (A common injectate is 40 mg of methylprednisolone and 4 cc of 1% lidocaine.) Make sure the extension tubing is primed and inject into the hip joint. There should be no resistance to injection. After half of the injectate is injected, take an AP image to make sure that the contrast is being diluted by the local anesthetic/corticosteroid mixture. (Saving this image is optional.) If dilution is occurring, inject the remainder of the injectate. Remove the extension tubing and flush the needle with 1 cc of 1% lidocaine and remove the needle.

Complications

Bleeding, infection, trauma to the cartilage, trauma to the labrum, and avascular necrosis are some of the potential complications. Good aseptic technique and adherence to proper setup will limit the chance for complications. Avoid movement of the leg during the procedure. Always review the imaging, if available, prior to the procedure.

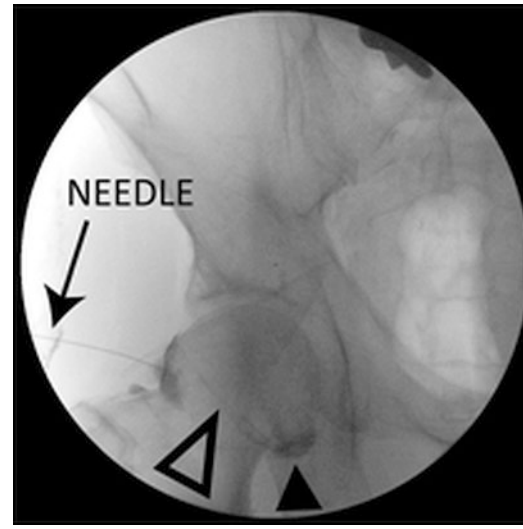

Fig. 98.1 AP view. Note the needle tip at the neck of the femur with the contrast flowing down the interface of the femoral head and neck of the femur (*open arrowhead*) to the inferior aspect of the femoral head (*closed arrowhead*)

Clinical Pearls

If the contrast pools at the end of the needle, the needle tip is not within the joint capsule and should be redirected.

Removing a needle through the skin with particulate steroid inside it can result in skin depigmentation and skin fat atrophy.

Obtain a pain score (groin pain with adduction and internal rotation of the hip joint) before and a few minutes after the procedure. This will allow you to determine if, and to what extent, the hip joint is the pain generator.

Position the patient at a point of comfort as they will be lying on the table for 5–10 min without moving. Position a pillow between the knees for added comfort.

There is no consensus on injectate or volume of injectate. Volumes vary from 2 to 25 cc and choice and dosage of corticosteroid varies widely

as well. A typical solution for injection is 40 mg of methylprednisolone mixed with 1 % lidocaine for a total volume of 4–6 cc.

The lateral approach to hip joint injections has been shown to be safe and reliable.

The fluoroscopic approach to hip joint injections will mostly likely be supplanted by ultrasound guidance in the near future.

Evidence

Intra-articular Steroid Use

A recent meta-analysis concluded that intra-articular steroid injections for hip osteoarthritis are an Ib indication after conservative care had been completed.

Another meta-analysis revealed that intra-articular steroid injections do not increase the risk of joint injection following future hip arthroscopy or total hip arthroplasty.

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Intra-articular Knee Joint Injection (Fluoroscopically Guided)

99

David V. Dent

Indications: Primarily used for documented knee joint osteoarthritis/meniscus tear/sprain.

Equipment/Materials: Fluoroscopy, 25G needle 1.5"+length, extension tubing, syringe for contrast, syringe for local anesthetic, syringe for corticosteroid, local anesthetic, contrast, +/− corticosteroid, +/− hyaluronan/hylan products.

Procedure

Position: supine
IV: usually not required unless
Antibiotics: not required

Steps:

1. Identify the patient and confirm the planned procedure with the patient. Mark the side and area to be injected. Perform a time-out.
2. Supine position with the affected knee joint in a few degrees of flexion and relaxed. Position the toes of the affected leg pointing straight up. Set the c-arm in an AP view to the knee with the entire patella visible.
3. Prepare the anterior and lateral knee using an antiseptic/antimicrobial cleaning solution and sterile technique.
4. Palpate the superolateral patellofemoral joint. The entry point will be the superior third of the superolateral patellofemoral joint. Keep in mind that the needle will be advanced in the coronal plane. Mark the entry point on the skin and anesthetize the skin. Once appropriate local anesthesia is obtained, insert the chosen needle and advance in the coronal plane with no anterior or posterior tilt to the needle. Once the needle comes into contact with the joint capsule, a slight increase in difficulty advancing the needle will be appreciated. If the bone is contacted, immediately stop advancing and reposition either posteriorly if the patella is contacted or anteriorly if the femur is contacted.
5. The target is under the superior third of the patella. Advance the needle in a medial direction in the AP view. Use caution not to come in contact with the bone as this can disrupt the articular surface of the patellofemoral joint.
6. Once the needle is in correct positioning (Fig. 99.1), place the extension tubing, which is connected to your syringe with contrast, onto the needle hub (make sure that your extension tubing is fully primed (all air is out of the extension tubing)). Use the length of your extension tubing to remove yourself as

CPTIntra-articular injection (major joint): 20610
Fluoroscopy (outside the spine) 77002

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R.J. Yong et al. (eds.), *Pain Medicine*, DOI 10.1007/978-3-319-43133-8_99

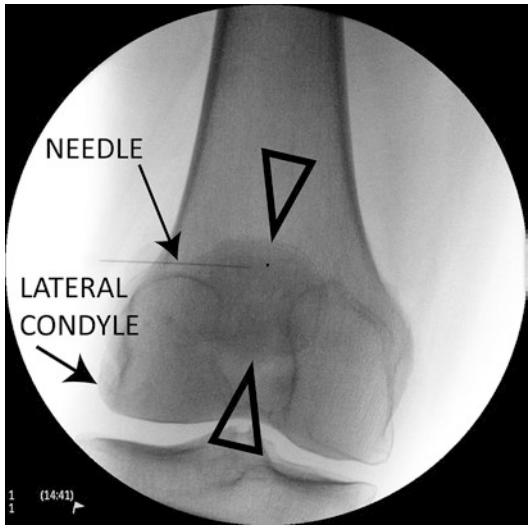

Fig. 99.1 AP view with the needle posterior to the upper third of the patella. The patella is between the *open arrowheads*

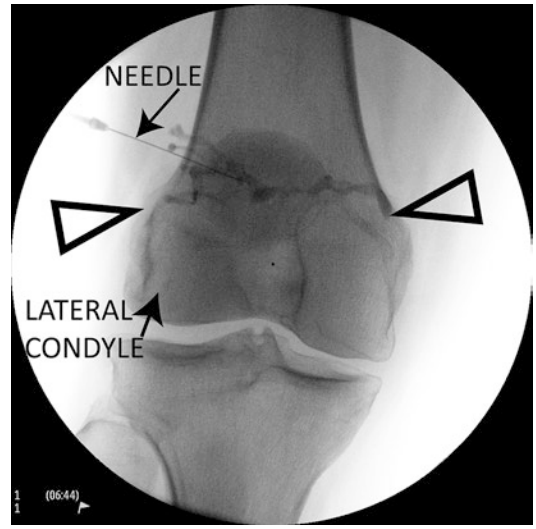

Fig. 99.2 AP view. Notice how the contrast is flowing medically and laterally to the edge of the knee capsule. The contrast then flows inferiorly (*open arrowheads*) toward the femorotibial joint

far as possible from the x-ray beam. If aspiration is negative, inject a small amount of contrast under a short burst of live fluoroscopy. There should be no resistance to flow. If resistance is encountered, slightly redirect the needle (resistance could mean that the needle is in the joint capsule, in a ligament, or in a tendon). Ideal contrast flow is medially and laterally and then inferiorly down toward the knee joint (Fig. 99.2). Once ideal contrast flow is seen, no further contrast is needed. Save this AP image (some like to rotate to a lateral fluoroscopic position and save an image in this trajectory as well).

7. Remove the extension tubing from the contrast syringe and place it on the syringe with your injectate. (A common injectate is 40 mg of methylprednisolone and 4 cc of 1% lidocaine.) Make sure the extension tubing is primed and inject into the knee joint. There should be no resistance to injection. After half of the injectate is injected, take an AP image to make sure that the contrast is being diluted by the local anesthetic/corticosteroid mixture. (Saving this image is optional.) If dilution is occurring, inject the remainder of the injectate. Remove the extension tubing and flush the needle with 1 cc of 1% lidocaine and remove the needle.

Complications

Bleeding, infection, trauma to the cartilage, trauma to the plica, and trauma to the menisci are some of the potential complications. Good aseptic technique and adherence to proper setup limit the chance for complications. Avoid movement of the knee during the procedure. Always review the imaging, if available, prior to the procedure.

Clinical Pearls

If the contrast pools at the end of the needle, the needle tip is not within the joint capsule and should be redirected.

Removing a needle through the skin with particulate steroid inside it can result in skin depigmentation and skin fat atrophy.

Obtain a pain score (knee pain with movement) before and a few minutes after the procedure. This will allow you to determine if, and to

what extent, the knee joint is the/a pain generator.

I suggest avoiding entering the knee joint from the medial aspect as this can result in damage to the plica.

I suggest avoiding entering the knee joint from an anterior approach as this can risk damage to the menisci.

Evidence

Intra-articular Steroid Use

A recent Cochrane review found a short-term benefit from intra-articular knee steroid injections. The review also found that the injection of hyaluronan/hylan products into the knee joint leads to a more "durable" improvement.

A recent meta-analysis concluded that intra-articular steroid injections for knee osteoarthritis are an Ia indication after conservative care had been completed.

Another meta-analysis revealed that intra-articular steroid injections do not increase the risk of joint infection following future knee arthroscopy or total knee arthroplasty.

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Ultrasound-Guided Ankle Joint Injection

100

Phuong Uyen Le, Marline Sangnil,
Karina Gritsenko, and Soo Yeon Kim

This chapter includes injection of the tibiotalar and subtalar joints and the five nerves for an ankle block.

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Indications

Indications for a tibiotalar joint injection include pain that is secondary to osteoarthritis, rheumatoid arthritis, acute traumatic arthritis, crystalloid deposition disease, mixed connective tissue disease, and synovitis.

Indications for a subtalar joint injection include pain that is associated with arthritis. Patients may present with heel pain that is worse with ambulation.

Equipment/Materials

Ultrasound probe 12–5 MHz (5–16 MHz to 17–5 MHz are preferable), 20- to 25-gauge 1.5-in needle, 1 % lidocaine for local anesthesia, 5-mL syringe, sterile ultrasound gel and probe cover, 4 × 4 gauze pads, sterile drapes, adhesive bandage and sterile cleansing solution,+/− corticosteroid.

Tibiotalar Joint Injection

Position: supine with knee bent and foot flat on the examination table (Fig. 100.1a).

Steps:

1. Clean the skin around the ankle thoroughly with an antiseptic agent such as chlorhexidine or alcohol. After the skin is dry, place sterile

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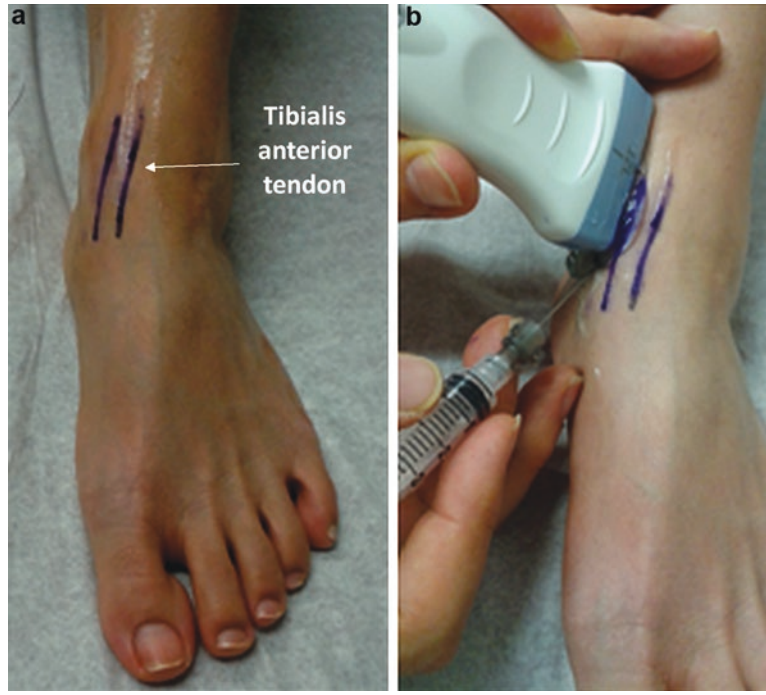

Fig. 100.1 Tibiotalar joint injection. (**a**) Patient position. (**b**) Probe and needle placement

ultrasound gel on the probe and cover the probe with sterile plastic.
2. Place the probe using the dorsal long axis approach. The probe is placed in the long axis with respect to the tibialis anterior tendon and positioned medially to the tendon (Fig. 100.1b).
3. Identify and avoid the dorsalis pedis artery.
4. When the anterior recess of the tibiotalar joint is localized, insert the needle, directing the needle from distal to proximal (Fig. 100.1b).
5. Aim the needle toward the underside of the tibia (Fig. 100.2) and aspirate to rule out intravascular injection.
6. Inject the medication, remove the needle, and apply an adhesive bandage.

Subtalar Joint Injection

Position: The ankle is positioned with the lateral side facing upward. Place the ankle in subtalar inversion (a towel may be placed under the ankle) (Fig. 100.3).

Steps:

1. Clean the skin around the ankle thoroughly with an antiseptic agent such as chlorhexidine or alcohol. After the skin is dry, place sterile ultrasound gel on the probe that is covered with sterile plastic.
2. The injection site is located by placing the probe on the sinus tarsi and scanning posteriorly. The lateral subtalar joint is identified anterior to the calcaneofibular ligament. The peroneal tendon and sural nerve are caudal to the subtalar joint at that location.
3. Position the probe parallel to the calcaneofibular ligament. The peroneal tendon and sural nerve are caudal to the subtalar joint at that location.
4. Aim the needle toward the subtalar joint line (Fig. 100.4) and aspirate to rule out intravascular injection.
5. Inject the medication, remove the needle, and apply an adhesive bandage.

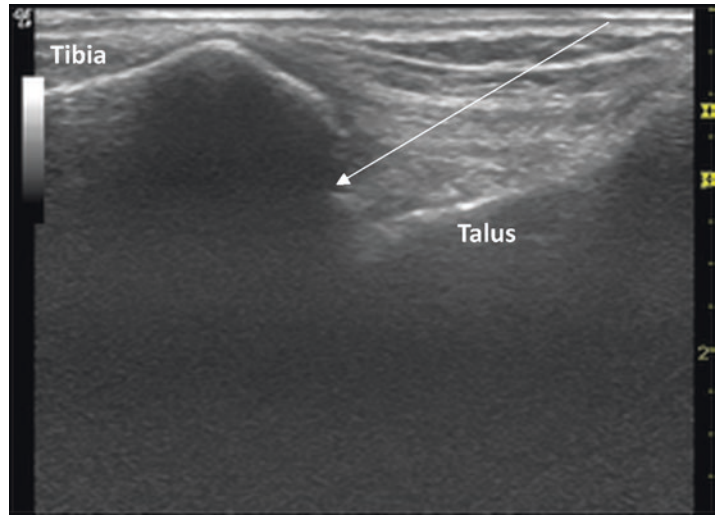

Fig. 100.2 Tibiotalar joint space

Complications

Infection, neurovascular injury, and damage to joint surfaces are potential complications. With corticosteroids, skin depigmentation and ligamentous and tendon injury may occur. It can also temporarily elevate blood glucose. Local anesthetic may cause flushing, hives, chest or abdominal discomfort, and nausea.

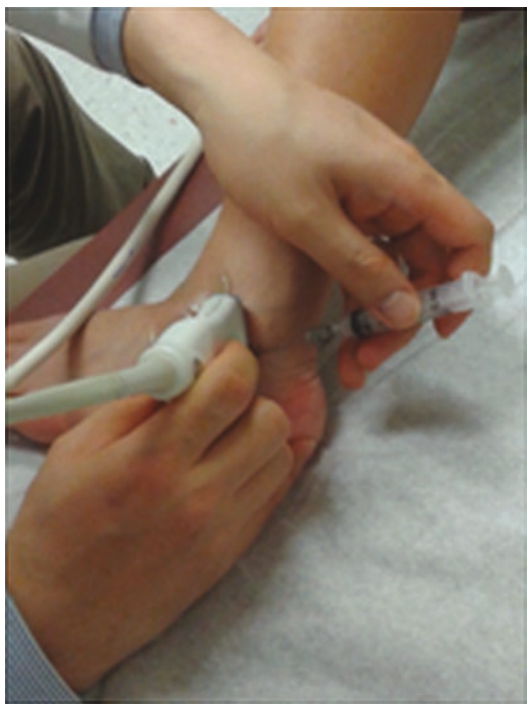

Fig. 100.3 Subtalar joint injection—probe and needle placement

Clinical Pearls

A typical combination of injectate may contain 0.5 mL 1 % lidocaine, 0.5 mL 0.5 % bupivacaine, and 0.5–1 mL 40 mg/mL triamcinolone or equivalent corticosteroid.

Evidence

The accuracy for US-guided injection of the tibiotalar joint was found to be 100 % versus 77.5–85 % for non-guided injections [1, 2].

The accuracy for US-guided injection of the subtalar joint was found to be 90 % [3].

CPT: peripheral nerve block 64400, 64530.

Sensation to the foot and ankle is innervated by five nerves. This chapter describes nerve block of the superficial peroneal, deep peroneal, saphenous, posterior tibial, and sural nerves.

Indications: Metatarsophalangeal joint fusions, plantar fasciotomies, bunionectomies, Morton's neuroma, hallux rigidus procedures, amputations of the lower digits or the midfoot,

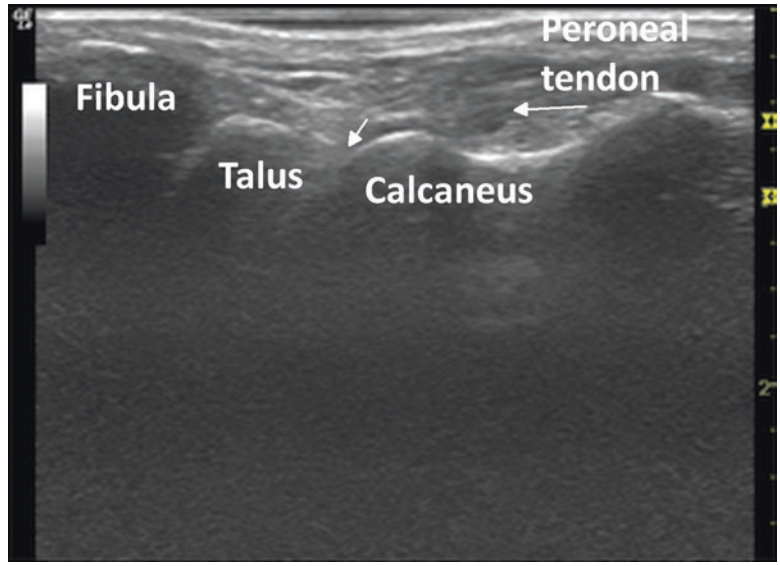

Fig. 100.4 Subtalar joint space

plantar neurectomy, excision of accessory navicular exostoses, and foreign bodies, complex regional pain syndrome.

Equipment/materials: Ultrasound probe 12–5 MHz, 20- to 25-gauge, 1-in needle, 5-mL syringe, sterile ultrasound gel and probe cover, 4×4 gauze pads, sterile drapes, adhesive bandage, and sterile cleansing solution.

Procedure

Superficial Peroneal Nerve (SPN) Block

Position: lateral decubitus position with target side on top

Steps:

7. Using a linear transducer and an in-plane, short-axis technique, the SPN is visualized between the peroneus brevis and extensor digitorum longus muscles (between the lateral malleolus and the anterior tibial surface) (Fig. 100.5).
8. Inject 1–2 mL of local anesthetic around the nerve. In addition, a subcutaneous field block can be conducted from malleolus to malleolus which will provide adequate analgesia.

Deep Peroneal Nerve (DPN) Block

Position: supine

Steps:

1. Using a linear transducer and an out-of-plane, short-axis technique, the DPN is visualized just lateral to the anterior tibial artery superficial to the interosseus membrane (Fig. 100.6).
2. Inject 5 mL of local anesthetic around the nerve.

Saphenous Nerve Block

Position: supine

Steps:

1. Using a linear transducer and an in-plane, long-axis technique, the saphenous nerve is visualized subcutaneously between the extensor hallucis longus tendon and the medial malleolus next to the great saphenous vein (Fig. 100.7).
2. Inject 3–5 mL of local anesthetic agent around the vein, and administer care to avoid puncturing the greater saphenous vein.

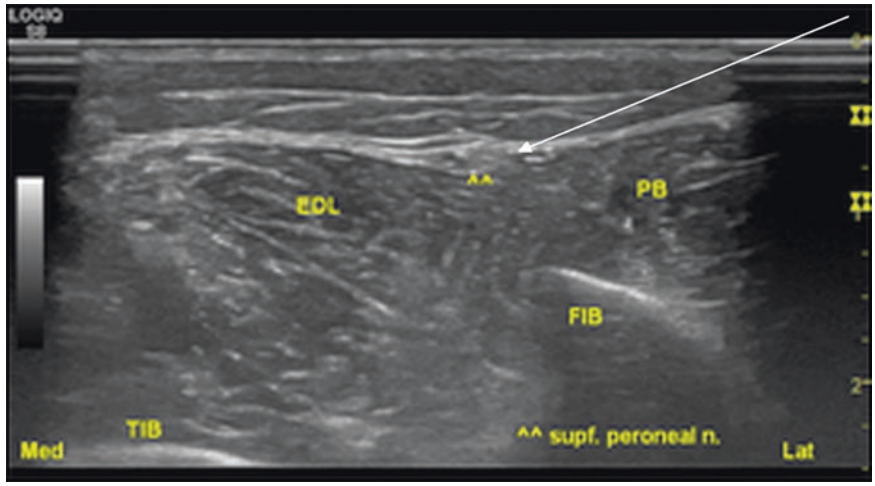

Fig. 100.5 Superficial peroneal nerve—needle placement. *EDL* extensor digitorum longus, *PB* peroneus brevis

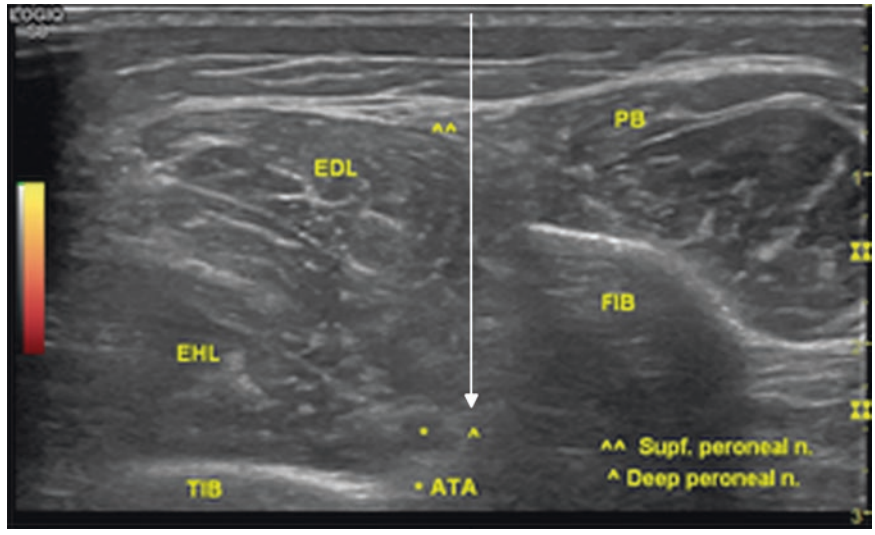

Fig. 100.6 Deep peroneal nerve—needle placement. *EDL* extensor digitorum longus, *PB* peroneus brevis, *EHL* extensor hallucis longus, *ATA* anterior tibial artery

Posterior Tibial Nerve (PTN) Block

Position: prone or supine

Supine: the foot rolled outward and knee slightly bent

Prone: elevate the ankle with pillow to flex the knee and situate the foot and ankle in a neutral position

Steps:

1. Using a linear transducer and an in-plane, long-axis technique, the PTN is visualized at the level of the Achilles tendon and the medial malleolus posterior to the posterior tibial artery (Fig. 100.8).
2. Inject 1–3 mL of local anesthetic agent around the nerve.

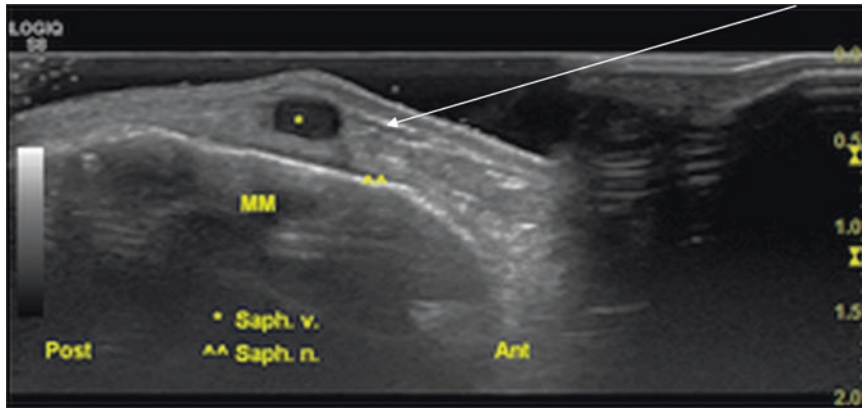

Fig. 100.7 Saphenous nerve—needle placement. *MM* medial malleolus

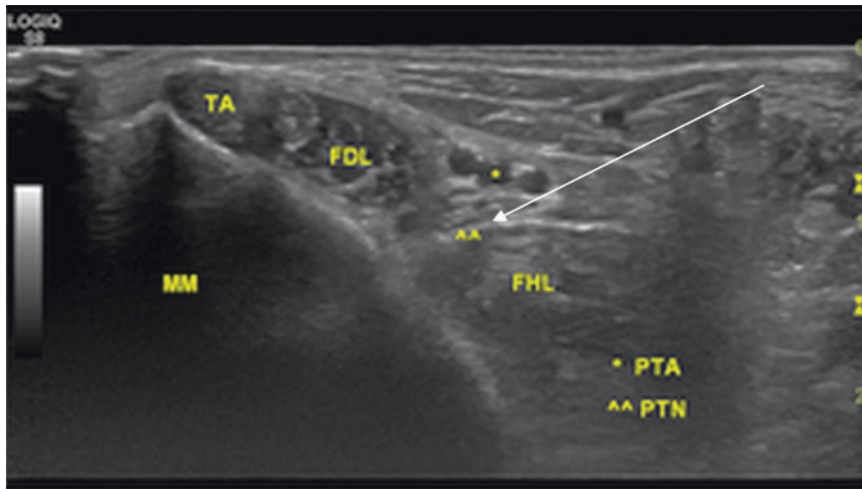

Fig. 100.8 Saphenous nerve—needle placement. *TA* tibialis anterior, *FDL* flexor digitorum longus, *FHL* flexor hallucis longus, *PTA* posterior tibial artery

Sural Nerve Block

Position: lateral decubitus position with knee extended

Steps:

1. Using a linear transducer and an in-plane, long-axis technique, the sural nerve is visualized between the Achilles tendon and peroneus brevis at the level of the lateral malleolus (Fig. 100.9).
2. Inject a maximum of 5 mL of local anesthetic agent 3–4 cm proximal to the ankle joint.

Complications

Complications of regional anesthesia of the foot and ankle include infection, neurovascular injury, and local anesthetic systemic toxicity.

Clinical Pearls

A typical combination of injectate may contain a 1:1 mixture of bupivacaine (long acting) and lidocaine (rapid onset).

Due to variable innervations, local infiltration should be performed and the neighboring nerve should also be blocked.

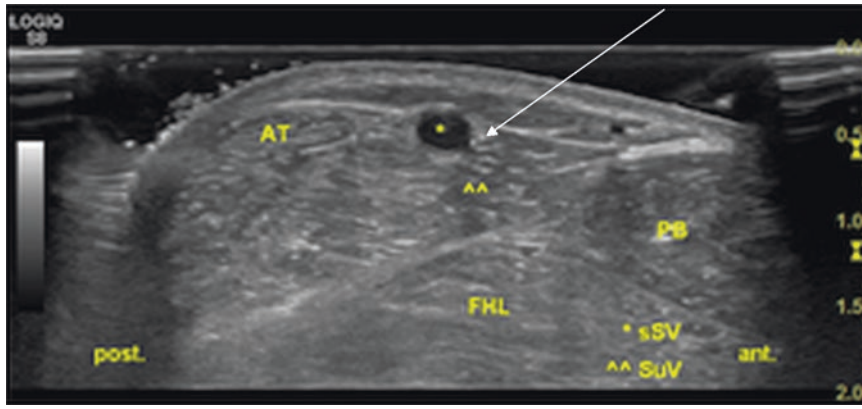

Fig. 100.9 Sural nerve—needle placement. *AT* Achilles tendon, *FHL* flexor hallucis longus, *PB* peroneus brevis, *sSV* superficial saphenous vein

Evidence

The use of ultrasound in regional anesthesia reduces the volume of local anesthetic solution [1] and decreases procedural time [2].

Saphenous nerve block in the ankle may not be necessary for bunion surgery based on a prospective study of 100 patients where mapping of the saphenous sensory distribution showed that it did not reach the level of the first tarsometatarsal joint in 97 % of cases [3].

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Small Joint Injections

101

Nehal A. Shah and Glenn C. Gaviola

Indications. Foot/ankle: Diagnostic injection to confirm the site of pain if not clinically apparent particularly in patients with hindfoot pain/instability; therapeutic injections for post-traumatic arthritis, osteoarthritis, and inflammatory arthritis; and presurgical diagnostic and therapeutic injections to aid in surgical planning of arthrodesis or ligamentous reconstruction. Sternoclavicular joint: diagnostic and therapeutic injection for nonsurgical management of degenerative disease).

Equipment/Materials: Fluoroscopy or CT, 25–22 g needles, short-acting local anesthetic, iodinated contrast material, and corticosteroid.

Procedure

Foot/Ankle

1. Patient positioning: Tibiotalar (Fig. 101.1a) and posterior subtalar joints (lateral decubitus with affected ankle upward); talonavicular, naviculocuneiform, and tarsometatarsal joints (Fig. 101.1b) (supine, knee flexed, and foot on small-angled wedge); and metatarsophalangeal joints (supine, knee bent, and foot flat on fluoroscopy table).
2. Palpate and mark the dorsalis pedis artery except for MTP joint injections.
3. Adjust C-arm angulation to adequately visualize the joint space.
4. Place radiopaque marker at the skin entrance site using intermittent fluoroscopy. Avoid the Achilles tendon for subtalar joint injection and the extensor hallucis longus tendon for MTP joint injection.
5. Following skin and subcutaneous tissue local anesthetic infiltration, advance 22 g needle into the joint space (use 25 g needle for TMT, intertarsal and MTP injection).
6. Once in the joint space or on the bone, inject minimal amount of local anesthetic to check for loss of resistance, followed by minimal amount of iodinated contrast material to document intra-articular location (Fig. 101.1).
7. Save this image and administer the injectate. Note dilution of the intra-articular contrast and save this final image.
8. Document pre-procedure and post-procedure pain score.

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Sternoclavicular Joint

1. Patient is positioned supine on the CT table.
2. Place the CT biopsy grid over the affected joint.

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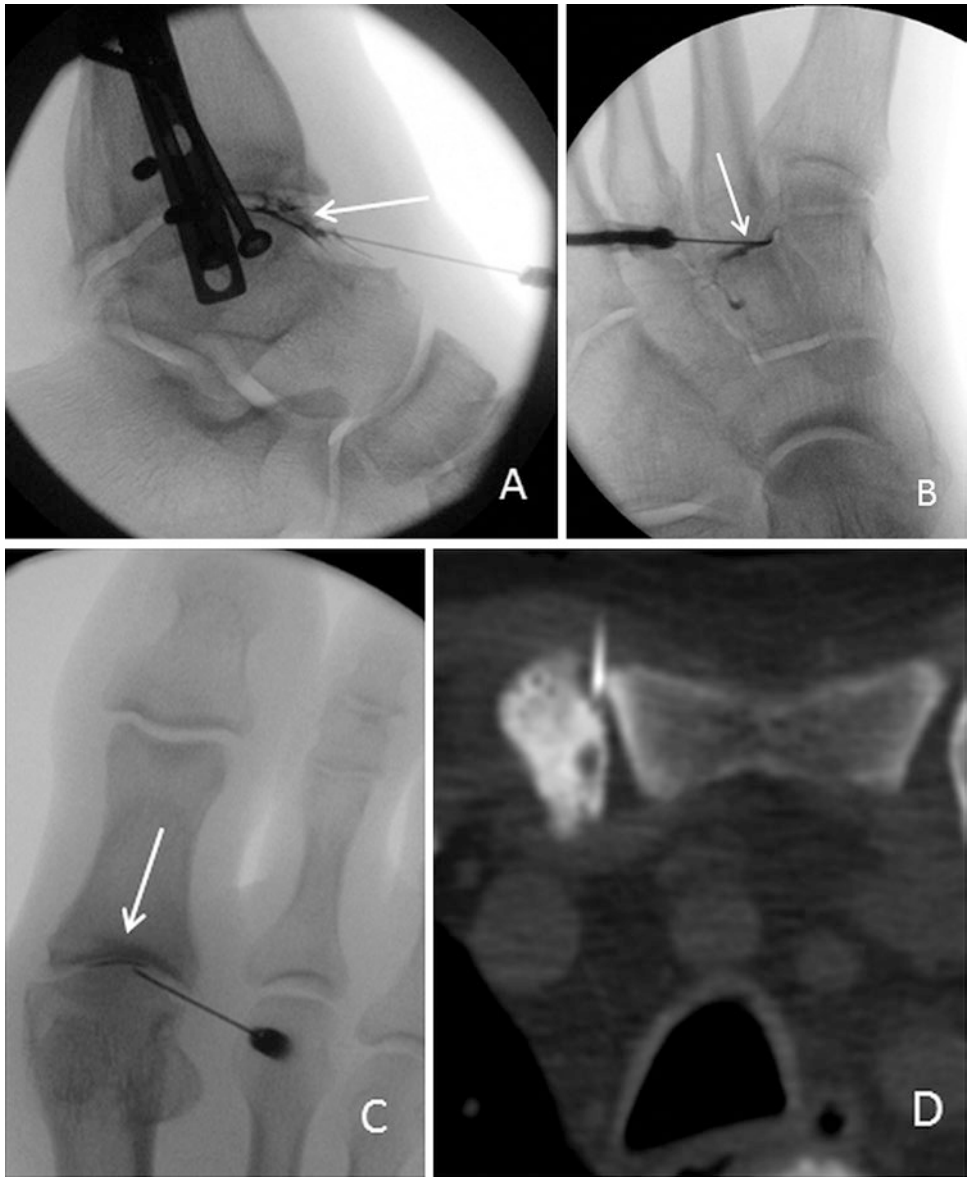

Fig. 101.1 Examples of small joint injections. (**a**–**c**). Fluoroscopic-guided injection of the tibiotalar joint (**a**), second tarsometatarsal joint (**b**), and first MTP joint (**c**) demonstrating iodinated contrast material within these joints (*arrows*). (**d**). CT-guided injection of the right sternoclavicular joint shows needle placement within the right SC joint

3. Place a CT grid, acquire CT images through the affected joint, and identify a suitable skin entrance site avoiding blood vessels.
4. Use a 22 g needle to advance into the SC joint utilizing intermittent CT guidance.
5. Inject minimal amount of iodinated contrast material to document intra-articular location followed by corticosteroid and short-acting anesthetic agent (Fig. 101.1d).
6. Document pre- and post-procedure pain score.

Complications: For small joint injections, bleeding, infection, and reaction to contrast medium are the typical complications.

Meticulous sterile technique is recommended to reduce risk of infection. For sternoclavicular joint injections, major bleeding and lung injury (pneumothorax) are possible complications due to the joint's proximity to the mediastinum and lung. Additionally, for any intra-articular steroid injection, postinjection synovitis flare reaction can be seen. A steroid flare presents as severe pain, swelling, and possibly redness of the injected joint. It is self-limiting and resolves in 2–5 days. Treatment is symptomatic with rest, ice, and NSAIDs.

Pearls: Review available imaging prior to the procedure to help guide access to the joint. CT guidance may be necessary for severely narrowed or hypertrophic joints. For patients with documented iodinated contrast reaction, intra-articular gadolinium and air are two alternatives. For small midfoot and MTP joints, we suggest injecting 20 mg of Depo-Medrol (40 mg/mL), 40 mg of Depo-Medrol (40 mg/mL) for tibiotalar and subtalar joints, and 60 mg of Depo-Medrol (40 mg/mL) for sternoclavicular joint. 1–2 mL of 1% Lidocaine is the suggested dose for long-acting anesthetic. Educate the patient at the time of injection to expect the anesthetic to wear off in 4–6 h and corticosteroid to be effective starting at 24–48 h postinjection.

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Part VIII

Surgical Pain Management

Intrathecal Drug Delivery

102

Christopher R. Abrecht and Sanjeet Narang

Indications: Intrathecal drug delivery may be performed for malignant pain, nonmalignant pain, and spasticity. In all cases, patients must have persistent, debilitating pain or spasticity not responsive to more conservative treatments. They must also first undergo a trial of neuraxially administered medication showing at least a 50 % improvement in pain or functional status. These patients must be very carefully selected; contraindications include but are not limited to concurrent active infection, severe psychological comorbidities (e.g., substance abuse), and an inability to comply with medication refill schedule.

The only FDA-approved medications for intrathecal delivery are morphine, ziconotide, and baclofen; in practice, however, a number of agents are used including hydromorphone, fentanyl, clonidine, and local anesthetic.

Equipment/Materials: Local anesthetic and the analgesic agent of choice, fluoroscopy, and all the components of the intrathecal system, including the catheter, the tunneling device, the paravertebral anchoring device, adapters, the spinal needle, and the pump, all provided by the device manufacturer.

Procedure

Position: lateral decubitus.

IV: required. Depending on physician preference and patient comorbidities, the procedure can be performed with local anesthesia and sedation or general anesthesia. Another option is the addition of a spinal anesthetic once the catheter has been threaded to the dermatomal level corresponding to the incision site.

Antibiotics: required (e.g., cefazolin). The agent should target the skin flora and be chosen based on patient's allergies, MRSA colonization status, and institutional guidelines.

Steps:

1. Mark the intended pump implantation site while the patient is in the sitting position, then proceed with positioning.
2. Obtain AP views of the lumbar spine showing the intended skin and interlaminar insertion sites as well as the intended catheter tip site.
3. After subcutaneous administration of local anesthetic, advance the spinal introducer needle using a paramedian approach to enter at the intended interlaminar space under fluoroscopic guidance. Confirm dural penetration by free flow of CSF, and then quickly replace stylet to stem CSF flow.

CPTImplantation, revision, or replacement of catheter 62350
Implantation, revision, or replacement of pump 62360

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4. Advance the catheter under "live" x-ray guidance until the tip is at the target level.
5. Withdraw the spinal needle 1–2 cm, but keep it in place to protect the catheter while making a 5–8 cm incision parallel to the axis of the spine and extending through the needle's entry point. Next, dissect to the lumbar paraspinous fascia.
6. Create a purse-string suture in the fascia and two anchoring sutures on either side of the catheter, then remove the spinal needle and stylet, and again confirm CSF flow.
7. Attach the anchoring device, tighten the purse-string suture, and again confirm CSF flow.
8. After subcutaneous administration of local anesthetic, make the pump pocket incision and dissect to approximate the level of the rectus sheath, ensuring that the pump will just fit within the space.
9. Tunnel the catheter from the back to the pocket using a tunneling tool.
10. After again confirming CSF flow, attach the catheter to the pump. Next, place the pump in the pocket and suture the pump in place.
11. After ensuring hemostasis, irritate all wounds with antibiotic solution and perform a multilevel closure at all sites.

Complications

Early complications include intraoperative injury to the nerve roots or spinal cord, minimized by intraoperative feedback from the patient as well as close examination of the patient's imaging prior to instrumentation. Epidural hematoma and other bleeding complications are another possibility, minimized by following ASRA guidelines for anticoagulant management and ensuring effective hemostasis prior to closure. Infection is also possible; superficial surgical site infections may be treated with antibiotics alone, but deeper infections often require explantation of the entire system. Another consideration is catheter-related malfunctions (e.g., kinks), which are common and usually treated without complete explantation of the system. A serious but fortunately rare complication is the formation of an intrathecal granuloma. This condition is often heralded by loss of analgesia and best identified by MRI. If neurological symptoms are present, neurosurgical decompression may be needed.

Clinical Pearls: The target for the catheter tip is often the dermatome corresponding to the middle of the patient's pain. Up to six spinal segments are usually covered well by an intrathecal opioid infusion, but up to ten segments may be reached.

Evidence: Intrathecal morphine compared to oral morphine in patients with advanced cancer has been shown to provide improved analgesia with fewer side effects. Intrathecal ziconotide compared to placebo in patients with advanced cancer or AIDS has been shown to provide some analgesia, although with frequent neurological side effects. Intrathecal baclofen compared to oral baclofen in patients with upper motor neuron spasticity has been shown to provide improved functionality with fewer side effects.

Additional Reading

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Spinal Cord Stimulation

103

Christopher R. Abrecht and Edgar L. Ross

Indications: Spinal cord stimulation (SCS) is a treatment option for severe neuropathic pain not responsive to more conservative treatments. Common indications include FBSS, CRPS types 1 and 2, and painful radiculopathies. Other indications include but are not limited to painful peripheral vascular disease, post-herpetic neuralgia, and axial low back pain. Careful patient selection is paramount; contraindications include but are not limited to certain severe psychological comorbidities, active infection, and an inability to pause anticoagulants for the procedure. Prior to implantation of the impulse generator, the patient must first undergo a trial with a percutaneous or surgically placed lead and show at least a 50 % improvement in pain or functional status.

Equipment/Materials: Local anesthetic, fluoroscopy, a prone Jackson table, and all the components of the SCS system, including the electrodes, the paravertebral anchoring device, the tunneling device, and the IPG.

CPT Implant or trial percutaneous SCS electrodes 63650
Implant IPG 63685
Revise or remove SCS electrodes 63660
Revise or remove IPG 63688

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Procedure

Position: prone and also lateral decubitus depending on the location of impulse generator (IPG).

IV: required. The procedure is usually performed under monitored anesthesia care.

Antibiotics: required (e.g., cefazolin) and based on patient history. The agent should target the skin flora and be chosen with regard to patient's allergies, MRSA colonization status, and institutional guidelines.

Steps for Percutaneous Technique Following a Temporary Trial

1. Mark the intended pump implantation site while the patient is in the sitting position, then proceed with positioning.
2. Obtain AP views of the spine and identify the target epidural entry site.
3. After subcutaneous administration of local anesthetic, insert the epidural needle at least one level below the target epidural entry site, aiming for an angle of 45°.

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Locate the epidural space using loss or resistance technique.

4. Advance the electrode under "live" x-ray guidance to the target, ensuring it remains 2–3 mm lateral of the midline, on the side of the patient's pain.
5. Withdraw the epidural needle 1–2 cm, then make a 5–8 cm incision parallel to the axis of the spine extending through the needle's entry point. Next, dissect to the paraspinous fascia.
6. Remove the epidural needle and attach the anchoring device.
7. After subcutaneous administration of local anesthetic, make the pump pocket incision and dissect so that the pump will just fit within the space. (Note: if the pump pocket is the abdomen, the patient must be turned from the prone to the lateral decubitus position.)
8. Tunnel the lead from the back to the pocket using a tunneling tool.
9. Attach the lead to the IPG, coil any excess lead behind the IPG to allow for patient movement, and suture the IPG in place.
10. Irrigate all wounds with antibiotic solution and perform a multilevel closure at all sites (Fig. 103.1).

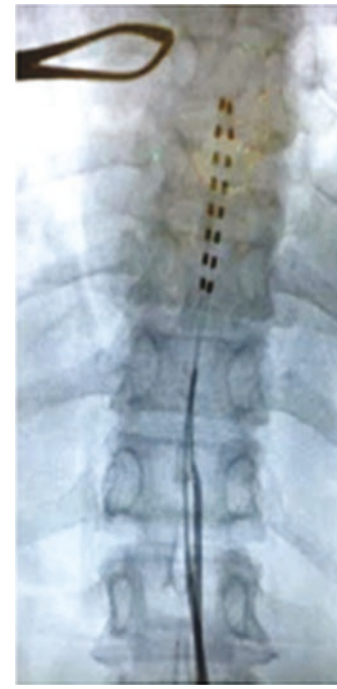

Fig. 103.1 Dual SCS electrode insertion, with radiopaque surgical instrument marking intended for catheter tip site

Complications: As with all open surgical procedure, bleeding and infection must be considered. Bleeding complications include hematoma formation in the pump pocket or epidural space, the latter of which will likely require emergent surgical drainage. Adherence to ASRA guidelines for anticoagulant management is paramount when performing epidural placement. Superficial infections may be treated with antibiotics alone, but deeper infections often require explantation of the entire system. Another concern is postdural puncture headache, especially given the use of a 14G modified Tuohy with an extended orifice to allow easy passage of the electrode. Equivocal loss of resistance with this instrument may lead to dural puncture. Spinal cord or nerve root damage is another concern, albeit an unlikely one and minimized by intraoperative feedback from the patient regarding a painful paresthesias. A more common complication is lead migration, often heralded by loss of analgesia. Proper attachment of the anchoring device and instructing the patient to avoid bending and twisting at the insertion site will minimize this problem. Lead fracture is also a possibility, especially in the cervical region, and would require surgical repair.

Clinical Pearls

For low back or lower extremity pain, a common epidural entry site is L1-L2 with an electrode tip at T9. For upper extremity pain, a common epidural entry site is T1-T2 with an electrode tip at C2. The skin entry site may vary significantly depending on the patient's habitus.

Evidence

For patients with FBSS, SCS has been shown in RCT to provide sustained pain relief and improved functional capacity compared to patients who received only conventional medical management.

Additional Reading

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Peripheral Nerve Stimulation

104

Christopher R. Abrecht and Assia T. Valovska

Indications: Peripheral nerve stimulation (PNS) best treats neuropathic pain localized to a specific nerve. Successful treatment of many conditions has been demonstrated: CRPS, headaches, cranial neuralgias, phantom limb pain, cancer pain, chronic pelvic pain, and coccydynia. PNS may be preferred over SCS if the painful area is small or if SCS lead placement will be difficult (e.g., in the patient with scoliosis). Patients must be carefully selected; they should have failed more conservative management. Contraindications included but are not limited to certain severe psychological comorbidities (e.g., substance abuse), severe coagulopathy, and infection, especially if close to the intended implantation site. In all cases, patients must first undergo a trial and show a 50 % reduction in pain or significant improvement in functional status. Targeted nerves include but are not limited to occipital, supraorbital, inguinal, and pudendal sites.

CPT Percutaneous peripheral nerve stimulator electrode implant 64555
Insertion peripheral nerve stimulator generator 64590

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Equipment/Materials

Local anesthetic, ultrasound, fluoroscopy, and all the components of the PNS system, including the leads, extensions, tunneling device, and IPG.

Procedure

Position: prone, supine, and lateral decubitus are all possible and depend on the targeted peripheral nerve.

IV: required. The procedure can be done with local anesthesia and minimal sedation or, depending on patient comorbidities and the extent and location of implantation, general anesthesia. Ideally, the patient will receive only minimal sedation so he or she can provide feedback during the procedure.

Antibiotics: required (e.g., cefazolin). The agent should target the skin flora and be based on the surgical trajectory. It should also be chosen based on patient's allergies, MRSA colonization status, and institutional guidelines.

Steps:

1. In the preoperative area, mark after visualization of the nerve with ultrasound the intended lead entry site. Also mark the intended IPG site.
2. In the OR, again visualize the nerve with ultrasound and confirm target with a region block nerve stimulation needle.

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3. After subcutaneous administration of local anesthetic, insert 14G Tuohy needle, then advance the lead under fluoroscopic visualization.
4. Perform lead testing and confirm the presence of appropriate paresthesia.
5. Anchor the lead in place.
6. After subcutaneous administration of local anesthetic, create the IPG pocket with a 5–8 cm incision followed by blunt dissection so that the IPG just fits in place.
7. Tunnel the lead from the stimulation site to the pocket site.
8. Attach the lead to the IPG, coil any excess lead behind the IPG to allow for patient movement, and suture the IPG in place.
9. Ensure hemostasis.
10. Irrigate all wounds with antibiotic solution and perform a multilevel closure at all sites (Figs. 104.1 and 104.2).

Complications

While multiple studies have assessed the complications associated with SCS, few studies have assessed those for PNS. That being said, possible complications include those associated with all open surgical procedures: bleeding and infection. Ensuring proper hemostasis prior to closure, holding anticoagulants prior to the procedure if feasible, and ensuring the patient does not have any active infections prior to implantation minimize these complications. Nerve damage is also possible; this complication may be minimized by the careful use of ultrasound and fluoroscopy and by eliciting intraoperative feedback from the patient. Damage to viscera during the tunneling process is also a possibility; a midway incision may be required if tunnel is difficult due to patient habitus. A less serious but more common consideration is lead migration, minimized by proper securing of leads.

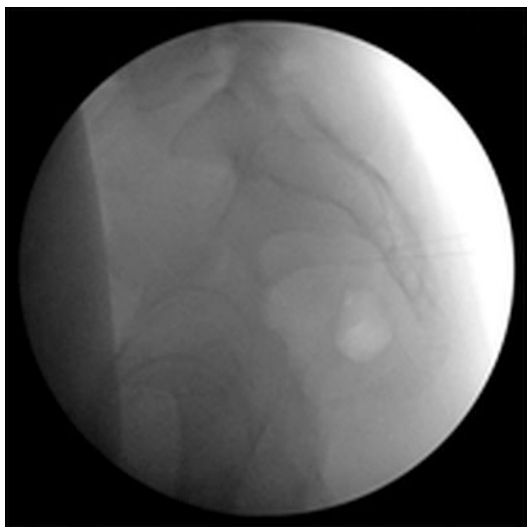

Fig. 104.1 Fluoroscopic insertion of spinal introducers into bilateral S3 foramina for sacral nerve stimulation, lateral view

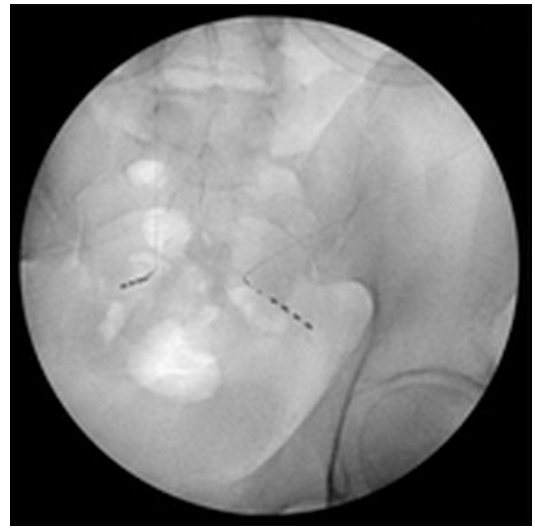

Fig. 104.2 Fluoroscopic deployment of leads for sacral nerve stimulation, AP view

Clinical Pearls

When deciding on the IPG implantation site, avoid placement at the bra or beltline because the irritation caused by these garments may contribute to lead migration. For this reason, many practitioners mark the IPG site with the patient fully clothed.

Evidence

One of the many studies demonstrating the benefit of PNS looked at 38 patients who underwent PNS implantation for pain from peripheral nerve injury or entrapment, with over 60 % showing at least 50 % reduction in pain.

Additional Reading

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Peripheral Nerve Field Electrostimulation

105

Tara Sheridan

Introduction

Peripheral nerve field stimulation (PNFS) is a form of neuromodulation in which one or more leads are placed in the subcutaneous tissues, adjacent to areas of chronic pain, in order to provide relief through the stimulation of small peripheral nerves. Leads are then connected to a temporary external pulse generator (PG) during trials, or to an implanted PG for permanent placement.

Percutaneous neurostimulation was initially described as a novel treatment for refractory occipital neuralgia by Weiner and Reed in 1999. Overall, there is limited data regarding the most promising indications for PNFS. However, case reports include the successful utilization of PNFS for multiple chronic pain states, including headache syndromes, diabetic peripheral neuropathy, complex regional pain syndrome and inguinal neuralgia. Currently, evidence based literature does not endorse PNFS for fibromyalgia, phantom limb pain, diffuse polyneuropathy, or angina pectoris.

In order to be an appropriate candidate for PNFS, the following criteria should be documented with regard to the patient's pain and function:

- At least 3 months of chronic and severe pain
- Lack of response to less invasive treatment modalities and medications
- No surgical contraindications, including infections and medical risks
- Appropriate patient education, including discussion of risks, benefits, and patient expectations
- No active substance abuse issues
- Favorable psychological assessment by a mental health professional
- Successful stimulation trial demonstrating ≥50 % reduction of target pain, or ≥50 % reduction of analgesic medications, and demonstrable functional improvement

The most reliable predictor of PNFS effectiveness is a successful stimulation trial. A repeat trial is usually not appropriate unless extenuating circumstances exist which led to trial failure, such as equipment malfunction or early lead migration.

Additional Reading

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Minimally Invasive Ligamentum Decompression (MILD) Procedure

106

Narayana Varhabhatla and Ehren Nelson

CPT: Percutaneous laminotomy/laminectomy (intralaminar approach) for decompression of neural elements (with or without ligamentous resection, diskectomy, facetectomy, and/or foraminotomy), any method under indirect image guidance (e.g., fluoroscopic, CT), with or without the use of an endoscope, single or multiple levels, unilateral or bilateral; lumbar (0275 T).

Indications: Neurogenic claudication present when standing or walking and relieved by sitting or bending forward. MRI evidence of ligamentum flavum hypertrophy and central canal stenosis.

Equipment/materials: Radiolucent table, C-arm, MILD procedure kit, fluoroscopy, local anesthetic, epidurography supplies (Tuohy needle, LOR syringe, preservative-free saline, extension tubing, contrast), scalpel, 4×4 Steri-Strips, dressing MILD kit—portal, trocar/handle, stabilizer, depth guide, bone sculptor rongeur, tissue sculpter, and surgical clamp.

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Procedure

1. Preprocedure—Confirm allergies (contrast, adhesives, antibiotics), images for verification (MRI), anticoagulant therapy, and VAS/ODI preoperative scores.
2. Obtain preoperative IV access. Administer IV Ancef 30 min preoperatively.
3. Place the patient in the prone position, with a pillow under the abdomen.
4. If needed, the patient may receive midazolam +/− fentanyl for the procedure.
5. In a sterile fashion, prep from T12 to the buttocks.
6. With AP views, mark spinous process and medial pedicular lines on the skin. This shows the approximate width of the lamina, which is the treatment area of interest.
7. Access the epidural space with a Tuohy and LOR syringe in the usual fashion, as close to the midline on the treatment side and as close to the superior lamina as possible. Verify epidurogram in contralateral oblique view.
8. Optional but recommended—Use a spinal needle to identify the trajectory for the portal placement, and use the needle to inject local for the portal as well. The needle in its final position should rest on the superior surface of the inferior lamina.
9. Insert the trocar and portal into the same trajectory as with the spinal needle, with its

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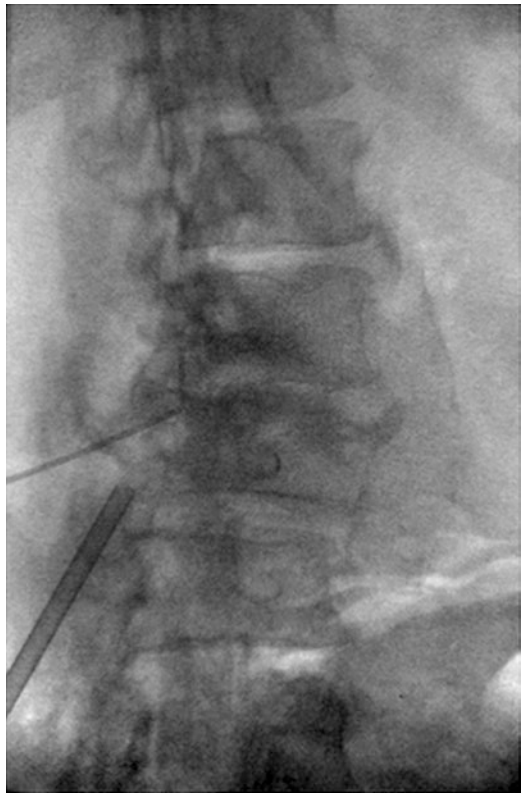

Fig. 106.1 A fluoroscopic view of the spine with the epidural needle in place just superior to the MILD trochar

final resting place on the superior aspect of the inferior lamina (see Fig. 106.1).

10. Remove the trocar and place the portal stabilizer. In certain patients, the surgical clamp can be used to stabilize the portal. However, it is recommended for most patients to use the stabilizer to hold the portal in place and prevent unintentional movement.
11. Insert the bone sculptor rongeur through the portal, which will be used to remove part of the lamina. Remove small pieces of lamina from the superior surface of the inferior lamina. Remove and clean the blade after each bite.
12. Then insert the tissue sculpter through the portal. This will be used to remove parts of the hypertrophied ligamentum flavum. The scooped part of the tissue sculpter must always be positioned on the bottom and never on top. Remove and clean after three bites.
13. After adequate decompression, confirm with epidurogram in the contralateral view to assess improvement in contrast spread.
14. Remove the instruments as a unit, and apply pressure to the area until adequate hemostasis achieved. Place adhesive strips and dressings.
15. There is no indication for postoperative antibiotics.
16. The outer dressings can be removed on the third postoperative day. Steri-Strips covering the incision will fall off within 7–10 days. The patient is instructed to only take sponge baths the first 3 days post-procedure, while the outer dressings are still in place.

Complications: The most common complications were soreness at the site and less commonly gluteal pain and back spasms.

Evidence: Kreiner and colleagues conducted a systematic review of the available literature to evaluate the MILD procedure. They found one prospective RCT, seven prospective cohort studies, four retrospective studies, and one case series in the literature. All the studies showed statistically significant improvement in VAS scores, and multiple of these studies showed improvement in ODI scores. The MILD procedure provided 40–49 % improvement in VAS scores at 4 weeks to 1 year post-procedure. There was 14–16 % improvement in ODI scores between 6 weeks to 1 year post-procedure. These studies reported no procedure-related complications including dural puncture, nerve root injuries, infections, or bleeding.

Additional Reading

Kreiner DS, MacVicar J, Duszynski B, Nampiaparampil DE. The mild® procedure: a systematic review of the current literature. Pain Med. 2014;15:196–205.

Vertebroplasty and Kyphoplasty 107

William J. Epps and M. Gabriel Hillegass, III

CPT

Percutaneous vertebroplasty, one vertebral body, unilateral or bilateral injection; cervicothoracic 22510

Percutaneous vertebroplasty, one vertebral body, unilateral or bilateral injection; lumbosacral 22511

Thoracic or lumbar, each additional level 22512

Thoracic percutaneous vertebral augmentation, including cavity creation (kyphoplasty) 22513

Lumbar percutaneous vertebral augmentation, including cavity creation (kyphoplasty) 22514

Thoracic or lumbar, each additional level 22515

*As of 2015, three new codes have been implemented for both vertebroplasty and kyphoplasty. These codes include bone biopsy when performed at the same level and all imaging guidance, so the supervision and interpretation codes 72291 and 72292 have also been deleted. If the radiological supervision is performed under CT guidance, also use CPT code 72292-26.

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Indications: Used in the treatment of symptomatic (painful) vertebral compression fracture due to osteoporosis, malignancy, or benign lesions such as hemangiomas.

Equipment/materials: Fluoroscopy machine (biplanar is optimal) or computed tomography in select cases, 22 gauge spinal needle, 11 or 13 gauge bone biopsy needle (for lumbar or thoracic levels, respectively), scalpel, sterile hammer, cement based on polymethyl methacrylate (PMMA), nonionic contrast, and local anesthetic with epinephrine.

Preparation

IV: Required for moderate sedation. Be careful to avoid over sedation as patient participation and ability to respond to questioning is key.

Antibiotics: 2 g cefazolin IV, unless allergic, as this procedure involves injecting foreign material. An antibiotic, such as gentamicin or tobramycin, may be mixed with the PMMA prior to injection to help reduce the incidence of infection as well.

Position: Prone with cushions under chest and pelvis to flatten the spinal curvature.

Monitors: Patient's heart rate, blood pressure, and oxygen saturation are continuously assessed during procedure. Supplemental oxygen should be provided and suction equipment available.

Exam: A pain assessment and neurological exam should be performed prior to the procedure and documented.

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Procedure

The typical approaches are transpedicular and parapedicular. The authors describe herein a transpedicular approach in the AP view as the intraosseous path of the needle helps to protect neural structures from damage.

1. Proper C-arm positioning and identification of bony landmarks are of utmost importance. Start with an AP view and center the spinous process between pedicles. Adjust caudal/cephalad tilt to align the vertebral body endplates, and place the pedicles in the middle of the affected vertebral body. The pedicles should appear circular or ovoid in shape (Fig. 107.1).
2. The skin entry point should be approximately 1 cm superolateral to the center of the pedicle. Utilize the spinal needle to anesthetize the skin, subcutaneous tissues, and periosteum with lidocaine or bupivacaine containing epinephrine to minimize bleeding. The spinal needle also allows assessment and adjustment of the proper trajectory prior to placement of the larger trocars to be used in subsequent steps.
3. Once the trajectory is verified, make a skin nick with the scalpel to ease the insertion of the 11 or 13 gauge biopsy needle. The needle should be advanced in an anteromediocaudal trajectory. When bone is encountered, the needle tip should be in the superior and lateral quadrant of the pedicle or the "10 o'clock" position (Fig. 107.1). Repositioning can prove difficult if the original needle placement is suboptimal, so taking the time to properly seat the needle on the pedicle is a vital step.
4. After initial bony contact is made, switch to a lateral fluoroscopic view, and adjust the craniocaudal angulation as necessary, keeping in mind that the ultimate destination is the center of the vertebral body in both the craniocaudal and mediolateral planes. In compression fractures with endplate depression, ensure that your trajectory avoids piercing the inferior vertebral endplate.
5. Utilizing the sterile hammer (hand pressure often suffices in osteoporotic bone), advance the biopsy needle in an anteromediocaudal trajectory. The authors recommend advancing the needle in the AP view in small increments and then rechecking in the true lateral view to ensure correct trajectory. In the AP view, the needle tip should never traverse the medial or inferior cortical borders of the pedicle until the needle tip is in the vertebral body in the lateral view otherwise the interventionalist risk injury to the nerve roots or spinal cord (Fig. 107.2).
6. Once the needle has crossed the pedicle completely and entered into the vertebral body, it is further advanced using the lateral fluoroscopic view. For vertebroplasty, it is advanced to the anterior two-thirds of the vertebral body where the cement will be deposited (skip to step 8). For kyphoplasty, it is advanced to the posterior third of the vertebral body to allow space for the inflatable balloon system.
7. **Kyphoplasty:** The procedure steps may vary slightly depending on the manufacturer of

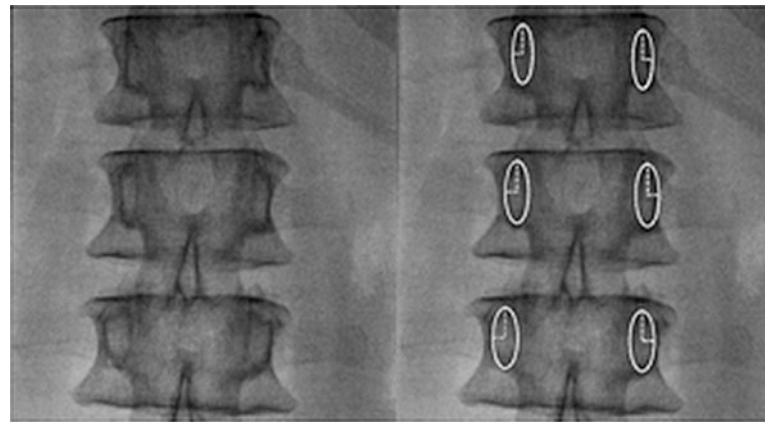

Fig. 107.1 AP view: Identify the ovoid pedicles at T12, L1, and L2 (outlined in *white* in right image). The *dotted line* denotes the upper outer quadrant, the starting point for your trocar/needle. Note: Do not violate the integrity of the medial or inferior margins of the pedicles

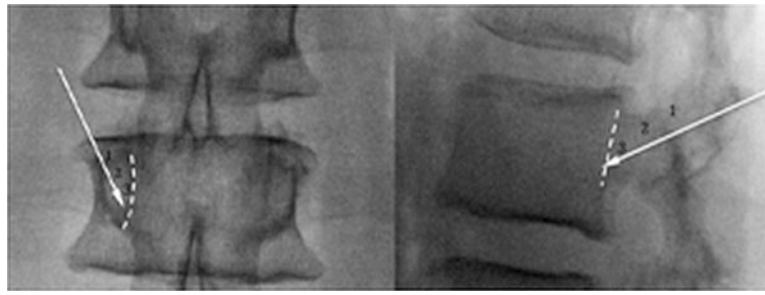

Fig. 107.2 AP and lateral views: *Arrow* denotes trajectory of trocar/needle. Note the numbered positions of the needle tip. They should correlate with each other in the AP and lateral views. For example, when the needle tip is at the midpoint of the pedicle in AP view, it should be at the midpoint of the pedicle in the lateral view also. *Dotted line* denotes the medial border of the pedicle in AP and posterior wall of vertebral body in lateral

the needle trocar cannula, drill and balloon system utilized.

(a) The needle is removed leaving the introducer cannula in place. A hand-operated drill is inserted and advanced to the anterior quarter of the vertebral body ensuring not to traverse the anterior cortical surface of the vertebrae.

(b) The drill is removed (along with a bone biopsy if indicated), and a balloon is inserted into the cavity. There are typically radiopaque markers denoting the distal and proximal ends of the deflated balloon. Ensure that these marks have cleared the cannula prior to inflation.

(c) The balloon is then attached to a syringe pump with a pressure gauge and carefully inflated with contrast under live fluoroscopy. Inflation continues slowly until the system reaches maximum pressure or balloon volume; the balloon reaches one of the cortical margins; or the vertebral kyphotic deformity is corrected.

(d) The balloon is then deflated and removed leaving a large cavity to be filled with cement.

8. **Vertebroplasty:** If a bilateral needle placement is being undertaken, then the second needle should be placed at this stage of the procedure utilizing steps 1–6 on the opposite pedicle.
9. Once the final needle position is verified in both AP and lateral views, the polymethylmethacrylate (PMMA) cement should be mixed per the manufacturer's specifications. The cement contains a contrast material and has a working time between 10 and 20 min once reconstituted. The consistency of the cement is frequently compared to toothpaste.
10. Once mixed, the cement is delivered through the cannula and into the affected vertebrae. The delivery system also varies with the manufacturer; it may be via a syringe or in small aliquots in stylets. Cement injection should be performed in the *lateral view* using continuous fluoroscopy. The goal is to deliver cement evenly in the vertebral body while avoiding extra-vertebral cement delivery. Care should be taken to deliver the cement at a controlled pace and to avoid over-pressurization of the delivery system.
11. Since there is no preformed cavity created in vertebroplasty, as the cement is injected, the needle should be slowly pulled backward to facilitate even distribution of cement throughout the vertebral body.
12. Finally, the needles/cannulae are removed. When removing the needles, make sure to clear them of cement using a stylet or by gently spinning the needle to avoid leaving a "cement tail." Apply pressure to the skin puncture sites to decrease incidence of hematoma, and then apply a sterile dressing.
13. Post-procedure: Typically, the authors keep the patient prone for approximately 10–15 min to allow the cement to set. After that, the patient will remain supine for about 2 h. A neurological exam should be

conducted prior to patient discharge and compared to the pre-procedure exam.

Complications

Most complications associated with vertebroplasty and kyphoplasty are minor and require no intervention. Reported complications include infection, bleeding, transient radiculopathy, spinal stenosis, pulmonary embolization, and death.

Neurologic complications occur in <1 % of patients; however when complications arise, the patient may require surgical decompression and result in significant permanent disability or even death. Extravasation of cement from the vertebrae into adjacent structures is frequently reported and usually asymptomatic. Leakage into the disc space may create increased stress in the adjacent end plate and lead to subsequent fracture.

Clinical Pearls

Absolute contraindications include asymptomatic fractures or those improving with nonsurgical care, history of vertebral body osteomyelitis, allergy to bone fillers or opacification agents, and irreversible coagulopathy. Relative contraindications are the presence of radiculopathy, cortical retropulsion against neural structures, greater than 70 % loss of vertebral body height, multiple pathologic fractures, and lack of surgical backup to manage potential complications.

Both bilateral and unilateral needle placements have been utilized in vertebroplasty and kyphoplasty. Unilateral approach may be less time-consuming and less traumatic to soft tissues. However, midline needle tip placement may be more technically challenging as compared to bilateral approach.

Evidence

Efficacy

The results of a 2013 meta-analysis showed that vertebral cement augmentation results in significantly greater pain relief, functional recovery, and improvement in health-related quality of life than did nonsurgical or sham treatment of symptomatic vertebral compression fractures. The results were significant for early and late follow-up end points (i.e., 6–12 months), favoring intervention [1].

Vertebroplasty Versus Kyphoplasty

Both modalities of cement augmentation have been used to treat symptomatic compression fractures for many years. Kyphoplasty provides the added advantage of vertebral body expansion and correction of kyphosis before the injection of cement. The radiographic advantages of kyphoplasty compared with vertebroplasty have been documented in the literature; however, the actual impact on clinical outcome is controversial. In a recent meta-analysis of the available evidence, there was no difference between the two in long-term pain relief or functional improvement [2].

Disclaimer The views expressed in this article are those of the author(s) and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the US Government.

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Radio-Frequency Venous Ablation 108

Aman Saw and Niharika Saw

Associated Procedures

Pre-ablation venous ultrasound to assess reflux (retrograde flow >0.5 s for axial veins), proper anatomy (prior stripping or ablation), and rule out deep vein thrombosis (DVT).

Post-ablation venous ultrasound to assess success/persistent reflux and rule out DVT (<72 h)

Indications

Symptoms after 3 months of medical therapy + documented reflux as above symptoms inhibit ADLs.

Symptoms not secondary to other etiologies.

Assess for significant venous reflux (>0.5 s): patient standing, rapid inflation/deflation BP cuff distal to vein segment in question; measure time to valve closure after release of compression using ultrasound (prolonged time to closure = prolonged reflux time).

Complications

Transient sensory disturbances—usually transient—reduce rates by using tumescent infiltration.

Unable to access vein (venous spasm, small caliber, tortuosity, catheter perforation).

Recanalization (initially occluded but recanalized on follow-up).

Groin reflux (vein trunk occluded but reflux visualized in groin)—likely accessory saphenous vein.

Cutaneous burn

Hematoma/fistula formation

Infection

Phlebitis

DVT (<1 %)

PE (case reports)

Pearls

Access location is important: avoid small and tortuous veins; avoid nerve bundles at access sites to minimize paresthesias (use of tumescence to separate nerve bundle from vein).

Create an anxiety-free environment (calm soothing music, PO anxiolytics, room lighting).

Reposition leg (semi fowler).

CPT CodesPrimary vein 36475
Subsequent vein +36476

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Warm room/patient leg.
J wire to assist catheter advancement due to tortuosity (confirm in lumen if resistance).
Map entire vein prior to anesthesia.
Adequate tumescence starting distally to proximally and ensure "halo" isolation of vein to prevent thermal damage to skin and saphenous nerve, thereby preventing nerve damage and pain.
Medical grade compression stocking post procedure with compliance education.
Phlebectomy and sclerotherapy can be adjuncts to ablation.
Radiofrequency ablation (RF): resistive heating contracts collagen fibers and venous endothelium.
Laser ablation: thermal energy heats blood and thereby destroys venous endothelium.
RF vs laser ablation: higher occlusion rates after RF compared to laser ablation at one year.
RF vs traditional ligation and stripping: RF + phlebectomy/sclerotherapy was as effective; advantages are minimally invasive, reduced post-op pain, and reduced post-op recovery time.

Anatomy

Axial veins: greater and small saphenous veins and saphenous accessory veins.
Deep veins: femoral vein, popliteal vein; lie deep in the fascial plane.
Perforating veins traverse the fascia to connect deep veins to superficial veins.
Saphenous nerve: largest cutaneous branch of femoral nerve, sensation to medial lower leg; adheres to saphenous vein in distal calf.
Sural nerve: sensation to lateral lower leg; runs alongside small saphenous vein.

Equipment

Duplex ultrasound machine
Table capable of Trendelenburg and reverse Trendelenburg positions
Tumescent anesthetic mixture (saline, lidocaine, bicarbonate)
Heparinized saline

Procedure Description

1. Position patient to allow maximal visualization and access to vein.
2. Sterile technique to prep the area of interest.
3. Ultrasound guidance to access the vein via Seldinger technique using a micropuncture kit.
4. Exchange the micropuncture sheath for 7 F sheath.
5. Advance ablation catheter to proximal location, 1–2 cm distal to saphenofemoral junction. If resistance due to tortuosity is noted, consider 0.025″ wire.
6. Readjusting leg and external compression to alter anatomy may also help facilitate wire/catheter advancement.
7. Circumferential tumescent anesthesia (0.1–0.2 % lidocaine) to separate vein from tissue and decrease pain and improve energy transfer.
8. Reconfirm ablation catheter is not in deep venous system.
9. Perform ablation from proximal to distal vein segment of interest.
10. Remove sheath and hold manual compression for hemostasis.

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109 Physical Medicine and Rehabilitation: Physical Modalities, Orthoses, Assistive Devices, and Manipulation

Aaron Jay Yang, Ryan Castoro, and Nitin B. Jain

Physical Modalities

Heat

Indications for heat are to provide analgesia, contracture reduction, decrease joint stiffness, increase collagen elasticity, and hyperemia in the setting of a chronic injury. The use of heat as a therapeutic modality is based on the physical properties of conduction, convection, conversion, and radiation. The therapeutic range of heat is 40–45 °C and is commonly maintained for about 5–30 min [1].

Application of heat can be divided into superficial and deep heat. Superficial heat is considered to be 1–2 cm and deep heat generally involves increasing tissue temperature to a depth of 3–5 cm or more. Examples of superficial heat include heating pads, hydrocollator packs, whirlpool baths, and paraffin baths which achieve maximal tissue temperature in the skin and subcutaneous fat.

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Deep applications of heat include ultrasound and shortwave and microwave diathermy. Ultrasound heats the greatest at the bone-tissue interface, while short wave diathermy heats fat more so than muscle. Ultrasound that is therapeutic in nature uses high-frequency energy to produce a deeper tissue response, and the most commonly used frequency is a range from 0.8 to 1.1 MHz. Thermal response in tissues involves energy absorption causing heat production in tissues, whereas nonthermal responses cause distortion and movement of tissues [2]. Shortwave diathermy is used to treat deep muscles and joints and commonly uses a frequency of 27.12 MHz. This type of modality can involve two condenser plates placed on either side of the body part or induction coils that can be molded to the body part. Through conversion, electromagnetic energy converted to thermal energy travels between the coils or condensers to cause deeper heating of tissues. General contraindications for heat modalities are acute inflammation, bleeding disorders or active hemorrhage, malignancy, impaired sensation, vascular disease, scars, and inability to respond to pain [3]. Caution should be used especially for superficial heat, and patients should be advised to avoid sleeping on heating pads. Superficial heat is one of the most common reasons for burns in therapy sessions, and patients should apply heat on the skin for a maximum of 20–30 min at a time with frequent skin checks to avoid risk of burns.

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Cryotherapy

Indications for cryotherapy are soft tissue or musculoskeletal edema, acute inflammation, muscle spasms, and spasticity. It is used to provide analgesia, slowing of nerve conduction velocity, and decreased local metabolism [4]. The physical properties for cold transfer are based upon conduction, convection, and evaporation. Cold packs are a common method for applying cryotherapy by conduction and are generally applied for 20–30 min with mild external compression [5]. Vaporized coolant sprays can also be used in combination with stretching or manipulation to relieve tight or contracted muscles [6]. General contraindications for cold therapy include cold intolerance or hypersensitivity, impaired sensation, communication or cognitive deficits, arterial insufficiency, and cryopathies such as paroxysmal cold hemoglobinuria or cryoglobulinemia. In general, cold application should be avoided over superficial nerves due to its effect on nerve conduction.

Electricity

There are no specific indications for electrical stimulation as it is most often used as an adjuvant therapy to a more active rehabilitation program. The most common form used is transcutaneous electrical nerve stimulation (TENS). It is based on the gate control theory proposed by Melzack and Wall in 1965 in which TENS stimulates the large myelinated afferent nerve fibers "gating" or blocking afferent pain transmission at the dorsal horn, thus modulating ascending pain signals to the brain [7]. Therefore, it is most useful in providing analgesia. General contraindications include circulatory impairment, pregnancy, active hemorrhage, malignancy, and decreased skin sensation.

Other modalities include iontophoresis and phonophoresis. Therapeutically, iontophoresis delivers medication directly to soft tissues with a small electric current that drives the medication away from the electrode into the target tissue. This modality is commonly used to treat various bursitis and plantar fasciitis [8]. Phonophoresis uses ultrasound on topically applied medications to facilitate migration of medication such as corticosteroids into the skin to treat bursitis, osteoarthritis, and contractures.

Orthoses

Spinal Orthotics

Indications for spinal orthoses include vertebral fracture, instability of the spinal column, or spinal ligamentous injury. Spine orthoses are divided into cervical, thoracic, and lumbar orthosis. One of the most commonly encountered cervical orthosis is the Philadelphia collar which is used for stable bony or ligamentous injuries in which limitation of flexion and extension is needed. The collar limits flexion and extension by 70 % and less with rotation. This collar is used to wean off a more rigid orthosis such as the sterno-occipital mandibular immobilizer (SOMI) brace. The SOMI brace is useful for bedridden patients due to the lack of posterior uprights and stabilizes the cervical and thoracic regions by limiting flexion and extension by 75 %. For best control of motion in all planes, the halo vests are used to treat unstable cervical fractures and dislocations and are used for approximately 3 months.

The three most commonly used thoracolumbar braces are the Jewett brace, thoracolumbosacral orthosis (TLSO), and Taylor brace. The Jewett brace is used to treat lower thoracic or upper lumbar compression fractures or for postsurgical stabilization. This brace limits flexion but allows extension and leaves the abdomen open. The TLSO extends from the sacrum to the inferior angle of the scapula and decreases the load on the axial spine. It is used to prevent progression of scoliosis or during the postoperative period after spine surgery to provide stabilization. The Taylor brace is similar to the TLSO in limiting flexion and extension and is used to treat

kyphosis in the setting of osteoporotic compression fractures.

Ankle Foot Orthoses (AFO)

Indications for AFOs are foot drop, spasticity, or contracture leading to persistent plantar flexion and resulting in limited function or pain. AFOs can be made of plastic or metal with a plastic design being advantageous due to its lightweight and cosmetic appearance. Metal designs are more compliant in patients with fluctuating edema. The most common types of plastic AFOs include the posterior leaf spring, semirigid, and solid AFO. It is important that the calf band is at least 1 in. below the fibular neck in order to avoid compression of the common peroneal nerve. The patient should also be closely monitored for any skin breakdown.

Knee Orthoses

Indications for knee orthoses may be for preventative, rehabilitative, or functional uses. Prophylactic knee bracing helps to prevent or reduce severity of injuries although evidence for this is lacking [9]. More rigid and durable rehabilitative orthoses include the Swedish knee cage or Lenox-Hill derotation orthosis that not only provide structural protection but also limits knee hyperextension. To date, bracing has demonstrated a small beneficial effect with a recent Cochrane review demonstrating that the use of a knee brace may increase walking distance but not lead to any difference in pain or function [10].

Assistive Devices

Canes

Indications for the use of canes are gait instability, pain relief, and to minimize weight bearing of an injured or affected limb. They can range from a single point cane to a quad cane, which provides a wider base of support. The function of the cane should be to increase the base of support, provide additional sensory feedback, and decrease loading on the lower limbs. In general, the cane should be held in the hand opposite of the affected lower limb and is advanced with the affected limb. This reduces the load on the affected limb 20–25 % [11]. The cane length should be from the bottom of the shoe heel to the height of the greater trochanters with the elbow flexed at 20–30° [12]. When climbing up and down stairs, patients should be counseled to ascend stairs with the strong and unaffected limb while descending stairs with the affected limb.

Walkers

Indications for a walker are the same as the cane and can allow up to 100 % of weight-bearing relief of the affected lower limb. The disadvantage of the walker over the cane is that walkers may promote a slow and disrupted gait pattern that may not only promote poor posture but also cause difficulty maneuvering stairs and small spaces. A proper fitting walker is set with the elbows flexed at 20° with the patient standing straight and shoulders relaxed. The three most common types of walkers include the rolling walker, hemi-walker, and platform walker. The rolling walker is used for patients who cannot lift the upper limbs to advance the walker and also when a smoother reciprocal gait is desired. The hemi-walker is used in hemiplegics who need a wide base of support, and the platform walkers are used to allow weight bearing at the elbow without putting pressure on the distal upper extremities.

Crutches

Crutches are more stable than canes due to the two points of contact with the body and are most commonly used in lower extremity injuries. The most commonly prescribed crutches are axillary, forearm (Lofstrand), and platform crutches. Axillary crutches require significant upper body strength and increased cardiac demand for the

patient. Forearm crutches are used when axillary pressure is not appropriate or to allow for hand use. Platform crutches are useful when there is a distal upper extremity injury, as they allow for upper body weight bearing through the humerus. Axillary crutches may be the most commonly encountered, and contrary to popular belief, the axillary part of the crutch should not be padded as it is not designed to take on body weight as this increases potential for nerve injury.

Splinting and Casting

Indications for splinting and casting are bony fractures, ligamentous sprains, and lengthening in the case of contractures. Generally, splinting should be done in a manner to provide anatomic support and limiting range of motion through the affected area especially in the acute phase of fractures or sprains. Casting is used for nonsurgical, non-comminuted fractures in order to prevent motion in the joint above and below the level of injury [13]. This is to limit stress on the bone from the muscles attached distal and proximal to the fracture.

Manipulation

The term manipulation is a broad term used to define modalities that help increase range of motion or strength and to relieve pain. These include osteopathic manipulation therapy (OMT) and massage therapy. OMT is an approach that allows the practitioner to manipulate the axial skeleton along with skeletal muscles to restore function and provide pain relief. Techniques in OMT overlap with massage therapy and physical and occupational therapy while focusing on a global approach based on anatomic structure and function [14]. Common OMT techniques are soft tissue massage, strain and counterstrain, and high-velocity and low-amplitude muscle energy techniques. Massage therapy can be used to relieve muscle tension, soreness, and pain.

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Work Rehabilitation

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Kathy Aligene, Akshay S. Garg, Karina Gritsenko, and Yury Khelemsky

Overview

Scope of the Chapter

Definitions and terminologies: are based on the accepted evidence-based consensus of the International Classification of Functioning (ICF), Disability and Health [1]. The ICF categorizes health conditions and disability based on functional metrics in comparison to the International Classification of Disease (ICD) that focuses mainly on disease-specific conditions [2].

Limitations: this chapter focuses on work rehabilitation and return to work (RTW), not work disability.

Definition

- Work rehabilitation (*vocational rehabilitation*, *RTW programs*) encompasses a diverse group of health-related functional conditions that may limit one's ability to actively and effectively participate in work-related task(s).
- ICF defines work rehabilitation as "a multiprofessional evidence-based approach that is provided in different settings, services, and activities to working age individuals with health-related impairments, limitations, or restrictions with work functioning, and whose primary aim is to optimize work participation."

Paradigm Shift

- The vocational rehabilitation and RTW programs create a cost-effective and functional improvement that reduces the burden of illness

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and injury by helping patients to return and maintain the ability to work.
- The ICF model provides a comprehensive, evidence-based, practical clinical approach that incorporates a biopsychosocial model to categorize, evaluate, measure, and manage health conditions.
- The goal is to reduce the associated burden of health conditions and enable those who are at risk or have experience a health-related condition to achieve and optimize their functional ability within their immediate environment.
- Main components of ICF evaluation and assessment focus on the complexity of the functional and physical aspects in relation to personal and environmental factors that impacts an individual's ability to participate.

Evidence-Based Approach

Evaluation

Fundamental Components ICF Evaluation*

1. *Body structure and functions:* focuses on the anatomical structures and neurobiological/systemic physiological function of the body.
2. *Impairment:* deviation from the normal body structure and functions that may limit or restrict the ability to execute an activity/task.
3. *Participation and activity:* integrates the individual ability (*i.e., psychological, social, cognitive, level of education, level of training level, etc.*) and environmental factors that limit or restrict the ability to efficiently and effectively accomplish a task.

*Impairment, limitation, and restrictions lead toward disability. The level of disability is influenced by personal and environmental factors.

Risk Factors

The literature recognizes the significant influence of psychosocial aspects related to work productively and participation. Notably, individuals that are unsatisfied with their work have an increased likelihood of injury, increased number of sick days, etc. Therefore, it is important to identify risk factors—especially preventable or reversible factors. Prevention is the most reliable cost-effective strategy.

✓ *Negative risk factors:* stress, lack of support group, lack of professional peer support, lack of skills or training, etc.

Assessment Tools

- *Conventional assessment*: usually based on three types of assessments—*self-reported assessments* (i.e*., validated questionnaires*), *clinically based assessment*, *and capacity-based assessment*. Individually, these assessments are significantly limited in providing a comprehensive evaluation of an individual's disability.
- *Core sets* (*evidence-based validated test*): a variety of categories that are tailored to specific health condition(s), to health-related event(s), and in different settings. The provider is able to generate a customized brief or comprehensive assessment incorporating the fundamental components of ICF.

Management

Disability evaluation will be different depending on underlying illness or condition (i.e., stroke, multiple sclerosis, spinal stenosis, rheumatoid arthritis).

Vocational rehabilitation intervention *classification* is based on absence from work:

✓ Not absent
✓ Short term (<6 weeks)
✓ Intermediate (6–12 weeks)
✓ Long term (>3 months)

Vocational rehabilitation intervention *outcomes* are highly dependent on:

- ✓ Coordinator for RTW
- ✓ Gradual/graded level of activity and work exposure
- ✓ Biopsychosocial orientation by vocational rehabilitation team

Concepts:

– Habituation versus rehabilitation

Model of a comprehensive vocational reintegration (VR) stepwise customized, multidisciplinary approach (based on SPZ ICF-VR study):

1. Initial phase
2. Assessment phase
3. Evaluation and decision phase
4. Interdisciplinary coordination of goals and measures
5. Intervention phase (skill training)
6. Goal evaluation
7. Discharge phase (vocational reintegration)

Multidisciplinary Approach

- ✓ Multidisciplinary team
- ✓ Setting
- ✓ Services

Treatment/Target Intervention

- ✓ Education: understanding the basics (definition of impairment, function, etc.).
- ✓ Special considerations
- ✓ Clinical pearls: question to ask—"how am I functioning in my work environment."

Interventions

Targeted functional interventions parallel the three components of ICF health conditions assessments. The goal is to balance multidisciplinary therapeutic approaches and the complexity of the underlying health condition(s) with a focus on prevention, restoration, and/or *maintenance*:

- ✓ Impaired body functions
- ✓ Limited activities
- ✓ Restricted participation

RTW services: job counseling, job placement, skill development and retraining, work conditioning, and workplace modifications.

Treatment Outcomes [3]

Strong evidence for cost-benefit and quality-of-life improvement with a vocational rehabilitation EBA leading to decreased work disability burden.

Prognostic factors: individuals with a greater chance of return to jobs **after vocational rehabilitation**:

– Younger, native, and highly educated with a steady job and high income
– Married, with stable social networks, self-confident, happy with life, not depressed, with low levels of disease severity, and no pain
– High work seniority and long working history and an employer that cares and wishes him or her back to the workplace
– Positive VR outcome focus on healthcare and accommodating work environment

Key Findings in Literature

- Waddell, Burton, and Kendall demonstrated for every unit of investment in vocational rehabilitation provides about fivefold return [4].
- **Employers have a critical role; studies show proactive, preventative interventions, such as temporary provisions when employee is sick; and work modification and accommodations are more cost-effective compared to worker's compensation** [5].
- Not only is higher pain intensity related with worse outcome, but higher interference of pain with activities is also associated with reduced treatment success.
- High levels of depression at baseline are associated with worse outcome, and reduction of

depressive symptoms is related to better outcome. This effect suggests that depressed patients have more to gain from treatment.

- Workers who have not returned to work within 2–3 months after injury are at high risk of disability and dropping out of the work arena completely. Therefore, encouraging early RTW by intervening at the workplace may be an efficient way to minimize socioeconomic and personal consequences.
- Education, follow-up by a case manager, occupational therapy, worksite visits, on-site management, vocational guidance, occupational health services, work hardening, work modification, job accommodation, work adjustments, work reintegration plans, or ergonomic interventions.

Summary

In brief VR is "anything that helps someone with a health problem stay at, return to, and remain in work." {2} ICF creates a dynamic, comprehensive, and interactive model to categorize and assess the interaction of an individual health conditions, personal, and environmental factors.

Key Concepts

Disability: diagnosis of disability (physical, mental, or emotional) is often used for legal determination of an individual's qualification for benefits or compensation (i.e., from workers' compensation, disability insurance, social security, etc.).

Work disability: individual's inability to perform daily work-related participation as a result of an injury or illness.

Functional assessment: evaluation of an individual's physical capacity, performance, and executive function.

Vocational rehabilitation: incorporates multidisciplinary and evidence-based approach (ICF) to optimize an individual ability to participate efficiently at work given underlying impairments and/or functional limitations (either health or injury related).

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Complementary, Alternative, and Integrative Therapies (CAIT)

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Overview

Many Americans, nearly 40 %, use health-care approaches outside of mainstream Western, or conventional, medicine to treat specific conditions, treat side effects of conventional medicine, and improve health or overall well-being [1–3]. It has been estimated that two-thirds of individuals that suffer from arthritis and other musculoskeletal disorders have used complementary and alternative treatments to control their symptoms [4].

The terms "complementary" and "alternative" can be defined in a variety of ways. For example, definitions offered by the National Center for Complementary and Integrative Health (NCCIH) (formerly National Center for Complementary and Alternative Medicine) are as follows:

> "Complementary" generally refers to using a non-mainstream approach **together with** conventional medicine.
> "Alternative" refers to using a non-mainstream approach **in place of** conventional medicine.

Complementary, alternative, and integrative therapies best describe the practices reviewed in this chapter. The modalities that are being described may be a complement to health care or they may also be an alternative. The alternative may not be "nonmainstream," just as an injection or surgery may be considered an alternative. "Alternative" in complementary and alternative medicine (CAM) may imply a "nonmainstream" treatment, used in place of conventional medicine, but often the therapies described in this chapter are not "instead of," but are "along with." Other terms that are used to describe this approach are complementary and integrative medicine and active self-care [3, 5].

For the purposes of this review, practices will be divided into **alternative medical systems** (e.g., traditional Chinese medicine, homeopathy, ayurvedic medicine), **mind-body interventions** (mindfulness, yoga, Qigong, Tai qi), **energy-based therapies** (e.g., healing touch, therapeutic touch, Reiki), and **biologically based therapies** (e.g., herbs, foods). Manipulative methods (e.g., osteopathy) are addressed in this chapter.

The quality of research on CAIT varies considerably and is somewhat limited. The National Institutes of Health (NIH) set up the National Center for Complementary and Integrative Health specifically "to define, through rigorous scientific investigation, the usefulness and safety of complementary health approaches and their roles in improving health care. NCCIH's vision is that scientific evidence will inform decision-making by the public, by health-care professionals, and by health policymakers regarding the use and integration of complementary health approaches." The amount of research on mind and body

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approaches varies widely depending on the practice. For example, acupuncture, yoga, spinal manipulation, and meditation have had many studies, and some of these practices appear to hold promise in pain management, whereas other practices have had little research to date [6–10].

The purpose of this chapter is to provide a brief overview of commonly used complementary, alternative, and integrative health approaches. Given the vast array of therapies and approaches available, only the most common have been included in this review.

Alternative Medical Systems

- **Traditional Chinese medicine**
- **Shiatsu**
- **Homeopathy**
- **Ayurvedic medicine**

Traditional Chinese Medicine

Traditional Chinese medicine (TCM) includes acupuncture and Chinese herbal medicine. These may be used in conjunction or as separate therapies. TCM may also include the use of Qigong or Tai Chi, but these will be described in the section Mind-body Interventions.

Based on thousands of years of practice, the premise of Chinese medicine is that when healthy and abundant supply of **qi** (pronounced chee) or "life energy" flows through the body's meridians (a network of defined yet invisible channels through the body). If the flow of qi in the meridians becomes blocked or there is an inadequate supply of qi, then the body fails to maintain harmony, balance, and order, and disease, illness, or pain can ensue.

Acupuncture has also been shown to have an effect on endogenous opioid and peptide systems. Acupuncture plays a modulatory effect on neurotransmitters involved in nociception such as serotonin, norepinephrine, beta-endorphin, encephalin, substance P, and others thus leading to analgesia. Functional imaging of the central nervous system indicates that acupuncture may work on the descending inhibitory system [4, 11, 12].

The practitioner of Chinese medicine formulates a Chinese medicine diagnosis and a treatment plan that will restore the flow of qi. This can be accomplished with Chinese herbal formulations and or needling of specific acupuncture points. Acupuncture technique may also include the use of moxibustion or percutaneous electrical nerve stimulation (PENS). Chinese herbal formulations will be discussed in this subheading, rather than in the "herbal remedies" section.

It is difficult to study the efficacy of acupuncture or Chinese herbs in reference to Western medical diagnoses, since Chinese medicine diagnoses are not categorized in the same way. Benefit has been found for treating back and neck pain, headache, myofascial pain, and a variety of other pain conditions (dysmenorrhea, osteoarthritis, postoperative pain, epicondylitis).

Complications and risks are very rare, but can include infection, pneumothorax, syncope or vagal reaction, retained needles, contact dermatitis, organ puncture, bruising, compartment syndrome, and temporary exacerbation of symptoms.

Side effects of acupuncture can include lightheadedness, anxiety, agitation, tearfulness, and fatigue.

Precaution must be taken to avoid electrical stimulation in patients with pacemakers. The use of certain points in pregnancy can stimulate uterine contractions.

Chinese herbal medications can be associated with drug interactions and allergic reactions and affect blood pressure, coagulation, and other physiologic effects. For example, the Chinese herb ephedra (ma huang) has been linked to heart attack and stroke. In 2004, the FDA banned the sale of ephedra-containing dietary supplements, but the ban does not apply to TCM remedies. There are reports of contamination of Chinese herbs with drugs, toxins, or heavy metals or that they may not contain the listed ingredients [4, 9, 10, 12–18].

Homeopathy

Homeopathy is based on two main principles, the law of similar and that highly diluted remedies (diluted natural substances) can be effective even

though they are unlikely to contain a single molecule of the original substance. A remedy is chosen individually for a sick person based on its capacity to cause, if given in overdose, physical and psychological symptoms similar to those a patient is experiencing. The meta-analysis of randomized or placebo control studies indicates that clinical effects are not entirely due to placebo. There is some evidence that homeopathy can be effective for treatment of rheumatoid arthritis and osteoarthritis. Homeopathy, given that very dilute substances are administered, is considered as safe as placebo. The use of arnica to treat myalgias is an example of a homeopathic remedy [3, 4].

Ayurvedic Medicine

Ayurvedic medicine has been practiced in India for more than 5000 years. The premise of this practice is that illness is a state of imbalance among body systems. This imbalance can be detected through diagnostic procedures such as reading the pulse and observing the tongue. Treatment of disease and restoration of balance involve incorporating nutritional counseling, massage, natural medications, meditation, and other modalities. Ayurvedic medicine is used to treat pain and there is some research to support its use in osteoarthritis [3, 19, 20].

Mind-Body Interventions

- **Mindfulness-based interventions**
- **Qigong**
- **Tai qi**
- **Yoga**

Mindfulness-Based Interventions

Mindfulness-based interventions (MBIs) "can be described as the ability to observe the experience of the present moment with openness and curiosity and without judgment" [21].

MBIs distill the use of meditative practices from Eastern traditions, while omitting original religious, ideological, and cultural constructs. The goal of MBI is to teach individuals techniques, which enhance one's ability to be mindful such as sitting and walking meditation, guided meditation, mindful movement, and other exercises. It has been increasingly incorporated into Western medicine to help with stress reduction and to serve as an intervention for the management of a variety of conditions including pain, depression, PTSD, and anxiety. There are studies that show that mindfulness-based interventions are associated with significant changes in brain function and architecture with subsequent effects on improving attention, memory, executive functions, improved sleep, and decreased emotional reactivity.

MBI can help patients to relate to their pain differently. In learning mindfulness, patients learn to experience body sensations, thoughts, emotions, and impulses without having to change them, avoid them, or suppress them. Patients are able to observe their pain, describe pain, and notice how pain and related emotions may change from moment to moment. They can separate the observation of the pain from the sensation of pain. MBIs are not necessarily associated with a decrease in pain, but can change the experience of pain.

Mindfulness can increase pain, depression, or anxiety within the first few weeks of incorporation. Some mindfulness programs indicate that this practice may not be recommended for all individuals. This may include a history of substance or alcohol abuse (with recent sobriety), suicidal attempts or ideation, recent or unresolved trauma, or being in the midst of major life changes.

[17, 21–24]

Qigong

Qigong (chi-kung) is a practice that has existed for thousands of years. There are many different forms of Qigong, which incorporate traditional Chinese energy exercises or therapies. The word "Qigong" means skill or cultivation of vital energy (qi). Qigong is also considered to be a form of traditional Chinese medicine. In TCM, good health is the result of a free-flowing, well-balanced *qi* (bioenergy) system, while sickness, pain, or physical disorders occur when there is a blockage or

imbalance of qi. Qigong practice refers to the mind-body movements, skills, or processes that integrate the adjustments of body, mind, and breath to stimulate and balance the flow of qi (chi), or vital energy, along the acupuncture meridians, or energy pathways. Qigong is used to reduce stress, improve blood circulation, enhance immune function, and treat a variety of health conditions [25].

Tai Chi

Tai Chi is a mind and body practice that originated in China as a martial art. Tai Chi is sometimes referred to as "moving meditation." Practitioners move their bodies slowly, gently, and with awareness, while breathing deeply circulating their qi or life force. The highly disciplined movements and forms are thought to unite the body and mind and to bring balance to the individual's life. Tai Chi has been used as part of treatment for pain but may also be helpful due to an effect on increasing range of motion, improving strength and balance, and creating a sense of well-being [25, 26].

Qigong and Tai Chi are considered to be safe practices. They involve gentle movements and have been used to relieve chronic pain. Research regarding efficacy for pain is limited but points toward benefit from their use.

Yoga

The word "yoga" comes from the Sanskrit root yuj, which means "to join" or "union." It is a practice that seeks to **join** the body and mind, using a system of techniques. There are many types of yoga and practices. It is suggested that yoga creates inner, physical, and emotional balance using postures and breathing techniques. Proposed mechanisms as to how yoga can affect pain include increased release of enkephalins and endorphins, increased tissue flexibility and oxygenation, relaxation effects, decreased sympathetic activity, and decrease in inflammatory markers. Yoga can also have positive psychological effects including increased mind-body awareness, improved outlook, and sense of empowerment in self-care. There is evidence that yoga alleviates pain, but research varies in terms of quality and strength of results obtained. Some studies have shown, for example, moderate evidence for long-term effectiveness for low back pain. Potential risks include injury and increased pain [10, 27, 28].

Energy-Based Therapies

- **Healing touch, therapeutic touch, Reiki**

The premise behind energy healing is that when energy paths of the body are blocked or disturbed, a disruption occurs in a person's "holistic harmony." This balance of energy and sustained flow of energy is needed to maintain health, and imbalance may result in disease, weakness, pain, illness, or psychological issues. Practitioners of energy-based therapy use direct or noncontact touch to influence the human energy field.

There is limited research evidence in terms of robust studies to show that Reiki is effective in healing or decreasing pain. Some research has shown decreased opioid requirements in patients receiving energy-based therapies.

Reiki is being used increasingly though in traditional health-care environments such as hospitals, hospice care settings, nursing homes, and other health-care settings. Reports of outcome include relaxation, decreased anxiety, and pain relief. Healing touch and Reiki are considered to be safe with negligible side effects. In studies of Reiki, side effects were no more common among participants who received Reiki than among those who did not receive it [17, 29–31].

Biologically Based Therapies

- **Chinese herbal medicine (see above)**
- **Herbal supplements**
- **Food as medicine**

Herbal Supplements

Many herbal medicines minimize pain via an anti-inflammatory effect. **Table** 111.1 provides a

Table 111.1 Commonly used herbs to treat pain

Herb	Conditions treated	Mechanism of action	Risks/side effects/drug interactions
Devil's claw (harpagoside)	Osteoarthritis (hip, knee, spine), back pain	Anti-inflammatory and analgesic effect	– Diarrhea, possible bradycardia, dyspepsia – Contraindicated in pregnancy – Can interact with antacids/H2 antagonists, beta-blockers/digoxin, anticoagulants, cytochrome P450 enzymes
Turmeric (*Curcuma longa*)	Rheumatoid arthritis, osteoarthritis	Anti-inflammatory (decreases COX_2 and lipoxygenase activity, inhibits production of inflammatory cytokines)	– Considered safe for most adults – High doses or long-term use of turmeric may cause indigestion, nausea, or diarrhea – May exacerbate cholecystitis or cholelithiasis – May interact with many drugs including anticoagulants/antiplatelet drugs, chemotherapeutic drugs, drugs metabolized by CYP3A4, CYP1A2, and CYP2A6 enzymes, midazolam, acetaminophen, ibuprofen, aspirin
Willow bark	Arthritis Headache Inflammation	Contains salicin	– Contraindicated if allergic or sensitive to salicylates – GI distress, allergic reaction, erythema, pruritus, bleeding complications – Increase risk of bleeding with warfarin or other anticoagulants
Avocado-soybean unsaponifiables (ASUs)	Osteoarthritis	Anti-inflammatory effect (inhibits interleukin-1 synthesis)	
Ginger	Osteoarthritis Low back pain	Anti-inflammatory effect (inhibits thromboxane formation and platelet aggregation)	SE: flatulence, bloating, heartburn, and nausea – Avoid during pregnancy or lactation – Interaction with NSAIDs, anticoagulants, antiplatelet drugs, hypoglycemic agents, insulin, some chemotherapeutic agents
Phytodolor (*Populus tremula*, *Fraxinus excelsior*, *Solidago virgaurea*)	Osteoarthritis, rheumatoid arthritis	Anti-inflammatory effect	Rare allergic reactions
Rose hip	Osteoarthritis	Anti-inflammatory effect	
Boswellia (*Boswellia serrata*)	Osteoarthritis	Anti-inflammatory effect (5-lipoxygenase inhibitor)	– Fewer adverse effects than steroids and NSAID
Capsicum	Muscle soreness Arthritis (topical formulations) Neuropathic pain	Capsaicin is active ingredient, causes initial release, subsequent depletion of substance P	– External application can lead to blister and ulcer formation – Can irritate mucous membranes, the eyes, and broken skin – Unclear if long-term topical use is skin carcinogenic – Increases pain with initial use

(continued)

Table 111.1 (continued)

Herb	Conditions treated	Mechanism of action	Risks/side effects/drug interactions
Butterbur	Migraine	Blocks leukotriene activity	– Raw, unprocessed plant contains pyrrolizidine alkaloids (PAs), which can cause liver damage – Limit use to products that are labeled or certified as PA-free – PA-free products are safe and well tolerated when used in recommended doses for up to 12 to 16 weeks. Safety of longer-term use is not established – SE: headache, ocular pruritus, GI distress, asthma, fatigue, drowsiness, eructation – May cause allergic reactions in those with sensitivities to ragweed, chrysanthemums, marigolds, and daisies
Feverfew	Migraine	– Blocks transcription of inflammatory proteins and decreases platelet activity	– SE: canker sores, swelling and irritation of the lips and tongue, loss of taste, nausea, indigestion, and bloating – After stopping long-term use: insomnia, headaches, joint pain, anxiety, myalgias – Contraindicated in pregnancy – If allergic to members of the daisy family, more likely to be allergic to feverfew – Drug interactions with cytochrome P450 3A4 substrates, anticoagulants, antiplatelet drugs
St John's wort	Depression		– Many drug interactions but most significant concern in pain management is the risk of serotonin syndrome if taken with SSRIs, monoamine oxidase inhibitors (MAOIs), SNRIs, Serzone, dextromethorphan, triptans – Photosensitivity
Thunder god vine	Rheumatoid arthritis		– Severe SE if not carefully extracted from the skinned root – leaves, flowers, and skin of the root are highly poisonous and can cause death SE: diarrhea, indigestion, nausea, hair loss, headache, menstrual changes, rash Increased risk of osteoporosis with use greater than 5 years – Decreases male fertility via effect on sperm

summary of more commonly used herbs to treat pain. Patients should be queried as to their use of herbs, since many patients are involved in active self-care. The list included in this review is not exhaustive and resources are provided to enable the practitioner to further investigate herbs that patients are taking. The table also summarizes side effects and possible drug interactions. Herbs are regulated by the FDA and fall under the category of "dietary supplements." It is not required that manufacturers have FDA approval before an herbal supplement goes on the market. Manufacturers can make claims as far as efficacy if there is supporting research and they provided a disclaimer that the FDA has not evaluated the claim. Herbal supplement manufacturers do need to meet certain quality standards in the USA, and foreign manufacturers must register their products with the FDA in order to sell them in the USA. The manufacture of herbal medicines in most countries is unregulated raising concerns regarding contamination with toxic substances, adulteration, and suboptimal quality. Patients who are taking conventional over-the-counter and prescribed substances may also be taking self-prescribed herbal supplements. This can lead to potential adverse herb-drug interactions [4, 9, 15–17, 32–39].

Food as Medicine

Food can contain substances that may have an effect on pain (see Table 111.2). Certain diets have also been identified as anti-inflammatory and may have an effect on pain including diets free of foods from the nightshade family or the Mediterranean diet. Research is limited but in practice one may have patients who are engaged in active self-care and utilizing diet to affect their pain. Many of the substances in food attributed to decreasing pain may do so by an effect on the inflammatory process. Some examples of foods that contain substances that have an anti-inflammatory effect are listed in table form below. This is not intended to be an exhaustive list; the entire topic of food as medicine is too broad a scope to be covered in this review [40–44].

Table 111.2 Foods that may have anti-inflammatory properties

Food	Active compound
Cherries, berries, black currants, eggplant, red and black grapes, and plums	Anthocyanins
Red and black grapes and plums	Anthocyanins
Green tea	Epigallocatechin-3-gallate (EGCG)
Salmon, herring, mackerel (not king), sardines, anchovies, rainbow trout, Pacific oysters, flaxseeds (ground and oil), chia, walnuts	Omega-3 fatty acids
Olive oil	Oleocanthal

Complementary, alternative, and integrative therapies (CAIT) are increasingly becoming a part of the Western medical landscape. Complementary, alternative, and integrative therapies are being incorporated into pain management programs and cancer treatment centers not only for the potential for decreasing pain but also for the improvements seen in mood and a sense of well-being [45]. Patient's use of CAIT in self-care is becoming more prevalent. Most have few risks. Most CAIT is not covered by insurance and cost varies. Evidence for efficacy is promising, but more robust research is needed.

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Part IX

Clinical States

Taxonomy of Pain Systems

112

Samuel Holmes and P. Jason Silvestri

Pain

An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. Inclusion of the descriptors "emotional experience" as well as "actual or potential tissue damage" is important: it is not pain without an emotional experience and tissue damage is not required. Emotional experiences of pain may be described as annoying, nagging, troublesome, tiring, exhausting, frightening, terrifying, dreadful, grueling, wretched, punishing, cruel, vicious, sickening, suffocating, blinding, miserable, agonizing, and unbearable.

Analgesia

Absence of pain in response to stimulation which would normally be painful.

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Anesthesia Dolorosa

Pain in an area or region which is anesthetic.

Dysesthesia

An unpleasant abnormal sensation, whether spontaneous or evoked.

Paresthesia

An abnormal sensation, whether spontaneous or evoked. Paresthesia is an abnormal sensation that is not unpleasant, while dysesthesia should be used preferentially for an abnormal sensation that is considered to be unpleasant.

Allodynia

Pain due to a stimulus that does not normally provoke pain.

Hyperalgesia

Increased pain from a stimulus that normally provokes pain.

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Hyperesthesia

Increased sensitivity to stimulation, excluding the special senses. Used to indicate both diminished threshold to any stimulus and an increased response to stimuli that are normally recognized. Hyperesthesia includes both allodynia and hyperalgesia, but the more specific terms should be used wherever they are applicable.

Hyperpathia

A painful syndrome characterized by an abnormally painful reaction to a stimulus, especially a repetitive stimulus, as well as an increased threshold. It may occur with allodynia, hyperesthesia, hyperalgesia, or dysesthesia.

Hypoalgesia

Diminished pain in response to a normally painful stimulus (Table 112.1).

Hypoesthesia

Decreased sensitivity to stimulation, excluding the special senses.

Table 112.1 Implications of key pain definitions

Allodynia	Lowered threshold (not required)	Stimulus and response mode differ
Hyperalgesia	Increased response	Stimulus and response mode are the same
Hyperpathia	Raised threshold: increased response	Stimulus and response mode may be the same or different
Hypoalgesia	Raised threshold: lowered response	Stimulus and response mode are the same

Neuralgia

Pain in the distribution of a nerve or nerves.

Neuritis

Inflammation of a nerve or nerves.

Neuropathic Pain

Pain caused by a lesion or disease of the somatosensory nervous system. May be described as paroxysmal, lancinating, sharp, thermal (burning, cold), numbing, electrical, shocking, tingling, pricking, itching, pulling, tugging, and shooting.

Central Neuropathic Pain

Pain caused by a lesion or disease of the central somatosensory nervous system.

Peripheral Neuropathic Pain

Pain caused by a lesion or disease of the peripheral somatosensory nervous system.

Neuropathy

A disturbance of function or pathological change in a nerve: in one nerve, mononeuropathy; in several nerves, mononeuropathy multiplex; if diffuse and bilateral, polyneuropathy.

Nociception

The neural process of encoding noxious stimuli. May be autonomic (e.g., elevated blood pressure) or behavioral (motor withdrawal reflex or more complex nocifensive behavior). Pain sensation is not necessarily implied as there is no requirement for emotional experience.

Nociceptive Neuron

A central or peripheral neuron of the somatosensory nervous system that is capable of encoding noxious stimuli.

Nociceptive Pain

Pain (with emotional response) that arises from actual or threatened damage to the nonneural tissue and is due to the activation of nociceptors. The term is used to describe pain occurring with a normally functioning somatosensory nervous system to contrast with the abnormal function seen in neuropathic pain. May be described as aching, dull, sore, deep, throbbing, cramping, pinching, gnawing, pressure, heavy, and crushing. This includes somatic, visceral, and vascular etiologies.

Nociceptive Stimulus

An actually or potentially tissue-damaging event transduced and encoded by nociceptors.

Nociceptor

A high-threshold sensory receptor of the peripheral somatosensory nervous system that is capable of transducing and encoding noxious stimuli.

Noxious Stimulus

A stimulus that is damaging or threatens damage to normal tissues.

Pain Threshold

The minimum intensity of a stimulus that is perceived as painful.

Pain Tolerance Level

The maximum intensity of a pain-producing stimulus that a subject is willing to accept in a given situation.

Sensitization

Increased responsiveness of nociceptive neurons to their normal input and/or recruitment of a response to normally subthreshold inputs.

Central Sensitization

Increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input.

Peripheral Sensitization

Increased responsiveness and reduced threshold of nociceptive neurons in the periphery to the stimulation of their receptive fields.

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Acute Pain

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Kay H. Lee and Karina Gritsenko

Acute pain: Normal, predicted, physiologic response to an adverse chemical, thermal, or mechanical stimulus, which generally resolves within 1 month.

- *Background*: Persistent but may vary over time
- *Breakthrough*: Escalates above a persistent background pain
- *Transitory* and *intermittent*: Episodic in the absence of background pain

Epidemiology of Postoperative Acute Pain

Approximately 75 million surgical procedures are performed each year in the United States, and more than half are in an inpatient setting.

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Physiologic and Psychological Effects of Inadequate Acute Pain Control

- Delay of recovery and return to daily activity and patient dissatisfaction
- Potential to produce chronicity
- *Neuronal plasticity*: Acute pain-induced CNS change, which can result in *sensitization* of the nervous system to result in *allodynia* and *hyperalgesia*

Major Classes of Drugs

Opioids: Morphine is considered the gold standard. The three main opioid receptors are mu, delta, and kappa. There is *no ceiling effect* of the drug, just a concern regarding side effects (Table 113.1).

Opioid rotation is a very useful technique to restore analgesic sensitivity in the highly tolerant patient. Methadone can be a useful alternative for opioid rotation with careful assessment of conversions* (Table 113.2).

Para-aminophenol: Acetaminophen 500–1000 mg PO or IV q4–6 h with maximum daily dose (MDD) of 4000 mg has both analgesic and antipyretic properties, similar to aspirin, but is devoid of any anti-inflammatory effects.

NSAIDs: Most commonly used and have anti-inflammatory, analgesic, and antipyretic effects.

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Table 113.1 Equi-analgesic dosing

Drug	IV/IM/SQ	PO (mg)
Morphine	10 mg	30
Hydromorphone	1.5–2 mg	6–8
Hydrocodone	N/A	30–45
Oxymorphone	1 mg	10
Oxycodone	10–15 mg	20
Levorphanol	2 mg	4
Fentanyl	100 μg	N/A
Meperidine	100 mg	300
Codeine	100 mg	200

Table 113.2 Morphine to methadone conversion ratio*

Morphine PO (mg)	Ratio
<100	3:1
100–300	5:1
300–600	10:1
600–800	12:1
800–1000	15.1
>1000	20:1

(e.g., 720 mg PO morphine × (1/12) = 60 mg PO methadone, *estimated values—always start conservatively)

Unlike opioids, they *do* exhibit *ceiling effect*.

Nonselective NSAIDs can cause platelet dysfunction, gastrointestinal ulceration, and an increased risk of nephrotoxicity. Examples are ibuprofen (400 mg PO or IV q4–6 h with MDD 3200 mg), naproxen (250 mg PO q6–8 h with MDD 1500 mg), ketorolac (30 mg IV q6–8 h not to exceed 5 days with MDD 120 mg), diclofenac (50 mg PO q8 h with MDD 150 mg), and selective COX-2 inhibitors, celecoxib (100–200 mg PO q12h) and meloxicam (7.5–15 mg PO q24 h).

NMDA antagonist: Low-dose ketamine (0.25–0.5 mg IV bolus followed by infusion of 2–4 μg/kg/min) can provide significant analgesia for neuropathic pain and is opioid-sparing.

α2-Adrenergic agonist: Clonidine (3–5 μg/kg PO with 0.2 mg/24 h of transdermal patch) and dexmedetomidine (loading dose of 1 μg/kg IV over 10 min followed by infusion of 0.2–0.7 μg/kg/h) administered perioperatively provide analgesia, sedation, and anxiolysis.

Anticonvulsants: Perioperative gabapentin and pregabalin exert analgesic and opioid-sparing effects and, as a result, decrease opioid-related side effects. Useful neuropathic analgesic.

Local anesthetic: Lidocaine (1.5–2 mg/kg) has been shown to be analgesic, antihyperalgesic, and anti-inflammatory following intravenous administration.

Glucocorticoids: Dexamethasone (8 mg IV) has shown to have analgesic, anti-inflammatory, and antiemetic effects.

Perioperative Pain Management

Preemptive Analgesia

Local anesthetic: Wound infiltration of local anesthetic decreases analgesic consumption but showed no difference in postoperative pain score.

Systemic: Ibuprofen 800 mg PO, ketorolac 30 mg IV, gabapentin 600 mg PO, or COX-2 inhibitors before induction showed to decrease postoperative narcotic requirements.

Neuraxial analgesia: Intraoperative neuraxial opioids reduce postoperative systemic opioid need. Opioids administered in subarachnoid space act on *μ (mu) receptors* in *substantia gelatinosa* of the dorsal horn of the spinal cord by suppressing excitatory neuropeptide release from type C nerve fibers.

- Morphine (0.1–0.2 mg) or fentanyl (10–20 mcg) as spinal anesthetic
- Intrathecal morphine reaches maximum effect in about 45 min locally with a second peak effect at 18–24 h through rostral spread.
- Morphine 3–5 mg for lumbar and low thoracic epidurals

Postoperative Analgesia

Epidural analgesia: Patient-controlled epidural analgesia (PCEA) is used when longer duration neuraxial analgesia is needed. Examples of infusions include bupivacaine (0.125%) or ropivacaine (0.2%) plus fentanyl (2–5 mcg/mL) or hydromorphone (20 mcg/mL).

Table 113.3 Sample IV opioid regimens in opioid-naive adult patient with 5–10 min lockout intervals

Opioid	Demand	Basal infusion
Morphine	1–2 mg	0–2 mg/h
Hydromorphone	0.2–0.4 mg	0–0.4 mg/h
Fentanyl	20–50 μg	0–60 μg/h
Sufentanil	4–6 μg	0–8 μg/h
Tramadol	10–20 mg	0–20 mg/h

IV Patient-Controlled Analgesia (PCA) (Table 113.3)

Peripheral nerve block: Local anesthetics can also be administered perineurally as either single shot or continuous infusion via catheter. Loading bolus, commonly 20–30 mL of 0.5 % ropivacaine, can be used for surgical anesthesia. For postoperative pain relief, a continuous infusion of 0.2 % ropivacaine may be used (rates may vary depending on nerve location).

Non-pharmacological Methods

There is a sound body of knowledge to support the use of these established *non-pharmacological* methods in the management of acute pain:

- Appropriate preoperative information giving
- Preoperative relaxation and hypnosis
- Guided imagery and breathing training
- Cognitive reframing
- Distraction in both visual and auditory (music) forms
- Massage, acupuncture, and TENS

Clinical Outcomes to Be Evaluated

Adequate postoperative acute pain management should lead to *earlier mobilization*, *shortened hospital stay*, *reduced hospital costs*, and *increased patient satisfaction*. Pain control regimens should not be standardized. Rather, they are tailored to the needs of the individual patient. The goal is minimizing dose of medications to lessen side effects while still providing adequate analgesia, which is best accomplished with *multimodal* and *preemptive analgesia*.

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Cancer Pain: Assessment

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Niharika Saw and Michael Nguyen

Pain is one of the most common and undertreated symptoms of cancer. Proper treatment of pain begins with its accurate assessment. New pain in a patient with malignancy should be assumed to be progression of the cancer until ruled out. Up to one quarter of cancer pain is secondary to cancer treatment, while the remainder is mostly related to the cancer's physical relation to viscera, soft tissue, bone, muscle, or nerves. Physical exam, especially motor or sensory changes, can help localize tumor or metastases. Plain films are useful to diagnose fractures and viscera. Bone scans and CT are helpful to determine bone pathology or destruction, and MRI is useful to evaluate soft tissue.

Cancer pain can be categorized as nociceptive pain versus neuropathic pain or acute pain versus chronic pain. It can alternatively be categorized as pain related to the cancer, pain related to its treatment, or pain related to comorbid conditions other than the cancer.

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Assessing Type of Pain

Nociceptive Pain

- Intact pain pathway.
- Somatic pain from the muscle, skin, or bone—sharp—can be localized.
- Visceral pain mediated by the autonomic nervous system—dull and cramping—cannot be localized.

Neuropathic Pain

- Abnormal pain pathway
- Damage to the myelin sheath or nerve itself secondary to ischemia, metabolic injury, or compression
- Alteration in central facilitation or "windup" causing pain secondary to a stimulus that is usually not painful
- Sensation: burning, shooting, stabbing, electric, tingling, numbness, or sensory deficit

Acute Pain Syndromes

- Pain physically related to tumor
- Pain from radiation therapy or chemotherapy
  - Oral mucositis
  - Chemotherapy-induced neuropathy

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- Other chemotherapy-related acute pain syndromes
- Radiation plexopathy
- Radiation enteritis and proctitis

Chronic Pain Syndromes

- Chronic pain related to cancer
- Nociceptive pain: tumor-related bone pain, tumor-related soft tissue pain, paraneoplastic pain syndromes, and visceral nociceptive pain syndromes (hepatic distension, intestinal obstruction, peritoneal carcinomatosis)
- Neuropathic pain: cranial neuralgias, plexopathies, and radiculopathies
- Chronic pain related to antineoplastic treatment
- Chronic postsurgical pain

Assessing Pain Severity

- Numeric analog scale.
- Visual analog scale.
- Facial scales such as Wong-Baker scale for pediatric patients or developmentally delayed adults.
- Consider temporal aspect of pain in relation to severity—i.e., pain worse at night or pain that is paroxysmal such as firing of a neuroma.
- Choice of analgesic for treatment of pain depends on severity of pain as appreciated by the three-step ladder of cancer pain management (i.e., start with step one analgesic for mild pain, step two analgesic for moderate pain, and step three analgesic for severe pain; add adjuvant medication at any point).

Psychological Considerations

Cancer patients' interpretation of their situation leads to individual thought processes which effect these patients' emotional reaction to their circumstances. Cognitive behavioral therapy is one technique that is used to alter thought processes that are harmful to these patients. These thought processes, or dysfunctional cognitive patterns, include dichotomous thinking, catastrophization, filtering, and overgeneralization:

- Behavioral skill training—teaches practical skills to encourage adaptation to illness such as relaxation techniques, pacing activities, and incorporating enjoyable activities in daily life
- Cognitive skill training—teaches how to identify maladaptive thought processes and substitute with more helpful and adaptive ones

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Cancer Pain: Pharmacological Treatment

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Principles of Treatment

Pain is a significant concern for most cancer patients, as it is estimated that up to 50 % of patients in active treatment and 90 % of patients with advanced disease will experience pain [1]. Fortunately, with appropriate pharmacologic therapy, the majority of cancer pain (up to 95 % of patients) can be adequately managed [2]. The remaining 5–10 % of cancer patients may require interventional procedures to relieve pain and improve quality of life; these procedures are discussed elsewhere in the text.

Types of pain: Cancer pain may be associated with the cancer itself (i.e., visceral compression from tumor, bony metastases), with antineoplastic therapies (i.e., post-radiation enteritis, oral mucositis following chemotherapy), or with the exacerbation of preexisting chronic pain syndromes (i.e., headache, low back pain) due to cancer progression or cancer therapies. Broadly this pain is classified as either nociceptive (somatic, visceral, or both) or neuropathic, though psychogenic pain may also occur. Temporally there is often some element of constant pain accompanied by intermittent, breakthrough pain symptoms; these temporal aspects of the pain should influence analgesic selection.

Treatment strategies: When possible, pain may be reduced or potentially eliminated by treatment of the underlying disease itself: via surgical removal, chemotherapy, radiation therapy, or hormone therapy. In addition, oral analgesic pharmacotherapy remains the primary treatment modality in cancer pain management. Interventional therapies may be utilized when pharmacotherapy has proven insufficient or is causing intolerable side effects. Behavioral therapy, biofeedback, and other alternative modalities such as hypnosis and aromatherapy may also be employed.

Analgesic Ladder Approach

The *World Health Organization* has proposed a simple, three-tiered "analgesic ladder" approach to cancer pain management which bases oral analgesic selection upon the severity of a patient's symptoms (Table 115.1) [3].

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Table 115.1 Analgesic ladder approach to cancer pain management

For mild cancer pain, begin pharmacotherapy with non-opioid analgesics (NSAIDs, acetaminophen) along with adjuvant analgesics (anticonvulsants, corticosteroids, TCAs) as needed
↓ *Step one = mild pain* ↓
Can start "weak" opioids here, such as tramadol and opioid/non-opioid formulations (i.e., Tylenol + codeine, Tylenol + oxycodone), along with adjuvant analgesics as needed
↓ *Step two = mild to moderate pain* ↓
For pain of moderate/severe intensity, opioid agonists (i.e., morphine, hydromorphone) are indicated and titrated to pain relief. Sustained-release preparations are often augmented by PRN immediate-release form used for breakthrough pain
↓ *Step three = moderate to severe pain* ↓
When escalating opioids are failing to adequately treat pain, or if side effects become intolerable, interventional techniques (i.e., neurolytic blocks, neuraxial opioids) and/or conversion to parenteral opioid therapy may be necessary
Step four = severe, intractable pain

Pharmacologic Management

Oral analgesics, particularly the opioids, are essential to the treatment of cancer pain. Goals of pharmacotherapy are to achieve adequate analgesia with minimal side effects and improve quality of life and functionality. Frequent evaluation and reassessment are necessary in order to monitor for therapeutic efficacy and manage adverse side effects:

- *NSAIDs*: Nonsteroidal anti-inflammatory drugs inhibit COX enzymes along the pathway of prostaglandin synthesis, which decreases the sensitization of peripheral nociceptors. They are useful in the initial management of mild to moderate cancer pain and can reduce pain from bone metastases (which themselves are thought to synthesize prostaglandins). While combining NSAIDs with opioids can allow for reduced doses and fewer opioid-related side effects, it is important to remember the well-established NSAID toxicities and use sparingly in patients with GI, renal, or cardiovascular comorbidities.
- *Opioids*: Clinicians should be comfortable prescribing opioids—which modulate pain by binding to peripheral and central opioid receptors (mu, kappa, delta)—for cancer pain at all stages of disease. Initial use in opioid-naive patients typically involves the so-called "weak" opioids such as Tylenol + codeine, progressing to pure opioids if pain continues to increase thereafter. Chronic, constant pain is addressed with regularly scheduled doses or sustained-release formulations, while intermittent breakthrough pain is mitigated by PRN doses of short-acting opioid (i.e., OxyContin 10 mg q12 h plus oxycodone 5 mg q4–6 h PRN). Sustained-release opioids should not be used independently to titrate pain, as this is inefficient and can lead to unnecessary suffering. Alternative routes of administration are available when conditions merit (buccal, transdermal, rectal, intranasal, subcutaneous, intravenous, neuraxial). When opioid rotation is necessary (due to side effects or diminishing analgesic efficacy), account for incomplete cross-tolerance by decreasing the equianalgesic dose of the new opioid by 30–50 %.
- *Methadone:* This synthetic opioid deserves special mention given its popularity in cancer pain management. It is inexpensive, long-acting (clinical duration of analgesia is 8–12 h, similar to other sustained-release opioids), and offers both MAO reuptake inhibition and NMDA antagonism in addition to its activity at opioid receptors. Risk of QTC prolongation merits ECG evaluation prior to starting methadone.
- *Adjuvant analgesics:* Numerous adjuvants have been utilized for cancer pain. Several classes are especially effective for neuropathic pain control, including the gabapentinoids (gabapentin and pregabalin, which act as calcium channel ligands), tricyclic antidepressants (amitriptyline, nortriptyline), and other

serotonin-norepinephrine reuptake inhibitors (duloxetine, venlafaxine). Bisphosphonates and corticosteroids can reduce the pain from bone metastases; corticosteroids are also utilized for painful headaches due to brain metastases, back pain in the setting of spinal cord compression, abdominal pain from bowel obstruction, and intractable nausea and vomiting [4].

Side Effect Management

Preemptive measures to limit side effects are an integral component of any cancer pain regimen that involves opioids; fortunately, tolerance to most adverse symptoms will occur within a period of weeks, with the exception of constipation which is ongoing. Therefore, antiemetics may be necessary during the initial period of opioid titration (nausea is common, present in as many as one-third of patients), and a bowel regimen should be instituted concomitantly with the initiation of opioids. Monitor closely for other known side effects including urinary retention, respiratory depression, dry mouth, pruritus, and CNS symptoms (sedation, dysphoria, confusion).

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Cancer Pain: Interventional Therapies

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Niharika Saw and Michael Nguyen

Interventional therapies are considered when intolerable side effects are noted with systemic medications or when systemic pain medications provide inadequate relief or there is concern for respiratory depression with increasing doses. Timing of interventional therapies and risks of interventional versus oral therapies is controversial, but certain studies have found fewer side effects with neuraxial techniques as compared to oral medications.

Anesthetic Approaches Include Peripheral Nerve Blocks

Celiac Plexus Block

Technique: two needles at L1 level 5–7 cm from midline; right needle advanced with retrocrural or splanchnic approach or anterocrural/transcrural approach (through the diaphragm); left needle—anterocrural approach necessitates transaortic advancement (or advancement anterolateral to aorta via CT guidance); alternatively, supine technique is transabdominal advancement via CT or ultrasound guidance.

Indications: upper abdominal cancers, including pancreatic cancer, with visceral pain component.

Risks

- Injection into the peritoneum, organ, or blood vessel rather than plexus
- Orthostatic hypotension (most common in retrocrural approach)—must rule out retroperitoneal hemorrhage before making this diagnosis
- Retroperitoneal hemorrhage—backache, hypotension, decreased hematocrit; necessitates surgical consult
- Transient diarrhea (most common in anterocrural approach)—treat with aggressive hydration
- Abdominal aortic dissection (most common with anterocrural approach)
- Paraplegia—due to spasm of lumbar segmental arteries (do not use alcohol neurolysis if aortic atherosclerosis)

Superior Hypogastric Plexus Block

Technique: two needles at L4–L5 level 5–7 cm from midline, directed medially for needle tips to

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lie anterolateral to L5–S1 interspace. If blood aspirated or fluoroscopy depicts intravascular injection, iliac vessels may have been traversed, in which case transvascular approach may be used.

Indications: pelvic pain with significant visceral component.

Risks

- Retroperitoneal hematoma
- Foot ischemia secondary to iliac artery plaque embolization

Ganglion Impar Block

Technique

- Left lateral decubitus position: needle into the anococcygeal ligament, bent to facilitate directing needle tip posteriorly to the sacrococcygeal junction
- Prone for transcoccygeal approach: needle through the sacrococcygeal ligament, advance until posterior to the rectum

Indications: perineal pain with visceral component.

Risks: none have been reported.

Interventional Radiologic Approaches

Neuraxial techniques for pain control include medication administration through epidural tunneled catheters, intrathecal catheters, or intraventricular catheters.

Medications

Opioids—infusion of opioids into the neuraxial space is useful for patients who require further pain control whose oral opioid dose escalation is limited by side effects. Oral to intrathecal morphine potency is 1:300, and oral to epidural morphine potency is 1:30:

- Alpha-agonists
- Baclofen
- Ziconotide—selective voltage-gated calcium channel blocker, inhibits central release of pro-glutamate, calcitonin, and substance P; monitor for central nervous system side effects

Neurolysis and neurosurgical destructive techniques: reserved for intractable pain not responding to local anesthetic or last means of pain control for end of life.

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Cancer Pain: Palliative Care

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Niharika Saw

- Palliative care: definition and scope, frequency of pain and multiple sites of pain, barriers to treatment, and importance of development of evidence-based practice in the management of cancer pain
- Benefit to burden ratio: variation according to stage, ethical issues of physician-assisted suicide and euthanasia, and doctrine of double effect and importance of intent

Palliative care is the multidisciplinary approach to care for a patient whose malignancy is not responsive to curative treatment. The fundamental thought process of this approach is that dying is a natural process, and every attempt is made at improving quality of life. Goals include control of pain as well as social, emotional, psychological, and spiritual support to improve quality of life for patients and their families. Palliative care is most beneficial when initiated early rather than during the last days or weeks of life. Assessment of pain at the end of life is similar to general assessment of pain, an important difference being inclusion of psychosocial assessment. Fears, concomitant depression or anxiety, religious and spiritual dimensions, and pain's effect on the patient and caregiver are all addressed.

End-of-Life Pain Syndromes

Intractable neuropathic pain: Interventional therapies are beneficial. In terms of pharmacologic therapy, lidocaine infusions are useful for intractable neuropathic pain, but severe hepatic or cardiac dysfunction may be contraindications to local anesthetic infusions secondary to potential toxicity. Dexamethasone, methadone, antidepressants, and anticonvulsants have been of benefit.

Malignant bone pain: Dexamethasone, bisphosphonates, radiation therapy, orthotics, and physical therapy are used to treat malignant bone pain. High doses of opioids or sedation are sometimes used for movement-associated bone pain.

Opioid neurotoxicity: Symptoms include myoclonus, seizures, delirium, and hyperalgesia. Treatment includes adding a benzodiazepine, opioid rotation, and reducing dose of current opioid. Switching to intrathecal opioids should be considered.

Malignant intestinal obstruction: Palliative surgery is sometimes beneficial, as are nonoperative measures such as octreotide, nasogastric suctioning, and venting gastrostomy. Dexamethasone for nausea and scopolamine for secretions are of benefit as well.

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End-of-Life Symptoms Besides Pain

Depression: Physical symptoms of depression such as fatigue and anorexia are often mistaken for symptoms of the cancer alone. Psychological symptoms pointing to the correct diagnosis include loss of self-worth, hopelessness, and in the more severe form, suicidal ideation. Patients should be asked about depression during palliative care visits. Selective serotonin reuptake inhibitors may take 2–4 weeks for onset, but other antidepressants such as serotonin-norepinephrine reuptake inhibitors, mirtazapine, and bupropion have faster onset of action. Methylphenidate or other stimulants with their rapid onset of action may be more beneficial for patients with days to weeks of life remaining as addiction and withdrawal is not of concern.

Anxiety: Anxiety in cancer patients can be secondary to medication use (bronchodilators, neuroleptics, corticosteroids, and others), inadequate pain control, pheochromocytomas, hypoxia, dyspnea, thyroid conditions, sepsis, and hypoglycemia. Benzodiazepines are used for treatment, and haloperidol has been used with success for immediate effect.

Dyspnea: "Air hunger" is a common phenomenon at the end of life. Non-pharmacologic measures include bedside fans and psychological support. Pharmacologic measures include small doses of opioids and short-acting benzodiazepines.

Airway secretions: Positioning patient on his or her side and stopping unnecessary intravenous fluids and enteral feedings are first measures. "Death rattle" is often more disturbing to family than patients themselves. Glycopyrrolate (intravenous, subcutaneous, or oral) is the preferred anticholinergic due to fewer central symptoms. Scopolamine patches are a second option for patients being managed at home.

Nausea: Opioid rotation for opioid-induced nausea may be used. Nausea may be secondary to cancer treatment or cancer itself. To treat the latter, therapies that may improve symptoms include haloperidol, oral or rectal prochlorperazine, dexamethasone, scopolamine, meclizine, and ondansetron.

Seizures: IV or subcutaneous lorazepam may be used to treat and prevent seizures for days. For patients who cannot take oral medications and are being transitioned at home without intravenous access, rectal diazepam and phenobarbital are options.

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Cervical Radicular Pain

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Andrew I. Gitkind and Karina Gritsenko

Anatomy

- Bony anatomy—made up of seven vertebral bodies and the occiput (insert diagrams):
  - The first two vertebrae are anatomically quite different from the remaining five cervical vertebrae; this is the only section of the spine vertebrae that may differ significantly.
  - C1 (atlas) does not have a body—it is a bony ring.
  - C2 (axis) body extends superiorly, articulating with posterior aspect of the anterior arch of C1, kept in close approximation by transverse ligament.
    - There is no intervertebral disk between C1 and C2.

See chapter 121 for full description of cervical bony anatomy.

- Neural anatomy:
  - There are *eight* cervical nerve roots.
  - This anatomy is different from the anatomy of exiting nerve roots of the thoracic and lumbar spine in multiple ways.
    - C2–C7 exit *above* their corresponding vertebrae—this is the only section of the spine where this occurs.
    - C8 exits between C7 and T1 and is the only nerve root in the body where there is no corresponding named vertebral level.

Differentiation of Radicular from Somatic Pain (Table 118.1)

History Taking and Neurologic Examination: Role and Limitations

- The most important part of diagnosis is the history and physical exam.
- The patient may report neck pain, upper extremity pain, or both:
  - Radiating pain typically radiates in a dermatomal pattern, not diffuse or somatic.
  - Radicular pain described as "electric," "lancinating," "burning," etc.
    - Pain typically increases in positions which reduce the foraminal area such as cervical extension.

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Table 118.1 Differentiation of Radicular from Somatic Pain

Symptom	Radicular pain	Somatic pain
Pain description	Electric, lancinating, lightning bolt	Achy, deep
Paresthesias	Present	Absent
Distribution	Dermatomal	Diffuse

  - There is typically associated numbness/tingling.
  - Sensory loss.
  - Weakness.
- History may reveal acute onset or aggravation of symptoms from sneezing, lifting, coughing, or other Valsalva-type maneuver.

Medical Imaging: Reliability and Validity

- X-ray
  - Best to show bony architecture and alignment of the cervical spine.
  - AP: best to study uncovertebral joints and their relationship to neural foramina. These joints lie just medial to the foramen, so in the setting of hypertrophy, this may contribute to foraminal stenosis.
  - Lateral: Shows degree of cervical lordosis or amount of straightening. Shows disk space height. Loss of disk height may also lead to a loss of foraminal space, potentially leading to radicular symptoms. Also best to show posterior element hypertrophy, which also may contribute to foraminal narrowing.
- MRI
  - Best imaging modality to demonstrate soft tissue structures.
  - Most common studies will include T1, T2, and commonly STIR (short-tau inversion recovery) sequences.
  - Excellent imaging modality to evaluate the nerve roots as they traverse the foramen.
- CT
  - Better outlines the bony elements of the spine than neural elements. Best option in a setting where MRI is not available or contraindicated.
  - Axial images through the neural foramen best to show foraminal stenosis as well as the relation of the nerve root itself to the surrounding structures.

Electrodiagnostic Studies

- Consist of motor conduction, sensory conduction, and needle EMG studies.
- Electrodiagnosis can help distinguish between acute, subacute, chronic, and non-radicular symptoms.
- Abnormal spontaneous activity in at least two muscles innervated by the same nerve root indicates a radiculopathy.
- Greater than 50 % loss in compound muscle action potential indicates a significant axonal loss.
- Sensory nerve action potential (SNAP) is typically normal in the setting of cervical radiculopathy.
- EMG may help identify a peripheral cause of symptoms if not a cervical radiculopathy.

Commonly Used Interventions

- Physical therapy:
  - Works to strengthen the cervical stabilizing musculature, providing increased support to the cervical spine.
  - Pain-relieving modalities may help to reduce pain. This may include manual or mechanical cervical traction which could increase foraminal size, reducing radicular pain from foraminal narrowing.
- Medications:
  - First-line agents include:

- Neuropathic pain medication
  - Antiepileptics
  - SSRIs
  - SNRIs
  - TCAs
- NSAIDs

- *See Medication chapter for full description.*
  - Injections
    - *See Injection chapter.*

Surgical Treatment: Indications and Use

- Surgical evaluation or intervention may be appropriate in the following instances:
  - In the setting of failure of conservative management
  - When muscle weakness is elicited on physical exam

Neck Pain

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Andrew I. Gitkind and Karina Gritsenko

Introduction

Neck pain is one of the leading causes of pain and disability in the US. Its frequency and intensity can result in both acute and chronic pain which can disrupt daily living. Neck pain can restrict recreational activities, lead to sleep disturbances, as well as result in loss of work and sometimes disability.

Anatomy

The cervical spine is made of seven vertebral bodies and the occiput. C1, also known as "*atlas*", is morphologically different from the rest of the vertebral bodies in that it is only vertebra in the spine that does not have a body. Instead, C1 is a bony ring. What developmentally would have been the body of C1 is known as the "*dens*" and is a cephalad bony projection extending from the body of C2, also known as "axis". The dens sits posterior to the anterior arch of C1 and is held in place by the transverse ligament.

The remainder of the cervical vertebrae, C3–C7, are all similar in structure. They are separated anteriorly by the intervertebral disc. Note that with no body of C1, there is no intervertebral disc between C1 and C2.

The cervical spine is the only section of the spine with bony articulations between vertebral bodies. The uncinate process is a superior projection of the lateral aspect of the cervical vertebral body, which articulates with the vertebral above at the *joint of lushka*.

Ligaments: The *anterior longitudinal ligament (ALL)* runs along the anterior surface of the vertebral column and is a broad, strong ligament originating at the atlas and continuing to the sacrum. Its deepest fibers bind with the intervertebral disc as it passes adjacently. The *posterior longitudinal ligament (PLL)* extends from the axis to the sacrum. It is proximally continuous with the tectorial membrane. It lines the posterior aspect of the vertebral bodies, forming the anterior border of the spinal canal. Like the ALL, its innermost fibers also blend with the intervertebral disc as it passes each level.

The posterior ligaments include the *ligamentum flavum (LF)*, the *interspinous ligament (ISL),* and the *supra-spinous ligament (SSL)*. The LF is

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highly elastic and lies between adjacent laminae and is typically NOT connected at midline. The ISL extends obliquely between adjacent spinous processes and the SSL is a thin ligament running posteriorly to the tips of the spinous processes. It originates at the occipital protuberance and provides significant contribution as a stabilizer of the head and neck.

Intervertebral Disc: located between all cervical vertebral levels except C1 and C2. It serves as a shock absorber, which over time can deteriorate and become a pain generator. It is comprised of an inner nucleus pulposus and a cartilaginous outer ring, the annulus fibrosus. The annulus fibrosus is composed of multiple parallel rings of collagen fibers called lamellae. The outer rings attach to the adjacent anterior and posterior spinal ligaments, while both inner and outer rings attach to the adjacent vertebral bodies. The nucleus palposus is composed of two fiber types, collagen fibers and elastin fibers. The functional purpose of the nucleus is to distribute loading forces exerted on the spine.

Musculature: Cervical musculature is more complex and intricate than in other areas of the spine, given the excessive mobility and need for stabilization of the cervical region. Muscle-related pain is one of the most common causes of neck pain (Tables 119.1 and 119.2).

Table 119.1 Muscles of the neck

Posterior muscles	Anterior muscles
Superficial	Platysma
Trapezius	Sternocleidomastoid
Levator scapulae	Hyoid muscles
Intermediate	Scalenes
Splenius capitus	Longus colli
Splenius cervicis	Longus capitus
Deep	
Iliocostalis cervicis	
Longissimus cervicis	
Longissimus capitus	
Spinalis cervicis	
Semispinalis capitis	
Semispinalis cervicis	

Table 119.2 Somatic vs. radicular pain

	Somatic	Radicular
Pain radiation	May or may not radiate May radiate in a non-dermatomal pattern	Radiates in a dermatomal distribution
Description	Achy, intermittent	Sharp, lancinating, electric, 'lightening bolts', associated with numbness or tingling
Exam findings	Pain may be reproduced by local palpation	Radicular symptoms may be reproduced by Spurling's maneuver
Neuro exam	No numbness, tingling, weakness	May be associated with focal weakness

Use of Conventional Imaging

Imaging of any type typically is not indicated in the immediate aftermath of the onset of pain unless there was preceding trauma, the severity of pain is beyond expected, or if there is an associated change in the neurologic exam.

X-Ray: used to evaluate for mal-alignment or degenerative spondylytic changes. Also, it can identify straightening (reversal) of normal cervical lordosis, which may indicate local muscles spasm. Post trauma, x-rays can help to identify any fracture or dislocation.

MRI: does not expose patient to any radiation. *This is the best imaging modality* to evaluate the neural structures of the cervical spine. Can evaluate both central canal and foraminal stenosis. Also, good to evaluate for muscle or soft tissue injury.

CT Scan: indicated in the post-trauma setting to evaluate for any bony pathology or dislocation. May be used to evaluate the neural structures if MRI is not an option.

CT Myelography: Performed by instillation of water-soluble contrast medium into the subarachnoid space, followed by CT scan. Used when MRI is not available to evaluate for central canal stenosis, disc herniation, or spinal cord compression.

Invasive Tests

See chapter on invasive procedures.

Nonsurgical Intervention

In the setting of neck pain, a quick return to function and work is recommended. Prolonged periods of rest have been shown not to be beneficial and greatly reduce the likelihood of return to work. Most axial neck pain from sprain/strain injuries will improve gradually over the course of weeks following pain onset. In the acute phase, the cervical spine should *not* be immobilized.

The use of non-steroidal anti-inflammatories can be helpful as patient increases their functional level.

Physical Therapy can be very helpful as most neck pain is at least in part related to myofascial pain. Components of a comprehensive PT program will include strengthening, gradual increase in range of motion, and pain relieving modalities when indicated. In certain conditions, manual cervical traction may be helpful in reducing pain from muscle spasm or nerve root compression. Overall, physical therapy will focus on postural training, improvement in cervical spine flexibility, and strengthening of the cervical musculature.

Lumbar Radicular Pain

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Erik Romanelli, Amaresh Vydynathan, and Karina Gritsenko

Anatomy

- Lumbar spine consists of five distinct lumbar vertebrae connected by paired facet joint articulations located between the pedicular processes.
- Intervertebral foramina formed by notches in articular processes of adjacent pedicles of adjoining vertebrae; disk is anterior and medial to the foramen.
- L1–L5 roots descend from conus medullaris (termination of adult spinal cord, between T12and L1 vertebral levels)—exit at the neural foramina of their respective level.
- Distal to intervertebral foramen, dorsal rootlets (somatic sensory input) and ventral rootlets (somatic motor fibers) join to form mixed spinal nerve, which divides once more:
  - Dorsal rami = innervation to para-spinal muscles and their overlying skin
  - Ventral rami = nerve fibers to the lumbosacral plexus (sensory and motor to trunk and legs)

Causes and Differentiation Between Low Back Pain and Somatic Referred Pain

- Radiculopathy defined by objective neurologic signs (i.e. loss of sensation and/or motor activity, weakness, muscle wasting, loss of reflexes).
- **Radicular *pain*** typically is evoked by ectopic discharges arising from dorsal nerve root or its ganglion, distributing painful sensations along the length of its dermatomal innervation.
  - *Etiologies*: *compression or irritation of spinal nerve roots* (numerous causes including disc herniation, formation of osteophytes, degenerative lumbar spondylosis, scar tissue from previous spinal surgery, foraminal stenosis, thickening of adjacent ligaments),

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neoplasms, inflammatory conditions (i.e. ankylosing spondylitis, Paget's disease), and *infectious disorders* (herpes zoster, Lyme, spinal epidural abscess).

- **Somatic referred pain** and **(non-radicular) lower back pain** both do *not* involve nerve root stimulation, and hence have no associated neurologic signs.
  - *Somatic referred pain*: arises following noxious stimulation of nerve endings in spinal structures (i.e. discs, facet joints)—"dull, aching, gnawing" in character.
  - *Non-radicular lower back pain*: nociception localized to the spine and paraspinous regions and do not necessarily involve radiation to the legs.

History and Neurologic Examination: Reliability, Validity, and Limitations

- Patients describe "sharp, shooting, lancinating, stabbing, shock-like sensation" affecting the associated dermatomes in one or both lower extremities, more-so of an "unpleasant" sensation distinct from classic nociceptive pain.
- Neurologic exam should assess lower extremity motor strength, sensation, and reflexes.
  - *Tell-tale Sign*: Pain on straight leg raise test (Lasegue's sign)—particularly sensitive for detecting radiculopathy due to disc herniation.
  - *Limitation of physical exam*: Patterns of lumbar radicular *pain* cannot be distinguished from one another unless they occur in combination with radiculopathy— must look for patterns of *numbness* or paresthesias along dermatomal distributions to best estimate at which lumbar segment there is likely nerve involvement.
- Also, one should elicit history for symptoms suggestive of neoplasm (fever, weight loss, chills) or neurosurgical emergency (i.e. cauda equine syndrome—bowel and/or bladder incontinence, leg weakness, and saddle anesthesia).

Medical Imaging and Electrodiagnostic Testing: Indications and Validity

- If radicular pain and/or radiculopathy is suspected, but patient is neurologically intact and has a low risk for neoplastic, infectious, or inflammatory etiologies → immediate diagnostic testing is *not* necessarily warranted, can implement 3–6 weeks of conservative therapy.
  - Proceed to immediate MRI if: neurologic deficits are progressing, cauda equina is suspected, or there is clinical suspicion of malignancy, infection, or inflammatory disorders.
    - If MRI is contraindicated (i.e. if patient has pacemaker or spinal cord stimulator), a CT myelogram may be an appropriate.
  - If conservative therapy fails, or there is onset or further progression of neurologic symptoms, further diagnostic testing with MRI can be utilized (especially if considering surgical intervention).
- MRI highly accurate for identifying abnormalities which may otherwise put patient at risk for developing lumbar radicular pain, particularly disk herniation.
- Normal MRI findings + persistent unexplained leg pain → may benefit from electromyography (EMG).
  - EMG performed in combination with nerve conduction studies (NMS) may localize symptoms to specific nerve root levels, measure severity of radiculopathy, and rule out alternative diagnoses such as neuropathy or plexopathy. Yield generally lower in patients with only pain or sensory loss as sole manifestation of radiculopathy.

Natural History and Relevance to Management

- Majority of patients have a self-limited course—symptoms appear to resolve in weeks to months, conservative approach in initial weeks to months often appropriate.
- Suggested that over 75 % of patients treated with nonsurgical options (even those experiencing neurologic symptoms) could expect complete or near-complete relief.
- Mainstay therapies include NSAIDs and/or acetaminophen, simple activity modification—aimed to help through the acute course and return to functional quality of life.

Commonly Used Interventions: Evidence-Based

- *Epidural steroid injections*: goal of providing short-term to moderate-term analgesia for acute radicular pain—may often require a series of three injections; efficacy is well documented. *See Chap. 61 (interlaminar epidural injection) and Chap. 62 (transforaminal epidural injection) for additional information.*
- *Physical therapy*: often attempted for patients with persistent mild to moderate symptoms; evidence of effectiveness generally lacking.
- *Other conservative measures*: patient education (i.e weight management, avoiding activities which exacerbate symptoms), chiropractic treatment, heat modalities, local anesthetic nerve blocks, and medications such as tricyclic antidepressants, low-dose narcotics, and muscle relaxants may be used.

Surgical Treatment: Indications and Efficacy

- Generally recommended that patients without severe neurologic deficits be initially trialed with non-surgical therapies.
- Consider surgical intervention if neurologic deficits progress and/or severe lumbar radicular pain refractory to conservative measures.
- Surgical options vary depending on presumed etiology of lumbar radicular pain; however, most geared towards nerve decompression and/or spinal stabilization (i.e. interbody fusion, cage implantation, microdiscectomy, laminectomy).
- May indeed result in faster relief of radicular symptomology and earlier return to function; however, long-term results appear to be similar when compared to patients receiving more conservative managements.
- Surgical outcomes could be expected in approximately 80–95 % of patients with clinical radiculopathy and correlating imaging. Recurrence rates reported at 2–12 %. Incidence of serious complications very low (<2 %).

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Low Back Pain

121

Kelly Yan Chen, Naum Shaparin,
and Karina Gritsenko

Anatomy

- Lower back consists of the nerves, spine, muscles, and ligaments.
- Each of these components, along with referred visceral diseases, can contribute to low back pain.

History and Physical Examination

Taking a detail history and physical exam is essential to determining the origin of low back pain.

- Patients can complain of *radicular pain*, sciatica (a form of radicular pain), or *radiculopathy*.
- Patient can also complain of *referred back pain*, where visceral diseases (prostatitis, pyelonephritis, pancreatitis, abdominal aneurysm, and many more) and non-mechanical processes (neoplasia, infection, inflammatory arthritis, and many more) can lead to lower back pain.
- *Axial skeletal pain*: Pain is localized to and is of origin from the lower back.
- A detailed history and work up is needed to rule out radicular pain, radiculopathy, and referred pain so that patients can be appropriately treated for axial skeletal back pain.

History

History gathering should include some of the differentials for axial skeletal back pain, which includes lumbar strain, degenerative diseases, spondylolisthesis, herniated disc, spinal stenosis, osteoporosis, fracture, congenital diseases, spondylolysis, and facet joint asymmetry, as well as diagnoses not related to the spine itself [1].

Physical Examination

Physical examination includes inspection and palpation of the spine, neurological examination of nerve roots with sensation and motor function,

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straight leg test for radiculopathy, and other maneuvers for detecting malignancy or infectious processes.

Imaging and Tests

- Given the favorable recovery of back pain, imaging with x-ray, MRI, or CT is typically not necessary unless the back pain does not resolve after 6–8 weeks [2].
- If red flags (cauda equina syndrome, malignancy, infection) are present and require immediate management, imaging with MRI or CT is recommended [3].
- Joint nerve blocks, such as lumbar facet joint injections, have been shown to diagnose effectively 89.5 % of patients and are able to provide pain relief in 80 % of patients [4, 5].
- Diskography is a diagnostic technique for disc herniation where the injection of a contrast medium into the nucleus pulposus reproduces pain [5].
- Lastly, epidural steroid injections of an isolated nerve can be useful to diagnose or treat patients with disc herniation or spinal stenosis [5].

Prognostic Risk Factors and Psychosocial Factors

- The majority of low back pain should resolve within 4–8 weeks. One study showed that as many as 90 % of patients complaining of back pain stop consulting physicians about their symptoms after 3 months [6].
- Studies have also shown that patients who participate in hard physical work, frequent lifting, and postural stresses are more likely to have disk degeneration, low back pain, and sciatica [7].
- Obesity, smoking, and poor health can increase the risk of low back pain [7].
- Worst prognosis is associated with those who have taken sick leave for low back pain, high disability level, and lower education [8].
- Up to 25 % of patients can get recurrence of low back pain in 1 year [9].

Interventions: Medical and Surgical

Medical Therapies

- First-line treatments have traditionally been NSAIDs for pain relief as well as a muscle relaxant [10, 11].
- If suited, the patients can also be referred for physical therapy and be recommended to use warm compression. Patients are advised to stay active and decrease bed rest.
- If these therapies fail and the patient is still complaining of axial skeleton or localized back pain, pain specialists can perform a trigger point injection for low-back strain and/or a medial branch neurotomy to block pain signals carried by facet joints [12].
- If both of these measures fail, the patient should be referred for surgical assessment and intervention.

Surgical Therapies

The type of surgical procedures offered is dependent on the etiologies of back pain.

- Discectomy for a herniated disc.
- Decompressive laminectomy for spinal stenosis, kyphoplasty.
- Vertebroplasty for compression fractures.
- Arthrodesis for spinal fusion.

Surgical and invasive interventions are last step treatment options and require patients to undergo intensive rehabilitation.

Multidisciplinary Therapy

There are multitudes of non-medical therapies for back pain that are becoming more popularized. Patients will often visit chiropractors and acupuncturist, do yoga, tai chi, and take herbal remedies. As long as the patients do not have contraindications to these modalities, like anatomic concerns with spinal manipulation for chi-

ropractors or medication interactions for herbal remedies, these therapies have been shown to improve low back pain [13–16].

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Degenerative Lumbar Spinal Stenosis

122

Jay M. Shah, Karina Gritsenko, and Sayed E. Wahezi

Brief Overview, Definition, and Epidemiology of Degenerative Lumbar Spinal Stenosis (dLSS)

- dLSS is a clinical definition which describes a small spinal canal diameter commensurate with standing and walking limitations due to back and/or leg pain.
- Stenosis is due to hypertrophy of lateral recesses, circumferential disc bulge, ligamentum flavum (LF) hypertrophy, or a combination of any of these.
- Symptoms are thought to result from compression-induced ischemia of cauda equina vaso nervosum.
- When symptomatic, can cause substantial disability, limit daily activities, and degrade quality of life. The course of disease can be unpredictable and vary with flares and asymptomatic periods over time.
- About 1.2 million Americans suffer from dLSS. This number is thought to double by 2024, due to an aging population. However, despite this high prevalence, very little is known about the epidemiology of dLSS.
- LSS is the most frequent indication for spine surgery in patients older than 65 years of age and is associated with a threefold higher risk of experiencing LBP.

Common Clinical Presentation

- The symptom most commonly recognized with dLSS is neurogenic claudication (NC), also referred to as pseudo-claudication. NC refers to leg symptoms that encompass the buttock, groin, thigh, and can also radiate down the legs to the feet.
- Patients will complain of bilateral leg pain, with or without back pain, which is worse with standing or walking. Vascular compromise decreases oxygen supply in the cauda

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equina during walking, thus increasing leg pain.
- As lumbar lordosis/extension increases in the standing position, the severity of stenosis increases with the constriction of the cauda equina and its associated vasculature.
- In the sitting position or when the trunk is flexed, mechanical compression of these structures is reduced and symptoms improve.
- Differentials to consider are:
  - *Vascular Claudication (VC)*: similar activity exacerbates leg pain in both conditions. However, VC is more likely to be associated with muscle atrophy, hair loss, and other signs of vascular disease. VC can be confirmed with lower extremity ultrasound or ankle-brachial index (ABI) studies.
  - *Lumbar disk herniation*: associated radicular pain can mimic neurogenic claudication that is worsened with walking and standing. Of note: pain from lumbar disk herniation is usually unilateral and localized to the distribution of the affected nerve root(s).

Imaging and Diagnostic Pearls

- A major difficulty in performing any epidemiologic analysis of LSS is the absence of universally accepted diagnostic criteria.
- Studies in asymptomatic populations have found that up to 20 % of subjects had imaging findings consistent with spinal stenosis.
- The gold standard imaging modality is T2-weighted MRI, which allows for assessment of the central canal and accurate measurement of the thickness of LF.
- A spinal canal AP diameter of 10 mm is considered absolute stenosis and 12 mm is suggestive of relative stenosis.

Conservative Management of dLSS

- Conservative measures typically consist of multidisciplinary treatment programs including medication management, physical therapy, and lumbar epidural steroid injections.
- NSAIDs are the mainstay of pharmacologic therapy, but must be used with caution in the elderly due to associated hypertension, renal, and gastric toxicity. Gabapentin, methylcobalamin, and prostaglandins may also improve walking distance due to symptoms of LSS.
- Flexion-based exercises (stationary bicycle, inclined treadmill) increase the cross-sectional area of spinal canal to improve spinal cord microcirculation. These exercises are better tolerated by patients and help to promote weight loss and cardiovascular fitness.
- Aquatic therapy strengthens hip flexors and hamstrings, while also strengthening the abdominal core and trunk musculature. There is also decreased axial load on the spinal column.

Non-operable vs. Operable Intervention

- dLSS may progress past the point of moderate symptom severity with significant neurogenic claudication impairing participation in therapy. This can exacerbate symptoms in an already deconditioned individual.
- Lumbar epidural steroid injections (LESI) are the most common conservative intervention, and randomized trials have demonstrated clinical efficacy and cost-effectiveness of LESI in managing pain from central spinal stenosis.
- Preliminary evidence suggests that procedures such as percutaneous image-guided lumbar decompression (PILD) and implantable interspinous spacers are safe interventions designed to address this population.
- When pain and neurologic deficits progress, surgical decompression improves symptoms in the majority of patients, but is associated with higher morbidities such as dural puncture, excessive intra-operative bleeding, and motor weakness.

Special Considerations in Contemporary Management of dLSS

- An effective assessment method for dLSS is one that examines symptoms, quality of life, and healthcare economics as key assessment factors.
- Treatment of dLSS can be clinically challenging and requires careful assessment of the patients' symptoms, physical examination, and correlation of imaging results when considering invasive therapies.
- As healthcare costs rise, patients and those paying for care request for accountability, clarification, treatment efficacy, and proof of the appropriateness of expensive medical care treatments.

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Musculoskeletal Pain

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Epidemiology

- Common in the general population and increases with age. One in five adults is diagnosed with arthritis and 60 % of those over 65 years have joint symptoms.
- Major cause of disability.
- Osteoarthritis and rheumatoid arthritis are the two most common joint disorders.
- Women have a higher prevalence then men.

Anatomy and Physiology

- *Basics*: collagen (tensile strength), elastin (elasticity), proteoglycans (water).
- *Muscle*: contractile unit composed of actin, myosin fibers, and myocytes. Type 1 slow twitch vs. type 2 fast twitch.
- *Tendon*: fibrous connective tissue composed of type 1 collagen and tenocytes that connects muscle to bone. Enthesis is the site of attachment into the bone and frequent site of a tear.
- *Bone*: rigid connective tissue composed of osteoclasts (absorption), osteoblasts (deposition), type 1 collagen, and calcium phosphate (hydroxyapatite). Periosteum is the outer covering rich in nociceptive fibers.
- *Cartilage*: flexible connective tissue composed of type II collagen, and chondrocytes. Avascular and aneural.
- *Types of Joints*: Diarthrosis (synovial) knee, Aphiarthrosis (fibrocartilagenous) intervertebral disc, Synarthrosis (fibrous) interosseous memebrane.

Mediators of Inflammation, Tissue Destruction, and Repair

- *Acute Phase*: Platelets (initiators), Neutrophils (minutes), Mast cells (histamine-mediated vasodiation), Macrophages (hours-days).
- *Chronic*: Macrophages (phagocytosis), Fibroblasts (collagen synthesis).
- *Inflammatory factors*: (also activate afferent sensory nerves)—TNF-A, IL-1, ILD-6, Arachidonic acid.
- *Metalloproteases*: degrade extracellular matrix.

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Molecular and Cellular Basis of Immunity and Autoimmunity

- *Antigen*: any substance that causes the adaptive immune system (B/Plasma cells) to produce antibodies.
- *Major Histocompatibility Complex (MHC)*: bind peptides from pathogens and display them to T-cells. MHC 1 (found on all nucleated cells) vs. MHC 2 (found on antigen-presenting cells, B-Cells).
- *T-cells*: Cytotoxic (CD8+) destroy virus-infected and tumor cells vs. Helper (CD4+) amplify the active immune response.
- *Human leukocyte antigen* (HLA) is a type of MHC found on human cells. HLA-B27 is associated with ankylosing spondylitis.
- *Compliment system*: part of the innate immune response that assists the adaptive immune system. Classical (C1 activation by antibodies) vs. Alternative (low level C3 activation).
- *Psychoneuroimmunology*: Psychological states, hypothalamic-pituitary-adrenal (HPA) axis, and the sympathetic nervous system can suppress the immune system.

Neurophysiology

- Primary afferent sensory neurons (nociceptors) are found in skin, muscle, joints, viscera, dura, faschia, and adventitia of blood vessels.
- Have receptors for glutamate, opiates, substance-P, somatostatin, and vanilloids.
- Divided into small unmyelinated C-fibers (slow) vs. large myelinated Aδ fibers (fast).
- Primary sensory afferent cell bodies found in the dorsal root ganglia (DRG).
- Synapse with secondary sensory afferents in the dorsal horn to form the spinothalamic tract.
- Interneurons can have a modulatory excitatory (glutamate-mediated) and inhibitory (GABA-mediated) effect at the spinal level.
- Second-order neuron types include wide dynamic range (mechanical, thermal and chemical input), high threshold (HS), and low threshold.
- Descending inhibitory pathways from the rostral ventromedial medulla (RVM) provide further inhibition via serotonergic and noradrenergic neurons.

Psychosocial Aspects

- All phases of pain and treatment responsiveness are influenced by personal, social, and cultural constructs.
- Depression is the most common psychiatric disorder associated with chronic pain.
- Physical, sexual, or emotional trauma resulting in post-traumatic stress disorder reduces the success of invasive interventions.
- Sleep deprivation is common and can amplify the awareness of pain.

Classification and Clinical Characteristics of Musculoskeletal Diseases

- *Inflammatory joint/muscle diseases* characterized by an auto-immune response (e.g. Rheumatoid arthritis, polymyositis) often systemic and involves multiple joints.
- *Non-inflammatory joint/muscle diseases* characterized by trauma and degeneration (e.g. osteoarthritis, meniscal tear).
- *Soft tissue or myofacial disorders* characterized by central neural sensitization (e.g. Myofacial pain syndrome, fibromyalgia, chronic fatigue syndrome).
- *Overuse injuries*: Physeal/growth plate and apophyseal/tendon insertion in children vs. tendinopathies and stress/compression fractures in adults.

Assessment of Activity and Severity of Rheumatic Disease

- At each office visit, assess for joint deformity, swelling, range of motion, strength, tenderness, and function/mobility
- Laboratory analysis (CBC. BMP, ESR, CRP, ANA, RF, anti-CCP)

- Imaging (CT, MRI, US, XR) to look for erosions
- Functional assessment—Activities of daily living (ADL's), arthritis impact measurement scales (AIMS), health assessment questionnaire (HAQ)

Treatment and Rehabilitation of Musculoskeletal Pain/Disability

- Treatment requires a multidisciplinary team approach which can include a psychologist, therapists, patient education, family, and other doctors.
- Start with the most conservative treatments including therapy and medications before advancing to invasive modalities such as injections and surgery.
- Chronic musculoskeletal disorders may be associated with widespread pain beyond the initial site of injury indicating a central neural sensitization disorder.

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Muscle Pain and Myofascial Pain 124

Naum Shaparin, Diana M. Nguyen,
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Myofascial Pain

- A common muscular disorder caused by multiple myofascial trigger points (MTrPs).
- MTrPs: The most tender or hyper-irritable foci in a band of skeletal muscle fibers which can cause point tenderness or referred pain when compressed.
- Active MTrPs: cause pain or referred pain either spontaneously or on palpation.
- Latent MTrPs: similar to active MTrPs, but do not cause spontaneous pain.

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Pathophysiology

"Integrated hypothesis" has three features:

1. excessive acetylcholine release
2. sustained sarcomere contraction
3. release of sensitizing substances

The environment surrounding an active MTrP is very acidic, which activates nociceptors to cause pain and down-regulates AChE. This increases Ach activity, which causes sustained sarcomere contraction and increases muscle fiber tension. Increased tension leads to ischemia and hypoxia, which stimulates the release of sensitizing substances, leading to more pain and increased Ach release. Through this cyclical process, nerves within these mysofascial bands become more sensitized and pain occurs at lower pressures.

Symptoms

- Compression of point of maximal tenderness within a muscle causes pain, referred pain, or local twitch response
- Palpable/visible band or muscle knot

Risk Factors

- Acute trauma or repetitive micro-trauma
- Overextension of a muscle

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- Sedentary lifestyle
- Poor posture
- Sports/occupational injuries
- Systemic or connective tissue disease

Diagnosis: Myofascial pain syndrome is primarily diagnosed clinically through history and physical exam, although there are novel techniques (ultrasound) being used as well.

Physical Exam: MTrPs identified when compression of a point of maximal tenderness induces pain over the point, referred pain, or a local twitch response. These points are visualized or palpated as taut "bands" or "knots" of muscle fibers.

Pressure Algometry: A hand-held pressure meter delivers a force with a 1 cm^2 rubber disc over a trigger point and measure the pain threshold.

Ultrasound: While a vibratory stimulus is applied to the muscle of interest, ultrasound measures the shear wave speed. Shear wave speeds in active MTrPs are higher than in normal tissue.

Clinical Management

Trigger Point Injections: Injections can be performed with an agent or without any substance (dry needling). Both methods cause muscle fiber relaxation and lengthening, ultimately disrupting the MTrP and alleviating pain.

– *Drug injection* causes vasodilation, disrupts fibrotic tissue, and can deliver an anesthetic.
– *Dry needling* physically disrupts fibrotic tissue that causes nerve entrapment, thus allowing inflow of blood which dilutes and removes nociceptive substances.

Injection Agents:

- Saline, steroids, local anesthetic
- Example: 50/50 solution of lidocaine and 0.9% saline
- Do not use long-acting anesthetics (e.g., bupivacaine) that can be myo-toxic
- Do not use Botulinum A toxin, which can cause motor dysfunction and muscular atrophy

Side Effects and Contraindications:

- Side effects include pain, nerve damage, infection, bleeding, vasovagal syncope
- Contraindications: Do not perform if the patient has:
  - A bleeding disorder or is on anticoagulants
  - Taken aspirin within 3 days
  - A local/systemic infection
  - An allergy to the injected medication
  - A recent muscular injury

Clinical Pearls

– Myofascial pain is defined by pain over points of maximal tenderness or hyperirritability within a muscle fiber.
– Palpation of these MTrps causes pain, referred pain, or a local twitch response. These trigger points are often seen or palpated as "bands" or "knots" of muscle.
– Myofascial pain syndrome is diagnosed clinically through history and physical exam, though new techniques such as pressure algometry and ultrasound are being utilized.
– Myofascial pain is treated with trigger point injections with medication or without any substance (dry needling). These injections relax and lengthen taut muscle fibers and disrupt fibrotic tissue, ultimately alleviating pain.

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Fibromyalgia

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Overview

Definition: Fibromyalgia is a medical condition characterized by chronic widespread pain and a heightened and painful response to pressure in multiple areas of the body.

– Fibromyalgia is more widespread and generalized than myofascial pain syndrome. It involves soft tissue and muscles more commonly than joints. In addition to diffuse generalized pain, other clinical features include sleep disturbances, memory loss, migraines, morning stiffness, and GI irritation. There can be debilitating fatigue. Some patients report difficulty in swallowing, bowel and bladder dysfunction, widespread numbness and tingling in the digits, and cognitive dysfunction. Depression is an associated symptom. Headaches of the tension-type are frequent.
– Fibromyalgia is much more prevalent in females than men and occurs within ages 20–60 years old.
– Many causes have been theorized and research has shown the following to be possible causes: decreases in serotonin, physical or emotional trauma, aberrant muscle blood flow, and heightened perceptions of pain.
– Genetics appears to be involved. Fibromyalgia tends to run in families, and it is theorized that certain genetic mutations make patients more susceptible to developing the disorder.

Evaluation

– Generalized pain in three or more sites for 3 or more months. Pain is widespread, bilateral, above and below the waist, and in the axial skeleton (the skull, spine, ribs, arms, and legs).
– No other preexisting medical conditions that can cause similar symptoms.
– Tenderness in 11/18 of the following sites (Fig. 125.1).

ICD-9 code: 729.1

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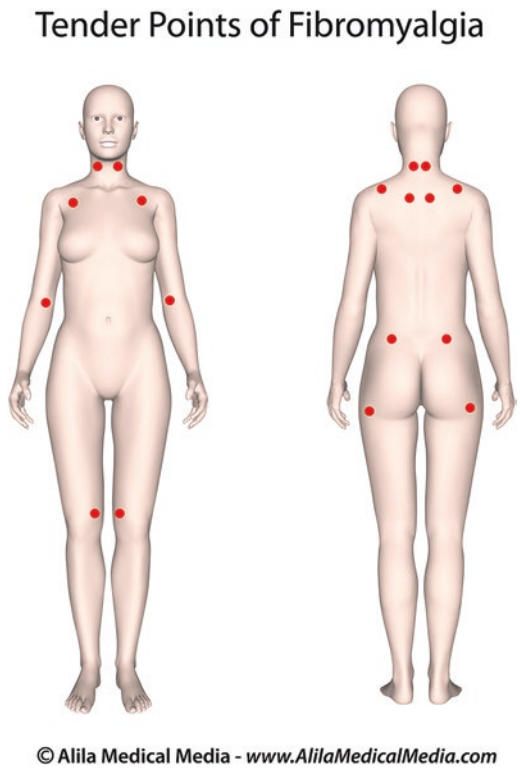

Fig. 125.1 Tender points of fibromyalgia. © Alila Medical Media—www.AlilaMedicalMedia.com

When trigger points are palpated you may feel:

- Ropy muscle band with possible twitching.
- "Jump Sign"-when the patient moves away from pressure.
- Note: referred pain does not follow dermatomes or nerve root distributions.

Treatment

Multidisciplinary: Best success is achieved when a Multi-Disciplinary approach is utilized—including Physical Therapy, Medications, Psychological Therapy, and Pain Management Service Input.

- Physical Therapy should include heat, exercise, stretching, movement therapy
- Trigger Point Injections with local anesthetics (with or without steroids)
- Transcutaneous electrical nerve stimulation (TENS)
- Pharmacologic Treatment includes both FDA-approved and adjunct medications:
  FDA-approved specifically for Fibromayalgia:
    Lyrica (Pregabalin)
    Duloxetine
    Milnacipran
  Adjunct medications:
    Amitriptiline (for sleep) ,
    SSRIs (for serotonin levels),
    Anti-anxiety agents
    Muscle Relaxants
    NSAIDS
- Psychologic—includes Stress Management, Coping Mechanisms
- Sleep hygiene, Relaxation techniques, Biofeedback
- Complimentary Treatments including herbs, massage, acupuncture, chiropracter therapy

Prognosis:

Fibromyalgia is a chronic, life-long condition with no single cure. The Multi-Disciplinary Approach with medications, PT, psychologic, and other modalities gives the best chance for improved outcomes.

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Piriformis Syndrome

126

M. Brigid Maruszak and Tara Sheridan

Definition

Piriformis syndrome (PS) is an entrapment neuropathy of the sciatic nerve by the piriformis muscle, causing non-diskogenic sciatica, buttock pain, gluteal tenderness, and possible radiation to the ipsilateral leg. It was first described by Dr. Yeoman in 1928, and the term was coined by Dr. Robinson in 1947.

ICD9: Piriformis syndrome (mononeuritis)—355.9
CPT: Trigger point injection, 1–2 muscles—20552
Ultrasound guidance—76942
Fluoroscopic guidance, non-spinal—77002

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Anatomy

- Piriformis Muscle
- Originating at the anterior surface of the S2–S4 foramina, the piriformis ("pear shaped" in Latin) muscle exits the pelvis through the greater sciatic foramen, inserts onto the greater trochanter, and is innervated by ventral rami of the first and second sacral nerves. It lies in close proximity with five other hip external rotators: superior and inferior gemelli, obturator internus, and the quadratus femoris.
- Sciatic Nerve
  1. In 70–90 % of patients, the anterior and posterior divisions of the L4, L5, S1, S2, and S3 nerve roots (the lumbosacral plexus) join to form the sciatic nerve before reaching the sciatic foramen. They remain united as the sciatic nerve passes beneath the piriformis muscle, dividing into the posterior tibial (anterior division) and common peroneal (posterior division) nerves.
  2. In the other 10–30 % of patients, variations of the posterior tibial and peroneal nerves occur, resulting in variable sciatic nerve relationships to the piriformis muscle at the greater sciatic foramen.
  3. There are six commonly described anatomical relationships between the sciatic nerve and the piriformis muscle, as first described by Beaton and Anson in 1938.

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4. It is not clear to what extent anatomic variations contribute to the pathology of PS.
   (a) In cadaveric studies, 70–90 % of anatomical variations are bilateral, but 90 % of PS cases are unilateral.

Mechanism of Injury

1. Hypertrophy and spasm of the piriformis muscle causes irritation of the sciatic nerve within the infrapiriformis canal. The sciatic nerve is compressed between the tendinous portion of the muscle and the bony pelvis.
2. Release of pro-inflammatory mediators (prostaglandins, histamine, bradykinin, and serotonin) worsens the cycle of spasm-inflam mation-pain.
3. A history of traumatic injury to the sacroiliac and gluteal region (i.e., rear end collision) is associated with 50 % of all cases, suggesting that post-traumatic hematomas, adhesions, and scarring contribute to nerve compression.
4. Insidious presentation may be associated with chronic overuse. Piriformis muscle hypertrophy is seen in athletes (rowing, hockey, pilates), and as a complication of total hip arthoplasty or cesarean section.

Incidence

- Six to eight percent of patients with low back, buttock, and sciatic pain.
- Annual incidence of 4.8–6.4 million cases.
- 6:1 female to male ratio.

Differential Diagnosis

Degenerative disk disease	Trochanteric or ischiogluteal bursitis
Spinal stenosis	Pudendal neuralgia
Facet syndrome	Pelvic mass, tumor, or endometriosis
Sacroiliac joint dysfunction	Aneurysm of inferior or superior gluteal arteries

Signs and Symptoms

1. Buttock pain, with sciatic radiation, tenderness to palpation over the piriformis muscle (at the greater sciatic foramen), and possible pain with defecation or sexual intercourse. Worsened by prolonged sitting, standing, lifting, or stooping.
2. Positive response to provocative maneuvers is suggestive:
   (a) FADIR sign—Pain reproduced by hip flexion, adduction, and internal rotation.
   (b) Laségue's sign (straight leg raise)—Pain with passive hip flexion to 90° and passive knee extension to 180°.
   (c) Freiberg's sign—Pain with forced internal rotation of extended hip.
   (d) Pace sign—Pain and weakness with seated hip abduction against resistance.
3. Physical exam may further reveal pelvic tilt, gluteal atrophy, a spindle-shaped mass, persistent external rotation, or limp on the affected side.

Imaging

Electromyography (EMG), computer tomography (CT), and magnetic resonance imagery (MRI) are all diagnostically helpful and are increasingly used to establish diagnosis and track response to treatment.

1. EMG: Prolonged H reflex (initiation and measurement of the Achilles tendon reflex) when the piriformis muscle is stretched against the sciatic nerve, suggesting sciatic nerve entrapment.
2. CT: Enlarged piriformis muscle or increased uptake of contrast.
3. Pelvic MRI: Enlarged piriformis muscle or anatomical variation in the sciatic nerve.

Treatment Options

1. Physical therapy, focusing on stretching exercises, lumbosacral stabilization, hip strengthening, and myofascial release over a 6-week period.

(a) Piriformis stretch, standing hamstring stretch, pelvic tilt, partial curls, and prone hip extension recommended.
2. Correction of biomechanical issues such as leg length discrepancy or pelvic obliquity.
3. Non-steroidal anti-inflammatories, muscle relaxants, acetaminophen, heat therapy, and transcutaneous electrical nerve stimulation (TENS) units recommended.
4. Variable evidence supporting acupuncture.
5. Piriformis muscle injection under fluoroscopic or ultrasound guidance (US).
   (a) US allows visualization of adjacent inferior gluteal artery.
   (b) Injection may involve steroids or Botox, with up to 3 months of relief.
   - Steroids helpful when sciatic radiation involved: 40 mg triamcinolone or methylprednisolone in 5 mL of normal saline or local anesthetic.
   - Botulinum toxin (Botox) inhibits presynaptic conduction at the motor end plate, resulting in muscle weakness, paresis. Atrophy and fatty infiltration, as seen on follow-up MRI.
   - Botox also inhibits release of pro-inflammatory substance P at the nerve terminal.
   - Multiple studies, using Botox A (50–150 units) or Botox B (5000–12,500 units).
   - Clonidine described as helpful in one study (Naja et al. 2009).
6. Caudal epidural steroid injections have shown positive results.
7. Failure to respond to physiotherapy or interventional injections may necessitate surgical consultation for piriformis tenotomy or sciatic nerve decompression (Filler et al. 2005).

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Carpal Tunnel Syndrome 127

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Carpal Tunnel Syndrome

Definition: Carpal tunnel syndrome (CTS) is a neuropathy caused by median nerve entrapment and compression within the carpal tunnel at the wrist. It is the most common mononeuropathy seen in clinical practice, causing pain, paresthesia, and weakness in the median nerve distribution.

Pathophysiology: The median nerve (C6, 7, 8, and T1) runs through the carpal tunnel, which is bound superiorly by the transverse carpal ligament and inferiorly by the carpal bones, along with nine flexor tendons from the forearm. In the hand, it innervates the thenar eminence, first 3 digits, and lateral half of the fourth digit. Increased pressure within the canal can lead to compression and damage of the median nerve. Causes include small anatomic canal, space-occupying lesions, inflammation, and trauma. Most commonly seen is an increase in connective tissue (CT) from noninflammatory synovial fibrosis.

Symptoms:

- Pain, tingling, weakness, or clumsiness of hands in median nerve distribution
- Discomfort may radiate to forearm/arm
- Often worse at night, waking patient from sleep
- Worsened with wrist extension/flexion
- Improved with shaking wrist/hand
- Severe cases may lead to thenar atrophy

Epidemiology and Risk Factors:

- Prevalence is 1–5 %.
- Female to male ratio is 3:1.
- Obesity, pregnancy, diabetes, rheumatoid arthritis, hypothyroidism, CT diseases, and use of aromatase inhibitors increase risk.
- Controversial whether workplace factors (e.g., computer use) play a role.

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Diagnosis: CTS is diagnosed clinically, with confirmatory studies including:

Provocative tests: Phalen's, reverse Phalen's, Tinel's sign, Durkan's, hand elevation, and Gillet tests. Paresthesia in the median nerve distribution in ≤1 min is a positive test.

Nerve Conduction Studies: Gold standard for CTS diagnosis. CTS is defined by sensory and motor conduction delays and diminished velocities of the median nerve.

Electromyography: Rule out a primary muscle disorder. Often paired with nerve studies.

Imaging:

X-ray/CT: Only indicated if there is trauma or limited ROM of hand, since it cannot visualize soft tissue. Should not be used routinely.

Ultrasound: Can provide high quality imaging of peripheral nerves and fascia, fibrosis, inflammation, edema, demyelination, etc. It is noninvasive, low cost, and time-efficient.

MRI: Provides excellent visualization of soft tissue, but limited use due to it being expensive, time-consuming, and not as readily available. Indicated for CTS refractory to surgery, long-lasting CTS, severe CTS post-trauma, etc.

Clinical Management

Non-surgical treatment: Conservative management of mild-to-moderate CTS. Neutral wrist splinting and corticosteroids are most commonly used. *Neutral wrist splinting* is recommended at night for 6 weeks, though studies have shown that full-time use is more effective. *Local corticosteroid injections* directly into the carpal tunnel are effective for short-term treatment. *Local anesthetic injections* (e.g., procaine hydrochloride) are effective as adjuncts to steroid injections, and some studies have shown they are as effective as steroids in short-term treatment. *Oral steroids* are another option.

Heated lidocaine patches and *acupuncture* provide significant pain reduction in patients with CTS. Some studies show that *NSAIDs* are comparable to placebo in relieving pain and treating CTS, while others show that NSAIDs are an effective treatment. Currently, there is not enough evidence to support the use of *ergonomic positioning*.

Surgical Treatment: Indicated in moderate-to-severe CTS. The transverse carpal ligament is divided to increase space within the carpal tunnel and relieve pressure on the median nerve. There are no significant differences in outcomes from open carpal tunnel release vs. endoscopic release. Surgical treatment has been shown to be significantly more effective at relieving symptoms than wrist splinting.

Clinical Pearls:

CTS is defined by pain, paresthesia, or weakness in the median nerve distribution. It appears that clinical signs and symptoms along with confirmatory electrodiagnostic testing are best for best diagnosing CTS. Ultrasound is a promising alternative and can be used when NCS are unavailable or when tests are nonconfirmatory. First-line treatments for mild-to-moderate symptoms are corticosteroid injections and wrist splinting. Surgery is an option for severe cases and those refractory to conservative treatment.

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Compression Fracture Pain

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Ilan Margulis and Joseph C. Hung

Introduction

Bone pain remains one of the most common sources of chronic pain in the elderly population. Over 30 % of women over the age of 65 are estimated to suffer from osteoporosis and are at risk for bone fractures. Fractures occur in vertebrae most often in this population, followed by wrist and hip fractures. However, only one-third seek medical attention for related back pain. The incidence of radiographically identified vertebral body fractures nearly doubles in women every 10 years starting from age 50. It is thought that women show a significant increase in osteoporosis risk after estrogen production decreases at menopause. Changes in bone metabolism and a longer expected life span compared to men are thought to be contributory. In men, the incidence of vertebral fractures also increases with age, but at a slower rate. The lifetime risk for vertebral fractures is thought to be as high as 40 % for women while only 13 % for men.

Pathophysiology

Osteoporotic vertebral fractures are classified into three forms based on morphology. These include:

- Crush fractures—involving compression of the vertebral body
- Wedge fractures—posterior height is unchanged but there is anterior collapse
- Biconcave—anterior and posterior heights are maintained but there is central compression

A vertebrae can simultaneously have more than one type of these classified fractures.

Bone is widely innervated and despite the loss of bone mass and strength with aging, the density of sensory nerve fibers does not change. Bone is mainly innervated by thinly myelinated A-delta fibers and peptide-rich CGRP+ nerve fibers. Subsets of acid sensing ion channels are present on sensory neurons including TRPV1 and ASIC-3. As a result, nociceptive neural excitability is potentiated in acidic environments normally created by osteoclast activation.

Vertebral compression fractures most commonly occur in the mid-thoracic spine and

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thoracolumbar junction. It has been suggested that vertebral fractures may occur secondary to contraction of paraspinal muscles causing an increased load on the spine.

Clinical Manifestations

Patients can present with back pain, progressive thoracic kyphosis and lumbar lordosis, change in posture, loss of height, and functional impairment including anxiety, sleep disturbances, emotional perturbations, and limited mobility.

However, it is thought that most vertebral fractures are asymptomatic, but despite a mild onset back pain can progress suddenly and severely to the point where any slight movement is difficult. Fracture-related pain may radiate to the anterior abdomen or flank. Movement is a common exacerbating factor and patients often feel much better when lying, sitting, or standing still. Acute pain directly related to the fracture typically lasts 3–4 weeks on average. In terms of location, lumbar fractures are thought to be more symptomatic than thoracic fractures. Neurologic deficits are uncommon, but nerve root compression can cause related discomfort in the legs and gluteal region(s). Spinal cord compression is very rare. Previous studies have noted that both degree of back pain and level of functional disability tend to correlate with the number of vertebral fractures.

Vertebral body deformity contributes to disturbances in spine alignment and stability. Chronic back pain occurring after the acute pain phase may be secondary to continued contraction of the paraspinal muscles in order to maintain posture. Fatigue and cramping are common due to excessive strain on adjacent muscles, ligaments, and intervertebral joints. Given stress on adjacent vertebral segments, patients are at risk for new fractures to develop. This risk increases as the number of baseline fractures increases. Patients with respiratory comorbidities may notice worsening dyspnea secondary to a stooped posture restricting full expansion of the lungs. Pressure on the abdomen may result in abdominal bloating, early satiety, and secondary weight loss. Higher levels of mortality from cardiac and pulmonary causes have been reported among women with vertebral fractures.

Management

Diagnosis can be made using conventional radiographs in the lateral projection and the degree of fracture staged based on percent height deformity (Table 128.1). Dual X-ray absorptiometry systems (DXA) and radionucleotide-labeled bone scans may serve as alternative or adjuvant evaluation methods.

Goals of treatment in patients with vertebral compression fractures include providing antiresorptive treatment to preserve bone density, ensure proper nutritional intake including calcium and Vitamin D, to improve physical conditioning, and to improve quality of life.

Bisphosphonates are mainstays in preventing bone remodeling and may also be effective for pain relief and increasing mobility. The speculated mechanisms of action behind their analgesic effect are through direct promotion of osteoclast apoptosis and modulation of K+ATP channels. Of note, GI upset and particularly erosive esophagitis may occur with the use of alendronate (one of the most widely used agents for osteoporotic vertebral fractures). Discontinuation of alendronate therapy within the first 6 months of initiation occurs approximately 30 % of the time due to these reasons. Calcitonin, a hormone typically produced by the thyroid bone, lowers plasma calcium and phosphate levels while promoting bone formation. Like bisphosphonates, some studies

Table 128.1 Classification of vertebral compression fracture

Type of fracture	Height reduction	Area reduction	Ratio of anterior to posterior vertebral body height
Mild	20–25 %	10–20 %	3 standard deviations below population mean
Moderate	25–40 %	20–40 %	
Severe	>40 %	>40 %	4 standard deviations below population mean

have shown calcitonin to decrease pain levels and improve movement in patients with vertebral fracture. Adjuvant hormone replacement therapy (HRT) has been shown to reduce bone loss, limit bone resorption, and increase bone mass in patients with estrogen insufficiency.

Oral analgesics including acetaminophen, NSAIDs, opioid medications, and muscle relaxants are often useful for acute pain. Back bracing may help to reduce spine motion and consequently incident pain. However, long-term use may lead to atrophy of back muscles and orthoses should be discontinued with improvement of acute pain. Rehabilitation in the form of progressive mobility and isometric contractions of paraspinal muscles should be initiated in the acute phase. Extension exercises are favored over flexion exercises as the latter may increase or worsen existing vertebral fractures. Of note, there is no evidence to support the use of epidural steroid injections for vertebral compression fractures.

Patients with ongoing pain, disability, or progressive fractures may be considered for vertebral augmentation. Both vertebroplasty and kyphoplasty involve injecting bone cement under image guidance into the body of fractured vertebrae. Kyphoplasty is a modification on vertebroplasty in that a balloon is passed through the needle into the fractured vertebral body and inflated to create a space prior to administration of bone cement. Studies comparing the two procedures have yet to definitively show any significant differences in outcome. Of note, the cost of performing kyphoplasty is usually much higher compared to vertebroplasty.

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Post-thoracotomy Pain Syndrome: PTPS

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Lucian M. Macrea and Konrad Maurer

What is PTPS?

Post-thoracotomy pain syndrome (PTPS) develops after a thoracotomy (open or laparoscopic) and is one of the most often reported chronic postsurgical pain syndromes.

Definition of Chronic Postsurgical Syndrome

The following diagnostic criteria [1] for a postoperative pain condition (including PTPS) must be fulfilled:

- Pain develops after a surgical procedure.
- Pain is of at least 2 months duration.
- Other causes of pain must be excluded (e.g. malignancy).
- The possibility that pain is continuing from a preexisting problem must be explored and exclusion attempted.

Depending on the PTPS phenotype, there may be neuropathic and/or inflammatory components. Elucidating the main pain mechanism and the neuropathic character according to the IASP definition [2] are fundamental for further pain treatment.

Epidemiology and Risk Factors for PTPS

In a very large epidemiologic study comparing pain intensity the first day after surgery (POD 1), sternotomy (for cardiac surgery) ranked 52, thoracoscopic lung resection ranked 67, and open lung surgery ranked 118 of 179 analyzed surgical procedures [3]. The incidence of chronic pain at 3 and 6 months after thoracotomy was 57 % and 47 % respectively, with mean pain scores of 30 and 32, respectively, on a 0–100 scale. The incidence has been stable since the 1990s [4]. These data suggest that patients undergoing major cardiothoracic surgery receive appropriate postoperative analgesia on POD 1, with pain scores <40 (NRS). However, they still may go on to develop chronic postoperative pain.

Patients with PTPS show a high pain-induced functional impairment and elevated pain intensities (in general >50 % having pain scores higher than 3). The nature of this pain is neuropathic in 30–50 % of patients.

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The risk factors identified for development of PTPS (also generally for chronic postoperative pain) are: age (younger ages tend to develop more chronic pain), presence of pain before surgery, psychological distress (high levels of anxiety or catastrophizing), presence of hyperalgesia, and the use of more invasive surgical techniques with intraoperative nerve lesions.

Chronic pain is a complex biopsychosocial condition and the underlying pathophysiology in the development of PTPS is not well-understood, but implies peripheral and central sensitization mechanisms.

Clinical Presentation of PTPS

The intensity of acute pain after thoracotomy seems to be a predictor for the development of chronic PTPS. PTPS show typically a constant pain pattern with triggers (touch, physical exertion, coughing, sneezing, moving heavy objects, vibration, etc.) exacerbating the symptoms. Clinical examination must document sensory changes in the pain area and the limitation in function/movements of the spine, shoulders, and abdomen.

Differential Diagnosis

Life-threatening diagnoses for pain from a cardiac or pulmonary origin must be excluded. Gallbladder-triggered pain symptoms can be confusing and a gastrointestinal origin must be excluded. In the diagnostic work-up of the PTPS, low-grade infection at the level of the ribs or cartilage must be excluded as well. Neuropathic pain states of the thorax (diabetes mellitus, postherpetic neuralgia) must be excluded in the evaluation of the neuropathic pain component of PTPS.

Prevention Strategies for the Development of PTPS

Preventing the development of severe postoperative pain is one of the most efficient strategies for prevention of PTPS. The multimodal perioperative management gives the best opportunities to deal with the complex issue of postoperative pain. The goal of the multimodal approach is to allow early mobilization, enteral nutrition, and attenuation of the perioperative stress. Medical treatments with gabapentin and ketamine had no impact on acute chronic pain after thoracotomy. Lidocaine seems to have an effect on the development of chronic pain and local hyperalgesia [5].

Regional techniques are proven to be very effective in reducing the perioperative stress and are considered the standard analgesic procedure in thoracic epidural anesthesia, reducing the risk of chronic PTPS in one out of four treated patients [6].

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Post-Mastectomy Pain Syndrome 130

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Introduction

Though there is no standardized definition for Post-Mastectomy Pain Syndrome (PMPS), it is considered a chronic pain condition involving the chest wall, axilla, and/or upper extremity beginning after complete or partial mastectomy. Criteria for duration of pain vary in the literature, but a time period of 3 months is most commonly cited. The incidence after surgery has been estimated to range from 25 to 60 %. Symptoms are thought to have a strong neuropathic component. Persistent discomfort affecting the chest wall, axilla, and ipsilateral upper extremity can affect mental health, activities of daily living, and social functioning.

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Risk Factors

Risk factors for PMPS identified in the literature include younger age, unmarried social status, need for axillary lymphadenectomy, adjuvant radiotherapy, adjuvant chemotherapy, and preoperative anxiety. The most consistent risk factor associated with chronic pain after breast cancer surgery is severe postoperative pain.

Pathophysiology

There are a number of pathophysiological factors that can contribute to the development of PMPS.

Musculoskeletal pain is very common immediately following breast reconstruction given unavoidable trauma to the chest wall during surgery. The pectoralis and serratous anterior muscles are frequently involved and can go into spasm. Trigger points can often be identified as palpable nodules in the surrounding back, neck, and chest wall muscles. Pectoral muscle shortening may result in a "tight" sensation and can lead to compensatory overuse of the retractor muscles. Other common causes of acute pain may include axillary hematoma formation and/or the development of lymphedema.

However, it is suspected that persistent pain and PMPS are most often caused by severance, compression, ischemia, and/or retraction of nerves during surgery. Branches of the brachial

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plexus, the lateral cutaneous branch of the second intercostal nerve, the long thoracic nerve, the intercostobrachial nerve, and the lateral and medial pectoral nerves are at risk. After nerve damage, central sensitization mechanisms similar to those responsible for Chronic Regional Pain Syndrome (CRPS) are suspected to contribute to persistent pain.

There is a high incidence of intercostobrachial neuralgia following breast surgery. It is estimated that this nerve is injured 80–100 % of the time during mastectomy or lumpectomy with axillary node dissection. Patients often present with pain and sensory changes affecting the medial aspect of the upper extremity, axilla, and shoulder. Some studies have reported that intercostobrachial neuralgia is the most common cause of PMPS.

Neuroma formation is also very common after peripheral nerve injury. Histologically, neuromas are a mass of tangled nerve axons in various stages of healing and regeneration. Due to their immaturity, these axons cannot reach their targets and become often entangled in scar tissue. Some studies have noted that neuroma formation is more likely following lumpectomy with axillary dissection and radiotherapy compared with modified radical mastectomy. Nerve tissue trapped within a neuroma has the tendency to discharge spontaneously and can lead to frequent episodes of neuropathic pain without clear triggering factors.

Remodeling of the central and/or peripheral nervous systems after surgical manipulation may explain the high incidence of phantom breast sensations experienced by patients. Various descriptions have been recorded in the literature including pin-prick, burning, and torsion sensations. These unpleasant feelings may involve the entire phantom breast and/or isolated areas such as the nipple or scar tissue. Emotional factors along with central nervous system plasticity following surgical deafferentation may both play a role. The relationship between preoperative breast pain and the development of postoperative phantom pain has been suspected, but not well-established in research studies.

Clinical Manifestations

Patients typically present with burning, electric, stabbing, and/or shock-type pain in the chest wall, axilla, and ipsilateral upper extremity. Associated neurologic symptoms include numbness, tingling, paresthesias, allodynia, and hyperesthesia. Sensory deficits are common. Focal motor deficits are rare, but patients may have limited range of motion and strength secondary to surgical manipulation of chest wall and shoulder girdle musculature. Lymphedema may be present especially after lymph node removal or dissection.

There are no specific radiologic or laboratory findings specific to PMPS. The differential diagnosis should include local disease recurrence, metastatic disease, infection, cervical radiculopathy, and musculoskeletal disorders.

Treatment

Treatment options remain elusive. A multidisciplinary approach in the treatment of this complex syndrome should be taken. Prevention would be ideal, but nerve sparing surgical techniques are nonexistent. Since acute postoperative pain has been strongly linked to persistent and chronic pain following breast surgery, there may be some utility in multimodal and dedicated acute pain control.

The majority of patients can achieve relief of post-surgical pain with non-steroidal anti-inflammatory therapy (NSAIDs) and/or opiates. Other adjuvant pharmacologic therapies include anticonvulsants, antidepressants, sodium channel blockers, acetaminophen, topical local anesthetics, topical capsaicin, and muscle relaxants. Pre- and post-surgical interventional techniques have been described including paravertebral blockade, epidural placement, intercostal nerve blockade, and Botox injections. It should be noted that no treatment regimen has been shown to effectively treat acute and/or chronic pain after breast surgery.

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Peripheral Vascular Disease

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Michael Nguyen and Jackson Cohen

Peripheral vascular disease refers to any pathology that affects the blood vessels outside the brain or heart. Peripheral vascular disease is usually the result of atherosclerosis of the blood vessels resulting in insufficient tissue perfusion. Arteries are more commonly subject to atherosclerotic disease as compared to veins. Peripheral vascular disease is normally a chronic process, but it may present in an acute manner when thrombi, emboli, or acute trauma occur which can affect perfusion. Thromboses often occur in the lower extremities more frequently than in the upper extremities and may result from atherosclerotic plaques [1]. Emboli tend to carry higher morbidity because the extremity has not had time to develop collateral circulation. Whether caused by embolus or thrombus, occlusion results in both proximal and distal thrombus formation due to flow stagnation. Ultimately, this can result in tissue ischemia and necrosis.

Peripheral vascular disease is a leading cause of disability among people older than 50 years and in those with diabetes. The number of people with the condition is expected to grow as the population ages. Peripheral vascular disease is associated with significant morbidity and mortality. Prevalence increases dramatically with age, and disproportionately affects the African American population [2]. Men are slightly more likely than women to have the condition. Peripheral vascular disease is more common in smokers, and the combination of diabetes and smoking normally results in more severe disease. Despite its prevalence and cardiovascular risk implications, only 70–80 % of patients will undergo recommended antiplatelet therapy or lipid-lowering therapy [3].

Risk factors for peripheral vascular disease include:

- Positive family history of cardiovascular disease
- Older than 50 years
- Obesity
- Inactive (sedentary) lifestyle
- Smoking
- Diabetes
- Hypertension
- Hypercholesterolemia
- Hypertriglyceridemia

Clinical presentation of peripheral vascular disease may be asymptomatic in many cases. However, intermittent claudication may be the sole manifestation of early symptomatic peripheral vascular disease. Aortoiliac disease manifests as pain

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in the thigh and buttock, whereas femoral-popliteal disease manifests as pain in the calf. Symptoms are precipitated by walking a predictable distance and are relieved by rest. Collateral circulation may develop, reducing the symptoms of intermittent claudication, but if peripheral vascular disease is not treated, the collateral circulation will not be able to prevent worsening of symptoms. The pain of vascular claudication usually does not occur with sitting or standing; whereas the pain of neurogenic claudication is usually worse with walking and relieved with sitting or bending forward.

If peripheral vascular disease is suspected, a complete work up may be warranted to assess the patient's condition. Doppler ultrasound studies are useful as primary noninvasive studies to determine flow status. Blood tests such as CBC, CMP, lipid profile, and coagulation tests may also be ordered. MRI may be of some clinical benefit due to its high visual detail. Plaques are imaged easily, as is the difference between vessel wall and flowing blood. MRI also has the benefits of angiography to provide even higher detail and has replaced traditional arteriography. The ankle-brachial index is used to compare pressures in the lower extremity to the upper extremity [4]. Blood pressure normally is slightly higher in the lower extremities than in the upper extremities. Comparison to the contralateral side may suggest the degree of ischemia. Normal ABI is more than 1; a value less than 0.95 is considered abnormal and less than 0.4 is severe.

Currently, treatment options include medication management with antiplatelet agents for prevention of cardiovascular events in patients with asymptomatic and symptomatic peripheral vascular disease [5]. Treatment of risk factors with smoking cessation, diet, and exercise are also crucial for successful outcomes in conjunction with these medications. Statins have been linked to improved prognosis in other vasculopathies, including renovascular and cardiovascular events, and may slow the progression of atherosclerotic disease systemically. When conservative measures fail to improve quality of life and function, endovascular procedures such as stenting, angioplasty, and bypass surgery are considered.

Treatment of pain due to peripheral vascular disease can be quite challenging. There is limited evidence for any specific interventional pain procedure that is effective for treating painful peripheral vascular disease such as lumbar sympathetic blocks. Opioid medications may be used to treat severe pain due to peripheral vascular disease, but there are no long-term studies showing the efficacy of opioid therapy for chronic pain due to this condition. On the other hand, multiple studies have shown proved efficacy of spinal cord stimulation in peripheral vascular disease [6]. The exact mechanism by which spinal cord stimulation acts in the treatment of peripheral vascular disease is not completely understood, but it may include stimulating the release of nitric oxide, modulation of the sympathetic nervous system, or modulation of prostaglandin production. Spinal cord stimulation should be reserved for patients with end-stage lower limb peripheral vascular disease unresponsive to medical therapy and not amenable to surgical reconstruction.

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Chronic Venous Insufficiency 132

Mary So, Namrata Khimani, and Michael Ngyuen

Introduction

Chronic venous insufficiency (CVI) is a pervasive and problematic disorder thought to affect between 10 and 35 % of the American population [1]. It encompasses a full spectrum of chronic venous disorders ranging from uncomplicated telangiectasias to debilitating venous ulcers.

Etiology

CVI can be broadly divided into three categories based on etiology: primary, secondary, and congenital. Primary CVI includes patients without an underlying mechanism for venous dysfunction. Secondary CVI is a result of venous malfunction precipitated by an event such as a deep vein thrombosis [2]. Congenital CVI include those born with venous malformations at birth [3].

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Pathophysiology

The underlying pathophysiology of CVI is not well-understood. Early theories proposed that CVI arose from incompetent venous valves (reflux), obstruction, and inadequate muscle pump function leading to elevated venous pressure. Recent theories have focused on structural and histologic abnormalities, including underlying connective tissue defects [1].

Risk Factors

Risk factors for chronic venous disorder include female gender, obesity, advanced age, family history, pregnancy, prolonged standing, and urban residence [1].

History and Physical Exam

Presenting symptoms include pain, aching, cramping, sensation of "heaviness" in the leg, itching, swelling, edema, and skin changes. Physical exam findings can include reticular and varicose veins, telangiectasias, skin pigmentation, lipodermatosclerosis, dermatitis, and ulcerations [3]. Differential diagnoses include arterial occlusive disease, vasculitis (small vessel disease), infection, and carcinoma [1].

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CEAP Classification

An international committee of the American Venous Forum developed a universal and systematic classification system for chronic venous disorders. The classification "CEAP" was based on (C) clinical manifestations, (E) etiologic factors, (A) anatomic distribution of disease, and (P) underlying pathophysiologic findings (Table 132.1).

Diagnosis

History and physical examination are integral to the diagnosis of CVI and can be aided with noninvasive testing, such as Venous Duplex Imaging. Venous Duplex Imaging can detect acute and chronic thrombosis, post-thrombotic changes, obstructive flow, and reflux. The presence of reflux is determined by the direction of flow and its duration is known as the reflux time. A reflux time of greater than 0.5 s for superficial veins and 1.0 s for deep veins is typically used to diagnose the presence of reflux [5, 6]. Other noninvasive testing include Air Plethysmography, Computed Tomographic, or Magnetic Resonance Venography. Invasive testing, including contrast venography and intravascular ultrasound, may also be used to establish the diagnosis, but is usually reserved for assessing disease severity or for further detailed evaluation prior to surgical intervention [7].

Table 132.1 CEAP classification of chronic venous disease

Clinical classification
C0: no visible or palpable signs of venous disease
C1: telangiectasies or reticular veins
C2: varicose veins
C3: edema
C4a: pigmentation or eczema
C4b: lipodermatosclerosis or atrophic blanche
C5: healed venous ulcer
C6: active venous ulcer
S: symptomatic, including ache, pain, tightness, skin irritation, heaviness, and muscle cramps, and other complaints attributable to venous dysfunction
A: Asymptomatic
Etiologic classification
Ec: congenital
Ep: primary
Es: secondary (post-thrombotic)
En: no venous cause identified
Anatomic classification
As: superficial veins
Ap: perforator veins
Ad: deep veins
An: no venous location identified
Pathophysiologic
Pr: reflux
Po: obstruction
Pr,o: reflux and obstruction
Pn: no venous pathophysiology identifiable

Adapted from [4]

Treatment

Conservative Therapy

The initial management of CVI involves conservative measures to reduce symptoms and prevent the development of secondary complications and progression of disease.

- Leg elevation
- Exercise Therapy
- Compression therapy
  - Apply graded external compression to the leg and oppose the hydrostatic forces of venous hypertension.
  - *Evidence*: A Cochrane meta-analysis of 22 trials showed that compression stockings were more effective than no compression in healing venous ulcers, and higher compression pressures were more effective than lower ones [8].

- Drug therapy
  - Venoactive Agents:
    - Heterogenic group of drugs from vegetal or synthetic origin.
    - *Evidence*: Available randomized control trials and meta-analyses support their effectiveness in relieving venous edema and related symptoms [3, 9].

- **Micronized purified flavonoid fraction (MPFF)**—mixture of flavonoids.
- **Hydroxyethylrutoside**—mixture of semisynthetic flavonoids.
- **Escin**—horse chestnut seed extract.

- Rheologic Agents
  - *Evidence*: Although pentoxifylline is well-tolerated, reported efficacy is variable [3].
    - **Pentoxifylline**—targets inflammatory cytokine release, leukocyte activation, and platelet aggregation at the microcirculatory level.

Vein Ablation Therapies

The choice of ablation method depends upon the size of the varicose veins, their location, and presence or absence of venous reflux. (See CVI Treatment Chapter.)

■ **Endovenous Ablation**
- Radiofrequency Ablation
- Laser Ablation
- Chemical Ablation (sclerotherapy)

■ **Surgical**
- Vein stripping and excision
- Repair of incompetent valves

Evidence: Randomized trials and meta-analyses comparing minimally invasive therapies, including radiofrequency ablation, laser ablation, and sclerotherapy with conventional surgical ligation and stripping, found that the short-term efficacy and safety of endovenous ablation and surgery are comparable, with improved quality of life, less post-operative pain, and earlier return to normal activity and work with ablation [10–14].

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Sphenopalatine Ganglion: Function and Block

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Satish Vembu, Boleslav Kosharskyy, and Karina Gritsenko

Innervation of Sphenopalatine Ganglion

- Preganglionic Parasympathetic originating in Superior Salvitatory Nucleus via Facial Nerve synapse at ganglion project.
- Sympathetic and post-ganglionic parasympathetic neurons pass through ganglion, innervates lacrimal glands, inferior and posterior septum, lateral wall of nasal cavity, and nasal glands.

Sphenopalatine Block

Indications: For medically resistant cluster headaches, trigeminal neuralgia, vasomotor rhinitis, TMJ pain, and pain from cancer of head and neck.

CPT:
Sphenopalatine Ganglion Block 64505
Fluoroscopic Needed Guidance 77002

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Equipment: Fluoroscopy, 5 mL local anesthetic (1–2 % Lidocaine), 1–3 mL contrast, 5 mL 0.25 % Bupivacaine, 22G Touhy needle, 16G Angiocatheter.

Procedure Steps

Infrazygomatic Approach [1]:

1. Place patient supine. Place standard non-invasive monitors. Prep and drape patient with ipsilateral side of face exposed. Anesthesia requirement may vary from light sedation, monitored anesthesia care, or heavy sedation if ablation is being used.
2. Fluoroscopy is not mandated, but highly recommended for block success. With fluoroscopy in lateral view, visualize patient anatomy including maxilla, lateral pterygoid plate, and turbinates.
3. Locate mandibular fissure and pterygopalatine fissure via manipulation of C-arm. This appears as V figure on fluoroscopy when left and right fissures overlap.
4. Anesthetize skin using Lidocaine with 25G needle.
5. With 16G Angiocatheter, advance through skin until medial to ramus. Remove needle leaving behind Angiocatheter.
6. Using blunt curved 2 in. 20G needle, or 3.5 in. 22G short bevel spinal needle, advance

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through angiocatheter, proceeding medial, cephalad, and anterior. Targeting the middle of ptereygopalatine fissure, check frequently with lateral images.
7. Using AP view, needle advanced to middle turbinate with tip adjacent to palantine bone. If resistance felt, withdraw and change direction. Check progress frequently with AP and lateral views.
8. When needle in fossa, inject 0.5–1 cm^3 contrast solution to rule out intravascular or intranasal injection.
9. Once placement verified. Inject desired local anesthetic with or without steroids.

Contraindications/Concerns: Patient refusal, infection at site of injection, anticoagulation status, altered anatomy, contrast allergies.

Complications

Diplopia, Epistaxis, Hematoma, Infection, Bradycardia, Dizziness.

Evidence

Sphenopalatine Block for Management of Cluster Headaches:

In a study of 56 patients with episodic cluster headaches refractory to medical management, 60 % received complete pain relief from a Sphenopalatine block over an average follow-up time of 29 months. [2].

Fifteen patients with chronic cluster headaches refractory to medical management treated with radiofrequency ablation of sphenopalatine ganglion experienced statistically significant decreases in attack intensity, attack frequency, and scores on disability index [3].

Repeat Sphenopalatine blocks have shown success with acute chronic migraine headaches. Patients given repeat blocks showed significant reduction in numerical pain rating scale and Headache Impact Test -6 up 24 h after blockade [4].

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Phantom Limb Pain

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Sivan Schipper and Konrad Maurer

Definition

Phantom Limb Pain (PLP) is the feeling of pain in a limb, portion of a limb, or organ after its amputation. PLP can also occur after nerve avulsions or spinal cord injuries. Around 80 % of people who undergo amputation experience some degree of PLP.

Differential Diagnoses

- Residual limb pain/Stump pain
- Post-amputation pain at the wound side/ Wound infection
- Osteomyelitis
- Poor prosthetic fit
- Heterotopic ossification
- Neuroma pain
- Non-painful phantom limb sensations:
  - Movement sensation
  - Phantom limb posture sensation
  - Touch, temperature, pressure, itchiness, heat, and tingling sensations
  - Telescoping sensation (feeling that phantom limb is gradually shortening over time)

Characteristics

Characteristics of PLP vary drastically; there is a vast phenotypical heterogeneity, indicating multiple pathophysiological mechanisms:

- Onset of symptoms hours to days to weeks to decades after amputation
- Frequency of pain episodes every few days to several episodes daily
- Length of episode 1 min to continuous pain
- Variety of pain descriptors: sharp, cramping, electric, jumping, crushing, shooting, squeezing, tingling, throbbing, stabbing, burning

Pathophysiology

Historically, PLP was widely believed to be psychogenic. This hypothesis has been abandoned in the last decade due to advances in research in this area. There is still ongoing debate as to whether the origin of PLP is central or peripheral. The heterogeneity of the disorder suggests that multiple mechanisms are involved. A paradigm

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shift in the conceptualization of phantom limb pain from a single disorder to a cluster of pain conditions, involving both peripheral and central mechanisms, was proposed [1].

- *Peripheral Mechanisms*:
  - ○ Abnormal firing of action potentials from neuromas in the residual limb. Pressure on neuromas of the amputation stump provokes PLP (Tinel Sign); however, there is evidence to suggest that blockage of the neuroma or nerve plexus does not consistently prevent PLP [2]. Furthermore, PLP can be present immediately after amputation, even before neuroma sprouting.
  - ○ Sympathetically mediated pain: Blockage of sympathetic activity may reduce PLP, whereas epinephrine injections will increase PLP [2].
  - ○ The "Loss of Sensory Input" Theory of PLP was challenged recently by Vaso et al. [3] by the alternative "Exaggerated Input" Theory, in which it is thought that ectopic activity in the dorsal root ganglia (DRG) of axotomized primary afferent neurons would be mainly responsible for PLP. Intrathecal and/or peridural DRG application of local anesthetics removed PLP as well as non-painful phantom limb sensations, suggesting that PLP is driven primarily by activity generated within the DRG.
- *Central Mechanisms*
- Central nervous system theories of PLP implicate neuroplastic changes in the spinal column (mainly the dorsal horn) and the brain (mainly the somatosensory cortex)
  - ○ Ongoing ectopic afferent input leads to central sensitization processes at the spinal level.
  - ○ Contralateral somatosensory cortical changes: augmentation, glial activation, inhibitory signaling inhibition, long-term potentiation, axonal sprouting, and more mechanisms have been described.
  - ○ Reorganization in multiple other brain areas, such as motor cortex, limbic pathways, and prefrontal cortex.
  - ○ "Maladaptive change theory": Loss of afferent input allows shift of the cortical representation from neighboring areas into the deafferentiated cortical amputation zone.

Treatment

Good evidence for treatment of chronic PLP is sparse. Efforts should be made to adapt a mechanism-based treatment approach. Proper history taking and examination as well as additional investigations are essential before initiating a proper treatment. Multifactorial individual pain drivers often demand a multidisciplinary approach.

- *Pharmacological Treatment* [4]
  - ○ Currently, the best evidence exists for oral morphine for intermediate to long-term treatment of PLP.
  - ○ There is mixed and only weak evidence for the efficacy of Gabapentin, Carbamazepine, Amitriptyline, Topiramate, and Tramadol.
- *Physical Treatment*
  - ○ Optimal prosthetic use is associated with reduction of PLP.
  - ○ Mirror Therapy: positive evidence from case studies and anecdotal data [5].
- *Psychological Treatment*
  - ○ Cognitive Behaviorial Therapy: Patient empowerment, alteration of erroneous or destructive self-concepts.
  - ○ Hypnotherapy, Eye Movement Densitization and Reprocessing (EMDR), electromyographic feedback, and many more.
- *Interventional Treatment*
  - ○ There is very little evidence and no consensus concerning interventional treatment therapies such as Pulsed Radio Frequency Therapy, Spinal Cord Stimulation, Deep Brain Stimulation, blocks of the sympathetic nervous system, Phenol instillation into neuroma, injections with botulinum toxin A, and more [6].

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Visceral Pain Syndromes

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Daniel Pak and Joseph C. Hung

Introduction

Chronic visceral pain is a common yet challenging disorder. There are over 12 million consultations a year alone for abdominal pain in the United States. Estimated prevalence rates are as high as 25 % for intermittent abdominal pain and 24 % for pelvic pain in women. Causes are many and varied, but generally thought to be related to activation of nociceptors of the thoracic, abdominal, or pelvic organs. Medical treatment decision making may be tricky as many pain medications can affect bowel motility and can actually lead to worsening discomfort.

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Pathophysiology

Visceral structures are sensitive to noxious stimuli including twisting, distention, ischemia, and inflammation. However, they are relatively insensitive to stimuli that typically cause somatic pain such as pinching, cutting, or burning.

The diffuse and poorly localized nature of visceral pain can be attributed to the low density of afferent nerve fibers located within viscera and also to the divergent nature of these inputs into the central nervous system. Visceral afferent fibers that transmit pain travel through prevertebral sympathetic ganglia as they transmit information back to the spinal cord. Examples include the celiac plexus (innervates abdominal viscera from the upper esophagus to the splenic flexure), the aortic plexus (mesenteric, pelvic, and urogenital viscera), the superior hypogastric plexus (pelvic viscera and bowel distal to the left colonic flexure), and the inferior hypogastric plexus (pelvic and perineal viscera). Most of the encoded pain information then travels through the spinothalamic tract and the medial aspect of the dorsal columns before preferentially acting on the perigenual portion of the anterior cingulate cortex. The close proximity between pain and emotion processing areas in this region of the brain may explain the stronger emotional response often seen compared to nonvisceral pain.

Viscerosomatic or visceromotor convergence is defined as visceral input into the dorsal horn asso-

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ciated with central sensitization of wide dynamic range (WDR) neurons. Since no second-order neurons receive only visceral input, a referred cutaneous pain pattern (referred pain) often results from these interactions. This pattern can comprise the same dermatomal regions as the spinal cord segments receiving the visceral stimulus or relate to input from several segments away. A classic example of viscerosomatic convergence is referred pain to the right shoulder from the hepatobiliary disease and/or diaphragmatic irritation.

Clinical Manifestations

Visceral pain is usually diffuse, poorly localized, and dull in nature. Discomfort is usually perceived in the midline regardless of the origin of the organ and may become more localized with time. Episodes of pain crisis may be associated with strong autonomic reactions, emotional reactions, and changes in visceral function. As stated above, referred pain (perceived at a location other than at the site of the stimulus) is also common.

Some of the most common chronic visceral pain syndromes are listed:

- *Thoracic pain syndromes*: angina
- *Upper abdominal pain syndromes*: chronic pancreatitis, biliary disease, splenic infarction, dyspepsia
- *Lower abdominal pain syndromes*: urolithiasis, disorders of the internal female reproductive organs (pelvic inflammatory disease, adnexal masses, endometriosis, leiomyoma, dysmenorrhea, interstitial cystitis, pelvic malignancy)
- *Diffuse abdominal pain syndromes*: bowel/mesenteric ischemia, bowel obstruction, irritable bowel syndrome, inflammatory bowel disease, malignancy

Management

Given the many potential causes of visceral pain, diagnosis and treatment work best when targeted at the primary pathology causing discomfort. In addition to underlying disease, impaired visceral function as a result of therapy or pain itself may further contribute to discomfort. Effective pain management should aim to restore visceral function in addition to targeting underlying pathophysiology.

Pharmacotherapy aimed towards central pain processing pathways including analgesics, antidepressants, and anticonvulsants remains mainstays of therapy. Some of these agents have the added advantage of treating the emotional component of pain symptoms (in addition to sensory aspects). Given that the gastrointestinal tract contains the vast majority of the body's serotonin (5-HT) receptors, serotonin-modifying drugs are also of particular interest, but evidence supporting their use remains limited. Other treatment agents have been used to improve visceral function and include muscarinic receptor antagonists, L-type calcium channel blockers, and anticholinergic medications. While opiate medications may also be an effective modality, their gastrointestinal side effects (nausea and constipation) may confound characteristics of the original visceral pain.

Invasive interventional techniques are reserved for patients in whom pharmacological therapy has proven to be inadequate. However, due to the complicated and often bilateral nature of visceral afferent pathways, regional blocks and/or isolated nerve blocks are often ineffective. Sympathetic blocks targeting visceral afferent fiber synapse points (autonomic ganglia) using local anesthetic and/or steroids remain primary interventional pain control options. Neurolytic blocks and ablative techniques are most often reserved for malignant pain and are useful options when opiate escalation is limited by medication-related side effects. Other invasive techniques including spinal cord stimulation (SCS) and neuraxial drug delivery systems can also be in those with intractable pain syndromes resistant to more conservative measures (Tables 135.1 and 135.2).

Table 135.1 Pharmacologic treatment options for visceral pain

Class	Treatment
Analgesics and anxiolytics	Opiates, NSAIDs, acetaminophen, benzodiazepines
Anti-spasmotics	Loperamide
Antidepressants	TCA, SSRI, SNRI agents
Anticonvulsants	Gabapentin, pregabalin
NMDA antagonists	Ketamine

Table 135.2 Interventional treatment options for visceral pain

Intervention	Anatomic target
Celiac plexus block	• Visceral pain from the proximal gastrointestinal tract—upper esophagus to the splenic flexure including the pancreas, liver, biliary tract, gallbladder, spleen, adrenal glands, kidneys, mesentery, stomach, small and large bowel
Splanchnic nerve block	• Alternative to celiac plexus blockade—the greater (T5-T9), lesser (T10-T11), and least (T12) splanchnic nerves provide afferent and sympathetic innervation to the abdominal viscera and travel through the celiac plexus
	• Better option when disease is located on or around the celiac axis (involving the body or tail of the pancreas)
Superior hypogastric block	• Visceral pain from the distal gastrointestinal tract (bowel distal to the left colonic flexure) or pelvic viscera
Ganglion of impar block	• Visceral pain from the perineum, vulva, distal vagina, anus, distal rectum, or distal urethra
Spinal cord stimulation (SCS), intrathecal/epidural drug delivery systems	• Intractable visceral pain resistant to more conservative measures

Additional Readings

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Chronic Urogenital Pain

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Gary Kim, Boleslav Kosharskyy,
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Anatomy

- Major structures involved include kidneys, ureters, bladder, urethra, testes, penis, vagina, ovaries, fallopian tubes.

Nerves-Plexus Blocks

- *The superior hypogastric plexus*—contains efferent sympathetic fibers to and afferent pain fibers from most of the pelvic organs.
- *The ganglion impar*—the point at the sacrococcygeal junction at which the two sympathetic paravertebral chains end. It contains visceral afferents from the perineum, distal rectum, anus, distal urethra, vulva, and the distal third of the vagina.
- *Pudendal nerve*—contains fibers from the S2-4 nerve roots and supplies sensory innervation to the perianal region, anal sphincter, posterior two thirds of the scrotum or labia major, muscles of the urogenital triangle, and the dorsum of the penis or clitoris.
- *Ilioinguinal nerve*—derived from the lumbar plexus, it innervates skin over root of penis, upper part of scrotum for males, skin of mons pubis, and labium majus for females
- *Genitofemoral nerve*—derived from lumbar plexus, it innervates cremaster muscle

Epidemiology

Women

- Affects approx. one in seven women in the US.
- Consists of 10% of all referrals to gynecologists
- Most common in women of reproductive age

Men

- For men, most common after age of 50
- Common causes include interstitial cystitis, prostatitis, and scrotal and vaginal pain

Clinical

Bladder pain syndrome (BPS): pain related to filling of bladder, characterized by aching, burning, or stabbing pain.

- Associated with increased urinary frequency, nocturia, or painful urination.

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– Interstitial cystitis is a specific subset of BPS which involves chronic inflammation of the bladder.
– Pain usually correlates with the amount of bladder filling, which is usually relieved by voiding but returns soon afterwards.
– Diagnosis can be made with urinalysis, cystoscopy with hydro-distension, and biopsy.

Causes: infectious, inflammatory, autoimmune causes, structural defects, hypoxia, or neurologic disorders.

Treatments: amitriptyline, pentosan polysulfate sodium, hydroxyzine, cyclosporin A, manual therapy via palpation of the pelvic floor (urinary and anal sphincters, pubourethralis, vaginalis, rectalis, iliococcygeus, obturator internus, and piriformis muscles)

Chronic Prostatitis (CP): pelvic pain originating from the prostate of non-infectious and unclear etiology. CP can be categorized into two categories depending on WBC levels in prostatic specimens:

– Type A (inflammatory)
– Type B (non-inflammatory)

Treatments: Antibiotics (quinolones), NSAIDs, 5-alpha-reductase inhibitors (in the presence of BPH), opioids, biofeedback, relaxation, prostate massages

Urethral pain syndrome: Characterized by pain from the urethra. Usually presents with tenderness and inflamed urethra, dysuria, frequency, urgency without evidence of urinary infection. Can be diagnosed with ureteroscopy. Possible causes include concealed infection of the periurethral glands/ducts, estrogen deficiency.

Treatment: Difficult and experimental. Treatments that have been studied are cortisone-antibiotic ointment, systemic antibiotics, alpha blockers, and laser therapy.

Scrotal pain: Scrotal pain can be the result of trigger points in the pelvis, but can also be caused by the lower abdominal musculature or due to the testicles. In the absence of clinical findings or negative urinalysis, there is limited evidence for the efficacy of ultrasound as a diagnostic tool for scrotal pain, except to rule out cancer.

Causes: infection, tumor, torsion, varicocele, hydrocele, spermatocele, trauma, previous vasectomy, diabetic neuropathy, polyarteritis nodosa.

Gynecologic pain: Various causes, but no identifiable cause in 30 % of cases.

Diagnosis relies on history and physical, laboratory, and radiographic studies, or sometimes laparoscopic surgery.

Causes: pelvic infections, cancer, endometriosis, dysmenorrhea, vulvodynia.

Treatment

– Systemic antibiotics for infection
– Surgery for chronic infections, dysmenorrhea, endometriosis, cancer (if operable)
– Dysmenorrhea can be treated with hormonal therapy

Vulvodynia: vulvar pain, often burning, without pertinent physical findings or a specific disorder, and is not associated with an identifiable cause of pain.

Cause: thought to be a combination of inflammation, genetics, hormonal changes, and/or neuropathic changes.

Treatment: options include topical lidocaine, tricyclic antidepressants, gabapentin, physical therapy, trigger point injections, surgical treatment. Low oxalate diet is also recommended as it is believed that oxalate in the urine may cause vulvar irritation and pain.

Interventional Treatments

– Pudendal nerve blocks (S2–S4 region)
– Superior hypogastric plexus block (gynecologic disorders, interstitial cystitis, suprapubic post-surgical pain)
– Ganglion impar block (perineum, rectum, and genitals)
– Ilioinguinal nerve block (neuralgia)
– Genitofemoral nerve block (neuralgia)
– Trigger point injections (ex. muscle spasms)

Blocks with local anesthetic or steroids can be temporary. Neurolysis (with phenol or alcohol),

radiofrequency ablation (radio energy waves via a special type of needle to either burn or stun the nerve), or cry-ablation can be used for long-term pain relief.

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Labor Pain

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Dominique Arce and Holly Ende

Mechanisms of Pain During Labor

Pain during the first stage of labor arises from stretching and dilation of the lower uterine segment and cervix. Visceral afferent neurons accompany sympathetics through the paracervical region, hypogastric plexus, and lumbar sympathetic chain and eventually transmit the signal to the dorsal horn of the spinal cord at the level of T10-L1. During the second stage of labor, somatic afferent neurons arising in the cervix, vagina, and perineum convey signals via the pudendal nerve, entering the spinal cord at S2-4 [1].

Benefits of Labor Analgesia

The surge of catecholamines, particularly epinephrine, which can occur during contractions, can lead to detrimental effects for mother and fetus. Relief of pain during labor prevents this pain-induced activation of the sympathetic nervous system and is beneficial in many ways, including:

1. Elimination of beta-adrenergically mediated tocolysis, possibly normalizing the labor pattern.
2. Prevention of increased peripheral vascular resistance and its associated decrease in uteroplacental blood flow.
3. Prevention of pain-induced hyperventilation leading to respiratory alkalosis, a leftward shift of the oxyhemoglobin dissociation curve, and decreased unloading of oxygen to the fetus.
4. Prevention of compensatory hypoventilation between contractions and associated maternal and fetal hypoxemia.
5. Prevention of delayed gastric and bladder emptying.

Irrespective of the physiologic benefits of controlling labor pain, epidural analgesia has added benefit of facilitating rapid conversion to surgical anesthesia should the need for emergency cesarean delivery arise [1].

Consequences of Labor Analgesia

While the treatment of pain during labor has many positive effects, there are some consequences to consider. Abrupt decreases in epinephrine-mediated tocolysis can lead to transient uterine hyperstimulation and tetanic contractions causing fetal stress and bradycardia. If neuraxial analgesia is utilized, blockade of ascending sacral spinal tracts leads to decreased secretion of endogenous oxytocin and could theoretically prolong labor.

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Management of Labor Pain: Inhalation Agents

Nitrous Oxide: Nitrous oxide has historically been used very infrequently in the United States (<1 % incidence). It is co-administered with oxygen typically in 50:50 mixture using a blender or premixed cylinder and via a mask or mouthpiece. It is believed to act by stimulating the release of endogenous opioids and inhibition of descending spinal pain pathways, but this has never been fully elucidated [2]. Pharmacologically, nitrous has rapid onset and offset due to its low solubility and undergoes minimal metabolism. Its physiologic effects are limited to slight reduction in tidal volume with some compensation through an increased respiratory rate. Nitrous oxide has little-to-no effect on cardiovascular or uterine functions. The most common side effects are nausea and vomiting [2]. A systematic review of 58 studies concluded that there is less pain relief with the use of nitrous oxide when compared to neuraxial analgesia, and Apgar scores were not significantly different between the two groups. Additional research is needed given the poor quality of most studies to date [3].

Anesthetic gases: Volatile halogenated agents have limited use secondary to concern for maternal amnesia, sedation, and loss of airway reflexes as well as environmental contamination. They are administered via facemask or mouthpiece. Sevoflurane is preferable to desflurane due to the latter's irritation to upper airways. None are currently used within the United States for labor analgesia.

Management of Labor Pain: Parenteral

Opioids: Due to their high lipid solubility and low molecular weight, opioids easily cross the placenta and have the potential to lead to neonatal respiratory depression. They can be administered either intramuscularly or intravenously. Intravenous dosing is delivered by intermittent boluses from healthcare providers or patient-controlled analgesia (PCA). Fentanyl PCA is one of the most ideally suited methods for use in obstetrics because of its rapid onset, short duration, and lack of active metabolites. Remifentanil is also used for labor analgesia given its pharmacologic profile—rapid hydrolysis by nonspecific plasma and tissue esterases leading to short elimination half-life, short context-sensitive half-life, extensive redistribution/metabolism by fetus, demonstrated by low umbilical artery:vein concentration ratio. Remifentanil has been shown in many randomized, double-blinded trials to offer superior pain control compared to fentanyl or meperidine [4] and nitrous oxide [5]. Studies comparing remifentanil PCA to epidural anesthesia are mixed, with either similar or lower pain scores in the epidural group and increased side effects with remifentanil including sedation, hypopnea, desaturation, and need for supplemental oxygen [6, 7].

Management of Labor Pain: Regional

Epidural: Of all methods listed, epidural is the most effective means of relieving pain during labor. It is associated with decreased pain scores and increased patient satisfaction when compared to nonpharmacologic techniques, parenteral, and inhaled medications [8]. It is also the most commonly utilized technique in the United States by laboring women [9]. Few absolute contraindications to its use exist, and these include: [1]

1. Patient refusal
2. Allergy to injectate
3. Intracranial lesions with associated increased intracranial pressure
4. Local infection at the site of needle insertion
5. Coagulopathy
6. Recent anticoagulant administration (see guidelines)
7. Uncorrected maternal hypovolemia

Following placement of an epidural catheter, local anesthetic (LA), opioid, or a combination of the two may be used for initial bolus and mainte-

nance of analgesia. Long-acting amide local anesthetics are typically utilized, and there appears to be no clinically significant difference between Bupivacaine and Ropivacaine, despite numerous studies comparing the two [10]. Low concentration-high volume dosing decreases the total dose required and increases patient satisfaction compared to high concentration-low volume administration of the same LA [11]. Addition of a lipid-soluble opioid to the LA decreases the concentration of LA required to achieve adequate analgesia [12] and decreases the total dose of LA in a dose-dependent fashion [13]. It has also been shown to speed onset, lengthen duration, and increase the quality of the block achieved [14]. Fentanyl and Sufentanil are most commonly used for this indication, and no significant difference has been found between the two [15]. Adjuvants including epinephrine, clonidine, and neostigmine are also occasionally utilized in epidural anesthesia, but no absolute indications for their use exist.

In addition to choice of medication and dosing regimens, methods of administration have also been studied in regard to epidural anesthesia. Currently, patient-controlled epidural anesthesia (PCEA) with or without background continuous infusion is most commonly utilized. Studies have shown that while background infusion improves analgesia, it also leads to administration of higher total doses of local anesthetic. The significance of this is questionable, since no increased motor block or difference in adverse obstetric outcomes between the two has been shown [16]. Although not yet mainstream, the use of programmed intermittent epidural boluses is being used to replace continuous infusions. Studies investigating this method of drug delivery report decrease in the overall consumption of LA and incidence of motor block while increasing patient satisfaction [17, 18].

Combined Spinal-Epidural (CSE): Advantages of this technique include its significantly faster onset to effective analgesia, faster onset to sacral analgesia, and decreased incidence of failed epidural catheter. Although the technique involves puncture of the dura, with use of a small-gauge pencil-point needle, the risk for post-dural puncture headache does not appear to be increased [19].

Dural Puncture Epidural: This technique involves puncture of the dura with a small-gauge spinal needle, but no intrathecal injection of medication. Sacral coverage following epidural injection of a LA and opioid has been shown to be superior to traditional epidural, likely secondary to spread of medications through the puncture site [20].

Paracervical Block: This technique can be used during the first stage of labor to relieve pain associated with cervical dilation. It involves injection of local anesthetic lateral to the cervix. Although uncommon, maternal complications include neuropathy, hematoma, abscess, and laceration. Fetal bradycardia and direct injection into the fetal scalp leading to systemic toxicity are both possible [1].

Pudendal block: Injection of local anesthetic into the bilateral vaginal wall can partially relieve pain associated with the second stage of labor. Maternal and fetal complications of this block are similar to those associated with paracervical block [1].

Management of Labor Pain: Nonpharmacologic

Many nonpharmacologic means of pain control are utilized during labor in an attempt to minimize fetal exposure. These include intradermal water injections, transcutaneous electrical nerve stimulation, acupuncture, hypnosis, biofeedback, and hydrotherapy.

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Part X

Headache and Facial Pain

Migraine Headaches

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Paul Rizzoli

ICD-10 G43 Migraine
G43.0 Migraine without aura
  G43.00 Migraine without aura, not intractable
  G43.01 Migraine without aura, intractable
  G43.1 Migraine with aura
G43.4 Hemiplegic migraine
G43.5 Persistent migraine aura without cerebral infarction
G43.6 Persistent migraine aura with cerebral infarction
G43.7 Chronic migraine without aura
G43.8 Other migraine
G43.9 Migraine, unspecified

Epidemiology

The 1-year prevalence of migraine in the US population is roughly 12 % (5 % males and 17 % females), with peak prevalence between the ages of 25 and 55 years old. At all ages, migraine is roughly 2–3 times more common in females than males. Geographically, the lowest prevalence areas are Africa and Asia and the highest prevalence is in North America.

In most populations studied, chronic migraine prevalence is consistently around 4 % of adults.

Migraine remains under-diagnosed and under-treated with less than half of epidemiologically identified patients ever being diagnosed.

Clinical Picture

Migraine Phases: Prodrome—Aura—Headache—Postdrome

Prodrome: This develops hours to days before headache in up to 60 % of patients. Multiple different symptoms are described from constitutional to psychological in nature, including depression, hyperactivity, cognitive changes, irritability, euphoria, neck stiffness or pain, fatigue, and drowsiness in some combination. Food cravings, e.g., chocolate, when satisfied and followed by headache, may result in the food being blamed for the headache when instead it was simply a prodromal food craving.

Aura: Focal neurologic phenomena that typically precede, but may accompany the onset of a headache. Most symptoms develop slowly over minutes and last less than 60 min. Most commonly seen are visual or sensory symptoms; however, weakness in any form is specifically excluded from the definition of aura.

Headache: Typically described as unilateral, throbbing, and of moderate to severe intensity

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that is aggravated by routine physical activity. Lost in the common experience of headache is the appreciation of the severity of migraine; this is a pain that is often easily recalled by the patient who will go to some lengths to prevent or limit further events. After onset, pain peaks in minutes to hours and usually clears within 4–72 h. The most typical onset is upon waking in the morning, though migraine may awaken patients from sleep at times. More atypical patterns may be difficult to distinguish from a tension-type pattern. Generally, during a headache, patients seek rest in a dark environment and avoid activity or even head movement. Scalp tenderness (Allodynia) is also present in some.

Headache frequency varies among patients for several per year to 10–12 days per month. The most common associated features, photophobia and nausea, are present in nearly all patients and are featured in the diagnostic criteria. Anorexia and vomiting, when present, are likely on the basis of gastroparesis, which can interfere with absorption of orally administered treatments for migraine. More recently, dizziness has become accepted as a migraine-associated symptom. Patients also experience symptoms of enhanced sensory perception: not only photophobia as above but also phonophobia and osmophobia. As a result, patients often seek a dark, quiet environment with reduced sensory stimuli.

Postdrome: Characterized by impaired concentration, feeling washed out and fatigue for a time after the headache. Alternatively, some patients report feeling refreshed or euphoric after a headache.

Migraine Without Aura

A highly prevalent disabling disorder characterized by moderate to severe episodic or chronic headache. It is divided into two major subtypes: migraine with and without aura. The headache, as defined by ICHD criteria, lasts 4–72 h with at least two of: unilateral location, pulsating quality, moderate or severe intensity, and aggravated by routine physical activity such as walking or climbing stairs. Nausea and/or vomiting or photophonophobia should also be present. Once a patient has had five such attacks, migraine can be diagnosed. The headache is most often frontotemporal in location; an occipital location in children is rare enough to prompt concern. A facial location for the pain is rarely reported. Episodic migraine frequency varies widely, with episodes occurring anywhere between once or twice a year to 12–14 days a month. When attacks are very frequent, >15 days a month with > 4 h of headache per day, chronic migraine is diagnosed.

Migraine with Aura

An aura is defined as a set of neurologic symptoms consisting of visual, sensory, or speech/language symptoms, but excluding motor weakness, that develop gradually over minutes, each lasting less than an hour. Symptoms are completely reversible and often precede or herald the onset of headache pain.

Most common is a visual aura which typically consists of both positive visual symptoms such as bright scintillating lights, zig-zag lines (so-called fortification spectra), or negative visual symptoms such as dark spots or visual loss that spread across the visual field at a slow but persistent rate. These may be followed by additional aura symptoms, usually unilateral sensory paresthesias or numbness. Later, these may be followed by speech or language dysfunction.

Chronic Migraine

Chronic migraine, defined as headache for more than 15 days per month and more than 4 h each day of headache, is present in 3–4 % of the headache population and is very debilitating. Factors contributing to the development of chronic migraine may include a higher frequency of episodic migraine at baseline, obesity, sedentary lifestyle, comorbid depression/ anxiety, and overuse of abortive migraine medications. Significant advances in the management of chronic migraine, including Botox (see separate chapter), have improved the prognosis.

Migraine Equivalent

Many types of transient recurrent neurologic symptoms occur that have been attributed to migraine or migraine aura, but without headache and thus termed migraine equivalents. These include visual scintillations, visual blurring or transient loss of vision, visual field cuts, language dysfunction, paresthesias, confusion, oculosympathetic palsy, confusion, cyclical vomiting, and diplopia.

Visual scintillating scotoma and blurred vision may reflect the occurrence of aura alone without headache. This pattern typically occurs in patients over age 40. Over half report a prior history of recurrent headache but not all do. Though scintillations may be considered pathegnomonic of migraine physiology, other visual symptoms may be caused by a number of conditions including TIA or stroke. At times, it may be a challenge to distinguish among these possible explanations.

Pathophysiology

Migraine pathophysiology may be thought of in terms of a functional system: the trigeminovascular system that contains both peripheral and central components. The trigeminal nerve supplies most sensory fibers innervating intracranial meninges and vessels. When stimulated, these fibers can release neuropeptides, locally causing neurogenic inflammation, amplifying afferent nerve transmission, and producing the characteristic throbbing headache aggravated by routine physical activity. Cervical nerve pathways may also be involved. These nerve transmissions converge on the brainstem, primarily in the trigeminal nucleus caudalis, and then travel to the thalamus and cortex. Symptom amplification and reinforcement may then be enhanced by a process of central neuronal sensitization. Central descending inhibitory systems may come into play to eventually stop the process and restore normal function. These processes may be located in the dorsal pons and midbrain.

Diagnostic Testing

In a patient with a clear diagnosis of migraine and no findings on neurological examination, there is likely little value in adding imaging to the evaluation. However, if the headache has any atypical feature or is recently changed in pattern, the decision may shift in favor of imaging. In the outpatient setting, MRI imaging is the most common modality and avoids patient exposure to radiation.

American Academy Guidelines on Imaging in Headache suggest considering imaging in patients with unexplained findings on neurological examination or in patients with atypical headache features or who have some additional medical condition such as immune deficiency that raises concern for secondary causes for headache.

Treatment

The goals of treatment broadly are to return the patient to a functional state following an attack and further to reduce the overall burden of the condition. Components of a treatment plan include patient education, lifestyle management and trigger reduction, acute treatment of an attack, preventive management, and periodic review of the plan.

Migraine can be described as a genetically induced hypersensitivity or reactivity to internal (e.g., hormonal changes) and external (e.g., weather change) environmental changes that act as triggers to initiate an attack. Based on this formulation, lifestyle management techniques could be considered including regular sleep hours, nutrition, exercise, and stress management. Dietary restrictions are commonly discussed and recommendations are widely available though with limited research evidence.

Acute abortive treatment of headache is with either non-specific agents such as non-steroidal anti-inflammatory drugs (NSAIDs), combination analgesics, anti-emetics, opioids, corticosteroids, dopamine agonists, or with migraine-specific agents such as ergotamine preparations, dihydroergotamine, and the selec-

Table 138.1 Selective serotonin (5-hydroxytryptamine), 5-HT 1B/1D receptor agonists, the triptans

Generic	Brand (e.g.)	Formulations	Half-life (h)	Metabolism
Sumatriptan	Imitrex	25, 50 and 100 mg tabs, 4 and 6 mg SC, nasal spray	2.5	MAO
Rizatriptan	Maxalt	5 and 10 mg tab and oral dissolving tablet (ODT)	2–3	MAO
Naratriptan	Amerge	2.5 mg tabs	5–8	Hepatic
Eletriptan	Relpax	20 and 40 mg tabs	4	CYP3A4
Almotriptan	Axert	6.25 and 12.5 mg tabs	3–4	Hepatic
Frovatriptan	Frova	2.5 mg tabs	26	Hepatic
Zolmitriptan	Zomig	2.5 and 5 mg tab/ODT	3	Hepatic

Table 138.2 Preventive agents used in migraine management

ACE inhibitors
Anticonvulsants: e.g., valproate, gabapentin, topiramate
Antidepressants: TCAs, SSRIs, SNRIs
Beta adrenergic blockers: e.g., propranolol, nadolol, metoprolol, atenolol
Calcium channel antagonists: Verapamil, flunarizine
Neurotoxins
Serotonin antagonists: methergine

tive 5-HT1 agonists, or triptans. Early treatment in the course of an attack is suggested for best results. The choice of agents may differ depending on headache severity. Medication overuse, which can lead to toxicity, dependence, and headache exacerbation, is a concern when attack frequency necessitates frequent use of abortive agents (Table 138.1).

Preventive therapy can be considered in migraine when headaches are frequent (>2/week) and/or disabling. Best results are obtained from starting agents at a low dose with slow increases as warranted and an overall adequate trial length. Patient follow-up and review of headache diaries or journals can be helpful (Table 138.2).

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Tension-Type Headache

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ICD-10

- G44.2 Tension-type headache
- G44.20 Tension-type headache, unspecified
  G44.201 …intractable
  G44.209…not intractable
- G44.21 Episodic tension-type headache
  G44.211 …intractable
  G44.219 …not intractable
- G44.22 Chronic tension-type headache
  G44.221 …intractable
  G44.229 …not intractable

Summary

- Most common primary headache disorder in the general population
- High socio-economic impact
- Most tension-type headaches do not come to medical attention

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Definition and Epidemiology

Tension-type headache (TTH) is a highly prevalent, mild—moderate pattern of headache with a likely neurobiologic basis. It is no longer considered to be psychogenic in origin. The somewhat vague clinical picture is based largely on the absence of symptoms. Prevalence is estimated at 30–78 % though some studies put it as high as 87 %. The infrequent episodic form is the headache that virtually everyone has had and usually does not come to medical attention. Chronic TTH may affect about 3 % of the general population. Nonetheless, TTH as a whole produces a large socioeconomic impact and significant disability. TTH is slightly more prevalent in females and some genetic factors may play a role; however, environmental features are generally considered more significant.

Pathophysiology

Pathophysiology is unknown. Debated is whether TTH shares migraine pathophysiology forming a spectrum of symptoms with a common cause, and many patients exhibit both migraine and TTH patterns; however, differences exist and the matter is under study. TTH patients have been shown to have general increased pain sensitivity suggesting abnormal pain processing. Though pain thresholds may not be abnormal, the response to pain dis-

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plays a left-shifted curve indicating altered pain physiology. Long-term peripheral nociceptive input may produce sensitization of neurons in the trigeminal nucleus caudalis, explaining the increase in pain sensitivity and central sensitization. TTH patients also frequently, but not invariably, report musculoskeletal complaints and show findings of pericranial muscle tenderness.

Clinical Features

TTH is in essence a mild to moderate bilateral steady, pressing or tightening headache lasting 30 min to 7 days that, unlike migraine, is not aggravated by routine physical activity (e.g., climbing stairs), and further, is usually unassociated with nausea or vomiting (anorexia may be reported) and photophonophobia. It may be classified as infrequent (<1/ month), frequent (1–14 episodes/month), or chronic (>14 episodes per month). The infrequent episodic category provides a way of classifying the nearly universally experienced pattern of headache while keeping it separate from more significant tension headache types. TTH may be further classified as being associated or unassociated with pericranial muscle tenderness. The pain may be described by patients as a vise-like or band-like discomfort.

The peak prevalence is estimated at between 30 and 39 years of age. Chronic TTH has a prevalence of 2–3 % of the population with a female predominance. All forms tend to persist in an individual over years. Conditions known to be comorbid with TTH include anxiety, depression, and fibromyalgia.

Treatment

Patient education and lifestyle modification form the cornerstones of treatment. Evidence for the efficacy of pharmacologic treatments in TTH remains scarce for a variety of reasons. Also, given the variability of TTH, treatment should be individualized. Acute treatment can be considered in all forms of TTH; preventive treatment can be considered in frequent and chronic TTH with the goal of reduced headache burden and improved quality of life.

It has been recommended that acute headache management be limited to 2 days a week or less (Wolff), primarily to avoid the risk of development of medication overuse headache. Nonsteroidal anti-inflammatory drugs appear more beneficial than acetaminophen. Acetylsalicylic acid has also been shown to be effective.

Tricyclic antidepressant medications, especially amitriptyline, may be effective in prevention and this effect is seen as separate from the antidepressant effect. A minimum trial of 6–8 weeks should be considered and dosage adjustment may be required. Continuing treatment for 3–6 months after control is achieved is suggested followed by an attempt to taper the medication. Tizanidine has also been suggested in preventive management.

Complementary and alternative therapies are attractive and becoming more frequently used in management of TTH, but often difficult to study and, apart from some evidence for biofeedback, no clearly superior therapeutic modality emerges. Psychological and behavioral therapies may play a role for some patients. Physical therapy may show a modest benefit in some. Lastly, treatment of comorbid conditions can be very helpful.

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Cluster Headaches

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ICD-10

- G44.0 Cluster headaches and other trigeminal autonomic cephalalgias (TAC)
  - G44.00 Cluster headache syndrome, unspecified G44.001 intractable, G44.009 not intractable
  - G44.01 Episodic cluster headache G44.011 intractable, G44.019 not intractable
  - G44.02 Chronic cluster headache G44.021 intractable, G44.029 not intractable

ICHD III Beta-Cluster Headache

3. Trigeminal autonomic cephalalgias
   3.1 Cluster Headache
      3.1.1 Episodic cluster headache
3.1.2 Chronic cluster headache

Definition and Diagnosis

Cluster headache (CH) is classified in the International Classification of Headache Disorders (ICHD) as a trigeminal autonomic cephalalgia (TAC). Others in that group are discussed elsewhere. TACs as a group are unilateral headaches combined with the local parasympathetic autonomic symptoms activated through normal trigeminal parasympathetic fibers. CH, the most commonly diagnosed TAC, is typically an episodic headache that is usually severe and localized to the orbital, periorbital, or temporal region. Each cluster attack lasts 15 min to 3 h, with attacks occurring every other day up to eight times per day. Along with the pain, one of the following autonomic features should be present: ipsilateral conjunctival irritation, tearing, nasal congestion, sweating, pupillary changes, or facial and eyelid edema. In addition and by definition, the patient is usually agitated and restless during an event in distinction to the typical migraine patient who usually seeks rest in a quiet, dark environment. Interestingly, typical migraine aura has been described in rare instances of cluster and can confuse the diagnosis.

Cluster Headache—ICHD Diagnostic Criteria

A. At least five attacks fulfilling criteria B–D
B. Severe or very severe unilateral orbital, supraorbital, and/or temporal pain lasting 15–180 min (when untreated)
C. Either or both of the following:
   1. At least one of the following symptoms or signs, ipsilateral to the headache:
   2. A sense of restlessness or agitation
      (a) Conjunctival injection and/or lacri mation

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(b) Nasal congestion and/or rhinorrhoea
(c) Eyelid oedema
(d) Forehead and facial sweating
(e) Forehead and facial flushing
(f) Sensation of fullness in the ear
(g) Miosis and/or ptosis

D. Attacks have a frequency between one every other day and eight per day for more than half of the time when the disorder is active

Epidemiology

CH is a relatively rare form of headache which, in distinction to migraine, predominates in men. Lifetime prevalence estimates vary widely, but may be around 120 per 100,000 or 0.1% of the population. Mean age of onset is between ages 26–30. For the most part, it is considered a sporadic illness with possible familial features. Smoking has been associated with development of the headache pattern; up to 85% of patients with the disorder are chronic smokers. Quitting, however, seems to have no effect on the course of the illness.

Pathophysiology

The pathophysiology is incompletely understood. In cluster, as distinct from migraine, an ipsilateral hypothalamic source triggering the trigeminal pathway may lead to unilateral hyperactivity in the spinal tract and nucleus of the trigeminal nerve and to the release of vasoactive peptides and production of autonomic changes. Secondary ipsilateral vasodilatation may explain some of the clinical findings, e.g., swelling, and research findings.

Clinical Features

CH is relapsing illness with periods or episodes, up to several weeks or months' duration, of headache attacks as above interspersed with headache-free remissions often lasting up to a year or more. The initial clinical presentation is usually quite characteristic and the diagnosis may be made clinically. Nevertheless, neuroimaging is suggested to exclude secondary causes, so-called secondary cluster headache. Distinguishing CH from the other TACs may also present a diagnostic challenge at times.

Pain quality is generally described as sharp and constant, burning or boring, described by some as a "hot poker in the eye". The typical duration of an attack is 30–60 min. Associated cranial autonomic features are ipsilateral to the pain and persist for the duration of the pain. Patients are typically unable to rest during an attack, and instead become restless and may pace, rubbing or compressing the affected area. An individual attack may tend to return at the same time daily during a cluster episode. Typical migraine triggers, including alcohol, may trigger a cluster attack and sleep, especially REM sleep, may also trigger an attack.

CH may become chronic in some patients transformed from an episodic pattern, or may arise de novo as a chronic pattern.

Diagnosis

Though the clinical picture for episodic cluster is typically quite characteristic, secondary forms of CH are described and imaging is usually warranted at some point in the course of the illness.

Treatment

Beyond avoiding alcohol and naps during a cluster bout, both of which can trigger headache, there is little in the way of lifestyle management to suggest. Quitting smoking is usually advised, but typically does not abort an episode. Abortive and preventive pharmacologic treatments are usually advised during a bout and are generally held if possible between bouts. Since individual headaches usually develop rapidly, oral abortive medications will be less effective than parenteral or inhaled treatments. Subcutaneous sumatriptan 4–6 mg is the treatment of choice for an individual attack. It has a rapid onset, is very effective, and well-tolerated even when used up to twice a day

during a cluster bout. Contraindications to use include coronary heart disease or uncontrolled hypertension. Nasally administered triptans may also be effective.

Inhalation of oxygen at high rates is both safe and effective in some patients. Effective treatment requires high flows of oxygen at 7–12 L per minute or higher through a non-rebreathing mask for 15–20 min at the onset of an attack. Barriers to use include the bulky delivery system and cost since the treatment may not be insurance-reimbursed for this condition.

For short-term prevention or to break an attack, corticosteroids, daily ergotamines, or daily triptans can be considered. An occipital nerve block administered at the onset of an attack episode may provide some benefit.

Longer episodic bouts or chronic cluster may warrant longer-term prevention. Verapamil and lithium are most commonly used. Verapamil may be used in doses ranging from 240 to 960 mg daily. The standard preparations may be more effective than longer acting preparations. Constipation is the most common side effect. At higher doses, heart block is possible and EKG monitoring is suggested as dosage titration progresses.

Evidence also supports the use of lithium 600–1200 mg daily, especially in chronic cluster. Side effects are multiple, including weakness, thirst, and tremor, and drug level monitoring is suggested to avoid toxicity.

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Medication Overuse Headache

141

Paul Rizzoli

ICD-10

G44.40 Medication Overuse Headache
G44.41 MOH-intractable

Definition

Those with frequent headaches often overuse analgesics and other abortive agents leading to medication overuse headache, a 'biobehavioral disorder' resulting in the headache condition becoming more refractory. Medication overuse headache is defined as headache on more than 15 days per month for more than 3 months after the regular overuse of acute or symptomatic headache medication(s).

Clinical Picture

The resulting headache tends to be featureless, daily and constant, often responsive, however, to the overused agent and thus tending to reinforce its use. Upon cessation, patients may report transient worsening in headache, but at about 10–14 days may note improvement overall and a return of responsiveness of their episodic headaches to treatment.

Pathophysiology

All abortive drugs can cause medication overuse including simple and compound analgesics, opioids, 5-HT 1B/D receptor antagonists (triptan) medications, and ergot preparations. The most commonly involved medications appear to be butalbital-containing combination preparations and acetaminophen-containing preparations. The period of exposure necessary to produce the condition may differ depending on the drug. For ergots, triptans, opioids, and combination analgesics, the definition requires use for more than 10 days a month, and for simple anlagesics or nonsteroidal anti-inflammatory medications, use for more than 15 days a month may be risky. The mechanism is unclear, possibly a down-regulation of serotonin or other receptors resulting from continued drug exposure. It is thought mainly or exclusively to occur in those with underlying headache disorders. Some patients may exhibit comorbid anxiety with anticipatory anxiety of an impending headache, leading to increased abortive treatment. Others may exhibit addictive personality features. The prevalence is uncertain, but medication overuse headache is frequently seen in patients presenting to a tertiary headache clinic.

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Clinical Pearl

Differentiation from chronic migraine may be challenging. Careful questioning about details of abortive medication use may help make the diagnosis.

Additional Reading

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Occipital Neuralgia

142

Paul Rizzoli

ICD-10: M54.81

Definition

- Unilateral (rarely bilateral) side-locked paroxysmal lancinating pain localized to the posterior scalp in the distribution of the greater, lesser, or third occipital nerves.
- Typical attacks last seconds to minutes; the pain is severe, sharp, and stabbing or shooting in quality. At times, an underlying dull pain is reported in between paroxysms.
- Associated dysesthesia or allodynia can be noted in the same distribution.
- A local block that temporarily relieves the pain serves to confirm the diagnosis.
- Distinguish from other posterior occipital-referred pains from intracranial or other cervical sources.

Anatomy

Sensation to the region of the posterior neck and scalp is supplied on each side by medial branches of the dorsal rami of mainly C2 and C3. The major peripheral nerves are the greater occipital nerve (C2), the lesser occipital nerve (C2, C3), and the third occipital nerve (C3). Combining these nerves provides sensation to the posterior cervical region upwards to the vertex and laterally to just behind the ear.

Pathophysiology

Compression of the greater or lesser occipital nerves in their course through cervical muscles has been suspected; however, no clear pathological evidence has been unequivocally demonstrated. Trauma, inflammation, and vascular compression have also been implicated, again without clear evidence.

Diagnosis

The incidence and prevalence of the condition are unknown. The rate of diagnosis in different centers may vary due to lack of consensus regarding the diagnostic criteria and clinical picture. Clinically, the condition often develops spontaneously, though at times a provocation such as a preceding flexion-extension neck injury is reported. When unilateral, pain is side-locked to one side and described as above. The pain often shoots forward in an arc-like distribution up and over the scalp. Referral of the pain forward to the fronto-orbital region is thought due to transmission through trigeminocervical interneuronal connections.

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Physical Examination

Palpation on the affected side in the occipitonuchal region: may elicit local tenderness, may increase the background discomfort, increase or elicit paresthesias, or may act as a trigger to the pain (Tinel's sign). Other findings may include reduced range of motion of the cervical spine or detection of spasm in cervical musculature. Less common findings would include reduced sensation or dysesthesia in the distribution of the affected nerve. The remainder of the examination is typically normal.

Differential Diagnosis

Many conditions could produce referred occipital pain, and thus, the differential diagnosis is broad and includes multiple causes of cervical spine joint and bone disorders, posterior fossa pathologic processes and, possibly, vertebrobasilar vascular pathology. Differentiation from cervicogenic headache, referred pain from cervical pathology perceived as a headache, may be challenging at times.

Testing

No clear guidelines exist on how to best evaluate the patient for structural or infiltrative processes producing posterior occipital region pain. Cervical MRI is probably overall the most informative modality, though there may still be a role for plain radiographic imaging or radionucleotide bone scanning in some patients.

Management

- For mild symptoms, local application of heat or ice has been recommended.
- For more severe discomfort, a local anesthetic nerve block may provide both transient relief and confirm the diagnosis (See Chap. 73 for description)
- Repeat blocks with a local anesthetic agent as needed are generally safe and well-tolerated. Blocks containing a mixture of an anesthetic agent with a steroid medication have been associated with local complications such as focal alopecia and are less frequently used.
- Lastly, oral neuropathic pain medications may be beneficial. Gabapentin and tricyclic antidepressants have been recommended.

Clinical Pearl

Inadvertent injection of local anesthetic into the CSF via an underlying long nerve root sleeve may cause complications including respiratory arrest.

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Trigeminal Neuralgia

143

Paul Rizzoli

ICD-10
G50 Disorders of the trigeminal nerve

G50.0 Trigeminal neuralgia

G50.1 Atypical facial pain
G50.8 Other disorders of the trigeminal nerve
G50.9 Disorder of the trigeminal nerve, unspecified

Definition

A distinctive recurrent painful facial pain disorder characterized by brief, severe shock-like pains limited to one or more divisions of the trigeminal nerve.

Pathophysiology

The trigeminal nerve supplies sensation to the face through three divisions, the ophthalmic (V1), maxillary (V2), and mandibular (V3) divisions. Sensory information from these divisions enters the gasserian ganglion located in Meckel's cave in the base of the middle cranial fossa. From there, information travels through a large sensory root to enter the mid-lateral pons. Compression at the level of the root entry zone by a vessel (usually the superior cerebellar artery) is a common cause; the resulting clinical picture is termed classical trigeminal neuralgia. Compression is thought to produce focal demyelination, which leads to ectopic impulse generation and ephaptic transmission responsible for generating symptoms.

Clinical Features

The classical form is a painful relapsing and remitting condition that most often strikes those over age 50 with a peak incidence in the fifth to seventh decades. Estimates of prevalence are between 4 and 13 cases per 100,000 per year, with a slight female predominance. Though most often sporadic, rare familial cases are described.

The pain has an abrupt onset and termination. Attacks are very severe and typically last from a fraction of a second to 2 min, described as brief, electrical, or shock-like. Pain may be triggered by an innocuous local stimulus such as touching the face, and patients typically avoid washing the face, talking, or chewing so as to avoid triggering an event. There may be a brief refractory period after a triggered event during which triggering further pain is not possible. Remissions may occur in some for long periods of months to years followed by a return of pain. Some patients report a less severe background pain in between attacks.

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Those with interictal background pain may be less likely to exhibit neurovascular compression by MRI and may respond less well to medical and surgical management. Rare cases of bilateral trigeminal neuralgia have been described, often in the setting of multiple sclerosis.

Diagnosis

ICHD 3-beta

13 Painful cranial neuropathies and other facial pains
- 13.1 Trigeminal neuralgia
  - 13.1.1 Classical trigeminal neuralgia
    - 13.1.1.1 Classical trigeminal neuralgia, purely paroxysmal
    - 13.1.1.2 Classical trigeminal neuralgia with concomitant persistent facial pain
  - 13.1.2 Painful trigeminal neuropathy
    - 13.1.2.1 Painful trigeminal neuropathy attributed to acute Herpes zoster
    - 13.1.2.2 Post-herpetic trigeminal neuropathy
    - 13.1.2.3 Painful post-traumatic trigeminal neuropathy
    - 13.1.2.4 Painful trigeminal neuropathy attributed to multiple sclerosis (MS) plaque
    - 13.1.2.5 Painful trigeminal neuropathy attributed to space-occupying lesion
    - 13.1.2.6 Painful trigeminal neuropathy attributed to other disorder

For diagnosis of classical trigeminal neuralgia, the ICHD 3-beta classification system requires three attacks of unilateral facial pain strictly within one or more divisions of the trigeminal nerve, along with at least three of the following pain features: (1) Paroxysmal attacks lasting from a fraction of a second to 2 min, (2) Severe intensity, (3) Quality that is electric shock-like, shooting, stabbing, or sharp, and (4) Precipitated by innocuous stimuli to the affected side of the face. The condition may be further classified as being purely paroxysmal or being associated with concomitant persistent facial pain.

Others with atypical presentations or secondary forms of trigeminal distribution pain are diagnosed as painful trigeminal neuropathies.

Examination in those with the classical pattern of symptoms is often normal, though a minority show sensory loss on the affected side.

MRI is the diagnostic study of choice and is done both to exclude secondary causes and to demonstrate the neurovascular compression.

Treatment

Pharmacologic therapy is first step in management with surgery reserved for those failing medical management. Carbamaezapine (typical recommended maintenance dose of 600–800 mg daily) is the best studied drug for TN with complete or near complete pain relief in well over 50 % of patients and as high as 100 % in some studies. Other tested medications include oxcarbazepine, baclofen, gabapentin lamotrigine, and onabotu linumtoxinA.

Surgical options include various ablative procedures and microvascular decompression. Decompression requires a craniotomy, but produces pain relief initially in up to 90 % of patients.

144 Trigeminal Autonomic Cephalalgias (TACs): Cluster Headache, Paroxysmal Hemicranias, SUNCT, SUNA

Paul Rizzoli

ICD-10

G44 Other headache syndromes
- G44.0 Cluster and other TACs
  - G44.00 Cluster, unspecified
  - G44.01 Episodic cluster
  - G44.02 Chronic cluster
  - G44.03 Episodic paroxysmal hemicrania
  - G44.04 Chronic paroxysmal hemicrania
  - G44.05 Short lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT)
  - G44.09 Other TACs

The trigeminal autonomic cephalalgias, including cluster headache, paroxysmal hemicrania, short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT), and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA), are grouped together as primary headache disorders charac terized by unilateral trigeminal distribution pain in association with ipsilateral cranial autonomic features. They differ in their attack frequency and duration (Table 144.1).

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Cluster Headache

This disorder in its episodic form is very distinctive; an episodic headache disorder more frequently appearing in men and characterized by attacks of daily severe unilateral orbital pain with ipsilateral autonomic features, episodes of which occur in clusters of up to 1–2 months duration, typically recurring annually at roughly the same time of the year. During a headache, the patient will usually become agitated and pace in distinction to the sensory-avoiding behavior of the migraine patient. Examination may disclose an ipsilateral Horner's syndrome. Functional imaging studies localize the disorder to the posterior hypothalamic region. An episode of recurrent cluster attacks lasting more than one year may be considered chronic cluster.

Diagnosis and Management

Cluster is a rare form of headache with a prevalence under 1 % of the US population. Multiple structural and vascular lesions may mimic cluster and imaging is warranted for a new or changed pattern of headache. Individual attacks may respond to injection of subcutaneous sumatriptan or inhalation of high flow oxygen administered by a non-rebreather mask. Initial and empiric treatment at the onset of a cluster period may include a course of PO corticosteroids and

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Table 144.1 Comparison of trigeminal autonomic cephalalgias

Name	Location	Duration	Attack frequency/day	Associated features	Treatment
Cluster	Unilateral orbital	15–180 min	1–8	Lacrimation, conjunctival injection, rhinorrhea	Verapamil, inhaled oxygen 15 L/min
Paroxysmal Hemicrania	V-1, ophthalmic division	2–30 min	2–40	Tearing, conjunctival injection, rhinorrhea	Indomethacin- with complete control
SUNCT	Unilateral orbital to temporal region	15 s to 4 min	3–200	Conjunct inject AND lacrimation	Lamotrigine, IV lidocaine
SUNA	Unilateral orbital to temporal region	15 s to 4 min	3–200	Conjunct inject OR lacrimation + rhinorrhea/ nasal congestion	Lamotrigine, IV lidocaine

anesthetic blockade of the ipsilateral occipital nerve. Verapamil is the most widely used preventive agent and, given early in a cluster period, may reduce attack frequency and shorten the overall duration of the cluster period.

Paroxysmal Hemicrania

This is a rare disorder seen predominantly in adult females who present with brief side-locked attacks of severe pain in the orbitofrontal region with ipsilateral autonomic features. Although generally limited to a duration of minutes, attacks as long as 2 h have been described and up to 1/3 of patients may report a more mild background headache in between attacks that can complicate the clinical picture. There is typically a delay of years after presentation before the correct diagnosis is made. The importance of making this diagnosis is the dramatic and complete remission possible with an adequate trial of oral indomethacin, 75–150 mg daily for 1–2 weeks. Thereafter, maintenance doses range from 25 to 100 mg daily. Otherwise, paroxysmal hemicrania is considered refractory to most other medication management.

SUNCT and SUNA

These very rare conditions are among the shortest duration headaches described with attacks lasting 5 s to 4 min, but recurring very frequently throughout the day. The pain is side-locked and periorbital, brief and severe, and stabbing or pulsing. The pattern of associated autonomic features may serve to determine which diagnosis is made. SUNCT requires associated ipsilateral lacrimation and conjunctival injection. SUNA has one but not the other and may have other ipsilateral autonomic features such as rhinorrhea or nasal congestion. Imaging is generally suggested in the initial evaluation. Secondary causes include lesions in the posterior fossa or pituitary gland. These are challenging headaches to treat. Transient response to IV lidocaine has been reported. Preventive agents used in this setting include lamotrigine and topiramate.

Part XI

Nerve Damage

Neuropathic Pain

145

Christopher R. Abrecht and Srdjan S. Nedeljkovic

Neuropathic Pain: Definition

"Pain caused by a lesion or disease of the somatosensory nervous system" is a definition for neuropathic pain according to the International Association for the Study of Pain. "Lesion" refers to an abnormality found on a diagnostic test (e.g., evidence of demyelination); "disease" refers to a known process causing a lesion (e.g., Guillain-Barre Syndrome). This lesion or disease-causing neuropathic pain may be in either the central or peripheral nervous system.

Prevalence

A recent systematic review of epidemiological studies has estimated that neuropathic pain has a prevalence of between 6.9 and 10 % in the population.

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Evaluation and Diagnosis

The onset and progression of neuropathic pain is often gradual, and symptoms may be spontaneous or evoked. Its hallmark dysesthesias may be described by a range of phrases (e.g., "burning," "pins and needles," "shock-like") and pain may be associated with hyperalgesia and allodynia, as well as motor and autonomic disturbances. Validated questionnaires are available to identify neuropathic elements of pain (e.g., the Neuropathic Pain Questionnaire).

The initial approach to assessing a patient with neuropathic pain is to determine the territory of neuropathic symptoms and signs. A common presentation is of a symmetric, length-dependent pattern of injury that starts in the feet, which are innervated by the longest axons, and progresses upward. Presumably, a systemic stressor (e.g., hyperglycemia) reaches all nerves, but has the greatest impact on those axons furthest from their cell body. In contrast, an asymmetric, non-length-dependent neuropathy affects both proximal and distal territories and is not symmetric (e.g., CIDP).

Next in the evaluation, take note of the affected modalities: sensory, motor, or autonomic axons. Sensory involvement is a predominant component of almost all neuropathies; motor involvement may occur as a late finding of a symmetric, length-dependent process, or early in the disease course when demyelination occurs

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(e.g., CIDP, Charcot-Marie-Tooth). Autonomic involvement is overall rare, but common in certain conditions (e.g., diabetic neuropathy).

Further in your evaluation, consider whether the pathology is occurring at the axon or myelin sheath. With axonal injury, deep tendon reflexes are preserved and muscles atrophy; with myelin injury, reflexes are lost and muscle bulk is preserved. If in doubt, NCS/EMG can confirm the etiology of the deficit. If a small fiber neuropathy is suspected, a skin punch biopsy may be performed.

While most patients presenting to a pain specialist with a painful neuropathy have an established diagnosis, understanding the basic pathophysiology of neuropathic pain is important as this may guide treatment.

Etiologic Classification

Painful neuropathies can be classified by their etiology.

Symmetric, length-dependent processes can be caused by metabolic (e.g., diabetic neuropathy), infectious (e.g., HCV, HIV), toxic (e.g., heavy metals, chemotherapeutics), nutritional (e.g., thiamine deficits in Beriberi), or genetic abnormalities (e.g., Charcot-Marie-Tooth, Fabry's). Non-length-dependent processes may be caused by autoimmune demyelinating (e.g., GBS, CIDP) or vasculitic (e.g., polyarteritis nodosa) disorders.

Examples of Common Painful Neuropathies

Diabetic neuropathy is the most common painful neuropathy and is discussed in detail elsewhere in this text, as are CRPS and PHN.

Trigeminal neuralgia typically manifests as paroxysmal, lancinating, unilateral pain in the distribution of the maxillary nerve, although the pain may also be bilateral and involve other branches of cranial nerve V. A common trigger is light touch, as occurs with daily activities such as shaving, tooth brushing, and eating. MRI can be used to evaluate for secondary causes such as vascular compression by the superior cerebellar artery or a demyelinating process such as multiple sclerosis. The clinical diagnosis, however, is made by history and does not require additional tests. An effective pharmacologic treatment is carbamazepine, the use of which requires frequent follow-up to evaluate for the development of agranulocytosis. Acute, severe exacerbations may be treated with IV phenytoin. Microvascular decompression or percutaneous, neuroablative procedures should be reserved for refractory cases.

Treatment Modalities

For patients with neuropathic pain, treatment should be provided for their underlying disease process—avoidance of hyperglycemia will, for example, help slow the progression of diabetic neuropathy.

Much of the research on pharmacologic interventions to treat neuropathic pain has been based on diabetic neuropathy; often, the promising agents from these trials are then applied to other painful neuropathies.

Another consideration is that neuropathic pain is stubbornly difficult to treat and often requires multiple medications to achieve satisfactory pain relief. Furthermore, many of the medications known to effectively treat neuropathic pain, such as tricyclic antidepressants and anticonvulsants, are known to have anti-cholinergic, anti-histaminergic, and other troublesome side effects. Therefore, a less effective agent but one with a better safety profile may be first used, especially in the elderly patient.

Pharmacologic treatment usually begins with an $\alpha_2\delta$ ligand such as gabapentin. Next, one may consider the addition of an SNRI such as duloxetine, a TCA, or another anti-convulsant. Additional pharmacologic treatments include topical agents (e.g., capscaicin) and, for patients who show benefit, opioids.

Spinal cord stimulation and peripheral nerve stimulation are additional treatment modalities appropriate for some patients with neuropathic pain (e.g., SCS for CRPS). These modalities are discussed elsewhere in this text.

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Diabetic Neuropathy

146

Srdjan S. Nedeljkovic and Syed Irfan Qasim Ali

Introduction

As per the American Diabetes Association, it was estimated that 29.1 million Americans had diabetes in 2012. Diabetes remains the seventh leading cause of death in United States. According to data from 2013, approximately $245 billion was spent treating patients with DM. By 2034, 44.1 million Americans are projected to have DM and annual diabetes-related spending may increase to $336 billion.

Diabetic Neuropathy

Along with other complications including atherosclerotic disease affecting coronary, carotid and peripheral arteries, nephropathy, and eye problems, the diagnosis of peripheral neuropathy related to diabetes increases morbidity and is associated with high health care expenditure. The total annual cost of diabetic neuropathy and its complications in the U.S.is estimated to be between $4.6 and $13.7 billion. Up to 50 % of diabetic patients may have neuropathy. Diabetic neuropathy is a significant contributing cause for diabetic foot ulcers.

Pathophysiology of Diabetic Neuropathy

Diabetic neuropathy may be symptomatic or asymptomatic and may be accompanied by sensory, motor, or autonomic changes. Symptomatic cases may present as tingling, numbness, pain, or allodynia. As illustrated in Fig. 146.1, there are multiple causative mechanisms associated with diabetic neuropathy, including metabolic derangements, inflammation, nerve ischemia, oxidative stress, and free radicals that may be responsible for the development of neuropathy. The key abnormality is poor glycemic control, which may lead to a cascade of reactions resulting in debilitating complications. Other associated risk factors for the development of diabetic neuropathy are elevated blood pressure, hyperlipidemia, tobacco & alcohol abuse, and the duration of diabetes.

Management

Treating diabetic neuropathy benefits from using a multidisciplinary approach involving primary care providers, endocrinologists, pain specialists, podiatrists/vascular surgeons, and physical therapists.

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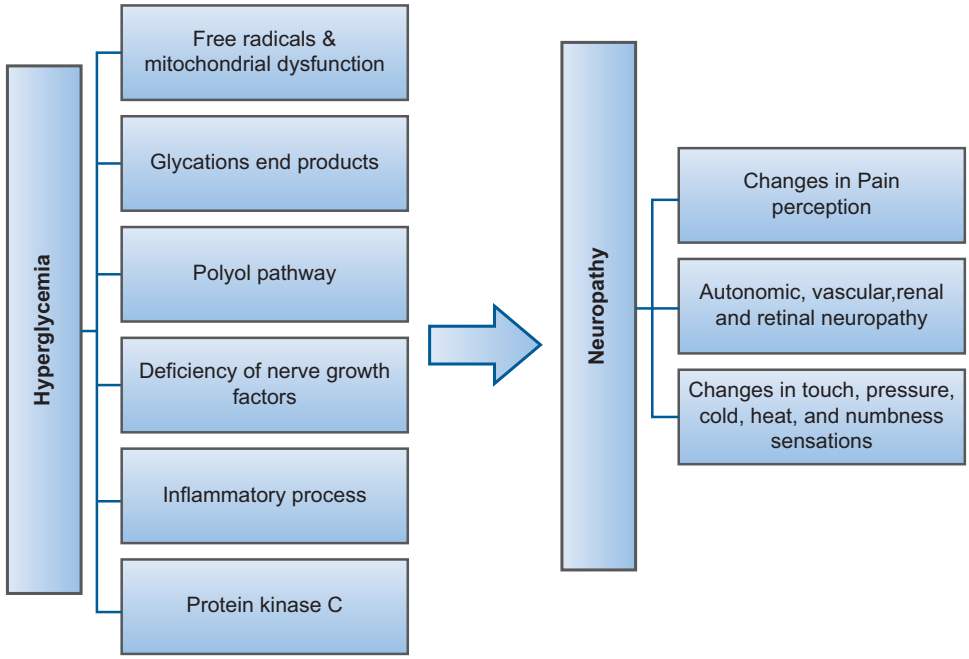

Fig. 146.1 Possible trigger and mechanism involved in development of diabetic neuropathy. Used with permission from Marrif Husnia I, Alsunousi Salma. Diabetic Neuropathy and the Sensory apparatus "Meissner Corpuscle and Merkel cells." Frontiers in Neuroanatomy. 8:2014(00079). http://www.frontiersin.org/Journal/FullText.aspx?s=742&name=neuroanatomy&ART_DOI=10.3389/fnana.2014.00079. Copyright 2014 Alsunousi and Marrif. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution, or reproduction in other forums is permitted, provided the original author(s) or licensor are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution, or reproduction is permitted which does not comply with these terms

A key component in managing diabetic neuropathy is maintaining better glycemic control, followed by patient counselling and education, foot care, pharmacotherapy, physical therapy, referral to a pain specialist, and consideration of using modalities including TENS, spinal cord stimulation, and surgical referral for advanced disease.

Pain management specialists have numerous pharmacologic options available. These include the use of drugs such as pregabalin, gabapentin, duloxetine, amitryptiline, venlafaxine, morphine, oxycodone, capsaicin, isosorbide dinitrate spray, and topical lidocaine.

Guidelines for the treatment of diabetic neuropathy have been issued by the American Academy of Neurology (AAN), American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM), and American Academy of Physical Medicine and Rehabilitation (AAPMR). Based on class 1 evidence, both pregabalin and gabapentin are useful in treating neuropathic pain related to diabetes. Class 2 evidence supports use of sodium valproic acid. Amitriptyline, venlafaxine, and duloxetine have also been used to treat symptoms of diabetic neuropathy, but there is no evidence to recommend one agent over the other. Several opiods including tramadol, oxycodone, morphine, and dextromethorphan may also be considered. Capsaicin and isosorbide dinitrate spray and topical lidocaine patches have also been used.

Evidence-based studies have not yet been done to support or refute the use of topiramate, vitamins, or alpha lipoic acid as treatment for diabetic neuropathy. Other agents like clonidine, pentoxyfylline, lamotrigine, oxcarbazepine, lacosamide, and mexilitine lack a sound

evidence-base to treat neuropathic pain in diabetic patients. In the US, the FDA has approved pregabalin and duloxetine for the treatment of pain due to diabetic neuropathy (2004) and later approved tapentadol extended release (2012), a centrally acting synthetic analgesic which is mu-opioid receptor agonist and norepinephrine reuptake inhibitor. Detailed dosing information of these medications can be found in the pharmacology chapters in this book. Research on improved treatments for pain due to diabetic neuropathy is ongoing regarding several other chemicals including NGF antibodies, N type calcium channel blockers, Nav 1.7 antagonists, aldose reductase inhibitors, angiotensin II type 2 receptor antagonists, and benfotiamine.

Evidence

Studies have shown that good glycemic control along with pharmacologic modalities leads to improved pain relief for patients with diabetic neuropathy. In a Cochrane review in 2012 by Callaghan BC et al., the authors showed that tight glycemic control delayed the onset of neuropathy. Another systemic review in 2014 by Griebeler ML et al. showed that the use of SNRI drugs, topical capsaicin, TCAs, and anticonvulsants was effective in reducing neuropathic pain in diabetic neuropathy compared to placebo.

Transcutaneous electric nerve stimulation (TENS) and spinal cord stimulators (SCSs) have also shown some benefit. A systemic review from 2013 by Stein C et al. showed that patients had pain relief with TENS. A multi-center RCT from 2014 showed that SCS was successful in 59 % patients in reducing pain.

Diabetic neuropathy is a debilitating complication leading to increased health care costs and disability. More research is needed to actually target metabolic and genetic elements responsible for neuropathy. Additional multi-center trials are needed to assess the efficacy of newer modalities and interventions for pain management of this expanding group of patients.

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Complex Regional Pain Syndrome 147

Ankur Dave

Description

Complex regional pain syndrome (CRPS) is a rare chronic pain disease affecting one of the extremities (arms, legs) and is usually secondary to trauma to that limb. The key defining feature of CRPS is the combination of excessive sensory response (pain) and physical changes disproportionate to the inciting nerve injury.

Types

- CRPS-I (Reflex Sympathetic Dystrophy, RSD): No confirmed nerve injury—most common
- CRPS-II (Causalgia): Associated nerve injury

Epidemiology

- Prevalence: 5–25/100,000
- Most common inciting events: Bone fractures, strains, trauma. Upper extremity more commonly affected than lower extremity.
- Increased risk factors
  - Severity of trauma
  - Females
  - Tobacco use
- CRPS I is more common than CRPS II
- CRPS II has worse outcomes compared to CRPS I

Pathophysiology

The exact mechanism of CRPS is not well-understood, but it is believed to be multifactorial. In 90% of cases, a trigger (such as burns, fractures, etc.) can be identified. In patients who develop CRPS, the initial injury may result in hypoxia and release of various inflammatory markers, neuropeptides, and cytokines. The continued release of these factors may lead to abnormal hyperactive responses of the central nervous system (neurogenic inflammation), peripheral nervous system (allodynia), and sympathetic nervous system (vasomotor dysfunction). As the disease progresses, peripheral and central wind-up of these pain responses and CNS sensitization (via NMDA receptor activation) can cause amplification of the symptoms. CRPS may also involve the sympathetic nervous system. In cases of sympathetically maintained pain, non-noxious stimuli may result in activation of sympathetic afferent fibers, thus leading to vasomotor dysfunction. In sympathetically independent pain, CRPS symptoms may occur in the absence of sympathetic nervous system involvement. There is some evidence suggesting psychological distress may further intensify the sympathetic response.

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Signs/Symptoms

- Traditionally, CRPS was characterized by three stages of progression.
  - Stage 1: severe pain at site of injury, decreased ROM, muscle spasms, joint stiffness, rapid hair/nail growth, skin/temperature changes
  - Stage 2: pain worsens and spreads throughout the limb, expansion of edema, reduced hair growth, brittle or cracked nails, severe/diffuse osteoporosis
  - Stage 3: severe pain of entire limb, muscle atrophy, contractures, limited mobility, skin thinning; often considered irreversible
- Signs and symptoms may overlap and presentation is highly variable.
- Increased temperature of the affected extremity is more common and has better prognosis.
- Decreased temperature of the affected extremity is more indicative of chronicity and holds worse prognosis.

Diagnosis

- No gold standard diagnostic test tests exist and CRPS is considered a diagnosis of exclusion.
- The "Budapest Criteria" has been used to aid in the diagnosis of CRPS in the clinical setting:
  - Must report at least 1 symptom in three of the four following categories:
    - Sensory: hyperesthesia and/or allodynia
    - Vasomotor: skin color changes, temperature asymmetry, and/or skin asymmetry
    - Sudomotor/edema: edema, sweating changes, and/or sweating asymmetry
    - Motor/Trophic: decreased ROM, motor dysfunction, and/or trophic changes
  - Must display at least 1 sign at the time of evaluation in two or more of the following categories:
    - Sensory: hyperalgesia and/or allodynia
    - Vasomotor: temperature asymmetry, skin color changes, and/or skin asymmetry
    - Sudomotor/edema: edema, sweating changes, and/or sweating asymmetry
    - Motor/Trophic: decreased ROM, motor dysfunction, and/or trophic changes
  - Must present with symptom of continued pain, which is disproportionate to any inciting event
- Imaging may serve as a tool in diagnosis, but should not be used as a unique diagnostic modality.
  - X-Ray and/or bone scans may show patchy osteoporosis as early as 2 weeks after injury.
  - EMG and/or nerve conduction studies may help differentiate CRPS 1 and 2.

Treatment

- Efficacy of treatment decreases as the disease progresses.
- Overwhelming evidence for treatment modalities does not exist.
- A multimodal approach is often recommended for the management of CRPS.
  - Physical/Occupational Therapy
    - First line treatment which should be started as soon as possible and considered a mainstay of CRPS management
  - Medication management: although commonly used, many classes do not have overwhelming evidence supporting use
    - Paracetamol
      - Generally accepted, given low side effect profile, but lack of evidence of benefit
    - NSAIDs
      - Mixed results and benefit versus risk must be weighed.
    - Corticosteroids
      - Benefit has been shown in setting of early/acute phases of CRPS.
      - Role in chronic CRPS is unknown.
    - Anticonvulsants
      - Gabapentin/pregabalin may reduce neuropathic pain and should be considered as a first line therapy for CRPS.
      - Carbamezepine and phenytoin can be considered if gabapentin is not tolerated.

- Antidepressants
  - A trial course of amitryptiline or nortriptyline can be considered in CRPS patients suffering from neuropathic pain.
  - Combination of gabapentin and nortryptiline has been shown to have better outcomes for neuropathic pain (such as CRPS) compared to individual drug treatment.
- Muscle Relaxants
  - Baclofen is considered first-line in cases of muscular dystonia or spasms.
- Opiates
  - Tramadol may have a benefit on neuropathic pain
  - Strong opiates should not be administered to this patient group; no data confirms long-term benefit of use.
- NMDA receptor antagonists
  - Ketamine may provide transient benefit in cases of severe, persistent CRPS
- Bisphosphonates
  - Have been shown to reduce pain in CRPS, but only on a trial basis.
  - Benefit versus risk must be weighed for long-term use.
- Calcitonin
  - Has been shown to reduce pain in CRPS.

– Interventional techniques
- Sympathetic Nerve Blocks (stellate ganglion blocks, lumbar sympathetic ganglion blocks)
  - Results have been controversial regarding efficacy as a treatment modality.
  - Long-lasting benefit has not been proven.
  - May be beneficial to restore functionality while a patient is undergoing physical therapy.
  - May be used to diagnose sympathetically mediated pain secondary to CRPS, but will not provide pain relief in patients with sympathetically independent pain.
- IV Regional Anesthetics
  - Most recent studies have shown no benefit in CRPS.
- Neurostimulation
  - Spinal cord and peripheral nerve stimulation have been shown to effectively reduce pain scores and improve quality of life.
  - Stimulation may not improve functionality.
- Epidural and plexus infusions
  - Epidural and brachial plexus infusions of bupivacaine and/or opiate may improve ROM and decrease pain scores; long-term evidence is lacking.
  - Benefits versus risks of procedure must be weighed.
- Intrathecal infusions
  - Intrathecal therapy has not been shown to provide long-term benefit.
  - Intrathecal baclofen may help in cases of dystonia secondary to CRPS.

Summary

- CRPS is a rare, often over-diagnosed disease usually affecting one of the upper or lower extremities.
- CRPS-I is the most common type and is not associated with nerve injury.
- CRPS-II (causalgia) is associated with nerve injury and associated with poor prognosis.
- The pathophysiology is not well-understood. The cause of injury results in hypoxia and release of inflammatory markers. With prolonged inflammation, peripheral, central, and sympathetic nervous systems are wound up and in a state of hypersensitivity.
- Symptoms of CRPS are highly variable and patient-dependent. As the disease progresses, there are sensory, motor, and physical changes to the affected limb.
- The disease is characterized by persistent pain disproportionate to the inciting event. Diagnosis is clinical and involves components

of sensory, vasomotor, sudomotor, and motor changes.

- Treatment is multimodal. Physical and occupational therapy is first-line and should be initiated once diagnosis is established.
- Medications should be utilized based on patient symptoms. Opiates have not been shown to have long-term benefit.
- Interventional techniques should be utilized after evaluating benefits versus risks. Neuromodulation has positive results and should be considered on a patient-by-patient basis.

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Post-Herpetic Neuralgia

148

Daniel Pak and Joseph C. Hung

Introduction

Primary varicella infection (chickenpox) is typically a mild and self-limited childhood illness presenting with a characteristic rash (pox), fever, malaise, and fatigue. Following primary infection, the varicella zoster virus (VZV) exists in a clinically inactive state in the dorsal root ganglia spinal nerves or sensory ganglia of cranial nerves. The virus can remain latent for years, but has the potential to reactivate as acute herpes zoster (AHZ)—typically seen as a blistering skin rash in the distribution of the affected ganglia. Symptoms are usually self-limited and resolve within several weeks. However, a subset of patients may have persistent pain that can last for months to years. If persistent, this neuropathic pain condition is known as post-herpetic neuralgia (PHN) and is the most common complication from AHZ. Though a 3-month time period for continued pain is typically used as a defining criterion for PHN, time frames in the literature range between 1 and 6 months.

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Risk Factors

The risk of AHZ increases with advanced age. In the general population, the lifetime risk of AHZ is 25% and escalates to greater than 50% in those older than 80 years. In general, immunocompromised patients are at increased risk for AHZ. Specific examples include advanced age (older than 50), patients with HIV, diabetes, respiratory diseases, and/or cancer, and patients that take medications (e.g., steroids, chemotherapy) that weaken the immune system.

There are several risk factors cited in the literature that increase the chance of developing PHN after AHZ. Like AHZ, the elderly are susceptible—nearly 75% of PHN cases are seen in those 60 years and older. Other named risk factors include: female gender, pain/neurologic symptoms prior to rash (prodrome), uncontrolled acute pain, and rash severity during AHZ.

Pathophysiology

The pain associated with acute herpetic neuralgia is likely due to inflammation and damage to the nerve structures during AHZ. Neural damage is amplified through peripheral and central sensitization mechanisms. Even innocuous afferent input may result in increased spontaneous activity of primary nociceptive and their associated second-order neurons.

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Table 148.1 Post-herpetic neuralgia treatment modalities

	Common agents/modalities	Side effects and limitations
Tricyclic antidepressants (TCA)	• Amitriptyline • Nortriptyline • Desipramine	• Anticholinergic side effects (drowsiness, dry mouth, constipation, urinary retention, blurry vision)
Anticonvulsants	• Gabapentin • Pregabalin • Valproic acid	• Somnolence, dizziness, confusion, ataxia
Topical Agents	• Capsaicin (may require multiple daily applications for pain relief)	• Burning sensation, erythema (more frequently seen with higher concentrations)
	• Lidocaine cream, ointment, or patch	• Local skin irritation
Opioids	• Morphine, oxycodone, tramadol, methadone, clonidine most commonly used	• Sedation, respiratory depression, tolerance, physical dependence, overdose
		• Not suitable for long-term use
Infusion therapies	• Ketamine	• Increased bronchial secretions, emergence reaction, cognitive dissociation
	• Magnesium • Lidocaine	• Arrhythmias, fatigue, sedation, blurred vision, respiratory and cardiac depression
Cutaneous/electrical nerve stimulation (TENS)	• TENS unit	• Skin irritation
	• Acupuncture	• Small risk for infection
Interventional pain techniques	• Intercostal nerve blockade/ neurolysis, cryotherapy	• Questionable efficacy
	• Sympathetic Blockade	• Deafferentation neuritis, nipple anesthesia
	• Epidural steroid injection	• Risk for bleeding and infection with more invasive techniques
	• Intrathecal steroid injection (therapeutic benefit not proven and thought to be unsafe)	• Arachnoiditis
Neurosurgical techniques	• Electrocoagulation of dorsal root, anterolateral cordotomy	• Permanent neurologic deficits
		• Questionable efficacy
	• Dorsal root and/or dorsal column stimulator	• Risk for bleeding and infection with more invasive techniques
		• Lead migration

Clinical Manifestations

AHZ and PHN most commonly affect thoracic and cervical sensory spinal nerves in addition to one or more divisions of the trigeminal ganglion. Patients present with pain and sensory disturbances along affected nerve distributions. Pain can be spontaneous, paroxysmal, and/or evoked with even innocuous stimuli. Allodynia, hyperesthesia, and dysesthesia are common. Sensory disturbances can include loss of thermal, tactile, and vibration sensations. Persistent pain can affect quality of life, interfere with activities of daily living, and result in chronic fatigue, sleep disorders, depression, and anxiety.

Management

No disease modifying agents currently exist for PHN. Therapy should be geared towards symptom control. Often multiple agents may be necessary to achieve optimal pain control. Topical agents, tricyclic antidepressants (TCAs), and anticonvulsants are recommended as first-line agents. Topical applications of lidocaine and capsaicin are generally well-tolerated, have minimal side effects, and may offer efficacious pain relief. Although opiates can also provide analgesia, they should not be offered as an initial option. If prescribed, close monitoring is recommended. Non-pharmacological treatments such as transcutaneous electrical nerve stimulation (TENS), acupuncture, and behavioral therapies should also be considered in patients who have failed first-line pharmacologic treatments. Of note, NMDA receptor antagonists and antiviral medications have not been shown to be effective for treating PHN.

The zoster vaccine is recommended for prevention of AHZ and PHN in patients 50 years old or greater, particularly those with a previous history of AHZ. The vaccine is not recommended in patients who have already received the varicella vaccine (Table 148.1).

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Part XII

Special Cases

Pain in Older Adults

149

J. Tasker Gundy

Background and Demographics

Chronic persistent pain is a prevalent syndrome in older adults (age ≥65 years), affecting as many as 50 % of community-dwelling elders and 80 % of those residing in nursing facilities [1]. Population studies demonstrate that this age group is growing faster than any other demographic, having doubled within the past 50 years and expected to double again over the next 50. Given the significant prevalence of pain in such a rapidly expanding demographic, pain practitioners should anticipate an increasing demand for their services in the multidisciplinary care of older adults in the decades to come [2].

Sequelae of untreated pain in elders: Persistent, unrelieved pain in elders can precipitate a cascade of deleterious secondary outcomes such as anxiety, depression, and insomnia. Impaired mobility may trigger the avoidance of customary social activities and increase the risk of falls. These sequelae are clearly hazards to an older adult's independence and their quality of life.

Physiologic Changes with Aging

Advancing age brings an expected, progressive functional decline of physiologic systems, and a decreased ability to adapt to stressors. As comorbidities accumulate, so too does the likelihood that complex pain may be generated from multiple pathologic territories. Several systems undergo changes that are relevant to the pain practitioner:

- *Nervous system*: Autonomic disregulation results from decreased synthesis of NE and GABA. An age-related decrease in C and A-delta fibers results in a slowed reflex response to pain and increased susceptibility to burns and other injuries. Balance issues are common, increasing fall risk.
- *Musculoskeletal*: Bone density and muscle mass decline with age, and some degree of degenerative osteoarthritis is common. Remember that radiographic evidence of degenerative disease does not always correlate with the existence of pain, and imaging should be ordered based upon the history and clinical exam in order to avoid unnecessary treatments.
- *Renal*: Renal impairment is common in older adults, as GFR decreases with age. This can result in a prolonged duration of renally cleared medications (i.e. gabapentin) or

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medication metabolites (i.e. morphine), and an increased risk for NSAID toxicity.
- *Hepatic*: As the liver ages, it loses tissue mass. Expect prolonged bioavailability for first-pass drugs, and delayed elimination of drugs metabolized in the liver (i.e. methadone).

Pain Assessment in Older Adults

Effective management of pain requires an accurate and comprehensive pain assessment. This begins with a thorough history and physical exam, the goals of which are not only to evaluate for objective evidence of inflammation, weakness, radiculopathy, etc., but also to evaluate the subjective experience of pain intensity, examining how this has influenced overall physical functioning (mobility, risk of falls) and ADLs (sleep, appetite, activity). Attention should be paid to any red flag symptoms (bowel/bladder dysfunction, unexplained weight loss, etc.), which warrant immediate investigation. Consider physiologic age as it compares to the chronologic age of the patient: is the individual physiologically "old" for their age (i.e. multiple comorbid conditions in addition to expected, age-appropriate changes)?

Assessment Tools: A variety of validated assessment tools are available for use in older adults. These include unidimensional scales such as VAS, NRS, and faces scales, as well as more evocative multi-dimensional scales such as the McGill questionnaire. Pain assessment in the cognitively impaired can be particularly challenging, placing these individuals at risk for under treatment (see below); know that unique assessment tools have been developed for use with these patients (Doloplus, PACSLAC).

Barriers to Effective Management

Studies show that many older adult patients in pain are either un- or under-treated, with the cognitively impaired and the "oldest old" (age ≥80) at increased risk [3, 4]. Practitioners should be cognizant of the variety of potentially unanticipated barriers to effective pain management in this demographic, which include:

- Difficulty accessing treatment (transportation, financial limitations)
- Polypharmacy (limits analgesic options)
- Comorbid conditions (limit analgesic options)
- Patient attitudes (stoicism, under-reporting)
- Provider attitudes (reluctance to utilize medications in fear of causing harm, agism)
- Sensory, cognitive impairment

Pharmacologic Management

Analgesic pharmacotherapy remains the most common method for managing pain in older adults. Though few controlled studies have evaluated medication management in this age group directly, clinical practice guidelines are available and offer evidence-based recommendations to support decision making [5]. Principles of pharmacotherapy in older adults include starting with low doses and up-titrating slowly, reevaluating frequently to assess for therapeutic efficacy and adverse side effects, and using combination therapy where possible (less toxicity, added opportunity for analgesic synergy).

- *Acetaminophen*: With an excellent safety profile compared to other agents, acetaminophen is the most commonly utilized analgesic in older adults and should be considered as a first-line agent for mild to moderate pain. It is important to emphasize daily dosing limits (4 g/day max) and to carefully evaluate the patient's medication list for other acetaminophen-containing products (hundreds exist) to avoid accidental toxicity.
- *NSAIDs*: Non-steroidal anti-inflammatory drugs may be used cautiously in this age group, but given the increased risk of adverse side effects, should be avoided in patients with significant cardiac, GI, or renal comorbidities. NSAIDs are best utilized for short-term treat-

ment of inflammatory conditions (rheumatoid arthritis, gout) or musculoskeletal pain (osteoarthritis).

- *Topical agents*: For patients with well-localized pain, topical NSAIDs (i.e. diclofenac gel) can be effective, and given minimal systemic absorption, are considered safer than oral preparations. Five percent of Lidocaine patches are similarly low-risk and are widely utilized for both neuropathic and non-neuropathic pain in older adults.
- *Opioids*: Despite questions regarding the long-term efficacy and safety of opioid medications in older patients, they have a well-established efficacy in short-term management (<12 weeks) of moderate to severe pain refractory to other treatments. One advantage of opioid therapy is the avoidance of NSAID toxicities. Potential analgesic benefit must be weighed alongside the potential negative side effects attendant with opioid use, which include nausea, pruritis, constipation, urinary retention, mental status changes, and falls. Constipation prophylaxis should be initiated whenever opioids are introduced. As in younger patients, initial risk assessment (i.e. SOAPPR) should be used to identify risk factors for abuse, and monitoring should include regular urine toxicology amidst frequent follow-up visits. Long-acting formulations should be reserved for the opioid-tolerant.
- *Adjuvants*: Antidepressant and anticonvulsant analgesics may be useful either as stand-alone or complementary agents in a number of pain conditions, most notably neuropathic pain. Gabapentinoids (gabapentin, pregabalin) are generally safe and effective analgesics, but patients must be monitored for side effects including fatigue (physical, mental) and peripheral edema. Tertiary tricyclic antidepressants (i.e. amitriptyline) are contraindicated in older patients, but nortriptyline can be safely used at low doses with the understanding that anticholinergic side effects may be limiting. SNRIs (duloxetine, venlafaxine) offer a more favorable side-effect profile; be aware of the risk of serotonin syndrome when using re-uptake inhibitors and avoid co-administration with Tramadol.

Sample suggested starting doses [5]

Analgesic	Starting dose
Acetaminophen	325–500 mg q4h
Celecoxib	100 mg qd
Ocycodone	2.5–5 mg q4–6 h
MSIR	2.5–10 mg q4h
Hydromorphone	1–2 mg q3–4 h
Duloxetine	20 mg qd
Venlafaxine	37.5 mg qd
Nortriptyline	10 mg qhs
Gabapentin	100 mg qhs
Tramadol	12.5–25 mg q4–6 h

Non-pharmacologic Management

Physicians should consider the wide variety of low- to no-risk alternative strategies for managing pain without oral medication. Exercise and PT can be remarkably effective in managing pain while simultaneously improving mood and functionality. Therapeutic injections (i.e. ESI, peripheral nerve blocks) may be preferable to oral pharmacotherapy from a risk/benefit perspective, though research regarding these treatments in older adults is lacking. Cognitive behavioral therapy can be useful for learning to control and transform chronic pain into a more manageable experience. Other alternatives to medication include:

- Acupuncture
- Chiropractic
- Massage
- TENS
- Hypnosis
- Biofeedback
- Meditation
- Yoga
- Tai chi

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Words That Hurt, Words That Help! 150

Heidi Nelson, Suyin G.M. Tan, and Allan M. Cyna

Introduction

Communication is an essential skill required for a clinician to practice effectively. For some, this is intuitive; for others, like any other skill, it needs to be learned and practiced to gain proficiency. Effective communication is associated with reduced error and harm, better health outcomes, and higher patient satisfaction. Indeed, the most common cause of malpractice suits is poor communication with patients and their families [1]. More recently, the impact of negative types of communication on patient outcome has been demonstrated. In particular, the use of warnings or negative suggestions are associated with increased pain and anxiety in patients having potentially painful procedures [2].

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Suggestions and Their Consequences

Patient's perceptions and behaviors are often subconscious responses to subtle verbal and nonverbal cues from their environment. When stressed, patients may become overwhelmed by their external situation and focus internally. Their ability to analyze and respond to communications on a logical level is likely to be impaired. Interestingly, when this occurs patients become highly receptive and responsive to suggestions—verbal or non-verbal communications that can alter perceptions and behavior independent of any conscious effort or reasoning [3]. As such, inadvertent suggestions or words with negative emotional content (sharp, pain, sting, nausea) can increase anxiety and pain [2]. On the other hand, words with therapeutic meaning and/or positive connotations can be associated with positive therapeutic benefit. Reframing phrases to exclude negative words, while suggesting healing and recovery, enable patients to refocus their attention in a more positive direction. For example 'we will give you pain killers to help with the pain after surgery' or 'we will give you something to help with nausea' suggests to the patient that it is inevitable that there will be pain and nausea, and that will be the only way to interpret these sensations. Alternatively, telling a patient that you will do whatever is required to ensure their comfort and safety while healing occurs or 'will give something to enable eating and drinking

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as soon as you feel like it' are alternative ways of describing the experience, enabling an interpretation of their sensations as part of the healing process. These effects are sometimes considered part of the placebo effect.

Communication and the Placebo Effect

The Placebo effect has been recently recognized to have widespread physiological and neurobiological effects as well as psychological effects [4]. One of the mechanisms by which placebo is therapeutic is by changing expectations through communication. There is a strong correlation between the degree of expected outcome and the subsequent placebo-induced analgesia or effect [5]. Words and language can be used as part of the placebo effect similar to pharmacological interventions. Just as positive words can impact on a patient's expectations, using negative language will perpetuate negative expectations—the so called, Nocebo effect [6].

Nocebo Effect of Communication

The nocebo effect is a non-pharmacological, unpleasant, or undesirable effect of an intervention, which is perceived as more negative and unpleasant than the experience would have otherwise been [6]. Like placebo, nocebo effects are clinical effects not attributed to the pharmacological component of the intervention. As such, nocebo effects are amenable to suggestion and are subject to the influence of communication. Patients warned of, or expecting, a negative experience are more likely to experience an adverse outcome [2, 7]. An example, prior to a potentially painful procedure telling a patient 'this will hurt' is more likely to make the experience of 'hurt' more likely. The use of a neutral alternative such as 'you will feel what you feel' allows the patient to experience the intervention without introducing or exacerbating any negative perceptions.

The use of local anaesthetic to facilitate comfortable placement of a cannula, nerve block, or an epidural is another example. This is frequently preceded by the negatively primed words 'this will sting' 'sharp scratch now' or the like. These well-meaning 'warning' phrases have been shown to be associated with not only increased pain, but worsening pain behaviors such as movement and vocalization of pain [8]. In telling the patient that the local anaesthetic will 'numb the area to facilitate more comfortable placement of the epidural' enables patients to expect that they will become numb and is associated with lower pain scores [9]. Using a modifier such as 'just a *tiny* scratch' or 'it will only hurt for *a moment*' does not displace the effect of the negative words scratch or hurt [10].

Recent studies have repeatedly shown that when patients are supplied with an explanation of why they are having the intervention without the associated negative suggestion, they are less likely to have a negative perceptual experience [2, 8, 9]. Similarly, a randomized study comparing post-operative patients being asked about 'pain' or 'comfort' scores found that the patients who asked about their 'pain' were more likely to request additional analgesia and report postoperative sensations of healing and recovery as unpleasant, compared with those patients who asked about comfort [11].

Ethical Communication

Clinicians frequently express concern that failure to warn patients about potentially aversive experiences is unethical. There is no evidence that warning of perceptions in a negative way (scaring patients) is helpful. It is essential to keep our language neutral as we do not know for certain how the intervention is going to be perceived. As practitioners, we need to provide accurate information to prepare patients, but also to avoid unnecessary pain and anxiety. This is possible while avoiding negatively loaded statements/communications. When a patient asks 'will this hurt?', it is as inaccurate to say 'no' as it is 'yes' as everyone's experiences are different.

Addressing patient concerns and avoiding platitudes such as 'you'll be fine' or 'it's only a

small needle' is essential. Sometimes intended helpful comments have the opposite of what is intended. For example, "there is nothing to worry about" implies to the patient that 'there is something to worry about'. These comments are invariably unhelpful and can result in increased anxiety.

Patients frequently know what they don't want—'I don't want pain' or 'I don't want to feel frightened', but have difficulty telling us what they do want. It might be helpful to ask patients whether it would be "OK to work on how you might feel more comfortable and relaxed". Part of the strategy to enhance the effectiveness of the placebo and nocebo effects of communication is to encourage ways in which patients can start focusing on what they wish to achieve and where they are going, so they can focus on times when things seem more comfortable or relaxed such as with family and friends or doing their favorite activity.

Summary

In summary, awareness is increasing of the impact that words and phrases have that can lead to adverse patient responses. Negative suggestions result in more negative evaluation of a particular stimulus or situation. In particular, patients who expect negative outcomes are more likely to have adverse outcomes [2, 8, 9, 11].

The noxious power of ill-chosen words can sabotage the patient's experience of pain-relieving procedures. There is an opportunity for clinicians to embrace the evidence. It remains depressingly common to hear expressions such as 'bee sting' and 'sharp scratch'. These clumsy verbal relics of the past are without evidence of benefit. The implications of teaching and using these obsolete language rituals are both professionally and ethically questionable [12]. The evidence is clear [13]. By managing expectations and avoiding negative suggestions, pain physicians can minimize the incidence and attenuate adverse patient perceptions. There has rarely been an opportunity to attenuate the distress of invasive medical procedures, so simply and, at such little cost [12].

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How to Communicate with Patients in Pain

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Cheryl S. Chooi, Suyin G.M. Tan, and Allan M. Cyna

Traditionally during training, clinicians focus upon gaining pharmacological knowledge and procedural and technological skills. This often leaves trainees failing to appreciate the effects of communication on patient perceptions and experiences and the power of communication to elicit positive therapeutic patient outcomes [1]. Effective communication skills can be taught and developed over time and have the potential to improve patient satisfaction and reduce medical error [2].

Levels of Communication

Conscious Communication

This is the provision of a specific instruction, explanation, or information. For example, when gaining 'informed consent' prior to a procedure.

Subconscious Communication

This type of communication is directed at the patient's subconscious, using voice pitch, tone, or words that can lead to non-volitional changes in perception and/or behavior. For example, using the LAURS approach [3] as detailed below. Any response begins with listening and noting patient's words and behavior and accepting where the patient is at that moment. Pacing or mirroring the patient's own behaviors such as breathing rate and speech pattern can reduce patient anxiety and distress.

The LAURS of Communication

The **LAURS** (Listening, Acceptance, Utilization, Reframing, and Suggestion) template helps to establish rapport and underpins therapeutic communication.

Listening

Listen, listen, listen……Listening is the act of being in the moment with the patient and not just thinking about what you need to ask next! Listening is the single most important part of any interaction. It involves four parts. Firstly, to hear the words. Secondly, to assess their meaning. Thirdly, to let the patient know they have been heard, and finally, to confirm that the patient has

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been understood. This requires a regular 'checking in' process with the patient.

- "It sounds like you are worried that…"
- Check that you understand what is meant. "It sounds like you are worried because…"

Communicate that you have heard and understood, rather than just silently listen.

- "Let me get this right…are you saying…?"
- "So you are telling me your shoulder has been painful since the bike accident and you have never had pain before that?"

Acceptance

Acceptance of the patient's beliefs, thoughts, actions, emotions, and perceptions is essential if useful therapeutic change is to take place. This needs to occur regardless of the clinician's personal opinion. This acceptance in a neutral way can be difficult—especially if the patient's values are in direct contradiction to those of the clinician. However, this acceptance needs to only be transient for the patient to subsequently engage in the therapeutic process. For example,

Patient: "I'm worried I will never be able to use my arm again."

Doctor: "It's okay to be worried, this frequently happens when…"

Patients in pain may not be able to be reasoned with logically, especially when distressed. Acceptance will facilitate greater future engagement with the patient (and family) and increase patient cooperation. For example:

Patient: "I'm in so much pain I can't listen to you."

Doctor: "That's okay, you don't have to *listen* to me just now."

Listening and *Acceptance* are frequently the only parts of LAURS that are required to gain rapport and start generating useful therapeutic interactions

Utilization

Utilize the patient's own words when they express concerns and reframe them into a solution that is helpful. For example,

Doctor: "You may not be able to *listen* right now, but you will inevitably hear a few strategies that you can choose between that will give us the best chance to help you…"

Reframing

Reframe the patient's perception such that it can be perceived as a possible means of solving the problem. For example,

"By not *listening*, the mind is frequently freed up to appreciate other ways of doing things…"

Suggestion

Verbal and nonverbal communications can be used to elicit subconscious changes in mood, perception, and behavior.

Direct suggestions refer to the patient as 'you'

- "You may start noticing that each time you take a slow relaxing breath in you will feel stronger and more in control"
- "You will find that each time you breathe out you can blow away some of the tension and feel yourself relaxing."

Indirect suggestions take the form of "most", "some", or "a patient I had last week found this helpful…"

- "Most people find that each time they take a slow relaxing breath in, they feel stronger and more in control".
- "Most people find that each time they focus on their breathing, as they breathe out they can blow away some of the tension."

Indirect suggestions are more easily accepted by the patient than direct suggestions. However, direct suggestions can work well in anxious patients and in an emergency.

Negative suggestions should be avoided as evidence demonstrates that negative language may increase the patient's perception of pain and anxiety [4–6]. For example, when injecting local anesthetic "This will sting" can increase pain [7].

Other Useful Language Structures

Double Binds

Double binds are statements of two comparable alternatives that give the patient a sense of choice and control even when there is none. For example, when the anxious or needle-phobic patients require intravenous access, "When you are able to *stay still*, would you prefer the drip in the left or the right arm?" It is implicit that when the patient makes the choice of arm, they have also agreed to then *stay still*.

Failure Words

The words 'try' and 'not' should be used with caution. 'Try' is a failure word and 'not' is not heard by the subconscious.

For example, when asked to "try not to move", the patient consciously will fail "not to move", but subconsciously only hear the word 'move' making movement more likely.

Similarly, this combination can be used therapeutically. For example, if the patient states that he/she can't relax, the pain physician could say, "That's OK" (Acceptance) "Try not to relax then….. and it will just seem to happen all on its own".

Avoid Jargon

Use language that is easy to understand. Words such as allergy, opioids, and local anaesthesia are commonly used, but are often not understood by patients [8].

The GREAT Template (Greeting, Rapport, Evaluation, Addressing Concerns, Termination)

This is a useful structure when thinking about a clinical interaction [3].

Greeting, Goal

- Introduction of all those present.
- Clarify the goal of the interaction, for example, to reduce and eliminate opioids that are no longer having any analgesia effect; or to work towards getting back to a usual activity where pain currently restricts the activity such as being able to go to a sporting event.

Rapport

- To establish trust, cooperation, effective communication of information.
- See LAURS concept in guiding communication, especially when standard communication techniques fail.

Evaluation, Examination, Explanation, Expectation

- Take a history, examine, and explain management options.
- Establish patient expectations to avoid misunderstandings.

Addressing Concerns

- Check patient's understanding.
- Address concerns.

Termination of Interaction

- Tacit agreement that the physician will provide a clearly defined strategy that has been agreed as optimal care and the patient accepts this.
- Thanks to those who are present (Patient and relatives).

Special Considerations

During potentially painful procedures, it may be useful to use a 'checking-in' process, as a way of getting repeated verbal consent during the procedure [9].

Ask the patient "Is it okay to carry on?" and "Please say 'stop' when you would like me to stop, and we can change position or give more local anesthesia and we can then continue when you are ready."

Summary

The LAURS framework provides a structure for clinicians to communicate more effectively with patients and colleagues, improving patient management and outcomes. Communication is not just an optional extra, but is a core clinical skill to optimize patient care [3, 6].

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Hypnosis for Pain Relief

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Johanna Saltis, Suyin G.M. Tan, and Allan M. Cyna

Introduction

Hypnosis can be defined as an altered conscious state of focused attention which involves absorption, some dissociative elements, and an increased responsiveness to suggestion. Suggestions are verbal or non-verbal communications leading to subconscious changes in perception, mood, or behaviour. This special state of focus can occur in many ways. For example, spontaneous trance states can occur in the form of 'daydreaming' or being 'in the zone' during physical training.

Hypnosis has been around for thousands of years in one form or another. Until the nineteenth century, hypnosis was the only means of having surgery comfortably. James Esdaile, a Scottish surgeon, is considered by many to be a pioneer in the use of hypnosis for pain relief before the discovery of pharmacological anesthesia in the 1840s. Recent research has also confirmed its value in the management of chronic pain [1] and anxiety. The effects of hypnosis as a means of dissociation from pain, its effect on decreased bleeding [2], and reduced infection [3] suggest an evolutionary basis for the ability to enter a hypnotic "trance-like" state when under extreme stress.

Evidence Base

Hypnosis is steadily accruing an evidence base for clinical efficacy in the management of pain. For example, in the context of Irritable Bowel Syndrome [4–6]. Jensen and Patterson [7] have reviewed the value of hypnosis in various areas of pain management. Hypnosis has been shown to be more efficacious than relaxation alone [1, 8] and to augment Cognitive Behaviour Therapy (CBT) [9, 10], improving outcomes for 70–90 % of clients [11].

Neuroimaging

More recently, neuroimaging studies have assisted with our understanding of the cognitive processes involved, providing insight into which parts of the brain are being modulated during hypnosis. It would appear that different

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suggestions activate different brain regions. For example, suggesting the pain is "less intense" leads to reduced activity in the somatosensory cortex, while suggesting that it is "less bothersome" leads to a reduced activity in the anterior cingulate gyrus [12, 13]. Some similarities appear with CBT and mindfulness. For example, CBT for Irritable Bowel Syndrome (IBS) [14] and fibromyalgia [15] have shown decreases in limbic activity and increases in prefrontal activity, suggesting reduced vigilance and attention to pain. Similarly, reductions in stress and pain sensitivity have been associated with reductions in grey-matter density in the amygdala of Zen [16] and Western [17] meditators. Further research is required to clarify whether the mediating systems for mindfulness and hypnosis are the same [16] or different [18].

Cognitive Neuroscience

Contrary to popular belief, hypnosis is not sleep, as patients can hear what's happening around them and can halt the process at any stage if they wish. Furthermore, hypnotic responses can be elicited in minutes or less. A cognitive phenomenon at play is highlighted by the Stroop Effect. In this experimental condition, reading time is slowed down markedly, by asking the subject to name the colour of the printed word, not the word itself. Hypnosis can bypass this interference effect [19] as can mindfulness [20] and meditation [21], which are likely identical conscious states to that of hypnosis.

Neuroplasticity, Hypnosis, and Different Ways of Processing Information

Hypnosis appears to have a clear role in enhancing neuroplasticity effects and there is renewed interest in the research and application of this topic in the management of pain [22].

Applications to Pain Medicine

The biopsychosocial model of chronic pain [23] provides a number of entry points in which to use hypnosis and/or self-hypnosis.

For example, harnessing the phenomenon of priming and attention shifting, Physicians, Psychologist, and trained clinicians can utilise hypnosis for directly reducing pain intensity and/or distress levels [12, 13]. Hypnosis can also be used for improving self-motivation for activity pacing and to improve sleep quality [24, 25]. Symptoms of depression coexisting with the pain experience can be moderated with hypnosis and self-worth can be improved through approaches such as "ego strengthening" [26].

Hypno-analgesia for childbirth and surgical procedures can be managed through a range of hypnotic techniques including: "glove analgesia" [25]. Lived-in imagination can be used for awake craniotomy [27], changing burns dressings [28] and for arm anesthesia [29].

The success of hypnosis in a clinical setting requires the development of rapport and trust between doctor and patient to engage with the process. However, it should be noted that partial or even frank hypnotic states can occur spontaneously in hospital settings. Particularly, where the overwhelming stress of being in a foreign environment and concern for the potentially painful procedure, or feelings of being a victim to illness, can facilitate an internal focus of attention and a dissociation from the external environment [30]. This state can be utilised by clinicians when using suggestions to help ease the patient's anxiety and shape positive expectations and experiences [31]. Hypnotic techniques can help patients feel more in control and to supplement and enhance their hospital experience. The main value of hypnosis as a technique is to assist patients as a supplement to standard clinical care. The belief that the patient can do more than he or she thinks (and more than the doctor believes is possible) is likely to generate surprising therapeutic responses.

Conclusion

Hypnosis can be used in multiple ways to supplement standard clinical management of patients both in acute and chronic pain settings, augment CBT for chronic pain management, and to reduce anxiety or depression. Training can be gained through formal Diploma channels (ASCH http://www.asch.net/Professionals/MembershipInformation.aspx and other groups such as the Society of Clinical and Experimental Hypnosis http://www.sceh.us/ijceh) to ensure clinical efficacy. Understanding that hypnosis is a way of harnessing normal cognitive process to supplement and enhance therapeutic outcomes should consolidate its place in the clinical practice of pain management.

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Regenerative Medicine for Pain Management

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Halland Chen, Joseph Purita, and Michael Nguyen

Terminology and Definitions

Stem cells have the potential to develop into many different cell types in the body during early life and growth. With the emergence of the field called **Regenerative Medicine**, we have the ability as clinicians to use the body's own healing mechanisms to treat medical conditions and pain symptoms.

Stem cells are distinguished from other cell types by two important characteristics:

1. Unspecialized cells capable of renewing themselves through cell division, sometimes after long periods of inactivity.
2. Under certain physiologic or experimental conditions, they can be induced to become tissue or organ specific cells with special functions.

Often patients and clinicians tend to think of stem cell therapy being controversial; however, that primarily relates to the early days when stem cell therapy was synonymous with the use of *embryonic stem cells*. These types of cells are now described in the context of **Totipotent stem cells** or **Pluripotent stem cells**.

In the clinical context of modern Regenerative Medicine, stem cell therapy uses *non-embryonic somatic cells* or *adult stem cells*. Most of these types of cells are described in the context of **Multipotent stem cells** (Fig. 153.1), and often in the clinical setting, refer to therapies with **Mesenchymal stem cells** (MSCs) and **Hematopoietic stem cells** (HSCs).

There's also another cell type that is becoming increasingly studied, we refer to them as **Adult Pluripotent stem cells** (APSCs). They were first discovered in mice in 2005 and then humans in 2006 by Professor Ratajczak at the University of Louisville. Some types of APSCs are referred to as Very Small Embryonic-Like stem cells (VSELs), Multilineage-differentiating stress-enduring cells (MUSEs), Marrow-Isolated Adult Multilineage Inducible cells (MIAMIs), and others. Since their discovery, APSCs have been widely studied due to their "embryonic-like" features. They are able to replicate and multiply freely and can become any other cells in the human body. Unlike embryonic stem cells, however, they do not have known cancer-causing properties. Also, they are found in infants, children, and adults, rather than embryos. As such, they present a potentially safer and more ethical alternative to embryonic stem cells.

Mesenchymal stem cells (**MSCs**) are present in many tissues and can give rise to a variety of

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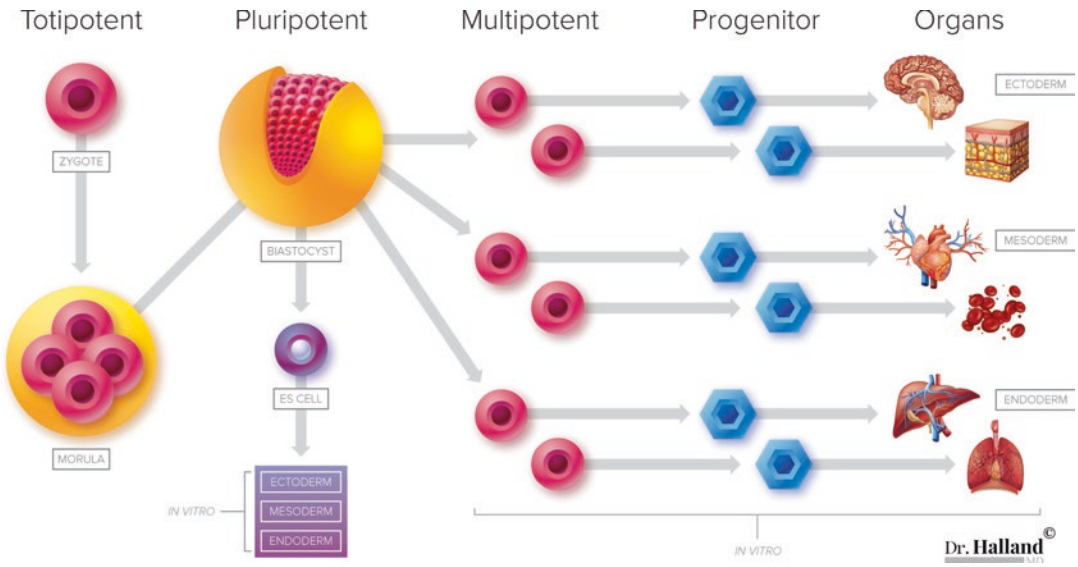

Fig. 153.1 Regenerative medicine utilizes adult stem cells for a variety of therapies, especially orthopedic and pain conditions. Illustration by Dr. Halland Chen, MD ©

cell types, including: bone cells (osteoblast and osteocytes), cartilage cells (chondrocytes), fat cells (adipocytes), myocytes (muscle cells) and stromal cells that support blood formation. In the clinical setting, adipose tissue is the most common source for MSCs. Mesenchymal stem cells are thought to be immune modulators and they typically will prepare the stem cell niche to receive many different types of cells.

Hematopoietic stem cells (**HSCs**) give rise to all types of blood cells: red blood cells, B lymphocytes, T lymphocytes, natural killer cells, neutrophils, basophils, eosinophils, monocytes, and macrophages. In the clinical setting, bone marrow is the most common source for HSCs and are the cells thought to drive tissue regeneration.

When describing stem cell or Regenerative Medicine therapies, vendors who manufacture the harvesting devices or kits often reference their system's ability to collect a certain number of cells from their processing system. A common metric that is often referenced is ***fibroblast colony forming units*** (***CFU-F***). These fibroblasts cells are multipotent and can differentiate into osteoblast, chondroblasts, adipocytes, and even myoblast. In *CFU-F* testing, a small portion of cells are watched under controlled conditions to see if stem cells divide and form colonies.

Another metric is ***total nucleated cell count*** (***TNC***), which can be measured using a flow cytometer device. It quantifies both living and dead cells; thus, the ***CFU-F*** metric is a more meaningful measure of whether stem cells are "viable" in a given sample.

Commonly, Hematopoietic stem cells express a cell surface protein called *CD34*. Therefore, *CD34+* cells can be used prospectively to predict the HSCs counts from a bone marrow sample (Fig. 153.2).

Types of Regenerative Medicine Therapies

The four most common Regenerative Medicine therapies are:

1. Platelet-rich plasma (PRP)
2. Bone marrow aspirate concentrate (BMAC)
3. Adipose tissue grafts / Micro-fractured fat / Stromal Vascular Fraction (SVF)
4. Adult Pluripotent stem cells (APSCs)

Each therapy can be used in combination or individually; likewise, there is no consensus on which protocols may work better than another when comparing the various techniques. Moreover, the difference between manufacturers may slightly influence outcomes; however, most systems are relatively comparable.

PRP is perhaps the most common and readily available treatment option available to clinicians and promote stem cell migration and healing when injected into joints and tendons for repair. Clinically, PRP is more effective when combined with other therapies such as bone marrow and/or adipose tissue.

Bone marrow contains mostly HSCs and is often used in orthopedic cases. Various systems on the market exist where bone marrow aspirates are often obtained from the pelvic iliac crest, which are then centrifuged and processed for injection.

Adipose tissue is rich in MSCs and is clinically used as a scaffold system; however, there are other newer clinical applications as technology with adipose tissue is evolving, particularly with *Stromal Vascular Fraction* (*SVF*) and microfragmented fat, such as *Lipogems*®.

Stem cell treatment therapy has evolved and more recently, these cells may also participate in an *endocrine* (having a distant effect on another cell), *paracrine* (secretions affecting neighboring cell populations), and/or *autocrine* (cell signals which affect themselves) functionality. This concept has been popularized by Dr. Arnold Caplan, who states that mesenchymal stem cells are showing themselves capable of far more functions than just healing and tissue regeneration, and therefore, suggests the acronym (MSC) should now stand for "Medicinal Signaling Cells".

PRP and Clinical Applications

PRP is prepared when whole blood is centrifuged and the platelets become separated and concentrated during the process; moreover, PRP consists of many other cellular elements including: platelets, neutrophils, monocyte, macrophages, fibroblasts, glycoproteins, endothelial cells, and keratinocytes.

Using a process known as differential centrifugation, PRP is prepared by the acceleration force

Assay End Point	Type (Method)	Time to Result	Advantages	Disadvantages	What Is Measured	Not Measured
TNC	Cell Count *(hemacytometer or automated cell counter)*	10 minutes	Simple Fast Inexpensive	Low biological relevance	Viable nucleated cells	Stem/progenitor cell number or function
$CD34^+$ Cells	Phenotypic *(flow cytometry)*	3 hours	Fast Standardized kits	Misses apoptotic cells Phenotypes can change High instrument cost High variability	Cell surface marker expressed on most HSPCs	Stem/progenitor cell function
CFU	Functional *(in vitro culture)*	7 to 14 days	Biological read-out Standardized reagents	Long assay duration Variability of manual colony counting	Viable and functional progenitor cells	Long-term repopulating HSCs

Fig. 153.2 Commonly used assays to evaluate hematopoietic cells for transplantation. ***TNC:*** total nucleated cells, ***CFU:*** colony forming unit, ***CD34:*** cluster of differentiation antigen 34

which causes sediment layers of certain cellular elements based on different specific gravity. There are three layers obtained after centrifugation: a bottom layer that consists mostly of RBCs, an intermediate thin layer that is known as the "buffy coat" and that is rich in WBCs and platelets, and finally an upper layer that is mostly plasma. Depending on which PRP Kit and manufacturer, there may or may not be an additional centrifugation step.

PRP is measured in terms of concentration above baseline. PRP devices can be divided into lower concentration systems (2.5x–3x times baseline) and higher concentration systems (5x–9x times baseline). An effective clinical PRP dose range should have between 1.5 to 3 million platelets/μL; moreover, ranges that are greater than 5 million platelets/μL can act inhibitory. Of note, there are currently no commercial kits that can produce platelets in these particular very high concentration ranges.

The key feature of PRP is that it contains a variety of growth factors, cytokines, and proteins that have direct effects for stimulating stem cells. Such properties include the stimulation of mesenchymal stem cells and also promoting blood supply formation.

There are several manufacturers of PRP systems, including: Harvest, EmCyte, Arteriocyte, and Arthrex.

Clinical Applications

PRP can be used to treat conditions affecting ligaments, tendons, and musculoskeletal injuries.

Typical Use Case Scenarios and Sample Therapy Protocol

Patients should refrain from taking NSAIDs 1 day prior and after any PRP treatment. Likewise, cortisone injections at the site of treatment or oral systemic use can decrease the efficacy of PRP.

Different kits use different amounts of whole venous blood, but typically 30 mL produce about 3 mL of PRP. The concentration above baseline is mainly dependent on the manufacturer and kit used in the process.

The injection volume/dosage can vary, but a rough guideline for the following treatment areas are approximate estimates that are safe and effective:

Shoulders: 2–6 mL
Knees: 3–10 mL
Hips: 3–6 mL
Tendinopathies: 1–3 mL
Muscle tears, sprains, trigger points: Varies, depending on the size of injury: 1–3 mL per area

PRP is most effective when combined with either bone marrow aspirate concentrate (*BMAC*) *and/or adipose tissue grafts* (*which serves as a scaffold and contains stem cells*).

Bone Marrow and Clinical Applications

Bone marrow aspiration is a minimally invasive procedure used to collect bone marrow, typically from the pelvic iliac crest. The final product that is processed is referred to as BMAC (Bone Marrow Aspirate Concentrate). During this procedure the physician collects bone marrow from the patient and concentrates it using a centrifuge, in a very similar fashion as PRP. In fact, some PRP machines often have the ability to process BMAC as well.

The aspirate contains mainly Hematopoietic stem cells (HSCs) and a smaller proportion of Mesenchymal stem cells (MSCs). It is likewise rich in growth factors and other important cell-signaling molecules needed for healing. Unfortunately, the MSCs count decreases dramatically with age in BMAC; hence, the importance of also using adipose tissue for stem cell procedures as it contains a significantly higher amount of MSCs over BMAC.

Clinical Applications

BMAC can be used to treat conditions affecting ligaments, tendons, and musculoskeletal injuries. It can likewise be applied to spinal facets.

Typical Use Case Scenarios and Sample Therapy Protocol

The most important factor for patient comfort is to adequately anesthetize the periosteum with a combination of lidocaine and bupivacaine. During

the aspiration process, it is important to pull the syringe slowly while harvesting the bone marrow to minimize the amount of whole blood pulled into the sample. Approximately 60 mL is aspirated and will produce about 10 mL of BMAC after centrifugation, although these numbers will vary depending on which manufacturer's kit is used to process the bone marrow. Recently, newer bone marrow aspiration needles take advantage of obtaining marrow aspirated from different geographic areas, which is an extremely important concept that differs from traditional techniques using standard systems. This needle design and modified aspiration technique allows for larger numbers of stem cells to be obtained while eliminating the need for centrifugation, which is a step that may actually discard important cells that make up the regenerative milieu.

The injection volume/dosage can vary, but a rough guideline for the following treatment areas are approximate estimates that are safe and effective:

Shoulders: 4–6 mL
Knees: 5–10 mL
Hips: 5–10 mL
Tendinopathies: 1–3 mL
Spinal facets: 1–2 mL per level

BMAC is most effective when combined with either PRP and/or adipose tissue grafts (*which serves as a scaffold and contains stem cells*).

Adipose and Clinical Applications

Adipose tissue is one of the richest sources of stem cells, particularly Mesenchymal stem cells. There is approximately 500x–2,500x times more MSCs in adipose when compared to bone marrow. Recently, MSCs have been relabeled as "Medicinal Signaling Cells" as they have endocrine, paracrine, and autocrine properties. There are four distinct ways fat can be processed:

1. Simple fat grafting, no centrifuging or processing involved
2. Fat harvesting with centrifugation
3. Enzymatic fat digestion, Stromal Vascular Fraction (SVF)
4. Micro-fractured fat, minimal manipulation (Lipogems®)

Simple fat grafting and fat harvesting with centrifugation are the most similar in that a simple liposuction technique is performed, using tumescent fluid mixed with anesthetic and epinephrine. Next, in a simple fat graft, the excess fluid and oil is decanted using gravity; versus, fat harvesting with centrifugation, the excess tumescent fluid and oils are separated into layers using a centrifuge system, often from the same manufacturers that make PRP and BMAC systems.

Stromal Vascular Fraction (SVF) is an isolation process that utilizes cell washings, centrifugation, and enzymatic digestion (collagenase). Usually about 50 mL of fat will produce 1–2 mL of SVF, which is referred to as the "SVF pellet." According to the FDA, there are certain criteria which make SVF controversial and not fully compliant within their guidelines; thus, we do not endorse its use in the USA.

The more recent technology for adipose processing is micro-fractured fat, with minimal manipulation, such as the Lipogems® system. In this process, fat is harvested and washed in a sterile chamber using saline and metal spheres. Once the process is complete, the adipose tissue is pushed through a small surgical grade mesh that further reduces the size of the fat to a smaller adipose-niche, which is rich in MSCs. This preserved structural niche leads to a higher survival rate of the regenerative cells.

Clinical Applications

Adipose derived stem cells can be used to treat conditions affecting ligaments, tendons, and musculoskeletal injuries. It can likewise be applied to spinal facets.

Typical Use Case Scenarios and Sample Therapy Protocol

When harvesting fat, one of the key elements is using adequate tumescent fluid to numb the area being harvested which also allows the liposuction/lipoaspiration to go smoothly.

Tumescent fluid mixture:
500 mL normal saline
50 mL 2 % lidocaine
1 mL of epinephrine 1 mg/mL (1:1000)

Usually, about 60 mL of tumescent fluid is injected into a harvest site, either the abdomen or side flanks. A liposuction tumescent infiltrator cannula is used to inject the fluid into the desired harvest site, and then a harvesting cannula is attached to an additional syringe under negative pressure to harvest the fat. Each manufacturer has its own kits with complete supplies to facilitate the process.

The injection volume/dosage can vary, but a rough guideline for the following treatment areas are approximate estimates that are safe and effective:

Shoulders: 6–9 mL
Knees: 5–12 mL
Hips: 3–15 mL
Tendinopathies: 1–3 mL
Spinal facets: 1–2 mL per level

Compliance with the FDA

Currently, only select embryonic stem cell lines have federal approval for use as part of specific research trials. While allogeneic stem cells are generally regulated as a drug, some autologous stem cell uses are exempt from federal guidelines. However, the clinical use of these autologous stem cells must meet the following criteria:

1. Cells must be the patient's own (*autologous*)
2. Cells must be used in the same surgical procedure
3. Cells may only undergo minimal manipulation in the cell processing steps
4. The cells' biological function must be identical between the harvest and delivery sites (*homologous use*)

One of the key points of the federal guidelines (21 CFR 1271) is that during cell processing, these cells are only minimally manipulated, which the FDA defines as it "does not involve the combination of the cells or tissues with another article, except for water, crystalloids, or a sterilizing, preserving, or storage agent, provided that the addition of water, crystalloids, or the sterilizing, preserving, or storage agent does not raise new clinical safety concerns." This particular definition forms the basis of the FDA's opinion on the use of Stromal Vascular Fraction (SVF). During the processing of adipose tissue into its Stromal Vascular Fraction, the structural tissue components are lost and thus the biological function of the tissue has changed. The FDA also contends that to use enzymatic digestion of adipose tissue to derive SVF, the cells biological function may be altered as well.

It is also important to note that, when considering treating patients with Regenerative Medicine therapy, one cannot make specific claims to cure specific diseases as that can have FTC violation implications.

Additional Reading

American Academy of Regenerative Medicine. http://aabrm.org/.

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