Anesthesiology In-Training Exam Review

Regional Anesthesia and Chronic Pain

Ratan K. Banik
Editor

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The book is dedicated to three women in my life.

My mom whose unconditional love and support inspired me to follow my dreams, do my best, and take nothing for granted.

My wife, who has enriched my life for 30+ years through her love, patience, kindness, and wisdom, despite my insane work hours and crazy life decisions. Without her, this book would not have been written and I would not be who I am today.

My mentor, teacher, and outstanding role model, Emeritus Professor Elise Delphin, MD, MPH. She has had the greatest impact on my anesthesiology training and continues to serve as a source of inspiration for moving forward.

Foreword

The science and clinical practice of pain management continue to evolve. Until 2016, there was only one subspecialty fellowship accredited by the Accreditation Council for Graduate Medicine Education related to pain medicine. In 2016, after a 3-year process of demonstrating the existence of a distinct subspecialty and developing new program requirements that I led, regional anesthesiology and acute pain medicine (RAAPM) became a postgraduate pathway for anesthesiologists. From my experiences with the first RAAPM fellowship program that I started in 2006 at the University of California, San Diego, to the RAAPM fellowship program that I currently direct at Stanford University, I have witnessed firsthand the dramatic improvement in curricular content and design within this subspecialty. Together, RAAPM and pain medicine now encompass the full spectrum of pain management science and clinical practice from prevention to mitigation, resolution, and, if needed, palliation.

Anesthesiology residents today are expected to have much more baseline knowledge in the realm of pain management than in years past. Anesthesiologists are dedicated perioperative physicians, and no specialty in medicine has as much training and experience managing patients across the continuum of acute to chronic pain. Anesthesiologists bear witness to the extreme trauma inflicted upon the human body during surgery and invasive procedures. They personally administer analgesic medications and interventions that relieve pain in the perioperative period. They assess and manage acute postoperative pain in the postanesthesia care unit and wards as part of an acute pain service. In recent years, there has been increasing attention to the potential for acute pain to become chronic and the importance of early detection and treatment in the form of anesthesiology-led transitional pain services. For patients who unfortunately go on to develop chronic pain, anesthesiologists trained in pain medicine offer their special expertise to palliate painful conditions and assist patients in maximizing their quality of life and function.

This new review book by Dr. Banik successfully covers all major topics related to regional anesthesiology, acute pain, and chronic pain for the purposes of in-training exam preparation. The topics specified by the American Board of Anesthesiology (ABA) make up the book's table of contents, and the standardized chapter format is easy to follow for the anesthesiology resident who is preparing for an exam or just looking for a quick answer to a clinical question. The contributor list represents a broad sample of the

RAAPM and pain medicine training programs across the country and presents diverse perspectives. I congratulate Dr. Banik and colleagues for assembling this impressive collection of high-yield reviews related to ABA pain management topics in a single review book and hope it may also serve to inspire anesthesiologists to pursue subspecialty training and further advance the fields of RAAPM and pain medicine to benefit future patients.

Edward R. Mariano

Foreword

Chronic pain is a composite field involving anesthesiology, internal medicine, physical medicine, neurology, psychiatry, psychology, neurology, interventions, and minimally invasive spine procedures. Pain management requires in-depth knowledge of fluoro-anatomy, sono-anatomy, physiology, pharmacology, physical exam, and surgical skills which are not typically taught during training. Currently available books are intended either for extensive review of the pain medicine or quick reviews in a few chapters. As a result, anesthesiology residents are uncomfortable in their chronic pain rotation and are inadequately prepared to enter pain medicine fellowship.

This book provides a valuable window to chronic pain and covers the necessary components from basic science to clinical medicine in an easy-to-read format, with extensive use of schematics, color figures, clinical pearls, and MCQs. The authors represent many major universities in the USA. This book is an innovation in the field as it is the first one that is structured in keyword-like chapters, with MCQs and high-yield concepts at the end of each chapter. In the new era of distractions, for example, Facebook, Twitter, and Instagram, medical students and residents have no time to read a thick textbook. Therefore, it is necessary to provide them state-of-the-art knowledge in a bulleted text with short succinct chapters and illustrations that are easy to consume. The book is a good step in that direction.

December 2021

Akron, OH, USA

Samer Narouze

Preface

You are never given a dream without also being given the power to make it true. You may have to work for it, however.
-Richard Bach

The impetus to work on this book arose during my surgery internship in the Drexel College of Medicine. At the time, I was introduced to ABSITE Review book by Dr. Fiser. The book is one of the most popular study guides for the American Board of Surgery In-Training Examination, which general surgery residents take each year. This easy-to-use book provides concise bulleted texts covering all components of the exam. Many of my co-residents got 99% percentile score by cramming this book in the final few weeks of their exam. When I started anesthesia residency and took American Board of Anesthesiology in-training exam, I felt a serious need for similar book.

Writing or editing a book is a daunting task. I never thought I would have time to work on a book. The Covid-19 pandemic made this opportunity. My basic research lab was closed, pain clinic changed to virtual visit at a limited capacity, and I got plenty of time in hand. I approached Gregory Sutorius at Springer Medical and Sarah Barth at Elsevier with this book proposal. Both were very enthusiastic, but ultimately Greg was superfast in developing a book contract. I signed the contract with Springer, and we agreed on a timeline that would see the book in the hands of readers by 2021.

I am a physician scientist with major focus on basic pain research. In many ways, the research challenges I faced prepared me for this book writing. I am indebted to contributing authors from more than 60 major universities in the USA, who have provided a solid, up-to-date, and evidence-based approach to their topics. Many of them have been extraordinarily helpful by giving permission to reproduce their work and by performing herculean writing efforts despite their busy work schedule.

Gregory Sutorius and Vijayasankara Gomathy Rajagopal were instrumental in the development of this book. I am grateful to Straive copyeditors, whose invisible copyediting skills improved the style and accuracy of the final text. The illustrators at Straive receives special thanks for their work on schematics and colorful figures. I owe a special debt of gratitude to Ed Mariano, MD, and Samer Narouze, MD for writing foreword for this book. In addition, without the loving support of my wife, Sheema, I could not have

contemplated taking on the task of writing this book. She was always there with me during ups and downs of my work on this book.

The contents of this book are intended to aid anesthesiology residents, regional anesthesia fellows, pain medicine fellows, and medical students in their study regarding patient care practices on regional anesthesia and chronic pain. They are based upon the available medical literature and clinical expertise at the time of writing. It is almost inevitable that errors remain, despite my best efforts and those of my editors at the Springer. Any errors that remain in the book are mine.

Minneapolis, MN, USA Ratan K. Banik

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Part I

Regional Anesthesia

1 Basic Science: Principles of Ultrasound: Obtaining an Image, Resolution, Depth, Frequency, Resonance

Jonathan Hausman and Gabriel Pollock

Introduction

- The use of ultrasound in the practice of anesthesiology has expanded greatly over recent decades. Ultrasonography allows rapid acquisition of images of anatomic structures.
- It has been well established in the administration of regional anesthesia as well as perioperative assessment through use of **Point of Care Ultrasound** (POCUS). A basic understanding of physics principles on which ultrasound imaging are based is critical in choosing the appropriate equipment and technique in order to optimize the images which are obtained. An understanding of these principles is also important in determining when an ultrasound image accurately reflects the target anatomy or when ultrasonic artifacts are interfering with appropriate imaging [1].

Physics of Ultrasound

- Piezoelectric elements are stacked in layers at the functional end of the ultrasound transducer. Mechanical vibrations occur when electrical energy is applied to the transducer. Returning vibrations are mechanically converted back to electrical energy with a time phase.
- **Frequency**: The number of cycles of a sound wave per unit time is expressed as hertz (Hz) or megahertz (MHz). Frequencies above the range of human hearing (20–20,000 Hz) are called ultrasonic frequencies. Modern ultrasound for diagnostic imaging utilizes high frequency sounds waves ***in the 2–15*** **MHz range**.
- Wavelength **is inversely proportional** to frequency, Wavelength = velocity/frequency (velocity of sound through tissue or 1540 m/s). Wavelength in millimeters can be calculated by dividing 1.54 by the Doppler frequency in megahertz.
- A frequency of 3 MHz (wavelength 0.51 mm) would have a resolution of 1 mm and a **penetration of up to 100–200 mm (10–20 cm)** whereas 10 MHz (wavelength 0.15 mm) corresponds to a resolution of 0.3 mm, but penetration depth of no more than 60–120 mm (**6–12 cm**).

Echogenicity

- The propagation of an ultrasound wave is variably affected by the differing types of organic tissue (see Table.1.1)
  - **Attenuation** refers to the cumulative energy which is lost between ultrasound

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Table 1.1 Echogenicity of anatomic structures

Structure	Anechoic	Hypoechoic	Hyperechoic
Artery and Vein	+		
Bone			+
Fat		+	
Muscle		+	
Nerve	+		+
Tendon			+

wave creation and measurement of returned ultrasound wave
- Absorption refers to the amount of acoustic energy which is converted to heat within the tissue. Absorption accounts for approximately **80% of total signal attenuation** [2].
- Reflection refers to when the ultrasound wave is redirected but continues as a single ultrasound wave. If this reflection results in the ultrasound wave **returning to the transducer then it results in an ultrasound image**. If this reflection results in the ultrasound wave not returning to the ultrasound probe, then it contributes to **attenuation**.
- **Scatter** refers the ultrasound is redirected in many directions. The ultrasound wave no longer propagates an individual wave and it is not measured by the ultrasound transducer
- A tissues resistance to propagation of an ultrasound wave is referred to as **acoustic impedance**. Each tissue type has a unique acoustic impedance based on its density and speed of sound in the tissue. For example, lungs which have a much lower acoustic impedance than soft tissues due to the vast number of air spaces. Bone, has a higher density and speed of sound and thus a higher impedance.
- Interfaces between two tissues that have different acoustic impedance results in a large degree of ultrasound wave reflection causing a structure to appear hyperechoic on an ultrasound image
- **Anisotropy**: When the ultrasound beam is incident on a fibrillar structure e.g., tendon or a ligament, majority of the sound beam reflects in a direction away from the transducer. Therefore, the transducer does not receive the returning echo which shows 'hypoechoic'. The artifact causes a normal tendon to appear hypoechoic, which falsely indicates a tendinosis or tear in the tendon [3].

Display Modes

- A-Mode refers to **amplitude mode**. In this mode, the amplitude of the measured sound wave is graphed over time. This mode is useful for precise **measurement of depth** and is used in ophthalmology
- B-Mode refers to **brightness mode**. In this mode, the time that passes between generation of a signal and measurement of a return signal are used to represent depth. The intensity of the return signal is used to generate darker grey dots for weak signals and brighter white dots for stronger return signals. These are combined to create a 2-dimensional grey-scale image that is traditional thought of as 2-dimensional ultrasound.
- M-Mode refers to **motion mode**. In this mode, a one-dimensional line is chosen using the 2-dimensional image created in B-Mode. This one-dimensional line is then graphed over time. This mode is useful when trying **to differentiate between stationary and moving tissues**. M mode is useful for diagnosis of pneumothorax (Fig. 1.1). **"Seashore sign"** indicates normal lung sliding and excludes **pneumothorax**. **"Barcode sign"** indicates absent lung sliding and is suggestive of a **possible pneumothorax**.

Common Types of Ultrasound Artifacts

- A-lines
  - Horizontal repetitions of the pleural line (Fig. 1.2a) [4]
  - Represent horizontal reverberation artifacts that are parallel and equidistant from each and found in healthy individuals.

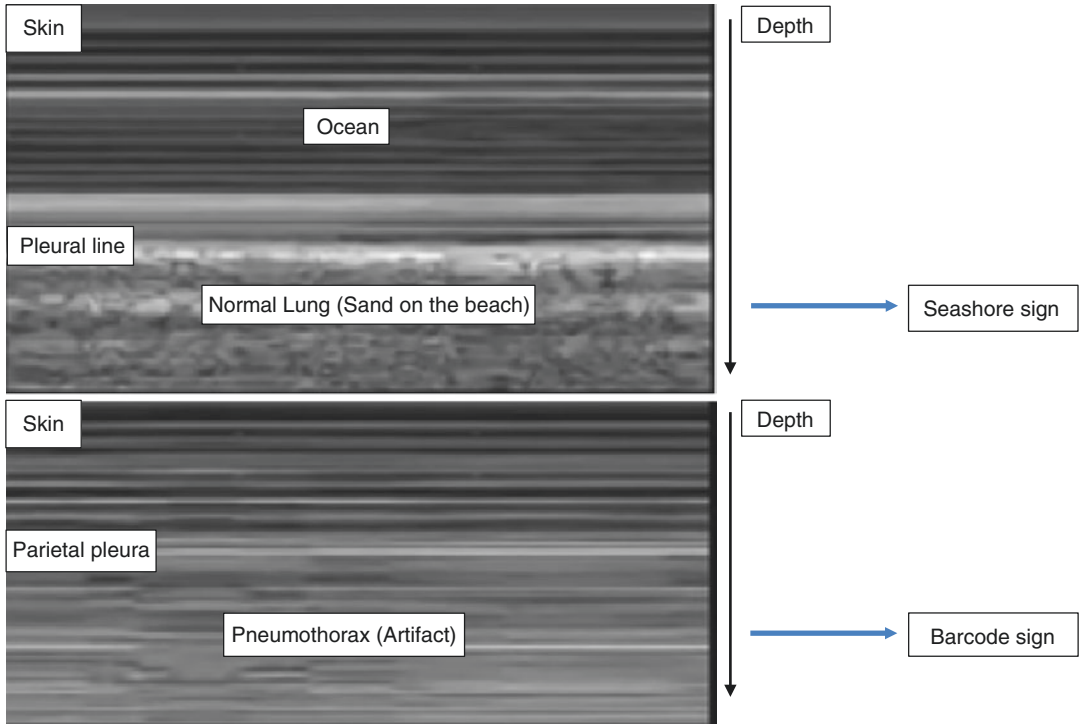

Fig. 1.1 M mode of the normal lung and pneumothorax

- B-lines
  - Multiple vertical bright lines originating at the pleural line to bottom of screen (Fig. 1.2b) [4]
  - Represent interlobular septa and appear as comet-tail like artifacts arising from and perpendicular to the pleural line with extension to the bottom of the screen, and move during respiration. May be seen in pulmonary congestion and interstitial lung disease. The presence of one to two B-line per intercostal space is a normal variant in 30% of healthy individuals.
- C-lines
  - Does not have a true linear appearance and presents as hepatization of lung parenchyma approaching the appearance of hepatic tissue on ultrasound.
  - Represent consolidated lung tissue that is often found in pneumonia (Fig. 1.2c) [4].
- Shadowing artifacts appear as a **hypoechogenic** area deep to a tissue (solid tissue, e.g., liver) with a higher level of attenuation than surrounding tissue. This artifact can confirm the presence of tissue with a high attenuation such as bone or gallstones (Fig. 1.2d) [4].
- Reverberation artifacts that appear as equally spaced echogenic areas due to reverberation of sound waves bouncing between two tissues with high levels of ultrasound reflectivity (Fig. 1.2e) [4].

Clinical Pearls

1. Wavelength **is inversely proportional** to frequency. High frequency transducers are ideally suited to image superficial structures. However, lower frequencies are required for deeper structures.

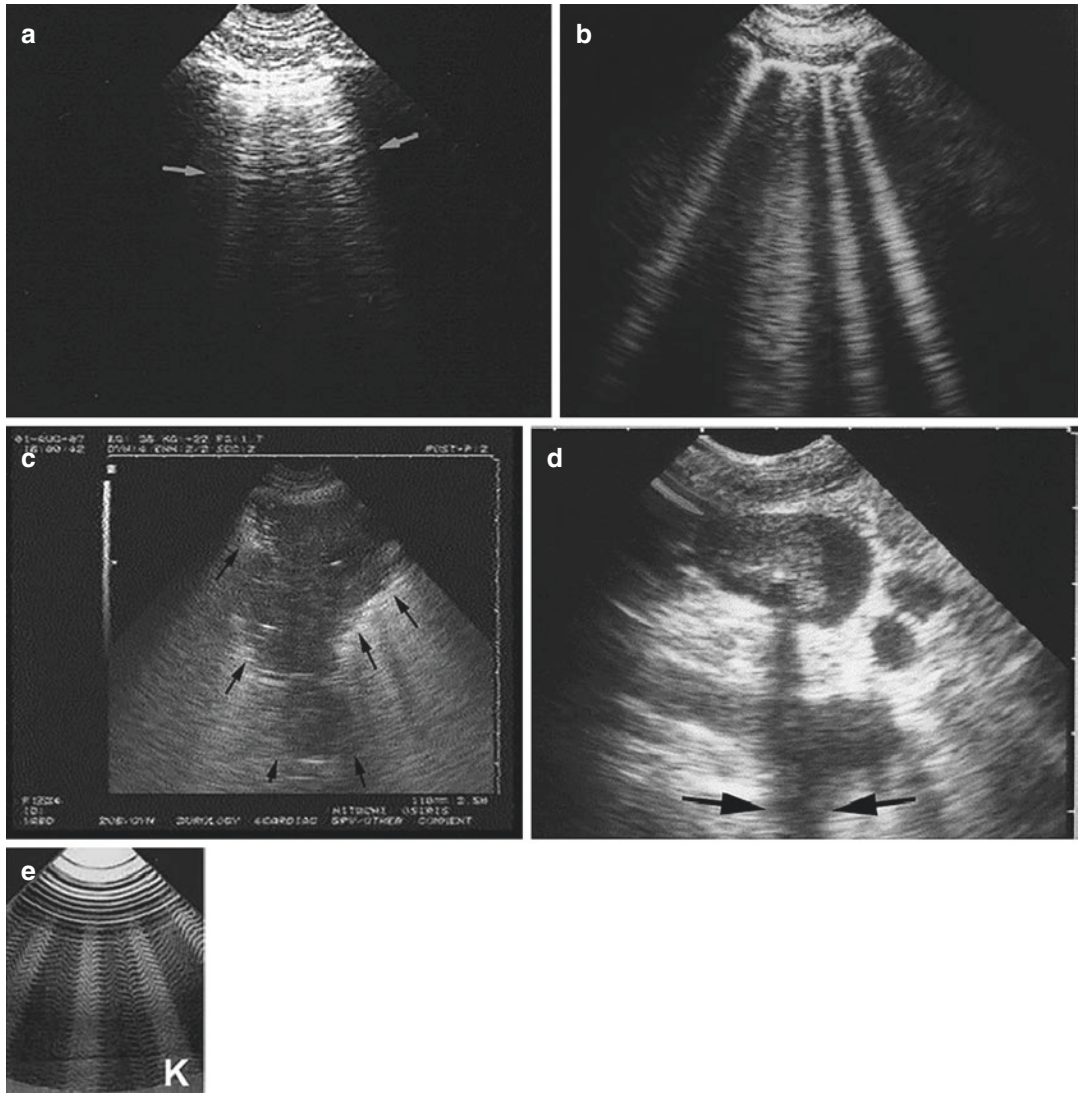

Fig. 1.2 (**a**) A-lines indicated by arrows showing three vertical ill-defined artifacts arising from the pleural line. (**b**) B-lines are seen as four distinct projections that are well-defined and arising from the pleural line. (**c**) C-lines represented as an anatomic structure (outline in arrows) instead of an acoustic barrier (consisting of A- or B-lines). (**d**) Shadowing shown as a vertical hypoechogenic image (within the arrows) deep to a solid structure. (**e**) Reverberations shown as equally spaced echogenic artifacts

Probe	Linear	Curvilinear	Phased array
Frequency range (MHz)	High frequency 5–10	Low frequency 2.5–5	Low frequency 2–8
Penetration	Lower	Higher	Higher
Image quality	+++++	+++	+++
Image foot print	Large	Large	Small

Probe	Linear	Curvilinear	Phased array
Ideal for movement	Poor	Poor	Great
Uses	Vascular, pleural, optic nerve, venous access	Abdominal, FAST, E-FAST, lung, pleural, GYN	Cardiac, lung, pleural, FAST, E-FAST, TCD

2. Phased array probes are most useful in ultrasound imaging of the heart, linear probes are most useful in imaging superficial tissue, and curvilinear probes are most useful in imaging deep structures.
3. M-Mode is a useful modality in differentiating moving vs stationary tissue. This is particularly useful in diagnosis of a pneumothorax.
4. A-lines represent horizontal reverberation artifacts that are parallel and equidistant from each and found in healthy individuals, B-lines represent comet-tail like artifacts arising from and perpendicular to the pleural line with extension to the bottom of the screen, and C-lines are not true lines but represent consolidated lung tissue that is often found in pneumonia (See Fig. 1.2).

Questions

1. What correctly describes the echogenicity of various anatomic structures?
   A. Bone is anechoic
   B. Arteries and veins are hyperechoic
   C. Nerves may be hyperechoic or hypoechoic
   D. Fat is hyperechoic
2. When scanning for specific nerve structures, what best describes the correct choice of ultrasound transducer in terms of ultrasound frequency, resolution, and depth?
   A. A low frequency transducer set to a shallow depth for imaging superficial nerves
   B. A high frequency transducer set to a shallow depth for imaging the neuraxial anatomy
   C. A low frequency transducer set to a deep depth for imaging the lumbar plexus
   D. A high frequency transducer set to a deep depth for imaging the proximal portion of the sciatic nerve
3. Artifacts on ultrasound imaging are most likely to be related to which of the following:
   A. Improper use of the ultrasound transducer
   B. Inappropriate interpretation of the ultrasound image by the person obtaining the image
   C. Abnormal patient anatomy
   D. Any scenario when the basic assumptions of the ultrasound imaging system are not accurate
4. Which of the following ultrasound imaging modes produces an image in which axial resolution is graphed on the X-Axis, depth is graphed on the Y-Axis, and signal intensity is represented by color on a greyscale?
   A. A-Mode
   B. B-Mode
   C. C-Mode
   D. M-Mode
5. What happens to the majority of the energy introduced to a biologic tissue by an ultrasound wave
   A. It is reflected back towards the ultrasound probe resulting in a 2-dimensional ultrasound image
   B. It is converted to heat due to absorption of acoustic energy
   C. It is reflected away from the ultrasound probe resulting in an ultrasound artifact
   D. It is scattered resulting in ultrasound wave propagation in many directions
6. Raising the frequency of an ultrasound transducer used from 3 MHz to 10 MHz, will result in which of following to tissue and ultrasound image
   A. Higher penetration but lower resolution
   B. Higher penetration with higher resolution
   C. Lower penetration but higher resolution
   D. Higher resolution with no change in tissue penetration

Answers

1. C, 2. C, 3. D, 4. B, 5. B, 6. C

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2 Basic Science: Local Anesthetics and Adjuvants for Nerve Blocks

Jeremiah Jeffers and Cale Kassel

Introduction

- Local anesthetics (LAs) are one of the oldest classes of medications used in the practice of clinical anesthesia
- Cocaine was the first clinically used local anesthetic, in 1884, during ophthalmic procedures
- The first spinal anesthetic was performed in 1898 using cocaine, by Augustus Bier at the University of Keil for an ankle surgery

Mechanism of Action and Properties

- LAs binds to voltage-gated sodium channels (Na) of nerve membrane, which become impermeable to Na → decreases action potential initiation and propagation.
- Diameter, myelination, and function of nerve fibers affects their responses to local anesthetics. In general, small unmyelinated sympathetic fibers are **blocked first,** followed by unmyelinated C fibers (pain and temp), then small myelinated fibers (proprioception, touch, pressure), and finally the large myelinated fibers (motor).
- **Lipid solubility** (high yield) is the primary determinant of potency of LA (Li**p**id has **p**otency). More lipophilic drugs can easily cross **lipid membrane** of nerve. Therefore lipid soluble anesthetics e.g. bupivacaine and tetracaine are more potent than less soluble anesthetics e.g. lidocaine.
- All local anesthetics are **weakly basic** molecules that have <50% fraction of non-ionized, lipid-soluble (active) molecules at physiologic pH (Table 2.1).
- **pKa** (high yield) is the pH at which uncharged and charged form of the drug exist in equal concentrations and determines onset of action. LAs with pKa closer to physiologic pH has a greater number of molecule uncharged form than the drug that has higher pKa. Uncharged molecule can rapidly diffuse across the nerve

Table 2.1 Properties of Local Anesthetics

Amides	pKa	Percent ioinized at physiologic pH (7.4); (cannot diffuse neuronal membrane)
Lidocaine	7.9	76%
Mepivacaine	7.6	61%
Bupivacaine	8.1	83%
Ropivacaine	8.1	83%
Prilocaine	7.9	76%
Esters		
Chloroprocaine	8.7	95%
Procaine	8.9	97%
Tetracaine	8.5	93%

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membrane while **ionized molecules cannot**. An exception is chloroprocaine, which has a fast onset of action that may be related to the higher concentration of drug used.
- **D**uration depends on **b**inding with protein: once local anesthetic reaches nerve cell, they bind with protein receptor sites. If a drug has high degree of protein binding it will bind with higher affinity resulting longer duration of action. Bupivacaine mostly bound with protein; hence it is longest acting.
- Placental transfer of LAs. 1. Highly protein-bound agents diffuse poorly across the placenta. Fetal acidosis → binding of hydrogen ions to the nonionized form of LA's → **trapping of the LAs** in fetal circulation.

Absorption, Metabolism, and Excretion

- Systemic absorption is dependent on site of injection, dose, and lipid-solubility
- Rate of absorption by site (highest-to-lowest):
  - Intravenous > tracheal > **i**ntercostal > **c**audal > **e**pidural > **bra**chial plexus > **s**ciatic/femoral > **s**ubcutaneous (high yield: mnemonic: **ICE BRASS**)
- Amide compounds are metabolized by cytochrome P450 enzymes (CYP3A4 & CYP1A2) in the liver by the steps of N-dealkylation followed by hydroxylation
- Prilocaine is unique as it is known to **cause methemoglobinemia** in high doses (>600 mg) via hemoglobin oxidation to methemoglobin by O-toluidine, a metabolic byproduct. (**methylene blue** is used to treat methemoglobinemia)
- **Ester** compounds undergo hydrolysis metabolism by plasma choline**sterases** and a small contribution from hepatic metabolism
- Ester metabolism is **significantly faster** than amid metabolism, decreasing the risk of toxicity. Cocaine is the exception, as it undergoes more hepatic metabolism than any other ester compound, increasing the risk of systemic toxicity
- Hepatic disease and increased levels of blood urea nitrogen both **slow the activity of plasma cholinesterases** and may impair ester compound metabolism

Allergic Reactions

- Allergic reactions to amide compounds or their metabolites are extremely rare
- PABA, a product of ester compound metabolism, is the most commonly cited cause of local anesthetic allergic reaction
- Preservatives such as methylparaben may evoke allergic reactions if they are included in the formulation of either ester or amide compounds
- Allergic reactions consist of type I (IgE mediated) or type IV (cell mediated) reactions
- There is no documented cross-reactivity between ester and amide classes of local anesthetics

Preservatives/Additives

- Epinephrine is the most commonly used additive in conjunction with local anesthetics. Effects include **prolongation of blockade**, increased intensity of blockade, and **decreased systemic absorption** of local anesthetic. Epinephrine may have direct analgesic effects via α-2 agonism in the brain and spinal cord (Table 2.2).
- Most LAs are marketed in acidic forms with pH of 5.0–7.0. LAs is more stable at this pH range and has a shelf life of 3–4 years at room temperature. The addition of sodium bicarbonate → pH increased toward physiological → greater proportion of **uncharged form** → enhanced effect and **decreased pain on injection**. For example, lidocaine preparations can be buffered by adding one part of 1 mEq/mL of sodium bicarbonate to 9 or 10

Table 2.2 Commonly Used Adjuvants in Regional Anesthesia

Medication	Mechanism	Indication	Dosing
Epinephrine	Alpha-1 agonism (vasoconstriction) Alpha-2 agonism	Marker for intravascular injection Prolong block duration	3–5 mcg/mL 1:200,000 = 5 mcg
Opioids	Opioid receptor agonism	Neuraxial (spinal, epidural) Described in some peripheral nerve blocks	Intrathecal: Morphine 100–200 mcg Fentanyl: 10–25 mcg Sufentanil: 5 mcg Epidural: Morphine: 1–3 mg Fentanyl: 2–10 mcg/mL Sufentanil: 0.25–1 mcg/mL
Dexamethasone	Unknown	Peripheral nerve blocks	2–4 mg
Clonidine	Alpha-2 agonism	Peripheral nerve blocks	1 mcg/kg
Dexmedetomidine	Alpha-2 agonism	Peripheral nerve blocks	0.5 mcg/kg

parts of 1 percent lidocaine or lidocaine with epinephrine.

- Opioids and LAs act synergistically in the neuraxial space, with the **exception of chloroprocaine** which may decreases efficacy of subsequently administered epidural morphine (controversial).
- Clonidine has been found to prolong the action of LAs. The drug has been shown to **inhibit impulse conduction** in primary afferents and especially in C fibers
- Dexmedetomidine is a highly selective α2-receptor agonist that has a faster onset and shorter duration of action compared with clonidine. Dexmedetomidine has **analgesic** properties, can potentiate neuraxial analgesia when injected with spinal LAs. It also has **direct inhibitory effects** on A and C nerve fibers.

Clinical Uses of Local Anesthetics

Peripheral Nerve Block Dosing

Local anesthetic	Typical concentrations (%)	Onset (min)	Duration (min)	Maximum dose[a] (Plain) (mg)	Maximum dose[a] (Epinephrine) (mg)
Bupivacaine	0.25–0.5	20–30	260–720	175	225
Ropivacaine	0.2–0.5	20–30	360–720	350	250
Mepivacaine	1–1.5	10–20	180–300	350	500
Lidocaine	1– 2	10–20	120–140	350	500
Chloroprocaine	2	5–10	30–60	800	1000

[a]Weight-based maximum dosing sometimes described
Bupivcaine: 2.5 mg/kg (plain), 3 mg/kg (with epinephrine)
Ropivcaine: 2.5 mg/kg (plain), 3 mg/kg (with epinephrine)
Lidocaine: 5 mg/kg (plain), 7 mg/kg (with epinephrine)
Mepivacaine: 5 mg/kg (plain), 7 mg/kg (with epinephrine)
Chloroprocaine: 9 mg/kg (plain), 12 mg/kg (with epinephrine)

Special Considerations for Local Anesthetics

Ester Local Anesthetics (Has One 'I')

Chloroprocaine
- Short plasma half-life as it is metabolized by plasma cholinesterase
- Rapid onset via epidural route and limited exposure to fetus (rapid metabolism) makes it especially useful in obstetrics
- Overall low risk of toxicity (CNS or cardiac)

Tetracaine
- Slow-onset, long acting local anesthetic
- Long duration increased with vasoconstrictor (epinephrine)
- Often used for local infiltration, spinal anesthetics

Benzocaine
- Typically used for topical anesthesia of mucus membranes
- Excessive dosing can lead to methemoglobinemia

Prilocaine
- Ester local anesthetic often combined with lidocaine for topical anesthesia in preparation of needle sticks
- EMLA (Eutectic Mixture of Local Anesthetics) 2.5% Prilocaine + 2.5% Lidocaine
- Contraindications include: allergy to amide anesthetics, use of class III anti-arrhythmic drugs, known congenital or idiopathic methemoglobinemia, children <12 months also concurrently receiving methemoglobinemia-inducing drugs

Amide Local Anesthetics (Has Two 'II')

Mepivacaine
- Similar in structure to bupivacaine but clinically similar to lidocaine in onset, duration
- Does not cause vasodilation (like lidocaine), prolonged duration compared to lidocaine. Metabolism prolonged in fetus, newborn; **generally avoided** in **obstetric** epidural anesthesia. The fetus poorly metabolizes **mepivacaine**.

Lidocaine
- Versatile local anesthetic used for infiltration, regional blocks, epidural, spinal, IV anesthesia (Bier Block), nebulization, and topicalization
- Causes some vasodilation, adding epinephrine can prolong blockade
- **Transient neurologic symptoms** (TNS) may result from intrathecal injection
  - Pain or sensory abnormalities in low back, buttocks following lidocaine spinal (other local anesthetics may cause TNS)
  - May be related to position (Lithotomy increases risk), spinal catheters, ambulator procedures
  - Treatment with NSAIDs, typically resolves in 1–7 days

Bupivacaine
- Long-lasting sensory blockade, longer than motor block
- Addition of epinephrine can be added to prolong block but is less effective as bupivacaine is more hydrophobic (**lidocaine is more hydrophilic, epinephrine has greater effect**)
- High affinity for sodium channels coupled with high lipid solubility increased morbidity, mortality
- mixture of R(+) and S(−) enantiomer compounds

Liposomal Bupivacaine
- Solution of bupivacaine encapsulated in liposomal vesicles
- Time-delayed release can give analgesic effects for up to 72 hours post-injection
- Currently FDA approved for **tissue infiltration, TAP blocks, and interscalene nerve blocks**
- Cannot be injected within 20 minutes of administration of a non-bupivacaine local

anesthetic, as bupivacaine may be released quickly leading to toxicity

Levobupivacaine

- S(−) enantiomer of bupivacaine
- Produces less CNS and cardiovascular side effects than bupivacaine
- Can be used in the same dosing and routes of administration as bupivacaine
- May have a slightly slower onset and slightly longer duration than bupivacaine
- Appears to have a less dense motor blockade than bupivacaine

Ropivacaine

- Less cardiotoxic than bupivacaine (made from enantiomer of bupivacaine)
- As a result, larger doses can be used
- Differential block noted with epidural dosing (greater sensory block without significant motor block)
- Intrinsic vasoconstricting effect, may improve duration and less cardiotoxicity

Questions

1. Which of the following adjunct and side effect pair is incorrectly paired?
   A. Buprenorphine – Nausea/Vomiting
   B. Dexamethasone – Hyperglycemia
   C. Clonidine – Bradycardia
   D. Sodium Bicarbonate – Delayed Block Onset
2. In a 70-kg male, which dose of local anesthetic is toxic for a single-shot femoral nerve block?
   A. 40 mL of 1% lidocaine with 1:200,000 epinephrine
   B. 30 mL of 0.25% bupivacaine
   C. 40 mL of 1.5% mepivacaine
   D. 30 mL of 0.2% ropivacaine
3. Which of the following concentrations of epinephrine corresponds to a 1:100,000 mixture?
   A. 0.1 μg/mL
   B. 10 μg/mL
   C. 100 μg/mL
   D. 0.1 mg/mL
4. Patients with a documented allergy to para-aminobenzoic acid (PABA) should not be given which of the following local anesthetics?
   A. Lidocaine
   B. Benzocaine
   C. Ropivacaine
   D. Mepivicaine
5. A 5-year-old with an upper airway mass at risk for obstruction presents to the preoperative area, where EMLA is applied in preparation for placing an IV prior to induction. The child is also given oral midazolam. Once in the OR, the child is noted to be cyanotic with an SpO_2 of 84% despite being arousable with good respiratory effort and adequate preoxygenation. Which medication is appropriate as an initial treatment?
   A. Atropine
   B. Succinylcholine
   C. Methylene blue
   D. Low dose epinephrine
6. Which of the following measures is not indicated in the treatment of a patient with signs of cardiovascular toxicity from local anesthetic administration?
   A. Supplemental oxygen
   B. CPR if pulseless
   C. Epinephrine 1 mg IV/IO
   D. Lipid emulsion 20% bolus and infusion

Answers

1. D. Sodium bicarbonate raises the pH of local anesthetic solutions. When pKa of the solution moves closer to physiologic pH, the fraction of non-ionized (active) compound increases. This increase in bioavailable drug increases drug onset, not decreases it. The other pairs of medications and side effects are correct.
2. C. The maximum safe dose for mepivacaine is 350 mg, or roughly 5 mg/kg for a 70 kg patient. This selection would allow for 600 mg of plain mepivacaine to be administered, roughly twice the upper limit of safety.
3. B. The amount of epinephrine in a 1:100,000 solution is 10 μg/mL. The amount of epineph-

rine in a 1:200,000 solution is 5 μg/mL. By dividing 1000 by the goal concentration, this will yield the concentration in mg/mL which can easily be converted to micrograms/mL by 3 orders of magnitude.

4. B. Benzocaine is an ester local anesthetic, often used for topical and mucosal membrane anesthesia. One of the products of ester metabolism is para-aminobenzoic acid (PABA).
5. C. This child has developed methemoglobinemia secondary to the EMLA (specifically the prilocaine in the mixture). The refractory hypoxemia despite preoxygenation is another cue that this may be hypoxemia as opposed to hypoxia. Central cyanosis may occur at levels >10%, with significant sequelae at levels >20%. Methylene blue at doses of 1–2 mg/kg IV over 5 minutes (repeated until 7–8 mg/kg) is the initial treatment. It acts to reduce methemoglobinemia back to functional hemoglobin. Methylene blue is contraindicated in G6PD deficiency, as it may cause hemolysis.
6. C. ASRA guidelines recommend a significantly reduced dose of epinephrine for treatment of local anesthetic systemic toxicity (LAST). The rational for this dosing is to avoid impairment of pulmonary gas exchange and also to avoid large increases in afterload which will further decrease cardiac output of a failing heart; the same rationale for avoiding vasopressin.

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3 Acute Postoperative Pain: Patient-Controlled Analgesia

Juhee Sharma, Bryant Tran, and Sabrina Dhillon

Introduction

- Patient-controlled analgesia (PCA) is a method of analgesic delivery that was first used in the 1960s.
- PCA is most frequently used for delivery of intravenous opioids, such as fentanyl, hydromorphone, or morphine (Table 3.1).
- PCA devices can also deliver medications through other routes such as an epidural or peripheral nerve catheter (Table 3.2).
- Patient-controlled epidural analgesia (PCEA) incorporates either local anesthetic or a combination of opioid and local anesthetic (Table 3.2).
- Patient satisfaction with PCA is improved due to timely administration of demand dosing.
- Patients who use PCA typically have a **higher** overall in-hospital opioid consumption compared to patients with nurse-administered drug dosing.

Background

- The goal of PCA is to achieve a minimal effective analgesic concentration, which is the smallest concentration of medication needed for pain relief.
- PCA will minimize peaks and troughs associated with traditional bolus regimens and ideally will mimic a continuous infusion.
- Most devices have settings for demand doses, hourly limits, lockout intervals, and continuous infusion rates.
- There is no validated method of anticipating opioid requirements in opioid-naïve patients, so close follow-up is essential at the start of PCA.
- Lockout intervals prevent a patient who presses the PCA button too frequently from receiving additional medication boluses for a set period of time.
- The patient may press the delivery button multiple times within the lockout period, but this **does not always mean** that they have severe pain.
- Patients with continuous infusions of opioids have increased incidence of respiratory depression due to greater total consumption of opioids.
- Disadvantages of PCA include risk of inappropriate analgesic delivery by relatives or staff as well as the risk of patients waking up

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Table 3.1 Intravenous patient controlled analgesia regimens

Opioid	Demand dose	Lockout time (min)	Continuous basal infusion rate
Fentanyl	20–50 mcg	5–15	0–60 mcg/h
Hydromorphone	0.1–0.6 mg	5–15	0–0.4 mg/h
Morphine	1–3 mg	5–15	0–2 mg/h

Adopted from formulary at Virginia Commonwealth University Medical Center. Opioid-naive patients are typically set at a lower range for demand dose and higher range for lockout time. Basal infusion rates may be considered in opioid-tolerant patients

Table 3.2 Patient controlled epidural analgesic regimens

Concentration	Continuous rate (ml/h)	Bolus dose (ml)	Lockout time (min)
0.125% Bupivacaine + Fentanyl 2 mcg/ml	3–5	2–5	10–20
0.125% Bupivacaine + Hydromorphone 10 mcg/ml	3–5	2–5	10–20
0.0625% Bupivacaine + Fentanyl 2 mcg/ml	5–8	5–8	10–20
0.0625% Bupivacaine + Hydromorphone 10 mcg/ml	5–8	2–5	10–20

Adopted from formulary at Virginia Commonwealth University Medical Center

in pain as they are unable to press their button for medication dosing when asleep. It then takes time to re-achieve satisfactory analgesia once awake.

Indications

- PCA is commonly used for pain management in the post-surgical period where moderate or severe pain is expected, such as **major thoracic or abdominal surgery**.
- PCA may be an option when enteral medications are contraindicated, such as when patients are NPO or there are anatomical limitations.
- When regional or neuraxial anesthesia are not viable options due to contraindications or patient refusal, one may consider a PCA.
- PCA is appropriate for medical comorbidities such as cancer pain or sickle cell disease.

Relative Contraindications

- Practitioners may consider other options for pediatric patients or patients with **dementia, altered mental status**, frailty, obstructive sleep apnea, and concurrent use of sedatives.

Technique

- A thorough history and physical should be completed on all patients, with special attention paid to previous **history of opioid use** as well as gender, **age**, cancer history, or sickle cell disease. This information must be taken into account when initiating PCA (Table 3.1).
- When choosing a regimen, one must consider doses for on-demand boluses, loading dose, hourly limits, lockout intervals, and if a basal infusion will be initiated.
- **Loading dose**: clinician bolus given during a pain crisis. It is typically 2× or 3× larger than on-demand bolus doses.
- **On-demand dose**: accepted starting bolus doses include morphine 1 mg, hydromorphone 0.1 mg, and fentanyl 20 mcg (Table 3.1).
- **Lockout interval**: standard lockout intervals exist, which range from 10 to 30 minutes.
- Frequent re-evaluation of a patient's PCA settings is indicated to ensure appropriate analgesic regimen. On-demand dose increase is indicated if patient requires frequent clinician boluses and/or if they report uncontrolled pain.
- **A basal rate** or continuous infusion should preferably not be initiated in **opioid-naive** patients, or should be done with extreme

caution, as it does not improve the analgesic effect and reduces the safety margin of PCA.
- A basal rate may be cautiously added for opioid-tolerant patients when PCA is initiated based on an **equi-analgesic conversion** (Chap. 34) of chronic, long-acting opioids and a subsequent 25–50% dose reduction for cross-tolerance.

Complications Nausea and vomiting, Pruritus, Sedation, Potential for respiratory depression in patients with undiagnosed OSA and PCA operated by patient's surrogate, Risk of opioid withdrawal.

Preventive Measures to Avoid Complications

- Consider **multimodal analgesic regimens** to minimize dosing of opioid PCA. Scheduled acetaminophen and NSAIDs, if appropriate, may offer additional analgesia. Additionally, use regional or neuraxial anesthesia as an adjunct to PCA.
- In patients with continuous infusions, respiratory status should be monitored with end-tidal capnography.
- Transition off PCA **as soon as clinically appropriate**, ideally well before the day of discharge to establish an appropriate oral pain regimen.

IV PCA Versus PCEA

- Patient-controlled epidural analgesia (PCEA) is a **highly effective** method to provide pain control for obstetric patients as well as for patients in the postoperative period who have an indwelling epidural catheter.
- This benefits of PCEA include improved pulmonary and gastrointestinal function, decreased sedation, and decreased opioid consumption (Chap. 15, regional anesthesia).
- PCEA incorporates either local anesthetic or a combination of opioid and local anesthetic to provide demand dosing in obstetric or post-surgical patients. PCEAs, like PCAs, can have demand dosing alone or demand dosing plus continuous infusions.
- PCEA offers **superior pain relief** compared to IV PCA specifically in the elderly and patients undergoing painful procedures, such as thoracic or thoracoabdominal surgery.

Clinical Pearls

- IV PCA or PCEA should be considered in patients after major surgery, patients with contraindications to enteral medications, and cancer patients.
- Reduced initial PCA dosing and increased monitoring is recommended in patients with risk factors for opioid-induced respiratory depression. These risk factors include **advanced age**, **frailty**, obstructive sleep apnea, concurrent use of sedatives, family member participation of PCA use by proxy, and impaired renal function.
- Opioid tolerant patients may require **higher dosing** to provide adequate analgesia but may still be at equal risk for respiratory depression, as well as other side effects, including nausea, pruritus, and excessive somnolence.

Questions

1. When compared to intermittent demand dose patient-controlled analgesia (PCA), a continuous basal infusion of opioid results in which of the following outcomes?
   A. Improved pain control
   B. Decreased opioid consumption
   C. Increased risk of respiratory depression
   D. Decreased monitoring requirement
2. When comparing usage of an opioid PCEA in men and women, women are more likely to exhibit which of the following:
   A. No differences in opioid consumption
   B. Lower likelihood of nausea
   C. Increased pain scores
   D. Decreased opioid consumption

3. If a hydromorphone PCA was programmed to allow for a demand dose of 0.2 mg every 10 minutes, which of the following settings on a morphine PCA would most closely align as an equianalgesic dose?
   A. 0.5 mg every 10 minutes
   B. 1 mg every 10 minutes
   C. 2 mg every 10 minutes
   D. 4 mg every 10 minutes
4. In which of the following scenarios is nursing administration of breakthrough opioid medication preferred over PCA administration?
   A. Shortage of nursing staff
   B. Frequent dosing requirement
   C. Pediatric patient
   D. Post-surgical patient
5. Which of the following is not an advantage of PCEA?
   A. Decreased opioid consumption
   B. Longer length of stay
   C. Increased mental clarity
   D. Improved pulmonary function
6. A 60-year-old man is getting hydromorphone via patient-controlled analgesia (PCA) pump after exploratory laparotomy. The pump is programmed to deliver a maximum dose of 0.2 mg every 15 minutes (lockout time) as needed for patient comfort. On the first 8 hours, patient received 32 doses but pressed the delivery button 45 times. What would you do next?
   A. Change to morphine PCA
   B. Increase the lockout time to 20 minutes
   C. Increase the dose to 0.3 mg every 15 minutes
   D. Reassurance

Answers

1. C, 2. D, 3. B (see Chap. 34, chronic pain), 4. C, 5. B, 6. C

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4 Acute Postoperative Pain: Regional Versus General Anesthesia

Bahar Kasimi and Jon Zhou

Introduction

- Regional anesthesiology (RA), the practice of using local anesthetics to provide analgesia to specific parts of the body, started over 100 years ago.
- Compared to general anesthesia (GA), RA results in decreased hemodynamic changes and in certain populations, decreased opioid requirements, reduced post-operative recovery times and decreased complications such as delirium, PONV, and inflammation.
- RA increasingly incorporated into the perioperative care environment as variety of blocks, equipment, and patient demographics qualified to receive blocks have broadened (Table 4.1).

Benefits of Regional Anesthesia (RA)

- *Neurological effects:* **Lower post-operative delirium** in elderly population, thought to be related to avoidance of systemic anesthetics used in GA (inhaled or intravenous) and less hemodynamic changes [1]
- *Cardiopulmonary effects:* Direct cardiac and pulmonary effects of peripheral nerve block are low. Only a small amount of local anesthetics are absorbed systemically. General and neuraxial anesthesia, on the other hand, have a more pronounced effect on cardiac output and peripheral perfusion. Inhaled and many intravenous anesthetics used in general anesthesia cause **systemic vasodilation and direct myocardial depression**, which can lead to hypotension. Inhaled agents also suppress carbon dioxide and hypoxia-induced respiration [2]. Neuraxial anesthesia, particularly spinal anesthesia, produces a rapid sympathetic block leading to vasodilation and potential profound hypotension.
- *Gastrointestinal effects:* Neuraxial anesthesia→ sympatholysis→ improved microcirculation→ **improved bowel function**. Moreover, avoidance of opioid from neuraxial anesthesia help in **reducing constipation and ileus** [3].
- *Anti-inflammatory effects:* It has been shown that RA **reduces cytokine production** and blocks sympathetic nerve activity after surgery. Martin and colleagues showed that combined sciatic and femoral nerve block **reduced clinical inflammation** (evaluated by local skin temperature and circumference of the knee) after major knee surgery compared with morphine analgesia [4]. Animal studies also demonstrated that thoracic epidural anesthesia can cause effective sympathetic block and a

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Table 4.1 Regional anesthesia vs general anesthesia

	Pros	Cons
General anesthesia	Secured airway Muscle relaxation Optimal operating conditions even if prolonged surgical time/change in surgical plan Ideal for patients with anxiety	Airway instrumentation Increased time for emergence Hemodynamic changes/myocardial suppression with systemic anesthetics
Regional anesthesia	Decreased hemodynamic changes (excluding spinal anesthesia) [1] Decreased opioid requirements Improved post-operative bowel function [3] Earlier mobility post-operatively after orthopedic surgery [6] Lower post-operative delirium in elderly [1] Preserve cerebral auto-regulation and allows neurological exam intraoperatively in awake craniotomy	Contraindication with anticoagulant use Procedural anxiety Risk of failed block Risk of damage to surrounding structures (depending on block type) Risk of local anesthetic toxicity Postdural puncture headache

Table 4.2 Common types of regional anesthesia

Upper extremity (Single shot or catheter)	Lower extremity (Single shot or catheter)	Field block (Single shot or catheter)	Neuraxial	IV Regional Anesthesia (IVRA)
Brachial plexus (Interscalene, supra/infra-clavicular Axillary) Terminal nerve blocks (ulnar, radial, musculoskeletal, intercostobrachial, digital)	Femoral Sciatic/popliteal Obturator Adductor canal Ankle block	Transversus Abdominus plane Superficial/deep cervical plexus Intercostal Erector spinae plane	Spinal Epidural Combined Spinal/Epidural (CSE) Caudal Paravertebral	Bier block

reduction in inflammation. Use of neuraxial anesthesia to supplement GA in patients undergoing CABG or AVR have been found to cause **decreased release of inflammatory markers** and catecholamines [5].

- *Effects on blood coagulation:* Some studies suggest that the incidence of perioperative venous thrombosis is significantly reduced after neuraxial anesthesia in orthopedic surgeries. Patients undergoing orthopedic surgery including total hip arthroplasty and total knee arthroplasty, have **earlier mobility with regional anesthetic** which lead to decreased risk of deep venous thrombosis and shorter hospital stay [6].
- *Preserved cerebral auto-regulation during craniotomy:* Patients undergoing neurological surgery including awake craniotomy can be kept awake with use of RA allowing **intraoperative assessment of neurological status**. RA also allows preserved cerebral autoregulation. GA with inhalation anesthetic causes decreased CMRO2 and **decreased CBF at <1 MAC**. On the other hand, decreased CMRO2 and **increased CBF at >1.5 MAC**.

Disadvantages of Regional Anesthesia

- Patients with anxiety or pediatric populations may have an **unpleasant experience** receiving regional anesthesia while awake and recollection of surgical procedure.
- Risk of **failure of regional anesthesia** due to incorrect placement or injection, catheter migration, ineffective local anesthetic in acidic tissue (i.e., in setting of sepsis)
- Risk of headache after neuraxial anesthesia including **post-dural puncture headache** during epidural placement.
- Risk of intravascular injection of local anesthetic and **local anesthetic toxicity (LAST)** (Table 4.2).

Clinical Pearls

- RA can be used as **primary anesthetic in many cases**, not only postoperative analgesia.
- RA offers benefits over GA in certain populations (**elderly**, patients with **difficult airways**, OSA, COPD, severe cardiac disease), including improved pain control, decreased opioid consumption, decreased PONV, earlier mobility, decreased hemodynamic and cerebral autoregulatory changes.
- Nerve blocks (landmark or US based) can be performed with a single injection of local anesthetic +/− adjuncts to increase potency, duration of analgesia, or decrease onset time (or catheter placement allowing bolus dosing.
- Contraindications to neuraxial anesthesia include **prior spine surgery** at the targeted site, local infection, and coagulopathy. Risks included procedural failure, **dural puncture headache**, nerve injury and intravascular injection (LAST).

Questions

1. Compared to general anesthesia, which of the following is true regarding neuraxial anesthesia when used for patients undergoing cardiac surgery?
   A. Increased inflammatory markers with spinal anesthesia
   B. T4 level sufficient for high spinal anesthesia
   C. Clear mortality benefit from spinal anesthesia
   D. Reduced incidence of SVT with use of thoracic epidural anesthesia
2. Which of the following is a proven benefit of regional anesthetic techniques over GA?
   A. Decreased incidence of UTI in patients after radical prostatectomy
   B. Improved respiratory status in patients with COPD who receive interscalene blocks
   C. Decreased incidence of DVT in patients after total hip replacements
   D. Decreased incidence of cancer recurrence in patients with a history of breast cancer
3. Compared to GA, which of the following is true when utilizing regional anesthesia as the primary anesthetic for AV Fistula surgery?
   A. There is definitive evidence that RA can decrease the rate of AVF graft failure in the long term (>30 days)
   B. RA is associated with decreased bleeding from AVF creation compared to GA alone
   C. RA and GA have required equal amounts of perioperative opioid for pain control
   D. RA techniques for AVF creation are contraindicated in patients with pulmonary disease
4. A 55 years old patient with a history of low back pain with lumbar spine fusion and uncontrolled type II diabetes mellitus who is status post ankle ORIF after motorcycle accident has returned to the hospital with tarsal hardware infection and is to undergo surgical removal of hardware. What is the best anesthetic option for this case?
   A. Ankle block + monitored anesthesia care
   B. Combined spinal epidural
   C. GA with perioperative opioid analgesics only
   D. GA with post-operative popliteal nerve block
5. Compared to parenteral opioids, which of the following is true about thoracic epidurals for rib fracture pain?
   A. Over 50% of patients with rib fractures receive thoracic epidurals
   B. Thoracic epidural is associated with decreased mortality in rib fracture patients
   C. On average, patients who receive thoracic epidurals have similar average numbers of rib fractures
   D. Thoracic epidurals have not been shown decrease the incidence of mechanical ventilation

Answers

1. D. According to ASRA "Neuraxial Analgesia for Cardiac Surgery," there is growing evidence supporting use of neuraxial anesthesia for cardiac surgery. Thoracic epidural anesthesia has been shown to decrease rates of

supraventricular tachycardia vs. GA alone in cardiac surgery. There is also a decreased net inflammatory response when using high spinal anesthesia based on serum biomarkers. Neuraxial blockade for cardiac surgery requires at least a T1 dermatomal level, not T4. However, there is no evidence yet that neuraxial anesthesia improves mortality in this population [5].

2. C. Urinary retention is a risk of neuraxial anesthesia, thus there is a higher chance of UTI with RA comparison with GA [3]. Interscalene blocks may cause phrenic nerve blockade and are relatively contraindicated in COPD patients. It was hypothesized that regional anesthesia during breast surgery may decrease the risk of cancer recurrence but subsequent studies suggest that this is not the case.
3. B. Patients with end stage renal disease (ESRD) often require arterial venous fistula (AVF) in order to have permanent hemodialysis access. Recent studies found that there is a 26% increased chance of bleeding in patients status post arteriovenous fistula placement under GA vs. RA [7]. This same study suggested that there is also a three times higher infection rate in the GA group. However, there is no definitive evidence that AVF formation under RA leads to decreased failure rates compared to GA [7].
4. D. The patient has an infection of the ankle with likely overlying cellulitis. Although regional as the primary anesthetic could otherwise be indicated for this procedure, local infection is a contraindication to an ankle block. GA is the appropriate option for this case. He is however a candidate to receive a perioperative popliteal nerve block to alleviate post-op pain, assuming he has no cellulitis at the popliteal fossa.
5. B. Thoracic epidurals decrease mortality rates associated with rib fractures by 97% compared to alternative care when controlling for age and injury severity [8]. Patients with thoracic epidurals are typically older and have a greater number of rib fractures. Only 2.2% of patients with rib fractures get thoracic epidurals for analgesia, possibly attributed to the lack of acute pain specialists available to place them in patients with multiple rib fractures. Thoracic epidurals not only decrease pain but also decrease the incidence of mechanical ventilation by allowing the patients to improve oxygenation and ventilation [8].

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5 Acute Postoperative Pain: Pediatric Regional Anesthesia

Cheryl Chooi and Andrea Gomez Morad

Introduction

- Pediatric regional anesthesia is **commonly performed** for perioperative pain management.
- **Potential advantages**: superior analgesia; decreased anesthetic and opioid requirement; attenuation of stress response to surgery; decreased time to extubation; reduced duration of hospital admission; facilitates early ambulation and return of gastrointestinal function.
- Useful in pediatric **chronic and cancer pain** to facilitate physical therapy and rehabilitation.
- **Block failure** is the most common problem associated with peripheral nerve blocks and **inadvertent vascular puncture** is most common with central neuraxial blocks [1].

Anatomy and Physiology

Spinal Canal

- In neonates, **spinal cord ends at L3 or L4**, and slowly **moves to L1 by 1 year of age.**
- In neonates, **Dural sac ends at S3–4**, and slowly **moves to S2** by 1 year old.
- Infants have relatively **high** cerebrospinal fluid volume (**4 mL/kg**) and flow compared to adults, and therefore local anesthetics are cleared faster [2].

Bones

- Mostly cartilaginous, therefore bone contact with sharp needles should be avoided.
- Sacrum is not fully ossified and intervertebral spaces are present, allowing sacral epidural access.
- Sacral hiatus becomes smaller with increasing age, and therefore caudal blocks become more difficult beyond 6–8 years of age.
- **Intercristal line** is at L5 in children and L5-S1 in neonates [3].

Nerves

- Nerves are smaller, more superficial, and closer to adjacent vascular and organ structures.

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- Immature myelination of nerve fibers results in **greater** local anesthetic penetration into nerve fibers, **faster onset** of action and **lower concentration** of local anesthetic required to achieve a dense block.
- Hypotension associated with sympathectomy is **uncommon** due to sympathetic immaturity.

Connective Tissue

- Loose attachment of fascia and aponeuroses to adjacent structures enables greater spread of local anesthetic and higher quality block.

Pharmacology

Neonates and Infants

- **Immature hepatic function** and **reduced activity of metabolic cytochrome enzymes** resulting in slower amide local anesthetic metabolism.
- **Reduced levels of alpha-1-acid glycoprotein** (AGP), resulting in lower protein binding and higher concentrations of unbound amide local anesthetic in plasma. Adult levels of AGP reached by 1 year of age.
- **Ester local anesthetics**, such as chloroprocaine, are metabolized efficiently by plasma cholinesterases, and therefore considered safer than amide local anesthetics.
- **Relatively larger dose** required compared to adults to achieve a thoracic level spinal blockade (1 mg/kg of bupivacaine in infants, compared to 0.2 mg/kg in adults)
- Average spinal anesthetic duration is **one third of the duration** of adults, despite administration of **threefold** higher dose.
- **Increased cardiac output and heart rate** results in faster systemic absorption of local anesthetic.
- **Clearance is reduced in patients less than 6 months.** Careful administration of boluses and infusions is recommended [2].

Local Anesthetic Choice

- **Weight based calculation** of dose (Table 5.1) is essential to minimize the risk of local anesthetic systemic toxicity (LAST).
- Considerations: **analgesia versus anesthesia**; site and extent of ***surgery***; expected duration of **hospital stay**; ropivacaine and levobupivacaine are less cardiotoxic than bupivacaine.

Adjuvants

- Additives, such as dexamethasone, clonidine and dexmedetomidine may be added to the

Table 5.1 Local anesthetics maximum recommended dose for blocks

Local anesthetic	Maximum dose, no epinephrine (mg/kg)	Maximum dose, with epinephrine (mg/kg)	Maximum infusion rate by age, no epinephrine (mg/kg/h)
Ropivacaine	3	Not recommended	4 months to 1 year = 0.25 1–4 years = 0.35 >4 years = 0.4
Levobupivacaine	3	4	4 months to 1 year = 0.25 1–4 years = 0.35 >4 years = 0.4
Bupivacaine	2	3	4 months to 1 year = 0.25 1–4 years = 0.35 >4 years = 0.4
Lidocaine	5	7	Not recommended
Mepivacaine	5	Not recommended	Not recommended
Chloroprocaine	7	10	Age <6 months = 12

Adapted from Suresh (2020) [2]

local anesthetic to prolong the duration and density of single injection blocks.
- Current evidence **is not strong** to recommend routine use of additives.

Controversies

General Anesthesia

- Most blocks are **performed under general anesthesia** or deep sedation due to limited cooperation and anxiety in children.
- Prospective multi-center data from the **Pediatric Regional Anesthesia Network** demonstrated no permanent neurological deficits when performing peripheral and central-neuraxial blocks while under general anesthesia, and should be considered as safe as when performing a block in an awake child or adult [1].

Compartment Syndrome

- No evidence that regional blocks increase the risk of compartment syndrome or delays its diagnosis.
- **Dilute concentrations** of local anesthetic are less likely to cause motor block and less likely to mask pain associated with compartment syndrome.
- Caution when using local anesthetic additives, as this may increase block density and duration.
- If compartment syndrome is suspected, surgical evaluation should be urgently sought [4].

Safety

- Small footprint linear transducers allow **improved resolution** of superficial structures.
- The use of **test dose 0.5 mcg/kg epinephrine** to identify inadvertent intravascular needle placement is controversial but still considered useful with neuroaxial techniques. Monitor heart rate, blood pressure and electrocardiographic (ECG) morphology. During inhalational anesthesia, increase in **T wave amplitude is the earliest sign**. When using propofol total intravenous anesthesia, increases in blood pressure is considered more reliable.
- **Test dosing may yield false negative results**, and therefore any injection of local anesthetic should be performed **slowly with frequent aspiration** [4].

Aseptic Precautions

- Use alcohol containing skin antiseptic, such as chlorhexidine or betadine.
- Do not use chlorhexidine on infants <2 months old due to risk of chemical burns.
- Additional precautions when placing a catheter, including sterile gloves, drape and face mask.

Local Anesthetic Systemic Toxicity

- Highest risk in **infants less than 6 months of age** due to unrecognized intravascular injection, rapid absorption and distribution, and decreased levels of alpha-1-acid glycoprotein.
- All providers must be familiar with the management of **local anesthetic systemic toxicity**
- Weight based dosing using **American Society of Regional Anesthesia LAST Checklist** [5].

Informed Consent

- Discussion with parents, primary anesthesiologist and surgeon. **Consider** site of surgical incision; single injection versus catheter; patient comorbidities.
- **Informed consent** (and assent when appropriate) must be obtained.

Specific Blocks

- The most commonly performed nerve block in children is the **caudal block** [3].
- The most commonly performed peripheral nerve blocks are **femoral**, transverse abdominis, ilio-inguinal and ilio-hypogastric, sciatic, supraclavicular, saphenous, and penile.

Caudal Block

- **Indications**: Mainly used for surgery below the umbilicus (eg inguinal hernia repair)
- **Contraindications**: sacral malformations, meningitis, intracranial hypertension, coagulopathy, skin infection at site of intended needle insertion [3].
- **Landmark technique**: Position in lateral decubitus position. Locate the sacral hiatus, at the apex of an equilateral triangle using the posterior superior iliac spines (Fig. 5.1a). Needle is passed through sacrococcygeal ligament into caudal space, using loss of resistance technique.
- **Ultrasound guided technique:** Place ultrasound transducer in transverse orientation just above gluteal cleft. Scan cephalad to identify sacral cornua and sacral hiatus (Fig. 5.1b). Then turn transducer longitudinally to identify sacral canal and sacrococcygeal ligament (Fig. 5.1c).
- **Local anesthetic volume**: 0.5 ml/kg (sacral block), 1 ml/kg (T10 block), 1.25 ml/kg (mid-thoracic block)
- **Complications**: Dural puncture, infection, hematoma

Spinal Anesthesia in Neonates

- Most commonly used in neonates undergoing inguinal hernia repair, who have increased risk of postoperative apneic episodes (e.g. prematurity, prior apneic episode, anemia)

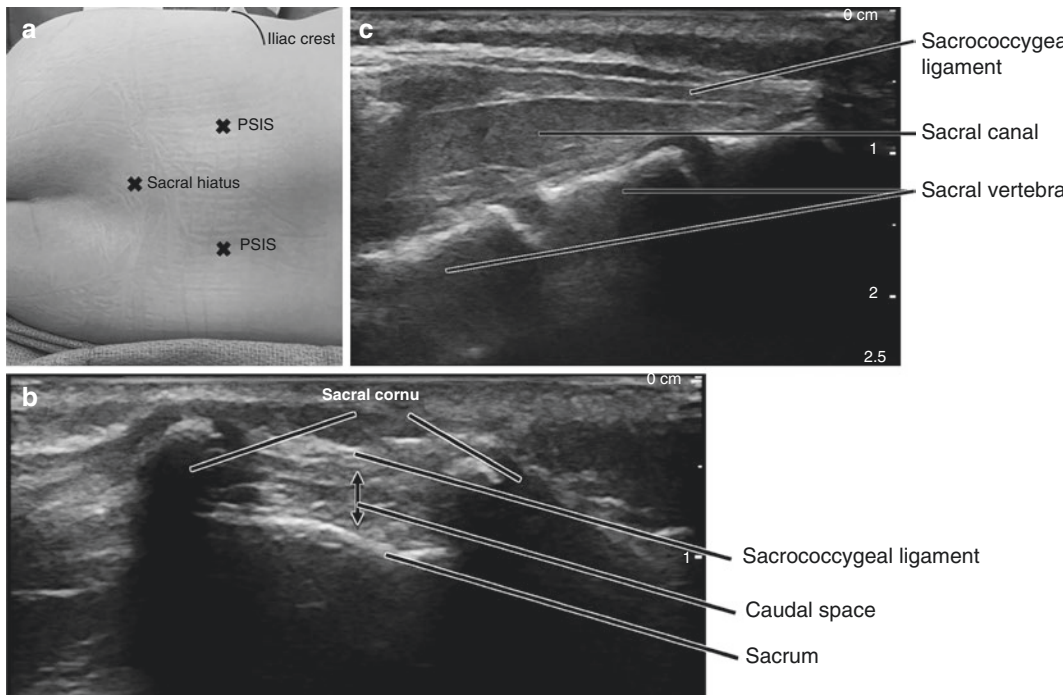

Fig. 5.1 Landmark and ultrasound guided caudal block (**a**) Anatomical landmarks (**b**) Transverse sonographic view of caudal space (**c**) Longitudinal sonographic view of sacral canal. PSIS: posterior superior iliac spine

- May reduce incidence of postoperative apnea compared to general anesthesia
- No significant difference in neurodevelopmental outcomes 5 years of age when comparing 1 hour of general anesthesia versus spinal anesthesia during early infancy.
- Technique of spinal anesthesia is similar to performing a lumbar puncture, however it may be technically challenging due to tiny anatomy and patient movement.

Continuous Nerve Catheter Infusions

- Peripheral nerve catheters are being increasingly utilized at pediatric centers.
- Allow longer duration of analgesia and may remain in situ for several days.
- Epidural catheters may be performed at the caudal, lumbar or thoracic level.
- Epidural catheters inserted via the caudal approach may be threaded cephalad to reach lumbar or thoracic epidural levels and this may minimize the risk of direct spinal cord injury. If available, ultrasound, nerve stimulation or fluoroscopy are recommended to confirm correct epidural catheter placement at desired level.
- See Table 5.1 **for maximum infusion rates**.

Clinical Pearls

- Single injection and catheter-based techniques are frequently utilized in pediatric patients.
- Any ultrasound-guided regional block described in adults could potentially be performed in children if the operator has the **appropriate training, assistance and equipment**.
- Ultrasound guided techniques allow **visualization** of needle, nearby anatomical structures, and local anesthetic spread.
- Local anesthetic **dose calculation** is essential prior to its administration.
- **Slow injection** of local anesthetic with **frequent aspiration**, while **monitoring** ECG morphology, blood pressure and heart rate may allow early detection of intravascular needle placement.

Multiple-Choice Questions

1. In neonates, the dural sac ends at:
   A. L3-L4
   B. S1-S2
   C. S2-S3
   D. S3-S4
2. A 6-week-old, ex-premature infant has a spinal anesthetic successfully inserted at the L4-L5 level for an inguinal hernia repair using a 22G spinal needle. Compared to spinal anesthesia in an adult, this anesthetic is most likely associated with:
   A. Shorter duration of action
   B. Bradycardia
   C. Apnea
   D. Tachycardia
3. A 10 month old, 10 kg male is booked for a hydrocelectomy and inguinal hernia repair. He undergoes an inhalational induction, endotracheal intubation and is turned into the lateral decubitus position for caudal injection. What is an appropriate dose of local anesthetic for this caudal block?
   A. 10 ml 0.2% ropivacaine
   B. 5 ml 0.5% bupivacaine
   C. 20 ml 1.5% chloroprocaine
   D. 10 ml 2% lidocaine
4. Which of the following statements is true?
   A. Intravascular needle placement can be excluded if no blood is aspirated
   B. Infants less than 6 months old are at greatest risk of local anesthetic toxicity
   C. The maximum dose of ropivacaine is 4 mg/kg
   D. The use of ultrasound reduces the risk of local anaesthetic systemic toxicity

5. Compared to 0.5% ropivacaine, the use of 0.2% ropivacaine in a sciatic nerve block will be:
   A. Less likely to result in a successful block
   B. Less likely to mask compartment syndrome
   C. More likely to cause motor block
   D. More likely to cause neurotoxicity

Answers

1. D, 2. A, 3. A, 4. B, 5.B

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6 General Topics: Regional Anesthesia for Enhanced Recovery After Surgery

Milly T. Rambhia, Anne L. Castro, and Amanda H. Kumar

Introduction

- Enhanced recovery after surgery (ERAS) protocols combine evidence-based strategies into standardized clinical pathways in order to **reduce surgical stress response, perioperative complications, postoperative pain, nausea and vomiting (PONV), and length of stay (LOS)**.
- Regional anesthesia techniques are often used as part of ERAS **multimodal analgesic regimens** to minimize opioid consumption, opioid-related side effects, and postoperative pain.

Colorectal Surgery

Innervation

- Sympathetic innervation of the gastrointestinal tract is via spinal nerves from **T5-L2** (Chap. 6, chronic pain)
- Preganglionic sympathetic fibers synapse in the celiac, superior mesenteric, and inferior mesenteric ganglia; postsynaptic fibers travel to innervate the target organ (Fig. 19.1, Chap. 19, chronic pain).

Thoracic Epidural Analgesia

- TEA placed at **mid-thoracic level (T7-9) for colon surgery or T10-11 for rectal surgery** are useful for **open** colorectal surgery [1].
- Advantages
  - Decreased inhaled anesthetic and muscle relaxant requirements; improved analgesia and decreased opioid use; reduced incidence of postoperative ileus, PONV, atelectasis and other pulmonary complications, respiratory depression, venous thrombosis, insulin resistance, and arrhythmia [2].
- Disadvantages/Risks
  - Increased incidence of hypotension, urinary retention, or motor blockade requiring longer hospital stay.

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- Epidural failure rate 13–32%.
- Multiple contraindications, including bleeding disorders and anticoagulation.

Fascial Plane Blocks

- Commonly performed in **laparoscopic** colorectal surgery.
- *Transversus Abdominis Plane (TAP) block (Chap. 28, regional anesthesia)*
  - Provides analgesia to the infraumbilical anterior abdomen with **classical approach** (T10-L1) or upper anterior abdomen with **subcostal approach** (T6-T9).
  - Advantages
    - Compared to TEA: procedural simplicity; preserved lower limb motor function, urinary function, and hemodynamic stability; fewer contraindications.
  - Disadvantages/Risks
    - Covers **somatic incisional pain** but not visceral pain.
    - Specific risks include intravascular injection and peritoneal puncture.
- *Rectus sheath block (Chap. 28, regional anesthesia)*
  - Targets terminal branches of T7-12 nerves between the rectus muscle and posterior rectus sheath.
  - Advantages
    - Useful adjunct for analgesia of **midline incisions** or umbilical hernia surgeries.
- *Quadratus lumborum (QL) block*
  - Provides **both somatic and visceral analgesia** to T7-L2 dermatomes.
    - Palliative coverage of entire abdomen with fewer needle punctures.
    - more technically challenging.
    - Contraindications include bleeding disorders and anticoagulation.
    - Patient positioning and ultrasound image shown in Fig. 6.1.

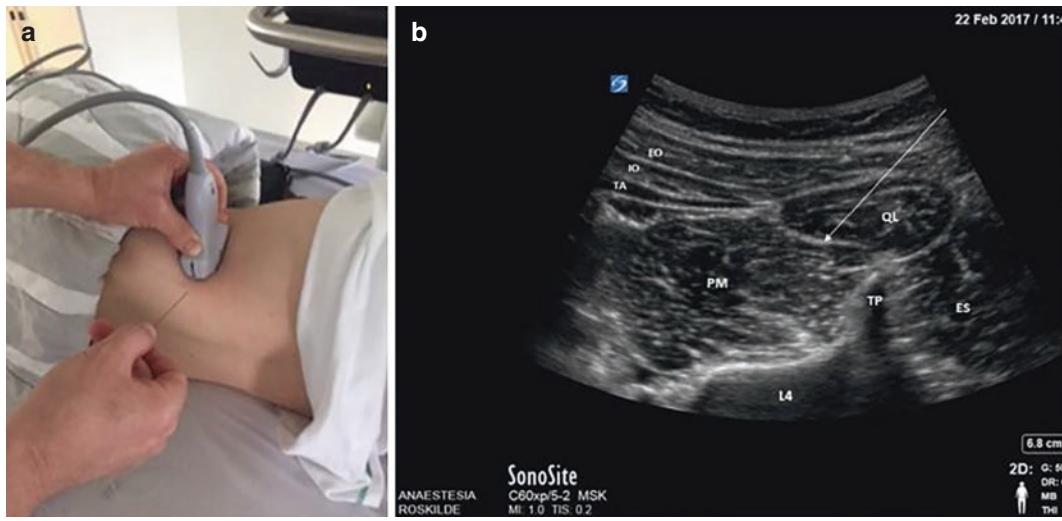

Fig. 6.1 The transmuscular quadratus lumborum (TQL) block. (**a**) Patient is in the lateral position. The curved arrary transducer is positioned transversely in the posterior axillary line just above the iliac crest. The needle is inserted in plane to the transducer. (**b**) The end-point of the injection is in the plane between the quadratus lumborum (QL) and psoas major (PM) muscles. EO external oblique, IO internal oblique, TA transversus abdominis, TP transverse process, ES erector spinae muscles, L4 vertebral body of L4. (Reproduced with permission from Blanco and Børglum [3])

Gynecologic Surgery

Innervation

- The superior hypogastric plexus provides sympathetic innervation and the pelvic splanchnic nerves form the inferior hypogastric plexus which supplies the pelvic viscera (Chaps. 6 and 19, chronic pain).

Thoracic Epidural Analgesia

- TEA is usually performed at **T9-12** and infused with a mix of low concentration local anesthetic (LA) and opioid.
- Advantages
  - After abdominal hysterectomy and gynecologic cancer surgery, TEA reduces pain, time to return of bowel function, and cardiopulmonary complications in higher-risk patients.

Transversus Abdominis Plane (TAP) Block

- Meta-analysis examining TAP blocks for laparoscopic surgery across a range of abdominal procedures found that **only pain at rest, and not dynamic pain, was reduced** [4].
- For laparoscopic hysterectomy, evidence has been mixed and there is no definitive benefit of TAP block for postoperative quality of recovery.

Breast Surgery

- 20–60% of mastectomy patients may develop chronic postsurgical pain; thus, there is increasing focus on multimodal analgesic protocols that incorporate regional anesthesia [5].

Innervation

- Sensory innervation of anterior and lateral chest wall primarily derived from anterior and lateral cutaneous branches of **intercostal nerves** (T2-T6), and lateral (C5-C6) and medial (C7-C8) **pectoral nerves**. Axilla innervation derived from T1-T2 (**intercostobrachial nerve**).

PECS I and PECS II Blocks (Chap. 34, Regional Anesthesia)

- Target the medial and lateral pectoral nerves between pectoralis major and minor (PECS I) and the T2-T6 thoracic intercostal nerves, thoracodorsal nerve and long thoracic nerve (LTN) in the fascial plane between pectoralis minor and serratus anterior (PECS II).
- Advantages
  - Procedural simplicity, supine positioning of patient, maintenance of hemodynamic stability.
- Disadvantages/Risks
  - Blockade of LTN with PECS II may result in inability of surgeon to stimulate this nerve to avoid inadvertent injury during axillary dissection.

Thoracic Paravertebral Block (PVB) (Chap. 29, Regional Anesthesia)

- Provides analgesia by blocking signal transmission at the level of the spinal nerves as they exit the intervertebral foramina; results in **unilateral somatosensory and sympathetic blockade**.
- May require multiple injections for surgical anesthesia, although single injection at T3 or T4 can be performed for analgesia.

- Advantages
  - Can be used as primary anesthetic.
  - PVB for acute postoperative pain may protect against development of **chronic postsurgical pain** at 6 months.
- Disadvantages/Risks
  - Important risks include pneumothorax, pleural puncture, sympathectomy causing hypotension and bradycardia, and epidural or intrathecal spread.
  - Must follow anticoagulation guidelines.
  - **Does not** provide analgesia to pectoral muscles.

Thoracic Surgery

- High risk of chronic pain (25–60%) with uncontrolled pain post-thoracotomy [6]; thus, regional techniques are highly recommended for thoracic surgery.

Innervation

- Anterior rami of spinal nerves (T2-T11) form intercostal nerves and terminate in anterior and lateral cutaneous branches to innervate anterior and lateral chest wall; dorsal rami of spinal nerves give off posterior cutaneous branches to innervate posterior thorax.
- Skin of the upper chest wall is also innervated by **supraclavicular nerves** from the cervical plexus.
- Innervation of the parietal pleura is primarily via **intercostal nerve branches**.

Thoracic Epidural Analgesia (TEA)

- **T5-T8** TEA has traditionally been used for analgesia after thoracic and esophageal surgery.
- Combination of low concentration LA and low dose opioid for at least 2 days confers maximal advantage. TEA typically maintained until **after chest tube removal**.
- Advantages
  - Lower incidence of pneumonia, decreased need for reintubation or prolonged ventilation.
  - Risk reduction of pulmonary complications in lung resection surgery, specifically in patients with **COPD and FEV_1 <60% predicted**.

Paravertebral Block (PVB) (Chap. 29, Regional Anesthesia)

- Trend in recent literature of the use of PVB over TEA for open thoracotomy and VATS cases.
- Advantages
  - Compared to TEA, PVB provides equal postoperative analgesia with equivalent 30-day mortality, major cardiopulmonary complications, and hospital LOS, with overall lower rates of PONV, itching, hypotension, and urinary retention [7].

Intercostal Nerve Block (ICB) (Chap. 27, Regional Anesthesia)

- Intercostal nerves can be blocked individually to produce a band-like segment of analgesia.
- Advantages
  - May be done intraoperatively by surgeon during video-assisted thoracoscopic surgery.
- Disadvantages
  - Risk of pneumothorax, rapid uptake of LA from intercostal space may reduce the duration of analgesia and increase risk of LA toxicity, multiple injections required.

Fascial Plane Blocks

- Fascial plane blocks may be utilized when TEP or PVB is not possible due to contraindications [8].
- Most fascial plane blocks have yet to be studied in large trials.
- All require relatively large volumes of LA in order to spread to multiple dermatomes.

- *Serratus anterior plane (SAP) block*
  - Targets lateral cutaneous branches of intercostal nerves (T2-T9), long thoracic, and thoracodorsal nerves. The block is an extension of the PECS II block, with a more inferolateral level of injection and a wider spread (fifth rib at mid-axillary line).
  - The reported spread of the SAP block involves approximate levels between T2 and T9 including anterior, lateral, and posterior chest wall, but sparing the mid chest. Requires LA volume >40 mL.
- *PECS I and II blocks (Chap. 34, Regional anesthesia)*
  - Useful for analgesia of anterolateral chest wall and axilla.
- *Erector spinae plane (ESP) block (Chap. 33, Regional anesthesia)*
  - Targets dorsal and ventral rami of spinal nerves and should provide analgesia of the hemithorax with possible midline sparing; site amenable to catheter placement.

Cardiac Surgery

- Uncontrolled post-sternotomy pain has been associated with chronic pain in up to 20% of patients. There is growing emphasis on **"fast-tracking,"** or more rapid extubation of patients, limiting the traditional practice of high intraoperative opioid dosing. Moreover, minimally invasive cardiac surgery has been growing. Therefore, fascial plane chest wall blocks are gaining popularity for procedures requiring thoracotomy or sternotomy.

Minimally Invasive Cardiac Surgery

- For minimally invasive anterolateral thoracotomy: PECS I and II, SAP, and ESP blocks.
- For transapical TAVR: unilateral left SAP and ESP blocks.
- For AICD/pacemaker placement and battery exchanges: PECS II, SAP blocks.

Sternotomy

- Parasternal blocks: pectointercostal fascial plane or transversus thoracis plane blocks, which target anterior cutaneous branches of intercostal nerves just lateral to the sternum.

Total Knee Arthroplasty (TKA)

Innervation

- The knee joint is innervated by branches of the femoral (**L2-L4**) and sciatic nerves (**L4-S3**).

Neuraxial Anesthesia

- Advantages

  When compared to general anesthesia, intraoperative neuraxial anesthesia is associated with equal or shorter length of stay and equal or lower rates of postoperative complications, including deep vein thrombosis (DVT) and cardiopulmonary complications [9].
  - Spinal anesthesia is usually preferred to epidural as its short duration facilitates early mobility.
- Disadvantages
  - Spinal opioids are associated with a higher risk of **urinary retention,** and itching, and are not routinely recommended; LA-only spinals are commonly used [10].

Peripheral Nerve Blocks

- Postoperative regional anesthetic options should provide pain control while preserving mobility.
- *Adductor canal block (Chap. 18)*
  - Targets the **saphenous nerve**, a sensory branch of the femoral nerve. The **nerve to vastus medialis** can also be covered with deposition of LA between the sartorius and vastus medialis muscles.

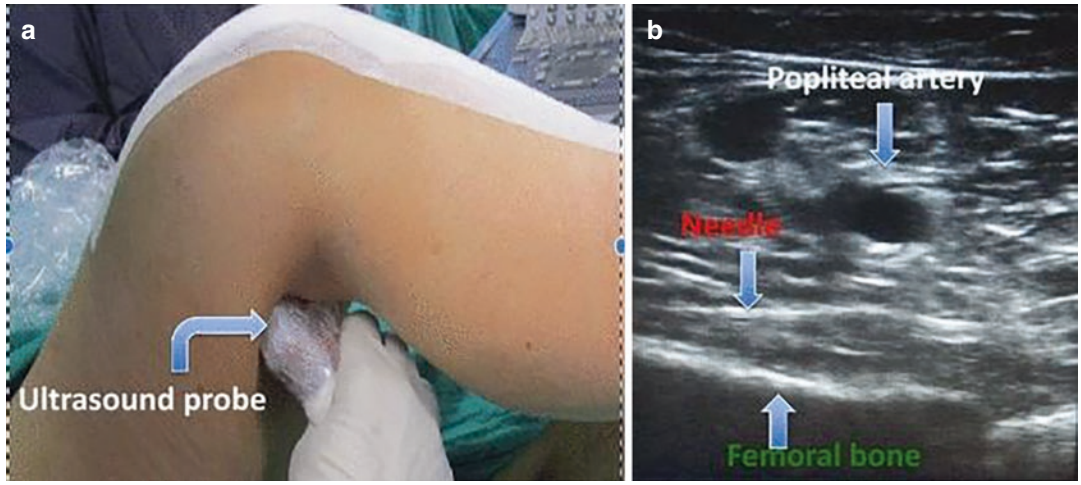

Fig. 6.2 Interspace between the popliteal artery and the capsule of the posterior knee (IPACK) block (**a**) The ultrasound probe is placed in the popliteal fossa on the lateral side and the needle introduced posteromedially with the patient placed in supine position. (**b**) Popliteal artery, femoral bone surface identified on the ultrasound and the needle placed in capsular space between the artery and femur and anesthetic injected [1]. (Reproduced with permission from Sankineani et al. [12])

  - Provides analgesia of the anteromedial knee with minimal quadriceps muscle weakness.
- *Femoral nerve block*
  - Results in **quadriceps muscle weakness**; thus may be appropriate only for patients who require more comprehensive postoperative pain control (e.g., chronic pain syndromes, extensive surgeries, planned **non-weight bearing status**). *(Chap. 18)*
- *iPACK (Interspace between the Popliteal Artery and Capsule of the Knee) block*
  - Targets **posterior knee pain** from terminal sensory branches of the tibial nerve.
  - The block is performed by scanning the popliteal fossa with a curvilinear 60-mm (2–5 MHz) US probe to the popliteal crease until the femoral condyles are visualized. The probe is then aligned until the condyles disappear and the femur shaft is visible. Here, the block needle is inserted in plane in the medial thigh using an anteromedial to posterolateral approach between the popliteal artery and the femur until the needle tip is 1 cm beyond the lateral edge of the popliteal artery. 20 mL of dilute LA is injected incrementally [11].
  - Has **opioid-sparing effects** as a single injection block.
  - Patient position and ultrasound image shown in Fig. 6.2.

Local Anesthetic Infiltration

- Local infiltration analgesia has been widely used for pain relief in patients undergoing total knee arthroplasty.
- A meta-analysis of randomized controlled trials comparing local infiltration analgesia with placebo infiltration in patients undergoing TKA shows local infiltration analgesia significantly reduced early perioperative pain and total narcotic consumption. However, postoperative functional outcomes were not significantly different. The pain-relieving effect of local infiltration analgesia was found to be **strong but short in duration.**
- Avoids motor blockade in comparison to femoral block and is supported by recent ERAS consensus guidelines.

Questions

1. Benefits of thoracic epidural analgesia for colorectal surgery include all EXCEPT:
   A. Decreased insulin resistance
   B. Decreased pulmonary complications
   C. Increased hemodynamic stability
   D. Decreased inhaled anesthetic requirement
   E. Improved analgesia postoperatively
2. A 77-year-old male with COPD and atrial fibrillation is scheduled to have an open thoracotomy for resection of lung adenocarcinoma. Pulmonary function tests reveal FEV1 38% of predicted, TLC 108% of predicted, and DLCO 50% of predicted. Which of the following is FALSE?
   A. Thoracic epidural analgesia (TEA) will decrease this patient's risk of postoperative pulmonary complications.
   B. Paravertebral blockade (PVB) has been demonstrated to have increased rates of major complications in comparison to TEA for open thoracotomy.
   C. INR of 1.8 will preclude the use of TEA in this patient.
   D. A combination of opioid and local anesthetic in an epidural solution will provide improved analgesia than either solution alone.
   E. TEA can be associated with hypotension, particularly in patients undergoing lung resection, as postoperative management may include limited fluid administration.
3. Spinal anesthesia for total knee arthroplasty:
   A. Has been shown to be associated with decreased rates of deep vein thrombosis.
   B. Has been linked to longer length of hospital stay than general anesthesia (GA)
   C. Is recommended to include a spinal injection of long-acting opioid, such as duramorph
   D. Is associated with higher risk of cardiopulmonary complications than GA
   E. May be followed postoperatively by a femoral nerve block to preserve quadriceps muscle strength and allow for early ambulation
4. A 53-year-old female with breast cancer presents for modified radical mastectomy with reconstruction. As part of an ERAS protocol, ultrasound-guided PECS I and II blocks are performed preoperatively with 0.25% bupivacaine. Which of the following is TRUE?
   A. A PECS I block will result in analgesia of the long thoracic nerve, which may interfere with nerve identification during the surgeon's axillary dissection
   B. PECS blocks as part of ERAS protocols have been shown to improve postoperative analgesia and increase PONV
   C. Paravertebral block provides better analgesia of the pectoral muscles compared to PECS blocks
   D. PECS blocks may provide increased hemodynamic stability intraoperatively compared to paravertebral block
   E. Risk of pneumothorax is higher with PECS blocks than with paravertebral block
5. A 79-year-old female with a history of hypertension, chronic kidney disease and advanced ovarian cancer presents for cytoreductive surgery via midline laparotomy. INR is 1.1. Which of the following regimens would be the best analgesic regimen for her as part of an ERAS protocol?
   A. Preoperative PO non-opioid analgesic medication, including acetaminophen, and thoracic epidural placement at T10
   B. Preoperative PO hydromorphone only with intraoperative TAP block with 0.5% ropivacaine
   C. Preoperative non-opioid analgesic medication, including acetaminophen, and thoracic epidural placement at T7
   D. Preoperative thoracic epidural placement at T9 with intraoperative bilateral TAP block with 1.5% mepivacaine
   E. Preoperative PO hydromorphone and ibuprofen, and thoracic epidural placement at T10

Answers

1. C, 2. B, 3. A, 4. D, 5. A

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General Topics: Nerve Injury in Regional Anesthesia

7

Cole Bennett and Ratan K. Banik

Introduction

- The incidence of nerve injury after peripheral nerve block is rare (8–10%) and most are transient. Permanent symptoms lasting >6 months are extremely rare (0.01–0.1%).
- Nerve injuries commonly occur due to intraneural (intrafascicular) injections. This can be avoided by not injecting local anesthetic if patient feels **paresthesias**, **requires high pressure to inject** medications, or if spread of local anesthetic is unsatisfactory (**not outside the perineurium**).
- Patients with pre-existing neuropathy, diabetes mellitus, and undergoing chemotherapy are more susceptible to developing nerve injury. Additional risk factors include extremes of body habitus, advanced age, hypertension, and tobacco use [1].
- It is recommended to perform a focused history, sensory and motor exam **prior to the nerve block** and document any neurological deficits. If a nerve injury is reported, other potential causes should be noted, including surgical manipulation or direct mechanical injury, tourniquet ischemia, hematoma, or positioning injury.

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Anatomy and Mechanisms of Nerve Injury in Regional Anesthesia

- Peripheral nerves are bundled by 3 separate connective tissue layers: epineurium, perineurium and endoneurium (Fig. 26.1, Chap. 26, chronic pain).
- The connective sheath covers entire length of the nerve fiber is called endoneurium, which protects the axons. Nerves are group together to form fascicles, which are surrounded by the perineurium. Fascicles are bundled into peripheral nerves, surrounded by an outer layer called the epineurium.
- **Neurapraxia** is a disorder secondary to an injury to the myelin sheath around an axon. The nerve usually returns to normal function within weeks. **Axonotmesis** is an injury to the axon along with the myelin sheath. The nerve can potentially regenerate on its own. **Neurotmesis** is complete transaction of the nerve, which includes the endo-, epi- and perinerium. Surgical repair is needed to regain nerve function (see Chap. 26, chronic pain).
- The pathophysiology of nerve injury during nerve blocks can include **direct trauma** of the needle, **rupturing of the fascicle** with high injection pressure, ischemia or **chemical neurotoxicity** from either the local anesthetic solution itself or from additives such as epinephrine (See Fig. 26.1, Chap. 26).

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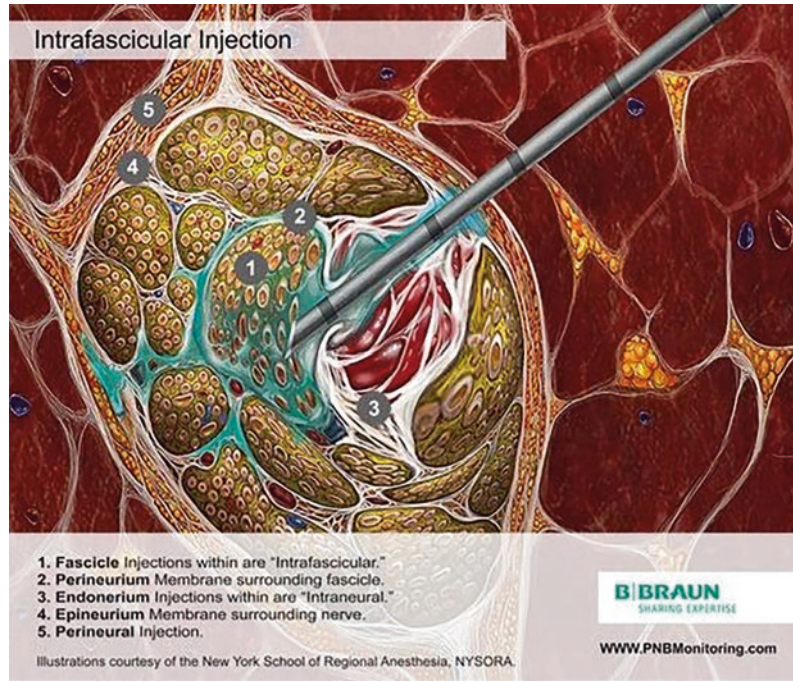

Fig. 7.1 Intrafascicular injection typically causes high pressure during injection. (Reproduced with permission from NYSORA)

- Even a small amount intrafascicular injection (Fig. 7.1) can lead to axonal degeneration and permanent nerve damage. The risk of nerve injury from intrafascicular injection is lower in certain nerves like the sciatic nerve as it contains **high proportion of loose connective tissue**, while it is higher in nerves such as the brachial plexus where most are entirely neural tissue.
- Direct needle trauma of a peripheral nerve can cause disruption of the perineurium thereby losing the protection over axons which **directly exposes them to LA toxicity** [2].

Prevention

- If patient reports paresthesia or severe pain during needle advancement or injection, injection should **stop immediately** and the needle should be repositioned as this may imply intraneural needle placement.
- **Heavy sedation** may eliminate patient's ability to report paresthesia; therefore should be avoided.
- If **high pressure** are required for injection, the needle may be intrafascicular, and the needle must be repositioned. Inline **pressure manometers** placed between the needle and syringe can aid in avoiding high injection pressures.
- Patients with pre-existing neuropathy or nerve injury on the intended nerve site may not be good candidate for nerve block.
- Use of hydrodissection to open a needle trajectory route and using a low number of needle passes may reduce the likelihood of nerve injury.
- Depositing local anesthesia **farther away from the nerves or plexus** approach rather than an intra-plexus approach may reduce the likelihood of nerve injury.

Management

- Any acute **motor deficit** requires urgent neurology consult and imaging. It is important to rule out non-regional anesthesia related causes, including **surgical injury** to nerve,

tourniquet, compressing hematoma, etc. All these causes require urgent management.
- If patient reports tingling, numbness or other sensory symptoms, reassurance is essential. 95% of postoperative sensory changes will resolve within **4–6 weeks**. If symptoms are either severe or persistent, the patient should be referred to a neurologist.
- Any motor deficits require referral to a neurologist. Investigations may include electromyography or nerve conduction studies (EMG/NCS).

EMG/NCS

- EMG and NCS typically show abnormalities in the muscles innervated by affected nerve. NCS is carried out by applying an **electrical stimulus to the skin overlying a nerve trunk**, followed by the recording of the generated electrical response over either the nerve trunk or muscle. EMG records the **electrical potentials generated in a muscle belly** through a needle electrode inserted in the muscle.
- In acute nerve injury, EMG and NCS provide limited information due to a **2–3 weeks** delay in the development of fibrillation potentials after acute motor axon loss. NCS can show loss of amplitude of compound muscle action potentials **1 week** after injury.
- A baseline EMG/NCS study may be required if a patient reports severe symptoms. Immediate EMG/NCS can be performed to rule out **baseline** neurological deficits.

Clinical Pearls

- Nerve injury after peripheral nerve block in regional anesthesia is a **rare** but potentially serious complication
- Most incidences of peripheral nerve injury **resolve spontaneously** in a short period of time
- The connective sheath over the entire nerve is the endoneurium, these are bundled together as fascicles and surrounded by the perineurium, and the fascicles are then bundled together and surrounded by the epineurium.
- A patient reporting parathesias or severe pain is an indication to **stop injection of local anesthetics** and reposition the needle. High injection pressures also may indicate the need to reposition the needle to avoid injury
- Risk factors for nerve injury may involve patient, surgical, or regional anesthesia variables, or a combination of these [3].
- Patient risk factors include body habitus (extremes), pre-existing neurological disorder (Diabetes, chemotherapy), male gender, hypertension, tobacco use, and advanced age
- Surgical risk factors include direct trauma or stretch, long tourniquet time, infection, hematoma, or tightly applied casts or dressings
- Regional anesthesia risk factors include mechanical **injury from the needle**, **chemical neurotoxicity** from the local anesthetic, or ischemic injury to the nerve.

MCQs

1. Which of the following can prevent peripheral nerve injury during regional anesthesia?
   A. Ultrasound use
   B. Heavy sedation
   C. Para-plexus deposition of local anesthetics
   D. Use of epinephrine
2. Which of following is correct for peripheral neve injury?
   A. Neuropraxia is least common.
   B. Neuropraxia defined as injury to the myelin sheath around an axon
   C. Axotemesis involves complete transection of nerve
   D. Endoneurium is not preserved in axotemesis
3. Which of the following is incorrect to define perineurium?
   A. Sheath that covers a nerve fiber
   B. Sheath that bundles fascicles
   C. Sheath overs a group of axons.
   D. None of the above

4. Which of the following is true regarding intrafascicular injection during peripheral nerve block?
   A. risk is lower in sciatic nerve
   B. risk is higher in brachial plexus trunk
   C. risk is similar in all nerves
   D. risk is higher in sciatic nerve
5. A healthy patient report tingling of the right thumb 2 days after an interscalene block. What is the next best step?
   A. electromyography
   B. tell him that symptoms will last 1 year
   C. Nerve conduction study
   D. focused history and clinical exam

Answers

1. C, 2. B (see Chap. 26, chronic pain), 3. B, 4. B, 5. D

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General Topics: Bier block

8

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Introduction

- First described in 1908 by August Karl Bier, a German surgeon [1].
- More widely accepted when it was reintroduced by C. Holmes in 1963.
- **Ideal for outpatient hand surgery** providing anesthesia and a bloodless surgical field [2].
- Safe and effective alternative to a peripheral nerve block.
- Indicated for surgical procedures that typically last **45–60 minutes**.
- Local anesthetic is injected intravenously into an exsanguinated arm distal to an inflated tourniquet.
- Less commonly used for surgery on the foot or ankle.
- Duration of anesthesia is limited by short duration of local anesthetics and tourniquet pain.

Mechanism of Bier Block

- Intravenously injected local anesthetic is carried to the intraneural capillary plexus where it reaches the terminal nerve endings anesthetizing them and it also **diffuses out of the vascular space to affect local nerves** [1, 3, 4].
- Inflation of the tourniquet leads to ischemia and nerve compression, a delayed and additional mechanism for anesthesia [3, 4].
- Onset of anesthesia is within 5 minutes and resolves rapidly once tourniquet is released.
- Mechanism of tourniquet pain: Unmyelinated C fibers function is preserved during prolonged tourniquet inflation. The fibers may get excited by hypoxia and other metabolites secondary to ischemia, resulting in tourniquet pain.
- Mechanism of hypotension after tourniquet deflation. Tourniquet→ ischemia→ accumulation of metabolites, Co2, anaerobic metabolism→ increased end-tidal Co2, acidosis→ vasodilation→ decreased blood pressure

Agents

- **0.5% Lidocaine** (Preferred)
  - **3 mg/kg is usual dose**
  - **40–50 ml for arm tourniquet**
  - **30 ml for forearm tourniquet for hand surgery**
- **0.5% Prilocaine** (alternative).
  - Popular in Europe. Potential for Methemoglobinemia.
- **0.5–1% Chloroprocaine** – preservatives can cause thrombophlebitis

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- **0.2% Ropivacaine** – gaining popularity. Tinnitus and dizziness are common, potential for cardiotoxicity. Increased duration of sensory / motor blockade.

Adjuvants

- Ketorolac (30 mg) has the best evidence for improving postoperative analgesia, speeding up onset of sensory/motor blockade and decreasing tourniquet pain.
- Clonidine improves tourniquet tolerance and postoperative analgesia but is associated with **sedation and hypotension** upon tourniquet release.
- **Bupivacaine should not be used** due to potential for severe cardiotoxicity following tourniquet release.
- **Epinephrine containing local anesthetics** increase risk of ischemia.
- Preservative containing solutions can increase risk of thrombophlebitis.

Indications

- Orthopedic procedures on wrist and hand
  - Closed reduction of Colles fracture
  - Carpal tunnel release
  - Trigger finger release
- Plastic surgery procedures on hand
  - Carpal tunnel release
  - Dupuytren's contracture
  - Tendon repair
  - Neuroma Excision
- Surgeries on the ankle and foot

Contraindications

Absolute Patient refusal**,** Allergy to local anesthetics, Local infection in the operative limb**,** Open fractures, Lymphedema**,** Berger's disease, Raynaud's disease, Sickle cell disease or trait**,** Methemoglobinemia (with Prilocaine)**,** Presence of Arteriovenous shunts / fistulas.

Relative Children – consider on a case by case basis if other anesthetic techniques are less preferable, Uncooperative patient, morbid obesity – cuff may not work reliably, Uncontrolled Hypertension >200 mm Hg, Scleroderma, Seizure disorder, Bilateral procedures.

Techniques

- A 20 Gauge IV catheter is placed in the operative hand and heplocked. A double pneumatic tourniquet is placed on the proximal upper arm or forearm (for hand surgery). Prior to the procedure the cuff should be checked for air leaks by inflating and leaving it on for 5 minutes.
- A stockinette or cotton padding can be used under the tourniquet to reduce discomfort. The double tourniquet enhances safety should one cuff fail.
- Ensure ready access to Intralipid to treat local anesthetic toxicity.
- Exsanguinate the arm passively by raising the arm up for one to two minutes.
- An Esmarch bandage is then wrapped tightly in an overlapping spiral, with the arm held up, starting distally from the hand, and working the way down to the axilla.
- The distal cuff of the tourniquet is inflated to about 100 mmHg above patient's baseline systolic blood pressure, usually about 250 mm Hg followed by inflation of the proximal tourniquet.
- Palpate the radial artery to confirm lack of a pulse as each tourniquet is tested sequentially.
- Release the distal cuff and remove the Esmarch bandage.
- 40–50 ml of 0.5% Lidocaine is slowly injected via the IV placed in the operative hand. 30 mL of 0.5% lidocaine is adequate if a forearm tourniquet is used for hand surgery.
- Keep the cuff inflated for a minimum of 20 minutes a to reduce toxicity nd for a maximum of 45 minutes to reduce incidence of tourniquet pain.

- The IV catheter in the operative arm is removed and pressure applied. Document cuff inflation pressure and duration.
- If patient complains of tourniquet pain, **inflate the distal cuff,** check for cuff integrity, and then **deflate the proximal cuff**. As the distal tourniquet is inflated over an area that was previously anesthetized, an additional 20–30 minutes of comfort is likely, before tourniquet pain recurs.
- Leave the tourniquet cuff inflated for **at least 20 minutes** after the injection of the local anesthetic to avoid Local Anesthetic induced Systemic toxicity (LAST).

Complications

- **Systemic toxicity** from premature release of a bolus of local anesthetic into the systemic circulation **(LAST**) See Chap. 9, regional anesthesia.
- Methemoglobinemia when prilocaine is used [5]. Treatment: IV **methylene blue** 1–2 mg/kg

Clinical Pearls

- If the tourniquet has to be deflated between 20 and 40 minutes, cycles of intermittent deflation (lasting 10 seconds) followed by inflation (lasting a minute), allows more gradual release of the local anesthetic into the systemic circulation, reducing the potential for LAST [5].
- In lower extremity Bier block, **30–50 mL of 0.5% lidocaine** is injected into an IV catheter in the foot, with a calf tourniquet.
- It is important to be aware of the potentially significant risk of systemic local anesthetic toxicity if the tourniquet is released prematurely or fails. **Intralipid** must be available.
- Tourniquet pain may be related to the **preserved function** of unmyelinated C fibers, which get excited by hypoxia and other metabolites of ischemia.
- After tourniquet deflation, hypotension can develop due to acidosis and vasodilation.

MCQs

1. Which of the following agents are unsuitable for a Bier Block?
   A. Lidocaine
   B. Prilocaine
   C. Bupivacaine
   D. Chloroprocaine
2. Commonest complication from a Bier Block
   A. Thrombophlebitis
   B. Compartment Syndrome
   C. Local Anesthetic Systemic Toxicity (LAST)
   D. Tourniquet pain
3. The best adjuvant to lidocaine in a Bier block to reduce tourniquet pain and improve postoperative analgesia is
   A. Ketorolac
   B. Morphine
   C. Decadron
   D. Tramadol
4. 20 minutes into a case of Duputryen's contracture release under Bier Block, patient complains of severe tourniquet pain. Appropriate steps to alleviate pain include all except:
   A. IV fentanyl
   B. IV Toradol
   C. Release of the proximal tourniquet followed by inflation of the distal tourniquet
   D. Inflation of the distal tourniquet followed by release of the proximal tourniquet
5. Preservative containing local anesthetics are not preferred for use in Bier Blocks due to the increased risk of
   A. Compartment syndrome
   B. Itching
   C. Thrombophlebitis
   D. Local Anesthetic Systemic Toxicity (LAST)

Answers to MCQs

1. C, 2. D, 3. A, 4. C, 5. C

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General Topics: Local Anesthetic Systemic Toxicity

9

Dustin Palm and Ratan K. Banik

Introduction

- **The Incidence of LAST: as high as 1.8/1000 cases**; ~1/5 involved a serious event (seizure 8.1%, major cardiac complication 6.8%) [1].
- The best ways to prevent this rare but potentially life-threatening complication are **risk reduction, early detection and expeditious appropriate treatment**.
- The majority of LAST cases have occurred after IV injection of LA or systemic absorption of LA after nerve blocks (20–30 minutes delay). LAST that occurred after inadvertent low dose intraarterial injection during interscalene block, cervical plexus block, or stellate ganglion block presented with brief seizures and no cardias effects [1].
- Potent local anesthetics such as bupivacaine are **more cardiotoxic** than lidocaine, ropivacaine and levobupivacaine.
- 20% of LAST occurred outside the hospital with 50% involving non-anesthesiologists. 20% of LAST was associated with local infiltration. The incidence of LAST was higher in peripheral nerve blocks compared to epidurals [2].

Mechanism of LAST

- Toxicity is related to:
  - **Rate of rise of [LA]:** varies with injection site: intravascular > intercostal > epidural > brachial plexus > femoral/sciatic > subcutaneous.
  - **Patient specific factor: acidosis**, liver/heart/kidney/CNS disease, frailty, malnourishment, low plasma protein concentration, mitochondrial dysfunction, carnitine deficiency, and extremes of age (<16 or >60) [3].
  - **Rate of clearance:** amides: liver (P450) metabolism and renal clearance; esters: plasma esterases. This may vary with comorbidities, medications, and nutritional status.
- LAs block **sodium channels** (slowing conduction time and action potentials in neurons and myocytes).
- **Intracellular [LA]** rises quickly in the **heart and brain** due to **high blood flow**.
- As weak bases, **LAs become** hydrogenated/polarized and **"trapped"** intracellularly in **acidotic conditions**. **Acidosis** decreases protein binding of LAs.

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- **Neurotoxicity**: initially, LA **blocks inhibitory pathways** in the cerebral cortex allowing **unopposed excitatory transmission (seizure)**. Further increases in [LA] inhibits excitatory pathways causing **CNS depression, coma, and respiratory arrest**.
- Seizures contribute to respiratory and metabolic acidosis; elevated PaCO2 increases cerebral blood flow and delivery of LA to the brain.
- **Cardiotoxicity: LAs inhibit myocardial contractility, cardiac conduction** (QRS prolongation→ VF)**, and systemic vascular resistance** through sodium channel blockade, metabolic signaling, and inhibition of oxidative phosphorylation.
- Cardiogenic shock contributes to metabolic acidosis.
- Low [LA] causes vasoconstriction whereas **high [LA] causes vasodilation**.

Prevention of LAST

- **Avoid and recognize intravascular injection**.
  - **Ultrasound guidance**.
  - **Incremental injection** (1–3 ml).
  - **Negative aspiration** (2% false negative rate).
  - **Test dose** (3 ml 1.5% lidocaine with 1:200,000 epinephrine) is negative if <10 BPM increase in HR or <15 mmHg increase in BP (in the absence of β-blockade, active labor, advanced age, or general/neuraxial anesthesia).
- Mitigate systemic uptake from tissues (consider addition of epinephrine).
- Consider patient specific factors which increase the risk of LAST:
  - Use the **lowest dose** possible based on **lean body weight**.
  - **Discuss LA dosing** as a part of the **preprocedural timeout**.
  - Monitor the patient for signs and symptoms of LAST for 30–45 minutes after injection to account for potential delayed peak plasma concentration.
  - **Peripheral nerve catheters** represent 15% of LAST, and present late (1–4 days after starting).
- Safe practice of peripheral nerve catheter **bolusing**:
  - Test dose prior to bolusing.
  - Monitor vitals for 30 minutes following a bolus.
  - Educate and communicate with the care team.
  - Be aware of the proximity of lipid rescue therapy and resources to treat LAST.
- **Ceiling doses** vary based on injection site and patient specific factors:
  - Ropivacaine 300 mg single injection; 770 mg/day.
  - Bupivacaine 175 mg single injection; 400 mg/day.
- Make LAST Rescue kit available (1 L 20% lipid emulsion, Large syringes for bolus administration, IV tubing with (1.2 μ) filter, ASRA LAST checklist) [4].
- Monitor patients after **tumescent liposuction** for 24 hours after the procedure. Patients receive large doses of lidocaine (up to 55 mg/kg of lidocaine with epinephrine). LAST may occur **as late as 20 hours following injection**.
- Seizure or cardiovascular collapse following **tourniquet deflation** should prompt suspicion for LAST.
- When liposomal bupivacaine is used, avoid additional local anesthetic for 72 hours. Caution in co-administration of anything other than saline and bupivacaine at the site of injection within 20 minutes of infiltration as this can cause **release of free bupivacaine** from liposomes.
- Monitor the patient for following early **signs/symptoms** of LAST for at least 30 minutes after the procedure:
  - Altered mental status (agitation, confusion, drowsiness, obtundation, coma).
  - Neurologic symptoms (**perioral numbness, dysgeusia, tinnitus**, diplopia, muscle twitches, dizziness, **seizure**, coma).
    (i) Spectrum of CNS presentation: seizure (47%), loss of consciousness (36%).

  - Cardiovascular instability (**bradycardia**, **conduction abnormalities**, **hypotension**, ventricular tachycardia, torsades, ventricular fibrillation, asystole).
    (i) Spectrum of CV presentation: dysrhythmia (34%), conduction delay (27%), cardiac arrest (23%) and bradycardia hypotension (16%).
  - Respiratory (**apnea**).
- Heavy sedation and or general anesthesia should be avoided during regional blocks as they may mask early signs and symptoms of LAST.
- Educate the whole perioperative and postoperative staff who are caring for patients who have received peripheral nerve block/catheter, or local infiltration.
- Consider developing **LAST kits** to include:
  - 1 L 20% lipid emulsion
  - Large syringes for bolus administration
  - IV tubing with (1.2 μ) filter
  - ASRA LAST checklist

Clinical Presentation

- Depends of serum concentration (Fig. 9.1).
- **Initial to late: perioral numbness → tinnitus**/diplopia, muscle twitches, lightheadedness-→ **seizure**→ coma→ respiratory arrest/apnea→ cardiac arrest.
- Cardiac manifestations may include **bradycardia**, **conduction abnormalities**, **hypotension**, ventricular tachycardia, torsades, ventricular fibrillation, and asystole.
- Sedation and or general anesthesia may abolish the ability to recognize early signs and symptoms of LAST.
- Most cases of LAST present with **isolated CNS signs and symptoms (43%)** compared to **isolated CV signs and symptoms (24%);** up to 1/3 cases of LAST present with **combined CV/CNS signs and symptoms** (Fig. 9.2).

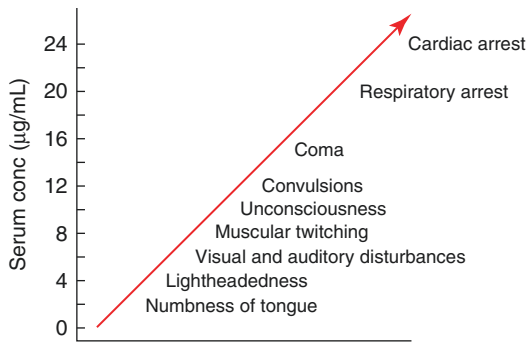

Fig. 9.1 Relationship of signs and symptoms of toxicity to serum lidocaine concentrations. (Source: Local Anesthetics, *Goldfrank's Toxicologic Emergencies, 10e*. Hoffman et al. [5]. Copyright © 2017 McGraw-Hill Education. All rights reserved)

Treatment

- Call for help and ask for lipid rescue kit. Order 12 lead EKG and monitor HR, BP, etco2, pulse oximetry. Prepare for **intubation** and **CPR**.
- Administer **1.5 ml/kg of 20% intralipid as a bolus** (infusion 0.25 ml/kg/min, may repeat bolus, **max total of dose 12 ml/kg**). For adults greater than 70 kg, give 100 ml bolus of intralipid 20%.
- Repeat bolus once or twice and double infusion rate for persistent cardiovascular instability. Propofol is **not a substitute** for lipid emulsion. Continue infusion for at least 10 minutes after hemodynamic stability is achieved.
- Administer **benzodiazepines** for seizure.
- Manage arrhythmias and cardiac arrest per ACLS protocol except use smaller doses of **epinephrine: <1 mcg/kg** boluses. Epinephrine→ vasoconstriction→ increased afterload, decrease efficacy of lipid rescue. Avoid vasopressin, calcium channel blockers, beta blockers, LAs, and amiodarone.
- Consider **early** cardiothoracic surgery **consult for ECMO**.
- Review the **ASRA Checklist**. **Early ventilation, intubation** and **CPR** are paramount in the treatment of LAST that has progressed to cardiac arrest.

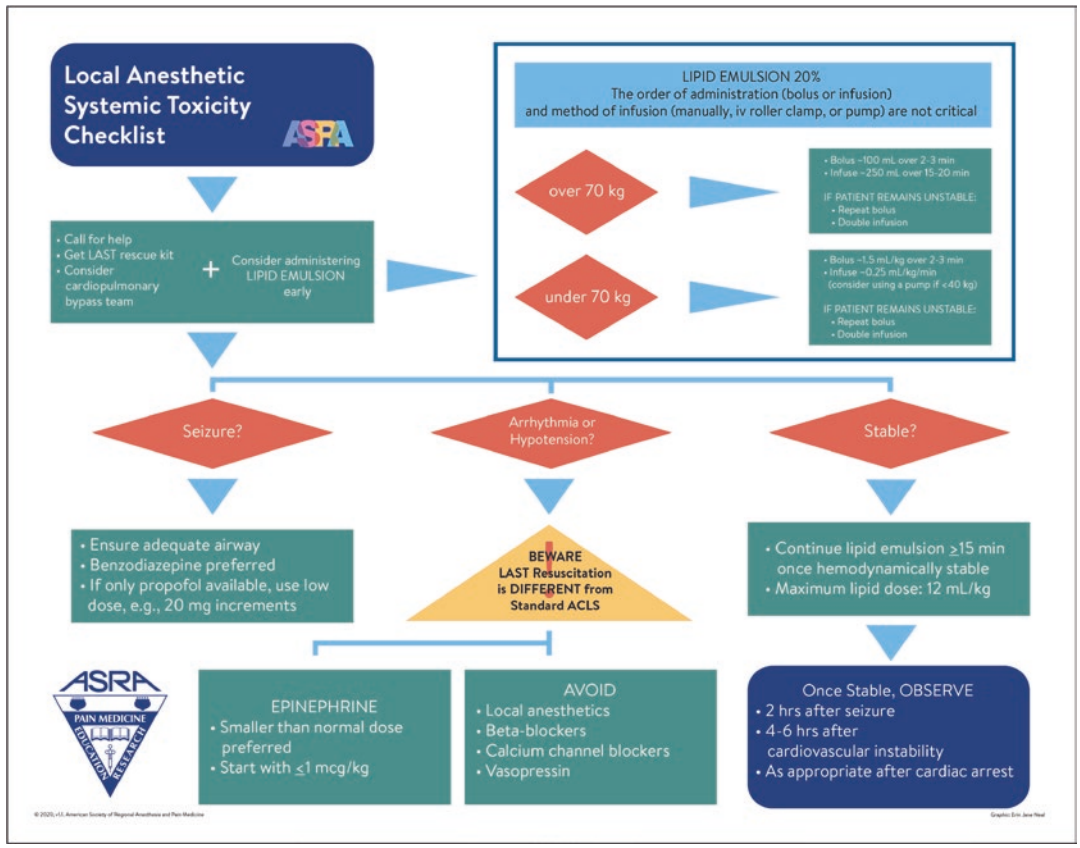

Fig. 9.2 Flowchart for treatment of local anesthetic systemic toxicity (Copyright: ASRA Pain medicine)

- **Montor patients for at least 2** hours following isolated neurologic and 4–6 hours after any cardiovascular involvement.
- If a LAST event is "short-lived" you may consider **proceeding with surgery** after an uneventful/asymptomatic 30-minute interval.
- If there is concern for LAST, **have a low threshold to give intralipid and treat expeditiously**. Review ASRA practice advisory. "At the first sign of arrythmia, prolonged seizure or rapid patient deterioration…we now unequivocally recommend lipid emulsion therapy soon after airway management in any LAST event that is judged to be potentially serious."

Mechanism of Intralipid

- LA readily binds to intralipid.
- Intralipid acts as a **dynamic shuttle, redistributing LA** from organs with high blood flow which are most susceptible to toxicity (heart and brain) to organs which store and metabolize LA (muscle and liver, respectively).
- Cardiotonic effect **enhances cardiac contractility** which improves redistribution of LA.
- Direct effect on peripheral vasculature **increases systemic vascular resistance**.
- Volume of intralipid contributes to preload.

MCQs

1. Twenty minutes following fascia iliaca block with 40 ml 0.25% bupivacaine, your patient becomes apneic and seizes. What is the best initial treatment?

   A. Initiate CPR
   B. Give naloxone 0.4 mg
   C. Ventilate with 100% oxygen, intubate and give 100 ml 20% intralipid
   D. Give midazolam 1 mg

2. What is the most common presentation of LAST?

   A. Isolated cardiovascular signs/symptoms
   B. Isolated neurologic signs/symptoms
   C. Combined cardiovascular/neurologic signs/symptoms
   D. Altered mental status

3. During a video-assisted thoracoscopic wedge resection, while the surgeon is infiltrating 50 ml of 0.5 ropivacaine intercostally, the BIS drops to 25 and the patient develops a second degree heart block. What is your initial response?

   A. Lighten the anesthetic
   B. Tell the surgeon to stop infiltration and give 1.5 ml/kg intralipid
   C. Give atropine 0.5 mg
   D. Give epinephrine 1 mg

4. What is the predominant mechanism of intralipid in the treatment of LAST?

   A. Blocks sodium channels
   B. Acts as a direct positive chronotrope
   C. Redistributes local anesthetic from the heart and CNS
   D. Enhances the metabolism of local anesthetic

5. What is the most important risk factor for the development of LAST?

   A. Acidosis
   B. BMI > 40
   C. Female gender
   D. Hypoalbuminemia

Answers

1. C, 2. B, 3. B, 4. C, 5. A

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General Topics: Post-dural Puncture Headache

10

Christina Spofford and Tyler Griebel

Introduction

- Post dural puncture headache (PDPH), is a common complication of lumbar puncture or inadvertent dural puncture during epidural injection/catheter or procedures (e.g. spinal cord stimulator lead placement).
- The incidence of PDPH after spinal anesthesia is 3–9%, unintentional dural puncture with an epidural needle for labor analgesia is 1–6%
- Not all dural punctures develop PDPH. The incidence of PDPH after dural puncture with an epidural needle are 76–85% [2]

Patient Risk Factors

- Female, 2–3 times higher incidence than male
- History of headache
- pregnancy (increased CSF pressure during labor→ larger CSF leak→ increased PDPH)
- 18–50 years of age (lower incidence in older patients)
- BMI <25 [4]
- History of depression

Procedural Risk Factors

- Accidental dural puncture with epidural needle
- Use of needle with sharp cutting tip. Pencil point spinal needles (e.g. Whitacre needles) reduces the risk of PDPH [1]
- Large bore needles for lumbar puncture (spinal tap)
- Paramedian approach to the spinal space
- Novice provider

Symptoms

- 90% of PDPHs occur within 72 hours after a dural puncture. Symptoms are worse if they occur in the first 24 hours;
- Positional headaches (exacerbated by sitting or standing and relieved with recumbency). They are bilateral and typically located in the fronto-occipital regions. Patient often reports generalized pressure-like or throbbing headaches [5].
- Other symptoms included nausea 60%, vomiting 24%, neck stiffness 43%, ocular changes (photophobia, diplopia, difficulty in accommodation) 13%, and auditory changes (hearing loss, hyperacusis, tinnitus), 12%.

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Pathophysiology

- CSF leak greater than CSF production → CSF hypotension (increases in upright position due to caudal redistribution of CSF)→ reflex meningeal venodilation → headache
- CSF hypotension → sagging of intracranial structures → and stretch of meningeal sensory nerves → headache
- sagging of intracranial structures → cranial nerve palsies (ocular, auditory symptoms)

Diagnosis

- **Exclude** worrisome headache red flags- "SNOOP" **S**ystemic symptoms (fever, weight loss), **N**eurologic symptoms (confusion, impaired consciousness), **O**nset: sudden, older: new onset and, **P**revious headache history (change in attack frequency, severity).
- Positional headache with history of lumbar puncture, epidural intervention within 72 hours
- Clinical diagnosis, labs/imaging not indicated

Treatment

Conservative

- Bed rest
- Caffeinated drink or supplemented IV
- Fluids, either orally or intravenously 3–5 liters/day
- Acetaminophen, NSAIDS, Fioricet (Butalbital-acetaminophen-caffeine)
- Abdominal binder (increased intra-abdominal pressure → increased pressure epidural space → decreased CSF leak)

Intervention

- Epidural blood patch (**gold standard**). Inject 15–20 mL of blood for blood patch at the same level of dural puncture, and stop injection if the patient complains of significant pain or pressure. Fluoroscopic guidance may be used for patients who had difficult neuraxial catheter placement. Mechanism: injection of blood into epidural space → compression of thecal sac → increased lumbar and intracranial cerebrospinal fluid (CSF) pressure → reverses CSF hypotension. Injected blood → clots plug the CSF leak. Complication: back pain, arachnoiditis, intrathecal injection, abscess, and cauda equina syndrome
- Intranasal sphenopalantine ganglion block (SPGB)- Least invasive [3] but **limited evidence** for efficacy. Methods: Cotton-tipped applicators soaked in 2% lidocaine or 0.25% bupivacaine are passed through both the nares and the end of the applicator tip is positioned just superior to the middle turbinate and anterior to the pterygopalatine fossa for 5 min with the patient in supine position (Fig. 10.2).

Clinical Pearls

1. PDPH are positional headaches (exacerbated by sitting or standing and relieved with recumbency). They are bilateral and typically located in the fronto-occipital regions.
2. Younger adults have a higher incidence of PDPH than older adults.
3. Severity of PDPH relates to the amount of CSF leakage through the dural puncture. The tip of the needle used is important; a cutting needle (e.g., Quincke) has a greater incidence of PDPH than noncutting needles (e.g., Whitacre, Sprotte) (Fig. 10.1).
4. Epidural blood patch is gold standard for treatment of PDPH, a procedure where the patient's venous blood (20–30 cc) in injected into the epidural space near the site of dural breach. Intranasal SPG block (Fig. 10.2) is least invasive and may be tried prior to blood patch.

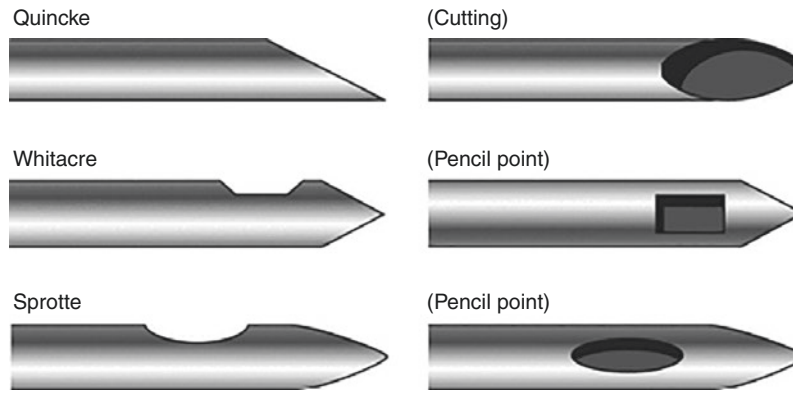

Fig. 10.1 Images of cutting vs pencil point needle [6]

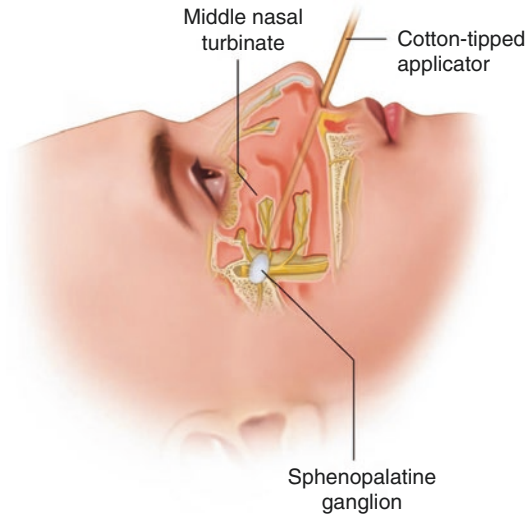

Fig. 10.2 Sphenopalatine ganglion block [7]. (to be drawn by Springer)

Questions

1. Which of the following is NOT a risk factor for PDPH?
   A. Pregnancy
   B. Female gender
   C. Obesity
   D. Patient with history of migraine headaches
2. Which of the following symptoms is rare in a patient with PDPH?
   A. Postural headache
   B. Tinnitus, visual chances, nausea and vomiting
   C. Headache lasting for over 2 months
   D. Headache onset within 48 hours after dural puncture
3. Which of the following would MOST LIKELY decrease the risk of a PDPH?
   A. Prophylactic EBP after dural puncture
   B. Using smaller gauge needle for neuraxial procedure
   C. Using a pencil point needle for spinal procedure
   D. Aggressive hydration and caffeine following accidental dural puncture
4. Which of the following decrease the incidence of PDPH after inadvertent dural puncture during epidural catheter placement?
   A. Placement of catheter in the subarachnoid space
   B. Remove Tuohy needle and attempt epidural at higher interspace
   C. Remove Tuohy needle and attempt epidural at lower interspace
   D. All of the above
5. Which of the following signs and symptoms are not associated with PDPH?
   A. Double vision
   B. Nausea and vomiting
   C. Hearing changes
   D. Fever

Answers

1. C, 2. C, 3. C, 4. D, 5. D

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Neuraxial Block: Overview

11

Ly Vu and Danielle Bodzin Horn

Introduction

- **Techniques**: spinal, epidural, and combined spinal/epidural (CSE)
- Important anatomy:
  - **Conus medullaris** = termination of spinal cord at L1-2 (adults) & L3 (newborns)
  - **Dural sac** termination = S2 (adults) & S3 (newborns)
- **Target**: between vertebrae, local anesthetic [LA] ± opioid is injected into the **epidural space** (for **epidural block**) or **subarachnoid space** (for **spinal block**) (See Fig. 11.1).
  - Pathway of needle via **midline approach**: Skin → subcutaneous fat → supraspinous ligament → interspinous ligament → ligamentum flavum → epidural space → dura → cerebral spinal fluid (CSF) in subarachnoid space
  - **Paramedian approach**: skin → subcutaneous fat → ligamentum flavum → dura mater → subdural space → arachnoid mater → subarachnoid space
- A spinal block is usually administered as a single injection but can also be performed via a catheter in the subarachnoid space for continuous spinal anesthesia [1].
  - Continuous spinal anesthesia is an effective and safe choice for high-risk surgical patients, but the provider should be aware of associated technical problems, risk of accidental overdose due to unfamiliarity and neurological damage (e.g., cauda equina syndrome).
- Epidural blocks commonly involve a continuous catheter technique, but can be performed as a single injection (either by interlaminar or transforaminal approach), especially in cases of chronic pain management involving steroid injections
  - **Caudal block** is a form of epidural technique performed at the **sacral hiatus**

    Analgesia/anesthesia for sub-umbilical surgery or chronic low back pain management (e.g. caudal epidural steroid injection for sciatica)

    Landmarks: equilateral triangle (base = 2 posterior superior iliac spines, apex = sacral hiatus), sacral canal roof = sacrococcygeal ligament, **sacral cornua** can be palpated at the rostral margin of the sacral hiatus

    Increasing LA volume will not spread analgesia past T8-T9 level [2].

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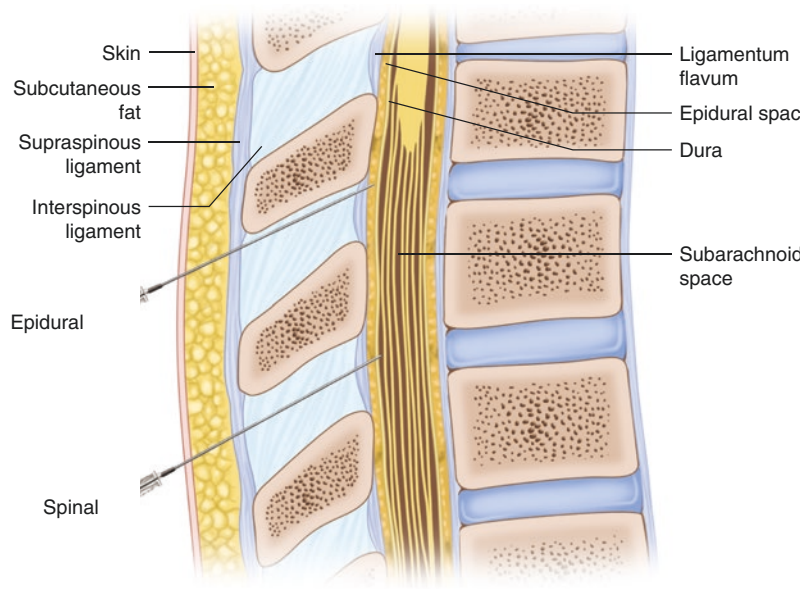

Fig. 11.1 Important landmarks of epidural versus spinal needle placement

Table 11.1 Neuraxial techniques and associated cases

Technique	Acute postoperative pain	Chronic pain examples
Cervical Epidural Steroid Injection		Chronic neck, shoulder, or arm pain Cervical radiculopathy
Thoracic Epidural	Thoracic surgery/acute pain Thoracotomy Thoracic aortic aneurysm repair Multiple rib fractures Abdominal surgery Esophagectomy/Gastrectomy Pancreatectomy Liver resection Abdominal aortic aneurysm repair Bowel resection Nephrectomy	Thoracic radiculopathy Post-herpetic neuralgia Post-traumatic (e.g. intercostal) neuralgia
Spinal Anesthesia/Lumbar Epidural	Obstetric surgery Labor analgesia Cesarean delivery Tubal ligation Orthopedic surgery Hip and lower extremity surgery Vascular surgery Amputation of lower extremity Revascularization procedures	Chronic low back pain, lumbar radiculopathy Postlaminectomy syndrome

Indications

- Supplement general anesthesia for surgical procedures, provide analgesia in the perioperative and intraoperative setting, function as primary anesthetic for surgeries from the mediastinum to lower extremities, and provide analgesia for chronic pain syndromes (Table 11.1).

Contraindications (Table 11.2)

Table 11.2 Contraindications of neuraxial blocks [3]

Absolute	Relative
1. Patient refusal 2. Patient inability to remain still during needle puncture 3. Infection at injection site 4. Uncorrected, severe hypovolemia 5. Allergy to drug utilized 6. Intracranial lesion that compresses normal brain tissue and causes midline or downward shift [4]	1. Coagulopathy 2. Bacteremia 3. Fixed cardiac output states (e.g. severe aortic stenosis) 4. Indeterminate neurological disease (e.g. severe demyelinating disease, Chiari malformation with unknown herniation/spinal cord involvement) 5. Prior spinal instrumentation with hardware (e.g. unable to place epidural at level of spinal fusion but spinal block can be performed)

Sites of Action

- Local Anesthetics
  - Unionized form diffuses across nerve sheath and membrane to bind **sodium channel** to inhibit sodium conductance
  - Spinal technique:
    Spinal nerve roots and spinal cord
    a larger dorsal nerve root creates a much larger surface area for LA penetration than the smaller ventral nerve root. This anatomic finding explains **the relative ease of sensory block** than motor block.
  - Epidural technique:
    Bathing spinal nerve roots as they traverse the epidural space and the spinal cord.
    LA diffusion into subarachnoid space through sleeves of dura mater that cover spinal roots [5]. LA injected into the epidural space have been shown to appear in the CSF after 10–30 minutes.
- Opioids
  - Directly inhibit ascending nociceptive transmission from **dorsal horn** of spinal cord
  - Activate pain control circuits that descend from the midbrain via the **rostral ventromedial medulla (RVM)** to the spinal cord dorsal horn
  - Bind to presynaptic and postsynaptic receptor sites in the spinal cord
  - Receptors are expressed in the **substantia gelatinosa** → inhibits release of substance P from the primary sensory neuron [3].

Influencing Factors

Onset

- Type of neuraxial block
  - Epidural has **slower onset** compared to spinal block because of incremental dosing of LA and slower onset of analgesia/anesthesia in the epidural space
  - The spread of epidural anesthesia varies individually and could be attributed to differences in the **surface area** of the lumbosacral dura (i.e. greater dural surface area can cause lower epidural LA longitudinal distribution), **epidural fat volume** (i.e. LA might have affinity for epidural fat thus preventing LA from reaching site of action), and **epidural blood flow** [6].
- Nerve fibers
  - **B fibers** (autonomic nervous system): smaller than A-delta fibers but larger than C fibers; It has highest sensitivity to LA, and therefore, block **faster than** sensory fibers (Table 11.3).
  - **C fibers** (temperature and pain): smallest in size, lack myelination → blocked rapidly
  - **A-alpha fibers** (motor): thick myelin sheath → require more LA and more time before adequate block is obtained
  - **Differential sensory/motor blockade**: normal occurrence in which sympathetic nerve fibers are most sensitive to LA (2–4 levels above sensory block), pain/touch fibers are moderately sensitive (2–3 levels above motor block), and motor fibers are least sensitive (Table 11.3) [7].
- LA properties
  - **pKa closer to tissue pH** → more unionized, lipid-soluble form available to cross cell membrane → faster onset (***pKa has sPeed***)
    Exception = Chloroprocaine 3% → fast onset due to high concentration

Table 11.3 Peripheral nerve fiber properties

Fiber type	Function	Size	Myelination	Conduction velocity	LA sensitivity
Aα	Motor	Largest	Yes	Fastest	+
Aβ	Tactile, proprioception		Yes		++
Aγ	Muscle tone		Yes		+++
Aδ	Pain, temperature, touch		Yes		+++
B	Preganglionic autonomic		Yes		++++
C	Postganglionic autonomic, pain, temperature, touch	Smallest	No	Slowest	+++

Table 11.4 Commonly used local anesthetics for neuraxial blocks [3]

Medication	pKa	Onset time (minutes)	Protein binding (%)	Duration (minutes)
2-Chloroprocaine	9.1	5–15 (epidural)	N/A	30–90 (epidural)
Bupivicaine	8.1	15–20 (epidural)	95	90–200 (spinal) 120–240 (epidural)
Lidocaine	7.8	5–15 (epidural)	64	30–90 (spinal) 60–90 (epidural)
Ropivacaine	8.1	15–20 (epidural)	94	90–200 (spinal) 120–240 (epidural)

- Opioid properties
  - **Lipophilic** opioids (e.g. **fentanyl**, **sufentanil**) have fast onset but short duration
- **Sodium bicarbonate**
  - Alkalinizes LA → increases concentration of nonionized form that can cross the nerve cell membrane
- Spread of spinal anesthesia
  - **Baricity**: Hyperbaric → follows gravity, greater **cephalad** spread e.g., 0.75% or 1% hyperbaric bupivacaine

Termination of Action

- Limited by resorption of medication from CSF to systemic circulation
- Duration of analgesia/anesthesia can be prolonged by using a continuous catheter for both epidural and spinal techniques
- LA properties
  - **Greater protein binding** → longer duration of action (***bondage brings discipline***)
  - Metabolism
    Esters undergo hydrolysis by **pseudocholinesterase** → short half-life
    Amides undergo enzymatic biotransformation primarily in the liver
  - Lidocaine is a vasodilator → increases absorption and metabolism → shorter duration compared to other LA (e.g. prilocaine, mepivacaine) (Table 11.4)
- Opioid properties
  - Can prolong sensory blockade when combined with LA
  - **Hydrophilic** opioids (e.g. **morphine**) have long onset and long duration
- **Epinephrine**
  - Concentration used: **5 mcg/ml** (**1:200,000**) or less
  - Vasoconstriction prolongs block; reduces vascular uptake of LA, delays metabolism
- **Clonidine** (alpha-2 adrenoreceptor agonist)
  - Proposed mechanism of increasing duration of blockade with LA: reduces SC blood flow and targets hyperpolarization-activated cation inward current [8].

Table 11.5 Complications of neuraxial blocks [3]

Complications	Precipitating factors	Preventive measures
Neurologic changes (e.g. cauda equina syndrome, peripheral nerve injury)	Intrathecal catheters Hyperbaric 5% lidocaine Lithotomy position Sensory/motor block eliminating normal protective reflexes	Catheter aspiration of CSF before and after LA injection Limiting amount of LA given in subarachnoid space
Postdural puncture headache (PDPH)	Younger age Female gender Larger gauge-needle Pregnancy Number of dural punctures Lower body mass index	Orient needle bevel parallel with length of neuraxis Use non-cutting needle
IV Injection / Local anesthetic systemic toxicity (LAST)	Inadvertent IV administration of LA	Confirm needle/catheter placement with aspiration and/or test dose
Infection (abscess, meningitis)	Chemical contamination & detergents Immunocompromised conditions (e.g. diabetes mellitus, HIV/AIDS, elderly, chronic steroid use)	Sterile technique
Total spinal anesthesia	Inadvertent IT administration of LA and/or opioids	Confirm needle/catheter placement with aspiration and/or test dose
Vertebral canal hematoma	Subarachnoid bleeding from injured artery or vein Coagulopathy Use of anticoagulant drugs Thrombocytopenia	Check for history of coagulopathy or anticoagulant drug use and platelet level
Spinal cord ischemia	Prolonged hypotension Addition of vasoconstrictors to local anesthetics Compression of arterial supply by vertebral canal hematoma	Maintain **spinal cord perfusion pressure** (SCPP) as determined by SCCP = MAP – ISP or CVP. Consider lumbar drain
Hypotension	Quick administration of large amounts of LA causing sympathectomy	Volume expansion Patient positioning (e.g. apply manual left uterine displacement for parturients)

Test Dose

- Purpose: to detect a malpositioned epidural catheter and avoid consequences of injecting a large amount of LA or opioid intravascularly (IV) or intrathecally (IT)
- Catheter aspiration should always be done, but is not always diagnostic, particularly with single-orifice catheters [7].
- **Standard Test Dose**
  - 3 ml of **Lidocaine 1.5%** with **1:200,000 epinephrine** (15 mcg epinephrine total)
- **Positive Test**:
  - Increase in heart rate by 10 beats within 1 minute of injection suggests IV uptake
  - Motor block within 3–5 minutes of injection suggests an IT catheter

Complications (Table 11.5)

Predicting the Difficult Neuraxial Block

- Poor landmarks
- Abnormal spinal anatomy (e.g., *kyphoscoliosis, previous spine surgery*)
- prolapsed discs
- Increased BMI

Clinical Pearls

- Absolute contraindications to neuraxial procedures include patient refusal, infection at the injection site, hypovolemic shock, and true allergy to LA/opioid used.

- Spinal anesthesia spread mainly depends upon *baricity* relative to CSF (hyperbaric → follows gravity; isobaric → follows gravity; hypobaric → nondependent spread); patient *positioning* (during/immediately following injection); medication *dose*; *injection site*
- Due to differential blockade of nerve fibers, it is important to check sensory levels to loss of pain sensation not cold sensation to ensure adequate neuraxial blockade prior to skin incision.
- Epidural anesthesia spread produces segmental block, spreads both caudally and cranially from site of injection (unlike spinal); drug dose and volume (not concentration) determine epidural spread and quality.
- Opioids provide analgesia by inhibiting the nociceptive information in the dorsal horn of the spinal cord and acting on opioid receptors found in the substantia gelatinosa to inhibit release of substance P.
- The pKa of a LA that is closer to physiologic pH, has faster onset of action. An exception to this rule is **2-chloroprocaine** (pKa of 9.1), which has a fast onset of action due to the high concentration that is used.
- Until age 5 years, very little hemodynamic effect/sympathectomy is elicited by spinal anesthesia.

Questions

1. Which if the following is most responsible for the duration of action of local anesthetics?
   A. Volume injected
   B. Baricity
   C. Protein binding
   D. pKa
2. Which of the following patients is not a candidate for a neuraxial technique?
   A. Patient who received heparin 5000 units subcutaneously 6 hours ago
   B. Patient who has cellulitis along the midline of his back
   C. Pregnant patient with 1-month history of lower back pain presenting for elective C/D
   D. A patient with asymptomatic mitral regurgitation
3. An 80-year-old man with history of COPD and renal cancer is scheduled for an open right nephrectomy. Which would be the best option for post-operative pain management?
   A. Opioid patient-controlled analgesia (PCA) using hydromorphone
   B. Lumbar epidural catheter with PCEA using bupivacaine and fentanyl
   C. Oral oxycodone-acetaminophen as needed
   D. Thoracic epidural catheter with PCEA using bupivacaine and fentanyl
4. A newborn is scheduled for hypospadias surgery, and you are planning a caudal block for postoperative pain control. At what vertebral level does the dural sac likely terminate?
   A. L1
   B. L3
   C. S2
   D. S3
5. Which of the following is an absolute contraindication to an epidural placement?
   A. Low platelet count
   B. Multiple sclerosis
   C. previous back surgery
   D. intracranial tumor
6. Two days after difficult epidural placement at L1-L2 level, the patient complains of bilateral lower extremity weakness (unable to lift both lower extremities). The epidural catheter was removed more than 10 hours ago. Which of the following is most likely?
   A. Residual anesthetics
   B. Anterior spinal artery syndrome
   C. Spinal cord injury during epidural placement
   D. None of the above

Answers

1. C (bin**d**ing→ **d**uration), 2. B, 3. D, 4. D, 5. D (Dural puncture is not recommended in patients with evidence of intracranial tumor causing increased intracranial pressure. Dural puncture → leakage of CSF → decreased CSF pressure → cerebellar herniation, 6. B (Answer is B. damage to the artery of Adamkiewicz by epidural needle)

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12 Neuraxial Block: Spine Anatomy; Epidural (Cervical, Thoracic, Lumbar, Caudal)

William Landphair and Timothy Lubenow

Spine Anatomy

- Vertebrae:
  - 33 vertebrae (7 cervical, 12 thoracic, 5 lumbar, 5 fused sacral and 4 fused coccygeal).
  - Cervical (except C1), thoracic and lumbar vertebrae have anterior body, two pedicles and two laminae.
  - Lamina connect to lateral transverse processes and posterior projecting spinous process.
  - Junction of the lamina and pedicles form inferior and superior articular processes.
  - 5 fused sacral vertebrae form the sacrum connecting the spine to the iliac wing of the pelvis.
- Ligaments:
  - Ligaments provide support and stability to the intervertebral column. Following from dorsal to ventral (See Fig. 11.1, Chap. 11 of regional anesthesia)
- Epidural Space:
  - Space between the periosteum and dura. Extends from foramen magnum to coccyx. Surrounded anteriorly by the posterior longitudinal ligament and posteriorly by the ligamentum flavum and laterally by the pedicles and intervertebral foramen (Fig. 12.1)
- Meninges: Dura Matter, Arachnoid Matter, Pia Matter (Fig. 12.1).
  - **Dura Matter** forms a sac surrounding spinal cord. Extends from Foramen magnum to **S2 in adults (S3 in neonates)**.
  - Subdural space contains small amount of serous fluid. Potential space between Dura and Arachnoid.
    - **Subdural injection**: Can occur if epidural needle pokes through dura, or if catheter migrates. Hypotension occurs more than expected from epidural anesthesia. Usually high sensory block with minimal motor block. Can track cephalad, and if not diagnosed, can cause dyspnea and loss of consciousness [2].
  - Subarachnoid space: Houses the CSF and spinal nerves. This is where spinal anesthetics placed.
  - Pia Matter: highly vascularized covering spinal cord. Lateral connections called denticulate ligaments (can lead to patchy or unilateral anesthesia)
- Spinal Nerves:
  - **31** pairs of nerves (cervical-8, thoracic-12, lumbar 5, sacral 5, coccyx 1)

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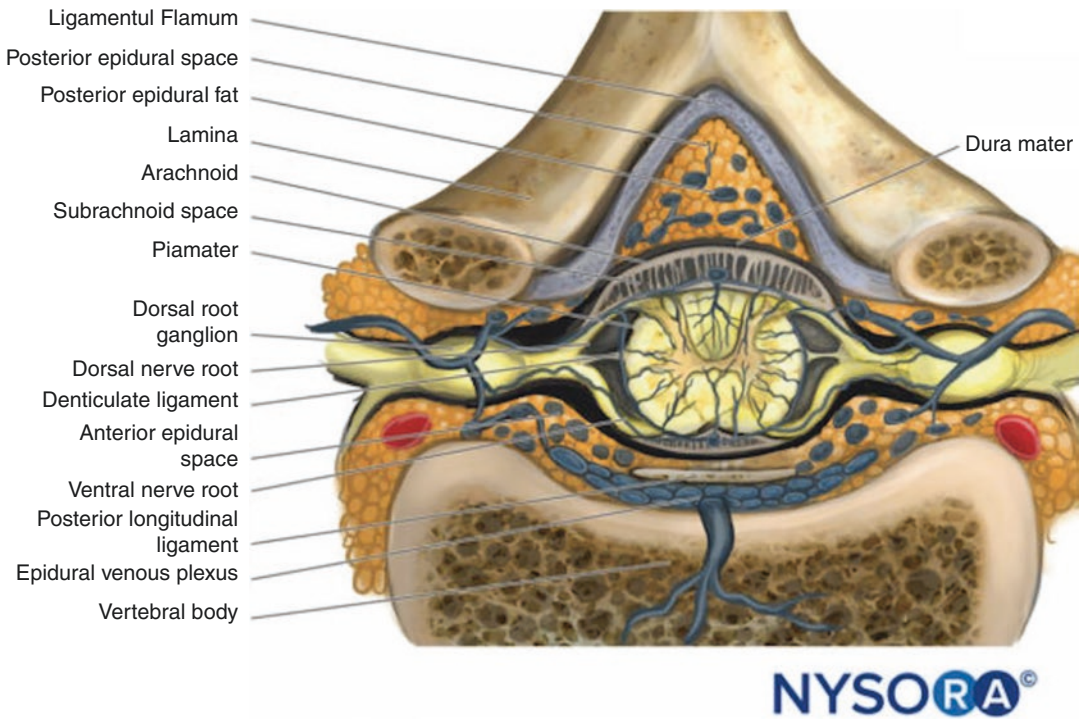

Fig. 12.1 Transverse view of the lumbar spine. (Reproduced with permission from NYSORA) [1]

- The first 7 ("**heavenly 7**") spinal nerves exit **above the neuroforamen** of the corresponding level. **C8 exits above T1**. T2 to L5 nerves exit **below their same numbered vertebrae** (high yield; Fig. 12.2).
- Important to know dermatomes when deciding where to place an epidural (See Fig. 10.1, Chap. 10 of chronic pain)

Blood Supply

- Anterior spinal artery supplies **anterior 2/3 of cord**.
- Posterior spinal artery: 2 on each side from vertebral or posterior inferior cerebellar artery. **Supplies 1/3 of cord** (Fig. 12.2).
- **Artery of Adamkiewicz**: supplies lower 2/3 of spinal cord
  - Largest of radicular arteries. Reinforcement to anterior spinal artery in lumbar area
  - If injured can lead to anterior spinal artery syndrome: Bowel and bladder dysfunction and lower extremity paralysis with sparing of proprioception and sensation.
- Six veins: median, longitudinal plexiform, 4 lateral longitudinal veins (communicate with internal vertebral and external vertebral plexus)

Regional Techniques, Epidural/Caudal

Indications and contraindications: See Chap. 11, regional anesthesia.

Technique

- Level of target for the epidural depends on the **dermatomal level** that one is looking to access based on pain or surgical procedure (Fig. 10.1, Chap. 10, chronic pain).
- Palpation of spine to assess for scoliosis and lordosis important as well as assessing landmarks and location:

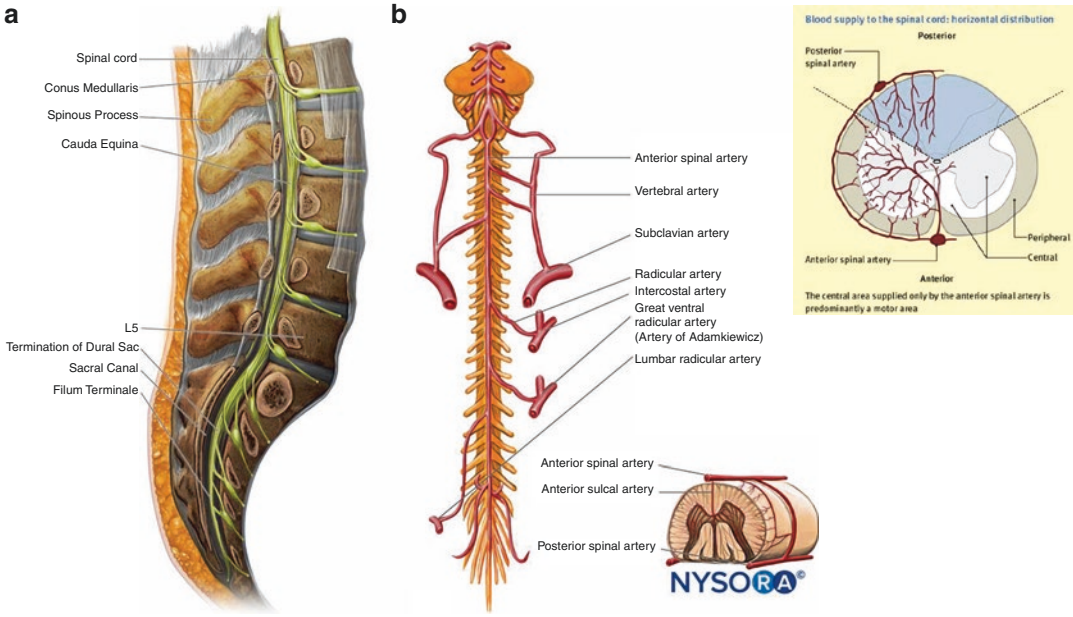

Fig. 12.2 (**a**) Sagittal view of the lumbar spine and (**b**) blood supply of the spinal cord. (Reproduced with permission from NYSORA) [1]

- **Iliac crest-L4; Twelfth rib- T12; Inferior scapula T7; Vertebra prominens** (most pronounced cervical spine at base of the neck) **C7**
- **Spinal cord** extends to **L2** in **adults** (**L3** in **Neonates**)

- Lumbar and Low Thoracic (Below T10) epidurals are typically placed at **midline**: The patient can be supine or lateral. The lateral position can be slightly more difficult due to difficulty keeping needle and catheter midline. This can cause difficulty in advancing the catheter and for unilateral anesthesia [3].
  - From posterior to anterior, the needle will pass through the following structures: **Skin, subcutaneous tissue, supraspinous ligament, interspinous ligament,** and finally **ligamentum flavum** before entering the epidural space (See Fig. 11.1, Chap. 11 of regional anesthesia).
  - Technique with loss of resistance: A syringe containing saline, air or both is attached to the needle once entering ligamentum flavum. There will be a noted resistance to injecting the air or saline when within the ligament. A Tuohy needle is advanced under continuous pressure until loss of resistance is found, which is likely indicating that the needle is within the epidural space.
  - The distance from skin to epidural space in adult male is approximately 5 cm at L3-L4 (can vary from 2 to 10 cm depending on patient weight, size, angle of needle, position of patient and age of patient).
  - Once within the space, a catheter can be advanced usually **3–5 cm** beyond the needle tip in the epidural space for continuous epidural anesthesia. Advancement beyond increases chance of **catheter exiting the foramen**.
  - The needle is removed over the catheter and the catheter is aspirated. Noted with **negative aspiration for blood** or CSF. A test dose is also given to rule out intrathecal and intravascular placement with lidocaine and **1:200,000** epinephrine. Then a local anesthetic is injected usually in distributed 5 ml aliquots until the desired level of anesthesia is reached.

- **Mid thoracic epidurals** are typically placed with a **paramedian approach:**
  - T4-T10 spinous processes of the upper vertebrae rest on the lower spinous process, making midline placement difficult and therefore a paramedian approach is favored. If done in midline, the needle approach must be advanced cephalad at an **acute angle** [3].
  - A Tuohy needle is inserted ~1 cm lateral to the superior tip of the spinous process and advanced until contact to the laminal of the vertebral body below. The needle is then redirected medially about 20°–30° and cephalad at about 45°. Once the tip is off the inferior laminae, the needle is advanced with a loss of resistance syringe. This is checked and achieved after entering the epidural space.
  - From posterior to anterior, the needle passes through the following structures: **Skin, subcutaneous tissue, ligamentum flavum**. There will be less "gritty" feeling with the needle due to not passing through the interspinous ligament.
- **Cervical epidurals** are typically performed for pain procedures and usually under fluoroscopy. **C7-T1 provides the widest space** and the largest width of dura (~3–4 mm). This becomes narrower in higher segments making placement above more dangerous for puncturing the dura and possible cervical spinal cord. **C7 is also a prominent landmark** [4].

Caudal Epidural

- This is typically done perioperatively in very young patients with or without general anesthesia. It provides analgesia below the umbilicus. It can also be accessed for analgesia in adults with chronic pain. This can be **more difficult** in the older population and fluoroscopy can assist in placement.
- The procedure is typically done in prone position, but it can be lateral.
- The caudal space is entered through the **sacral hiatus**, which is formed by the **unfused S5 spinous process**. Unfused laminae on the lateral aspects form the cornua, which can be palpated in the prone position. The hiatus is covered by the sacrococcygeal ligament. The epidural needle is advanced perpendicular through the skin and passes through the sacrococcygeal ligament. Typically, a "pop" can be felt. The needle angle is decreased and advanced about 1–2 cm into the caudal canal. Air or 5 ml of saline can be injected while palpating to ensure the needle is not within the subcutaneous tissue.
- Use caution not to advance too far in the canal to avoid dural puncture. The **dural sac ends** at **S3 in neonates**, **S2 in adults** [2].

Preventive Measures to Avoid Complications

- Intravascular or intraosseous injection can lead to **seizure or cardiac arrest** from local anesthetic toxicity (Chap. 9, regional anesthesia). Make sure there is a negative test dose and aspiration. Always have **intralipid available** when using local anesthetics.
- **Post Dural Puncture Headache**: (See Chap. 10 of regional anesthesia)
- **Epidural Hematoma**: A careful history and physical, PT/INR and platelet levels, anticoagulant use and following American Society of Regional Anesthesia (ASRA) guidelines can decrease the incidence. Patients present with **severe localized constant back pain** with or without radiculopathy. There may be numbness, tingling, paraplegia or quadriplegia and/or urinary or fecal incontinence. MRI is the gold standard for diagnosis. **Emergent surgical evacuation** is the definitive treatment [4].
- **Epidural abscess**: Rare complication that can occur during or after placement. This can be prevented with aseptic technique with placement of epidural and catheter, **decreasing length of time the epidural is in place**, and not to use in patients with local or systemic infection. Classic triad of **back pain, fever, and neurologic deficits**. Obtain complete

blood count, erythrocyte sedimentation rate, and c-reactive protein (all elevated). MRI imaging is the gold standard for diagnosis. Emergent surgical evacuation is the definitive treatment [4].

Clinical Pearls

- Important anatomical landmarks: Iliac crest- L4; Twelfth rib- T12; Inferior scapula T7; Vertebra prominens (most pronounced cervical spine at base of the neck)- C7.
- The anterior spinal artery supplies about 75% of the blood flow (anterior 2/3) to the spinal cord (**motor tracts**) and arises from the vertebral arteries and radicular arteries from the aorta. The two posterior spinal arteries supply about 25% of the blood flow (posterior 1/3) to the spinal cord (**sensory tracts**) and arise from the posterior and inferior cerebellar arteries, the vertebral arteries, and the radicular arteries.
- The artery of Adamkiewicz and is one of the "feeder" arteries for the **anterior spinal artery**. Damage to this artery can lead to paraplegia. The origin of this artery is **T9-T12 in 75% of cases**, L1-L2 in 10% of cases.
- Know structures passed by a touhy needle in the midline and paramedian approach to enter into epidural space (high yield).

Questions

1. A 50-year-old male with history of osteoarthritis of the left knee presents for left total knee arthroplasty. You intend to place an epidural for intra-op and post-op analgesia. What level would be the best to place your epidural at?
   A. C3-C4
   B. T7-T8
   C. T9-T10
   D. L3-L4
2. You intend to place an epidural for a patient undergoing a Whipple procedure and want to place your epidural at T7. What landmark best signifies this area of the spine?
   A. Twelfth Rib
   B. Iliac Crest
   C. Inferior Scapula
   D. Vertebra Prominins
3. When placing an epidural in the lumbar spine, what is the correct order of anatomical structures the needle will pass through from superficial to deep?
   A. Skin, subcutaneous tissue, supraspinous ligament, interspinous ligament, ligamentum flavum
   B. Skin, subcutaneous tissue, interspinous ligament, supraspinous ligament, ligamentum flavum
   C. Skin, supraspinous ligament, subcutaneous tissue, ligamentum flavum, interspinous ligament
   D. Supraspinous ligament, interspinous ligament, skin, subcutaneous tissue, ligamentum flavum
4. The Dura Mater forms the sac surrounding the spinal cord and extends from the foramen magnum to S3 in Neonates. Where does the dura matter normally end in adults?
   A. L4
   B. S2
   C. L1
   D. S5
5. The artery of Adamkiewicz most frequently arises from the aorta at which spinal level?
   A. T1-T4
   B. T5-T8
   C. T9-T12
   D. L1-L4
6. Which of the following symptom is not associated with epidural hematoma
   A. Paraplegia
   B. Bowel and bladder dysfunction
   C. Numbness and tingling
   D. Fever and chills
7. Which of the following structure an epidural needle would pass during a paramedian epidural catheter?
   A. Posterior longitudinal ligament
   B. Anterior longitudinal ligament
   C. Supraspinal ligament
   D. None of the above

Answers

1. D, 2. C, 3. A, 4. B, 5. C, 6. D, 7. D

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13 Neuraxial Block: Epidural Adjuvants

Paragi Rana and Musa Aner

Introduction

- **Spinal nerve roots, dorsal root entry zones and long tracts of the spinal cord white matter** serve as the primary sites of action of epidural local anesthetics.
- Local anesthetics utilized for epidural blockade are divided into three major categories: **short- (2-chlorprocaine), intermediate- (Lidocaine) and long-acting (Bupivacaine, Ropivacaine)**
- opioids, α-adrenergic agonists, cholinesterase inhibitors, ketamine, midazolam and semisynthetic opioid agonist-antagonists have been investigated to evaluate for their ability to augment the quality and duration of neuraxial blockade.

Epinephrine

- common adjuvant to epidural local anesthetic solutions; **concentration 1:200,000**
- vasoconstriction→ decreased vascular absorption of local anesthetic → prolonged duration of the blockade
- can decrease systemic absorption by 30% for lidocaine and 10–20% for bupivacaine(binds to tissues more avidly)
- can cause tachycardia and hypertension. Not advisable in patient with angina, pre-eclampsia

Clonidine

Mechanism of Action

- Selective alpha2 adrenergic receptor agonist. Alpha adrenergic receptors are located on both pre- and postsynaptic terminals of small primary afferents within the **substantia gelatinosa (Rexed Laminae II)** of the dorsal horn.
- nociception → activation of **descending inhibitory neurons** → release of norepinephrine → activation of synaptic α2-adrenergic receptors → decreased release of Substance P → analgesia [1]

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Table 13.1 Opioid receptor activity [2]

Receptor	Subtypes	Location	Function	Agonists
Delta δ	δ_1 δ_2	Brain (pontine nuclei, amygdala, deep cortex) Peripheral sensory neurons	Analgesia Behavioral/Antidepressant Epileptogenic	Exogenous: N/A Endogenous: Leu-enkephalin β – endorphin
Kappa k	k_1 k_2 k_3	Brain (Hypothalamus, Periaqueductal Grey) Spinal Cord (substantia gelatinosa) Peripheral Sensory Neurons	Spinal Analgesia Sedation Miosis	Exogenous: Morphine Nalbuphine Butorphanol Oxycodone Endogenous: Dynorphin
Mu μ	μ_1 μ_2 μ_3	Brain (Cerebral corex, Periaqueductal Grey, Substantia Nigra) Spinal Cord (Substantia gelatinosa) Peripheral Sensory Neurons Intestinal Tract	μ_1 - analgesia, physical dependence μ_2 - respiratory depression, miosis, euphoria, physical dependence, reduced gastrointestinal mobility μ_3 – vasodilation	Exogenous: Morphine Fentanyl Endogenous: Met-enkephalin β – endorphin

- Clonidine acts on descending inhibitory pain pathway using similar mechanisms [1]. In addition, it **blocks conduction** in **C and Aδ fiber**s and has local vasoconstrictive effect

Benefits

- Prolongs the duration of anesthesia and analgesia
- Synergistic effects with opioids
- Modulation of stress response
- Analgesic effect **without motor impairment**

Adverse Effects

- Sedation
- **Bradycardia**
- **Hypotension**
- Dry Mouth

Administration

- Single bolus dose 150–400 μg (adult); 1–2 μg/kg (pediatric)
- Continues epidural infusion rate 30–40 μg/h (adult); 0.1–0.5 μg/kg/h (pediatric)

Opioids

Mechanism of Action

- Opioids produce analgesia by binding to primarily mu receptors, as well as, kappa receptors

Opioid receptors are widespread throughout the body including cerebral cortex, thalamus, hypothalamus, amygdala, basal ganglia, brainstem, reticular activating system (Chap. 2, Chronic pain).

- **μ_1 mediates analgesia and physical dependence**; activation of **μ_2 facilitates respiratory depression, miosis, euphoria and physical dependence** and **μ_3 is implicated in vasodilation** (Table 13.1) [2].
- Presynaptic effects include a reduction in afferent neurotransmitter release e.g. **substance P and glutamate**, postsynaptic effects promote the release of spinal adenosine and hyperpolarization [3].

After epidural administration, opioids diffuse across the dura and arachnoid mater into the subarachnoid space to bind opioid receptors in the dorsal horn of the spinal cord.

- Lipophilic drugs have **faster** onset of action, **shorter duration** of action secondary to rapid clearance/redistribution, fewer adverse effects, and a bolus dose will demonstrate segmental analgesia. E.g. fentanyl.
- Hydrophilic drugs will have a **slower onset of action** and longer duration of action.eg morphine

Adverse Effects

- Dose dependent respiratory depression, incidence 0.1–0.9%
  - Reversal naloxone 100–400 μg increments, if infusion is required 0.5–5.0 μg/kg/h
- Urinary retention
- Nausea/vomiting
- Pruritus

Morphine

- μ-opioid receptor agonist
- Morphine is **hydrophilic**. Extended release epidural morphine (EREM) may provide analgesia for up to **48 hours** after a single bolus dose
- Epidural administration of morphine can cause **delayed respiratory depression up to 24 hours** after a single bolus dose, close monitoring is required
- Single bolus dose 30–100 μg/kg or 1–5 mg (adult); 10–30 μg/kg (pediatric). Continues epidural infusion rate 0.1–1.0 mg/h (adult); 1–5 μg/kg/h (pediatric)

Hydromorphone

- **semi-synthetic μ-opioid receptor agonist**.
- **Intermediate lipid solubility** may provide favorable profile for use in epidural analgesia [3, 4].
- rapid onset of action 20–30 minutes, low incidence of adverse effect, and **lower risk of delayed respiratory** depression as compared to epidural morphine.
- Single bolus dose 0.5–1 mg. Continues epidural infusion rate 100–200 μg/h.

Table 13.2 Epidural opioids pharmacology [5]

Opioid	Relative lipid solubility	Time	
		Onset (min)	Duration (h)
Morphine	1.0	30–90	12–24
Hydromorphone	1.4	20–30	6–18
Fentanyl	580	10–15	2–3

Fentanyl

- **synthetic μ-opioid receptor agonist**.
- High **lipid solubility** facilitates rapid onset of action, short duration of action, and mitigates cephalad spread (Table 13.2) [5].
- Epidural fentanyl is associated with a **reduced risk of delayed onset respiratory depression**, as well as, **lower incidence of postoperative nausea and vomiting (PONV)** as compared to epidural morphine.
- Rapid clearance from CSF contributes to an inability to provide analgesia at sites distant from the point of administration (**segmental analgesia)** [5].
- Single bolus dose 50–100 μg.
- Continues epidural infusion rate 0.5–1.0 μg/kg/h, 25–100 μg/h.

Clinical Pearls

- Epidural adjuvants can be utilized to augment the intensity and duration of epidural local anesthetic blockade while reducing adverse effects such **as motor blockade**.
- Epidural clonidine acts synergistically with epidural opioids such as fentanyl, when used in combination the dose of each agent can **be decreased by 60%**.
- The lipophilicity of an epidural administered opioid will determine its **onset of action, duration of action, and spread**.
- Hydrophilic drugs such as morphine and hydromorphone demonstrate **a slow onset of action**, longer duration of analgesic effect, and more prolonged half-life in the CSF.
- Administration of a hydrophilic opioid maybe advantageous when the epidural catheter placement site is **incongruent with the surgical incision**.

– Fentanyl produces **less pruritus and PONV** as compared to morphine [4].
– Analgesia with epidural fentanyl or morphine is decreased when administered after **2-chlorprocaine**, via an unclear mechanism.

Questions

1. Which of the following organizes opioids in order of increasing lipid solubility?
   A. Hydromorphone = Morphine > Fentanyl
   B. Morphine > Hydromorphone > Fentanyl
   C. Fentanyl > Hydromorphone > Morphine
   D. Morphine > Fentanyl > Hydromorphone
2. Activation of which of the following opioid receptors mediates vasodilation?
   A. μ_1
   B. δ_1
   C. μ_3
   D. k_1
3. Which of the following is not an adverse effect commonly associated with epidural administration of clonidine?
   A. Urinary Retention
   B. Hypotension
   C. Bradycardia
   D. Sedation
4. The duration and intensity of analgesia by epidural fentanyl or morphine is adversely affected by which of the following local anesthetics?
   A. Bupivacaine
   B. Lidocaine
   C. Ropivacaine
   D. 2-chlorprocaine

Correct Answers MCQs

1. B, 2. C, 3. A, 4. D

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14 Neuraxial Block: Spinal and Combined Spinal Epidural

Glenn Mann and Naum Shaparin

Introduction

- An epidural catheter provides prolonged anesthesia and an option to use for postoperative analgesia. A single-shot spinal is limited to the duration of action of the injected drug (60–90 minutes) [1].
- The combined spinal–epidural (CSE) technique is the performance of a single shot spinal block and the placement of an epidural catheter in the same setting.
- A CSE combines the advantage of a single shot spinal (rapidity and predictability of block) with epidural anesthesia and analgesia (modify and extend the block as needed) [1, 2].
- Epidural volume extension: a low subarachnoid block can extend cephalad by an epidural 'top-up' of 10 ml of normal saline given within 5 minutes of the spinal block [2, 3]. Compression of the subarachnoid space by the saline in the epidural space presumably results in cephalad spread of local anesthetic within the subarachnoid space [3].
- In morbidly obese patients, the preferred anesthesia technique for a cesarean section is a CSE since length of surgery is unpredictable and general anesthesia is associated with increased complication risk [2].
- Disadvantages include relatively longer duration of anesthetic technique and delayed confirmation of functional epidural catheter [1, 2].

Indications for CSE

- Rapid pain relief in obstetrical cases
- Complicated surgery that will last longer than 3 hours [1–3]
- Sole anesthetic for a wide range of orthopedic, urological, gynecological surgery [2]

Contraindications

- See Chap. 16 - Implications of Anticoagulants and Platelet Inhibitors: American Society of Regional Anesthesia and Pain Medicine (ASRA) Guidelines.

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Technique for Combined Spinal Epidural

Approach [1–4]

- Standard ASA monitors
- Patient position
  - Sitting (most common) or lateral decubitus
  - Flex neck, push out lower back
- Identify lumbar interspace below L3
- Local anesthetic administration to the skin
- Midline: Tuohy needle passes through tissue layers until encountering resistance from the ligamentum flavum.
- Tuohy needle is advanced while checking for loss of resistance with a syringe
- Loss of resistance indicates introduction in to the epidural space
- Spinal needle is passed through the Tuohy needle until a "pop" is felt and free-flowing cerebrospinal fluid (CSF) is encountered indicating penetration through the dura and in to the subarachnoid space
- Once free-flowing CSF is established local anesthetic is administered and the spinal needle is removed
- An epidural catheter is then threaded through the Tuohy needle in to the epidural space [4]
- The catheter should be threaded to ensure that 3–5 cm of catheter rests in the epidural space (i.e. if epidural needle entered the epidural space at 5 cm the catheter should be secured at the 8–10 cm mark at the skin) [4]

Medications

- Preservative free, hypobaric, isobaric, or hyperbaric local anesthetics (Table 14.1).
- The neonate has an increased CSF volume (4 mL/kg vs 2 mL/kg). They need a larger dose of local anesthetic and it has a shorter duration of action compared to adults (See Chap. 5 on regional anesthesia) [5].
- Use a hyperbaric solution if the desired level of blockade is higher than T10 [2].
- Use a isobaric solutions for a sensory level lower than T10 (e.g., lower extremity procedures) [2].
- The addition of adjuvants will lower the required dose and prolongs the duration of anesthesia (see Chap. 15 of regional anesthesia) [1].

Complications of CSE

- In addition to complications related to the neuraxial blockade, the spinal or epidural may not provide an adequate block [1].
- The spinal needle may not pierce the dura.
- Normal saline use during CSE placement can be mistaken as CSF.
- Problems encountered with inserting an epidural catheter following the spinal; significant hypotension from the subarachnoid block may limit time required to troubleshoot insertion of epidural catheter [2].

Clinical Pearls

- Hyperbaric solutions if the desired level of blockade is higher than T10.
- Isobaric solutions if the desired level of blockade is lower than T10.
- For CSE spinal doses are given in a single shot spinal and supplemented through epidural catheter

Table 14.1 Local anesthetics for single shot spinal

Local anesthetic	Typical concentrations	Baricity	Dose (mg)	Duration (min)
Lidocaine	5%	Hyperbaric	50–10	45–75
Bupivacaine	0.75%	Hyperbaric	6–15	90–150
Mepivacaine	1%, 1.5%, 2%	Isobaric	50–70	45–75
Bupivacaine	0.5%	Isobaric	6–15	90–120
Chloroprocaine	2–3%	Isobaric	30–60	30–50

- Significant hypotension from subarachnoid block may limit times required to troubleshoot difficulties (if any) in insertion of epidural catheter [2].
- With CSE, a low subarachnoid block can extend cephalad by an epidural 'top-up' [2, 3].

Questions

1. A 75-year-old male is undergoing a inguinal hernia repair under spinal anesthesia. 30 minutes into the procedure the patient becomes restless, bradycardic, hypotensive and states "I cannot breath." The most likely cause of these symptoms in this patient is
   A. local anesthetic toxicity
   B. perforation of perineum
   C. upper thoracic neuraxial block
   D. mid thoracic neuraxial block
2. An 85-year-old male patient is undergoing orchiectomy under neuraxial blockade. What is the desired dermatomal level to achieve surgical anesthesia?
   A. T10
   B. L2
   C. L4
   D. S1
3. Which of the following is an absolute contraindication to placing a spinal anesthetic?
   A. Aspirin administration within the last 6 hours
   B. Bacteremia
   C. Increased intracranial pressure
   D. Pre-existing CNS disorder
4. Which of following statement is true of local anesthetic dose in infant in comparison with adults?
   A. Greater dose and longer duration
   B. Greater dose and shorter duration
   C. smaller dose and shorter duration
   D. Smaller dose and longer duration
5. All of the following are indications for placement of a spinal anesthetic EXCEPT:
   A. Total hip replacement
   B. Cesarean section
   C. Laparoscopic robotic prostatectomy
   D. Hemorrhoidectomy
6. A 5-kg, 2-month-old male infant undergoes bilateral orchiectomy with a spinal anesthetic. What is the duration of 0.5% bupivacaine solution?
   A. 10–30 minutes
   B. 30–60 minutes
   C. 60–90 minutes
   D. 90–120 minutes

Answers

1. C, 2. A, 3. C, 4. B, 5. C, 6. C

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Systemic Effects of Neuraxial Block

15

Calvin Feng and Laura DeVita

Somatic Blockade [1]

- Somatic nerves innervate **peripheral nervous system**
- Divided into **afferent (sensory)** or **efferent (motor)**
- Control all voluntary movement and voluntary reflex arcs
- Synapse between upper motor neuron and lower motor neuron located in ventral horn of spinal cord
- Input from motor cortex **corticospinal tract** ventral horn of spinal cord alpha motor neurons muscle movement
- **Pre-synaptic and post-synaptic neurotransmitter is Acetylcholine (Ach)**

Autonomic Blockade [1]

- Nervous system is divided into 2 groups: Sympathetic and Parasympathetic, (see Fig. 6.1, Chap. 6 of chronic pain)
- Sympathetic nerves originate from **thoracolumbar** regions (T1-L2)
- **Pre-ganglionic sympathetic** nerves originate in intermediolateral gray columns of thoracolumbar regions ventral nerve root to merge with spinal nerve project to paravertebral sympathetic ganglia via white rami communicans
- **Post-ganglionic sympathetic** nerves synapse in autonomic ganglia post-synaptically join spinal nerves via gray rami communicans (See Fig. 19.2, Chap. 19, Chronic pain).
- **Neurotransmitters:** Preganglionic nerves utilize Ach as their neurotransmitter, post-ganglionic nerves will vary (**adrenergic will utilize NE and cholinergic will utilize Ach**)
- Neuraxial block will inhibit sympathetic fibers leading to **unopposed parasympathetic** control
- Parasympathetic nerves originate from **cranio-sacral** regions (CN III, VII, IX, X - S2/S4) (see Fig. 6.1, Chap. 6 of chronic pain)

Cardiovascular Effects

- Neuraxial block sympathectomy vasodilation **in both arterial and venous systems** [1]
- Venous vasodilation is **greater** than arterial vasodilation redistribution of central blood volume in splanchnic circulation and lower extremity **decreased preload** [2]
- Inhibition of cardioaccelerator fibers (T1-T4) can lead to **bradycardia** and **hypotension** [1]

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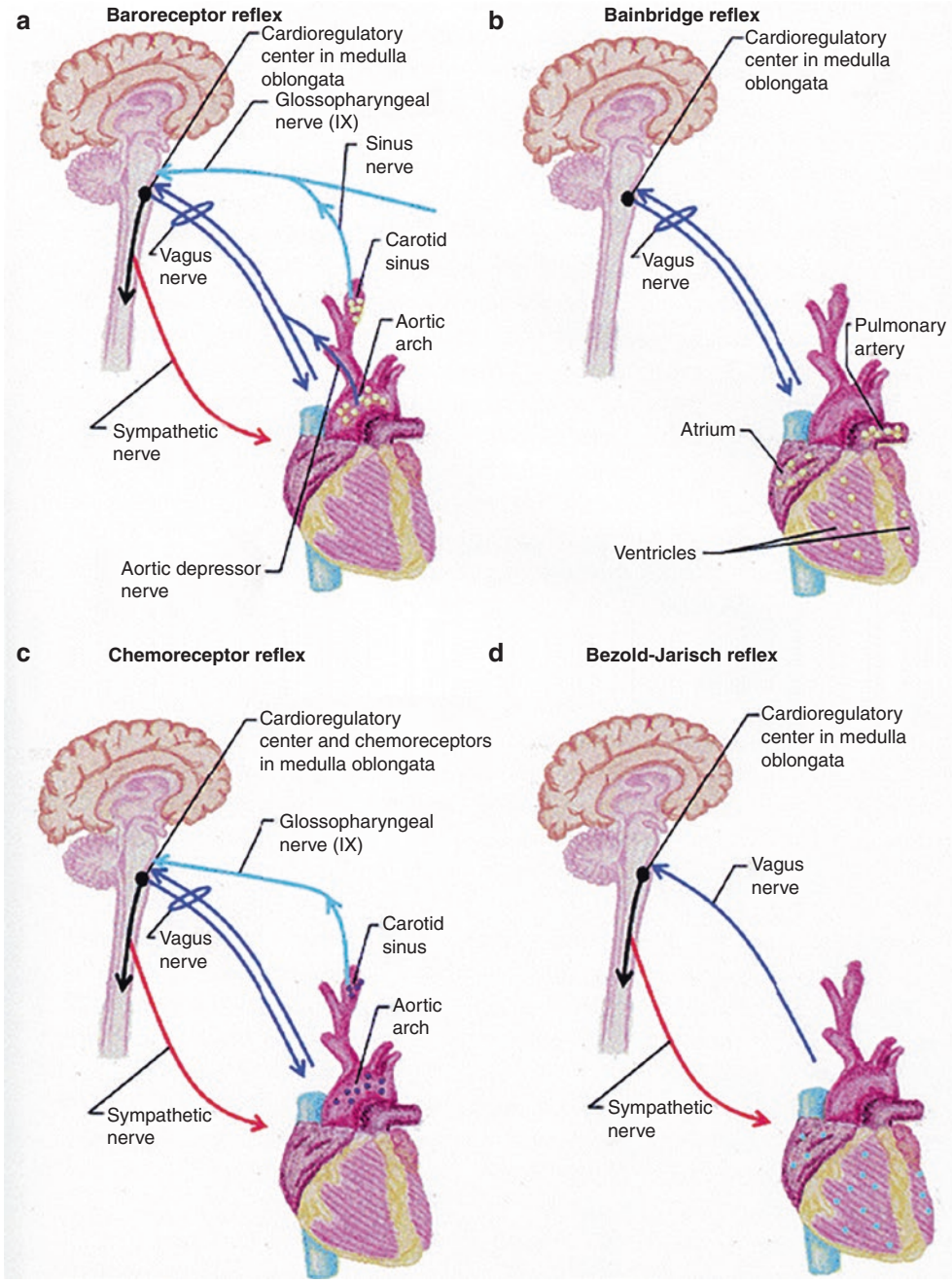
- **Bezold-Jarisch reflex (cardioprotective):** decreased preload → myocardial ischemia or infarction → activation of LV chemoreceptors and mechanoreceptors → increased parasympathetic activity → triad of hypotension, bradycardia, and coronary artery dilatation [1].
- **Bainbridge and reverse Bainbridge reflex:** distension of large veins or right atrium → activation of stretch receptors send vagal afferent signals to the cardiovascular center in the medulla → **inhibit parasympathetic activity** → tachycardia. Elderly patients have blunted reflex, which may cause persistent hypotension and "reverse" of the Bainbridge reflex.



Pulmonary Effects [2]

- Midthoracic block: has minimal effects since diaphragmatic function **phrenic nerve (C3-C5)** is maintained. FEV1/FVC ratio are unchanged, minimal changes in the inspiratory volume, vital capacity. It decreases pulmonary dysfunction after major thoracic or abdominal surgery by permitting **earlier extubation** and pain free ventilation
- Upper thoracic block or high spinal with **paralysis of accessory muscles** decreased peak expiratory flow, and expiratory reserve volume. Patient with COPD/chronic asthma may develop **hypoxia** as they rely on accessory muscles. These patients need extra caution.

Gastrointestinal Effects

- Gastrointestinal organs have sympathetic control from **T6-L1** and parasympathetic control from vagus nerve **(CN 10)** [2]
- Neuraxial anesthesia sympatholysis increased parasympathetic activity relaxed sphincters and peristalsis improved gastrointestinal motility after abdominal surgery (reduced the time to first flatus and first bowel movement)

Genito-Urinary Effects

- The urinary bladder innervation: the visceral afferent fibers (Aδ and C) arise from the bladder wall (stretch receptors). The parasympathetic fibers (S2-S4) cause c**ontraction** of the detrusor and relaxation of the neck, permitting micturition. The sympathetic fibers (T10 to L2) **relaxes** the detrusor muscle and close the internal urethral sphincter [3].
- Neuraxial blockade sacral spinal cord segments (S2-S4) blockade of afferent and efferent from and to the bladder **no sensation of urgency to void**; a dull feeling of maximal filling of the bladder present [3].
- The recovery of detrusor block (regaining ability to contraction) takes **several hours** and depends on duration of sensory block above the S2 and S3 sacral segments [4].

Central Nervous System

- Neuraxial blockade can cause sedation by **decreasing afferent input to the reticular activating system** in the brain. Sedatives should be administered in **decreased** dose.
- Cerebral blood flow remains **unchanged** unless systolic blood pressure drops <50.
- Decrease in metabolic rate below the level of the block decreases heat production, **shivering**, and vasoconstriction.

Endocrine Effects

- The hypothalamic–pituitary axis and the sympathetic nervous system are activated by surgical trauma [1].
- Neuraxial blockade can reduce the glucose, ACTH, cortisol, GH and epinephrine release due to **acute stress response** but cytokine responses are unchanged [5].

Metabolic Effects

- Normal surgical stress response causing catabolism leading to loss of muscle is inhibited
- Neuraxial blockade in the absence of surgical stress exerts only minimal influence on metabolism but it has been shown to **ameliorate stress induced hyperglycemic response** to surgery [5]
- Sympathetic efferent blockade at T2 impaired the acute **plasma insulin response to an intravenous glucose** load in patients before elective surgery but T9-T12 blockade had no effect [6]

- **Preserves renal function** by preventing loss of excretory function

MCQ

1. Which set of nerve fibers is most sensitive to local anesthetics?
   A. Visceral nerve fibers
   B. Pain nerve fibers
   C. Sympathetic nerve fibers
   D. Motor nerve fibers
2. A 25-years-old F G2P1 presents for labor and delivery for urgent C-section. A spinal with 12 mg of bupivacaine, 0.2 mg morphine, 15 mcg of fentanyl is given intrathecally. The patient soon experiences a decrease in blood pressure. What is the mechanism for this change?
   A. Arterial vasodilation
   B. Decreased preload
   C. Direct myocardial depression
   D. Venous vasoconstriction
3. A 30-years-old F G3P2 presents for scheduled C-section. She is administered a CSE. What is the expected effect on the GI system?
   A. Decreased peristalsis
   B. Decreased secretions
   C. Relaxation of sphincter tone
   D. Increased acid reflux
4. Which of the following is correct effect of neuraxial blockade on urinary bladder?
   A. T10-T12 blockade cause urinary retention
   B. No sensation of urgency to void
   C. No sensation of maximal filling of the bladder
   D. S1-S2 blockade cause urinary retention
5. What pulmonary function parameters are affected by mid-thoracic neuraxial blockade?
   A. Decreased FEV1/FVC
   B. Increased FEV1/FVC
   C. Decreased TV
   D. normal FEV1/FVC

Answers

1. C, 2. B, 3. C, 4. B, 5. D

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16 Neuraxial Block: ASRA Guidelines on Implications of Anticoagulants and Platelet Inhibitors

Adrian J. Maurer and Linda Le-Wendling

Introduction

- **The incidence of spinal and epidural hematomas increased significantly after the introduction of enoxaparin** to United States in 1993. Subsequently, in 1998, the American Society of Regional Anesthesia and Pain Medicine (ASRA) developed a Consensus Statement to guide anticoagulation management in patients receiving regional or neuraxial interventions, which has been revised three times (2003, 2010, 2018) [1].
- There is a **separate set of guidelines for chronic, interventional pain procedures**, stratified by procedure and risk of bleeding. The most notable difference between these two set of guidelines is for nonsteroidal anti-inflammatory drugs (NSAID)/aspirin cessation, unfractionated heparin (UFH), and the direct oral anticoagulants [2].

Fibrinolytics/Thrombolytics or Clot Busters (Alteplase, Streptokinase, Urokinase)

- Drugs used after myocardial infarction when percutaneous coronary intervention is not available. They dissolve fibrin clots and may decrease levels of both plasminogen and fibrin. Moreover, clot lysis fibrin degradation products inhibits platelet aggregation. Patients also receive IV heparin to maintain PTT of 1.5–2 times normal and clopidogrel/aspirin.
- **Avoid neuraxial anesthesia for 48 hours after discontinuation of thrombolytic/fibrinolytic medications**, and obtain documentation of normal clotting parameters and fibrinogen level.

Unfractionated Heparin (UFH) – IV/Subcutaneous

- Subcutaneous heparin effects are **delayed by 1–2 hours**.
- Heparin activity can be monitored with aPTT, anti-factor Xa assay, and ACT.
- May be rapidly reversed with protamine.
- To evaluate the possibility of **heparin-induced thrombocytopenia**: in patients receiving UFH for > 4 days, **check platelet count** prior to neuraxial procedure or catheter removal.

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- subcutaneous low-dose UFH can be given **IMMEDIATELY** after epidural placement.
- High-dose prophylactic subcutaneous UFH is 7500–10,000 U/dose; total dose < 20,000 U/day. Therapeutic UFH is considered >10,000 U/dose; total dose > 20,000 U/day.

Low-Molecular Weight Heparin (LMWH) (Enoxaparin, Dalteparin, Tinzaparin)

- **LMWH are partially REVERSIBLE with protamine**. **Renal function affects clearance.**
- Over **100 neuraxial hematomas** have been reported in patients receiving enoxaparin, including more than 40 within the first five years of introduction.
- Heparin-induced thrombocytopenia can also occur in patients receiving LMWH, and platelet counts should be checked prior to neuraxial procedure or catheter removal.
- In the setting of bloody placement of a neuraxial needle/catheter, initiation of LMWH should be delayed for **24 hours postoperatively.**
- Prophylactic LMWH (30 mg BID or 40 mg once daily)
  - Once daily dosing:
    - Indwelling neuraxial catheters ARE NOT CONTRAINDICATED.
  - BID dosing:
    - For any neuraxial technique, wait ε 12 hours after needle placement before restarting LMWH; ideal resumption is on POD1, **and indwelling neuraxial catheters should be removed** prior to starting postoperative LMWH.
- Therapeutic LMWH (1 mg/kg BID, or 1.5 mg/kg once daily)
  - If neuraxial procedure is strongly desired, wait 24 hours before placement. Consider checking **anti-factor Xa activity**, especially in the elderly and in patients with renal insufficiency.
  - Low-bleeding-risk surgery: wait ε 24 hours to resume postoperatively.
  - High-bleeding-risk surgery: wait 48–72 hours to resume postoperatively.
  - Indwelling neuraxial catheters not recommended. LMWH can be restarted ε 24 hours after needle/catheter placement OR 4 hours prior to the first postoperative dose of LMWH, whichever is greater.

Fondaparinux

- Inhibits factor Xa indirectly by binding to antithrombin. It is a long-acting drug with half-life of 20 hours but can be prolonged in ESRD.
- No ASRA recommendation. ESA recommends waiting 48 hours after the last dose.

Direct Oral Anticoagulant (Rivaroxaban, Apixaban, Edoxaban, Betrixaban)

- These are highly selective factor Xa inhibiting agents and their clearance highly depends on renal function. Agent-specific anti-factor Xa assays can be used, but there are no recommendations for abnormal values.
- **Andexanet alfa is reversal agent for rivaroxaban and apixaban**; unactivated/activated prothrombin complex concentrates (PCCs/aPCCs/FEIBA), recombinant factor VIIa used for reversal.

Vitamin K Antagonists (Warfarin)

- In general, warfarin should be stopped, **ideally ε 5 days prior to surgery,** and **INR normalized** prior to neuraxial procedure.
- Patients are **paradoxically hypercoagulable** within the **first 24 hours of initiating warfarin therapy**. Removal within 12–14 hours after initial warfarin administration does not appear to increase neuraxial bleeding risk. In patients receiving postoperative warfarin, neuraxial catheters should be removed when the INR is <1.5. The guidelines do not recommend correction of INR for epidural removal **unless it is >3.0**.
- These guidelines **do NOT apply to elevated INR from causes other than warfarin**.

Aspirin (ASA)/Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

- Aspirin irreversibly inhibits COX enzymes; NSAIDs are competitively reversible.
- **The acute and chronic pain guidelines differ with respect to NSAIDs;** perioperative regional guidelines have no specific recommendations for altered timing or dosing of aspirin or NSAIDs.
- In interventional chronic pain procedures, in high-risk procedures (eg. Spinal cord stimulator, intrathecal drug delivery device, vertebroplasty, etc.), aspirin should be stopped 6 days prior to procedure (if used primary prevention) and 4 days prior to procedure (if used for cardiovascular disease treatment). NSAIDs should be held based on 5-half-life elimination schedule.

Thienopyridines (Ticlopidine, Clopidogrel, Prasugrel)

- **Neuraxial hematomas and fatal hemorrhage** have occurred when performing neuraxial or deep blocks in patients on these agents, though recent updates in these guidelines allow a shorter time interval after stopping them and performing a regional procedure, based on surgical literature and experience.

Ticagrelor/Cangrelor

- Indwelling neuraxial catheters should be **avoided** with these drugs, which potently and reversibly inhibit platelet activation.

Platelet GP IIb/IIIa Inhibitors (Abciximab, Eptifibatide, Tirofiban)

- These are often administered in conjunction with ASA and heparin. Neuraxial procedures should be **avoided until platelet function has recovered** (abciximab: 24–48 hours, eptifibatide: 4–8 hours, tirofiban: 4–8 hours)

ASRA perioperative regional anesthesia antithrombotic/thrombolytic guidelines – fourth edition					
Agent	Min. interval before neuraxial procedure	Min. interval after neuraxial procedure	Recommendations during indwelling neuraxial catheter	Min. interval for indwelling catheter removal	Min. interval after indwelling catheter removal
Fibrinolytics/Thrombolytics	ε 48 hours, plus normal labs	Generally avoid	Optimize for neuro exam	Normal fibrinogen level	
UFH - IV	4–6 hours	1 hour	Optimize for neuro exam	4–6 hours	1 hour
UFH - SQ					
5 K U BID or TID	4–6 hours	Immediately		4–6 hours	Immediately
7.5–10 K U BID or TID (<20 K U QD)	12 hours AND assess coagulation status	Not established		Not established	Not established
>10 K U/dose (>20 K U QD)	24 hours AND assess coagulation status	Not established		Not established	Not established
LMWH					
(Prophylactic)	12 hours	12 hours	OK if once/daily dosing	12 hours	4 hours
(Therapeutic)	24 hours	24–72 hours (assess surgical bleeding risk)			24 hours after placement or 4 hours after removal, whichever is greater
Fondaparinux					6 hours
Rivaroxaban	72 hours	6 hours		22–26 hours	
Apixaban	72 hours	6 hours		26–30 hours	
Edoxaban	72 hours	6 hours		20–28 hours	
Betrixaban	3 days	5 hours		72 hours	
Direct thrombin inhibitors - IV	Avoid in general				
Direct thrombin inhibitors - oral	120 hours, less if renal function OK			34–36 hours	6 hours
Warfarin	5 days		With caution if INR < 3.0; daily INR and frequent neuro checks	When INR < 1.5	
Aspirin	No restrictions				
NSAIDs	No restrictions				
Thienopyridines	Clopidogrel and prasugrel: 5–7 days Ticlopidine: 10 days	Immediately if not loading dose; otherwise 24 hours postop	May be maintained for 1–2 days; AVOID if on prasugrel		6 hours
Ticagrelor	5–7 days	Immediately if not loading dose. If patient undergoes surgery: 24 hours postoperatively			No loading dose: immediately Loading dose: 6 hours
Cangrelor	3 hours	8 hours, or 24 hours if patient underwent surgery	Avoid	Remove prior to starting	8 hours
Platelet GP IIb/IIIa inhibitors	Abciximab: 24–48 hours Eptifibatide and tirofiban: 4–8 hours		Avoid		
Cilostazol	2 days		Avoid		6 hours
Dipyramidole	24 hours		Avoid		6 hours

Clinical Pearls

1. Neuro exams should be performed at least every 2 hours in patients at high risk for neuraxial hemorrhage. The most common presenting symptom is **progressive sensory and motor block**.
2. Renal function is important in the elimination of most of these agents. Suboptimal renal function may **prolong the interval** needed to safely perform neuraxial procedures.
3. Chronic pain procedure guidelines differ with respect to ASA and the NSAIDs; they are more conservative than the perioperative regional anesthesia procedure guidelines.

Questions

1. A 45 years old man with history of DVT is receiving 5000 U of SQ heparin BID. Which of following will need to be checked prior to neuraxial anesthesia?
   A. INR
   B. ATT
   C. ACT
   D. Platelet count
2. What is the minimum time interval to stop aspirin if a patient is taking it for cardiovascular disease for epidural placement for a Whipple procedure?
   A. no restriction
   B. 3 days
   C. 4 days
   D. 6 days
3. A patient with multiple bilateral rib fractures undergoes thoracic epidural catheter placement for analgesia. Subsequently, the primary service wishes to start enoxaparin. Which of the following is the best application of ASRA guidelines?
   A. Once-daily dosing, wait 12 hours after placement before first dose, hold 12 hours prior to removal.
   B. Once-daily dosing, wait 4 hours after placement before first dose, and hold for 12 hours prior to removal.
   C. Twice-daily dosing, wait 12 hours after placement before first dose, and hold for 12 hours prior to removal.
   D. Twice-daily dosing, wait 24 hours after placement before first dose, and hold for 12 hours prior to removal.
4. A patient held her clopidogrel appropriately prior to total knee arthroplasty, performed under spinal anesthesia. Postoperatively, what is the optimal time frame for restarting this agent?
   A. Immediately
   B. 6 hours
   C. 12 hours
   D. 24 hours
5. ASRA guidelines do not recommend correcting INR prior to removal of epidural catheter for patients receiving warfarin, unless it is above what threshold?
   A. 1.5
   B. 2.5
   C. 3.0
   D. 3.5

Answers

1. D, 2. A, 3. A, 4. D, 5. C

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Further Reading

https://rapm.bmj.com/content/rapm/43/3/263.full.pdf.

17 Lower Extremity Blocks: Sciatic Nerve Block and Lateral Femoral Cutaneous Nerve Block

Nasir Hussain and Michael Kushelev

Introduction

- Sciatic nerve block provides anesthesia to the leg below the knee, with the exception of the saphenous nerve distribution. Combined with adductor canal block, it provides analgesia for surgery of the distal anterior thigh; anterior knee; and lateral calf, ankle, or foot.
- The long path of the sciatic nerve allows for varying techniques for needle positioning.
- The lateral femoral cutaneous nerve block is a less frequently utilized nerve block that targets the lateral aspect of the thigh and is thought to be a purely sensory nerve.

Sciatic Nerve Block

Anatomy

- The sciatic nerve is the **largest and longest peripheral nerve** in the body and originates from the L4-S3 (Fig. 17.1a) spinal nerve roots.
- The spinal nerve roots converge to form the sciatic nerve on the anterior surface of the sacrum and exit the pelvis through the greater sciatic foramen (Fig. 17.1b) inferior to the piriformis muscle. The nerve then emerges approximately halfway between the greater trochanter of the femur and the ischial tuberosity at the infragluteal crease.
- At this point the sciatic nerve is positioned lateral to the long head of the biceps femoris (Fig. 17.1b) for 3–4 cm, before diving deep and medial to it as the muscle traverses obliquely along the posterior thigh.
- The nerve subsequently courses through the posterior thigh, providing several smaller cutaneous and muscular branches, and divides into the common peroneal and posterior tibial nerves around the popliteal fossa.
- The tibial component **is medial** and the fibular/peroneal component **is lateral**.

Indications

- Primarily used for orthopedic surgery of the lower leg including hip, tibia, fibula, knee (posterior), ankle, foot and amputations above and below the knee.
- Does not cover skin on medial aspect, especially in foot and ankle procedures (Fig. 17.1c).
- Most surgical procedures of the knee may require a sciatic nerve block for maximum analgesic benefit.

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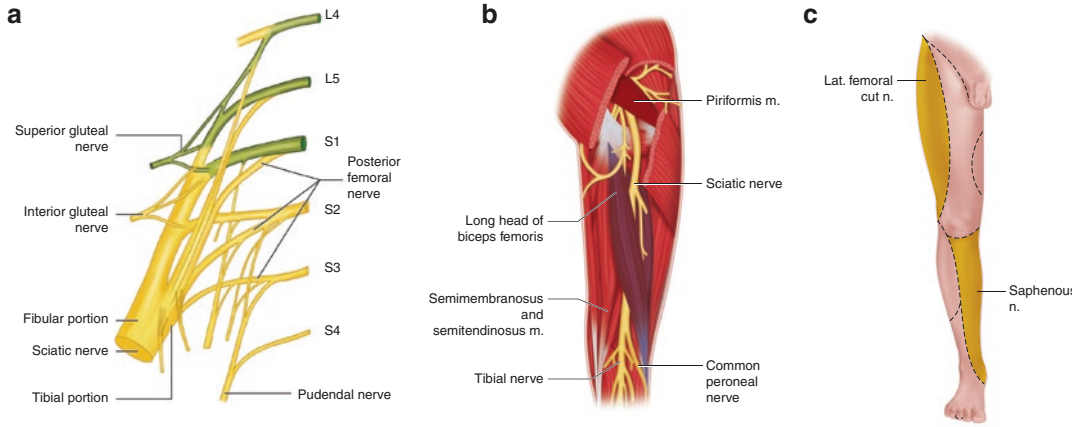

Fig. 17.1 (**a**) Lumbosacral plexus depicted with its branches; (**b**) Anatomic course of the sciatic nerve as it courses through the posterior thigh; and (**c**) Nerves and the corresponding distributions that are not covered by the sciatic nerve

Technique

- The long course of the sciatic nerve allows for multiple approaches. The ideal approach depends on anticipated surgical approach, body habitus, underlying coagulopathy, and underlying trauma that may limit the patient's ability to be positioned. Below are all approaches, with the most common ones being discussed in more detail.

Approaches

- *Parascaral* – most proximal approach and may supplement lumbar plexus blockade for major hip surgery.
- *Classic posterior (Labat)* – may be less predictable with patients of larger body habitus.
- *Anterior* – used as an option in patients that will not tolerate repositioning. Must be careful to identify and avoid the femoral nerve.
- *Infragluteal* – an **ideal proximal approach** with easily identifiable and reproducible landmarks (Fig. 17.2a).
  - Other proximal approaches have a greater risk of vascular puncture (especially classic posterior).
  - Excellent site for catheter placement as it typically cephalad to surgical tourniquets for lower extremity surgeries.
  - Can be performed using any combination of nerve stimulator or ultrasound guided techniques (Table 17.1).
  - Patient is placed in the lateral decubitus position with the side to be blocked as non-dependent and with the hip and knee flexed approximately 90° (Fig. 17.2a).
  - For young children, a high-frequency linear probe (10–5 MHz), and adult patients, a curved, lower-frequency (5–2 MHz) probe may be used.
  - The sciatic nerve can be first located in the sub-gluteal region at approximately the midpoint between the greater trochanter and ischial tuberosity and then traced proximally.
  - The gluteus maximus muscle will be visible superficial and posterior to the sciatic nerve (Fig. 17.2c).
  - The needle is inserted in-plane from the lateral aspect of the transducer and positioned with the tip of the needle adjacent to the nerve. Ideally want to deposit local anesthetic on both medial and lateral borders of sciatic nerve. After negative aspiration, approximately 20 mL of local anesthetic is injected in 5 mL increments.

Ultrasound Versus Nerve Stimulation

- Use of nerve stimulation **highly suggested** for most proximal approaches since one may have **poorer visibility** on ultrasound.
  - Plantar flexion/inversion preferred over dorsiflexion/eversion.

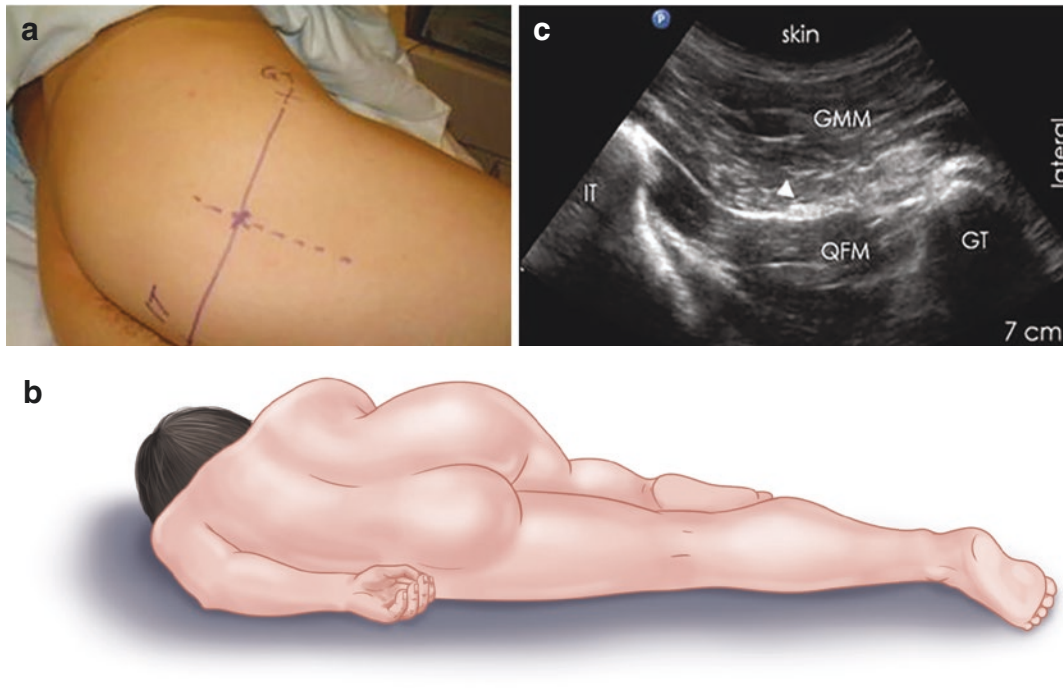

Fig. 17.2 (**a**) Anatomic landmarks for infragluteal approach for sciatic nerve block. Note that the sciatic nerve location is marked between the ischial tuberosity and greater trochanter; (**b**) Positioning of patient in lateral position for infragluteal approach for sciatic nerve block; and (**c**) ultrasound image for the infragluteal approach. Note that the gluteus maximus muscle (GMM) is visualized in addition to the greater trochanter (GT), ischial tuberosity (IT), and quadratus femoris muscle (QFM). The arrow indicates the location of the sciatic nerve

Table 17.1 Motor response and necessary needle redirection when performing the sciatic nerve block in the infragluteal location

Motor response	Needle contact	Needle adjustment	Comments
Foot dorsiflexion	Deep peroneal nerve	Slight medial adjustment	Adequate especially for catheter placement
Foot eversion	Superficial Peroneal nerve	Medial adjustment	Significantly lower success rate
Foot plantar flexion	Posterior tibial nerve	None needed	Associated with high rate of success
Foot inversion	Combination of tibial and peroneal nerves	None needed	Indicator of block of both branches of sciatic nerve
Bony contact	Femur	Medial adjustment	
No stimulation	Likely biceps femoris	Lateral adjustment	Reassess landmarks and palpate the long head of biceps femoris

  - Plantar flexion or inversion at <0.4 mA associated with nearly 100% sensory and motor blockade [1].
- Ultrasound for sciatic nerve blocks have consistently demonstrated to decrease needling time and increase the rate of complete sensory blockade [2].

Clinical Pearls

- The sciatic nerve provides motor function to all the skeletal muscles **below the knee** and sensory innervation for the **lateral half of the leg** and **most of the foot** (Fig. 17.1).
- Sonoanatomical landmarks can aid in recognizing the sciatic nerve at the Sub-gluteal

space: gluteus maximus, (superficial), ***ischial tuberosity*** (medial), ***greater trochanter*** (lateral) and quadratus femoris (deep) (Fig. 17.2c)
- For distal foot surgeries that are less invasive, like a bunionectomy, an ankle block (Chap. 21, Regional anesthesia) may be a better choice as distal blocks are associated with lower incidence of postoperative nerve injury [3].

Lateral Femoral Cutaneous Nerve (LFCN) Block

Introduction

- Purely sensory nerve, no motor component, and a branch of lumbar plexus (See Fig. 19.1, Chap. 19, Regional Anesthesia).
- Innervates anterolateral and lateral thigh (Fig. 17.1c).
- Arises from the anterior branches of L2-L3 and emerges from the lateral border of the psoas major muscle. It then divides into an anterior and posterior branch (Fig. 17.3a). The anterior branch courses inferiorly and laterally toward the anterior superior iliac spine, underneath the inguinal ligament, to the sartorius muscle, and into the thigh.

Indications

- Skin graft of lateral thigh.
- Diagnosis of meralgia paresthetica.
- Surgical procedures of anterolateral and lateral thigh.
  - Anesthesia of thigh along with other nerve blocks
  - Analgesia for total hip arthroplasty
  - Skin graft donor sites

Technique

- *Infiltration*
  - 2 cm medial and inferior to the anterior superior iliac spine (ASIS)
- *Ultrasound*
  - Identification of the anterosuperior iliac spine (ASIS) is performed by palpation. Skin

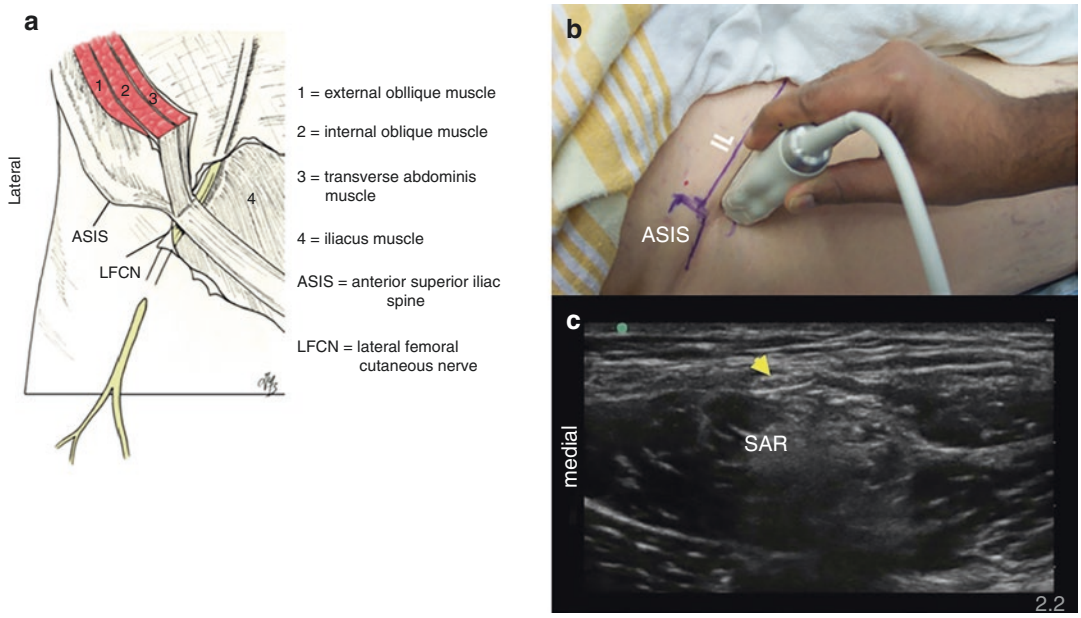

Fig. 17.3 (**a**) Anatomic course of the lateral femoral cutaneous nerve; (**b**) Location of ultrasound transducer placement for nerve identification. Note that the probe is placed medial to the anterior superior iliac spine along the inguinal ligament; and (**c**) Ultrasound guided image of nerve block with the nerve located over the sartorius (SAR) muscle when scanned proximally

marking is placed with surgical ink ~2 cm inferior and ~2 cm medial to the ASIS.
  - A linear transducer (10–12 MHz) is placed immediately medial to the ASIS along the inguinal ligament. The lateral end of the transducer is placed on the ASIS (Fig. 17.3b).
  - Inferior and medial to the ASIS, the lateral femoral cutaneous nerve is identified between the fascia lata and fascia iliacus using ultrasound.
  - Doppler is utilized to locate and avoid any nearby blood vessels.
  - The needle is passed in plane towards the lateral femoral cutaneous nerve under ultrasound guidance until the fascia is punctured and the needle tip is in the vicinity of the nerve (Fig. 17.3c).

Clinical Pearls

- Lower volume of local anesthetic (~5 mL) can be used to block the LFCN if careful ultrasound identification is performed.
  - The variations of the LFCN require careful tracing of the nerve to appreciate bifurcation points to ensure adequate block and allow for multiple locations for the nerve to be targeted.
- Up to 10 mL of local anesthetic is used for landmark guided approach with a fanning technique recommended.

Questions

1. The sciatic nerve derives from:
   A. L1-L5
   B. L2-S1
   C. L3-S2
   D. L4-S3
2. While performing a sciatic nerve block in a patient positioned prone utilizing an out-of-plane popliteal fossa approach a lateral angulation of the block needle is most likely to cause the needle to make initial contact with which branch of the sciatic nerve?
   A. Common peroneal
   B. Superficial peroneal
   C. Posterior tibial
   D. Saphenous
3. Inversion of the foot with a nerve stimulator at 0.5 mA while performing an infragluteal sciatic nerve block indicates stimulation of which nerve?
   A. Common peroneal
   B. Posterior tibial
   C. Sural
   D. Combination of common peroneal and posterior tibial
4. The biceps femoris is found where in relation to the sciatic nerve when performing an infragluteal sciatic nerve block?
   A. Lateral
   B. Medial
   C. Cephalad
   D. Caudad
5. While performing a sciatic nerve block utilizing a classic posterior (Labat) approach which of the following landmarks is not typically utilized?
   A. Posterior superior iliac spine
   B. Greater trochanter
   C. Anterior superior iliac spine
   D. Sacral hiatus
6. The lateral femoral cutaneous nerve can be found where in relation to the following anatomic structures?
   A. Superficial to the inguinal ligament
   B. Medial to the adductor longus muscle
   C. In between the fascial layers of the fascia lata and fascia iliaca
   D. Originating from the sacral plexus
7. Sciatic nerve block can be used for surgery in all except:
   A. Femur
   B. Ankle
   C. Foot
   D. Tibia
8. A 55-year-old man receives a sciatic block for foot surgery. During the surgery, the patient cries as the surgeon is touches the medial foot. What nerve needs to be blocked?
   A. Deep peroneal nerve
   B. Superficial peroneal nerve
   C. Sural nerve
   D. Saphenous nerve

9. Which of the following nerves does not originate from the sacral plexus?
   A. Femoral nerve
   B. Tibial nerve
   C. Superficial peroneal nerve
   D. Deep peroneal nerve
10. The LFCN derives from:
   A. L2
   B. L3
   C. L1 and L2
   D. L2 and L3
11. Landmark based LFCN block is performed using which of the following:
   A. 2 cm medial and 2 cm inferior anterior inferior iliac spine
   B. 2 cm medial and 2 cm inferior anterior superior iliac spine
   C. Just inferior to ASIS
   D. Just inferior to AIIS

Answers

1. D. The sciatic nerve is the originates from the lumbosacral plexus at the L4-S3 spinal nerves and is the largest and longest nerve in the human body.
2. A. The common peroneal is lateral to the posterior tibial nerve in the popliteal fossa. The superficial and deep peroneal nerve separate distal to popliteal fossa. The saphenous nerve is a branch of the femoral nerve.
3. D. The inversion motion is associated with stimulation of both the posterior tibial and peroneal branch of the sciatic nerve and is caused by muscular contraction of the tibialis posterior (innervated by the tibial nerve) and the tibialis anterior (innervated by the deep peroneal nerve)
4. B. At the gluteal fold the sciatic nerve lies just lateral to the long head of the biceps femoris with and is a useful marker for identifying the nerve with either US or NS.
5. C. The classic posterior approach is performed by identifying the posterior superior iliac spine, greater trochanter of the femur and the sacral hiatus typically with the patient in the lateral decubitus position.
6. C. The LFCN has significant anatomic variation, but is a distal branch originating from the lumbar plexus, exits below the inguinal ligament and is situated between the fascia lata and fascia iliaca.
7. A. The sciatic nerve primarily innervates muscles of the posterior thigh. In contrast, for surgeries of the femur, a nerve block targeting the femoral nerve would need to be performed which would anesthetize the anterior and medial thigh.
8. D. The saphenous nerve supplies the medial aspect of the foot and is a branch of the femoral nerve. It can be blocked by depositing anesthetic at the anterior border of the medial malleolus.
9. A. The femoral nerve derives from the lumbar plexus, specifically from the L2-L4 nerve roots. The tibial, superficial, and deep peroneal nerves are derived from the sciatic nerve, and thus the sacral plexus.
10. D. The LFCN is a branch of the lumbar plexus and is derived from the L2-L3 nerve roots.
11. B. Both under ultrasound guidance and through an anatomic approach, the LFCN can be found between the tensor fasciae latae muscle and sartorius muscle. This is located 2 cm medial and inferior to the anterior superior iliac spine.

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18 Lower Extremity Blocks: Femoral Nerve Block and Adductor Canal Block

Asma Khan and Mian Ahmad

Introduction

- Femoral nerve blocks were first described in the literature in 1952 [1]. Femoral nerve block provides effective anesthesia for anterior thigh surgery and post op analgesia for femur and knee surgeries.
- Femoral block with high volume of local anesthetic can also block **lateral femoral cutaneous**, and **obturator nerves**.
- When performed in combination with Sciatic nerve blocks, femoral block can provide adequate anesthesia for the lower extremity surgery **below the knee**.

Femoral Nerve

Anatomy

- Largest branch of the lumbar plexus.
- Origin- Posterior divisions of anterior rami of Lumbar 2, 3 and 4 nerves (Fig. 18.1).
- Course- It emerges from the posterior aspect of psoas muscle at the junction of its lower and middle third and passes under the inguinal ligament posterior to the iliac fascia to lie lateral to the femoral vessels in the femoral sheath. Divides 4 cm below the inguinal ligament into anterior and posterior divisions (Fig. 18.2). After giving off motor branches in the thigh it travels through the adductor canal as a sensory (saphenous) nerve and provides sensory supply to the medial aspect of leg and foot.

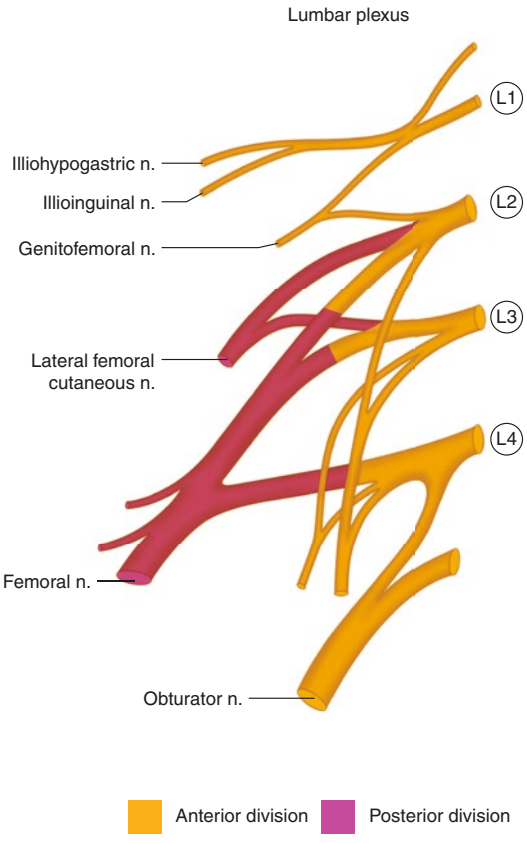

Fig. 18.1 Lumbar plexus

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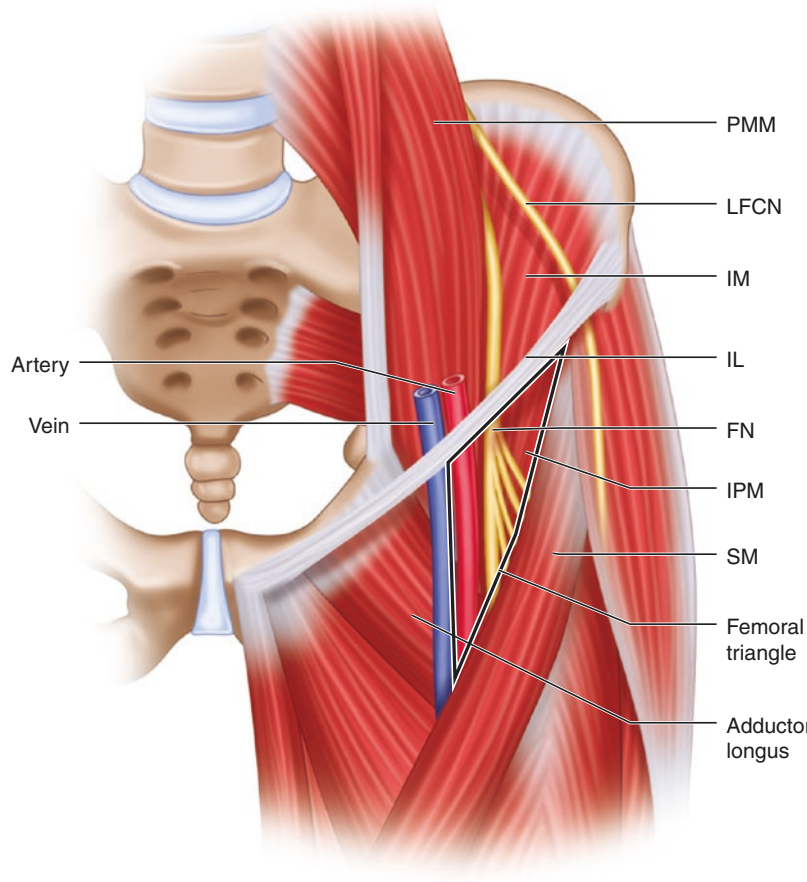

Fig. 18.2 Anatomy of femoral nerve and subinguinal region. FN femoral nerve, IL inguinal ligament, IM iliac muscle, IPM iliopsoas muscle, LFCN lateral femoral cutaneous nerve, PMM psoas major muscle, SM sartorius muscle. (Image is from 3D4Medical's Essential Anatomy 5 application. *Nerve Blockade and Interventional Therapy* pp. 217–219 by Springer. Reproduced with permission from springer))

- Femoral triangle: (Fig. 18.2)
  (a) Boundaries: Base- Inguinal ligament.
  Lateral border- Sartorius ms.
  Medial border- Adductor Longus ms.
  (b) Contents: Medial to lateral **(VAN)-** Femoral **VEIN,** Femoral **ARTERY** and Femoral **NERVE** (Fig. 18.2)
- Branches
  (a) Above the inguinal ligament- Motor supply to **Iliacus and Psoas major** muscles.
  (b) Below the inguinal ligament-
    (i) Anterior division: anterior cutaneous branches, branch to **Sartorius** and Pectineus.
    (ii) Posterior division: branch to **Quadriceps Femoris** and **Saphenous nerve**.

Indications

- Surgery on anterior aspect of thigh- Quadriceps tendon repair or quadriceps biopsy. Femur neck or shaft, knee, patella, medial aspect of leg (saphenous branch)- long saphenous vein stripping
- Post operative analgesia - hip fracture, femur or knee surgery.

Single Shot Anatomical Landmark/ Nerve Stimulator Technique

Patient position Supine.

Limb position Abducted (<45°), **externally rotated** and lateral border of foot resting on table.

Anatomical landmarks Inguinal ligament, femoral crease and femoral artery pulse.

Needle insertion Below the femoral crease, **1–2 cm lateral** to where the femoral artery is palpated.

Needle direction 30–45° to the skin in cephalad direction.

Current strength 1 mA or 0.1 msec/ 2 Hz.

Response

- Two pops of piercing Fascia lata and Fascia iliaca.
- Patellar twitch due to quadriceps stimulation
- Gradual decrease in stimulation with advancement of needle- inject 10–15 ml of local anesthetic.

Trouble Shooting Nerve Stimulation

Needle position	Response	Correction
Medial to femoral nerve	Vascular puncture- blood on aspiration	Withdraw and reinsert 1 cm lateral to the insertion point.
Anterior and medial to femoral nerve	Sartorius stimulation	Redirect needle medially and 1–3 mm deeper
Too deep	Bone contact and local stimulation of pectineus and iliopsoas muscle	Withdraw to skin and reinsert in another direction

Continuous Femoral Nerve Block [2]

Indication

- Postoperative analgesia for total hip replacement or major knee surgery.
- Analgesia in the emergency room or for manipulation of fractured femur or hip for exam.
- Analgesia for femur shaft or neck fracture.

Technique

- Femoral nerve is located with use of nerve stimulator after piercing fascia lata and iliaca.
- Catheter is inserted 5 cm beyond the tip of the needle.
- Optional to expand perineural space with fluids before insertion of the catheter [3].
- If the needle tip is not under fascia iliaca there will be difficulty in threading the catheter. Withdraw the needle and reinsert the needle, identify the loss of resistance for placement of needle tip under fascia iliaca.

USG Guided Femoral Nerve Block

- USG probe- High frequency linear probe. In morbidly obese patients sometimes curvilinear probe can be used.
- Probe position: Parallel to inguinal ligament in the inguinal or femoral crease.

Anatomy

- Femoral nerve- located approximately 2–6 cm deep to the skin surface. Identified as hyperechoic glistening oval/ triangular structure next to femoral artery.

Technique

- Identify femoral artery at femoral or inguinal crease.
- Sometimes two arterial structures could be seen- Deep artery of the thigh and femoral artery. Move the probe proximally till a single vessel (Femoral artery) is seen and identify the nerve lateral to femoral artery covered by fascia iliaca.

"3 in 1" Femoral Nerve Block

- Variation of femoral nerve block.
- Useful in severe proximal lower limb injuries.

- Nerves blocked- Femoral nerve, lateral femoral cutaneous nerve and obturator nerve.
- Same technique but pressure distal to the point of entry of the needle to force the local anesthetic spread proximally toward the above mentioned nerves.

Adductor Canal Block (Subsartorial or Hunter Canal) [4]

Anatomy

- Saphenous nerve- largest and terminal sensory branch of Femoral nerve.
- Origin- in the femoral triangle saphenous nerve branches off from the femoral nerve.
- Nerve root- L3-4 (Fig. 18.1).
- Supply- Prepatellar skin, anteromedial, medial and posteromedial aspect of leg.
- Branches- infrapatellar branch, sartorial branch and medial crural cutaneous branches.
- Approximately 10 cm above the medial femoral epicondyle saphenous runs a superficial course.

Indication

- Varicose vein surgery
- Saphenous vein harvest
- As part of multimodal analgesia for knee surgery
- Along with Sciatic nerve block to supplement for ankle or medial foot surgery.

USG Guided Adductor Canal Block

Patient Position Supine.

Limb Position abducted and **externally rotated** to expose medial aspect of the thigh.

Technique
Probe is placed transversely and anteromedially in the middle thigh. Femoral artery is identified deep to upturned boat shaped sartorius muscle.

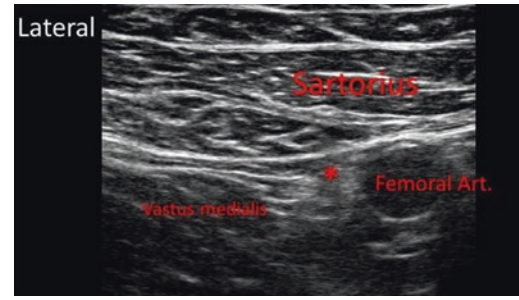

Fig. 18.3 Short axis ultrasound image of the adductor canal at the midthigh. *Saphenous nerve. (*Curr Anesthesiol Rep.* 2019;9:291–294) By Springer. Reproduced with permission from Springer)

Saphenous nerve can be identified as a **hyperechoic** structure positioned anterolateral to the femoral artery (Fig. 18.3). Needle is introduced from lateral to medial direction and spread of local anesthetic is observed around the artery while repeated aspiration is performed to avoid intravascular injection.

Complication Specific for Adductor Canal Block

- Vastus medialis nerve block resulting in Quadriceps weakness.

Clinical Pearls

- For Femoral nerve block in obese patients retract and **tape the abdominal wall** laterally. Downward displacement of the inguinal crease in obese patients compared to the inguinal ligament may make the needle entry too low (distal to the motor branches take off) leading to block failure.
- While utilizing nerve stimulation technique, do not confuse stimulation of medial side of thigh with patellar tap which is secondary to stimulation of the motor branch to sartorius muscle and will lead to block failure. **Place a hand on the patella** to confirm quadriceps stimulation.
- Femoral nerve is enclosed in sheath different from sheath enclosing femoral artery. During ultrasound guidance technique, ensure the

spread of the local anesthetic around the nerve.
- If it is difficult to identify the femoral artery, it can be traced down from the femoral crease down or popliteal crease up.

Questions

1. During performance of femoral nerve block using a nerve stimulator, a Sartorius twitch is noted in the thigh. What adjustment should be made to the tip of the needle to get the twitch of the quadriceps tendon (patellar tap)?
   A. Tip is too deep and medial, pull it back and direct laterally
   B. Tip is too superficial and lateral, go deeper and medial
   C. Tip is slightly medial and superficial, pull it back and direct it deeper and laterally
   D. Tip is slightly lateral, pull it back and move it medially
2. Femoral Nerve is formed by the:
   A. Dorsal rami of Lumbar L 2, 3 & 4 nerves
   B. Anterior divisions of the ventral Rami of Lumbar L2, 3 & 4 nerves
   C. Posterior divisions of ventral rami of lumbar L 2, 3 & 4 nerves
   D. Posterior divisions of anterior rami of L 3, 4 & 5 lumbar nerves
3. According to ASRA (American Society of Regional Anesthesia) practice advisory which of the following medication may be given for local anesthetic toxicity?
   A. Vasopressin
   B. Labetolol
   C. Atropine
   D. Low dose epinephrine
4. While performing an ultrasound guided adductor canal block, you are also using a nerve stimulator to ensure that the identified structure is really a nerve. What kind of response will reassure you that the identified structure is saphenous nerve?
   A. Muscle twitch on medial side of leg
   B. Muscle twitch on medial side of thigh
   C. Patellar tap
   D. No twitch

Answers

1. C
2. C
3. D
4. D

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Further Reading

NYSORA- New York school of Regional Anesthesia.
Open Anesthesia- Keywords.
USRA- Ultrasound for Regional Anesthesia.

19 Lower Extremity Blocks: Lumbar Plexus Block and Obturator Nerve Block

Ronny Chan, Yamah Amiri, and Tariq Malik

Lumbar/Psoas Plexus Block

Introduction

A lumbar plexus block/psoas compartment block used as a supplement to general anesthesia for lower extremity surgery and for management of postoperative pain.

Anatomy

- Lumbar plexus is located within the substance of the psoas muscle (Fig. 19.1).
- It is formed by the ventral rami of L1-L3 and contribution from L4. T12 contribute in few people.
- L1 divides into upper and lower branches: upper form iliohypogastric and ilioinguinal nerves(L1), while lower with a branch from L2 form genitofemoral nerve(L1, L2) (Fig. 19.1).
- L2-L4 split into dorsal and ventral branches. Ventral branches form obturator nerve (L2, 3, 4) and dorsal branches give rise to femoral nerve (L2, 3, 4), lateral femoral cutaneous nerve (L2, L3) (Fig. 19.1).
- Obturator nerve (L2, L3, L4) emerges on the medial side of the psoas muscle at pelvic brim (Fig. 19.1) and runs into the thigh via the obturator foramen where it divides into anterior and posterior division to innervate obturator externus and the three adductor muscles with articular branches to hip and knee joints. Obturator nerve has very variable skin supply within 57% of population it has no cutaneous supply, in 23% it innervates upper part of popliteal fossa, and in 20% it supplies inferomedial side of the thigh.

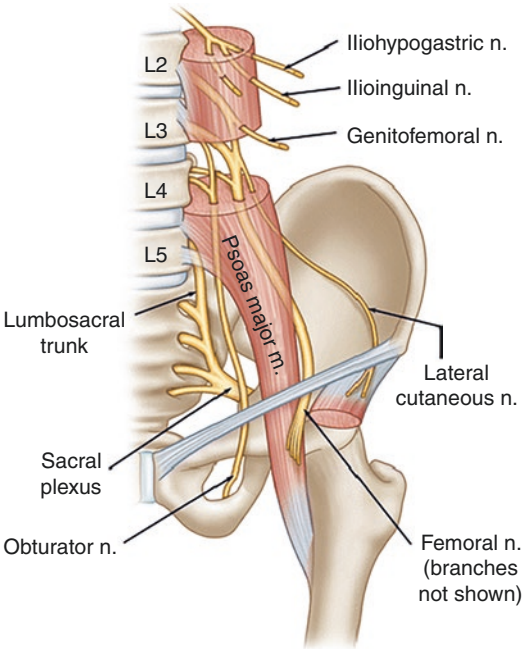

Fig. 19.1 Lumbar plexus anatomy. (Walji and Tsui [4])

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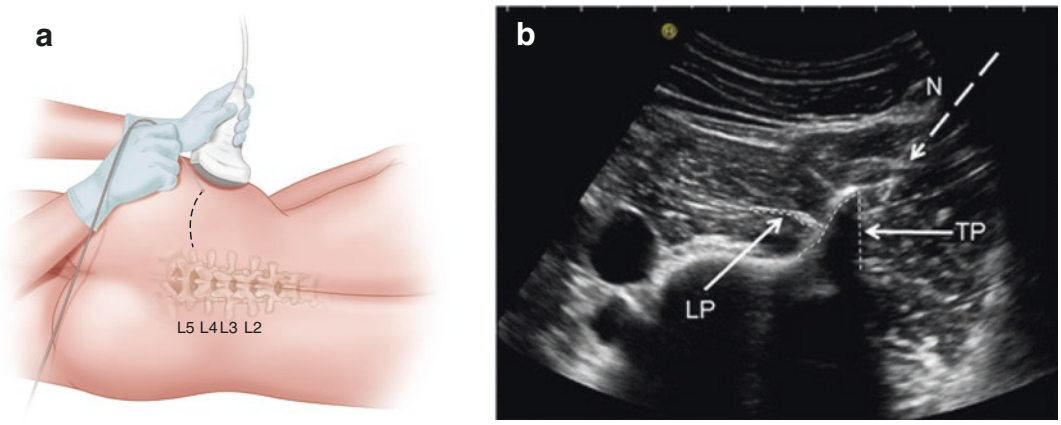

Fig. 19.2 (**a**) Schematic diagram of the probe placement and the puncture site during lumbar plexus block. (**b**) Ultrasound image and needle path. *TP* transverse process, *LP* lumbar plexus, *N* needle. (Reproduced from open access article by Lu et al. [5])

- The lumbar plexus lies deep within the posterior one-third of the psoas major muscle, which can be difficult to visualize with ultrasound.

Indications

- Hip and knee arthroscopy or replacement surgery

Contraindications

The lumbar plexus block is considered a deep block and contraindications should be considered similar to neuraxial epidurals or spinals.

Technique

Ultrasound-guided approach.

- Ultrasound guidance provide real-time view of psoas muscle improving safety of the block
- Lumbar plexus itself is not usually visible.
- Block is done at L4 level (Fig. 19.2).
- Capdevilla approach: Three lines are drawn: a horizontal over the L4spinous process (Tuffier's line), another vertical line from posterior.

  superior iliac spine up parallel to the midline. The needle is inserted.

  2/3 rd of the way on the L4 spinous process line from the midline (Fig. 19.2).
- US guidance: Patient is placed in lateral position (Fig. 19.2).
- The curved, low-frequency ultrasound transducer is placed just above the iliac crest directing ultrasound beam towards the L4vertebral body visualizing spinous process, transverse process/facet.

  joint, and side of the vertebral body. The three muscles attached to the.

  side of the vertebral body are visualized: quadratus lumborum,

  erector spinae, and psoas major (Fig. 19.2b). The three muscles looks like a shamrock leaf, hence technique is also called the shamrock technique.
- The full length of the needle should be seen as it approaches the target structure, which is the posterior third of the psoas major muscle. After negative aspiration, a large volume of local anesthetic is injected in 5 mL increments, up to 0.5 mL/kg is required.

Complications

- Epidural spread (1–10%)
- Intrathecal spread
- Intravascular uptake
- Renal capsule puncture
- Nerve damage
- Vascular puncture/ hematoma requiring blood transfusion

Clinical Pearls

- The lumbar plexus is **very close to neuraxial space**; test dose is strongly recommended to rule out intravascular or intrathecal placement.

- It's a volume block, requiring injection of 20–30 ml given slowly over 5–10 minutes
- In-plane needle approach using **shamrock technique** with real time visualization of local anesthetic on injection is best way to avoid complications.

Obturator Block

Obturator Nerve (L2, L3, L4; Fig. 19.1)

- Motor Innervation
  - Anterior branch: adductor longus, part of brevis, gracilis
  - Posterior branch: obturator externus, adductor brevis, magnus
- Sensory innervation:
  - Hip joint/ knee joint
  - Femur
  - Adductor muscles
  - Skin over the medial side of the thigh

Indications

- Transurethral resection of bladder Tumor or prostate surgery under spinal to prevent adductor contraction when electrocautery is used intraoperatively
- Analgesia for total knee replacement
- ACL reconstruction
- Analgesia for harvesting of gracilis tendon for ACL reconstruction

Technique

- Landmark
  - Supine position with hip abducted, knee flexed, and leg in external rotation
  - Palpate the pubic tubercle A nerve stimulating needle is inserted 1–1.5 cm lateral and inferior to tubercle
  - Advance the needle to contact bone
  - Withdraw the needle a little and redirect trajectory laterally (45°) slowly; advance until adductors muscle twitch is obtained with the nerve stimulator at appropriate setting (0.3–0.5 mA) After negative aspiration, 5–10 mL of LA is injected in 5 mL increments, with gentle aspiration between injections.
- Ultrasound guidance: The ultrasound probe is placed in the inguinal crease and the femoral vein is identified. The probe is moved medially to visualize the pectineus and adductor longus muscles. The needle is inserted in-plane and is directed to the two intermuscular fascial planes. After negative aspiration, 5–10 mL of local anesthetic (LA) is injected into each of the intermuscular fascial plane (Fig. 19.3).

Clinical Pearls

- The obturator nerve runs **close to the lateral bladder wall**, where direct stimulation with the scope can result in adductor spasm.
- This block provides anesthesia of the **medial distal thigh** and can be used in conjunction with femoral and sciatic blocks for procedures on the distal thigh and to prevent tourniquet pain during lower leg surgery.

Questions

1. The lumbar plexus gets contribution from:
   A. Ventral rami of L1-S1
   B. Dorsal rami of L2-L4
   C. Ventral Rami of L1-L4
   D. Dorsal Rami of L1-L5
2. Which of the following option best describes the correct location of the needle tip for lumbar plexus block?
   A. Contraction of the psoas muscle
   B. Contraction of psoas muscle at
   C. Contraction of quadriceps femoris
   D. Contraction of erector spinae muscle
3. During placement of lumbar plexus block, the patient receives 20 ml of 0.5% bupivacaine after negative test dose. Immediately she develops severe hypotension followed by cardiac arrest. The most likely diagnosis is
   A. Intraperitoneal injection of local anesthetic
   B. A common side effect of a properly done psoas plexus block

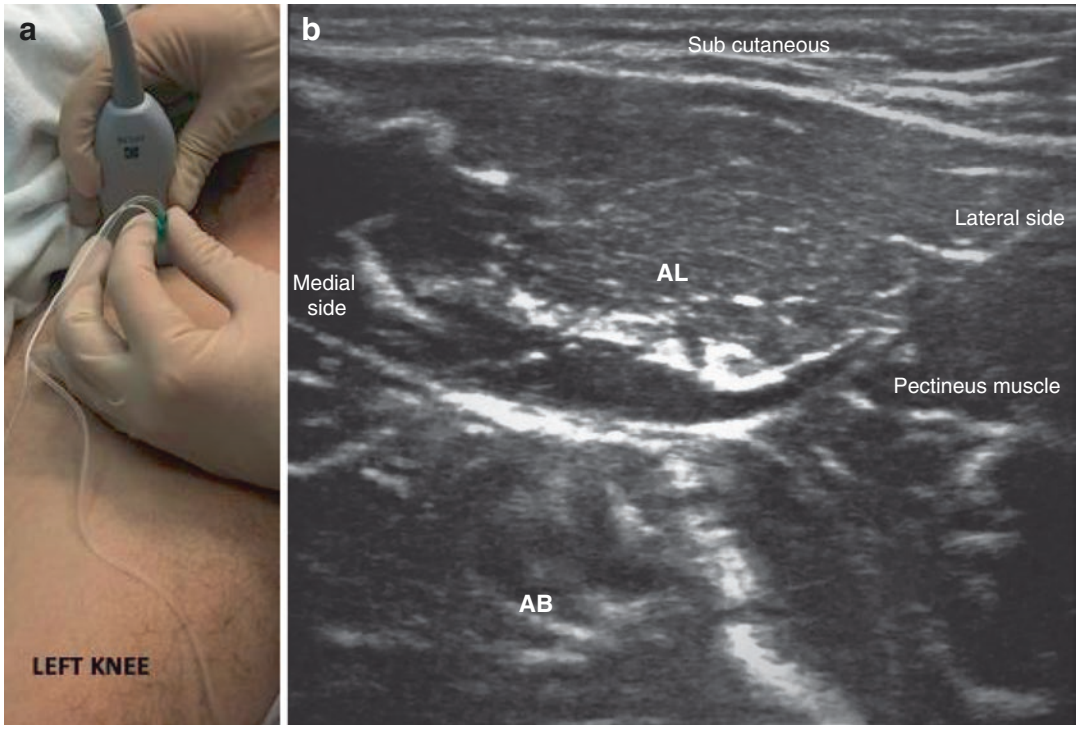

Fig. 19.3 Obturator nerve block. (**a**) Probe is positioned medial to the femoral artery (**b**) adductor longus (AL) muscle is visualized. Local anesthetic (LA) infiltrated between intermuscular plane of adductor longus (AL) and brevis (AB)

C. Spread of local anesthetic to epidural space
D. Intrathecal injection of local anesthetic

4. The Obturator nerve originates from:
   A. the dorsal branches of lumbar plexus
   B. the ventral branches of the lumbar plexus
   C. has contribution from L1
   D. has contribution from L5
5. The block of the obturator nerve is best demonstrated with which of the following findings?
   A. Sensory loss to pinprick on the medial side of the thigh
   B. Sensory loss to temperature in the back of the knee
   C. Sensory loss to touch on the medial side of the knee
   D. Weakness of abductor muscle group of the hip joint.

Answers

1. 1. C, 2. C, 3. D, 4. B (Fig. 18.1, Chap. 18, regional anesthesia), 5. A

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Lower Extremity Blocks: Popliteal Sciatic Block

20

Katherine L. Koniuch and Jacob E. Pollard

Introduction

- Blocking the sciatic nerve at the level of the popliteal fossa provides reliable anesthesia and/or analgesia of the lower extremity with the exception of the **medial aspect** of the lower leg, ankle and foot
- The block can be performed under ultrasound guidance or with nerve stimulation
- A peripheral nerve catheter can be placed to provide prolonged analgesia

Anatomy

- The sciatic nerve originates from the spinal cord roots of L4-L5 and S1-S3
- It exits the pelvis through the sacrosciatic foramen and courses down the posterior thigh into the popliteal fossa
- The popliteal fossa is bordered medially by the semimembranosus and semitendinosus muscles, laterally by the biceps femoris, and inferiorly by the heads of the gastrocnemius (Fig. 20.1b)
- In the popliteal fossa, the sciatic nerve branches into the tibial and common peroneal nerves
- The tibial nerve continues down the posterior leg while the common peroneal nerve courses laterally around the head of the fibula
- At the level of the popliteal fossa, the nerves lie superficial and lateral to the popliteal artery and vein
- The sensory distribution of the sciatic nerve at the popliteal fossa includes the lower leg, ankle, and foot with the exception of the medial portion of the leg and ankle [1]

Indications

- Surgical anesthesia of the foot, ankle, or lower leg
- Analgesia of the foot, ankle, or lower leg

Technique

- Sciatic nerve blockade at the popliteal fossa can be performed from a posterior, lateral or medial approach
- The block can be performed with prone (Fig. 20.1a), lateral decubitus, or supine position

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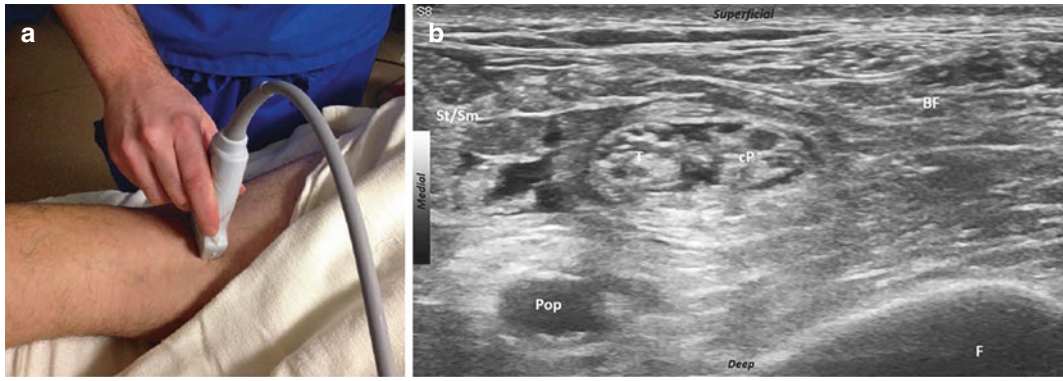

Fig. 20.1 (**a**) popliteal block with prone positioning. (**b**) Optimal site for popliteal sciatic nerve block as tibial (T) and common peroneal (cP) nerves branch out distally from sciatic bifurcation. *Pop* popliteal artery, *St/Sm* semitendinosus/semimembranosus muscles, Bf biceps femoris muscle, F femur. ((**b** is reproduced with permission from Springer) Ref: *Cardiovasc Intervent Radiol*. 2018; 41:43–48)

- **Ultrasound-guided**:
  - The ultrasound probe is placed on the posterior thigh in transverse orientation at the level of the popliteal crease
  - The popliteal artery and vein are visualized superficial to the femur
  - The sciatic nerve is identified as a hyperechoic honeycomb-like structure superficial and lateral to the popliteal artery and vein (Fig. 20.1b)
  - Branching of the sciatic nerve into tibial and common peroneal nerves can be visualized as the transducer is moved distally in the popliteal fossa
  - **Tilting the ultrasound probe in a caudad** direction can improve visualization of the sciatic, tibial and common peroneal nerves. This process is termed **anisotropy**.
  - Nerve blockade can be performed proximal or distal to the branching of the sciatic nerve. Studies have shown that blockade **distal to the point of branching** results in shorter **block onset** time [2].
  - Needle advancement can be performed in an in-plane or out-of-plane approach relative to the ultrasound transducer
  - Typically, **20–30 ml of local anesthetic** is injected with the goal of circumferential spread around the target nerve(s)

Clinical Pearls

- Blockade of the sciatic nerve in the popliteal fossa as opposed to the infragluteal region results **in sparing of the hamstring muscle** preserving the patient's ability to ambulate [3].
- Blockade of the sciatic nerve does not provide analgesia of the **medial aspect of the lower leg, ankle or foot**. Saphenous nerve blockade is also required for complete anesthesia or analgesia of the lower leg.
- **Anisotropy** is the technique of angling the ultrasound transducer **caudally**. This will improve nerve visualization in most patients.
- Blocking the tibial and common peroneal nerves in the popliteal fossa separately at the bifurcation provides a **faster onset than does a block proximal to the bifurcation of the sciatic nerve**.
- During popliteal block, a nerve stimulator can be used to elicit an evoked motor response in the ankle or foot. Depending on how proximal or distal on the posterior thigh the needle is inserted, different motor responses may be obtained. More proximally, sciatic nerve stimulation results in foot twitch. More distally, tibial nerve stimulation results in **plantar flexion of the foot** or toes and inversion of the foot and common peroneal nerve stimulation is indicated by **dorsiflexion of the foot**, toe extension, and foot eversion [1, 4].

Questions

1. By blocking the sciatic nerve at the popliteal fossa as opposed to the infragluteal region, the patient should retain the ability to:
   A. Dorsiflex the foot
   B. Flex the knee
   C. Plantarflex the foot
   D. Evert the foot
2. During ankle arthroscopy under surgical popliteal fossa block, the patient complains of pain at the medial malleolus. This likely results from failing to block the:
   A. Saphenous nerve
   B. Common peroneal nerve
   C. Tibial nerve
   D. Sural nerve
3. A surgical block is attempted at the popliteal crease under ultrasound guidance. Thirty minutes later the patient lacks sensation on the bottom of the foot and cannot plantar flex. However, the patient still has sensation on the top of the foot and the ability to dorsiflex the foot at the ankle. Which nerve was likely missed during the procedure?
   A. Tibial nerve
   B. Saphenous nerve
   C. Obturator nerve
   D. Common peroneal nerve
4. With the patient in the prone position, the structures encountered in the popliteal fossa from superficial to deep should be:
   A. Popliteal vein, popliteal artery, sciatic nerve, femur
   B. Popliteal artery, popliteal vein, sciatic nerve, femur
   C. Sciatic nerve, popliteal vein, popliteal artery, femur
   D. Sciatic nerve, popliteal artery, popliteal vein, femur
5. While performing a sciatic popliteal fossa block with nerve stimulation, the motor response elicited is a twitch of the foot. The next step is to:
   A. Redirect the needle medially
   B. Inject local anesthetic
   C. Redirect the needle laterally
   D. Withdraw the needle 1 cm

Answers

1. B, 2. A, 3. D, 4. C, 5. B

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Further Reading

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Lower Extremity Blocks: Ankle Block

21

Galaxy Mudda and Pedram Aleshi

Introduction

- Ankle block provides surgical anesthesia to the foot by blocking five peripheral nerves at the level of the ankle.
- It is a great alternative to general anesthesia in patients with multiple co-morbidities.
- Compared to combined sciatic / femoral nerve blocks, ankle block has the advantage of sparing motor blockade of lower extremity which allows early mobilization.
- Ankle block is as effective as sciatic nerve block as the primary anesthetic for patients undergoing foot surgery but with the disadvantage of a shorter postoperative analgesia duration [1].

Anatomy

- Innervation of the foot is provided by the sciatic and the terminal branch of the femoral nerve (saphenous nerve) (Fig. 21.1).
- Four of the peripheral nerves involved in an ankle block are branches of the sciatic nerve:
  - Posterior tibial nerve
  - Superficial peroneal nerve
  - Deep peroneal nerve
  - Sural nerve
- Saphenous nerve is a terminal branch of the femoral nerve.
- Posterior tibial nerve further branches off into three terminal nerves: medial calcaneal branch, and medial and lateral plantar nerves.

Indications

- Foot surgeries including amputations, bunionectomies, fractures, arthrodesis and arthroplasties
- Foot soft tissue injuries and removal of foreign bodies
- Analgesia for gout arthritis
- Diagnostic and therapeutic for sympathetically mediated pain (i.e. chronic regional pain syndrome)

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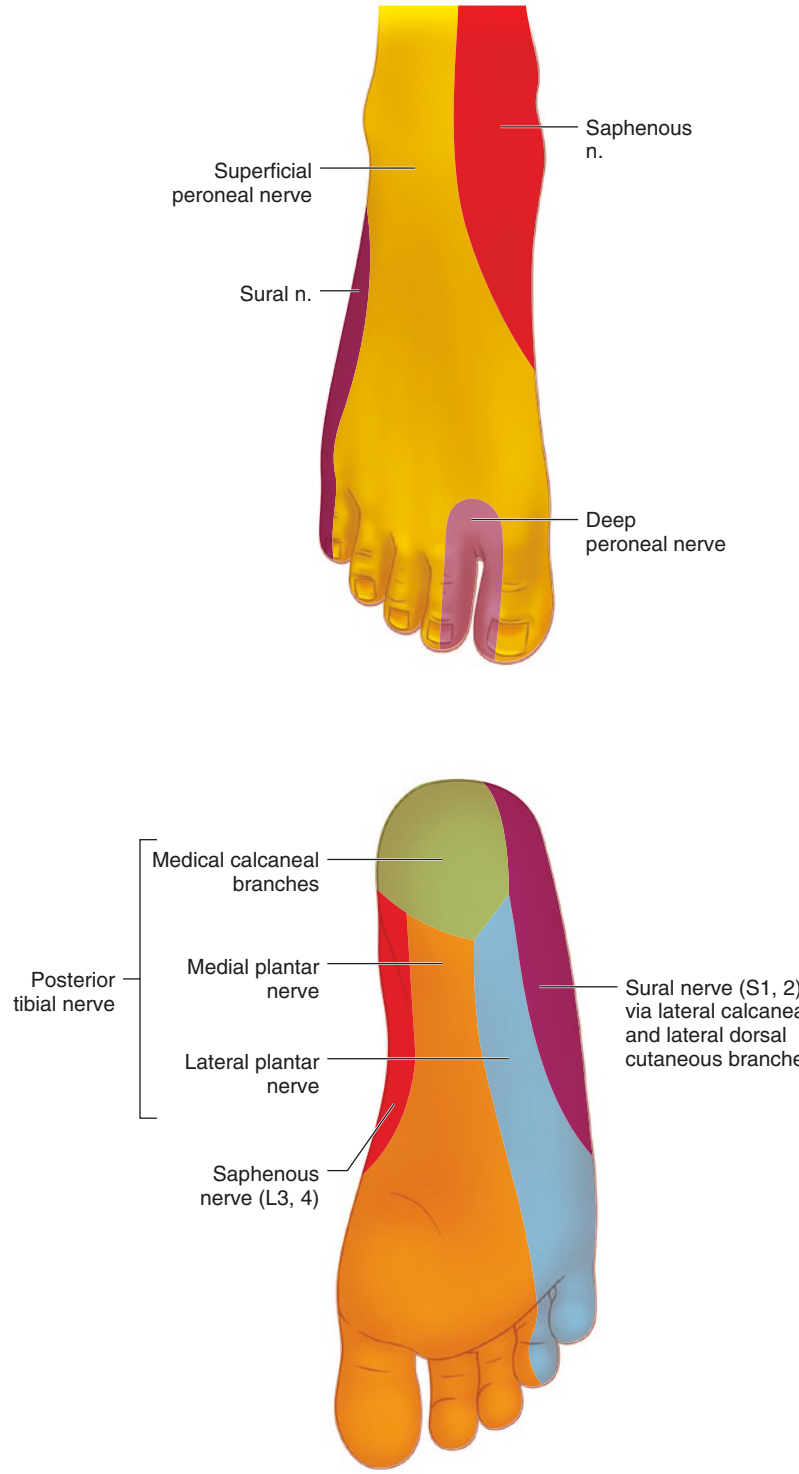

Fig. 21.1 Innervation of the foot (picture of dorsal and plantar surface of the foot to illustrate the innervation of the foot and ankle). (Source: Atchabahian A, Gupta R: *The Anesthesia Guide.* www.accessanesthesiology.com. Copyright © The McGraw-hill Companies, Inc. All rights reserved)

Technique

Typically, ankle blocks are done utilizing anatomic landmark based "blind" injection of local anesthetic. Instead of relying on a single injection, a "fan" technique is recommended to increase the success rate. Note however, that some providers may choose to do the block with ultrasound guidance; particularly for the posterior tibial nerve and deep peroneal nerve (Fig. 21.2 and Table 21.1) [2].

- Ankle block is performed in the supine position with the foot slightly elevated.
- **Superficial peroneal, saphenous and sural nerves** are all superficial and easily blocked using a simple circumferential injection of local anesthetic subcutaneously.
- The infiltration of local anesthetics may start circumferentially from **anterolateral aspect of the Achilles tendon towards the lateral malleolus**, and then **from anterior of the lateral malleolus**, injecting anteriorly until the **medial malleolus** is reached. A total 10 ml is injected.
- **Posterior tibial nerve** is blocked by palpating the posterior tibial artery located behind the medial malleolus and injecting **just posterior to the artery** (Fig. 21.2). The nerve is located deeper to the superficial fascia. The needle is

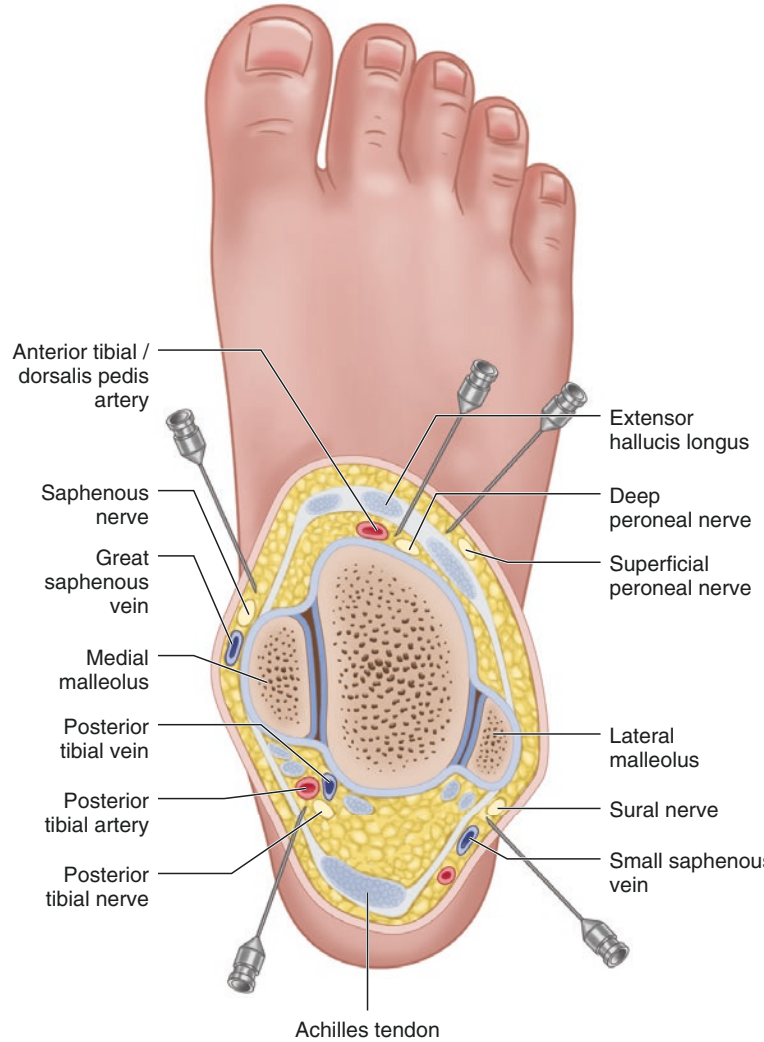

Fig. 21.2 Needle insertion sites for anatomic landmark technique of ankle block

Table 21.1 Anatomical location and function of the peripheral nerves involved in ankle block

	Motor	Sensory	Location
Posterior tibial nerve	Flexors of foot	Most of the sole of the foot	Posterior to medial malleolus and posterior tibial artery and anterior to the Achilles tendon
Superficial peroneal nerve	None	Dorsum of foot (except web space between first and second toes)	Lateral and superficial to extensor digitorum longus
Deep peroneal nerve	Extensors of foot	Web space between first and second toes	Lateral to the extensor hallucis longus and lateral to anterior tibial artery
Saphenous nerve	None	Medial foot/sole	Anterior to medial malleolus and lateral to great saphenous vein
Sural nerve	None	Lateral foot	Between lateral malleolus and Achilles tendon

introduced in the groove behind the medial malleolus and advanced until contact with the bone is felt. At this point, the needle is withdrawn and 2–3 mL of local anesthetic is injected in fan like distribution.

- For **deep peroneal block**, the anterior tibial artery (dorsalis pedis artery) is palpated between the flexor hallucis longus and extensor digitorum longus tendons (identified by flexing the great toe). The nerve lies just lateral to the artery. At the mid-tarsal portion of the foot, the needle is inserted just lateral to the artery and advanced until bone is encountered. A 2–3 mL of local anesthetic (LA) is injected in a fan like distribution.

Clinical Pearls

- Ankle block anesthetizes four branches of the sciatic nerve (superficial peroneal, deep peroneal, posterior tibial, and sural nerves) and one cutaneous branch of the **femoral nerve** (saphenous nerve). Each nerve is independently anesthetized.
- The **deep peroneal nerve** is one of the terminal branches of the common peroneal nerve and innervates the first web space of the foot.
- The **superficial peroneal nerve** is a branch of common peroneal nerve and supplies the skin over the dorsum of the foot.
- The **posterior tibial nerve** is terminal branch of tibial nerve and provides sensation to the calcaneus and sole of the foot.
- **The sural nerve** is a purely sensory nerve and branch of tibial nerve. It provides cutaneous sensation over the lateral ankle, foot and fifth toe and is adjacent the small saphenous vein. The **saphenous nerve** is another pure sensory nerve, which supplies sensation to the skin over the medial aspect of the ankle and foot.
- Sensory innervation of the foot is variable; it is best to block all five peripheral nerves despite the location of the foot surgery. Saphenous nerve has a large variability in its innervation of the medial aspect of the foot.

Questions

1. A patient is scheduled for amputation of the great toe under regional anesthesia. In order to have a successful block, it is necessary to block all of the following nerves EXCEPT:
   A. Sural nerve
   B. Superficial peroneal nerve
   C. Deep peroneal nerve
   D. Posterior tibial nerve
2. All of the following nerves are involved in the innervation of the plantar surface of the foot EXCEPT:
   A. Posterior tibial nerve
   B. Superficial peroneal nerve
   C. Lateral plantar nerve
   D. Sural nerve
3. Which of the following nerves involved in an ankle block have both sensory and motor components?
   A. Superficial peroneal nerve and posterior tibial nerve
   B. Saphenous nerve and superficial peroneal nerve

C. Deep peroneal nerve and posterior tibial nerve
D. Deep peroneal nerve and saphenous nerve

4. All of the following are indications for an ankle block EXCEPT:
   A. 25 years old female undergoing an open reduction internal fixation of her right ankle
   B. 50 years old male undergoing a left transmetatarsal amputation
   C. 48 years old female with complex regional pain syndrome s/p right fifth metatarsal open reduction and internal fixation
   D. 70 years old female scheduled for a left bunionectomy
5. Which of the following is NOT true regarding ankle block;
   A. Deep peroneal nerve is located adjacent to anterior tibial artery
   B. Superficial peroneal nerve is located in between lateral and medial malleolus on dorsal surface
   C. Sural nerve is located adjacent to great saphenous vein
   D. Saphenous nerve is located anterior to medial malleolus

Answers

1. A. The sural nerve only innervates the lateral aspect of the foot.
2. B. Superficial peroneal nerve only innervates the dorsal surface of the foot.
3. C. Of the five nerves, only deep peroneal nerve and posterior tibial nerve have both sensory and motor innervations. The others are sensory nerves only.
4. A. The ankle block provides a more distal block and is great for foot surgery, but not ankle surgery. A block of the sciatic nerve at or near its bifurcation in the popliteal fossa and a more proximal saphenous nerve or an adductor canal block is more suitable to provide anesthesia and analgesia for an ankle fracture.
5. C. The sural nerve – is located between lateral malleolus and Achilles tendon

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22 Upper Extremity Blocks: Interscalene and Superior Trunk Block

Jordan Starr and Mohammed Issa

Introduction

- The **interscalene brachial plexus block** is commonly used for post-operative analgesia for **shoulder surgery**, as this block reliably anesthetizes the **C5-C7** nerve roots [1].
- While some coverage of C8 or T1 may occur, this block cannot be relied upon for surgery below the elbow [1]. This block is associated with **phrenic nerve blockade** nearly 100% of the time, due to its course on the anterior surface of the anterior scalene muscle [1, 2].
- To reduce this adverse-effect, the **superior trunk block** was developed, which targets the C5 and C6 nerve roots distally as they form the superior trunk of the brachial plexus [3]. The superior trunk block is associated with less hemidiaphragmatic paralysis and provides non-inferior analgesia compared to the interscalene block [2].

Anatomy

- The plexus is formed by the **C5-T1 nerve roots**, which form trunks, divisions, cords, and branches as they run distally (**R**eal **T**exans **D**rink **C**old **B**eer) (Fig. 22.1) [4]. C5 and C6 roots merge to form the upper trunk. The C7 root forms the middle trunk. C8 and T1 roots merge to form the lower trunk.
- The upper trunk divides into the lateral and posterior cords. The middle trunk divides to the lateral and posterior cords. The lower trunk divides to the posterior and medial cord. The lateral cord branches form the musculocutaneous nerve and median nerve.
- The posterior cord branches form the axillary nerve and radial nerve. The medial cord branches contribute to the median nerve and the ulnar nerve. The interscalene block is performed on the brachial plexus nerve roots as they extend distally past the common carotid artery and internal jugular vein, and then converge between the anterior and middle scalene muscles.

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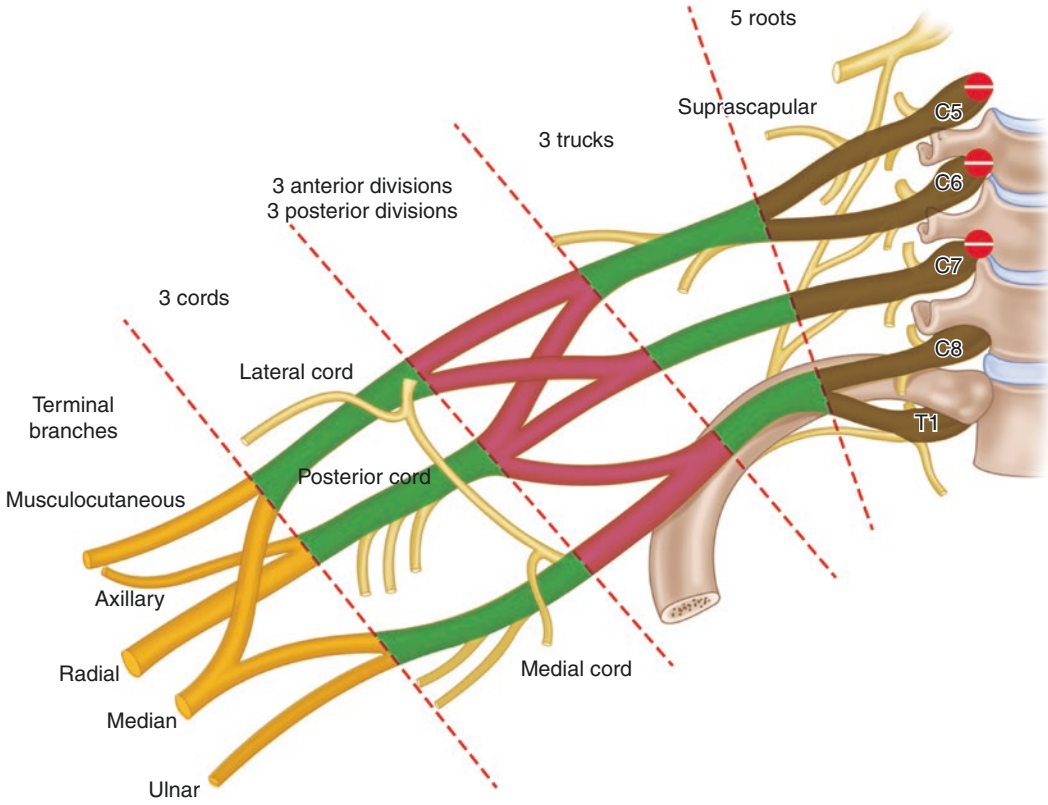

Fig. 22.1 Schematic diagram of the brachial plexus. (Source: Springer [4])

Indications

- The primary anesthetic, or **post-operative pain control**, for surgeries involving the clavicle (combined with superficial cervical plexus block), **shoulder**, or upper humerus.
- Management of acute or chronic pain in the clavicle, shoulder, or upper humerus.

Contraindications

- Severe **pulmonary disease** (COPD, OSA, contralateral pneumothorax) in addition with other contraindications for peripheral nerve blocks

Technique

- Position the patient supine with the bed at approximately a 30-degree incline. Turn the patient's head towards the contralateral side. Expose the ipsilateral neck and shoulder area then widely apply skin antiseptic and drape.
- Place the sterilely-draped ultrasound probe parallel and adjacent to the mid-clavicle, then scan to identify the brachial plexus (**1–3 cm deep**). Trace the brachial plexus proximally until it is bordered anteriorly by the anterior scalene and posteriorly by the middle scalene (Fig. 22.2) [5].
- **(Superior Trunk Block only)** After finding the brachial plexus as above, trace the C5 and C6 nerve roots distally until they coalesce into the superior trunk but proximal to the take-off of the **suprascapular nerve** (Fig. 22.3) [2].
- Inject local anesthetic into the skin, then insert the needle in a lateral to medial orientation using an in-plane technique.
- Place a catheter adjacent to the brachial plexus if desired.
- Confirm **negative aspiration** of blood, then incrementally inject local anesthetic with any adjuncts. Confirm injectate spread around the brachial plexus. Typical injection volumes are 7–20 mL.

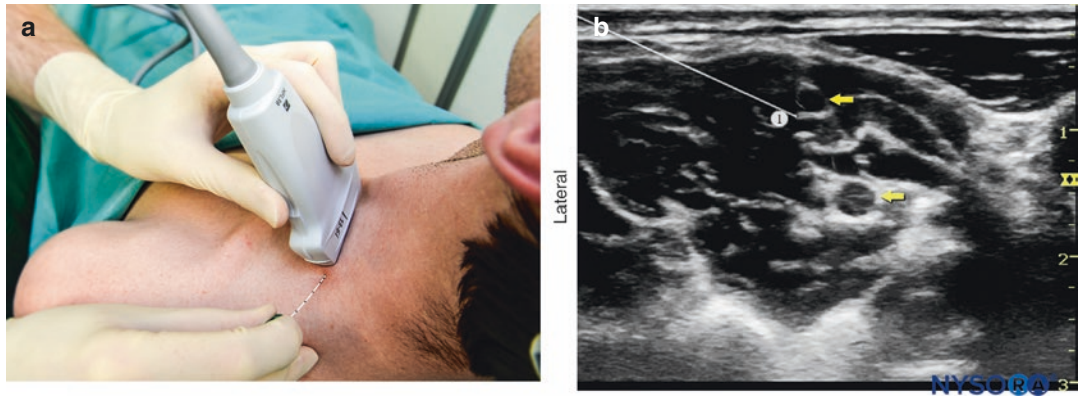

Fig. 22.2 (**a**) Transducer placement and needle insertion. (**b**) Position of the needle [1] for the interscalene brachial plexus block using an in-plane approach. The needle tip is seen in contact with the elements of the brachial plexus (yellow arrows). (Source: NYSORA.COM [5])

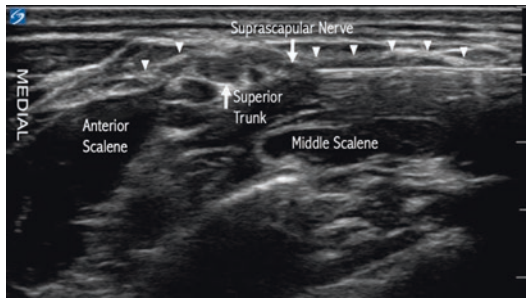

Fig. 22.3 Ultrasonographic image of the superior trunk block. *White down-pointing triangles* indicate the deep cervical fascia. (Source: Wolters Kluwer [2])

- Withdraw the needle, ensuring if a catheter was placed that it has not been displaced.
- If placed, secure the catheter with a relief loop and adhesive skin glue, then cover with clear sterile dressings and tape.

Complications

- Inadequate surgical blockade or pain relief
- **Phrenic nerve blockade**
  - Interscalene block: partial (25%) or complete (72.5%) paralysis [2]
  - Superior trunk block: partial (70%) or complete (5%) paralysis [2]
- Horner's syndrome (miosis, ptosis, anhidrosis)
- Recurrent laryngeal nerve blockade leading to voice hoarseness
- **Pneumothorax**
- Local anesthetic toxicity
- Epidural or intrathecal injection

Preventive Measures to Avoid Complications

- Avoid these blocks for analgesia **below the elbow**
- **Superior trunk blocks** may be preferable for patients with mild to moderate pulmonary disease.
- Use of color Doppler over the anticipated needle trajectory
- Aspiration prior to injection, incremental injection of 3–5 cc at a time

Clinical Pearls

- It is important to perform a quick neurological exam prior to the block to exclude pre-existing neurological deficits. Remember the four P's (Push, Pull, Pinch, Pinch). Have the patient push or extend the forearm (radial), pull or flex the forearm (musculocutaneous nerve), pinch the index or second finger (median nerve), and pinch the little finger (ulnar nerve).
- The brachial plexus starts out at the root level from the ventral rami of C5-T1 with a small contribution from C4 to T2. These roots at the level of the **scalene muscles**

become the three trunks: superior, middle and inferior. The trunks then divide into the dorsal and ventral divisions at the **lateral edge of the first rib**. When the divisions enter the axilla, they become **the cords**: posterior, lateral and medial. At the lateral border of the pectoralis muscle they become the musculocutaneous, median, ulnar, and axillary nerves.

- When using color Doppler, avoid excessive pressure with the ultrasound probe, as this can collapse veins and make them unidentifiable.
- High resistance during injection may indicate an intrafascicular injection, which should be avoided.
- The major disadvantage of the interscalene block for hand and forearm surgery is that blockade of the inferior trunk (C8-T1) is often incomplete. Supplementation of the ulnar nerve often is required.

Questions

1. What nerve is most commonly missed with an interscalene block?
   A. Median
   B. Axillary
   C. Ulnar
   D. Radial
2. Systemic absorption of local anesthetic is lowest in which location?
   A. Brachial
   B. Intercostal
   C. Tracheal
   D. Paracervical
3. A patient with pulmonary hypertension undergoes a superior trunk block and develops arm and shoulder numbness, but the patient reports pain proximal to the acromioclavicular joint with incision. The best next step is:
   A. General anesthesia
   B. Superficial cervical plexus block
   C. Deep cervical plexus block
   D. Repeat superior trunk block
4. During interscalene block, a patient becomes bradycardic, hypotensive, and cyanotic. The cause was most likely:
   A. Total spinal
   B. Stellate ganglion block
   C. Phrenic nerve block
   D. Carotid artery injection
5. During a superior trunk block, the anesthesiologist is least likely to inject into or block the:
   A. Vertebral artery
   B. Phrenic nerve
   C. Epidural space
   D. Basilar artery

Correct Answers

1. C, 2. A, 3. B, 4. A, 5. D

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23 Upper Extremity Blocks: Supraclavicular Nerve Block

Nicholas Heiser and Raime Robinson

Introduction

- **Supraclavicular Nerve Block** blocks the brachial plexus at the level of the nerve trunks (upper, middle, and lower) just distal to the shoulder (Fig. 23.1).
- The plexus is **tightly packed** at this level, resulting in a high-quality block. For this reason, the supraclavicular block is often called the "**spinal of the arm**."
- This block is good for surgery of the **distal two-thirds** of the upper extremity including hand surgery.
- The intercostobrachial nerve (T2) **is not blocked**, which supplies a strip of skin along the **medial aspect of the upper arm**. It can be blocked by infiltrating 10 cc of local anesthetic from the upper border of the biceps to the lower border of the triceps at the anterior axillary line.

Anatomy

- Nerve plexus involved: Brachial Plexus (C5-T1), visualized as a bundle of hypoechoic structures directly lateral to the subclavian artery [1] (Figs. 23.1 and 23.2)
- The brachial plexus (in a superficial position 1–3 cm deep to the skin's surface) travels with the subclavian artery between first rib and clavicle at the middle third of the clavicle.
- The block is performed at the level of the distal **trunks**.
- The brachial plexus is bordered deep by the first rib and pleura. The dome of the pleura lies medial to the first rib.
- The plexus runs initially posterosuperior and then lateral to the subclavian artery.

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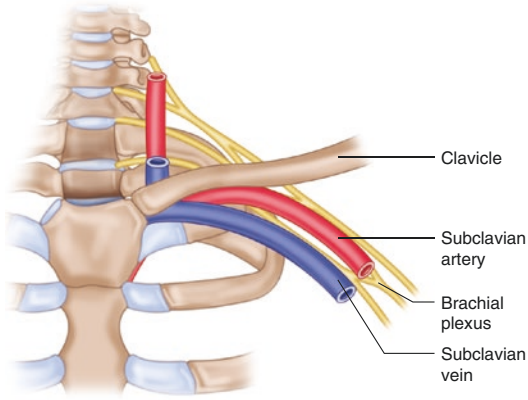

Fig. 23.1 Brachial plexus anatomy. Key landmarks from lateral to medial along the first rib are brachial plexus, subclavian artery, anterior scalene muscle (not shown)

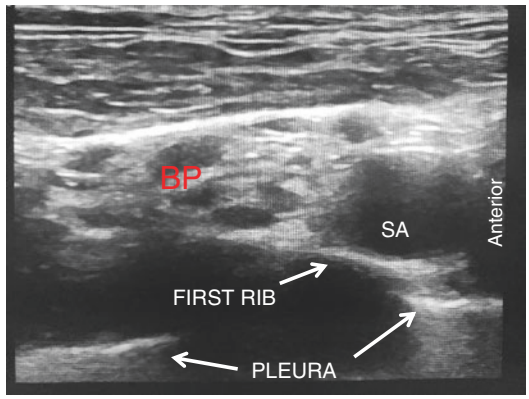

Fig. 23.2 Ultrasound image of the brachial plexus (BP) at its supraclavicular position coursing with the subclavian artery (SA). BP is lateral to SA

Indications

- Post-operative analgesia as part of a multimodal pain protocol.
- Primary surgical anesthesia for procedures of the shoulder, arm, and hand.
- Post-operative analgesia via continuous perineural catheter.

Contraindications

- Severe Chronic Obstructive Pulmonary Disease (relative contraindication due to potential hemidiaphragmatic paresis associated with phrenic nerve blockade). Along with other contraindications for peripheral nerve blocks

Block Technique

- Place patient in the supine position (often with a slight incline of ~30°) with neck extended and chin rotated towards the contralateral shoulder.
- With covered ultrasound probe apply firm pressure while placing the probe proximal to the middle-third of the clavicle.
- Identify the brachial plexus by locating it in its **lateral position relative to the subclavian artery** (Fig. 23.2).
- Caudal and/or cephalad tilting of the ultrasound probe may be necessary for optimal anatomical visualization (Fig. 23.3).
- Anesthetize skin with a wheel of local anesthetic prior to fully advancing through the skin.

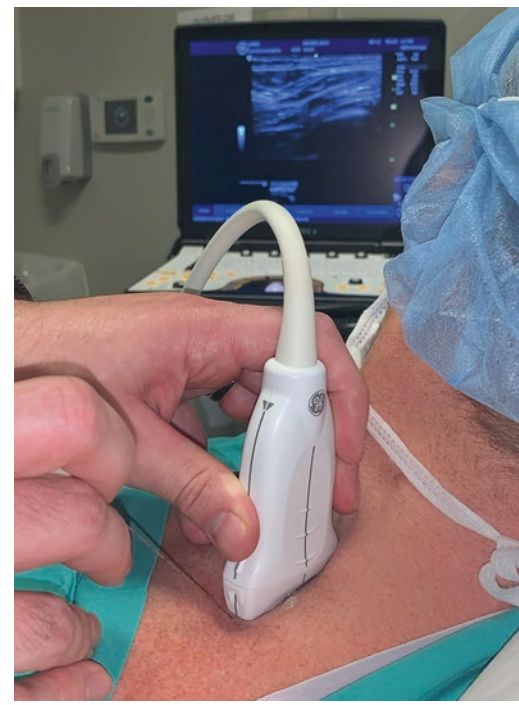

Fig. 23.3 Ultrasound guided approach to the Supraclavicular nerve block with needle insertion lateral to the probe

- Advance the needle in an in-plane technique towards the brachial plexus with complete visualization of the needle tip at all times.
- The needle tip and shaft should be visualized in real time to avoid inadvertent pleural puncture. Advance the needle toward the junction of the subclavian artery and first rib. This is inferomedial to the plexus, and superior to the first rib, which is also called as "the corner pocket."
- In multiple injections, after first aspirating and after confirming negative blood return, inject small aliquots (typically ~5 mL) of local anesthetic.
- STOP injection if patient complains of pain and/or you have **increased resistance** –this could indicate an **intrafascicular needle location**, which may result in **nerve injury**.

Complications

- Pneumothorax is a potential complication.
- Hoarseness due to temporary blockade of the ipsilateral recurrent laryngeal nerve and/or a cervical sympathetic blockade.
- Horner syndrome from blockade of the **stellate ganglion**, and hemi-diaphragmatic paresis (50–60%) from phrenic nerve involvement [2].
- The use of lower volumes of local anesthetics (20 mL) is recommended for patients with compromised pulmonary function to reduce incidence of phrenic nerve blockade.

Clinical Pearls

- The supraclavicular block is performed at the distal level of the trunks just before they become divisions. The plexus at this level appears as a "**bundle of grapes**" lateral to the subclavian artery. Unlike an axillary or interscalene block, no part of the plexus is spared at this level. Hence, the block is called the '**spinal of the arm'**. However, a **intercostobrachial nerve block** may be required.
- The block is good for anesthesia of the upper arm distal to the shoulder. Care should be taken in patients with respiratory disease because of the high incidence of **phrenic nerve block and pneumothorax**.
- A pneumothorax should be considered if the patient begins to complain of **chest pain** or shortness of breath or **begins to cough** during placement.

Questions

1. Following an uncomplicated supraclaviclar nerve block on a 59 year old male with a PMH of HTN, CAD, and COPD, he complains of difficulty breathing. You note his oxygen saturation on room air to be 85%. His baseline O2 saturation on room air is 92. Which known complication of this block is most likely to explain this clinical picture?
   A. Pneumothorax
   B. Local anesthetic systemic toxicity (LAST)
   C. Phrenic nerve block
   D. Hematoma
2. You have performed an uncomplicated supraclavicular nerve block for an arteriovenous fistula with 20 mL of 0.5% bupivacaine. Upon surgical incision, the patient moves abruptly and complains of pain. Failure to anesthetize which of the following nerves likely lead to this event?
   A. Ulnar Nerve
   B. Radial Nerve
   C. Median Nerve
   D. Intercostobrachial Nerve
3. The supraclavicular block is performed at which section of the brachial plexus?
   A. Roots
   B. Trunks
   C. Divisions
   D. Cords

4. If the patient complains of pain on injection of local anesthetic during a supraclavicular nerve block, which of the following would be the most appropriate next step?
   A. Administer more sedation to comfort the patient.
   B. Stop injection and redirect the needle
   C. Counsel the patient that this is normal and continue injection.
   D. Abort the procedure.
5. In the supraclavicular nerve block, which of the following structures lies deep to the brachial plexus?
   A. First rib
   B. Subclavian artery
   C. Medial scalene muscle
   D. Anterior scalene muscle

Answers

1. C, 2. D, 3. B, 4. B, 5. A

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24 Upper Extremity Blocks: Infraclavicular and Axillary Nerve Block

Alex Suginaka and James Flaherty

Infraclavicular Nerve Block

Introduction

- Blocks the brachial plexus at the level of the cords (lateral, posterior, medial).
- Provides anesthesia for surgeries of the distal 2/3 of the arm, similar to supraclavicular block, but conveys less risk of pneumothorax or phrenic nerve block.
- Deeper location can make ultrasound visualization difficult in obese patients.

Anatomy [1, 2]

- See Chap. 22, regional anesthesia for brachial plexus anatomy.
- Each trunk divides into an anterior and posterior division behind the clavicle and emerges from under the clavicle to form the lateral, posterior, and medial cords (Fig. 24.1), named for their position relative to the axillary artery in the infraclavicular fossa.
- The infraclavicular fossa is bounded by the pectoralis minor and major muscles anteriorly, ribs medially, clavicle and the coracoid process superiorly, and humerus laterally.

Indications

- Similar to the supraclavicular nerve block (See Chap. 23); not suitable for shoulder surgery due to lack of suprascapular nerve coverage.

Technique [1]

- Place the patient in the supine position with the arm abducted and elbow flexed. This arm positioning displaces the clavicle posteriorly which improves needling conditions.
- Place the ultrasound transducer in the parasagittal plane below the clavicle, just medial to the coracoid process (Fig. 24.1).
- Identify the pectoralis major and minor muscles. The artery is easily visualized deep to the muscles at approximately 3-4 cm and can be confirmed by color doppler. The axillary vein is identified medial to the artery. The hyperechoic nerves are arranged around the axillary artery (Fig. 24.2) at the 9 o'clock (lateral cord), 7 o'clock (posterior cord), and 5 o'clock positions (medial cord), though considerable anatomic variability exists.

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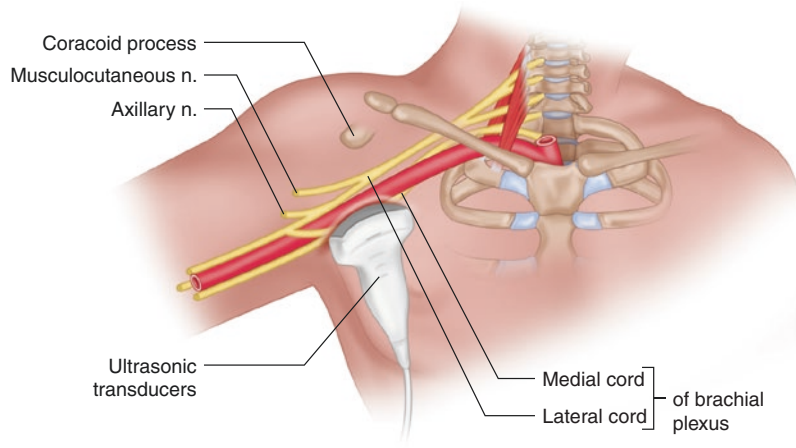

Fig. 24.1 Anatomy of the infraclavicular nerve block

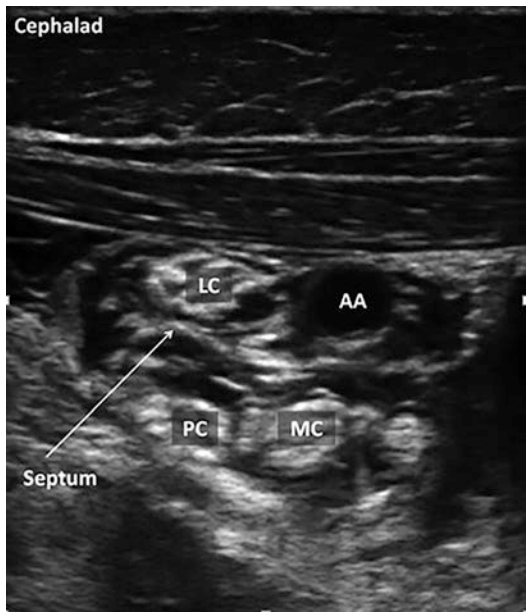

Fig. 24.2 Post-injection ultrasound image of the infraclavicular brachial plexus, illustrating the septum that separates the lateral cord (LC) from the posterior (PC) and medial (MC) cords. (Chin [4])

- Insert a 100 mm needle below the clavicle at an angle of 45° in-plane and advance the needle from cephalad to caudad.
- Place the needle tip at the 6 o'clock position of the artery and aspirate prior to injection of 15–20 mls of local anesthetic around the axillary artery. A "U-shaped" spread of local anesthetic around the artery produces reliable blockade even when cords are difficult to visualize.

Complications [2, 3]

- Pneumothorax,
- Radial nerve injury – loss of finger and wrist extension (wrist drop),
- Median nerve injury – loss of index and middle finger flexion and thumb opposition (hand of benediction),
- Ulnar nerve injury – loss of ring and pinky finger extension (claw hand),
- Musculocutaneous nerve injury – weakened elbow flexion, forearm supination

Axillary Nerve Block

Introduction

- Blocks the brachial plexus at the level of the terminal branches (median, ulnar, radial, musculocutaneous).
- Provides anesthesia for surgeries of the distal 2/3 of the arm, similar to infraclavicular block, but is performed at a compressible location and reduces the risk of pneumothorax and phrenic nerve block.
- The musculocutaneous nerve and intercostobrachial nerve are typically spared unless individually targeted

Anatomy [1, 2]

- See Chap. 22, regional anesthesia for brachial plexus anatomy
- The axillary artery courses superficially within the axilla; the median, radial, and ulnar nerves are arranged radially around the artery. The musculocutaneous nerve lies within the belly of the coracobrachialis muscle at this level.
- The neurovascular bundle is bounded by the biceps muscle, coracobrachialis muscle, and the conjoint tendon of teres major and latissimus dorsi.

Indications (See Infraclavicular Block)

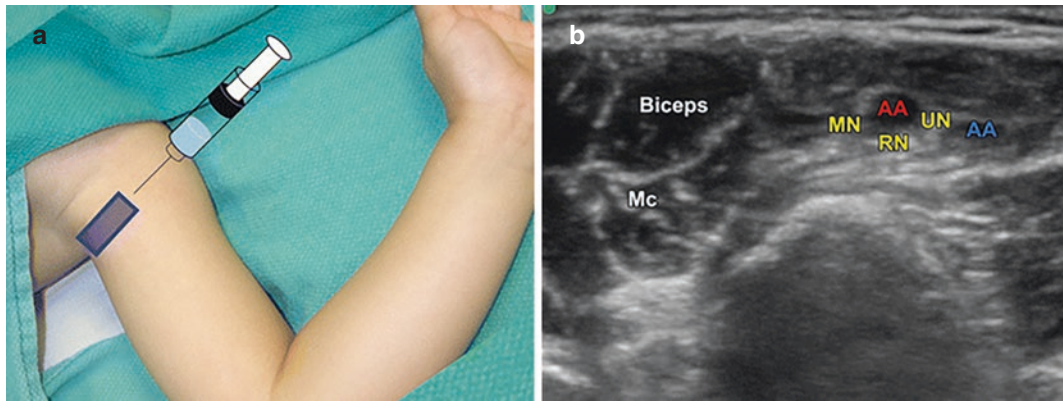

Fig. 24.3 (**a**) Patient position of axillary block. (**b**) Ultrasound image of axillary brachial plexus block. *Mc* musculocutaneous nerve, *MN* median nerve, *RN* radial nerve, *UN* ulnar nerve, *AA* axillary artery, *AV* axillary vein. (Tsui [5])

Technique [1]

- Place the patient supine with the arm abducted 70–80° and externally rotated, the elbow flexed at 90°, and the dorsum of the hand facing the table.
- Place the ultrasound transducer in an oblique parasagittal plane in the axilla (Fig. 24.3a).
- Identify the pulsatile axillary artery. The nerves are classically oriented at the 9 o'clock (median), 6 o'clock (radial), and 3 o'clock (ulnar) positions (Fig. 24.3b), though anatomic variability is the rule rather than the exception.
- Insert a 50–100 mm needle in plane from anterior to posterior and advance toward the axillary artery. Perform either a single 15–20 ml injection at the 6 o'clock position relative to the artery, or separate 5 mL injections targeting each of the median, radial, and ulnar nerves.
- Retract the needle into the biceps muscle and redirect toward the musculocutaneous nerve within the coracobrachialis muscle (Fig. 24.3b). Advance adjacent to this nerve and inject an additional 3–5 mL of local anesthetic.

Clinical Pearls [1]

- Parts of the arm that are not covered by the brachial plexus block include upper medial portion of the arm which is innervated by the **intercostobrachial nerve** (T2) and top of shoulder which is innervated by the **supraclavicular nerve** (originates from the cervical plexus) (Fig. 24.4).
- The musculocutaneous nerve provides sensory innervation to the lateral aspect of the forearm. It typically leaves the axillary sheath proximal to the level of the axilla and is therefore frequently missed during axillary block unless targeted.
- Subcutaneous injection of local anesthetic along the axillary crease blocks the intercostobrachial nerve, which provides cutaneous sensation to the medial/posterior upper arm. This is particularly important to block pain associated with tourniquet inflation.

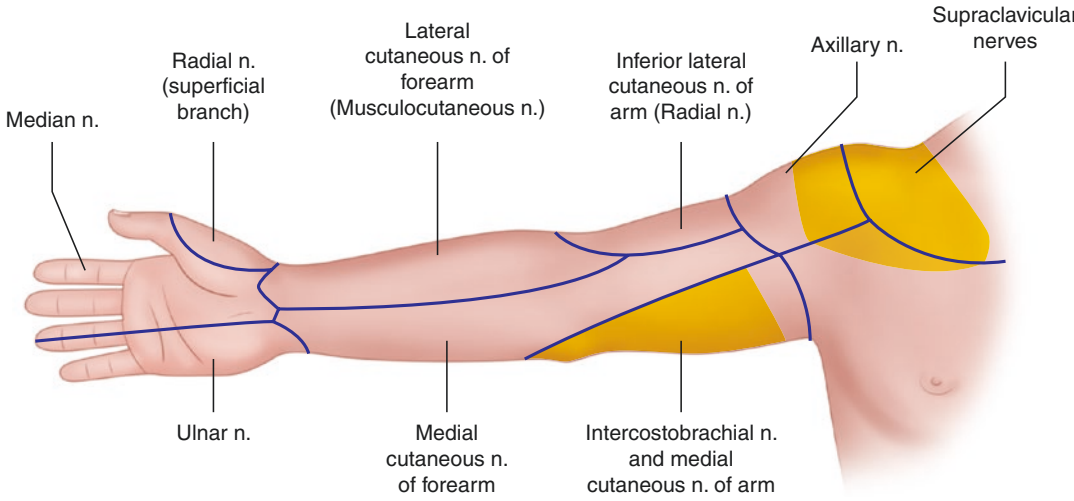

Fig. 24.4 Cutaneous innervation of the arm spared by brachial plexus block (marked yellow)

Questions

1. The plastic surgeon has requested an infraclavicular nerve block for repair of a distal radius fracture. Match the correct artery and level of the brachial plexus where local anesthetic should be deposited.
   A. Carotid artery, roots
   B. Axillary artery, cords
   C. Axillary artery, branches
   D. Subclavian artery, trunks
2. A patient undergoing repair of a distal radius fracture endorses pain from the tourniquet on the upper arm after receiving an infraclavicular nerve block preoperatively. Which supplemental block could have mitigated this?
   A. Intercostobrachial nerve
   B. Suprascapular nerve
   C. Lateral antebrachial cutaneous nerve
   D. Dorsal scapular nerve
3. A patient receives an axillary block for a tumor excision on the forearm. Upon incision of the lateral aspect, the patient grimaces and flexes the elbow in response. Inadequate block of which nerve most likely contributed to this?
   A. Ulnar nerve
   B. Median nerve
   C. Intercostobrachial nerve
   D. Musculocutaneous nerve
4. Which of the following would NOT be an appropriate target for providing sensory block of the fifth finger?
   A. C6 nerve root
   B. Ulnar nerve
   C. Medial cord
   D. Inferior trunk
5. A new resident is practicing an axillary nerve block on a mannequin. The instructor points out that the radial nerve has been transected by the needle. How would this injury manifest clinically?
   A. Ipsilateral diaphragmatic paralysis
   B. Loss of finger extension
   C. Loss of wrist extension
   D. Inability to oppose thumb

Answers

1. B, 2. A, 3. D, 4. A, 5. C

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25 Upper Extremity Blocks: Wrist Blocks: Ulnar, Radial, Median Nerve Blocks

Kaylyn Sachse and Brian Allen

Introduction

The terminal branches of brachial plexus (ulnar, median, or radial nerves) can be anesthetized for surgeries of the hand or fingers. These blocks are also used for supplementation of incomplete brachial plexus blocks. Indications include: surgical procedures on the wrist, hand, and fingers such as carpal tunnel release, metacarpophalyngeal joint arthrodesis, Dupuytren's contracture release, and fractures of the hand or wrist (Table 25.1).

Table 25.1 Nerve functions [1]

	Sensory (Fig. 25.1a)	Motor (Fig. 25.1b)
Median	Palmar aspect of thumb → medial half of fourth finger Dorsal tips of thumb → medial half of fourth finger	Forearm flexion and pronation Wrist and finger flexion Thumb flexion, opposition, abduction
Musculocutaneous	Lateral forearm	Elbow flexion
Radial	Posterior arm and forearm Lateral dorsum of the hand + thumb	Elbow extension and flexion Forearm supination Wrist extension Finger extension Thumb abduction
Ulnar	Dorsal and palmar aspects of medial hand	Wrist flexion and adduction Finger flexion Hand flexion Thumb adduction Fifth finger abduction

Median Nerve Block

The median nerve arises from the **medial and lateral cords of the brachial plexus** (C5-7 and C8-T1, respectively) (Fig. 22.1, Chap. 22, regional anesthesia) [2]. It has no branches above the elbow but supplies the opponens pollicis, abductor pollicis brevis, the first two lumbricals, and the flexor muscles of the forearm (except flexor carpi ulnaris). Sensory fibers supply the palmar surface of the radial three and a half fingers (Fig. 25.1) and their nailbeds. The recurrent branch of the median nerve supplies the three thenar muscles.

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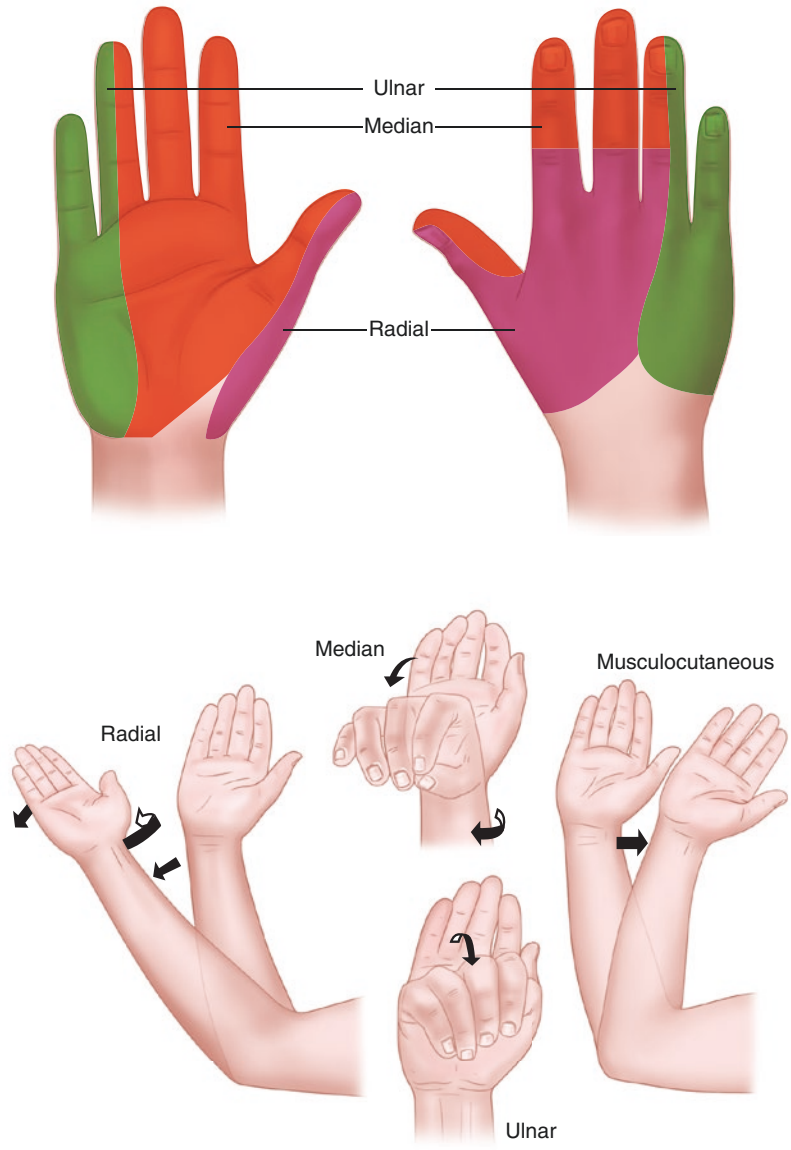

Fig. 25.1 (**a**) Sensory innervation of hand. [Instructions for illustrators: Hand on the right should be labeled "Palmar", hand on left should be labeled "Dorsum". Green is "Ulnar Nerve", Orange is "Median Nerve", Purple is "Radial Nerve". Each colored portion of the hand should have a line extending from it to the label in quotation marks]. (**b**) Tests for adequate motor blockage or motor deficits of the terminal branches of the brachial plexus. Ask the patient to push the forearm against resistance or extend the forearm (**radial nerve**), pull against resistance or flex the forearm (**musculocutaneous nerve**), pinch the index or second finger to the thumb (**median nerve**), pinch the little finger to the thumb or flex the fingers (**ulnar nerve**). Inability to perform these tasks represent injury or motor blockage of the respective nerve

Block Technique

Antecubital Fossa (Fig. 25.2):

- In the antecubital fossa, the median nerve can be identified just medial to the brachial artery.
- Using either an in-plane or out-of-plane ultrasound-guided technique, localize the skin and then inject approximately 3–5 mL of local anesthetic around the median nerve with the goal of circumferential spread around the nerve as well as visualization of local anesthetic spreading distal and proximal along the path of the nerve [3, 4].

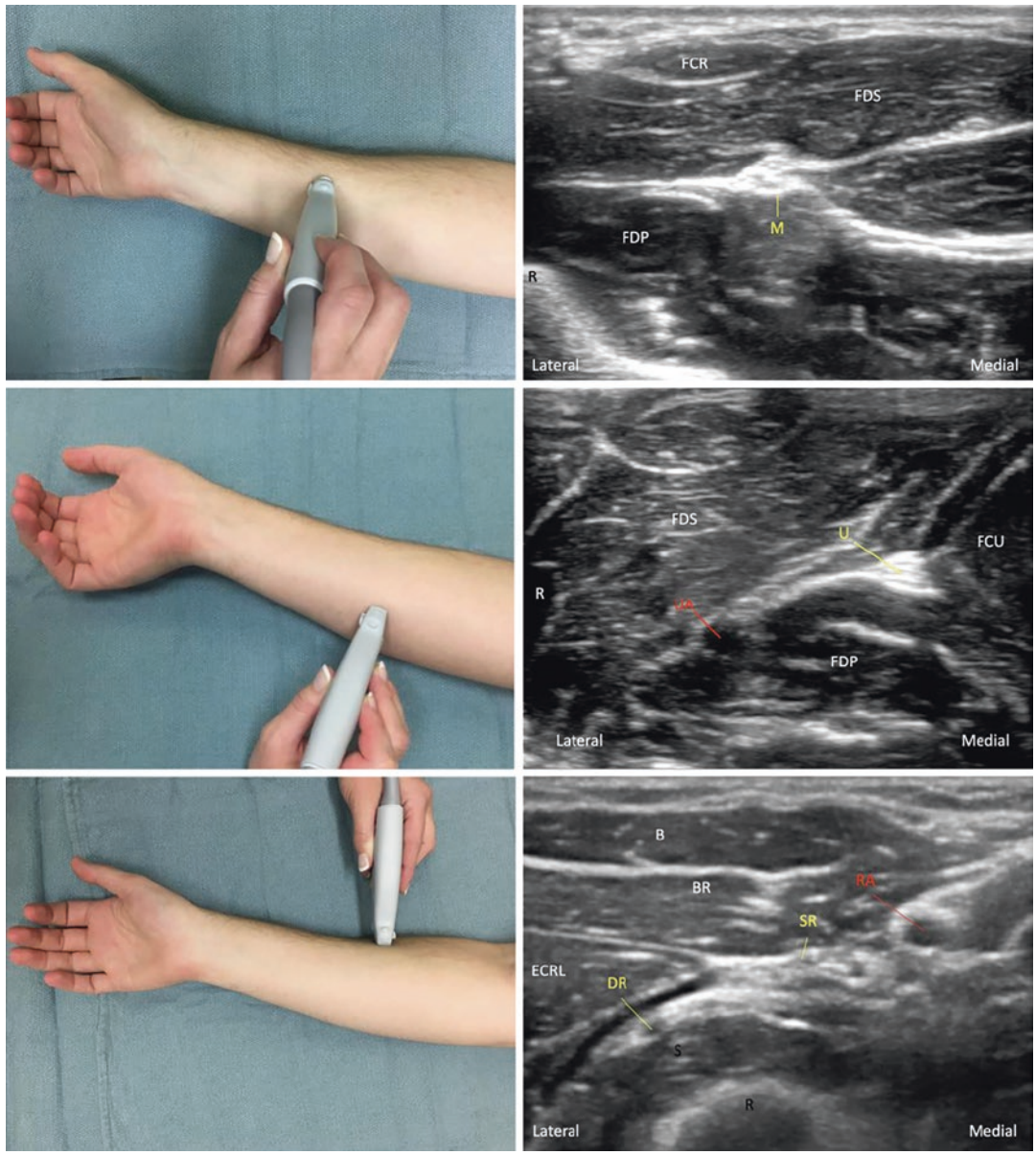

Fig. 25.2 Ultrasound probe positioning and the corresponding ultrasound image for median (upper), ulnar (middle), and radial (lower) nerve blocks at the mid-forearm. Abbreviations for ultrasound images. *B* brachialis muscle, *BA* brachial artery, *BR* brachioradialis muscle, *DR* deep radial nerve, *ECRL* extensor carpi radialis longus muscle, *F1* flexor carpi ulnaris muscle, ulnar head, *F2* flexor carpi ulnaris muscle, humeral head, *FCR* flexor carpi radialis muscle, *FCU* flexor carpi ulnaris muscle, *FDP* flexor digitorum profundus muscle, *FDS* flexor digitorum superficialis muscle, *M* median nerve, *ME* medial epicondyle of the humerus, *LE* lateral epicondyle of the humerus, *O* olecranon of the humerus, *PT* pronator teres muscle, *R* radius, *S* supinator muscle, *SR* superficial radial nerve, *U* ulnar nerve, *UA* ulnar artery

Mid forearm block (Fig. 25.3):

- The anterior interosseous nerve (AIN), which provides motor innervation to the deep flexors of the forearm, branches off the median nerve distal to the antecubital fossa. In the mid-forearm, the median nerve can be found deep to the flexor digitorum superficialis and superficial to the flexor digitorum profundus.
- Using either an in-plane or out-of-plane ultrasound-guided technique, localize the skin and then inject approximately 3–5 mL of local anesthetic around the median nerve.

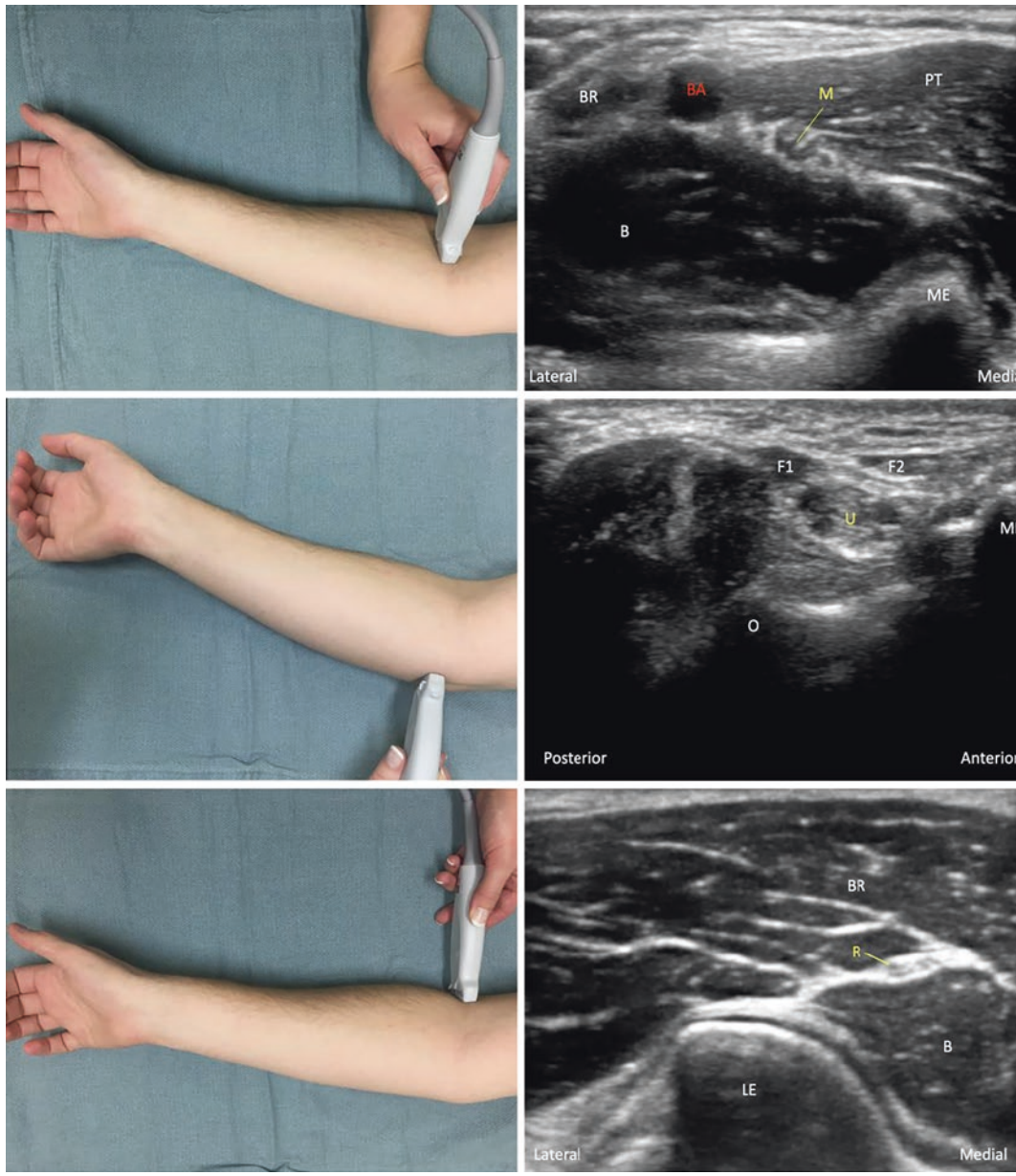

Fig. 25.3 Ultrasound probe positioning and the corresponding ultrasound image for median (upper), ulnar (middle), and radial (lower) nerve blocks at the antecubital fossa. Abbreviations for ultrasound images. *B* brachialis muscle, *BA* brachial artery, *BR* brachioradialis muscle, *DR* deep radial nerve, *ECRL* extensor carpi radialis longus muscle, *F1* flexor carpi ulnaris muscle, ulnar head, *F2* flexor carpi ulnaris muscle, humeral head, *FCR* flexor carpi radialis muscle, *FCU* flexor carpi ulnaris muscle, *FDP* flexor digitorum profundus muscle, *FDS* flexor digitorum superficialis muscle, *M* median nerve, *ME* medial epicondyle of the humerus, *LE* lateral epicondyle of the humerus, *O* olecranon of the humerus, *PT* pronator teres muscle, *R* radius, *S* supinator muscle, *SR* superficial radial nerve, *U* ulnar nerve, *UA* ulnar artery

Ulnar Nerve Block

The ulnar nerve originates from medial cord with fibers from roots C7, C8, and T1 (Fig. 22.1, Chap. 22, regional anesthesia) [2]. In the forearm, it supplies flexor carpi ulnaris and half of the flexor digitorum profundus. In the hand, it supplies 3 hypothenar muscles, the medial two lumbricals, all the interossei, and the adductor pollicis. Digital branches provide cutaneous sensation for the medial one and a half fingers and medial palm (Fig. 25.1).

Block Technique

Elbow/Antecubital Fossa (Fig. 25.2):

- Trace the ulnar nerve starting from the cubital tunnel between the medial epicondyle and olecranon on the posterior medial surface of the elbow. Just distal to the medial epicondyle, the ulnar nerve can be found deep to the two heads flexor carpi ulnaris. The prominence of the bony structures at the elbow may make ultrasound transducer contact and subsequent visualization challenging. It is often helpful to begin scanning distal to the elbow and trace the nerve proximally [3–5].
- Using either an in-plane or out-of-plane technique, localize the skin and then inject approximately 3–5 mL of local anesthetic around the ulnar nerve, identified by its "honeycomb" appearance of interlaced hyperechoic fascia and hypoechoic fascicles.

Forearm block (Fig. 25.3):

- Scanning distal from the elbow, trace the ulnar nerve into the medial mid forearm, where it lies immediately medial to the ulnar artery. To avoid inadvertent ulnar artery puncture, move the probe approximately 2 cm proximal to where the artery and nerve are separated and perform the block. Distal ulnar nerve block at the level of the wrist often spares the dorsal branch (sensation of the medial portion of the dorsum of the hand – see Fig. 25.1). It is therefore advised to perform the block a minimum of 8 cm proximal to the wrist [5].
- Using either an in-plane or out-of-plane ultrasound-guided technique, localize the skin and then inject approximately 3–5 mL of local anesthetic around the ulnar nerve, using care due to the proximity of the ulnar artery.

Radial Nerve Block

Originates from posterior cord of the brachial plexus with fibers from C5-8, T1 (Fig. 22.1, Chap. 22, regional anesthesia) [2]. Provides sensory supply to the skin of the lateral aspect of the arm, posterior aspect of the forearm, web space between thumb and index finger (Fig. 25.1), and skin of the radial side and base of the thumb.

Block Technique

Elbow/Antecubital Fossa (Fig. 25.2):

- Trace the radial nerve around the lateral epicondyle and into the lateral portion of the proximal forearm. The radial nerve can be found deep to the brachioradialis muscle and superficial to the brachial muscle [3, 4].
- Using either the in-plane or out-of-plane technique, localize the skin and then inject approximately 5 ml of local anesthetic around the superficial branch of the radial nerve.

Forearm block (Fig. 25.3):

- The superficial radial nerve is small and difficult to visualize at the wrist, it is often easier to find near the mid-forearm. Starting from the lateral epicondyle, trace the radial nerve into the lateral forearm as it divides into superficial and deep branches. Follow the superficial branch distal to the division, where it should be seen just lateral to the radial artery.
- Using either an in-plane or out-of-plane ultrasound-guided technique, localize the skin and then inject approximately 3–5 mL of local anesthetic around the radial nerve.

Clinical Pearls

- Each of these distal upper extremity blocks can be performed anywhere along the path of the nerves in the arm or forearm but are most commonly performed in the proximal forearm/antecubital fossa, and at the wrist. Ultrasound visualization of the nerves is **easiest** in the **mid forearm**.
- Blocks performed at the at or near the antecubital fossa will provide both motor and sensory blockade, while blocks performed distal to the mid forearm or near the wrist are more likely to provide **only sensory blockade**.
- Small volumes of local anesthetic (3–5 mL) are needed for each of these distal upper extremity blocks.
- The median nerve may be injured at the antecubital fossa by extravasation of IV drugs that are toxic to neural tissue, or by direct injury caused by the needle during attempts to cannulate the medial cubital or basilic veins. The median nerve provides sensory innervation to the palmar surface of the lateral three and one-half fingers and adjacent palm.
- The function of the distal branches of brachial plexus include**: arm flexion** at the elbow (musculocutaneous nerve), **arm extension** at the elbow (radial nerve), **forearm pronation**, wrist flexion and thumb opposition (median nerve), ulnar deviation of the wrist, little finger flexion, **thumb adduction** and flaring of the fingers (ulnar nerve), wrist and finger **extension** (radial nerve).

Questions

1. Twenty minutes after receiving an axillary brachial plexus block with 20 mL mepivacaine 2%, the patient has fully preserved sensation over the dorsum of the hand and is able to extend wrist and fingers. Supplemental blockade of which distal nerve is MOST likely to result in complete anesthesia of the hand?
   A. Median nerve
   B. Musculocutaneous nerve
   C. Radial nerve
   D. Ulnar nerve
2. A patient is scheduled to undergo carpal tunnel release with regional anesthesia as the primary anesthetic. Blockade of which of the following nerves is NOT necessary for surgical anesthesia?
   A. Median nerve
   B. Ulnar nerve
   C. Radial nerve
   D. All of the above
3. The lateral antebrachial cutaneous nerve is a sensory division of which terminal nerve of the brachial plexus?
   A. Median nerve
   B. Musculocutaneous nerve
   C. Radial nerve
   D. Ulnar nerve
4. A 62-year-old woman undergoes urgent exploratory laparotomy, with arterial blood pressure monitoring via a right brachial arterial line. Postoperatively, she complains of numbness and tingling of the lateral palmar aspect of her right hand. Injury to which nerve would MOST likely explain her symptoms?
   A. Median nerve
   B. Ulnar nerve
   C. Radial nerve
   D. Musculocutaneous nerve
5. Which of the following motor functions are correctly paired with appropriate nerve?
   A. Elbow extension—musculocutaneous nerve
   B. Thumb adduction—radial nerve
   C. Finger flexion—ulnar nerve
   D. Wrist extension- median nerve

Answers

1. C, 2. C, 3. B, 4. A, 5.C

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Upper Extremity Blocks: Suprascapular Nerve Block

26

John J. Finneran IV

Introduction

There are two ultrasound-guided approaches that may be used to block the suprascapular nerve, an anterior supraclavicular technique [1] and a posterior supraspinous fossa technique. The posterior approach will be the **focus** of this chapter.

- The **suprascapular nerve** is a branch of either the C5 nerve root or upper trunk of the brachial plexus, which innervates the **glenohumeral** and **acromioclavicular** joints as well as the infraspinatus and supraspinatus muscles.
- The **suprascapular nerve block** provides a motor sparing alternative for partial analgesia following **shoulder surgery** when interscalene block is contraindicated due to coexisting pulmonary pathology (assuming patient will not tolerate phrenic nerve block).
- This block may be used in combination with axillary or infraclavicular nerve block but these still provide less analgesia in comparison with interscalene block.
- **Chronic pain** conditions of the shoulder may also be treated effectively with suprascapular nerve blocks.
- Nerve localization techniques for suprascapular nerve block include **fluoroscopy**, **computed tomography**, **nerve stimulator, blind landmark**, and **ultrasound guidance**. This review will focus on ultrasound-guided suprascapular nerve block.

Anatomy

- For brachial plexus anatomy, review Fig. 22.1, Chap. 22, Regional anesthesia
- The **upper (superior) trunk** of the brachial plexus is formed by the **ventral rami of C5 and C6** nerve roots, the **suprascapular nerve** is a branch from this trunk.
- The suprascapular nerve branches from the upper trunk as it passes deep to the **omohyoid muscle** in the posterior triangle of the neck.
- The nerve then passes through the **suprascapular notch** (Fig. 26.1) deep to the **superior transverse scapular ligament** to enter the **supraspinous fossa**, where it may be found in proximity to the **suprascapular artery**.
- The nerve terminates and supplies the innervation to the **glenohumeral** and **acromioclavicular** joints as well as the **infraspinatus** and **supraspinatus** muscles.

Supplementary Information The online version of this chapter (https://doi.org/10.1007/978-3-030-87266-3_26) contains supplementary material, which is available to authorized users.

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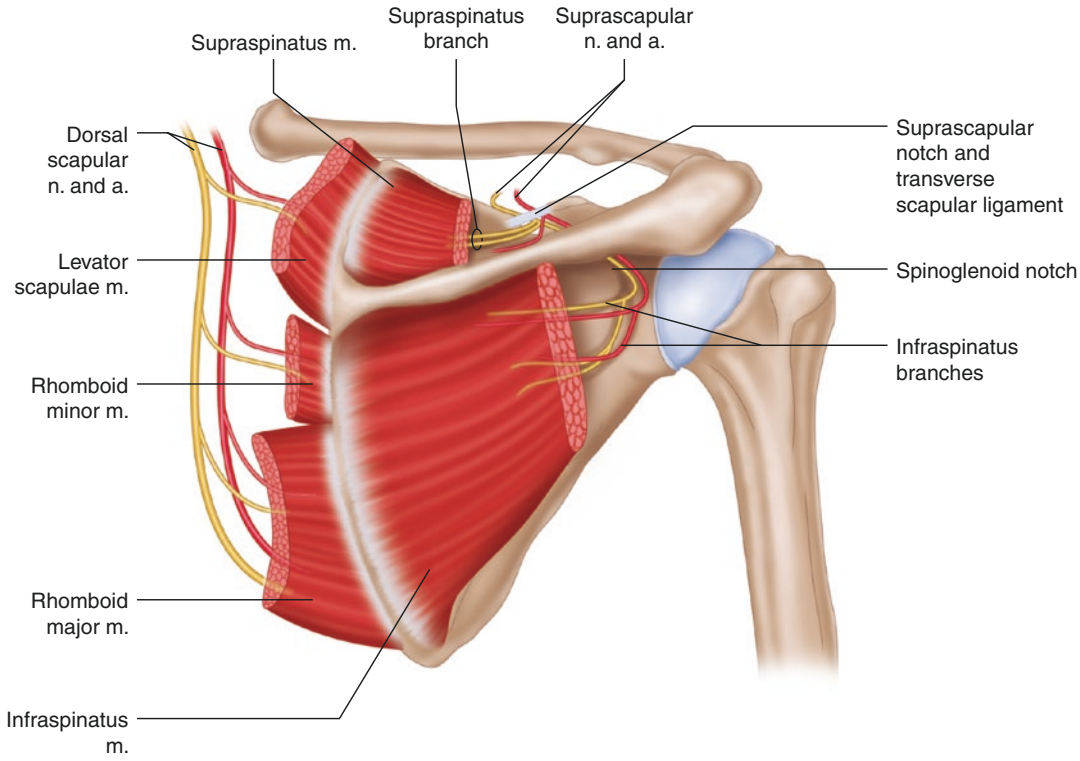

Fig. 26.1 Suprascapular nerve branching from upper trunk of the brachial plexus, running with suprascapular artery on posterior aspect of scapula, and innervating the glenohumeral joint

Indications

- Acute pain
  - Shoulder surgery
    Total shoulder arthroplasty, Reverse total shoulder arthroplasty, Shoulder arthroscopy [2], Proximal humerus hemiarthroplasty, Rotator cuff repair
  - Distal clavicle surgery
    Open reduction and internal fixation of distal clavicle fracture or dislocation
- Chronic pain
  - Adhesive capsulitis [3],
  - Rheumatoid arthritis [4]

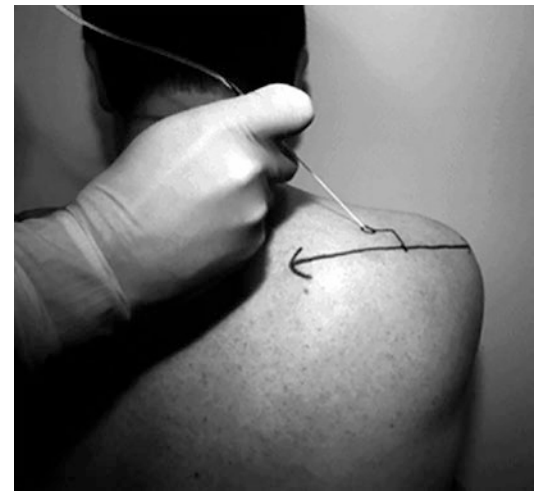

Fig. 26.2 Landmark technique for suprascapular nerve block

Technique

Landmark Technique

The patient is in the sitting position with arm adducted. A line is drawn from lateral part of the acromion to the medial end of the spine of the scapula. The needle entry point is located 2 cm medial and 2 cm cephalad to the midpoint of this line. The needle is inserted 4–6 cm in a lateral and caudal direction at an angle of 45° to the skin. Approxiamtely 10 ml of local anesthetic is then injected (Fig. 26.2).

Ultrasound Technique

Patient is positioned **sitting** (or prone), facing the ultrasound screen. The hand is placed over the contralateral shoulder, which moves the scapula laterally and provides adequate space for ultrasound scanning. The anesthesiologist stands behind the patient (Fig. 26.3a).

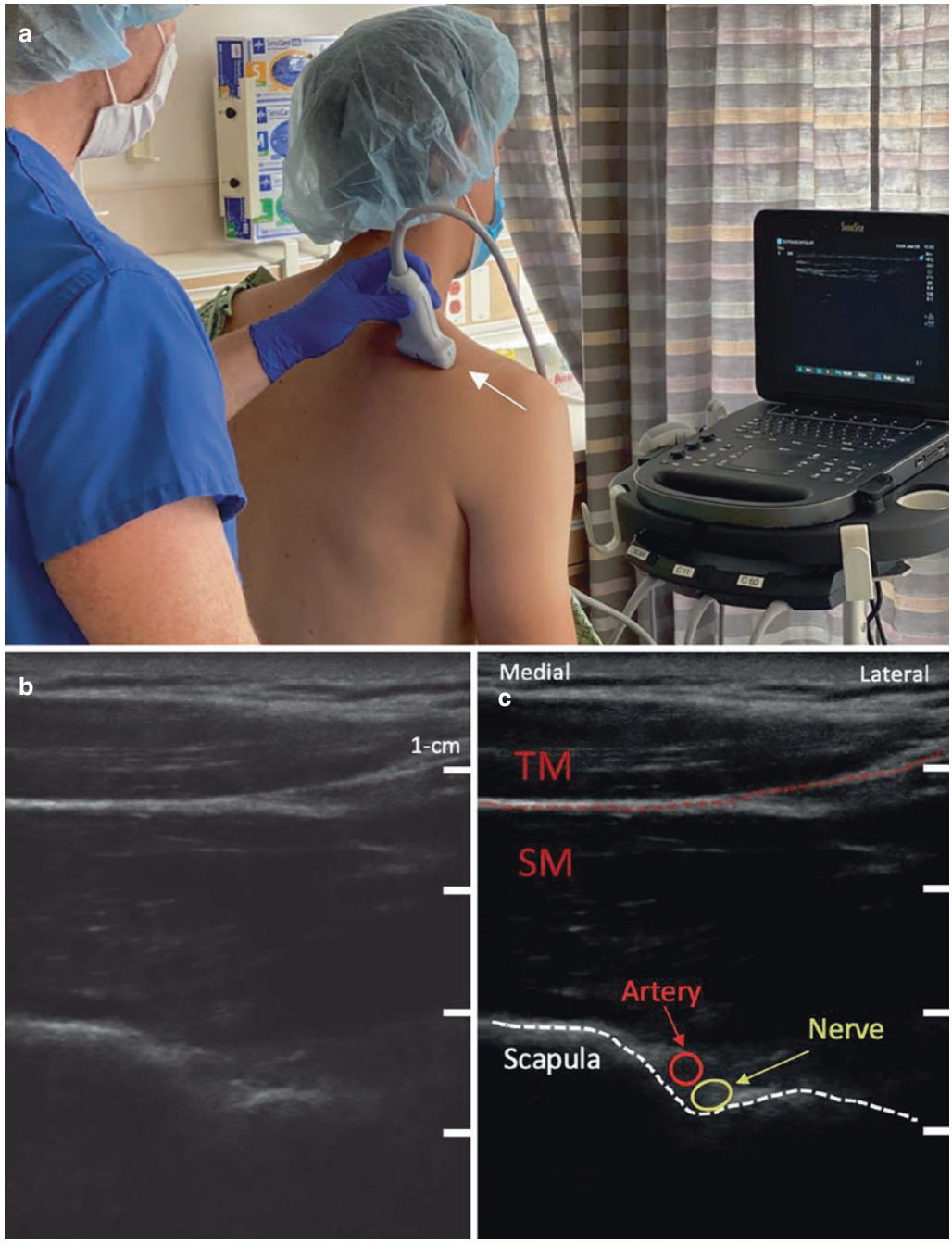

Fig. 26.3 (**a**) Positioning for the posterior supraspinous fossa technique with anesthesiologist standing behind a sitting patient; white arrow indicates the needle entry point for the block. (**b**) Ultrasound image of the suprascapular nerve in the supraspinous fossa of the scapula. (**c**) Trapezius muscle, supraspinatus muscle, suprascapular artery and suprascapular nerve are labeled

- A linear high frequency transducer probe is positioned on the lateral shoulder in a **coronal orientation**.
- The supraspinatus and overlying trapezius muscles are identified and the probe may be moved laterally to visualize the acromion. The transducer is then angled slightly anteriorly to visualize the suprascapular notch. Pulsation from the suprascapular artery can help confirm location of the nerve (Supplementary Video 26.2).
- The suprascapular nerve is visualized as a **hyperechoic** structure in the supraspinous fossa and may be associated with the suprascapular artery (Fig. 26.3b, c).

The needle is inserted in-plane from posteromedial to anterolateral, penetrating the trapezius and supraspinatus muscles until the needle is adjacent to the nerve. Local anesthetics is then injected beneath the fascia of the supraspinatus muscle after negative aspiration for blood. 5–8 mL is sufficient.

Complications

Possible complications include pneumothorax and nerve injury in addition to other complications of a nerve block. These complications are less likely with the posterior approach compared to the anterior approach.

Clinical Pearls

1. Suprascapular nerve injury can be caused by the lateral decubitus position, repetitive motion of shoulder e.g. baseball pitcher, volleball player, weight lifter. Symptoms include pain along the scapula radiating to shoulder and exacerbated by adduction of arm.
2. The suprascapular nerve innervates the supraspinatus and infraspinatus muscles; it injury can cause pain, atrophy, and weakened **abduction and external rotation** of the shoulder which is difficult to distinguish from rotator cuff tears.
3. This block may be used in combination with axillary or infraclavicular nerve block for patients with significant pulmonary comorbidities, but these provide less analgesia in comparison with interscalene block.

Questions

1. The suprascapular nerve is a branch of which part of the brachial plexus?
   A. Posterior Cord
   B. Upper trunk
   C. Lower trunk
   D. C8 nerve root
2. Which of the following muscles is innervated by the suprascapular nerve?
   A. Teres major
   B. Triceps brachii
   C. Infraspinatus
   D. Biceps brachii
3. The primary innervation to the glenohumeral joint is supplied by which nerve?
   A. Lateral pectoral nerve
   B. Axillary nerve
   C. Suprascapular nerve
   D. Radial nerve
4. Suprascapular nerve originates from which of the following nerve root?
   A. C4
   B. C5
   C. C7
   D. C8

Question Answers

1. B, 2. C, 3. C, 4. B

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Trunk Block: Intercostal Nerve Block

27

Poovendran Saththasivam
and Sanjib Das Adhikary

Introduction

- Provide effective analgesia **for acute pain from rib fractures, thoracic surgeries, chest tube placement,**
- Useful for diagnosis and management of chronic chest wall pain secondary to posthoracotomy syndrome, postmastecomy pain syndrome, mestastatic cancer pain, postherpetic neuralgia.
- Can be used as diagnostic block prior to the destruction of intercostal nerves for chronic cancer pain.

Anatomy

- Arise from ventral rami of **T1-T12 thoracic spinal nerves** (Fig. 27.1). They pass through the intervertebral foramina where they are divided into the anterior and posterior rami.
- The anterior rami of T1-T11 enter intercostal spaces (Fig. 27.1). The anterior ramus of T12 forms the subcostal nerve runs inferior to the corresponding twelfth rib.
- The posterior rami of intercostal nerves skin, muscles, and bones of the back (Fig. 27.1a).
- These nerves usually travel in the subcostal groove of each corresponding ribs **laying inferior to the intercostal vess**els (vein, artery, nerve)
- T12 spinal nerve is also known as subcostal nerve
- The intercostal nerve is located between the **internal intercostal** and **innermost intercostal muscle**
- In mid axillary line, the intercostal nerve gives branch to **lateral intercostal nerve** (Fig. 27.1) that supplies sensation to the anterolateral and posterolateral thoracic wall.
- **Anterior cutaneous branches** of T2 to T6 supplies sensation to the anterior thoracic wall around the midline of the sternum (Fig. 27.1)

Indications

1. Postoperative pain management after thoracotomy, sternotomy, mastectomy or chest tube placement
2. Analgesia for rib fracture
3. Chronic chest wall pain due to postherpetic neuralgia, postmastectomy or post thoracotomy pain syndrome, or costochondritis

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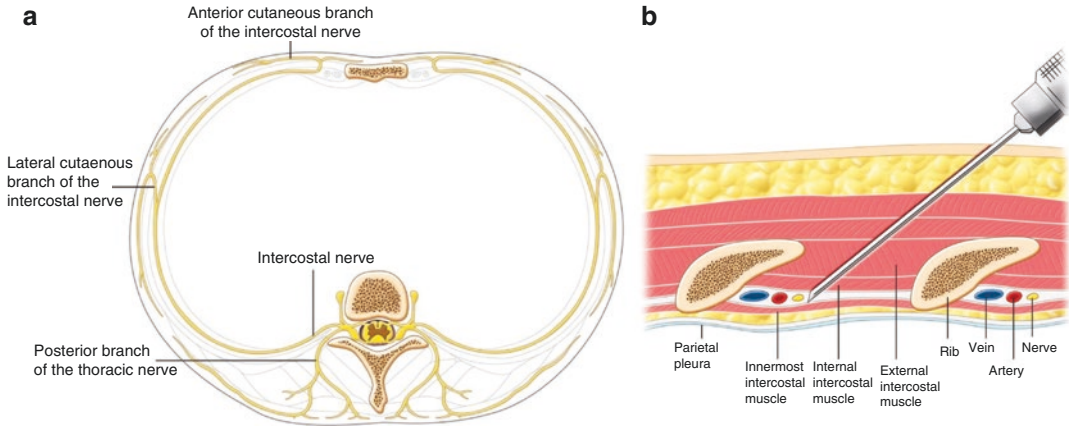

Fig. 27.1 Branches of intercostal nerves (**a**) and their anatomical location in the intercostal groove (**b**). (Chiu and Gulati [1])

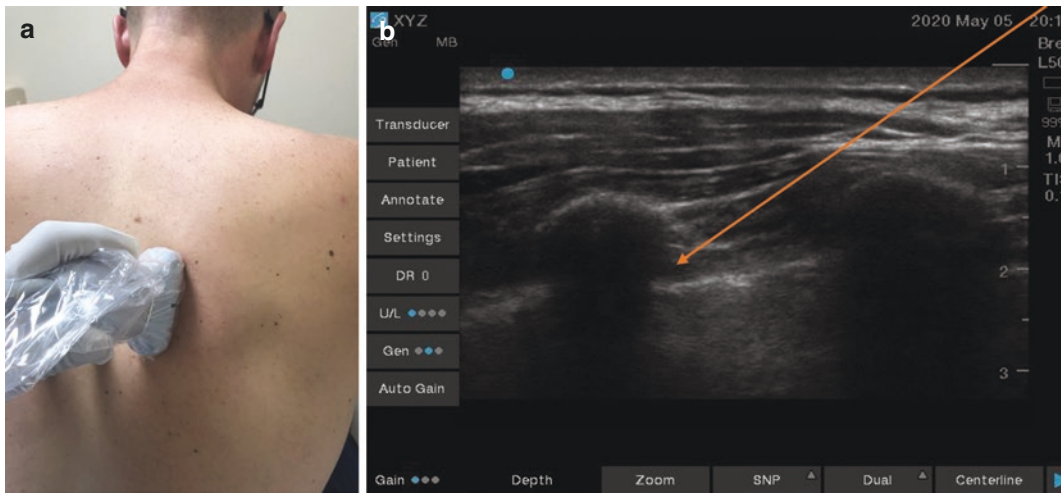

Fig. 27.2 Location of ultrasound probe (**a**) and needle trajectory for intercostal block under ultrasound guidance (**b**)

Technique

Ultrasound Approach

- Patient position can be prone, lateral or sitting
- Place the transducer 6–8 cm **lateral to the spinous process** of the corresponding vertebra (Fig. 27.2)
- The pleura is identified as a prominent **hyperechoic** which is gliding with respiration. The target intercostal nerve lies between innermost intercostal muscles;
- After localizing the skin with 1 cc of 1% lidocaine, a 22 gauge needle can be inserted at 20° in-plane just deep to the internal intercostal muscle which should be placed **2–3 mm above pleura**.
- The needle entry site is the **upper margin of the rib one level caudal** to the targeted intercostal nerve.
- caution is advised for not to advance the needle too deep to avoid pleural puncture and

pneumothorax. The spread of local anesthetics is visualized in real time, injectate is seen pushing the external intercostal muscle upward, and pleura downward.
- If a pneumothorax is present, the **pleura will no longer glides** with respiration.

Landmark Technique

- Preferably done in **sitting** position
- Palpate and mark the inferior border of the rib, about 6–8 cm lateral from the spinous process
- Using sterile technique, palpate and lift the skin using with hand. Using a 27 or 30 G 1 cm needle, direct about 20° and make a contact on the rib with the needle tip. "Walk" the needle inferiorly to the inferior border of the rib
- Advance the needle 2–3 mm until a "pop" is felt which signifies penetration of the facia close to the internal intercostal
- Inject 3–5 cc of local anesthetic agents after negative aspiration
- single-shot intercostal nerve blocks can provide adequate analgesia for approximately 6–8 hours

Complication

- Pneumothorax
- Injury to neurovascular bundle
- Local anesthetic systemic toxicity
- Local skin infection

Preventive Measures to Avoid Complications

- Ultrasound guidance with need tip visualization
- Epinephrine (5 mcg/ml) additive to the local anesthetic to decrease systemic absorption of local anesthetic
- Availability of resuscitative equipment for local anesthetic toxicity
- Post procedure chest radiograph

Clinical Pearls

- Intercostal block has **the highest risk** of local anesthetic systemic toxicity
- From superior to inferior, the neurovascular bundle in the subcostal groove consist of vein, artery and nerve (**VAN**).
- **Pneumothorax** is a common complication and can be disastrous in patients with already compromised cardiopulmonary status
- The safest needle insertion site is at the angle of the rib, about 7 cm from the spinous process because at this location, the subcostal groove is the largest.
- **Epidural analgesia** is safer compare to bilateral intercostal block because of increased risk of local anesthetic toxicity and bilateral pneumothorax

Five MCQ Questions

1. Which of following is true for intercostal nerves?
   A. Covers only the thoracic area
   B. Intercostal nerve runs above the adjacent rib
   C. Give branch to lateral intercostal nerve
   D. No sympathetic innervation from the intercostal nerve
2. The sternum is usually innervated by
   A. Anterior cutaneous branch of intercostal nerve
   B. Anterior branch of lateral cutaneous intercostal nerve
   C. Pectoral nerve
   D. Dorsal rami of intercostal nerve
3. Which of following is incorrect for intercostal nerves?
   A. Gives rise to the lateral cutaneous branch at the midaxillary line
   B. Pierces the posterior intercostal membrane approximately 3 cm lateral to the intervertebral foramen
   C. Travels in between the intercostal artery and vein
   D. Terminates as the anterior cutaneous branch, which supplies the skin over sternum and rectus abdominis

4. Which of the following statements concerning intercostal nerve block is true?
   A. Block at the midaxillary line provides analgesia for the anterior chest walls
   B. Epinephrine (5 mcg/ml) additive to the local anesthetic to decrease paravertebral spread
   C. Angle of needle entry into the subcostal groove is about 20° caudad
   D. None of above
5. Which of the following statement is true regarding intercostal block?
   A. Plasma level of the local anesthetic is higher compare to axillary block after the injection
   B. Pneumothorax is the least common complication
   C. Paravertebral spread is the primary mechanism of action of this block
   D. Intravascular injection of the local anesthetic is less likely to occur

Answer

1. C, 2. A, 3. C, 4. D, 5. A

Reference

1. Chiu YM, Gulati A. Intercostal nerve block. In: Peng P, Finlayson R, Lee S, Bhatia A, editors. Ultrasound for interventional pain management. Cham: Springer; 2020. https://doi.org/10.1007/978-3-030-18371-4_5.

Suggested Further Reading

Page 600, The New York School of Regional Anesthesia Textbook of Regional Anesthesia and Acute Pain Management 1st edition, page 983, Barash 6th edition.

28 Trunk Block: Transversus Abdominis Plane Blocks

Jacob Hutchins and Brian Vaughan

Introduction

- Transverse abdominis plane (TAP) blocks provide analgesia for somatic (incisional) pain of the abdominal wall but do not provide visceral analgesia.
- The **rectus sheath block** (injection between the rectus muscle and the posterior sheath) provides midline analgesia for several dermatomes near midline incisions (Fig. 28.1; green color). **Conventional (lateral) TAP blocks** (injection between the internal oblique and transversus abdominis muscles) placed near the mid-axillary line between the iliac crest and costal margin provide analgesia for lower abdominal surgery (Fig. 28.1; purple color). **Subcostal TAP blocks** (injection between the rectus abdominis muscle and transversus abdominis muscle) placed at the costal margin can provide analgesia for upper abdominal surgery (Fig. 28.1; yellow color).

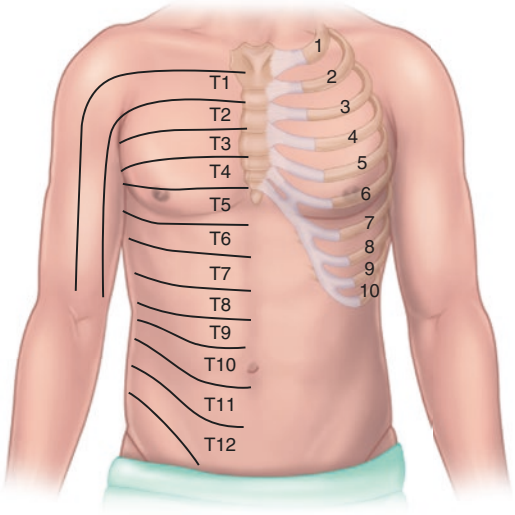

Fig. 28.1 Anatomic basis of the TAP block- conventional (purple), subcostal (yellow), and rectus (green)

Anatomy

- The abdominal wall is innervated by thoracolumbar nerves (T6-L1), which begin as **intercostal nerves** (T6-T11), subcostal nerve (T12), or ilioinguinal and iliohypogastric nerve (L1) (Fig. 28.1).
- These nerves run in a neurovascular plane between the internal oblique and transversus abdominis muscles; the plane allows adequate spread of local anesthetic.

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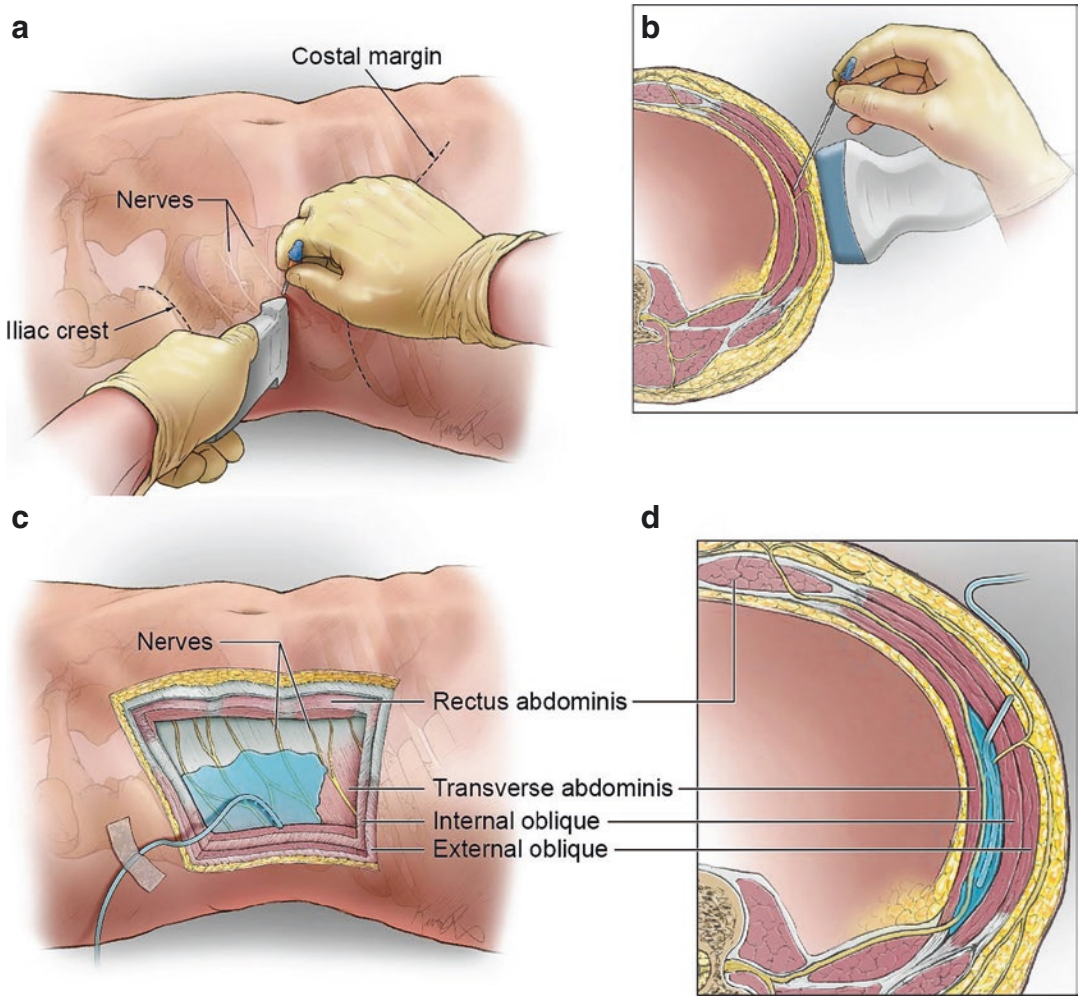

Fig. 28.2 Conventional TAP block using in-plane technique

- Lateral abdominal wall consists of three muscle layers: external oblique, internal oblique, and transversus abdominis (Fig. 28.2c, d)

  The rectus abdominis muscles (Fig. 28.2c, d) are paired vertical muscle (in contrast to others) separated in the midline by the linea alba. The rectus sheath encloses the rectus abdominis muscle.

  The rectus sheath block aims to place local anesthetic between the posterior aspect of the rectus sheath and the rectus abdominis muscle. The posterior wall of the sheath is not attached to the muscle and thus can be separated during the block injection.

Indications

- Surgical procedures with abdominal incisions that are midline or near midline (medial to the anterior axillary line)

- As laparoscopic incisions can usually be well localized with local anesthetic injection around the port sites, pure laparoscopic cases usually **do not need** TAP blocks. However, a rescue TAP block may be needed in PACU if a patient is experiencing more severe pain than is typically seen with pure laparoscopic cases.
  - Laparoscopic hernia repairs often benefit from TAP blocks due to the large number of tacks placed in the abdominal wall
  - As laparoscopic bowel resections, robotic prostatectomies, and hand-assist procedures still require a significant incision in the abdominal wall, these procedures typically benefit from TAP blocks
- More lateral abdominal incisions, such as flank incisions, are better treated with other techniques such as **paravertebral or erector spinae plane blocks**

Techniques

With the patient in a supine position, place a high-frequency ultrasound transducer perpendicular to the long axis of the body at the mid to anterior axillary line at the level of umbilicus (Fig. 28.2a). Visualize the external, internal oblique, and transverse abdominis muscles and peritoneal cavity (Figs. 28.2b, d and 28.3b). Under ultrasound guidance, insert the needle in-plane from medial to lateral (Fig. 28.2b). The needle tip is visualized as it penetrates the fascial layer between the internal oblique and transverse abdominis muscles. After negative aspiration, inject 20–30 mL of local anesthetic per side at 5-mL increments after negative aspiration. Expansion of the interfascial layer should be visualized (Fig. 28.3c), with downward displacement of the transverse abdominis muscle.

For subcostal TAP blocks, the transducer is placed along the costal margin to visualize the rectus abdominis muscle and its posterior fascial sheath. Insert the needle in-plane approach between the rectus abdominis (or internal oblique) and transverse abdominis muscles. After negative aspiration, inject 20–30 mL of local anesthetic per side at 5-mL increments after negative aspiration.

For rectus sheath blocks, the transducer is placed below the costal margin on the lateral edge of the rectus muscle. Identify the rectus muscle, and anterior and posterior rectus sheaths. Insert the needle in an in-place approach from a lateral-to-medial direction through the rectus muscle. Place the tip between the muscle body and the posterior sheath. After negative aspiration, inject 10–20 mL of local anesthetic at 5-mL increments after negative aspiration.

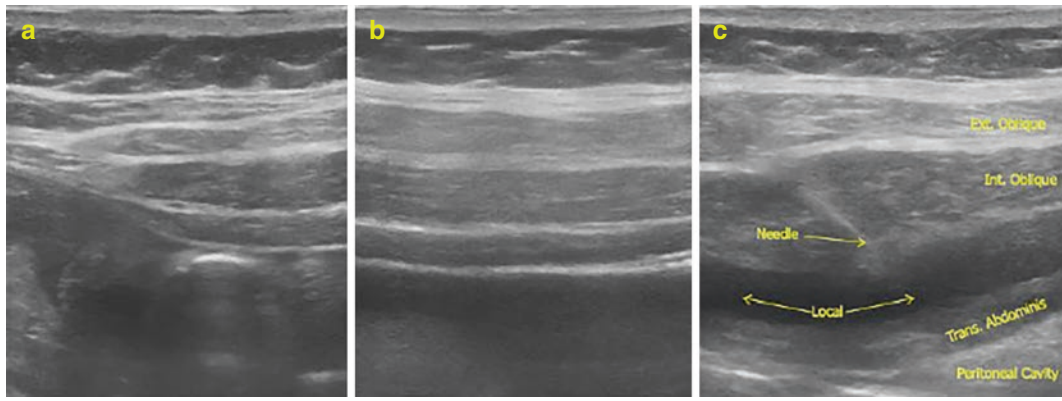

Fig. 28.3 Conventional TAP block ultrasound anatomy before (**a** and **b**) and after (**c**) injection

Clinical Pearls

- Benefits of TAP blocks compared to epidural:
  - Similar analgesia
  - Decreased side effects/complications- e.g. no motor block (weak legs); sympathetic block (hypotension); or urinary retention
  - Technically easier to place and ultrasound-guided as opposed to blind/landmarks based technique
  - Little concern with anticoagulants
  - Simpler for nurses to manage
- For an optimal block, create a layer of local anesthetic between the fascia and the muscle (Figs. 28.2d and 28.3c). Injection into the muscle limits the spread of local anesthetic and increases the risk of local anesthetic toxicity.
- Like all plane blocks, TAP blocks are volume dependent for their effectiveness- use up to 30 mL per side (60 mL total)
- When adjusting local anesthetic dose for patient size or comorbidities, decrease the concentration rather **than the volume** to give the appropriate milligram dose of local anesthetic
- Midline incisions require bilateral blocks for adequate analgesia; also consider rectus block.

Questions

1. In which potential space is the correct location to inject local anesthetic when performing a TAP block?
   A. Superficial to the external oblique muscle
   B. Between the external and internal oblique muscles
   C. Between the internal oblique and the transversus abdominis muscles
   D. Deep to the transversus abdominus muscle and superficial to the deep fascia of the transversus abdominus
2. Which is a benefit of a TAP block compared to an epidural?
   A. Improved analgesia
   B. Decreased risk of lower extremity weakness
   C. Sympathetic blockade
   D. Decreased risk of bowel injury
3. TAP blocks are NOT effective for which of the following procedures?
   A. Radical nephrectomy
   B. Hysterectomy
   C. Bowel resection
   D. Anterior spinal fusion
4. Which of the following is a risk of a TAP block?
   A. Hypotension
   B. Urinary retention
   C. Headache
   D. Bowel injury
5. TAP blocks provide analgesic coverage to which of the following?
   A. Bowel
   B. Liver
   C. Parietal peritoneum
   D. Iliac crest
6. The triangle of petit is formed by the latissimus dorsi, iliac crest and?
   A. Internal oblique
   B. External oblique
   C. Transversus abdominis
   D. Rectus abdominis
7. Which of the following nerves are blocked by a TAP block?
   A. Ilioinguinal
   B. Genitofemoral
   C. T4 intercostal
   D. Axillary

Answers

1. C. Local anesthetic should be deposited in the potential space between the internal oblique and transversus abdominis.

2. B. As only sensory nerves of the abdominal wall are typically affected by a TAP block, there is little risk of lower extremity weakness.
3. A. Typically a flank incision is used for a radical nephrectomy which it too lateral for a TAP block to be effective. A paravertebral or erector spinae block would be a better choice for analgesia.
4. D. Although rare, bowel injury can occur if the block needle enters the peritoneal cavity. All other choices are risks of epidural analgesia.
5. C. TAP blocks provide incisional coverage only and do not provide visceral coverage.
6. B. The triangle of petit is formed by external oblique, latissimus dorsi, and iliac crest.
7. A. TAPs block the T7-T11 intercostal nerves, subcostal (T12) and ilioinguinal and iliohypogastric nerves (L1).

Further Reading

Chinn JK, McDonnell JG, et al. Essentials of our current understanding: abdominal wall blocks. Reg Anesth Pain Med. 2017;42:133–83.

29 Trunk Block: Thoracic Paravertebral Nerve Block

Asif A. Ansari and Christina L. Jeng

Introduction

- Thoracic PVB (TPVB) is used for surgical and post-operative analgesia for chest wall, thoracic and abdominal surgeries [1]. This block anesthetizes spinal nerves as they emerge from intervertebral foramina and run through the paravertebral space.
- Also used for nonsurgical indications including rib fractures and chronic pain conditions. TPVB can be performed unilaterally or bilaterally depending on surgical or nonsurgical indication.

Anatomy

- TPVB space is a **triangular-shaped area** which starts at T1 and terminates at T12. The thoracic spinal nerves run through the space from the intervertebral foramina to become intercostal nerves (Fig. 29.1).
- The borders of the TPVB space include:
  - Medial – Vertebrae
  - Antero-lateral – Pleura
  - Posterior – Costo-transverse ligament
- This space contains adipose tissue, anterior and posterior rami, sympathetic chain, and the rami communicantes.
- Laterally, the paravertebral space is continuous with the **intercostal space**, medially it communicates with the epidural space via the **intervertebral foramina**, and with the contralateral paravertebral space through the prevertebral fascia. Superiorly, the paravertebral space is in close proximity to the adipose tissue associated with the **brachial plexus** and inferiorly it ends in **psoas major** muscle.

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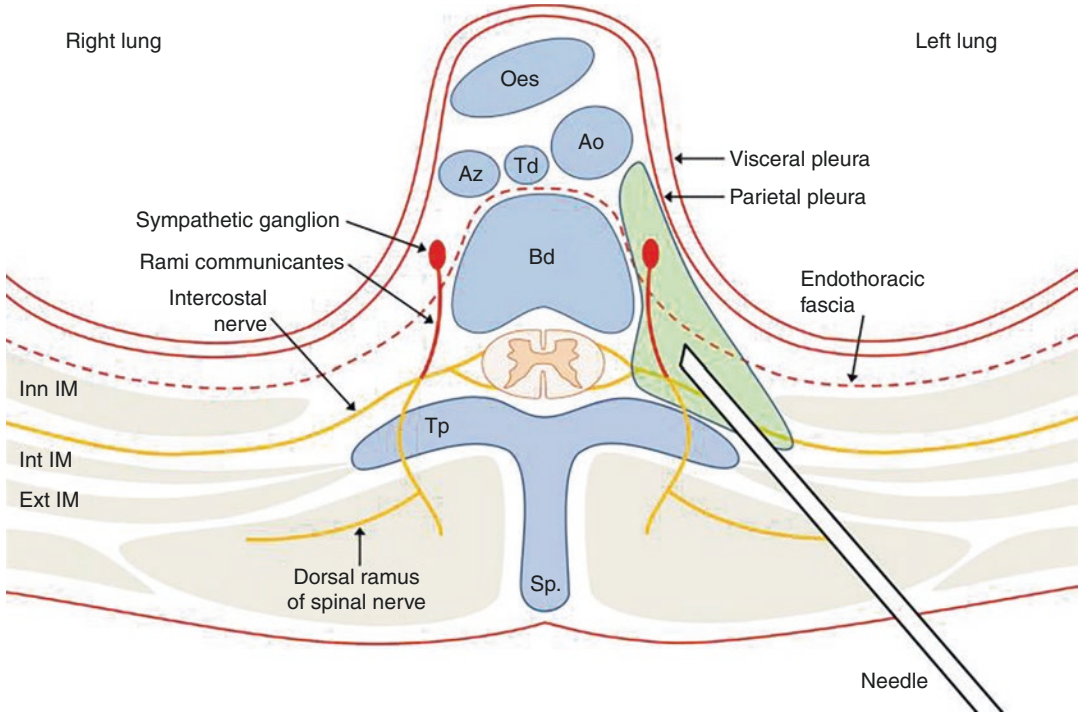

Fig. 29.1 Anatomy of the thoracic paravertebral space (triangle). Tp transverse process, Sp spinous process, Bd vertebral body, Oes esophagus, Ao aorta. (Reproduced with permission from Springer)

Indications

- Can be used as primary anesthetic for breast surgery, herniorrhaphy, and chest wound exploration
- Post-operative analgesia for:
  - Breast surgery
  - Thoracic surgery including thoracoscopy, thoracotomy, VATS
  - Abdominal surgery, renal surgery, herniorrhaphy, cholecystectomy, and appendectomy
- Also used for treatment of chronic pain conditions such as post-herpetic neuralgia

Technique

- Patient can be positioned in the sitting, prone, or lateral position. The spinous process of **C7** is identified as the **most prominent** in this region. The spine of the scapula corresponds to **T3**, and the lower border of the scapula corresponds to **T7** [2].
- A high-frequency (5- to 19-MHz) linear transducer is placed approximately 2 cm lateral to the midline of desired spinal level (Fig. 29.2a). Identify the junction head of rib and transverse process. The probe is rotated into a **cranio-caudal** orientation until the optimal ultrasound image is achieved (Fig. 29.2b).
- A needle is then introduced in a caudad to cranial manner in plane until it traverses the costo-transverse ligament. Often a "pop" is felt when it passes through the ligament.
- Local anesthetic is injected, after negative aspiration (no heme or CSF aspirated); the pleura will be shown to be displaced downward.
- Typically, local anesthetic can spread **4–5 levels** - 2 levels above and 2 below from the point of injection.

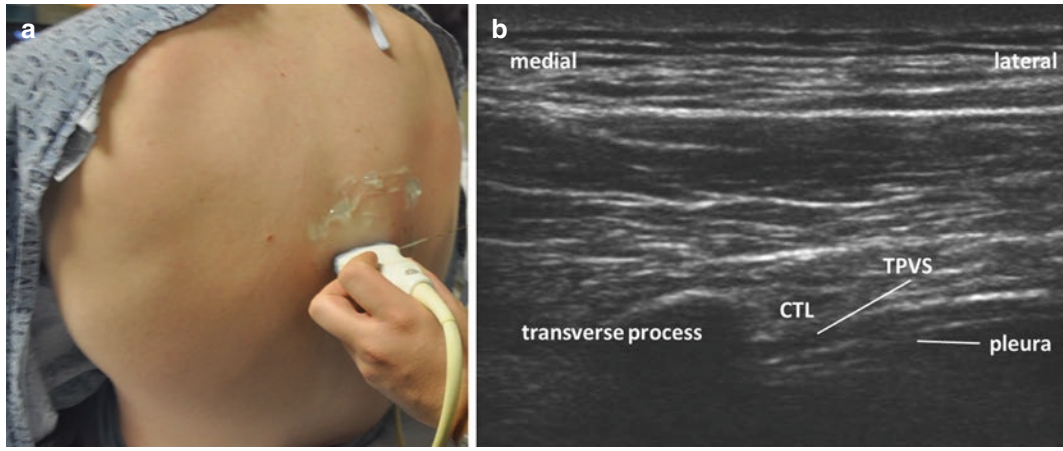

Fig. 29.2 (**a**) Transverse scan for thoracic paraverterbral nerve block (left). (**b**) Sonographic image shows the thoracic paravertebral space (TPVS) and related structures; CTL costotransverse ligament (right). (Reproduced with permission from Springer)

- 20 milliliters of local anesthetic is sufficient to produce adequate analgesia.
- Indwelling catheters may be placed through 18-gauge Touhy needle for continuous TPVB. After injecting either LA or saline through the needle, a multi-orifice epidural catheter is threaded far enough past the needle tip. The catheter is then secured to the skin with Dermabond and a sterile dressing.
- Continuous infusion of local anesthetic (typically 0.125 or 0.0625% bupivacaine) is administered at 6–14 mL/hour postoperatively.

Complications

- Unique complications for PVB include [3]:
  - Hypotension
  - Epidural or intrathecal spread
  - Pleural puncture
  - **Pneumothorax**

Clinical Pearls

- The TPVB space contains adipose tissue, anterior and posterior rami, sympathetic chain, and the rami communicantes (Fig. 29.1). This space communicates with the epidural space medially and the intercostal space laterally.
- The spinal nerves in the TPVB are devoid of a fascial sheath, making them sensitive to local anesthetics. The unique feature of TPVB is **blockade of sympathetic trunk** in addition to neuraxial blockade.
- TPVB is superior to intercostal block as it blocks **posterior branch of intercostal nerves** (innervates the skin of the back) which are missed in typical intercostal blocks.

Multiple Choice Questions

1. Which of the following structures lie within the paravertebral space?
   A. Adipose tissue
   B. Anterior and posterior rami
   C. Sympathetic chain
   D. All of the above
2. Which of the following factors would increase epidural or intrathecal spread during PVB?
   A. Directing the needle medially
   B. Low velocity and low pressure when injecting local
   C. Keeping the bevel pointed laterally during block placement
   D. Foraminal stenosis

3. The paravertebral space communicates with which of the following structures medially?
   A. Epidural space
   B. Intercostal space
   C. Peritoneal cavity
   D. Pleural space
4. Which of the following structures is the medial border of the paravertebral space?
   A. Pleura
   B. Vertebrae
   C. Costo-transverse ligament
   D. Costo-transverse junction
5. While performing a paravertebral block at T6, your patient becomes hypotensive and complains of difficulty breathing. Which if the following is least likely the cause?
   A. Pneumothorax
   B. Anaphylaxis
   C. Phrenic nerve irritation
   D. Epidural injection

Answer

1. D, 2. A, 3. A, 4. B, 5. C.

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3. Riain SC, Donnell BO, Cuffe T, Harmon DC, Fraher JP, Shorten G. Thoracic paravertebral block using real-time ultrasound guidance. Anesth Analg. 2010;110(1):248–51.

Trunk Block: Ilioinguinal and Iliohypogastric Nerve Block

30

Peter Yi and Gabriel Nam

Introduction

- An ilioinguinal nerve block provides intraoperative and postoperative analgesia to the hypogastric region of the abdomen, mons pubis, portions of the labia majora or penis and scrotum, upper medial thigh
- Provides a potential low risk alternative to general or neuraxial anesthesia for **inguinal hernia repair** in the ambulatory setting [1]

Anatomy

- The ilioinguinal and iliohypogastric nerves are primarily from the **L1 spinal nerve** (Fig. 30.1) and emerges from the lateral border of the psoas major muscle [2]
- Travels across the quadratus lumborum and iliacus, penetrating the transverse muscle above the iliac crest [3].
- Both the ilioinguinal and iliohypogastric nerves travel inferomedially from the anterior superior iliac spine (ASIS) in the **fascia plane between the internal oblique and transversus abdominis muscles** [4] (Fig. 30.2b and c)
- Provides afferent innervation to the cremasteric reflex

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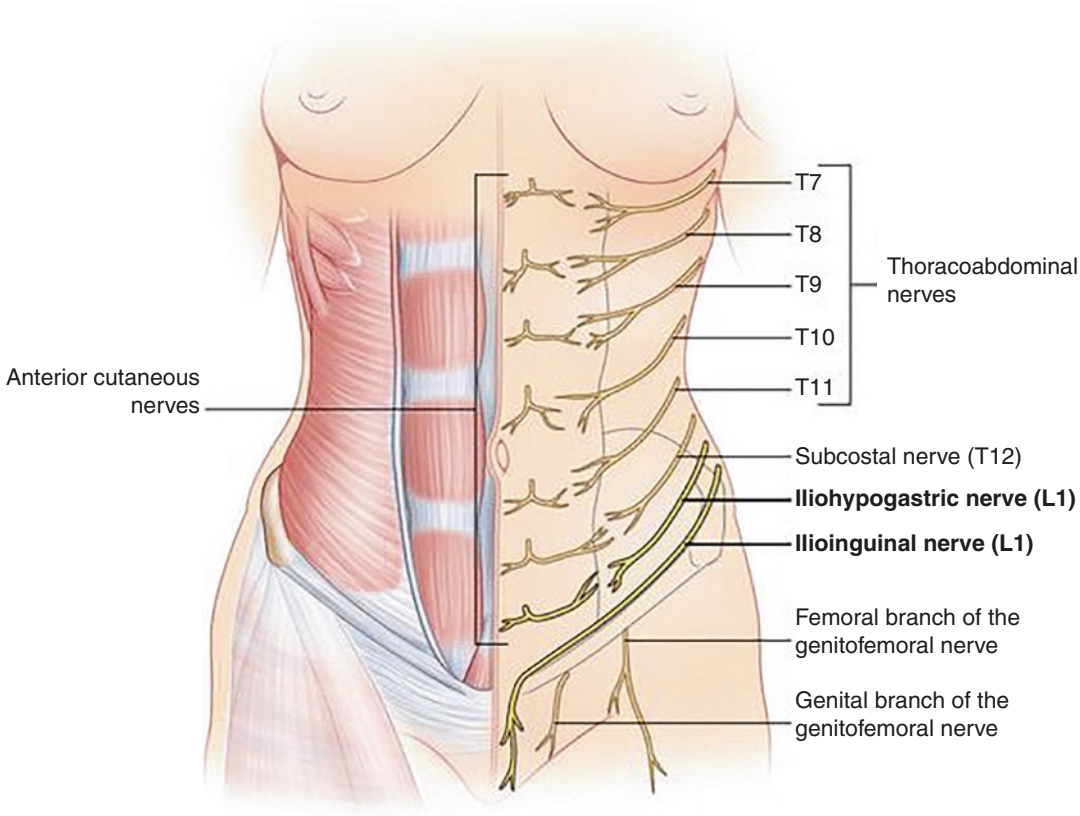

Fig. 30.1 Anatomy of the anterior abdominal wall ((Image by Springer) Amin et al. [6])

Indications

- Analgesia for inguinal hernia repair, elective caesarean section, orchidopexy, hydrocele or varicocele repair [5]
- Diagnostic tool in patients with chronic inguinal, lower abdominal, and/or pelvic pain

Technique

- Identify the ASIS. Place a linear ultrasound transducer (6- to 18-MHz) is initially placed **perpendicular** to the anterior superior iliac spine (Fig. 30.1a; (a) and then rotated parallel to the ilioinguinal and iliohypogastric nerve (Fig. 30.1a; (b). the final position of the transducer will be in parallel to the line drawn from ASIS to umbilius [3].
- Visualize the external oblique, internal oblique, and transversus abdominis muscles (Fig. 30.2b, c).
- A 50 or 100-mm, 22-gauge needle is inserted in plane in a medial-to-lateral direction until it reaches facial plane between internal oblique and transverse abdominis. After negative aspiration, inject 10 mL of LA in 5-mL increments, with gentle aspiration between.

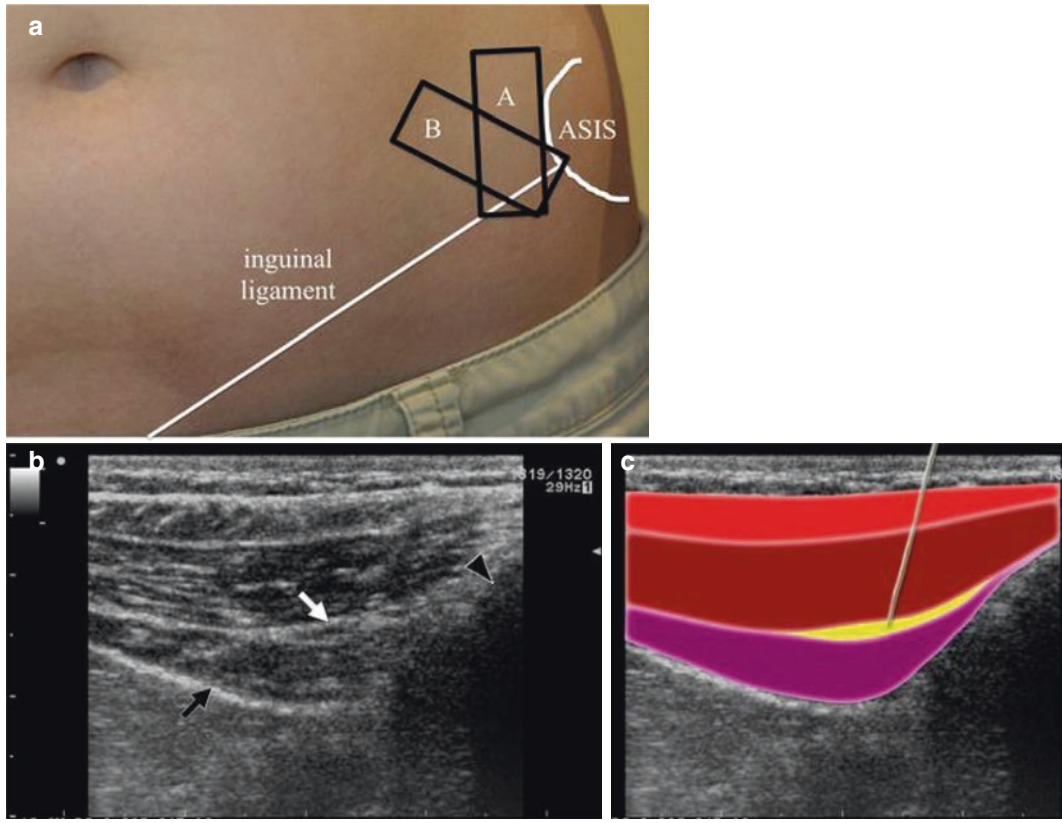

Fig. 30.2 (**a**) Location of the ultrasound probe. Probe is initially placed perpendicular to the anterior superior iliac spine (site *A*) and then rotated parallel to the ilioinguinal and iliohypogastric nerve (site *B*). (**b**) Ultrasound image of the ilioinguinal and iliohypogastric nerves (*white arrow*) and simulation of the ultrasound placement of a needle onto the ilioinguinal nerve. (**c**) *Orange* external oblique muscle, *red* internal oblique muscle, *yellow* location of ilioinguinal and iliohypogastric nerves with local anesthetic, and *pink* transversus abdominis muscle. *Black arrow* represents peritoneum; *black arrowhead* represents anterior superior iliac spine. (Amin et al. [6])

Clinical Pearls

- Ilioinguinal nerve block is often used for inguinal hernia repair, particularly in the pediatric population [1]
- The ilioinguinal nerve originates primarily from the **L1 spinal nerve** with the iliohypogastric nerve and travels between the internal oblique and transversus abdominis muscles [3]
- Ilioinguinal nerve innervates the anterior surface of the **scrotum or labia majora, root of the penis or mons pubis**, part of the upper antero-medial thigh

Multiple Choice Questions

1. At which spinal level does the ilioinguinal nerve primarily arise from?
   A. T11
   B. T12
   C. L1
   D. L2
2. An ilioinguinal nerve block does NOT provide analgesia for which procedure?
   A. Anorectal exam
   B. Elective cesarean section
   C. Inguinal hernia repair
   D. Orchidopexy

3. Which nerve can be blocked as a complication of performing an ilioinguinal block?
   A. Sciatic nerve
   B. Obturator nerve
   C. Intercostal nerve
   D. Femoral nerve
4. Which muscle is NOT usually penetrated to perform a successful ilioinguinal nerve block?
   A. Transverses abdominus
   B. External oblique
   C. Internal oblique
   D. None of the above
5. If a patient receives a spinal for cystoscopy and cautery is used, which nerve should be blocked to avoid inadvertent leg muscle contraction?
   A. Lateral femoral cutaneous nerve
   B. Ilioinguinal nerve
   C. Obturator nerve
   D. Iliohypogastric nerve

Answers

1. C, 2. A, 3. D, 4. A, 5. C.

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Further Reading

Pages 984–985, Barash 8th Edition; Pages 1691–1692, Miller 7th Edition; Page 1021, Morgan & Mikhail 5th Edition.

Trunk Block: Erector Spinae Block

31

Danielle M. Lindenmuth and Rachel Stahl

Introduction

- Erector spinae plane (ESP) block is an interfacial plane block which was first described in 2016.
- While primarily performed in the thoracic region, there are reports of this block being performed anywhere from the cervical to the lumbar region.
- ESP block for rib fracture patients has been shown to be beneficial as it results in [1]:
  - Improved Incentive Spirometry Volumes
  - Improved Pain (VAS) Scores
- The target of the ESP block is between the **deepest layer of the erector spinae muscles and the tip of the transverse process** (Fig. 31.1). Following a single injection of 20 ml, it has been shown that the local anesthetic spreads in both cephalad and caudad directions over an average of **3–6 spinal segments.**
- The mechanism of analgesic action is believed to result from diffusion of local anesthetic anteriorly to the **ventral and dorsal rami of the spinal nerves**.
- Variably, the local anesthetic can continue to the paravertebral space where the spinal nerves and sympathetic chain are located. In some cases, local anesthetic may even cross to the contralateral side via the epidural space [2].
- The ESP block has a **better safety profile** than epidural and paravertebral nerve blocks because the site of injection is distant from the pleura, major blood vessels, and spinal cord.

Anatomy

Anatomy of the Erector Spinae Plane

- The ESP muscle group contains 3 groups of muscles: **iliocostalis, longissimus, spinalis**
- Each of these muscle groups contains 3 individual muscles; each individual muscle has a unique site of insertion along the cervical, lumbar, or thoracic spine

Anatomy of Nerves of the Erector Spinae Block

- **Thoracic dorsal rami** (Fig. 31.1) arise from the spinal nerve and innervate skin and deep muscles in the back
- **Thoracic ventral rami** (Fig. 31.1) arise from the spinal nerve and give rise to intercostal nerves in the thoracoabdominal region

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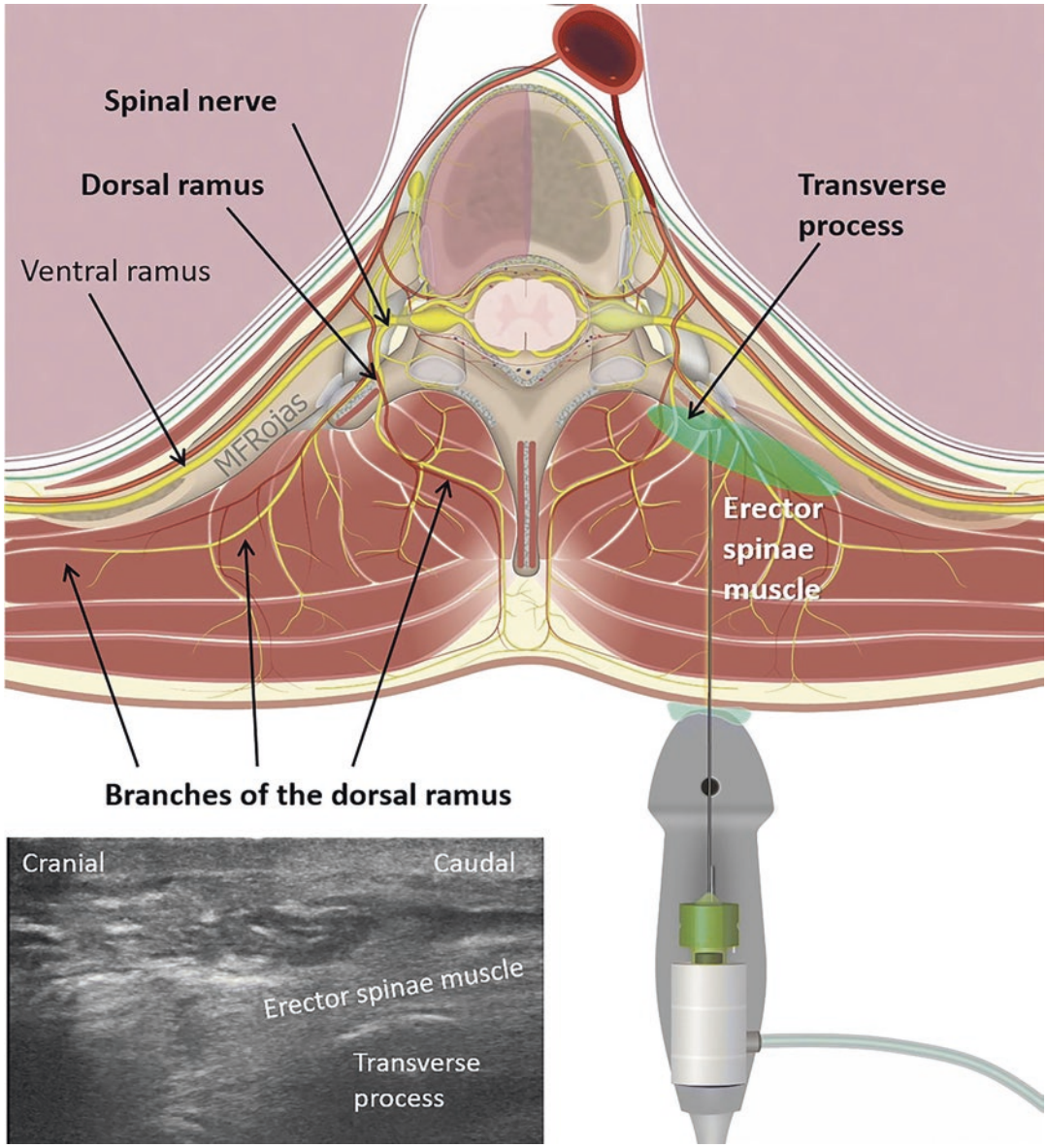

Fig. 31.1 The erector spinae plane block is performed by injection of local anesthetic into the musculofascial plane between the deep aspect of the erector spinae muscle and the transverse processes. This local anesthetic (green oval) spreads to effectively anesthetize the branches of the dorsal rami of the spinal nerves that travel through this plane. (https://www.springer.com/gp/rights-permissions/obtaining-permissions/882. Chin et al. [4])

Indications

- C7 to T5: Chronic or post-surgical shoulder pain
- T2 to T4: Breast surgery +/− axillary lymph node dissections
- T2 to T12: Rib fractures: anterior, posterior, or lateral
- T4 to T10: Open thoracotomy and VATS, sternotomy, post-herpetic neuralgia, chronic post-thoracotomy pain, metastatic cancer to the chest wall
- T7 to T12: Nephrectomies, hysterectomies, ventral hernia repair with mesh, chronic abdominal pain syndrome, chronic pelvic pain syndrome

- T8 to L4: Hip surgery
- Postoperative pain after lumbar or thoracic spine surgery [3, 4]

Relative Contraindications

- Anticoagulation
  - While patients have undergone cardiac surgery after receiving these blocks, risks and benefits should be weighed before performing an ESP block on a fully anticoagulated patient.
  - Caution with large gauge Tuohy needle for catheter placement is warranted.

Technique

- The patient can be in the prone, sitting or lateral position.
- Place a linear, high-frequency ultrasound transducer over the spinous process in the parasagittal plane.
- Place transducer 4–5 cm lateral to the spinous process and identify skin, subcutaneous tissue, muscles of the back (trapezius, rhomboid muscle at T3-T6, and erector spinae), ribs, and intercostal muscles (Fig. 31.2).
- Slide the transducer medially to identify the transition between transverse process and ribs (Fig. 31.3) The transverse processes will appear **more square-shaped in contrast to the ribs which appear more rounded in shaped** (Fig. 31.2).
- Insert the needle in-plane with the transducer in a cephalad to caudad direction and advance the tip of the needle to the area between the **erector spinae muscles and the tip of the transverse process** [5].
- Following negative aspiration, inject 20–30 mL of LA in 5 mL increments, aspirating between injections.

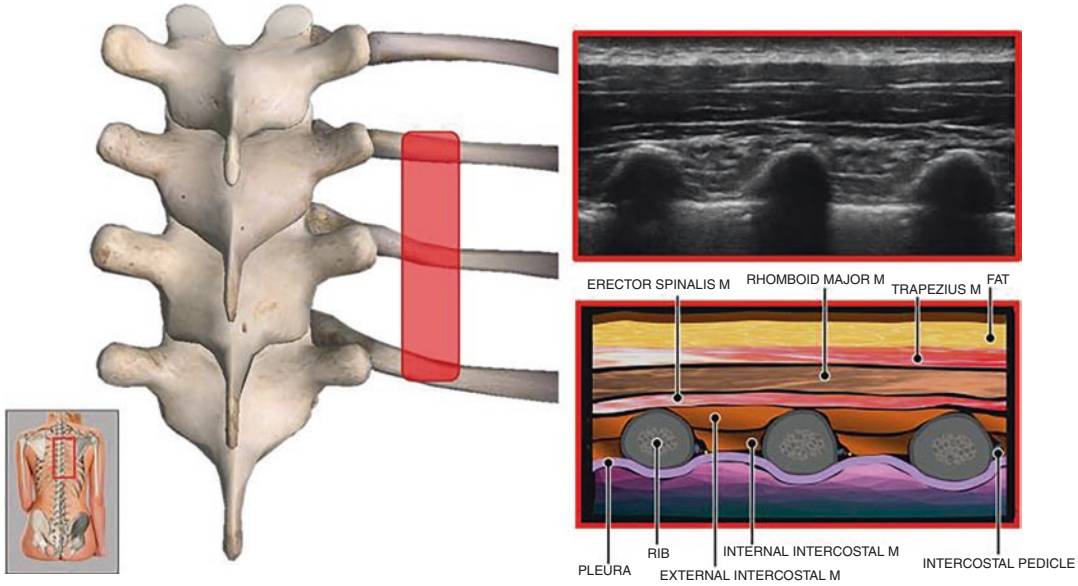

Fig. 31.2 Lateral Scan of ribs during ESP block

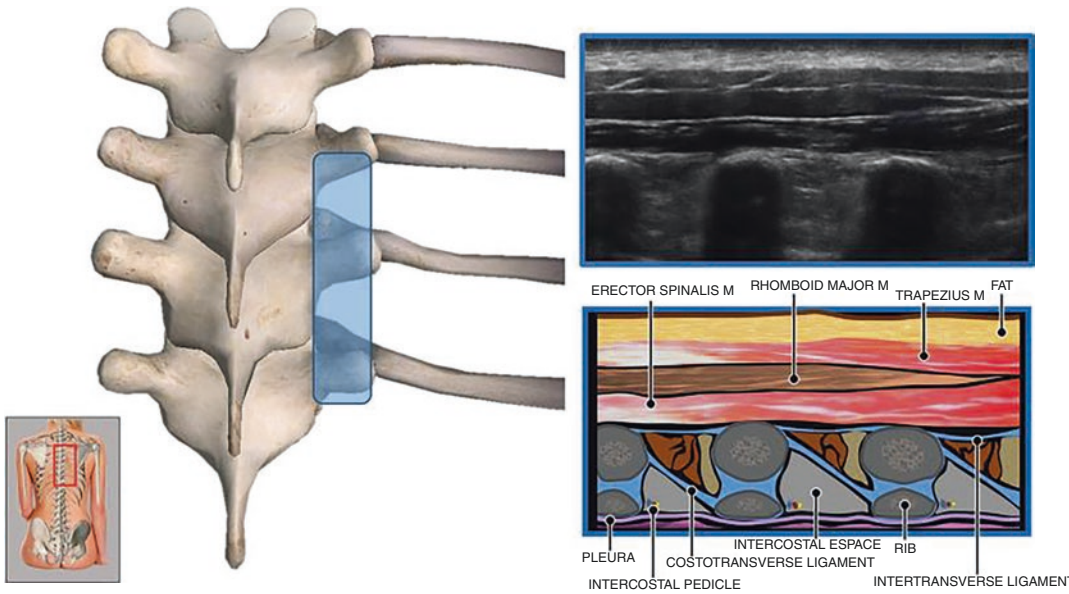

Fig. 31.3 Target Scan of the tip of the transverse process during ESP block

Complications

- Harlequin Syndrome has been reported following an ESP block at the T3 level.
- Priapism has been reported following an ESP block at the L4 level.

Clinical Pearls

- The block has been widely used for the treatment of acute postoperative pain after superficial and deep surgery in the chest wall and axillary regions (e.g., mastectomy, VATS, breast surgery, chest tube placement, multiple rib fractures) as well as for spine, hip, and shoulder surgery.
- Positioning the patient in the prone or sitting position may be easier than lateral.
- If visualization of the ultrasound anatomy is difficult, location of the tip of the transverse process may be visualized by rotating the probe 90 degrees and scanning medial to lateral in the transverse plane. Identify this point on the patient with a marking pen, prior to scanning in the parasagittal plane.
- In addition to somatic coverage, there is evidence of visceral pain relief in patients with pancreatitis, preoperative appendicitis pain, and chronic visceral abdominal pain [6].

Questions

1. The erector spinae plane block is performed between:
   A. Transverse process tip and trapezius muscle
   B. Transverse process middle and erector spinae muscles
   C. Transverse process tip and erector spinae muscles
   D. Erector spinae muscles and trapezius muscle

2. Which muscle is not part of the erector spinae muscle group:
   A. Rhomboid major
   B. Iliocostalis
   C. Longissimus
   D. Spinalis
3. What is an absolute contraindication to performing an ESP block?
   A. Therapeutic heparin stopped 4 hours ago
   B. Patient refusal
   C. Plavix stopped 2 days ago
   D. Anterior location of rib fracture pain
4. The ESP block can be used for which of the following:
   A. Anterior rib fractures and sternal fractures
   B. Posterior rib fractures
   C. Postoperative spine surgery pain
   D. All of the above
5. What is the correct order of structures encountered during a thoracic ESP block from most superficial to deep?
   A. Subcutaneous tissue, rhomboid muscle, trapezius muscle, erector spinae muscle, transverse process
   B. Subcutaneous tissue, trapezius muscle, rhomboid muscle, erector spinae muscle, transverse process
   C. Subcutaneous tissue, trapezius muscle, rhomboid muscle, erector spinae muscle, interspinous ligament, transverse process
   D. Subcutaneous tissue, rhomboid muscle, trapezius muscle, erector spinae muscle, interspinous ligament, transverse process
6. All of the following complications have been noted in case reports after an ESP block except:
   A. Harlequin Syndrome
   B. Priapism
   C. Pneumothorax
   D. Epidural spread

Answers

1. C, 2. A, 3. B, 4. D, 5. B, 6. C.

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Truncal Block: Pectoralis Nerve Block

32

Trina M. Kleiver

Introduction

- Pectoral (PECS) blocks provide analgesia for the chest wall and can provide postoperative pain relief for breast surgery and for a variety of other procedures. While paravertebral blocks are considered the gold standard for chest wall analgesia, PECS blocks provide a simple and less invasive alternative for postoperative pain control. They have proved non-inferior to paravertebral blocks.
- The PECS 1 block targets the **lateral pectoral nerve and the medial pectoral nerve**, both of which run between the pectoralis major and pectoralis minor muscles and originate from the brachial plexus. PECS 2 block targets the lateral branches of the **intercostal nerves,** as well as the **long thoracic and thoracodorsal nerves. Additionally,** the **intercostobrachial nerve** is blocked for axillary coverage (Fig. 32.1a).
- These blocks spare the anterior branches of the intercostal nerves (Fig. 32.1b); therefore, the **medial half of the breast will be spared**, as well as the overlying skin and subcutaneous tissues in the parasternal areas of the chest wall.

Chest Wall Innervation

- Several nerves provide sensation to the chest wall including (Fig. 32.1):
  - Anterior branches of T2-6 intercostal nerves
  - Medial pectoral nerve (Brachial plexus: C8-T1)
  - Lateral pectoral nerve (Brachial plexus: C5-7)
  - Intercostobrachialis nerve (branch of T2)
  - Long thoracic nerve (Brachial plexus: C5-7); innervates serratus anterior muscle)
  - Thoracodorsal nerve (Brachial plexus: C6-8); innervates latissimus dorsi muscle)

Types of PECS Blocks

PECS 1

- Local anesthetic is injected between the **pectoralis major and pectoralis minor muscles** at the level of the third rib
- Blocks the **medial and lateral pectoral nerves**

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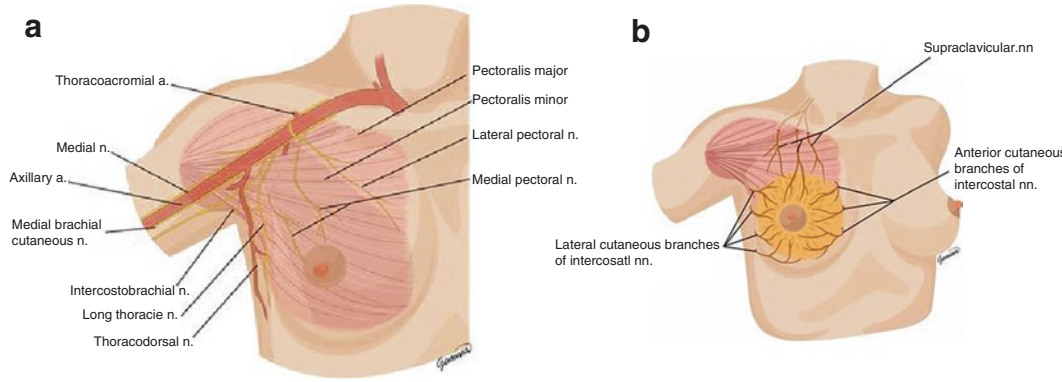

Fig. 32.1 Sensory innervation of the breast: PEC 1 and 2 blocks target the lateral branches of the intercostal nerves, as well as the long thoracic, thoracodorsal, and intercostobrachial nerves; (**a**) but it spares anterior cutaneous branches of the intercostal nerves. (**b**) Therefore the block will miss the medial half of the breast, as well as the overlying skin and subcutaneous tissues in the parasternal areas of the chest wall. (Prendergast [5])

- Indications:
  - Placement of breast tissue expanders
  - Subpectoral prosthesis
  - Superficial chest wall injuries
  - Port placements
  - Pacemakers

PECS 2

- PECS 2 involves PECS 1 block and deeper injection in the plane between the **pectoralis minor muscle and the serratus anterior** muscle at the level of the fourth rib. It aims to block the pectoral nerves, intercostobrachial nerve, anterior branches of intercostal nerves 3 through 6, thoracodorsal nerve, and long thoracic nerve.
- Indications:
  - Mastectomies
  - Reconstructive breast surgeries
  - Surgeries involving the axilla
  - Sentinel lymph node biopsy
  - Chest tube placement

Techniques

1. Position the patient supine with the arm abducted approximately 45°.
2. Place the ultrasound probe (high-frequency linear 10–15 hz) inferior and perpendicular to the clavicle, similar to that of probe placement for an infraclavicular block (Fig. 32.2a).
3. Identify the axillary artery and the accompanying vein, remembering that the vein is compressible. Identify the second rib, usually located caudad to the vessels, and appears as a bright, hyperechoic line with drop out deep to it. The pleura can be seen on, next to, and below the rib.
4. Identify the muscle layers including the pectoralis major and minor.
5. Slide ultrasound probe lateral and caudal moving from the second rib on the image to the fourth rib.
6. Maximize view to identify fascial layers between muscles by sliding and/or tilting probe slightly.
7. Use color doppler to identify any vessels in the fascial layers. Specifically, look for the thoracoacromial artery that is located between the pectoral muscles.
8. Using in-plane, real-time ultrasound guidance, insert needle at superomedial side of probe keeping needle in view.
9. Best to perform PECS 2 block first, as it is the deeper of the two blocks. Performing the PECS 1 block first may distort the ultrasound

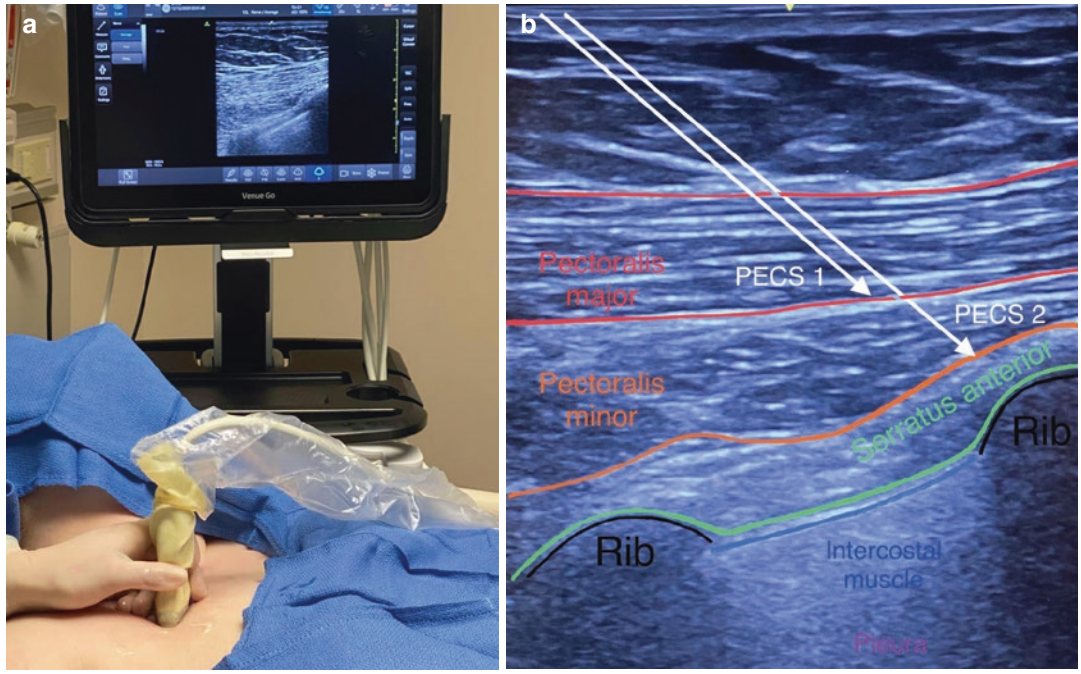

Fig. 32.2 (**a**) PECS block is performed by placing the ultrasound probe on the chest just below the clavicle, moving caudad and lateral. (**b**) Ultrasound image of blocks: PECS 2 block is performed by placing local anesthetic between the pectoralis minor and serratus anterior muscles (see corresponding arrow). PECS 1 block is performed by placing local anesthetic between the pectoralis major and minor muscles (see corresponding arrow)

image, making it more difficult to identify the anatomy for the PECS 2 block deep to it.

10. Advance needle to fascial plane between pectoralis minor and serratus anterior muscles. Alternatively, if the fascial plane is difficult to identify, place needle between the serratus anterior and the fourth rib (Fig. 32.2b).
11. After aspirating to rule out intravascular needle placement, inject local anesthetic into the plane. Incremental aspiration and injection every 5 ml is recommended. Approximately 15–20 ml of a local anesthetic (usually bupivacaine or ropivacaine) should be used for the PECS 2 block.
12. Next, withdraw the needle to the fascial plane between the pectoralis muscles to perform the PECS 1 block (Fig. 32.2b). Inject approximately 5–10 ml in the plane, aspirating with incremental injections.

Clinical Pearls

- Cutaneous innervation of the breast is **complex**. Branches of the brachial plexus and cervical spinal cord give way to the **supraclavicular nerves** (C3-C4), as well as the **lateral** (C5-C7) and medial (C8-T1) **pectoral nerves**. These nerves innervate the infraclavicular region including the pectoral muscles (**upper breast**). The intercostobrachial nerve (T2) and lateral branches of T2-T6 intercostal nerves innervate the **lateral breast** (Fig. 32.1b). The anterior branches of the T2-T6 intercostal nerves innervate the medial breasts and are spared when PECS blocks are performed. Additional blocks may be required for **medial breast analgesia**.
- The PECS blocks are relatively easier to perform with the arms abducted, and may be done after induction of general anesthesia.

- The cephalic vein and throraco-acromial artery are located in the needle path for the PECS 2 block. Doppler scan is recommended to avoid puncture of vessels.

Questions

1. Which of the following is not an indication for a PECS 1 block?
   A. Mastectomy
   B. Surgery for tissue expanders of breast
   C. Placement of port for chemotherapy
   D. Pacemaker placement
2. Which of the following nerves are blocked by a PECS 1 block?
   A. Long thoracic nerve
   B. Medial pectoral nerve
   C. Intercostobrachial nerve
   D. Thoracodorsal nerve
3. Which of the following is a possible complication of a PECS 2 block?
   A. Pneumothorax
   B. Phrenic nerve palsy
   C. Epidural hematoma
   D. Horner's Syndrome
4. Which of the following is not an advantage of PECS blocks when compared to paravertebral blocks?
   A. May perform in anticoagulated patients
   B. Requires a single injection
   C. Blocks serratus anterior muscle
   D. Covers the muscles and fascia
5. A patient presents for reconstructive breast surgery. Which blocks will provide the best analgesia for the surgery and in what order should the blocks be performed?
   A. PECS 1 then PECS 2
   B. PECS 2 then PECS 1
   C. PECS 1 only
   D. PECS 2 only

Answers

1. A, 2. B, 3. A, 4. C, 5. B

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33 Head and Neck: Glossopharyngeal, Superior Laryngeal, Transtracheal Block

Carina Jackman

Glossopharyngeal Nerve Block

- The block is primarily indicated for blunting airway reflexes in **awake endotracheal intubation** or diagnosis of **glossopharyngeal neuralgia.**
- Glossopharyngeal neuralgia is characterized by paroxysmal, severe, stabbing pain involving the ear, tonsillar fossa, or base of the tongue. Pain is elicited by chewing, swallowing, or coughing and radiates upward from the oropharynx toward the ear. Each pain episode last seconds to minutes and may occur many times a day. Glossopharyngeal neuralgia may be idiopathic or secondary to compression by **cerebellopontine angle tumor**, **peritonsillar abscess**, carotid aneurysm or the vertebral artery.

Anatomy

- Exits **jugular foramen** along with the vagus and accessory nerves (Fig. 33.1)
- Lies in groove between internal carotid artery and internal jugular vein
- Posterior to the styloid process of the temporal bone
- GPN is a **mixed motor and sensory nerve**; sensory branches innervate **posterior 1/3 of tongue**, palatine tonsil and mucous membrane of mouth and pharynx (Fig. 33.1); motor branch elicits **pharyngeal (gag) reflex**

Block Technique

- Anesthetize tongue with viscous lidocaine first.
- Supine position, mouth open, displace tongue medially with a tongue blade. Identify anterior tonsillar pillar or palatoglossal arch (U-shaped structure starting at the soft palate and running along the lateral aspect of the pharynx).
- Apply 4% lidocaine-soaked pledget at the tonsillar pillar for 3–5 min on each side (Fig. 33.2).

Superior Laryngeal Nerve (SLN) Block

- Branch of the vagus nerve; internal branch provides sensory innervation to pharyngeal mucosa from base of tongue to upper vocal cords. It also innervates the cricothyroid muscle of the larynx, which stretches, tenses, and adducts the vocal cord.
- Lies **inferior to the greater horn of the hyoid bone** close to superior laryngeal artery, travels

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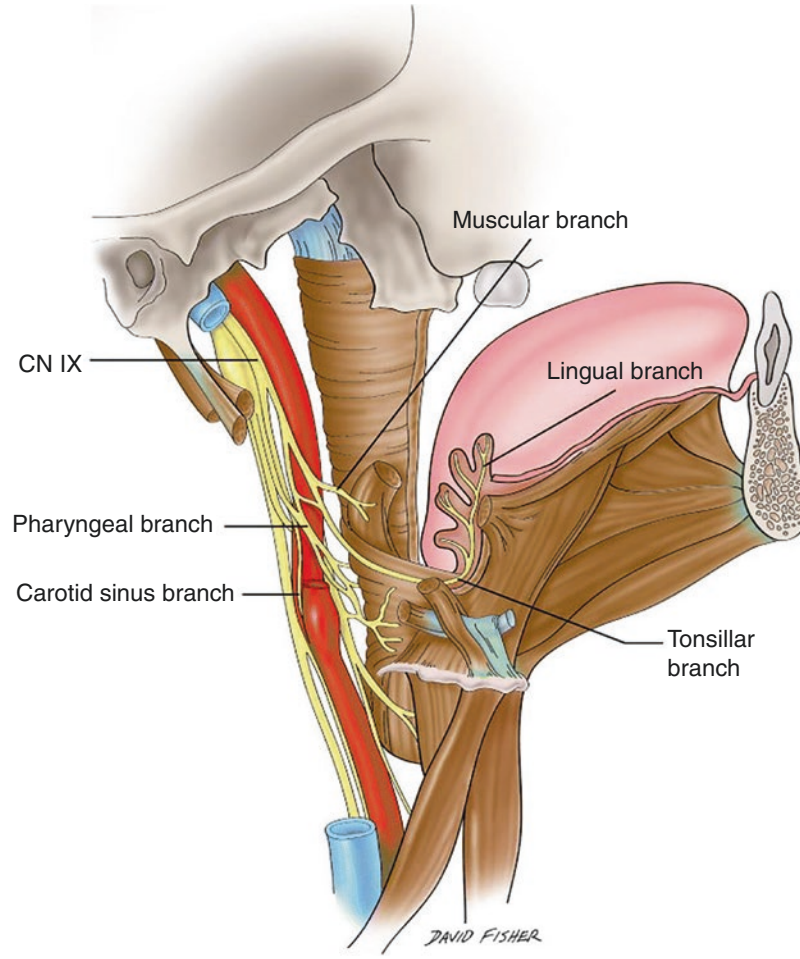


Fig. 33.1 Branches of the glossopharyngeal nerve. (Reproduced with permission from Springer https://www.springer.com/gp/rights-permissions/obtaining-permissions/882. Shereenet al. [6])

through thyrohyoid membrane then under the mucosa in the pyriform recess.

- The superior laryngeal nerve block provides anesthesia of the hypopharynx and upper glottis, including the valleculae and the laryngeal surface of the epiglottis.

Block Technique (Fig. 33.3)

- The patient is placed in a supine or sitting position with the neck maximally extended. The hyoid bone is displaced ipsilaterally.
- Identify greater cornu of hyoid bone and a 25-gauge needle is inserted and walked of the greater cornu inferiorly. The needle is then advanced 2–3 mm. After negative aspiration, 2 ml of 1% lidocaine is then injected. If air is aspirated, the needle will need to be redirected.

Transtracheal Block (Fig. 33.4)

- Targets small branches of the **recurrent laryngeal nerve** along the lumen of the trachea, below the vocal cords
- By percutaneously injecting local anesthetic into the tracheal lumen, the block elicits coughing which cause **local anesthetic to nebulize**. This provides additional anesthesia of the inferior larynx and vocal cords.

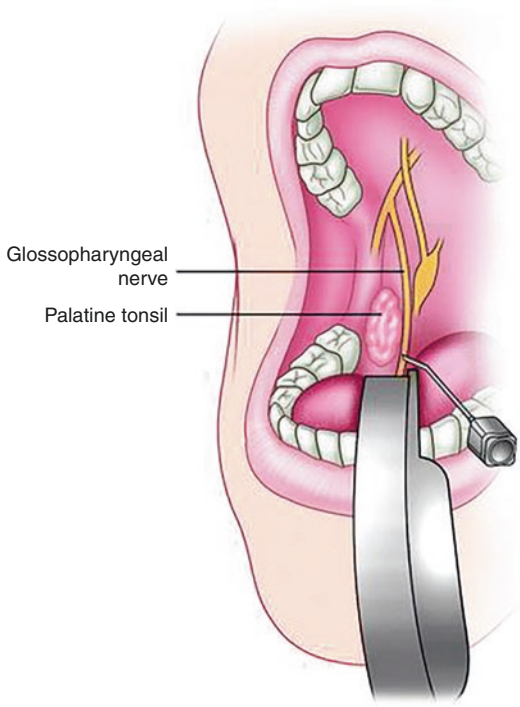


Fig. 33.2 Glossopharyngeal nerve block – intraoral approach. (Reproduced with permission from Springer https://www.springer.com/gp/rights-permissions/obtaining-permissions/882. Ellender et al. [7])

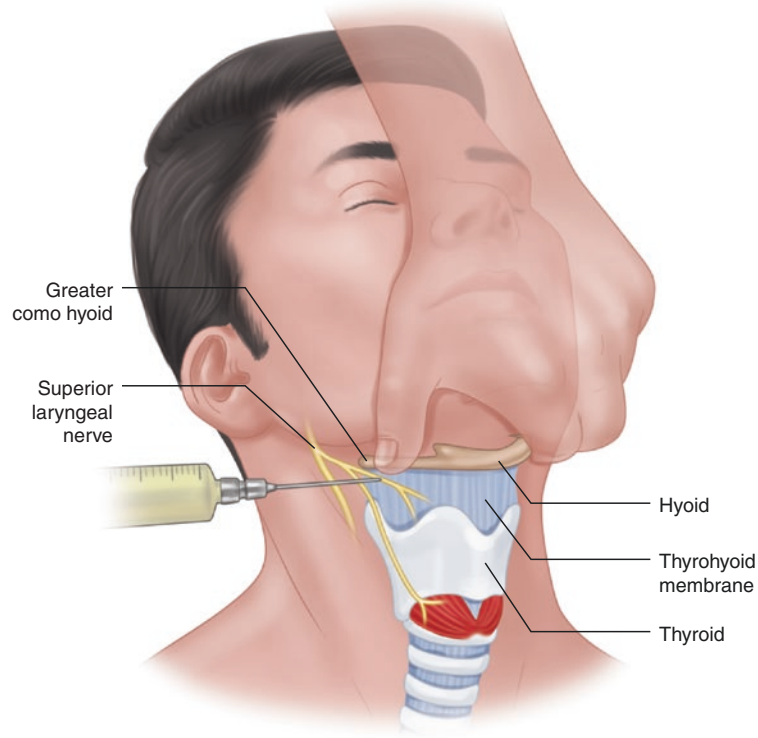
Block Technique

- Supine position, maximum head extension
- Palpate cricothyroid space and locate midline
- Aim posteriorly to avoid vocal cords; advance through cricothyroid membrane while aspirating
- After exhalation, inject lidocaine; expect cough

Complications

- Glossopharyngeal nerve block: Inadvertent block of the vagus nerve (dysphonia, bradycardia, reflex tachycardia), spinal accessory nerve (trapezius weakness), or motor portion (dysphagia).
- Superior Laryngeal nerve block: Aspiration may occur during the duration of the block without secure airway
- Transtracheal: Trauma to tracheal wall or esophagus

Fig. 33.3 Superior laryngeal nerve block



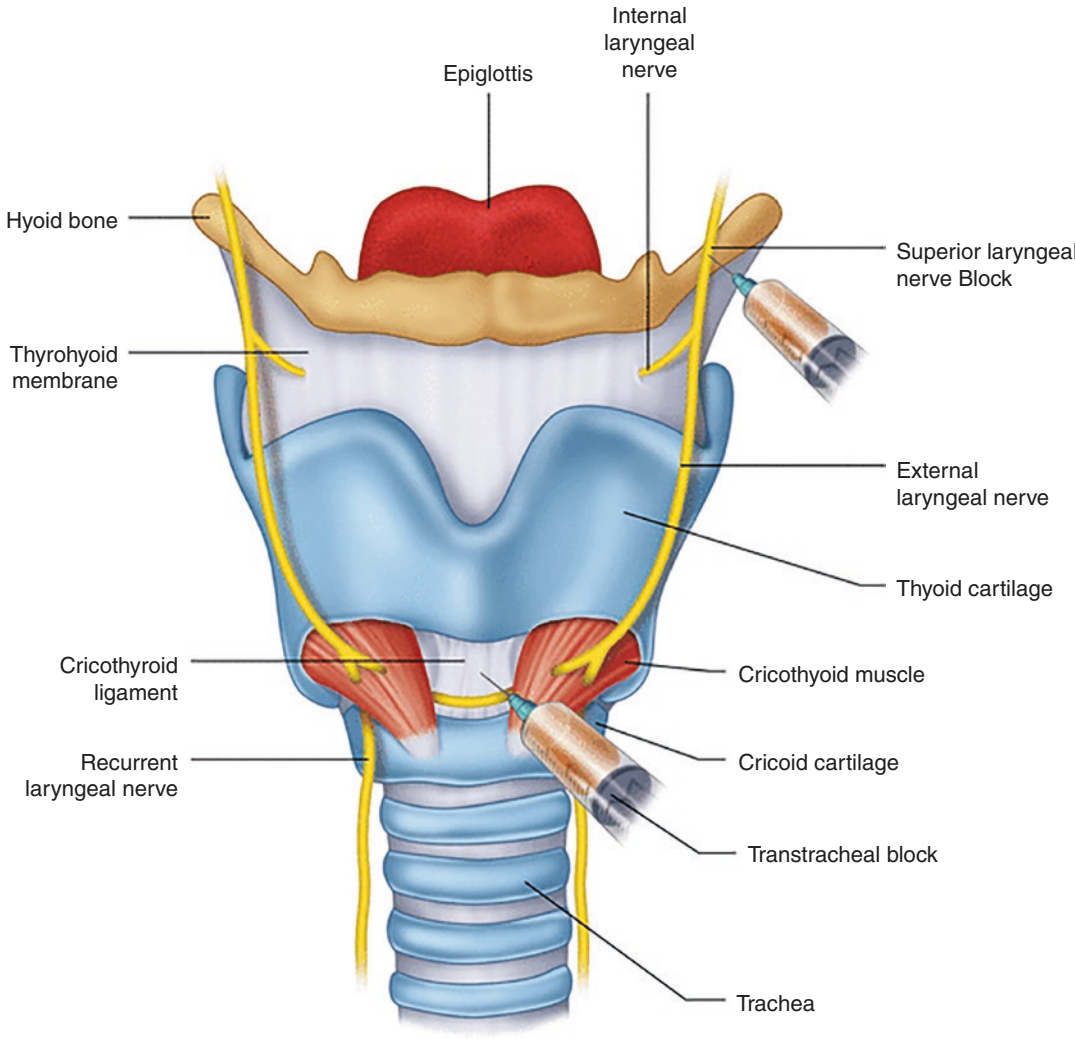


Fig. 33.4 Transtracheal nerve block. (Reproduced with permission from Springer https://www.springer.com/gp/rights-permissions/obtaining-permissions/882. Irefin and Kopyeva [8])

Clinical Pearls

- Knowledge of the facial anatomy is critical prior to attempting these blocks
- Nerves can also be targeted for endotracheal intubation preparation via **nebulized method of local anesthetic** or "spray as you go" technique to avoid external approaches to blocks.
- Consider ultrasound guidance for transtracheal block in obese patients or others with landmarks that are difficult to palpate. Cricothyroid membrane appears as a **hyperechoic line** known as the "airline."
- SLN block applied for treatment of pain in upper airway malignancies. While treatment usually requires bilateral block, minimize complications by performing only unilateral block in one visit.

Questions

1. The glossopharyngeal nerve exits through the
   A. Foramen ovale
   B. Julgular foramen
   C. Foramen rotundum
   D. Carotid canal

2. Which of the following is not an expected complication following an extraoral approach to the Glossopharyngeal nerve block?
   A. Dysphagia
   B. Dysphonia
   C. Bradycardia
   D. All of the Above may be complications
3. Which vessels are in close proximity to the location for the glossopharyngeal nerve block?
   A. Internal carotid artery
   B. External carotid artery
   C. Internal jugular vein
   D. Both A and C
4. The superior laryngeal nerve is a branch of the
   A. Trigeminal nerve
   B. Facial nerve
   C. Vagus nerve
   D. Recurrent laryngeal nerve
5. In order to block the pharyngeal reflex, the following cranial nerves (CN) must by anesthetized:
   A. CN 7
   B. CN 9
   C. CN 10
   D. CN 9, 10

Answers

1. B, 2. D, 3. D, 4. C, 5. D

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Head and Neck: Retrobulbar Block and Peribulbar Block

34

Nitin Goyal

Introduction

- Ocular anesthesia goals include **akinesia and anesthesia** of the orbit for eye surgeries [1]
- Commonly performed by anesthesiologist or ophthalmologist

Retrobulbar Anesthesia (RBA) (Fig. 34.1)

- **Intraconal** injection
- Targets the ciliary nerves, ciliary ganglion, CN III, IV, and VI
- **Does not block CN VII**, resulting in retained function of orbicularis oculi (blinking)
- Atkinson's technique (developed in the 1930s) involved an "up-and-in" gaze to reduce the distance of needle insertion to the muscular cone
  - Abandoned due to a high rate of optic nerve injury [2]

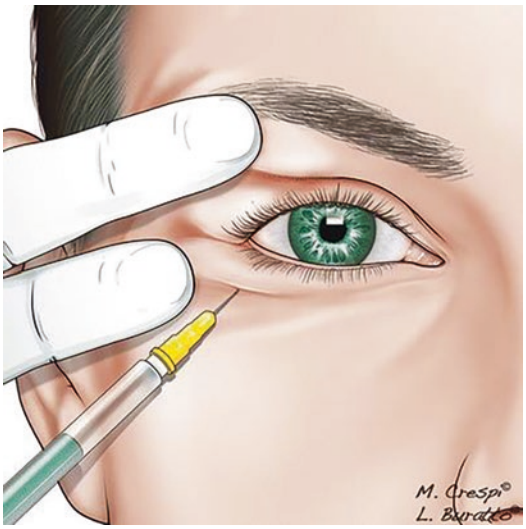

Fig. 34.1 Retrobulbar anesthesia used in glaucoma surgery. (Reproduced with permission from Caretti et al. [7])

Peribulbar Anesthesia (PBA) (Fig. 34.2)

- **Extraconal** injection
- Targeting the superior and inferior aspects of the orbit, blocking ciliary nerves, CN III, VI, and can result in block of orbicularis oculi muscle
- Multiple injections sites, but may achieve adequate anesthesia with a single injection of high volume

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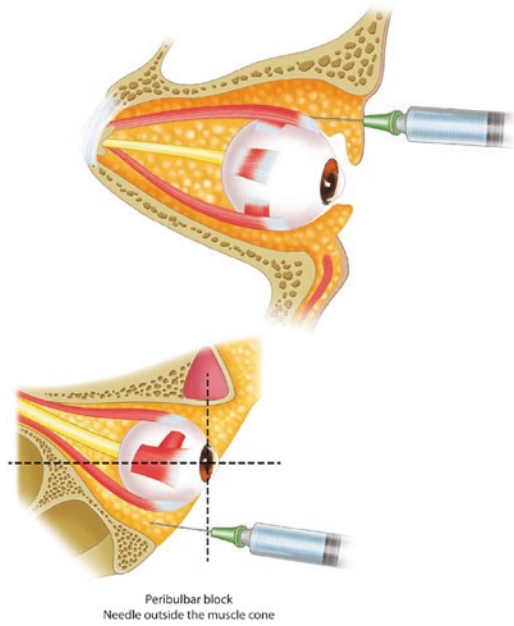

Fig. 34.2 Lateral view of orbital anatomy and needle trajectory during ocular blocks with lateral rectus resected. Figure above represent needle insertions and endpoints for peribulbar blocks. The figure below represents needle insertion and endpoint for peribulbar block. (Reproduced with permission from Chouhan [8])

- PBA carries a **lower risk of retrobulbar hemorrhage**, perforation, optic nerve injury, intraocular and intradural injections [3]
- Sub-Tenon block uses a small incision and insertion of a blunt cannula to reach the posterior globe

Anatomy

Orbit

- Pyramidal shaped: Apex (optic foramen) is posterior, globe is anterior
- Spherical globe has average axial length 25 mm, **myopic eyes have length >26 mm**
- Tenon's fascia: surrounds globe, separating globe from fat that surrounds ocular muscles

Muscles

- Levator palpebrae superioris
- 4 rectus muscles: superior, inferior, lateral, medial
- 2 oblique muscles: superior and inferior
- The acronym 'LR6SO4 rest 3' may help you memorize the nerves supplying ocular muscles. The abducens (VI) nerve innervates the ipsilateral lateral rectus. The trochlear (IV) nerve innervates the contralateral superior oblique. The oculomotor (III) nerve innervates the rest.

Muscular Cone

- Inter-muscular membrane between the recti, connecting circumferentially into a fibromuscular cone
  - Allows for small volume infiltration intraconal to block the nerves within it
  - Extraconal injections require higher volume to allow diffusion of medication intraconal
- Remaining muscles (oblique muscles and levator palprebrae) are extraconal

Optic Nerve

- Passes through optic foramen and annulus of Zinn
- Can be injured with long needle use during RBA or using Atkinson's gaze ("up-and-in") [4, 5]

Oculomotor Reflex or Oculocardiac Reflex

- Traction of extra-ocular muscles results in bradycardia
- Pressure or traction of orbital contents/ocular muscles → activation of ophthalmic portion of the trigeminal nerve → reticular formation and nuclei of the vagus nerve → efferent link through the vagus nerve to SA node → bradycardia/hypotension. Treatment: remove stimulus, anticholinergics, deepen anesthesia, local anesthesia

Indications

- **Any ocular surgeries**, including: Cataract surgery, Corneal transplant, enucleation [6]

- **Contraindications specific to this block**
  - Traumatic injury: open ocular trauma, perforated globe
  - **Myopic eye** (long eye shape), >26 mm length; higher risk of globe injury [4]
  - Patient's **inability to cooperate or lie still** with neutral gaze during regional block

Equipment and Technique

Injectate

- Local Anesthetic: 1:1 mixture of 0.5% bupivacaine and 2% lidocaine
- Hyaluronidase: 5–70 iU/mL, adjunct to hasten block onset and spread [4]

Retrobulbar Block

- Equipment: Long needles: 25 g, 30 mm length
- Place finger between globe and inferior orbital rim to displace globe slightly superiorly (Fig. 34.1)
- Insertion at lateral 1/3 of lower orbital ridge (inferotemporal corner)
- Needle **passed parallel to orbital floor**, until estimated to pass the globe's equator
- Angle needle **superiorly and medially** to pass posteriorly and enter the intraconal space
- Avoid globe rotation during insertion, as this may indicate engagement of the sclera
- After negative aspiration, inject **volume of 2–4 ml** of local anesthetic [5]

Peribulbar Block

- Equipment: Short needles: 27 g, 15–25 mm length
- First injection:
  - Periconjunctival insertion in far inferotemporal corner of eye
  - **Insert parallel to orbital floor** until it lies just beyond the globe's equator (Fig. 34.2)
  - After negative aspiration, inject **volume of 6–10 ml** of local anesthetic
- Second injection can be performed if there is incomplete akinesia
  - Between caruncle and medial canthus
  - Insert with angle towards upper medial quadrant, depth of 15–20 mm
  - After negative aspiration, inject volume of 3–5 ml of local anesthetic [5]

Complications

- **Retrobulbar hemorrhage** (most common)
- Central retinal artery occlusion
- Injury of globe, optic nerve, muscles
- Inadvertent brainstem anesthesia
- Seizures
- Blindness

Risk Reduction/Preventive Measures

- **Avoid Atkinson's "up-and-in" gaze** due to high risk of optic nerve damage
- Provide patient with a method to communicate during procedure (squeaky ball or bell)
- Blunt needle or use of blunt cannula reduces risk of puncturing globe or optic nerve
- **Slow injection** while watching for difficulty on injecting, increased pain, or globe rotation
- Risk of complications: RBA > PBA > Sub-Tenon Block

Clinical Pearls

1. Retrobulbar (intraconal) and peribulbar (extraconal) injections can provide adequate analgesia and akinesia for most ocular surgeries
2. RBA will block the ciliary nerves, ciliary ganglion, CN III, IV, and VI, but not CN VII, resulting in retained function of the orbicularis oculi muscle and ability to blink
3. PBA targets the superior and inferior aspects of the orbit, blocking the ciliary nerves, CN III, VI, and can result in block of the orbicularis oculi muscle

4. PBA reduces the risks involved with intraconal injections, including retrobulbar hemorrhage, optic nerve injury, and intraocular injections; however, with the high volume 6–10 mL used, local anesthetic can spread causing **brainstem anesthesia**
5. **Oculocardiac reflex** (high yield): decrease in heart rate and/or blood pressure in response to pulling of ocular muscles.
6. Ocular blocks can be safely performed on a cooperative patient that can tolerate the supine position, does not have a myopic eye shape, and has an expected surgical duration of less than 90–120 minutes
7. The most common complication from RBA is **retrobulbar hemorrhage**, which is characterized by inability to close eyelids, increased ocular pressure, loss of pupillary reflexes, and optic disc or retinal pallor, and proptosis; this is a serious concern that must be identified early to prevent blindness.

Questions

1. Which of the following muscles most likely retains function following a retrobulbar block?
   A. Lateral rectus muscle
   B. Superior rectus muscle
   C. Orbicularis oculi muscle
   D. Levator palpebrae superioris muscle
2. What is the most common complication of a retrobulbar block that can result in motor block, closing of the upper lid, increased intraocular pressure, proptosis?
   A. Perforation of the globe
   B. Retrobulbar hemorrhage
   C. Optic nerve injury
   D. Central spread of local anesthetic
3. What is the afferent and efferent pathway involved with the oculocardiac reflex, respectively?
   A. Afferent: Cranial nerve III; Efferent: Cranial nerve V
   B. Afferent: Cranial nerve III; Efferent: Cranial nerve X
   C. Afferent: Cranial nerve V; Efferent: Cranial nerve VII
   D. Afferent: Cranial nerve V; Efferent: Cranial nerve X
4. Which aspect of a normal peribulbar block increases the risk of brainstem anesthesia?
   A. Large volume (6–10 mL)
   B. Needle insertion into the optic sheath
   C. Injection at the muscular cone
   D. Intradural injection
5. What is (are) the target(s) for depositing local anesthetic in a peribulbar block?
   A. Inside the muscular cone
   B. Superior and inferior borders of the orbit
   C. Inside the optic sheath
   D. Inside the inferior part of the globe

Answers

1. C, 2. B, 3. D, 4. A, 5. B

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35 Head and Neck: Superficial Cervical Plexus Block for Awake Carotid Endarterectomy

Elizabeth J. Webber and J. Tasker Gundy

Introduction

- **Carotid endarterectomy (CEA)** is a revascularization surgery performed to reduce the risk of stroke in patients with symptomatic carotid artery stenosis due to atherosclerosis.
- Both general and regional/local anesthetic approaches have been utilized to facilitate CEA. Whether one approach is safer or results in superior outcomes, has been the subject of debate. General anesthesia remains the most common technique.
- Peripheral nerve blocks for CEA include **superficial cervical plexus block** or **deep cervical plexus block**.
- One undisputed advantage of a **cervical plexus block (CPB)** technique is that CEA can be performed with a patient awake during carotid cross-clamping, allowing for ongoing **real-time neurological assessment** and early recognition of cerebral ischemia or thromboembolic insult (indicating potential utility of shunt placement) [1].
- Some data have suggested CEA under regional anesthesia may offer improved hemodynamic stability (less hypotension), decreased incidence of cerebrovascular events and myocardial ischemia, and decreased mortality [2, 3].
- Compared with a deep or combined cervical plexus block, the **superficial cervical plexus block** is both safer and simpler to perform.

Anatomy

- The origin (roots) of the cervical plexus are the anterior (ventral) rami of **cervical nerves C1-C4**.
- The **superficial cervical plexus** is formed as the **terminal branches of C1-C4** travel superficially from beneath the posterior border of the **sternocleidomastoid muscle**, above the **prevertebral fascia** (Fig. 35.1).
- These four terminal branches—the **lesser occipital**, **greater auricular**, **transverse cervical** and **supraclavicular nerves**—provide sensory innervation of the anterior and lateral neck (Fig. 35.1).

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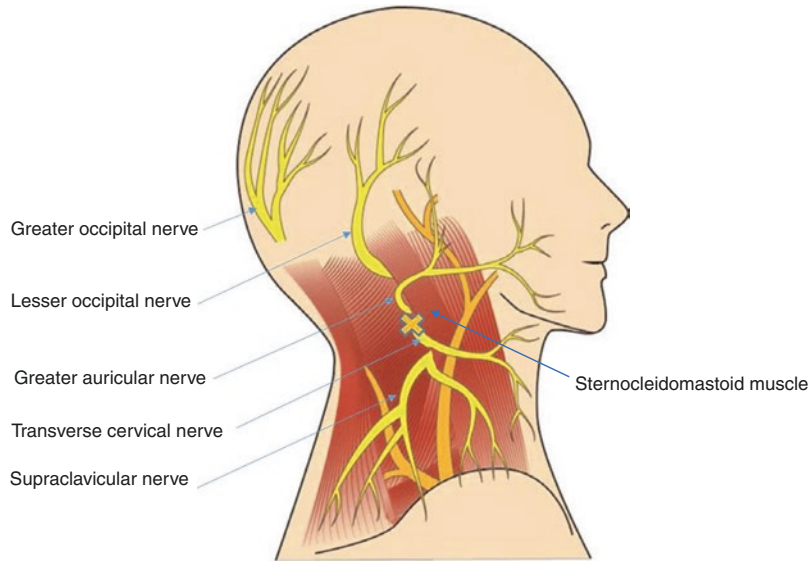

Fig. 35.1 Anatomy depicting the terminal branches of C1-C4 (the targets of the superficial cervical plexus block) that emerge from the posterior border of the sternocleidomastoid muscle to innervate the head, neck, and shoulder areas. Cross indicates injection point for landmark technique. (Original image taken with permission. Nishie [6])

General Technique Considerations

- For both the landmark and ultrasound-guided techniques of the superficial CPB, the patient is in the supine or semi-recumbent position, with head turned away from site of injection 30–45 degrees.
- 10–15 mL total of local anesthetic is sufficient to perform the superficial CPB.
- Given that there is no motor component with this particular block, a lower concentration local anesthetic may be utilized (i.e. 0.25% bupivacaine) [4].

Landmark Technique

Superficial Cervical Plexus Block

- First identify the **sternocleidomastoid muscle (SCM)**.
- Draw a line from the mastoid process to the C6 transverse process along the posterior border of the SCM. Insert the needle at the **midpoint of this line**.
- After depositing 3–5 mL of local anesthetic at this position, use a "fan" technique to redirect the needle both 2–3 cm superior and 2–3 cm inferior along the posterior border of the sternocleidomastoid muscle (depositing 3–5 mL of local anesthetic in both directions).
- Deep needle insertion of greater than **1–2 cm** should be avoided.
- The goal is to deposit local anesthetic **under the sternocleidomastoid** muscle.

Ultrasound-Guided Technique

Superficial (Intermediate) Cervical Plexus Block (Fig. 35.2)

- The superficial (intermediate) CPB can be accomplished with both in-plane and out-of-plane techniques. The posterior, in-plane technique will be described.
- Place the linear ultrasound transducer, in the transverse position, on top of the **sternocleidomastoid muscle** at its midpoint (generally around the level of the cricoid cartilage).
- Translate the ultrasound probe posteriorly until the tapering end of the sternocleidomastoid muscle is visualized and centered on screen.
- If visible, the **superficial cervical plexus** is seen as small hypoechoic nodules superficial to the **prevertebral fascia** overlying the interscalene groove [4].
- Traveling laterally to medially with the needle, using an in-plane technique, the goal is to

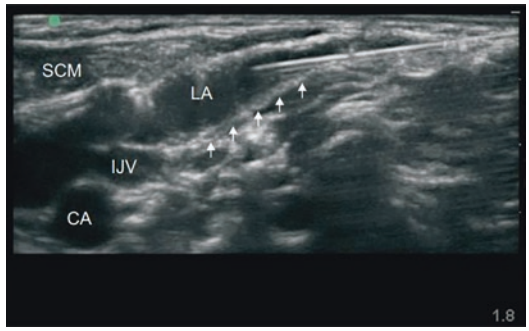

Fig. 35.2 Ultrasound image of the superficial (intermediate) cervical plexus block with needle placement under the sternocleidomastoid (SCM) muscle. Local anesthetic (LA) is deposited below the investing layer of the deep cervical fascia but superficial to the prevertebral fascia (indicated by white arrows). IJV: internal jugular vein. CA: carotid artery. (Original image taken with permission. Kim et al. [5])

deposit local anesthetic **below the sternocleidomastoid** muscle and investing layer of the deep cervical fascia, while remaining superficial to the prevertebral fascia (Fig. 35.2).

- After careful aspiration, 10–15 mL of local anesthetic may be deposited.

Complications Specific to CPB

- Theoretical risk of causing phrenic nerve palsy. One may decrease the risk by taking meticulous care not to puncture the **prevertebral fascia** with the needle, and by always injecting superficial to the prevertebral fascia [5].
- Bilateral deep and/or superficial (intermediate) CPB should not be performed given the risk of paralyzing bilateral vagus (recurrent and superior laryngeal nerves) and/or hypoglossal nerves which could lead to **fatal airway obstruction**. Blockade of these cranial nerves may also result in hoarseness (dysphonia) and/or dysphagia [5].
- The risk of developing blockade of a cranial nerve (vagus, hypoglossal, facial, glossopharyngeal) with CPB may be decreased by minimizing likelihood of medial and cephalad spread of local anesthetic (LA) along the **carotid sheath**. If able to visualize the internal jugular vein and/or carotid artery while performing the CPB, care should be taken to redirect the needle if medial spread of LA toward these structures is visualized.
- **Horner's syndrome** (ptosis, miosis, facial anhidrosis) is an unpleasant side effect encountered when LA spreads to the cervical sympathetic chain and has been reported after both superficial and deep CPB. The risk is minimized by avoiding puncture of the **prevertebral fascia**.

Clinical Pearls

- Superficial cervical plexus blocks anesthetize the anterior and lateral neck and scalp, enabling neuromonitoring during awake carotid endarterectomy thus aiding in the **prevention and detection of embolic stroke**.
- CPB targets the greater auricular, lesser occipital, transverse cervical, and supraclavicular nerves, which are peripheral branches of **C1-C4**.
- The block can be used for neck surgeries (e.g. **thyroid surgery**, cervical lymph node dissection) and chronic neck pain due to malignancy.
- The patient may develop transient **facial nerve paralysis** after the block due to concurrent auriculotemporal nerve blockade.
- The intermediate cervical plexus block refers to a slightly more posterior superficial cervical plexus block and local anesthetics are deposited deep to the investing layer of the deep cervical fascia but superficial to the prevertebral fascia.

MCQs

1. Which of the following is NOT an anatomic structure relevant to superficial cervical plexus block performed using a landmark technique?
   A. Chassaignac's tubercle
   B. Conjoint tendon
   C. Posterior border of sternocleidomastoid

D. C6 transverse process

2. Which of the following is NOT correct regarding anatomy for cervical plexus block?
   A. C1-C4 roots contribute to the cervical plexus
   B. The sternocleidomastoid muscle lies atop the superficial cervical plexus
   C. Branches of superficial cervical plexus emerge midway along the anterior border of sternocleidomastoid
   D. Phrenic nerve palsy is a risk of cervical plexus block, based upon the proximity of this nerve to the plexus
3. The intermediate cervical plexus block refers to injecting local anesthetic:
   A. Superficial to the investing layer of the deep cervical fascia.
   B. Deep to the investing layer of the deep cervical fascia but superficial to the prevertebral fascia.
   C. Into the sternocleidomastoid muscle.
   D. Deep to the prevertebral fascia, along the transverse processes of C2-C4.
4. A superficial cervical plexus block may be beneficial in all listed surgeries below, EXCEPT:
   A. Carotid endarterectomy
   B. Total thyroidectomy
   C. Clavicular surgery
   D. Distal biceps tendon repair surgery
5. The nerves that are involved in the superficial cervical plexus block include all EXCEPT:
   A. Lesser occipital nerve
   B. Supraclavicular nerve
   C. Transverse cervical nerve
   D. Suprascapular nerve

MCQ Answers

1. B, 2. C, 3 B, 4. D, 5. D

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Part II

Chronic Pain

Basic Science: Pain Mechanisms and Pathways

36

Yinan Chen and Salahadin Abdi

Introduction

- Pain definition: an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.
- Pain physiology: the neural networks activated by painful stimuli and responsible for reaction to pain. It is composed of (1) peripheral sensory neurons that sense the stimuli (**nociceptors**); (2) pathways that transmit the stimuli from peripheral to central nervous system (**pain transmission pathways**); (3) sets of neurons that elicit excitatory or inhibitory influences on pain and pain reactions (**pain modulation**).
- Pain reactions: protective somatic and autonomic reflexes, endocrine actions, emotional responses, learning and memory about the event, and cortical awareness of pain.
- Pain matrix: The responses to nociceptive stimuli in cortical networks including somatosensory, insular and cingulate areas, frontal and parietal areas of brain, which are collectively called as "pain matrix". This multi-level interaction and information exchange results in perception of pain, a subjective phenomenon with discriminative, affective, and cognitive dimensions.

Nociceptors and Afferent Fibers (Fig. 36.1)

- Nociceptor is defined by the IASP subcommittee on Taxonomy as "a receptor preferentially sensitive to a noxious stimulus or to a stimulus which would become noxious if prolonged". It is the **starting point** of pain perception.
- A nociceptor contains a peripheral axon, cell body, and a central axon. Peripheral nerve endings are located in skin, muscle, joints, viscera, meninges, and blood vessels. Damaging or potentially damaging stimuli are sensed at those nerve endings, transmitted via the peripheral axons, or known as primary afferent fibers (Table 36.1), to the cell bodies of the nociceptors in the dorsal root ganglia (DRGs) or cranial nerve ganglia outside the spinal cord or brainstem. The stimuli are then converted to chemical signals in the forms of neurotransmitters and neuropeptides secreted by the DRG neurons to the spinal cord dorsal horn (SCDH) via central axons of the nociceptors (Fig. 36.1).
- Afferent fibers form the axons of sensory neurons and carry impulses to the central nervous

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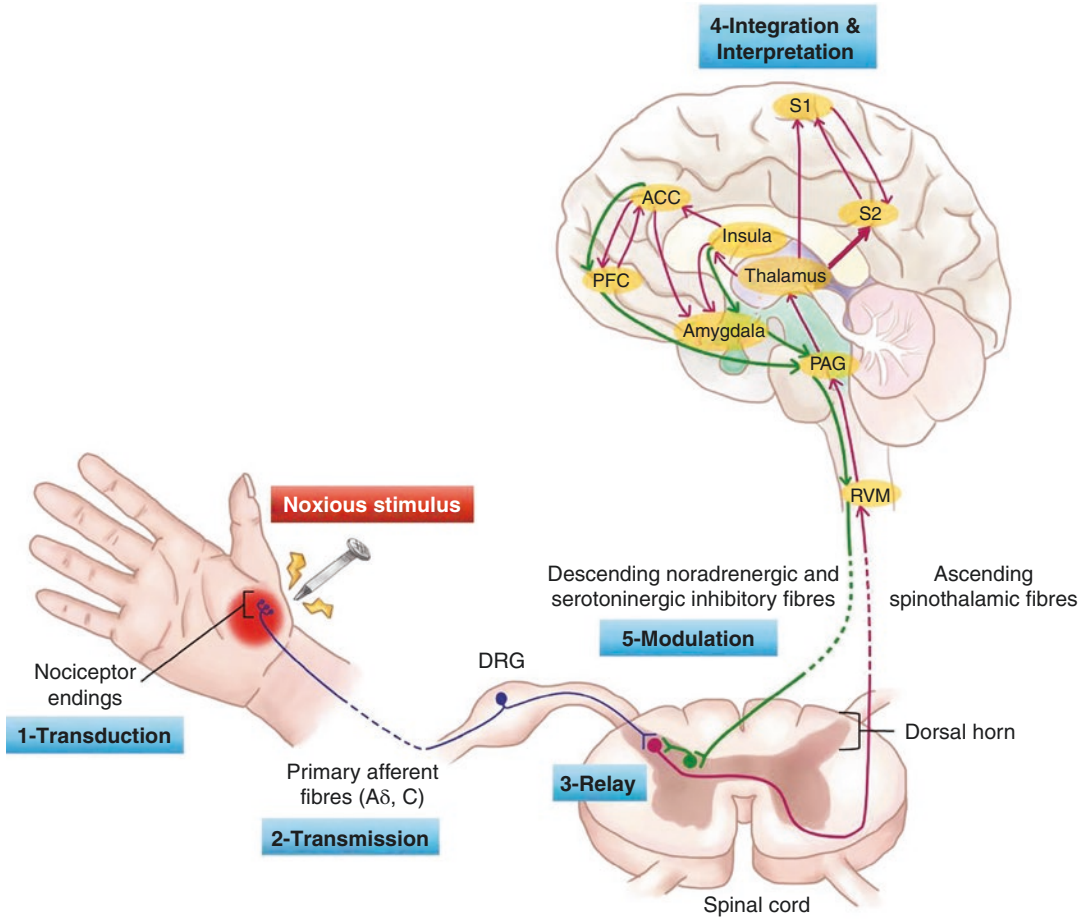

Fig. 36.1 Nociceptors and afferenet fibers. (Ref. Martin [6])

Table 36.1 Different classes of primary afferent fibers (high yield)

Fiber category	Myelinated	Diameter (microns)	Conduction velocity (meters/second)	Function
Aα	Y	13–20	80–120	Proprioception (self-movement and body position)
Aβ	Y	6–12	33–75	Fine touch, pain
Aδ	Y	1–5	3–30	Pain and temperature
C	N	0.2–1.5	0.5–2.0	Pain and temperature

system (CNS). They are further categorized based on their size and conduction velocity (Table 36.1) [1]. The predominant primary afferent fibers transmitting pain signals are **small unmyelinated (C) fibers and myelinated (Aδ) fibers**. C fibers are **more abundant**, smaller in size, and respond to mechanical, thermal, and chemical stimuli. They are responsible for the **slow, burning, spread out pain**. Aδ fibers respond to mechanical and cold thermal stimuli and transmit the **fast, sharp, localized pain**.

- Peripheral sensitization can occur in the event of tissue injury, peripheral nerve injury or chronic inflammation, during which nociceptors develop **increased sensitivity** and produce higher-than-normal level of pain to noxious stimuli (**primary hyperalgesia**) or

pain to non-noxious stimuli (**primary allodynia**) [2].

- Changes can occur at transcriptional, translational and posttranslational levels. Tissue injury → release of inflammation mediators (calcitonin gene related peptide, CGRP and substance P) by cells including nociceptors → increased vascular permeability and accumulation of more inflammation mediators (prostaglandin E2, bradykinin, leukotrienes, cytokines, growth factors) → formation of an "inflammation mediator pool" → signaling cascade that sensitizes and excites nociceptors, i.e. **peripheral sensitization**. It can initiate and sustain **central sensitization** and contributes to the development of chronic pain [3].

Dorsal Horn/Spinal Modulation and Transmission

- Wind-up: Noxious stimuli → depolarization of nociceptor cell membranes → impulse generation with Aδ and C fibers → repetitive low frequency (0.5–2 Hz) stimuli of the same strength → Wind-up phenomenon (discharge gets bigger on each subsequent stimulus)
- Central sensitization: normal or sub-threshold afferent input → central neurons hypersensitivity to noxious stimuli (**secondary hyperalgesia**), responsiveness to non-noxious stimuli (**secondary allodynia**), and increased pain response to noxious stimuli outside of the injury site (**expanded pain receptive field**). Central sensitization can present with or without wind-up.
- Peripheral vs central sensitization: peripheral sensitization is mediated by inflammatory factors and occurs at site of injury (Fig. 36.1). Central sensitization, on the contrary, is an abnormal state of the neurons in CNS that alters how it responds to sensory inputs, rather than the reflection of the presence of noxious stimuli.

First Pain Transmission

- Spinothalamic tract (STT): Main ascending pathway that transmits pain from the peripheral stimuli to somatosensory cortex, carrier of the sensory discriminative component of pain (**first pain**) [4].
- Anatomy of STT: Central axons of nociceptors enter the spinal cord dorsal root, and synapse with second order neurons (STT neurons) in the ipsilateral dorsal horn. The axons of STT neurons immediately cross over the midline via the anterior white commissure (Fig. 36.1), ascend in the contralateral white matter in the lateral and ventrolateral funiculi, and terminate in the ventral posterior and ventral basal thalamus. The **third order** neurons in the thalamus, which, after synapsed with the STT neurons, ascend through the internal capsule and corona radiata to the postcentral gyrus of the cerebral cortex and pain matrix (see above), in a manner that different parts of the body are represented in an ordered arrangement (**somatotopy**).

Dorsal Horn Anatomy [5]

- Lamina I; nociceptive, cutaneous C, somatic and visceral C and Aδ
- Lamina II: also called substantia gelatinosa, opioid responsive, nociceptive, predominantly C and some Aδ
- Lamina III and IV: non-nociceptive, touch, proprioception
- Lamina IV and V: abundant wide dynamic range neurons respond to both nociceptive and non-nociceptive stimuli
- While Aδ and cutaneous C fiber endings are distributed rather focally in the same and adjacent segments, visceral C fibers can extend **more than five segments** which compensates for the relatively sparse innervation of viscera and partly explains why visceral pain is poorly localized.

Second Pain Transmission

- The affective-motivational component of pain (**second pain**) is transmitted separately from the first pain. The ascending pathways that carry the second pain are spinoamygdalar and spinohypothalamic pathways [4]. The ascending axons mostly arise in laminae I, VII and X, and synapse with the third order neurons in **the central nucleus of amygdala and the lateral hypothalamus**, respectively. The two pathways are involved in the **affective responses to pain**, including anxiety, increased attention, and suffering, which is not only the important transition from unconscious nociception to conscious pain, but also part of pain modulation.

Pain Modulation and Descending Pathways

- Pain modulation includes both **inhibition** and **facilitation**. Dorsal reticular nucleus, also known as subnucleus reticularis dorsalis (DRt) in the brain stem balances the descending inhibition and facilitation processes. DRt receives nociceptive inputs from the ascending spinoreticular pathway and communicates with the periaqueductal grey matter (PAG) and rostral ventromedial medulla (RVM) as well as the thalamus and amygdala and sends pain modulatory projections to the spinal cord. Electrophysiologic studies and lesioning experiments propose that pain modulation occur through a PAG relay to RVM and then to the spinal cord (Fig. 36.1).
- Descending projections from RVM travel through the dorsolateral funiculus (DLF) to the dorsal horn of spinal cord, where they synapse with primary afferent fibers, secondary neurons as well as interneurons. The modulation effect is **biphasic**. Low intensity stimuli to RVM produce inhibitory effect of nociception, while high intensity stimuli enhance the response.
- **Endogenous opioids, serotonin, noradrenaline** are the main neurotransmitters involved in the descending pathway. Descending facilitation and loss of descending inhibition pathway may be involved in chronic pain. Understanding of pain pathways and their modulations will provide basis for multimodal analgesia and chronic pain (Chap. 28).

Clinical Pearls

- **Peripheral sensitization** is mediated by inflammatory factors, stimulus dependent, and results in painful response to non-noxious stimuli (primary allodynia) and increased painful response to noxious stimuli (primary analgesia)
- **Central sensitization** is not necessarily stimulus dependent. It is an abnormal state of central neurons that display responsiveness to subthreshold stimuli (secondary allodynia), increased response to suprathereshold stimuli (secondary analgesia) with expanded pain responsive field
- Repetitive low frequency stimuli to C fibers can cause **wind-up phenomenon** – increased response to the same subsequent stimulus within the same synapse
- Central transmission of pain from spinal cord to supraspinal CNS are through various ascending pathways. The spinothalamic pathway carries the somatosensory discriminative component of pain. The spinoamygdalar and spinohypothalamic pathways transmit the affective-motivational component of pain.
- The DRt, along with the PAG and the RVM, form parts of a **spinal-supraspinal-spinal feedback** loop that modulates pain. The descending pathways can suppress and enhance pain via neurotransmitters including **endogenous opioids, serotonin, and noradrenaline**.

MCQ Questions

1. Which of the following nerves conduct nociceptive stimuli?
   A. Aβ fibers and C fibers

B. Aα fibers and Aβ fibers
C. Aδ fibers and C fibers
D. A-δ fibers and A-β fibers
E. B fibers and C fibers

2. Which one of the following correctly describe the wind-up phenomenon:
   A. Increased stimuli recruit nearby neurons that were previously unresponsive
   B. After the same repetitive stimuli, neurons increase the discharge frequency
   C. When repetitive stimuli are abruptly haltered, neurons immediately upregulate the neurotransmitter receptors to the postsynaptic membranes
   D. Neurons are hyperpolarized without stimuli
3. Which of the following statements is incorrect regarding the mechanisms of neuropathic pain?
   A. Injured and neighboring non-injured sensory neurons can develop spontaneous discharges
   B. Central sensitization represents a state of heightened sensitivity of dorsal horn neurons
   C. After peripheral nerve injury C fiber input may drive central sensitization
   D. Allodynia, essentially reflect loss of sensation owing to axon/neuron loss
4. Which one of the following describes the concept of pain modulation?
   A. A peripheral noxious stimulus is transmitted to the thalamus via the spinal cord
   B. A peripheral noxious stimulus is processed in the limbic system, and elicits an emotional response
   C. A noxious stimulus is modified by inhibitory and excitatory neural inputs
   D. A noxious stimulus is converted to an action potential and propagated by neurotransmitters

Answers

1. C, 2. B, 3. D, 4. C

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Basic Science: Opioid Receptors

37

Joseph R. Holtman Jr

Pain

- Opioid receptors are important targets for the treatment of pain
- **Drugs acting at opioid receptors**, morphine the prototype, are useful in the treatment of **moderate to severe acute and cancer pain;** their use in chronic nonmalignant pain is controversial due to questionable long term efficacy and misuse/abuse

Terminology

- **Opiate** – any compound **structurally related to compounds found in opium** (poppy plant)
  - Morphine, codeine – found in opium
- **Opioid** – more inclusive term. **Any drug that acts at opioid receptors**

Multiple Opioid Receptors

- Pharmacological actions are mediated through **multiple opioid receptors** which are part of the **G-protein coupled receptor family (GPCR)**
- Hypothesized late 1960's – 1970's; confirmed by receptor cloning in 1990's
- **Site of action** of **opioid drugs (e.g. morphine)** as well as **endogenous opioid peptides (e.g. enkephalins)**

Endogenous Opioid Peptides

- Act on opioid receptors in CNS regions important in **pain processing**
  - Three endogenous opioid peptide families: **Endorphins** (beta-endorphin), **Enkephalins** (met and leu-enkephalin), **Dynorphins** (dynorphin A and B)

Opioid Receptor Classification

- Three receptor types form basis of opioid pharmacology:
  - **Mu receptor (MOR)**
  - **Kappa receptor (KOR)**
  - **Delta receptor (DOR)**
- Role of a fourth receptor, the **opiate receptor like protein (ORL-1) or NOR** (Nociceptin) **receptor,** not completely characterized
- Most **clinically useful opioid analgesic drugs** all have primarily **MOR agonist activity**

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Opioid Agonists and Antagonists (Table 37.1)

- Drugs acting at opioid receptors are classified as follows:
  - **Agonist** – binds to receptor and activates it to produce a **maximal response**
    Has high intrinsic activity
    Morphine, codeine, methadone, heroin, hydrocodone, oxycodone and fentanyl are examples of **full agonists**
  - **Partial Agonist** – binds to receptor producing **less response than full agonist**
    Partial agonists produce similar effects as full agonists but tend to have ceiling effect, i.e., increased doses do not produce additional analgesia
    Buprenorphine, used to treat opioid dependence, is a classic example of a partial mu agonist also with kappa receptor antagonism
    - 25–100 times as potent as morphine
    - Strong affinity for mu receptor can displace other opioids making them less effective when continued in perioperative period
  - **Antagonist** – binds but **does not activate receptor**
    Reverses effect of agonist by displacing it from receptor
    Naloxone, a pure mu, kappa and delta receptor antagonist, is most clinically useful opioid **antagonist**
    Naloxone is commonly used to **reverse** opioid effects, in particular, **respiratory depression** from opioid overdose
    - Needs **careful titration** (20–40 ug IV, onset 1–2 min)
    - Rapid administration can cause pain, arrhythmias, hypertension, pulmonary edema and opioid withdrawal

    Naltrexone is a long acting PO opioid antagonist
    - Used in treatment of opioid use disorder (DSM-V)
    - Use only after stopping opioid as can induce opioid withdrawal
    - Recent use for treatment of fibromyalgia

    Peripherally selective opioid antagonists (do not cross blood-brain barrier) such as **methylnaltrexone, naloxegol and alvimopan**, are used to **reverse opioid induced constipation**
  - **Agonist-Antagonist –** produces an **agonist effect at one opioid receptor** and an **antagonist effect at different opioid receptor**
    Developed as opioid drugs that would produce analgesia with less respiratory depression and addictive potential
    Nalbuphine – agonist at kappa receptor and antagonist at mu receptor
    - **Ceiling effect** on respiratory depression
    - May precipitate withdrawal in patients physically dependent on mu opioid agonists

Table 37.1 Opioid drug receptor interactions [1, 2]

Drug	MOR	DOR	KOR
Morphine	+++		+
Methadone	+++		
Fentanyl	+++		
Hydrocodone	+		
Oxycodone	++		
[a]Buprenorphine	+		–
Butorphanol	–		+++
[b]Nalbuphine	–		++
Naloxone	–	–	–
[c]Methylnaltrexone	–	–	–

+, ++, +++ = agonist; – = antagonist
[a] Buprenorphine – partial agonist
[b]Nalbuphine – agonist/antagonist
[c]Methylnaltrexone – peripheral selective antagonist

Localization of Opioid Receptors

- **Brain, spinal cord and periphery** at sites involved in processing of pain information
- **Suprasinal sites – Periaqueductal Gray (PAG)** and **Rostral Ventrolateral Medulla (RVM)**
- **Spinal site – dorsal horn (substantia gelatinosa)**
  - **Presynaptic terminals of nociceptors** (A delta and C fibers)

  - **Postsynaptic on pain projection neurons** to CNS
- **Peripheral site –** terminals of **primary afferent nociceptors**

Effects of Clinically Used Opioid Drugs (Table 37.2)

- Primary clinical use as **analgesics** for **moderate to severe pain**
- Administered by oral, rectal, topical, IV, epidural and intrathecal routes
- Important **side effects** include: respiratory depression, sedation, constipation, miosis, nausea/vomiting, urinary retention, pruritis (morphine-histamine release), hormone changes (decrease testosterone with chronic use), immunosuppression

Opioid Receptor Effect on Pain Transmission

- **Spinal cord opioid effect**
  - **Inhibit release of pain neurotransmitters** (glutamate, substance P) from nociceptor nerve terminals
  - **Hyperpolarize (decrease excitability)** pain projection neurons
  - Site of action of epidural and spinal administered opioid agonists
- **Brain opioid effect**
  - **Inhibit GABAergic neuron (disinhibition) allowing for activation of descending inhibitory nociceptive pathway** from PAG and RVM to spinal cord
  - Net effect in spinal cord is inhibition of neurotransmitter release from nociceptor nerve terminals
- **Peripheral opioid effect**
  - Activate opioid receptors on **peripheral sensory nerve terminals of nociceptors** inhibiting transmission of pain stimuli to spinal cord
  - Important **mechanism in damaged or inflamed tissue**
  - Morphine action after **intra-articular administration** (e.g. after knee arthroscopy)

Table 37.2 Opioid effects by receptor

Receptor	Subtype	Effect
MOR	mu_1	Analgesia
		Physical dependence
		Prolactin release
	mu_2	Euphoria
		Respiratory depression
		Constipation
		Pruritus
		Miosis
		Growth hormone release
KOR	$kappa_{1,2,3}$	Analgesia
		Dysphoria
		Diuresis Miosis
DOR	$delta_{1,2}$	Analgesia
		Convulsions
NOR	ORL_1	Anxiolysis Analgesia Modulation mu receptor

MOR mu opioid receptor, *KOR* kappa opioid receptor, *DOR* delta opioid receptor, *NOR* nociceptin receptor

Molecular/Cellular Effects of Opioid Receptor Activation (Fig. 37.1)

- Opioid receptors are one of the family of **G protein – coupled receptors (GPCR's)**
- Binding of agonist (e.g. morphine) to MOR causes **coupling with the G protein (Go/Gi)** resulting in three actions:
  - **Decrease** of intracellular **cyclic AMP (cAMP)** and protein kinase A (PKA)
  - **Inhibition** of voltage-gated **calcium channels –** decrease calcium influx
  - **Stimulation** of **potassium channels** – stimulate potassium efflux

Opioid Receptor Desensitization and Tolerance (Fig. 37.1)

- **Receptor desensitization** sometimes referred to as **acute tolerance** is a phenomenon which occurs during **short-term opioid agonist binding**. It involves the termination of receptor activation by receptor phosphorylation

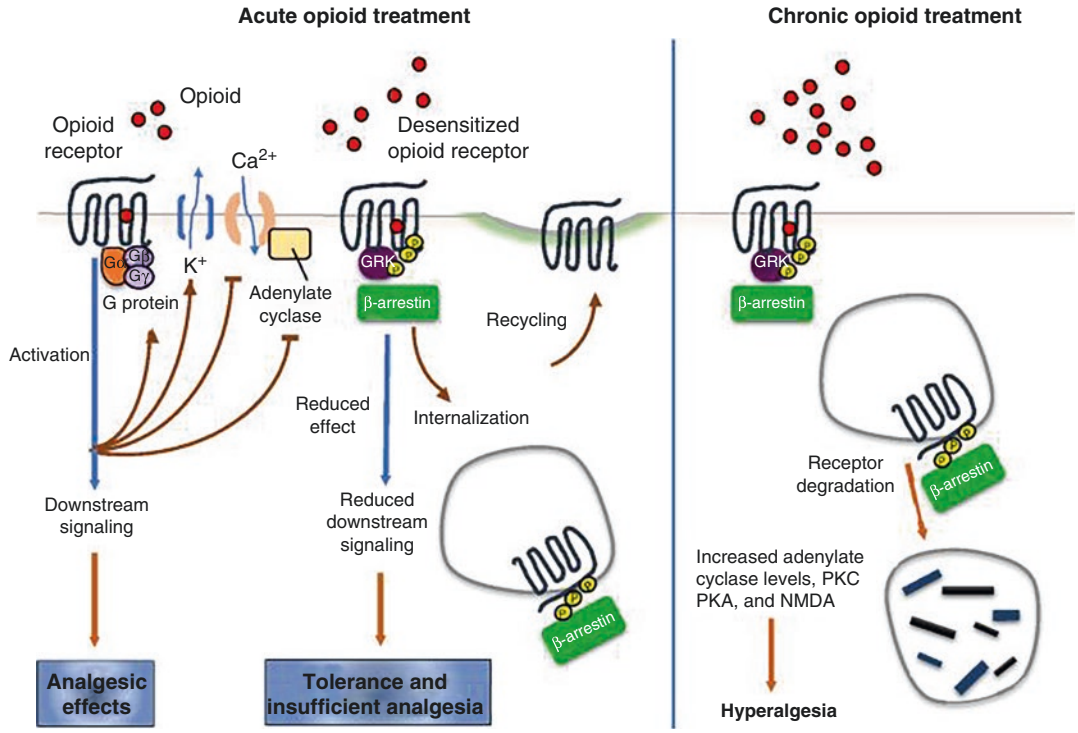

Fig. 37.1 Mechanism of opioid induced analgesia, tolerance, and opioid-induced hyperalgesia. Left: Agonist binding to mu opioid receptor produces analgesia by increasing potassium (K^+) efflux, decreasing calcium (Ca^{++}) influx and decreasing the production of cyclic AMP. Middle: repeated administration of opioid desensitizes receptors, which interact with beta arrestin (β-arrestin) to cause receptor uncoupling, internalization and recycling processes. Also reduced downstream signaling may cause tolerance and insufficient analgesia. Right: chronic opioid therapy produces hyperalgesia by increasing the level of cAMP. (Reproduced with permission from Springer. Reference Mercadante et al. [6])

mediated by G-protein coupled receptor kinases (GRK's) or protein kinase A/C

- **Tolerance** is defined as a **decreased effectiveness** of an opioid agonist to produce an effect (e.g. analgesia) upon **repeated administration** of the drug. Increased doses of drug required to produce a similar clinical effect
- **Different degree of tolerance development** for the various opioid effects. **Minimal** to none –miosis, constipation; **Moderate** – analgesia, sedation, respiratory depression; **High**-euphoria
- **Cross-tolerance** that develops between **opioid agonists** is often **incomplete**. Basis for the clinical practice of **opioid rotation** where one opioid is substituted for another to achieve a more favorable analgesic effect or reduce side effects

Cellular Tolerance Mechanism

- Differs between opioid agonists (e.g. morphine vs. fentanyl) – **biased agonism** may be factor whereby opioid agonists acting at GPCR may differentially activate one intracellular pathway over another
- **Mechanisms** complex but may involve:
  - **Receptor uncoupling/desensitization** – receptor phosphorylation and beta-arrestin binding
  - **Receptor internalization** – endocytosis with beta-arrestin binding resulting in receptor degradation or reactivation
  - **Alterations in post-receptor signaling** – rebound increase in intracellular cAMP
  - **N-methyl-D-Aspartate (NMDA) receptors**-ketamine decreases tolerance

Opioid Dependence

- **Physical dependence** develops along with opioid tolerance. **Abrupt cessation of the opioid or administration of an antagonist** (e.g. naloxone) causes **withdrawal state**
- Characterized by dysphoria, anxiety, insomnia, hyperalgesia, diarrhea, hypertension and mydriasis
- Avoiding withdrawal is often a motivation to continue either licit or illicit opioids

Opioid Induced Hyperalgesia

- Opioid induced hyperalgesia (OIH) is characterized by a **paradoxical increase in pain** typically associated with chronic high dose opioid treatment but observed with short-term opioid infusion (e.g. remifentanil)
- **Pain** is often at locations **distinct from the original site**
- Unlike tolerance it is **improved with a decrease in opioid dose** rather than an increase
- Possible role **NMDA receptors**-ketamine modifies OIH
- Along with opioid misuse/abuse, OIH is another reason long term opioid therapy in chronic pain patients is controversial

Clinical Pearls

- Multiple opioid receptors (MOR, DOR, KOR) – part of the G-protein coupled receptor family (GPCR); MOR most clinically relevant for analgesia
- Opioid drugs are agonists, partial agonists, agonist-antagonists or antagonists
- Receptors located in brain, spinal cord and periphery at sites involved in pain processing
- Physiological effects (analgesia) include: activation of descending inhibitory pain pathways (brain), decreased release of pain neurotransmitters (glutamate, substance P) from A-delta and C-fibers with resulting inhibition activity of pain projection neurons (spinal cord) and inhibition of nociceptor activity (periphery)
- Chronic opioid receptor activation results in molecular effects opposite to those of acute administration
- Differential degree of tolerance develops to various opioid effects
- Incomplete cross tolerance to opioid analgesic effect forms basis for opioid rotation
- OIH – paradoxical increase in pain typically with chronic high dose opioid use
- Know difference between tolerance, dependence and addiction (Chap. 33)

Multiple Choice Questions

1. The most clinically useful opioid agonist analgesics act primarily at which opioid receptor?
   A. Delta receptor (DOR)
   B. Mu receptor (MOR)
   C. ORL-1/NOP receptor
   D. Kappa receptor (KOR)
2. Which of the following drugs is a partial MOR agonist?
   A. Morphine
   B. Naloxone
   C. Buprenorphine
   D. Nalbuphine
3. Opioid receptors at which of the following sites are involved in opioid analgesia?
   A. Periaqueductal gray (PAG)
   B. Dorsal horn of spinal cord
   C. Primary afferent nociceptor terminals
   D. All of the above
4. Morphine binding with a G-protein coupled receptor (GPCR) causes all of the following actions
   EXCEPT:
   A. Inhibition voltage-gated calcium channels
   B. Stimulation of potassium channels
   C. Inhibition of intracellular cAMP
   D. Increased release of substance P from C fibers

5. Minimal to no opioid tolerance occurs with which of the following opioid effects?
   A. Analgesia
   B. Miosis
   C. Respiratory depression
   D. Euphoria

Answers

1. B; 2. C; 3. D; 4. D; 5. B

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38 Basic Science: Social, Vocational, and Psychological Influences on Pain Perception

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Introduction

- Pain perception is both a physical and a subjective experience. How individuals react to painful stimuli depends on psychological, emotional, and social factors. Awareness of these factors is critical for understanding chronic pain syndromes.
- Primary afferent neurons transmits painful stimuli to the dorsal horn of the spinal cord; impulses are then transmitted through the spinothalamic tract to the somatosensory cortex via thalamic projections, resulting in perception of the intensity of painful stimuli (Fig. 38.1). Impulses are also transmitted to the cingulate and insular cortices via connections in the brain stem and amygdala, which contributes to the **affective component of pain.**
- Lobotomized patients can register pain, but it doesn't make them uncomfortable; suggesting that pain perception is a product of the brain's processing of afferent inputs; the perception of pain involves numerous sensory, affective, and cognitive components (Fig. 38.1)
- The perception of acute pain is highly dependent on the context. A simple example is this: pain perceived in the battlefield is different from pain perceived in normal conditions. Soldiers in battle who suffer a compound fracture report only mild pain.
- Management of both acute and chronic pain symptoms often has psychological, social, and behavioral factors. Consideration of these factors into pain management would improve outcomes.

Anatomy of the Pain pathway (Also See Chap. 1)

- Noxious stimuli → Primary afferent neuron → dorsal horn of the spinal cord → spinothalamic tract → thalamus → somatosensory cortex (Fig. 38.1, **location and intensity of the painful stimulus**).
- Noxious stimuli → Primary afferent neurons → dorsal horn of the spinal cord→ brainstem (parabrachial nucleus) → amygdala → cingulate and insular cortices (Fig. 38.1, **affective component of the pain experience**).
- Noxious stimuli → Primary afferent → dorsal horn of the spinal cord → Rostroventral medulla and periaqueductal grey → **descending feedback system** to regulate output from spinal cord.

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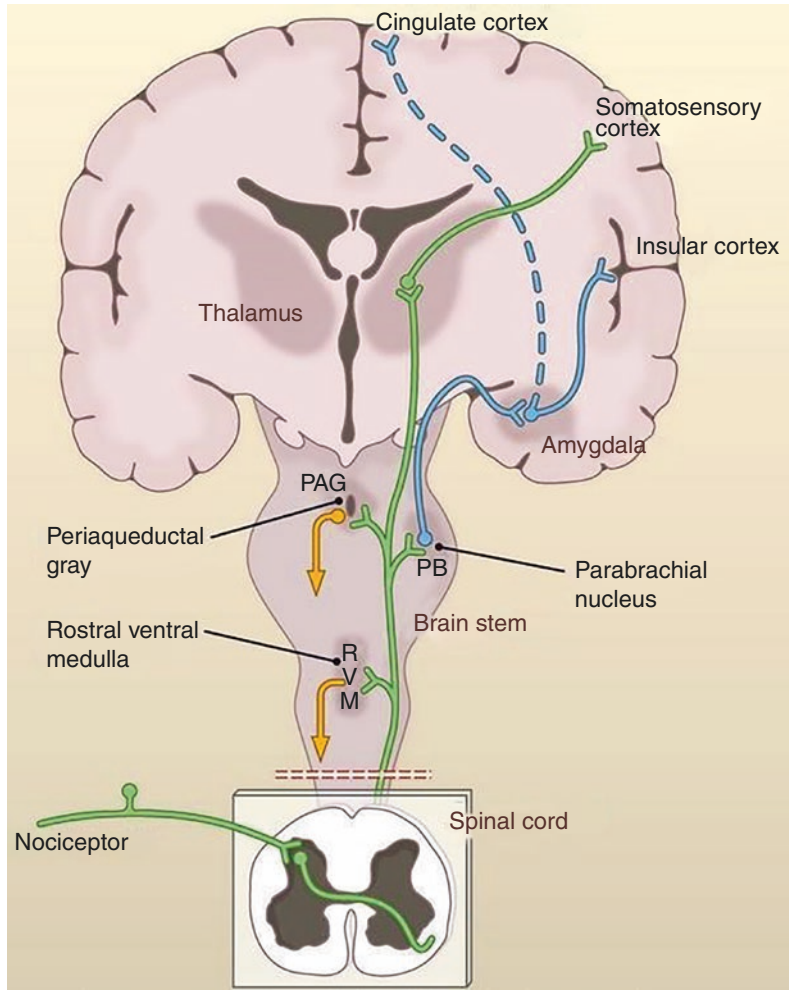

Fig. 38.1 Anatomy of the pain pathway. Primary afferent nociceptors convey noxious information to projection neurons within the dorsal horn of the spinal cord. A subset of these projection neurons transmits information by the spinothalamic tract to the somatosensory cortex via the thalamus, providing information about the location and intensity of the painful stimulus. Other projection neurons engage the cingulate and insular cortices via connections in the brain stem (parabrachial nucleus) and amygdala, contributing to the affective component of the pain experience. This ascending information also accesses neurons of the rostral ventral medulla and midbrain periaqueductal gray to engage descending feedback systems that regulate the output from the spinal cord. (Reproduced with permission from Basbaum et al. [1]). (Source: Fig. 28.6)

Pain Catastrophizing

- A significant factor that affects pain perception is fear. Fear of pain develops as a result of a cognitive interpretation of pain as threatening (pain catastrophizing), and this fear affects attention processes (hypervigilance).
- A patient's understanding of pain can become amplified, prolonged, or disabling if there is distorted cognitive processing of pain. Catastrophizing involves an **exaggeration of the meaning, severity,** and impact of pain on a patient's life.
- Insomnia, anxiety, depression have been shown to be associated with pain catastrophizing. Depression, anxiety disorders are categorized in the DSM-IV classification of psychiatric disorders.
- Treatment: Cognitive behavioral therapy (CBT) (Also see Chap. 28). The therapy iden-

tifies and develops skills to change negative thought and behaviors. A person may say, "I can't do any work!! My pain is awful. Nothing is going to help!!" Thinking, behaving, and feeling like this may start a downward spiral, which will make pain experience worse, and likely trigger a phenomenon of nocebo.
- The goal of CBT is to change negative thoughts, to develop coping skills, although the pain level stays the same. The therapy changes negative thoughts to positive ones, which will reduce stress and anxiety related painful experiences. CBT requires weekly or bi-weekly sessions, during which time the client and therapist work together to understand problems and develop strategies to tackle them.

Anxiety and Depression

- Chronic pain and depression often coexist. It is unclear if depression causes chronic pain or whether chronic pain is a manifestation of a form of depression (chicken vs egg). Patients with preexisting depression are more likely to develop more severe reactions to acute pain, which therefore is more likely to develop into a chronic pain syndrome. Underlying depression may be evaluated by Patient Health Questionnaire- 4 (PHQ-4) or PHQ-9.
- If a patient screens positive for depression on the PHQ-4, the patient should be assessed by the Patient Health Questionnaire (PHQ-9).
- Anxiety disorders are classified as GAD, panic disorders, and phobia. Anxiety disorders are also prevalent in chronic pain populations. Anxiety is characterized by fear and worry, heart palpitations, and shortness of breath. A 7-item anxiety scale—the (General Anxiety Disorder) GAD-7—has been used for identifying probable cases of GAD. There is evidence to implicate anxiety to worsening of the pain experience in acute surgical or procedural situations.
- The Minnesota Multiphasic Personality Inventory (MMPI) is a common clinical tool used by health psycholoogist to diagnose mental illness. Version 2 (MMPI-2) is the most often used revision. This test consists of 567 items, taking on average 60–90 minutes to complete. The MMPI-2 contains 10 clinical scales (hypochondriasis, depression, hysteria, psychopathic deviate, masculinity-femininity, paranoia, psychasthenia, schizophrenia, hypomania, social introversion).
- Mainstays of treatment of depression and anxiety are psychological and pharmacological. In the acute pain setting, especially in the perioperative period, patient education with reassurance is key. Providing detailed information of the surgery, addressing patient concerns, allowing for relaxation techniques, including breathing techniques and self-hypnosis, have been found to be beneficial. Anti-anxiety medications in the perioperative setting may be considered as well. These may include midazolam or dexmedetomidine.

Social and Vocational Influences of Pain

- **Low-income** patient populations are more likely to experience chronic, disabling pain.
- Adults living in **poverty** (annual income less than $25,000), with **public health insurance** (such as Medicaid) and with no higher than a **middle school education** are more likely to report higher levels of pain or development of chronic pain.
- There are racial and ethnic differences in pain perception. For example, African American subjects reported higher levels of clinical pain as well as greater pain-related disability than white participants. In addition, African Americans demonstrated less pain tolerance than whites. American Indians and Alaska Natives had a higher prevalence of pain symptoms and painful conditions when compared with the general US population.
- Studies have shown differences between majority and minority populations in countries in which they live, with minority groups (eg Asians, Black, Latinos) being more sensitive to pain. Moreover, multidisciplinary pain

treatment studies were less effective in improving pain severity in individuals with minority backgrounds.
- A pharmacokinetic study found ethnic differences (non-Hispanic whites vs African–Americans vs Asian) in the effectiveness of codeine. In addition, a number of genetic studies suggest altered response to analgesics based on the patient's ethnicity.

Miscellaneous

Anxiety Disorder Versus Somatic Symptom Disorder

Preoccupation with having an illness or getting an illness and constantly worrying about health. Somatization is the manifestation of physical symptoms from emotional distress and significant adversity. The development of somatization may occur when emotions and feelings become **overwhelming and appear as a physical ailment** (including pain). The direct treatment of these physical symptoms are regularly inadequate.

Factitious Disorder

A condition involving the presentation of an illness in the form of a symptom or constellation of symptoms that are often intentionally brought about for secondary gain (ie. financial compensation, attention, avoidance of social obligations, access to medications). Those with this condition, however, may or may not directly benefit from the situation, as well.

Conversion Disorder

A condition involving physical ailments that may regularly include a handicap (ie. numbness, blindness, or trouble walking) without an associated explanation or cause. Symptoms may vary in severity and may come and go or be persistent. Notably, these symptoms cannot be intentionally produced or controlled. Risk factors for conversion disorder include a history of mood disorders, history of significant physical or emotional trauma.

Clinical Pearls

- The affective component of pain is attributed in part to both medial thalamic projections and brainstem projections (from the periaqueductal grey and parabrachial area) to the hypothalamus and amygdala, among other cortical and subcortical brain structures.
- Pain catastrophizing is an exaggerated, negative cognitive and emotional response toward actual or potential pain, and can involve magnification of pain, rumination, and the feeling of hopelessness.
- Chronic pain and depressed mood are closely correlated in occurrence and development, and mutually influence the severity of each other.
- An inverse relation exists between economic status and chronic pain, as well as education and chronic pain.

MCQs

1. The condition in which a patient is found to have received monetary gain from feigning illness is best defined as:
   A. Malingering
   B. Factitious disorder
   C. Somatization
   D. Conversion disorder

   Answer (A): Malingering can be defined as feigning a physical or psychological condition in order to gain a reward or escape a duty. Conversion disorder is defined as a condition in which the patient presents with neurologic symptoms, such as blindness or paralysis, that cannot be explained, despite medical workup, and often can be traced back to a psychological trigger. Factitious disorder is a mental disorder characterized by the patient purposely injuring themselves or getting sick, without necessarily gaining any benefits from the intended illness. Somatization is a somatic symptom disorder in which a patient presents

with symptoms unexplained despite medical workup, but are not intentionally feigned.

2. Which of the following interventions is considered a form of cognitive behavioral therapy?
   A. Iontophoresis
   B. Electroconvulsive therapy
   C. Guided imagery
   D. Transcutaneous magnetic stimulation

   Answer (C): Cognitive behavioral therapy (CBT) is a psychosocial intervention that aids in the development of coping strategies to address a problem. It is often described as a form of "talk" therapy to treat a wide variety of issues. Guided imagery is an example of a CBT intervention in which the patient is guided into imagining an experience, which can modify and improve behaviors, such as pain coping skills. Iontophoresis is a physical therapy modality for transdermal drug delivery. Electroconvulsive therapy is a medical therapy that utilizes electrical stimulation to treat various mental disorders. Transcutaneous magnetic stimulation is a medical therapy employing magnetic fields to stimulate certain areas of the brain to treat conditions such as depression.

3. Personality disorders, somatization, depression, and post-traumatic stress disorders can best be assessed by which of the following tools:
   A. CAGE-AID
   B. Minnesota Multiphasic Personality Inventory (MMPI)-2
   C. Beck Depression Inventory
   D. Karnofsky Performance Score

   Answer (B): The Minnesota Multiphasic Personality Inventory (MMPI) is a common clinical tool used by mental health professionals to diagnose mental illness. Version 2 (MMPI-2) is the most often used revision. This test consists of 567 items, taking on average 60–90 minutes to complete. The MMPI-2 contains 10 clinical scales (hypochondriasis, depression, hysteria, psychopathic deviate, masculinity-femininity, paranoia, psychasthenia, schizophrenia, hypomania, social introversion). CAGE-AID can help to assess substance abuse. Beck Depression Inventory is a psychometric test to measure severity of depressed mood. Karnofsky Performance Score measures a cancer patient's general well-being and functional capacity.

4. Which of the following factors is found to be associated with a higher prevalence of chronic pain and less effective pain management?
   A. Ethnic minority groups
   B. Poverty
   C. Lower education levels
   D. All of the above

   Answer (D): Poorer and less-educated older individuals have a higher likelihood of experiencing chronic pain, compared to those with higher education and greater wealth. Those with less than a high school education, for instance, were found to be 370% more likely to report severe chronic pain, compared to those with graduate degrees. Studies have also shown differences in the prevalence of chronic pain between majority and minority populations in the countries that they reside.

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39 Gender and Age Differences in Pain Perception

Nasir Khatri, Nadia Hernandez, Stuart Grant, and Ratan K. Banik

Introduction

- The elderly population accounts for approximately 40% of 234 million surgeries performed each year worldwide. However, clinical studies typically do not include elderly subjects [1]. Therefore, recommendations for diagnosis and management of postoperative pain in older adults are derived from research in younger populations. This "one size fits all" approach to acute pain management is problematic for elderly patients. Specifically, empirical use of analgesic medications **without dosing modification for age** can lead to excessive sedation, delirium, and respiratory complication [2].
- Elderly patients have lower analgesic requirements; sufentanil, alfentanil, remifentanil, and **fentanyl are twice as potent in elderly patients** [3]. Remifentanyl's increased potency is due to a reduction in clearance. Additionally, the elderly have an increased duration of systemic and neuraxial effects of opioids.
- The etiology of increased sensitivity to opioids and anesthetics in the elderly is multifactorial. The combination of age-related degeneration of the sensory system, altered pharmacokinetics due to decreased volume of the central compartment and decreased clearance leads altered drug potency and increased duration of action.
- Epidemiological studies show that several **chronic pain conditions are more prevalent in women than men**, including fibromyalgia, migraine, auto-immune disease, eg. Systemic lupus erythematosus, rheumatoid arthritis, irritable bowel syndrome, temporomandibular disorders, and interstitial cystitis. There is also literature to suggest that women are more likely to report pain and describe pain affecting multiple sites as compared to their male counterparts.

Pain and Aging

- Multiple retrospective studies have reported that older patients report lower postoperative pain intensity and consume lower doses of opioids following surgery. In addition, older patients report minimal pain symptoms in several acute pain conditions. Approximately 35–42% of adults over the age of 65 experi-

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ence a silent or painless heart attack [4] and report little or no pain associated with peritonitis, intestinal obstruction, pneumothorax [5], and peptic ulcer diseases [6]. This data indicates a **fundamental change in pain regulation** associating with aging.

- Morphologic studies of the peripheral nervous system have shown that aged primary afferent nociceptors undergo several degenerative changes over time, including the loss of both myelinated and unmyelinated nerve fibers.
- The sensory system undergoes significant degenerative changes as a consequence of aging. Widespread disorganization and decreased myelin thickness has been demonstrated. There is a reduction of neurochemicals that are responsible for neurogenic inflammation, lower levels of growth factors necessary for ion channel synthesis as well as decreased expression of ion channels that convert noxious stimuli into electrical signals. It is very likely that such morphologic, biochemical and molecular changes in the sensory system are attributable to age-related diminished pain sensitivity [1].
- Although the prevalence of chronic pain is higher in the elderly population, **they have less pain symptoms** compared to their younger counterparts. For example, in a study of 193,158 patients aged 65 years and older, the mean reported pain score was lower with each increment in age (5 years) for men and women [7]. Further, older elderly individuals exhibited lower levels of pain compared with the younger elderly individuals after adjusting for a variety of potential confounding variables [7].
- Elderly patients on opiate therapy for chronic pain have a **higher incidence of adverse effects**. A cross sectional study [8] found that patients on long-term opioids performed significantly worse on attention tasks and had significantly lower self-efficacy beliefs over patients not receiving opioids. In a meta-analysis, opioids have shown to reduce attention of older patients when compared with patients who do not take medication that affects the central nervous system [9]. When opioids are used together with antidepressants and/or anticonvulsants, this effect increases [9].

Gender and Pain

- Both acute and chronic pain are reported more frequently by women than men, and several chronic pain conditions (eg, migraine, fibromyalgia, irritable bowel syndrome, and temporomandibular disorders) are considerably more common in women than in men [10] with female to male ratios ranging from 2:1 to 9:1. Females report higher numeric pain scores and a have a higher incidence of severe pain events after surgery [11].
- In basic science research, sex differences in the opioid receptor density, neurotransmitters, receptors and impact on pain of sex hormones have been documented [12]. It is possible that some chronic pain conditions that are common in females are genetic, likely transmitted via sex-linked inheritance. There are also differences in the prevalence of the psychosocial contributors to pain between men and women. There is a higher incidence of depression and anxiety among women, which increases the risk for pain. Pain catastrophizing, which is associated with greater pain intensity, (See Chap. 4) is also more common in women than in men,
- The mechanisms underlying sex differences in responses to pain is not clear. Existing hypotheses include genetic differences such as cognitive-affective factors, sex hormones, anxiety/depression, and familial factors.

Clinical Pearls

- Sensory system undergoes significant degenerative changes including widespread disorganization and decreased myelin thickness, reduction of neurochemicals that are responsible for neurogenic inflammation, reduction in the expression of ion channels that convert natural stimuli into electrical signals, and reduction in the levels of growth factors necessary for the synthesis of ion channels
- Although the prevalence of chronic pain is higher in the elderly population, **they have less pain symptoms** compared to relatively younger subjects.

- Elderly patients have lower analgesic requirements after surgery. Empirical use of analgesic medications without considering age as a risk factor can lead to excessive sedation, delirium, and respiratory complication.
- Female patients tend to report more pain compared to their male counterparts.

MCQ

1. After open exploratory laparotomy, severe acute postoperative pain is uncommon in the
   A. Middle age
   B. Adolescent
   C. Women
   D. Elderly
2. Which of the following is not a cause of increased sensitivity to opioid medications in the elderly?
   A. Age related degeneration of the nervous system
   B. Increased volume of the central compartment
   C. Decreased cardiac output in some elderly patients
   D. Altered pharmacokinetics of medications
3. Which of the following is not an effect of opioids in the elderly population?
   A. Increased incidence of respiratory depression
   B. Increased duration of systemic effects
   C. Increased incidence of pruritus
   D. Increased duration of neuraxial effects
4. Regarding gender differences in pain, which of the following statement is correct?
   A. No gender difference in the prevalence of migraine and temporomandibular joint disorder
   B. Females reports lower numeric pain scores than males
   C. Females are genetically more tolerant to pain
   D. Higher pain catastrophizing is associated with greater pain intensity.

Answers

1. D, 2. C, 3. C, 4. D

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40 Basic Science: Pathophysiology of Acute and Chronic Pain; Somatic Versus Visceral Pain

Braden Schuster, Timothy Ness, and Alethia Sellers

Introduction

- Nociceptive pain is associated with tissue damage or potential tissue damage and can be caused by a variety of stimuli. It is broken down into two types; **somatic and visceral**
- The duration of symptoms determines if the pain is acute (generally present **3–6 months**) or chronic (>6 months.)
- Somatic and visceral pain have several defining characteristics that help **distinguish each from the other** which include localization, quality of pain and evocative stimuli (Table 40.1).

Anatomy

Primary Afferent Neurons

- Both somatic and visceral primary afferent neurons have pseudo-unipolar axons with cell bodies located in the dorsal root ganglion.
- One axonal branch is located peripherally and acts as a sensory transducer; the other axonal branch synapses in spinal dorsal horn with second order neurons

Table 40.1 Correlation of visceral afferent levels of entry and referred pain

ORGAN	Spinal levels of greatest Primary afferent input	Typical site of referred pain
Heart	$C_{2-4,}$ C_8–T_6	Neck, arm, chest
Esophagus	$T_{1–10}$	Chest, upper abdomen
Stomach	$T_{6–10}$	Upper abdomen
Liver/gall bladder	$C_{3–5}$; $T_{6–10}$	Shoulder, upper abdomen
Pancreas	$T_{6–10}$	Upper abdomen through to back
Small intestines	$T_{6–12}$	Abdominal
Kidney/ureter	T_8–L_2	Back, flank, lower abdomen
Colon	T_6–L_2; $S_{1–4}$	Abdominal, pelvic
Rectum	$S_{1–4}$	Pelvic/perineal
Urinary bladder/ prostate	T_{10}–L_2; $S_{1–4}$	Abdominal, pelvic, perineal
Ovary/uterus/ vagina	T_{10}–L_2; $S_{1–4}$	Abdominal, pelvic, perineal

- Two types of peripheral sensory nerve fibers (myelinated A-δ fibers and unmyelinated C fibers) are responsible for both somatic and visceral pain sensation
- Additional myelinated fibers (A-β fibers) responsible for other sensations are also common in somatic structures (light touch, vibration) but rare in viscera
- Substances of interest that activate somatic and visceral primary afferents include sero-

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tonin, bradykinin, glutamate, neuropeptides (substance P, calcitonin gene-related peptide), purines (e.g. adenosine, ATP), potassium, acids and TRPV1/TRPA1 agonists.
- Somatic primary afferents have a high density of sensory nerve innervation in the periphery and are more well organized with distinct peripheral nerves.
- Visceral afferents have a low density of sensory nerve innervation in the periphery and are more diffusely organized **with few distinct nerves**; they travel along with sympathetic and parasympathetic efferent fibers along web-like perivascular paths.
- Primary afferents from a **specific somatic site** enter the spinal cord **unilaterally** at a limited number of spinal levels (3–5) and interact with neurons in only a few spinal laminae.
- Primary afferents from a **specific visceral site** enter the spinal cord **bilaterally** at numerous spinal levels (>10) and interact with neurons in almost all spinal laminae.

Second Order Neurons

- These have axonal projections that transmit sensory information to third order neurons residing in the spinal cord, the brainstem and/or the thalamus (Fig. 40.1).
- Second order somatic pain pathways are discrete and project to somatotopically organized sites in the brain.
- Second order **visceral pain pathways are diffuse** leading to **widespread activation** of brainstem, cortical and limbic structures.
- An important path for axons of second order neurons related to pain is the contralateral anterolateral spinothalamic tract but there is evidence that **dorsal column pathways** may also be involved in visceral pain.

Other Viscerosensory Neurons

- Third order neurons may be involved in local spinal reflexes or may transmit sensory infor-

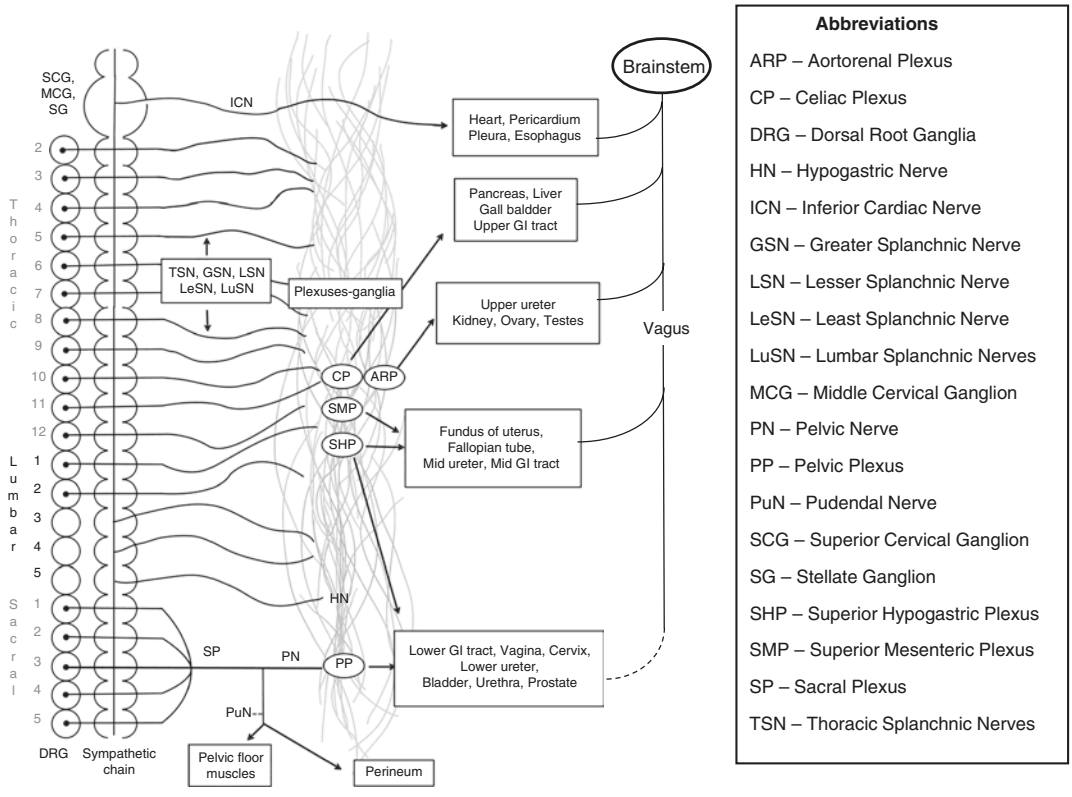

Fig. 40.1 Peripheral pathways of visceral sensation. (Adapted from Ref. [4])

mation to various brain subcortical and cortical sites, including the **somatosensory cortex and limbic structures** associated with emotion and autonomic responses.
- The vagus nerve also contains primary afferent neurons associated with typically non-painful visceral sensations (e.g., nausea) which have cell bodies in the nodose ganglion and synapse on second order neurons in the medulla.
- Enteric nervous system neurons contained within the many layers of the gut are likely not associated with pain sensation.

Physiology

Acute Somatic Pain Is Organized and Predictable

- Stimuli which reliably produce cutaneous pain include extreme heat, extreme cold, certain chemicals (associated with tissue damage/inflammation) and extreme pressure focally (pinprick/pinch) or broadly (crushing)
- After injury, skin can become hypersensitive to hair movement, light pressure, heat and cold

In Contrast, Visceral Pain Is Diffuse and Unreliably Evoked

- Healthy viscera are normally minimally sensate on a conscious level
- After injury, viscera may become highly sensate but with poor localization unless process extends to **somatic structures (e.g. abdominal wall**)
- Visceral sensations are generally referred to somatic structures whose afferents enter the spinal cord the same levels as visceral afferents.
- Organs with bilateral afferent pathways including the digestive tract, bladder, uterus and pancreas are generally perceived bilaterally in the midline
- Organs with **lateralized** afferent pathways including the kidneys, ureters, hepatobiliary structures and the ovaries are often felt **ipsilaterally**.

There Are No Stimuli Which Reliably Produce Visceral Pain

- **Stretch** is the principal mechanical stimulus involved in visceral nociception
- In addition, **distention, contraction, traction, compression**, and torsion all stimulate visceral nociceptors.
- Acute inflammation and ischemia may result in greater visceral pain sensation in response to external stimuli

Transduction Mechanisms of Visceral Primary Afferents

- Quantitative studies of sensory nerve fibers with endings in viscera demonstrate many, if not a majority, to be **"silent"** (mechanically insensitive)
- Following local acute inflammation in the viscera, *silent* nerve fibers become spontaneously active and sensitive to numerous stimuli (mechanical, thermal, chemical) –they acquire visceral hypersensitivity
- Following chronic inflammation, neuronal responses are less predictable as both hypersensitivity and hyposensitivity have been observed
- It has been hypothesized that certain chronic visceral pain disorders such as irritable bowel syndrome, may be associated with **hypersensitive afferents**.
- During surgery or other procedures involving viscera – if tissues have been inflamed or experienced ischemia, robust reflex responses (e.g., cardiovascular) to manipulation, traction, torsion and distension may be elicited due to activation of previously *silent* nerves.

Clinical Features

Superficial Somatic Pain

- From nociceptors located in skin, subcutaneous tissues and mucous membranes
- Pain is well localized and intensity corresponds to stimulus intensity
- Characterized by **sharp, throbbing, and burning type pain**

Deep Somatic Pain

- From nociceptors located in muscles, tendons, joints, and bones
- Pain felt unilaterally and regionally (limb, trunk)
- Characterized by **deep and aching pain which can be localized by movement/palpation**

Visceral Pain

- Arises from nociceptors located in internal organs.
- Pain tends to be **poorly localized**
  - Perceived in general location (chest, abdomen, pelvis - depends on organ of origination) and referred to somatic structures
  - Pain predominately is sensed in midline of body
  - Pain may migrate (e.g. movement of ureteral stone as travels through ureter)
  - Physical exam may help localize pain
- Associated symptoms include autonomic **responses (e.g. nausea, diaphoresis,** changes in heart rate and blood pressure) and **pain out of proportion** to exam
- Visceral pains thought to produce stronger autonomic and emotional responses than somatic pains
- Visceral pains are commonly made **worse** by psychological stress

Treatment

- Significant overlap in treatment options for somatic and visceral pain, with limited types of treatment options that are specific for visceral pain (noted in Table 40.2 by asterisks).
- Procedural and etiological therapies dependent on site of pain generation
- Pharmacological and nonpharmacological interventions are same for somatic and visceral pain.

Clinical Pearls

- Somatic and visceral are two types of nociceptive pain distinguished by **differing** neurobiology and by differing clinical presentation
- Cell bodies for sensory afferent neurons are located in the dorsal root ganglia
- Somatic pain is characterized by **good localization** of pain, and a well-organized system of primary afferents

Table 40.2 Therapies for nociceptive pain. Asterix denotes visceral pain-only treatments

Pharmacological	Non-opioid analgesics (NSAIDs and acetaminophen)	Opioid Analgesics (Hydrocodone, oxycodone, tramadol)	Adjuvant Agents (anti-convulsants/ depressants/ spasmodics, anxiolytics, steroids)
Procedural	Peripheral Nerve (axillary, sciatic) and Plexus Blocks (celiac*, hypogastric*)/ Neuroablative (RFA)	Neuraxial therapy (Spinal cord stimulation, epidural steroid injection)	Surgical (endoscopic procedures*, resection)
Nonpharmacological	Psychosocial therapy (Cognitive behavioral therapy and pastoral counseling)	Physical therapy (heat/cold application, exercise, TENS unit, OT/PT aids)	Education (peer group support)

- Visceral pain is characterized by **poor localization** of pain, and diffuse afferent innervation peripherally and centrally
- Visceral pain **may be referred** to (sensed in) somatic sites. A classic example of this is arm/neck/chest pain with myocardial infarction
- Autonomic and emotional responses are more **robustly evoked** by visceral pain when compared to somatic pain
- Treatment modalities can be broken down into three main categories; pharmacological, non-pharmacological, and procedural – all have role in both somatic and visceral pain

Multiple Choice Questions

1. What nerve contains visceral sensory afferent fibers?
   A. Greater Splanchnic Nerve
   B. Long Thoracic Nerve
   C. Median Nerve
   D. Peroneal Nerve
   E. Spinal Accessory Nerve
2. Which descriptor is appropriate when describing visceral pain
   A. Discretely localized to site of origin
   B. Reliably evoked in healthy tissues
   C. Rarely evokes autonomic responses
   D. Poorly localized
   E. Untreatable
3. Stimuli which always produce reports of visceral pain
   A. Burning
   B. Ischemia
   C. Cancer
   D. Pinch
   E. None of the above
4. A patient presents to pain clinic with uncontrollable abdominal pain related to pancreatic cancer, which of the following is the best treatment option
   A. Stellate ganglion block
   B. Spinal cord stimulator
   C. Hypogastric plexus block
   D. Celiac plexus block
   E. Epidural steroid injection
5. Which of the following may be present with visceral pain
   A. Tachycardia
   B. Nausea
   C. Diaphoresis
   D. Hypotension
   E. All of the above

MCQ Correct Answers

1A, 2D, 3E, 4D, 5E

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Basic Science: Autonomic Nervous System Physiology

41

Bharat Sharma and Yawar J. Qadri

Autonomic Nervous System Physiology

I. General Anatomy
   (a) The autonomic nervous system (ANS) manages physiologic functions via the sympathetic and parasympathetic branches [1] as shown in Fig. 41.1.

II. Sympathetic Nervous System:
   (a) The **preganglionic neurons** are located in the **lateral horns** of the cord from **T1 to L2/3** (Fig. 19.2, Chap. 19)
   (b) The **postganglionic neurons** are found in the **paravertebral** (cervical, stellate, thoracic, lumbar, impar) and **prevertebral ganglia** (celiac, aorticorenal, superior mesenteric, inferior mesenteric), from where they course to their end organ. Some sympathetic preganglionic fibers synapse **directly on the chromaffin cells** of the adrenal medulla.
   (c) The preganglionic neurons also travel more rostrally or caudally to synapse with postganglionic neurons in ganglia at other levels. A single preganglionic neuron may synapse with several postganglionic neurons. This divergence of the preganglionic neuron cause concurrent stimulation of many organs and tissues in the body.
   (d) Unlike the parasympathetic system, the postganglionic neurons of the sympathetic system travel within each of the 31 pairs of spinal nerves.

III. Parasympathetic:
   (a) **Parasympathetic preganglionic neurons** are located in **brainstem nuclei and lateral horns of the sacral cord (segments S2-S4)**. Cranial nerves III (oculomotor), VII (facial), IX (glossopharyngeal), and X (Vagus) mediate the cranial outflow of the parasympathetic fibers
   (b) 75% of all parasympathetic fibers are in the vagus nerve (Cranial Nerve X).
   (c) **Parasympathetic postganglionic** bodies lay **on ganglia on the organs innervated** by the vagus or sacral nerves or within ciliary, otic, pterygopalatine, and submandibular ganglia.
   (d) The axons of the preganglionic neurons are longer and synapse with postganglionic neurons within terminal ganglia which are close to or embedded within the effector tissues (Fig. 41.1)
   (e) The preganglionic neurons that arise from the sacral region of the spinal form

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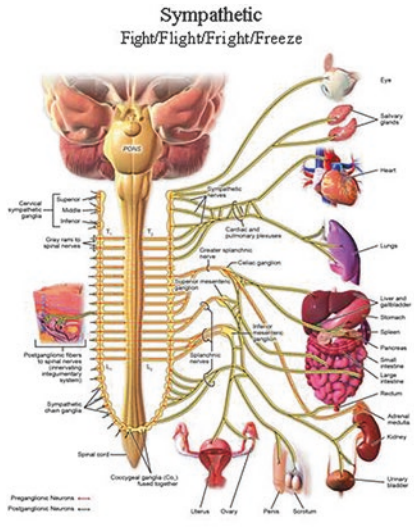

Organ	Sympathetic action	Parasympathetic action
Eye	Dilate pupils	Constrict pupils
Salivary Gland	Inhibit salivation	Salivate
Heart	Increase HR	Decrease HR
Lungs	Dilate airways	Constrict airways
Liver	Stimulate glucose release	Stimulate bile release
Intestines	Stimulate peristalsis	Inhibit peristalsis
Kidneys	Increase renin	Decrease renin
Adrenals	Release catecholamines	
Bladder	Relax bladder	Contract bladder
Sexual organs	Promote ejaculation	Stimulate arousal

Fig. 41.1 Shows the anatomic arrangement of the ANS, as divided between the sympathetic and parasympathetic nervous systems, with a table showing the functions of the two on the end organs. (Modified from Blausen.com staff [3])

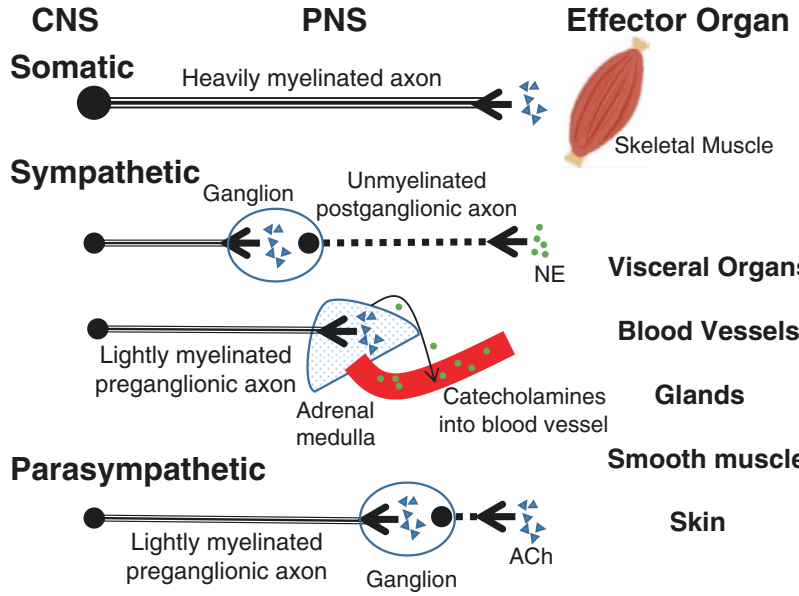

Fig. 41.2 Shows the schematic arrangement of somatic and autonomic neurons, with a cell body in the central nervous system, a pre- and post-ganglionic axon in the peripheral nerve system, with release of acetylcholine(ACh) or Norepinephrine (NE) as directed on the end organ

pelvic nerves and supply large intestine, renal and reproductive systems (Fig. 41.1)

(f) **White ramus communicans fibers** carry **afferent pain signals** back from the viscera.

IV. The **primary neurotransmitters** are acetylcholine and norepinephrine [2].

(a) **Acetylcholine** (ACh) acts on the **muscarinic** (M1-M5) or **nicotinic** (N2) receptors.

(b) **Norepineprhine** (NE) targets **α-** or **β-adrenergic** receptors

(c) All preganglionic fibers of the ANS release ACh (Fig. 41.2)

(d) Postganglionic fibers of the parasympathetic system release ACh; and sympathetic postganglionic fibers release NE except those innervating **sweat glands** which release ACh (Fig. 41.2).
(e) There is **systemic epinephrine and catecholamine release** by the direct sympathetic action on the **adrenals**.
(f) There is also a role of other peptide or small-molecule transmitters such as substance P, CGRP, ATP, glutamate, glycine, etc.

V. **Stimulation in the periphery generate the afferent signals** at various end organs [2].
(a) Activation of ANS can be by small molecules such as glucose, nicotine, or fatty acids, mechanical effects such as **stretch** or **flow**, or by light and temperature.
(b) Spinal visceral nociceptive fibers express **TRPV1** (activated by **heat/capsaicin**), **TRPA1**(activated by **chemical irritants/eicosanoids**), **Na_v1.8 or 1.9** (voltage gated), and/or **TRPM8**(activated by **cold/menthol**).
(c) Other channel families include the Acid Sensing Ion Channels (**ASIC3 – activated by low pH**) and Piezo family (**Piezo2** activated by **mechanical stretch/pressure**)
(d) These channel families and others can be modulated by inflammation or agents such as CGRP (calcitonin gene-related peptide) or Substance P. This modulation can awaken sleeping or silent nociceptors through a process of sensitization.

VI. **Visceral pain** is characterized typically as diffuse, dull, deep, and/or cramping pain with tenderness to palpation on physical exam. Visceral pain is typically **NOT characterized** as superficial or pinprick [1].
(a) Parasympathetic and Sympathetic autonomic innervation to visceral sites is mediated by **vagus (CN X), thoracolumbar, sacral outflows**
(b) Visceral structures are innervated by **A-Delta** and **C-fibers** that have cell bodies in the dorsal root ganglia with afferent inputs to the dorsal columns of the spinal cord.
(c) The spinal cord structures communicate with multiple brain stem regions including the **nucleus tractus solitarius**, **periaqueductal gray**, and **rostral ventromedial medulla** as well as higher structures including the **amygdala**, **thalamus**, and **hypothalamus**.
(d) There is **extensive arborization between the visceral and somatic pain pathways in the spinal cord**. This **viscerosomatic convergence** occurs on both sides and over multiple levels of the spinal cord. This is the reason for the diffuse, referred and often bilateral nature of visceral pain. This also leads to **referred pain** to sites that are distant from the pain generator based on the autonomic afferent signal interacting with the DRG or spinal cord levels.
(i) **Cardiac**: **Left arm/shoulder**, left thorax, and the neck
(ii) **Esophageal**: left thorax, and **left shoulder/upper arm**
(iii) **Liver**: **Left upper abdominal quadrant**
(iv) **Stomach**: **Epigastric** pain, and **lower left thoracic pain**
(v) **Colon**: **Lower abdominal pain**
(e) Similarly, there is **bidirectional signaling** within the ANS and somatic/pain systems, contributing to **autonomic motor symptoms** such as **sweating**, nausea/vomiting, diarrhea, tachycardia, hypotension, or **lacrimation** seen in pain states. This is primarily through nociceptive spinal neurons projecting to higher structures.

Clinical Pearls

- Visceral pain is generally **diffuse, dull,** and difficult to localize
- Referred pain due to viscerosomatic convergence can localizes based on convergence of

afferent inputs by arborization at the entering spinal cord levels

- Autonomic preganglionic signaling is primarily with **acetylcholin**e acting on the N2 Nictoninic receptors while postganglionic signaling is primarily via **norepinephrine** acting on adrenergic receptors.
- Parasympathetic preganglionic neurons are in the brainstem and sacral cord while sympathetic preganglionic neurons are in the **lateral horns** of the thoracolumbar cord (Fig. 19.2, Chap. 19).
- Parasympathetic postganglionic neurons are on the target organ while sympathetic postganglionic neurons are prevertebral and paravertebral ganglia.

Questions

1. Which of the following neurotransmitter and receptor combinations is appropriate for the preganglionic synapses of the autonomic nervous system?
   A. Epinephrine – Beta1 adrenergic receptors
   B. Norepinephrine – Muscarinic M1 receptor
   C. Acetylcholine – N1 receptors
   D. Acetylcholine – N2 receptors
2. Which of the following channels and activator combination is involved in visceral nociception?
   A. TRPA1 – cold temperatures
   B. TRPV1 – capsaicin
   C. TRPM8 – hot temperatures
   D. ASIC3 – intracellular calcium
3. Which combination of pre- and postganglionic neuron bodies locations is anatomically correct?
   A. Parasympathetic preganglionic neurons are located in the brainstem nuclei and synapse on postganglionic neurons in the thoracic paravertebral space.
   B. Parasympathetic preganglionic neurons are located in the sacral cord and synapse on postganglionic neurons in the prevertebral ganglia.
   C. Sympathetic preganglionic neurons are located in the dorsal columns of the thoracolumbar cord and synapse on postganglionic neurons on effected end organs.
   D. Sympathetic preganglionic neurons are located in the lateral horns of the thoracic cord and synapse on postganglionic neurons on paravertebral ganglia in the thoracic spine.
4. Which of the following qualities is least likely to describe visceral pain as compared to somatic pain?
   A. Localized
   B. Colicky
   C. Dull
   D. Pressure
5. A patient reports a superficial pain in their left shoulder after placement of a left chest tube. This referred pain pattern is explained by what neurologic phenomena?
   A. Central sensitization due to windup
   B. Peripheral unsilencing of sleeping nociceptors
   C. Viscerovisceral convergence due to temporal summation
   D. Viscerosomatic convergence due to arborization

Answers

1. D, 2. B, 3. D, 4. A, 5. D

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Suggested Reading

Wall and Melzack's Textbook of Pain, 6th edition pages 28–30, 198–210, 703–717.
Bonica's Management of Pain, 5th edition Chapter 9.

Noncancer Pain: Myofascial Pain Syndrome

42

Leath Abdullah and Scott Brancolini

Introduction

- Pain disorder caused by the presence of trigger points within muscles or their fascia
- Characterized by hyperirritable nodules of taut muscle tissue causing pain known as trigger points (see Fig. 42.1)
- Common source of chronic pain in the general population (~30%)
- Pain is of a deep aching quality, burning or stinging.
- Trigger points are **hallmarks of myofascial pain**, and may result from acute trauma, repeated microtrauma, or the sudden muscular strain of sedentary people.
- Sometimes pain radiates a significant distance from the site of the trigger point, mimicking radiculopathy pain

Clinical Picture

- **Non-inflammatory syndrome** that induces pain **identified by the palpation of trigger points** [1]
- Two types of trigger points: active and latent [1]
  - **Active trigger points:** regions of contracted, tight muscle tissue which induce pain, referred pain, or autonomic symptoms when stimulated, and reduce range of motion possibly inducing fatigue/weakness (Fig. 42.1)
  - **Latent trigger points**: also induce pain or referred pain on stimulation, and can actually induce any symptoms of active trigger points but to a lesser extent
- Pain develops in an **asymmetrical, nondermatomal pattern** on the body
  - Worsened by overuse, active stretching, palpation, further contraction, cold temperature, or viral infections.
  - Alleviated by rest, passive stretching, warm temperatures, myofascial pain therapies, or non-isometric contraction
- **Strong association with psychological disorders** such as anxiety and depression

Pathophysiology

- **Trigger points associated with muscle overuse** [2]
  - Contractions at even low levels of maximal strength generate large internal pressures
  - Varies muscle to muscle but only 20 mmHg of pressure required to stop blood flow
  - Creates a localized depletion of oxygen and hence ATP via increased reliance on anaerobic metabolism

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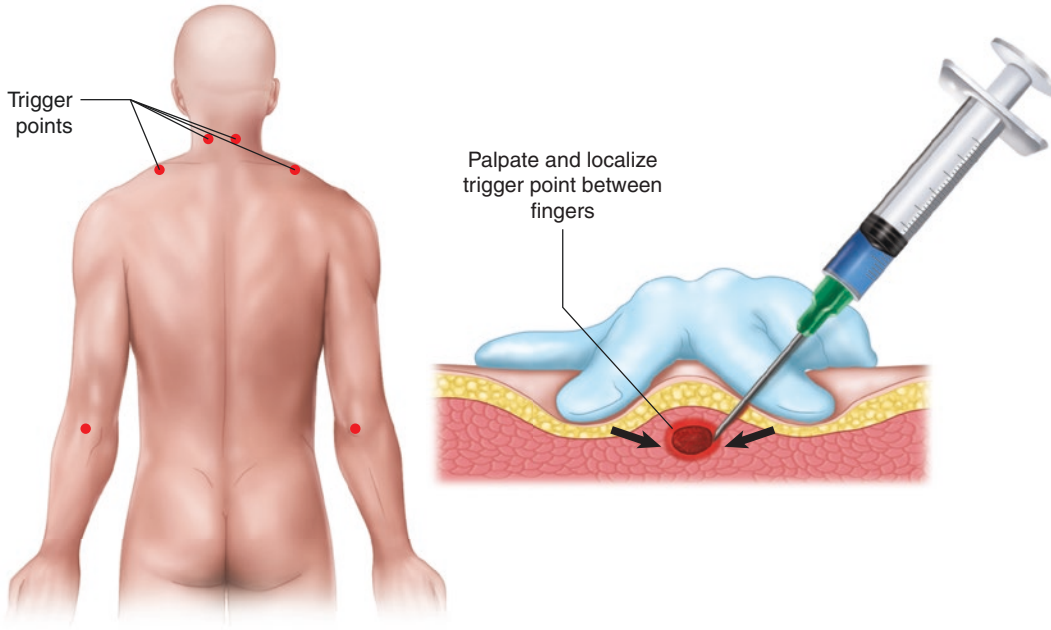

Fig. 42.1 Pictured above are common sites of trigger points and how to palpate and perform injections

  - Also creates lactic acid buildup which cannot leave muscle during contracted state
- Ischemia within this trigger point decrease pH to below 5 [3]
  - Ischemia and acidity excite nerve endings creating hyperalgesia and central sensitization
  - Ischemia decreases energy available for calcium ATPase to pump calcium from the sarcoplasm into the sarcoplasmic reticulum, preventing contraction from ceasing
  - Creates prolonged contractions which damage the muscle
- Injury or stress alone is sufficient but not required for trigger point development [3]
  - Overuse/micro-trauma may cause only brief soreness in people, but be enough to promote trigger point development

Treatments

General Principle

1. Identifying and treating the underlying factors for development of myofascial pain (eg, poor posture, repeated activities, anxiety disorder, certain medications such as statins)
2. Deactivating the trigger point with massage, dry needling, or trigger point injection (Fig. 42.1)
3. Building muscle strength with PT
4. Topicals: Topical analgesic and anti-inflammatory agents, applied as creams, gels, or patches, heat/cold therapy, TENS
5. Medications

- Dry needling [3]
  - **Insertion of needles without injection** of medication into the myofascial trigger points
  - Needle manipulated around the site using an **in-and-out technique** in many directions to break up the taut band (Fig. 42.1)
  - **Can cause a muscle twitch**, a spinal reflex, to occur
  - After relaxation, the blood flow to muscle is restored, breaking the positive feedback loop and allowing the trigger point release
  - Needle may cause post-procedural soreness

Injection of **lidocaine improves soreness without any additional benefit** over dry needling

Non-inflammatory condition, so steroid injections are of little benefit

- Massage and manual therapy [2]
  - Known to improve macroscopic blood flow but not capillary blood flow
  - Includes deep-pressure massages, stretch therapy (manual trigger point stretching after cold spray), and cutaneous heat
  - Improvement tends to be **short term**
- Transcutaneous electric nerve stimulation (TENS) [2]
  - Mechanism of action is based on the Melzack and Wall's gate-control theory
  - Modulation of the nociceptive stimulus to the brain **by presynaptic inhibition** in the spinal cord.
  - Evidence indicating a significant placebo component of the effect of TENS
- Neurotoxin botulinum type A toxin [2]
  - Enters acetylcholine producing neurons, then cleaves soluble NSF attachment protein receptors (SNARE proteins)

    SNARE proteins assists in acetylcholine vesicle fusion to the cell membrane.

    Botulinum inhibits release of acetylcholine at the synapse leading to muscle relaxation
    - Consequently blocks subsequent recruitment of proinflammatory mediators such as CGRP, glutamate and substance P

    Botulinum toxin blocks the alpha- and gamma-motor neurons leading to decreased abnormal pattern of muscle contraction eg, spasm, dystonia.

    Each 100-unit vial is diluted in 10 mL of preservative-free saline, and 1–2 mL are injected into each palpable trigger point and tender area.
  - Repeat injections may be considered 12 weeks after the first injection.
- Local heat and cold [2]
  - Local application of heat has short-term beneficial effects
  - Some find ice application also helpful for short term pain
- Medications [2]:
  - Acetaminophen
  - Non-steroidal anti-inflammatories (NSAIDs)
  - Muscle relaxants
  - Tizanidine

    Centrally-acting alpha-2 adrenergic agonist
  - Cyclobenzaprine

    Centrally acting muscle relaxant, likely inhibits 5-HT2 receptors

    Most widely studied muscle relaxant
  - Methocarbamol
- Psychiatric therapies [2]
  - Treatment of underlying anxiety and depression
  - Referral to pain psychology

Clinical Pearls

- Myofascial pain syndrome is **characterized by tender, tight nodules of contracted muscle tissue called trigger points**
- These are **non-inflammatory hypercontracted muscle tissue**
- **Muscle overuse, repeated micro-trauma, or acute trauma** to the muscle can lead to the development of trigger points.
- They may develop during occupational, recreational, or sports activities when muscle use exceeds muscle capacity and normal recovery is disturbed
- Identifying and treating the underlying factors for development of myofascial pain (eg, poor posture, repeated activities, anxiety disorder, medications such as statins)
- **Deactivating the trigger point** with massage, dry needling, or trigger point injection
- **Build muscle strength** with physical therapy and exercises
- **Topical analgesic and anti-inflammatory agents**, applied as creams, gels, or patches, heat/cold therapy, TENS

MCQs

1. The addition of a local anesthetic medication to saline for injection at myofascial pain locations provides which added benefit?
   A. Improves long term pain relief
   B. Acts to provide a localized nerve block for a short period of time
   C. Improves short term pain relief for pain associated with injections
   D. None of the above
2. Which term best describes myofascial pain?
   A. Visceral
   B. Somatic
   C. Inflammatory
   D. Post-traumatic
3. Which of the following statements about myofascial pain syndrome is correct?
   A. Symmetric distribution
   B. First line therapies include antidepressants
   C. Many therapies target improving blood flow
   D. Monotherapy is recommended for initial treatment
4. All the following are defining features of myofascial pain except:
   A. Distal numbness
   B. Referred pain
   C. Improvement with rest
   D. Taut muscle bands
5. The first line procedural therapy for myofascial therapy is:
   A. TENS
   B. Dry needling
   C. Laser therapy
   D. Ultrasound therapy

Answers

1. C, 2. B, 3. C, 4. A, 5. B

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Further Reading

Barash sixth edition, page 1515.

Noncancer Pain: Fibromyalgia

43

Danielle Bodzin Horn and Carlos C. Marrero-Prats

Introduction

- Fibromyalgia is a constellation of symptoms including chronic, **widespread musculoskeletal pain** with multiple **tender points** (19 have been described) +/− **fatigue**, sleep disturbance, cognitive dysfunction, **depression/** anxiety, **headaches**
  - Widespread pain typically bilateral involving both upper and lower body, usually muscle pain +/− joint pain [1, 2]
- Common comorbid conditions include irritable bowel syndrome, interstitial cystitis, depression, anxiety, headache, chronic fatigue syndrome, restless leg syndrome, temporomandibular joint dysfunction, systemic lupus erythematosus, and rheumatoid arthritis [3, 4]
- 2–5% of the U.S. population is estimated to have fibromyalgia [4]
- Peak incidence between age 50 and 59 years [4]
- 2–7 X more common in women than men [4]

Diagnosis

- American College of Rheumatology diagnostic tool for fibromyalgia (see Fig. 43.1)
  - adults may be diagnosed with fibromyalgia when the following criteria are met [5]:
    1. Diagnosis is explained by fibromyalgia regardless of other diagnoses
    2. Generalized pain (in ≥4 out of 5 regions)
       - 5 regions = 4 quadrants + axial
    3. Symptoms for ≥3 months
    4. **Widespread pain index (WPI)** ≥7 and **symptom severity scale (SSS)** score ≥5; OR WPI 4–6 and SSS ≥9
       - **Fibromyalgia severity (FS) score = WPI + SSS** (ranges 0–31)
       - WPI score ranges from 0–19 points – each of the following areas the patient has had pain over the past 1 week = 1 point:
         - Left jaw, right jaw, left shoulder girdle, right shoulder girdle, left upper arm, right upper arm, left lower arm, right lower arm, left hip/buttock/trochanter, right hip/buttock/trochanter, left upper leg, right upper leg, left lower leg, right lower leg, neck, upper back, lower back, chest, abdomen (Fig. 43.1)

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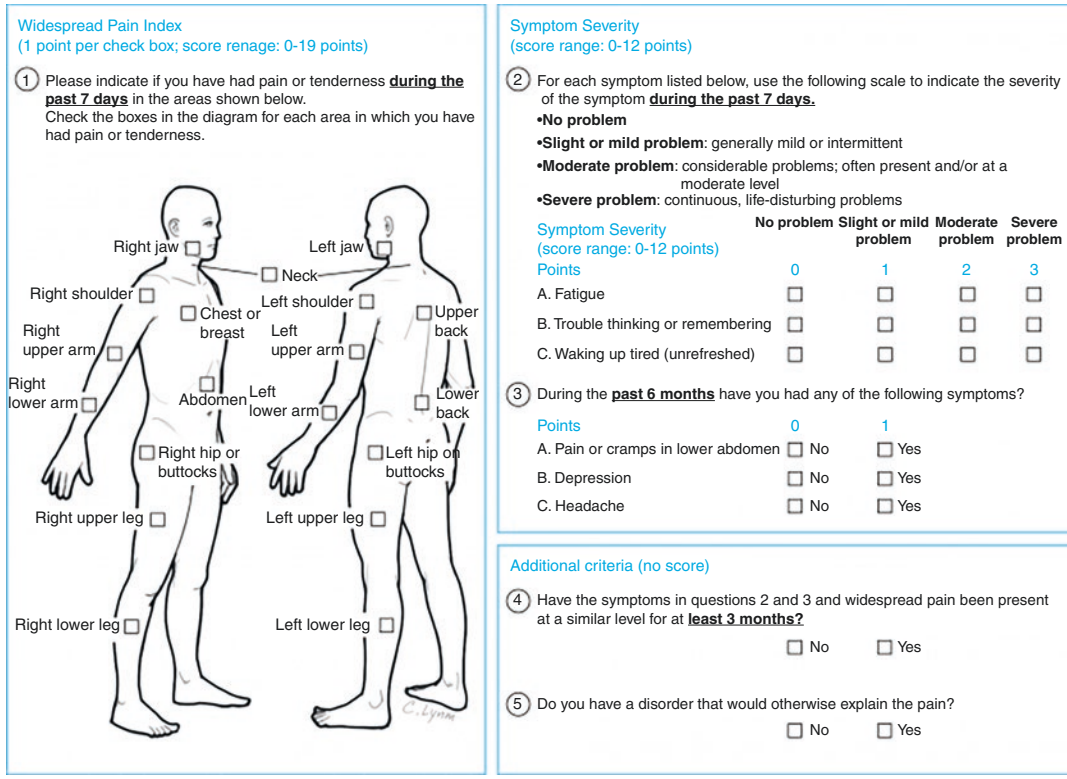

Fig. 43.1 Fibromyalgia ACR Diagnostic Criteria [6]. Number of painful body sites. Patients are asked to check the areas in which they experience pain on the 2-view manikins (ignoring the pre-shaded areas). Alternatively, patients may use the checklist of body sites. The number of separate sites are summed from a maximum of 9 body sites. (Reproduced with permission from Elsevier)

  - SSS ranges from 0 to 12 points (Fig. 43.1)
    - 9 of the 12 points are obtained from identifying severity level over the past week for the following symptoms (0 = no problem, 2 = slight/mild problem, 3 = moderate problem, 3 = severe problem):
      - **Fatigue** (0–3)
      - **Waking tired or unrefreshed** (0–3)
      - **Cognitive symptoms** (trouble thinking/remembering) (0–3)
    - The final 3 of the 12 points are obtained from identifying (yes or no) whether the patient has been bothered by any of the following symptoms in the past 6 months (0 = no, 1 = yes):
      - Headaches (0–1)
      - Lower abdominal pain or cramps (0–1)
      - Depression (0–1)
- The Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks (ACTTION), a public-private partnership with the U.S. Food and Drug Administration (FDA) and the American Pain Society (APS), developed the ACTTION-APS Pain Taxonomy (AAPT) which created the following 3 working group diagnostic criteria for FM:
  1. Musculoskeletal pain defined as 6 or more pain sites from a total of 9 possible sites (Fig. 43.2)

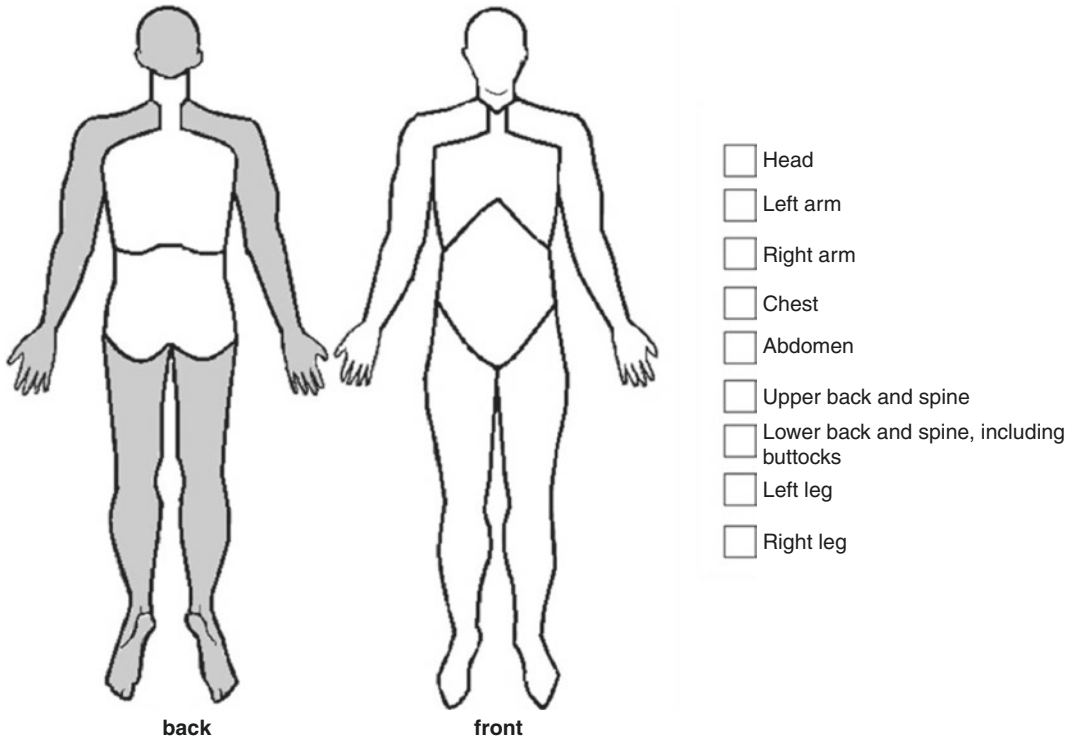

Fig. 43.2 Fibromyalgia AAPT Diagnostic Criteria. (Reproduced from Ref. [1])

2. Moderate to severe sleep problems OR fatigue
3. Musculoskeletal pain plus fatigue or sleep problems must have been present for at least 3 months

- Differential diagnosis includes [7, 8]:
  - Common – myofascial pain syndrome, chronic fatigue syndrome, hypothyroidism, polymyalgia rheumatica, metabolic or inflammatory myopathies (i.e., statin-related), autoimmune disorders such as rheumatoid arthritis, systemic lupus erythematosus, Sjogren's syndrome
  - Less common – hepatitis C, sleep apnea, Chiari malformation, celiac sprue

Pathophysiology

- Etiology of fibromyalgia is unknown and pathophysiology is not completely understood, but it is thought to be a **disorder of central sensitization** with CNS mediated pain amplification [9]
- The levels of the following neurotransmitters (which typically augment pain transmission) have been found to be increased in the CSF of patients with fibromyalgia: **Substance P, glutamate, nerve growth factor** [10]
- The levels of the following neurotransmitters (which typically inhibit pain transmission) have been found to be decreased in the CSF of patients with fibromyalgia: **serotonin, norepinephrine, dopamine** [10]
- Endogenous opioids in the brain of patients with fibromyalgia are altered [10]
  - **Elevated** levels of encephalins
  - Decreased availability of **mu-opioid receptors** in the nucleus accumbens and cingulate gyrus (opioid receptors are more greatly occupied at baseline)
- Temporal summation of pain – patients experience increased intensity of pain when rapidly repetitive short noxious stimuli are administered
- Decreased endogenous pain inhibition – decreased functional connectivity in the descending pain-modulating system

- Functional magnetic resonance imaging (fMRI) demonstrated that FM patients had **greater neuronal activity** in pain-processing brain regions compared with controls, following the same pressure stimuli
- Premature aging of brain: a significant **reduction in total gray matter** volume and a threefold increase in age-associated loss of gray matter
- Possible genetic predisposition [10]
  - Individual with first degree relative with fibromyalgia **8.5 times** more likely to develop fibromyalgia than an unrelated person
  - May be related to polymorphisms in genes involved in catecholamine and serotonin metabolism (i.e., catecholamine*O*-methyltransferase (COMT), GTP cyclohydroxylase, KCNS potassium channel, mu-opioid receptors, voltage-gated sodium channels, and gamma-aminobutyric acid (GABA) ergic pathways)

Treatment for Fibromyalgia [11, 12]

- Non-pharmacologic treatments (evidence level in parentheses):
  - **Patient education** (1A) – explain fibromyalgia, set expectations, encourage self-management and multimodal approach. Reassure that **FM is a real disease** not 'pain in the head'.
  - **Graded exercise** (1A)
    Best evidence for aerobic exercise; stretching and strengthening also beneficial
    Slow, *graded* exercise plan advised; symptoms may worsen if exercise progresses **too quickly**
  - **Pain based cognitive behavioral therapy (CBT)** (1A)
    May be individual, small group, or remote (via Internet) therapy
  - **Complementary and alternative medicine (CAM) therapies** (1A)
    Lack of adequate evidence
    Tai chi, yoga, balneotherapy, acupuncture possibly effective
- Pharmacologic treatments
  - At the time of writing this chapter, only 3 medications are FDA approved for fibromyalgia: **pregabalin, duloxetine, milnacipran**
  - Gabapentinoids (1A):
    Gabapentin (800–3600 mg/day in divided doses)
    Pregabalin (300–450 mg/day [typically divided in 2 doses])
    - Studies of 600 mg/day found no additional benefit and increased adverse reactions to doses above 450 mg/day [13]

    Common side effects: sedation, weight gain, dizziness
  - Serotonin-norepinephrine reuptake inhibitors (1A): ***duloxetine*** (30–120 mg/day), ***milnacipran*** (100–200 mg/day)
    Common side effects: nausea, palpitations, tachycardia, hypertension, headache, fatigue
  - Tricyclic antidepressants (TCA) (1A): *amitriptyline* (10–70 mg/night)
    Common side effects: dry mouth, weight gain, constipation, sedation
  - Muscle relaxants: *cyclobenzaprine* (1A; 5–10 mg up to TID) – centrally acting muscle relaxant, structurally related to TCA, side effects similar to those of TCA
  - *Low-dose naltrexone (LDN)* (4.5 mg/day) – shown to be effective in a few clinical trials, no serious adverse events [14]
  - Cannabinoids – *nabilone* (0.5 mg QHS or BID)
    Common side effects: sedation, dizziness, dry mouth
  - Nonsteroidal anti-inflammatory drugs (NSAIDs) (5D) – no evidence for fibromyalgia, but may help with comorbid pain
    Possible adverse gastrointestinal, renal, and cardiac effects

Clinical Pearls [5–10]

- **FM characterized by:**
  - Widespread pain, >3 months, fatigue, sleep disturbances, headaches, bowel disturbances
  - Physical examination: Widespread tenderness, otherwise normal
  - Labs: normal (must ensure CBC, BMP, ESR, CRP, and TFT are evaluated since fibromyalgia is a diagnosis of exclusion)
- Most common in **middle-aged women**
- Fibromyalgia may be a disorder of central sensitization, and is commonly comorbid with other somatic and psychiatric diagnoses such as irritable bowel syndrome, interstitial cystitis, depression, anxiety, headaches, chronic fatigue syndrome, and certain autoimmune disorders; some resources will combine multiple conditions and diagnose a single "chronic overlapping pain syndrome"
- Treatment should be multidisciplinary including **pharmacological and nonpharmacologic** measures: patient education, treatment of comorbidity, slow graded exercise as tolerated; if symptoms do not improve, may add low dose TCA vs SNRI nightly +/− gabapentinoids; other medications including low dose naltrexone may be trialed as last resort

Questions

1. A patient presents with widespread myofascial pain. In addition to fibromyalgia, what other diagnoses may be considered in the differential diagnosis?
   A. Polymyalgia rheumatica
   B. Hypothyroidism
   C. Rheumatoid arthritis
   D. All of the above
2. Which of the following medications have been FDA-approved for the treatment of fibromyalgia?
   A. Duloxetine
   B. Gabapentin
   C. Pregabalin
   D. A & C
3. Which of the following statements is true regarding fibromyalgia?
   A. Fibromyalgia is more commonly diagnosed in men than women
   B. There is large variability of patient presentation, but all patients with fibromyalgia will present with headaches within the past 6 months
   C. Fibromyalgia patients commonly complain of sleep disturbance
   D. Fibromyalgia may be reliably diagnosed based on the results of imaging and laboratory studies
4. A 42-year-old woman with a past medical history of irritable bowel syndrome and depression is complaining of widespread myofascial pain, headaches, and fatigue. Her lab work is significant for TSH level that is significantly elevated. Which of the following is true?
   A. This is a classic presentation of fibromyalgia and she should be diagnosed and treated as such
   B. Fibromyalgia cannot be diagnosed in this patient.
   C. This patient is likely suffering from a psychosomatic disorder
   D. Fibromyalgia is an unlikely diagnosis in a patient under the age of 60 years old
5. Which of the following statements is true regarding the pathophysiology of fibromyalgia?
   A. Decreased descending inhibition
   B. elevated androgen levels
   C. elevated serotonin metabolism in the CNS
   D. Decreased substance P in the CSF

Answers

1. D, 2. D, 3. C, 4. B, 5. A

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Noncancer Pain: Facet Arthropathy and Axial Low Back and Neck Pain

44

Jakun Ing and Elizabeth Feenstra

Introduction

- Facet arthropathy of the thoracic or lumbar spine usually presents with low back pain that is primarily localized to the **midline** but **may radiate to the hip or ipsilateral posterior thigh**; pain usually does not radiate past the knee (Fig. 44.1a) [1].
- Facet arthropathy often coexists with intervertebral disc degeneration (**spondylosis**). Symptoms are typically **worse in the morning** and are increased by stress, exercise, lumbar spine extension, rotary motions, and prolonged standing or sitting.
- Cervical facet arthropathy presents with primarily axial neck pain which **may radiate into the shoulders (C6/C7 joint,** Fig. 44.1b) or even present as **headaches (C2/C3 joint). Pain may be aggravated by neck rotation or lateral flexion** [1].
- Occurs due to degenerative changes in the facet (zygapophyseal) joints.
- Physical examination usually reveals paraspinal tenderness and **exacerbation of pain with extension and/or lateral rotation** of the back or neck [2].
- Sensory innervation to the facet joint is provided by the **medial branch of the posterior division (ramus)** of the spinal nerves (Fig. 44.2) [2].
  - Each facet joint is innervated by **two medial branches**, the medial branch at the same level and the branch at the level above. For example, L4/5 facet joint is innervated by the L4 and L3 medial branch nerve [3].
  - In the **thoracic** and **lumbar** spine, nerve roots exit the foramina **below** the vertebral bodies for which they are named (example: T10 nerve root exits the foramen below the T10 vertebral body).
  - In the **cervical** spine, nerve roots exit the foramina **above** the vertebral bodies for which they are named **until the level of C7**. The C7 nerve root exits above C7 through the **C6-C7 neural foramen** and C8 exits in between **T1 and C7 neural foramen** [1].

Diagnosis

- Limited utility of radiologic studies in diagnosing facet syndrome
- Local anesthetic may be injected directly into the facet joint itself or may be targeted to

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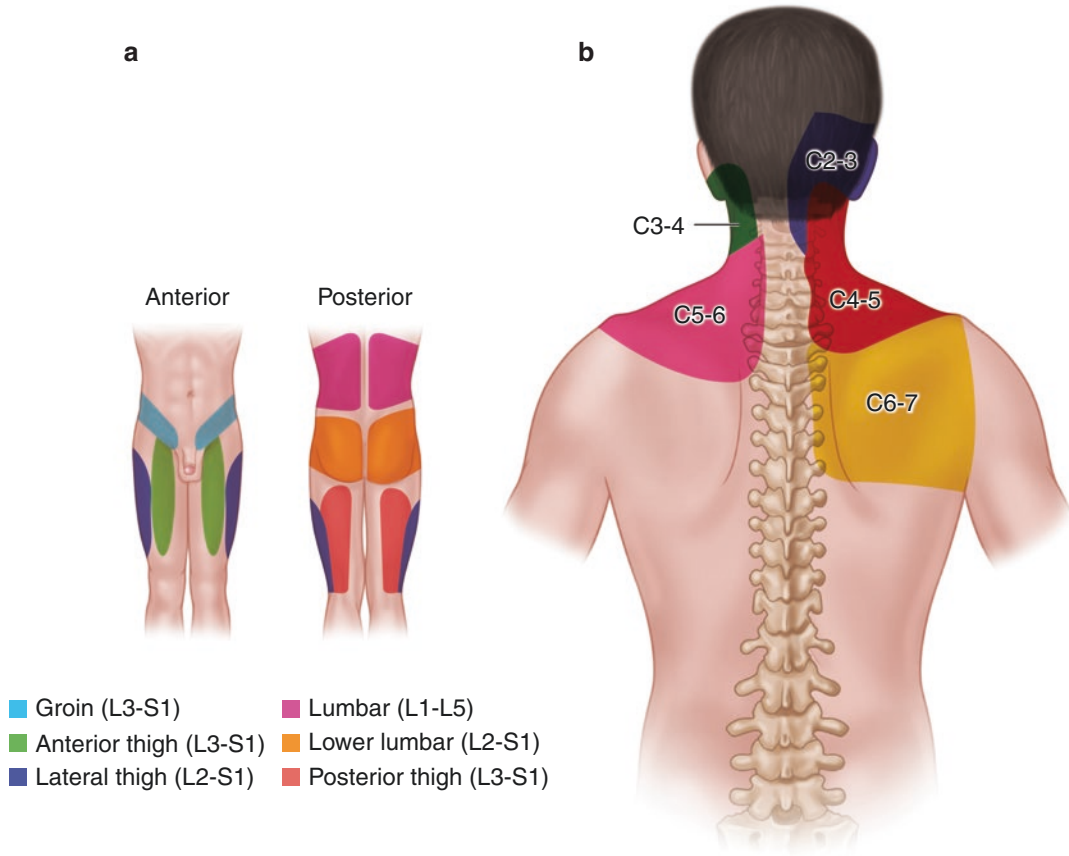

Fig. 44.1 Pain distribution of lumbar (**a**) and cervical (**b**) facet joints

block the medial branches which innervate the facet joint [4].

- Clinically meaningful pain relief of at least 50% following either of these two procedures is the **gold standard** for diagnosing facet arthropathy.
- High rates of false positive results occur after both facet joint injections and medial branch blocks.

Treatment

- Conservative management of axial back or neck pain involves use of nonsteroidal anti-inflammatory medications, muscle relaxants, antidepressants, weight loss, and physical therapy for core strengthening [1, 2].
- The patients who had >50% pain relief with diagnostic intra-articular injections or medial branch blocks can be offered for percutaneous radiofrequency ablation of medial branch nerves.

Technique

- Place the tip of a radiofrequency needle at the location of the targeted nerve under fluoroscopic guidance.
- In the cervical facets, the medial branches often cross the middle of the articular pillars (Fig. 44.3) [5].
- In the lumbar facets, the medial branches are generally located at the intersection of the superior articular process and the transverse process (Fig. 44.4) [5].

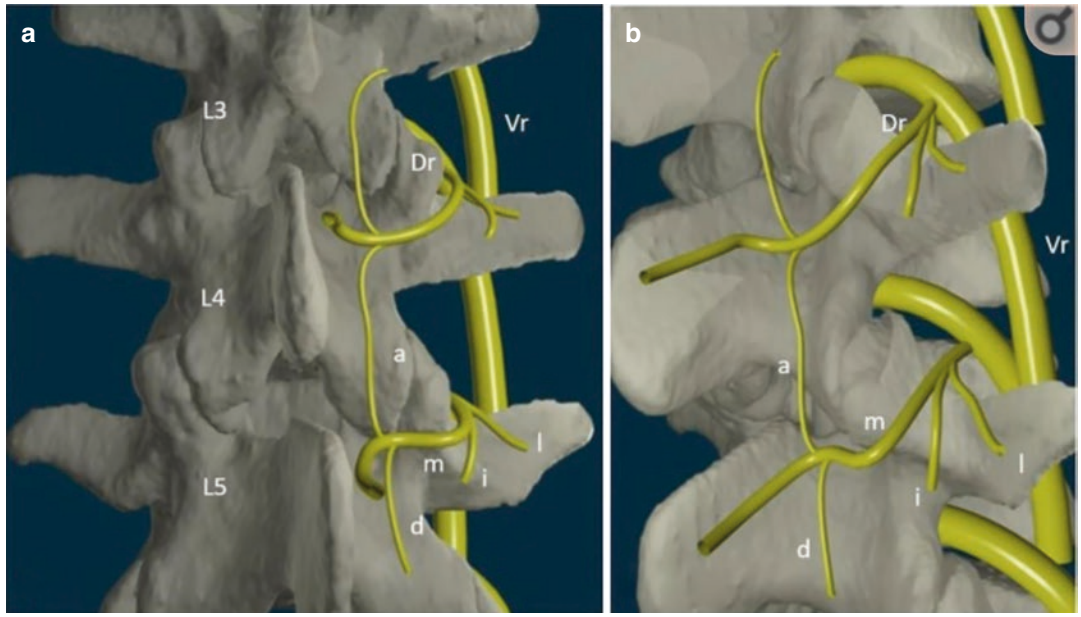

Fig. 44.2 Innervation of lumbar facet joints. A: AP view. b: anterolateral view. Vr: ventral ramus. Dr: Dorsal ramus. m: medial branch. i: intermediate branch. l: lateral branch a: ascending branch. d: descending branch. Posterior (**a**) and posterolateral (**b**) view of the lumbar spine. (From Perolat et al. [5]. Open access under Creative Commons Attribution 4.0 International License- no permission needed to use this image as long as appropriate credit to the source is provided)

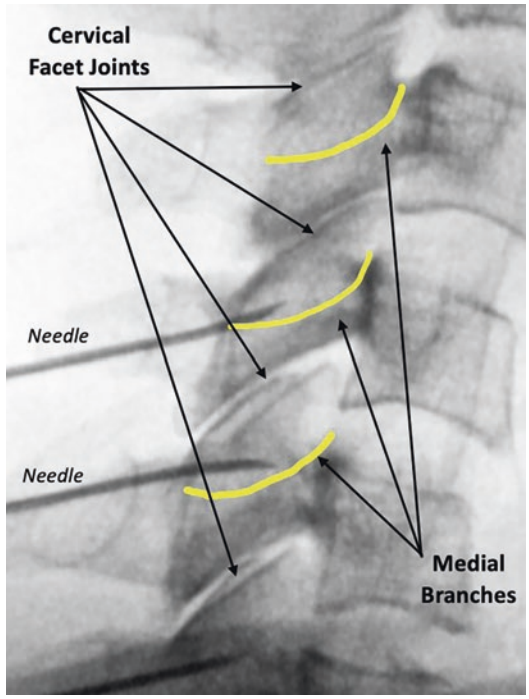

Fig. 44.3 Lateral radiograph of cervical spine to show the articular pillars, demonstrating location to cervical medial branch nerves (yellow lines)

- Sensory and motor stimulation is often performed prior to denervation.
- Local anesthetic and/or steroids are usually injected prior to denervation to enhance lesion size and to reduce the incidence of procedure-related pain and neuritis [5].

Complications

- Accidental intravascular injection of local anesthetic or steroid
- Thermal damage to the ventral nerve root
- Post-denervation neuritis [4]

Clinical Pearls

- Axial back and neck pain are primarily localized to the **midline** and may involve the facet joints, intervertebral discs, spinal nerve roots, paraspinal muscles and ligaments.
- Lumbar facet arthropathy may radiate down the **hip, buttock, and posterolateral thigh**

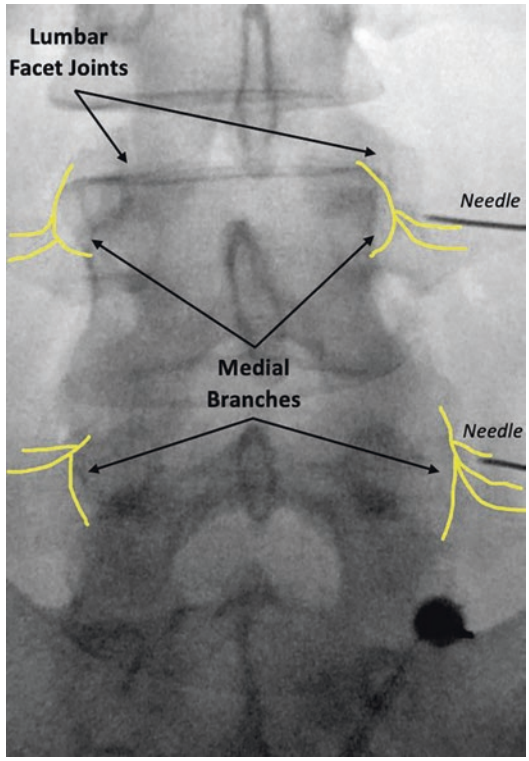

Fig. 44.4 Anterior-posterior radiograph of lumbar spine to show location to lumbar medial branch nerves

(Fig. 44.1a) whereas cervical facet arthropathy may radiate down **the shoulders or cause headaches** (Fig. 44.1b) [3].

- Medial branch blocks are the gold standard for diagnosing facetogenic back or neck pain [1].
- In the cervical spine, nerve roots exit the foramina above the corresponding vertebral bodies until the level of C7. For example, C7 nerve root exits above C7 through the C6-C7 neural foramen but C8 exits in between **T1 and C7 neural foramen** [1].
- In the thoracic and lumbar spine, nerve roots exit the foramina below the corresponding vertebral bodies. L4 nerve root exits **below the L4** vertebral body [3].
- Radiofrequency denervation of the medial branches of the posterior ramus is indicated for patients who experience >50% pain relief following medial branch blocks.

Practice Questions

1. A 71-year-old man presents with new onset back pain. He is being evaluated in clinic for a medial branch block. Which of the following would be an indication for medial branch block in this patient?
   A. Inability to void
   B. Pain with standing that is relieved with lying down
   C. Paresthesia of the S3–5 dermatomes
   D. Pain localized to the left paraspinal muscles
2. A 67-year-old woman presents with midline neck pain which radiates to her left shoulder. Extension of her neck while turning her head to the left exacerbates her pain. What is the gold standard for diagnosing her condition?
   A. Cervical MRI without contrast
   B. Cervical MRI with contrast
   C. Cervical X-ray
   D. Cervical medial branch block
3. Which nerve root emerges between the C7 and T1 vertebrae?
   A. C6
   B. C7
   C. C8
   D. T1
4. A 65-year-old man complains of pain in his lower back and buttocks which is worsened when he walks downhill and improves with sitting. He has a normal ankle-brachial index (ABI). What is his most likely diagnosis?
   A. Spinal stenosis
   B. Lumbar facet arthropathy
   C. Peripheral vascular insufficiency
   D. Sacroiliac (SI) joint pain
5. Sensory innervation to the facet joint is provided by which division of the spinal nerves:
   A. Lateral branch of the anterior ramus
   B. Medial branch of the anterior ramus
   C. Lateral branch of the posterior ramus
   D. Medial branch of the posterior ramus

Correct Answers

1. B, 2. D, 3. C, 4. A, 5. D

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Noncancer Pain: Radiculopathy and Epidural Steroid Injections

45

Asad Hashmi, Aparna Jindal, and Amy Pearson

Introduction

- Radiculopathy is a common source of chronic back and neck pain and may be accompanied by **signs of nerve root damage** including loss of sensory and/or motor function, which may present as numbness, paresthesia, weakness, atrophy or loss of reflexes [1].
- Radiculopathy refers to a disease process that affects the function of one or more **nerve roots**.
- The most common causes of radiculopathy due to nerve compression include **disc herniation** or **foraminal stenosis**, which is most often a result a narrowing of the spinal canal due to degenerative changes affecting the spine.
- Non-mechanical causes include chemically mediated non-cellular inflammatory reactions, including infection, neoplasm, and vascular injury.
- All lumbar and sacral nerve roots originate at the T10 to L1 vertebral level. A dorsal and a ventral nerve root join in the spinal canal to form the dorsal root ganglion. The roots exit at their respective neural (intervertebral) foramina. In thoracic and lumbar regions, they exit **below the vertebral body**. For example L4 nerve roots exit **below the L4 vertebra**. In the cervical spine, the nerve roots exit above the corresponding vertebral body. For example, the C4 nerve roots exit **below the C3 vertebra** and above the C4 vertebra. **The exception is C8**, which exits between C7 and T1.
- Nerve roots may be injured at their exit from neural foramina or central disc herniation. For example, the L5 root can be compressed by a *central* disc protrusion at the **L2–3** or **L3–4** level or a *paracentral* disc herniation at the **L4–5 level** or at the **L5–S1 foramen**.
- Classic radiating pain from spinal nerve root injury follows a specific lumbosacral dermatome (see Fig. 45.1; **high yield**)
- Radiculopathy can be present without an obvious compression in MRI e.g. chemical radiculitis due to the rupture of the **intervertebral** disc and release of chemical mediators. EMG can be useful for diagnosis in the cases.

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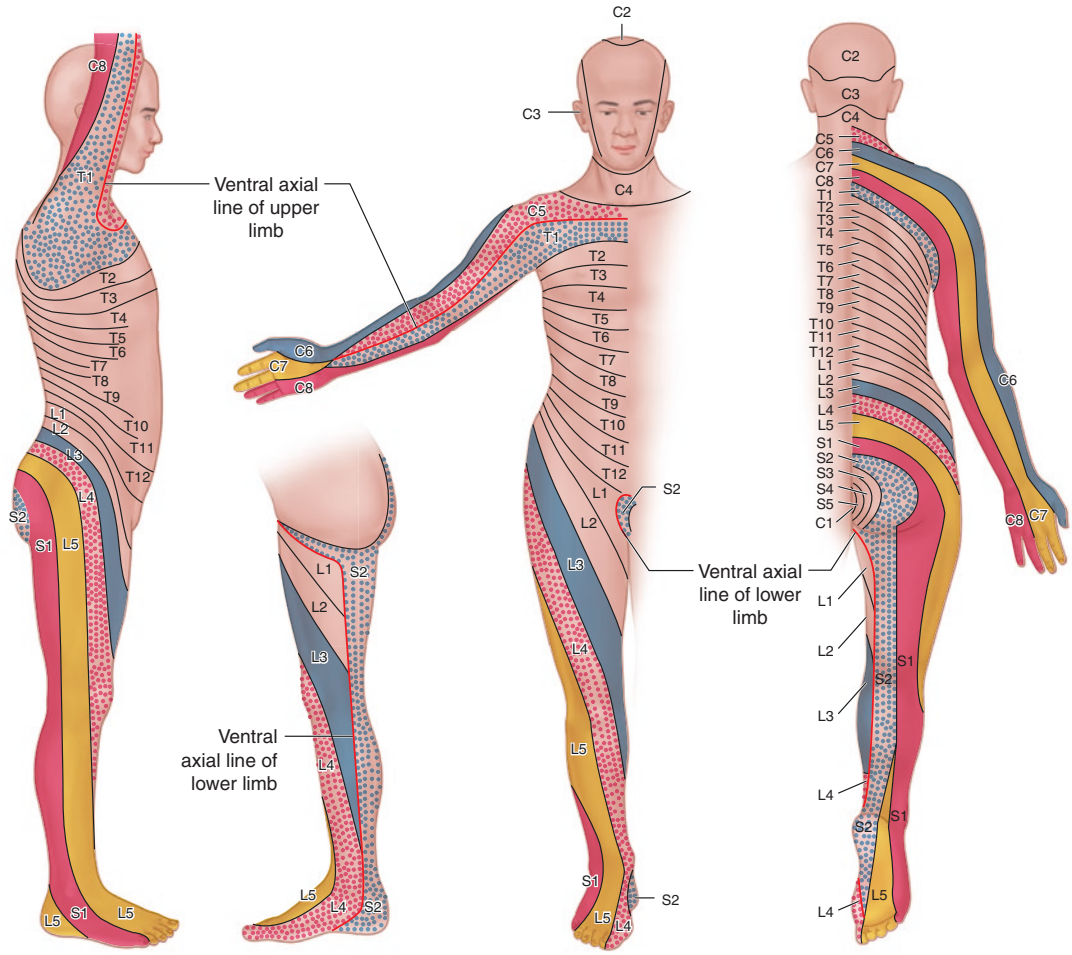

Fig. 45.1 The area of the skin supplied by a spinal sensory nerve root named as dermatome

Clinical Presentation of Radiculopathy Pain

Lumbar

L1 radiculopathy: Symptoms include pain, paresthesia, sensory loss in the inguinal region, and rarely mild weakness with hipflexion.

L2 radiculopathy: Symptoms include pain, paresthesia, and sensory loss in the anterior midthigh, and weakness with **hip flexion**.

L3 radiculopathy: Symptoms include pain, paresthesia, sensory loss in the distal anterior thigh, and weakness with **hip flexion and knee extension**. There may also be a diminished patellar reflex.

L4 radiculopathy: Symptoms include pain, paresthesia, sensory loss in the medial lower leg and foot, and weakness with knee extension and **ankle dorsiflexion**. There may also be a diminished patellar reflex.

L5 radiculopathy: The **most common** form of radiculopathy. Presents with back pain that radiates down the **lateral** aspect of the leg into the foot (Figs. 45.1 and 45.2), and weakness with dorsiflexion, toe extension, foot inversion, and foot eversion.

S1 radiculopathy: Symptoms include pain radiates down the **posterior** aspect of the leg into the foot from the back. **Weakness of plantar flexion**, leg extension, knee flexion and loss of ankle reflex may be present.

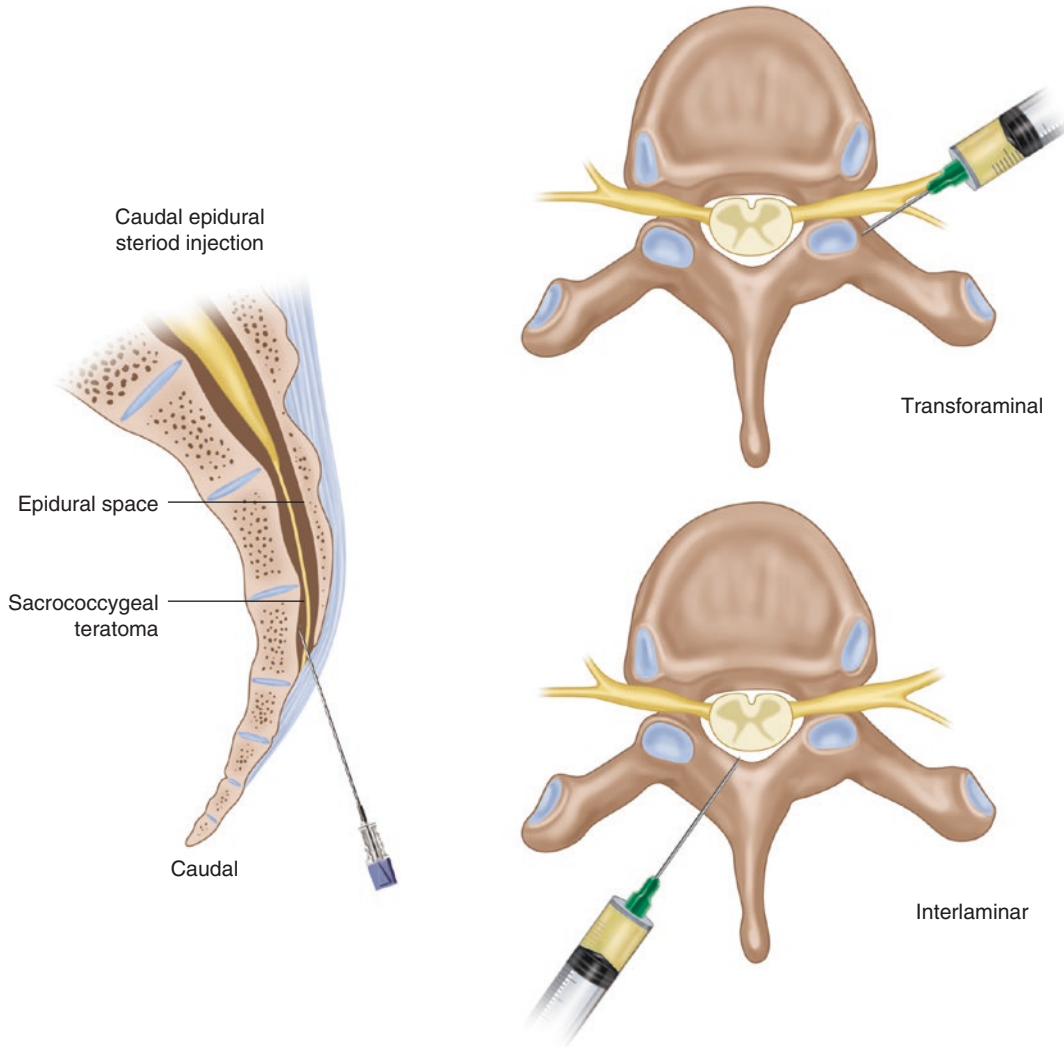

Fig. 45.2 Epidural injections are performed utilizing three approaches in the lumbar spine: caudal, interlaminar, and transforaminal and two approaches (transforaminal and interlaminar) in the thoracic and cervical spine

Cervical

C5 radiculopathy: pain in the neck and **shoulder** which may radiate to lateral arm along the axillary nerve.

C6 radiculopathy: pain in the neck and shoulder, which my radiate to lateral arm, lateral forearm, lateral hand (**thumb** and index finger).

C7 radiculopathy: pain in the neck, shoulder, and **middle finger.**

C8 radiculopathy: pain in the neck, shoulder, medial forearm, **fourth and fifth digits**, medial hand.

Diagnosis

- Acute onset of symptoms with bending, lifting, or trauma.
- Symptoms consistent with radiculopathy including pain, paresthesia, sensory loss, weakness.
- Positive straight leg raise, reverse straight leg raise, contra lateral straight leg test, Patrick test.
- For cervical radiculopathy, positive **Spurling test** (extension and rotation of neck to the side of the pain, followed by applying downward pressure on the head→ paresthesia

- **Lhermitte phenomenon**: a shock-like symptoms with neck flexion if there is compression of the cervical cord by a disc herniation
- MRI imaging if patient presents with radiculopathy, myelopathy symptoms or other alarm symptoms such as urinary retention or bowel/bladder incontinence. If MRI is contraindicated then consider performing a CT myelogram.
- Electromyography (EMG) with nerve conduction study (NCS) may help differentiate radiculopathy from other causes if MRI is negative. Note that it takes **2–3 months** after the injury to see EMG changes.

Treatment

- The mainstay of treatment for chronic back and neck pain are primarily symptom management and include the use of non-opioid analgesics, activity modification, and formal physical therapy. If conservative therapy fails, further treatment is indicated and includes a range of therapies from short-term opioid therapy, surgery, and systemic or epidural steroid injections. Of note, epidural steroid injections are **not effective** for chronic back and neck pain **without a radicular component** [2]. Indications are listed in Table 45.1.
- Acute radiculopathy with **myelopathy** due to sudden disc herniation will require **immediate** intervention.
- Epidural steroid injections may be performed using three different approaches: the translaminar approach, transforaminal approach, and caudal approach. These typically are beneficial in the short-term (less than 3 months) [2].

Indications [2]

Table 45.1 Indications for Epidural Steroid Injections

Intervertebral disc herniation
Spinal stenosis
Synovial cysts
Radicular pain

Contraindications [1]

- Relative contraindications to epidural steroid injections include uncontrolled diabetes, congestive heart failure, and states in which fluoroscopy is not advised such as pregnancy.
- Absolute contraindications include a local infection **at the site of injection** or systemic infection, a fully anticoagulated state, a significant allergy to contrast or corticosteroid without prophylaxis, acute spinal cord compression, inability to obtain informed consent, or patient refusal.
- The clinician should carefully weigh the risks and benefits of **holding anticoagulation** for an elective procedure such as an epidural steroid injection.

Technique

- The interlaminar approach is performed by placing the patient in the prone position. Under fluoroscopic guidance, the interlaminar space of interest is identified and marked in the anterior-posterior view. After sterile preparation, a skin wheal is raised using local anesthetic. An epidural needle, typically Tuohy or Hustead, is directed between the lamina of the upper and lower vertebra and advanced via coaxial fluoroscopic technique. The epidural space is identified by loss of resistance to air and/or saline. Contrast dye approved for epidural use is injected to confirm the placement of the needle by fluoroscopy. The corticosteroid preparation is then injected into the epidural space. The needle is removed and gentle pressure is applied to the insertion site.
  - A pillow under the abdomen can help to flatten the lumbar lordosis and increase the opening of the interlaminar space
  - Often for cervical sources of radicular pain, an interlaminar approach may be used in the upper thoracic region such as between T1 and T2. A catheter is then threaded up to the level of interest and contrast spread is confirmed with fluoroscopy after the desired level is reached.

- The transforaminal approach is performed by placing the patient prone. An ipsilateral oblique view is obtained with the superior articular process (SAP) at the desired level. The target is approximately at the 6 o'clock position of the pedicle at the same level in the anterior-posterior view (the lateral surface of the SAP is marked along a line that bisects the sagittal plane of the pedicle). The skin is prepared and a skin wheal is raised with local anesthetic. Under fluoroscopic guidance, the needle is advanced coaxially in the oblique view until it reaches this 6 o'clock position. Needle placement is confirmed by injecting non-ionic contrast, typically under digital subtraction angiography, followed by injection of the corticosteroid preparation.
- The caudal approach is performed by placing the patient in the prone position. A lateral fluoroscopic image is obtained and the sacral hiatus is identified as an opening at the end of the S4 lamina. A needle is advanced under fluoroscopic guidance towards the sacral hiatus. A subjective "give" may be experienced when the needle pierces the sacrococcygeal ligament. Contrast medium may be injected to verify placement of the needle within the epidural space and to confirm there is no intravascular uptake.

Complications [3]

- Procedural complications include direct tissue injury due to disruption of the tissue by the needle tip including vascular injury, dural injury, and direct neural injury.
  - Bleeding associated with these procedures is typically minor, but care must be taken to avoid the development of an **epidural hematoma**, a potentially catastrophic complication.
  - Anterior spinal artery syndrome may occur while performing TFESIs. This is believed to occur due to injury to segmental medullary arteries that supply the anterior spinal artery.
  - Post dural puncture headache may occur if inadvertent dural disruption occurs and has an incidence far less than 1%.
  - The patient may also complain of transient back pain after the procedure.
  - Infections such as **epidural abscess** and meningitis are very rare.
- Drug-related complications may also cause injury. For example, stroke and spinal cord injury can occur due to **embolized particulate steroid** and is more common with cervical TFESI given the proximity of the ascending cervical and vertebral arteries [4]. Repeated ESI have a number of long-term complications associated with their repeated use including osteoporosis and osteopenia, avascular necrosis, steroid induced myopathy, and cushingoid signs and symptoms.

Clinical Pearls

- In thoracic and lumbar regions, nerve roots exit **below the vertebral body**. For example L4 nerve roots exit **below the L4 vertebra**. In the cervical spine, the nerve roots exit above the corresponding vertebral body. For example, the C4 nerve roots exit **below the C3 vertebra** and above the C4 vertebra. **The exception is C8**, which exits between C7 and T1.
- L5 root can be compressed by a ***central*** **disc protrusion at the L2–3** or **L3–4** level or a ***paracentral*** **disc herniation at the L4–5 level**.
- Epidural steroid injections are commonly performed for radiculopathy pain after conservative measures have been attempted.
- Epidural injections are typically **not beneficial** for idiopathic chronic back or neck pain **without** radiculopathy.
- Non-particulate steroids are favored over particulate steroids.

Multiple Choice Questions

1. Epidural steroid injections are typically NOT indicated in which of the following:

A. Lumbar spinal stenosis
B. Discogenic pain
C. Chronic low back pain
D. Lumbar radicular pain

2. Particulate steroid formulations in epidural steroid injections have been associated with
   A. Stroke and spinal cord injury due to arterial embolization
   B. Increased long-term effectiveness compared to non-particulate steroids
   C. Increased pain due to chemical irritation
   D. Nerve damage due to osmotic effects
3. The typical initial fluoroscopic approach for a transforaminal epidural steroid injection is
   A. Anterior-posterior view
   B. Lateral view
   C. Contralateral oblique view
   D. Ipsilateral oblique view
4. A standard interlaminar epidural technique includes
   A. Non-ionic contrast dye
   B. IV sedation
   C. A particulate steroid preparation
   D. Lateral fluoroscopic approach
5. An absolute contraindication to epidural steroid injection includes
   A. Pregnancy
   B. Local infection at the site of injection
   C. Diabetes
   D. Immunocompromised status
6. A patient complaints of pain and paresthesia in the lateral leg and foot, and weakness with dorsi flexion. The most likely diagnosis is
   A. A, L3 radiculopathy
   B. L4 radiculopathy
   C. L5 radiculopathy
   D. S1 radiculopathy
7. A 43-year-old patient mentions that his right thumb tingles and then becomes numb if he extends his head. This symptom most likely represents
   A. C7 radiculitis
   B. C6 nerve root irritation
   C. Carpal tunnel syndrome
   D. C8 radiculopathy

Answers

1. C, 2. A, 3. D, 4. A, 5. B, 6, C, 7. B

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Suggested Further Reading

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Noncancer Pain: Discogenic Low Back Pain

46

Marc Korn and Dost Khan

Introduction

- **Lower back pain** is a ubiquitous medical issue with a lifetime incidence of 80–90%
- A patient's constellation of symptoms, physical exam findings and radiologic findings allow providers to identify likely etiologies of the pain.
- Low back pain can be due to a myriad of underlying issues (vertebral compression fracture, lumbar facet arthropathy, disc herniation, spinal stenosis, foraminal stenosis, myofascial pain, and sacroiliitis)
- The **intervertebral disc** is the most common cause of low back pain, accounting for approximately 40% of patient complaints [1].
- **Discogenic low back pain (DLBP)** is a condition in which pain emanates from the intervertebral disc without adjacent nerve compression.

Anatomy

- The intervertebral disc is the primary joint between consecutive vertebrae.

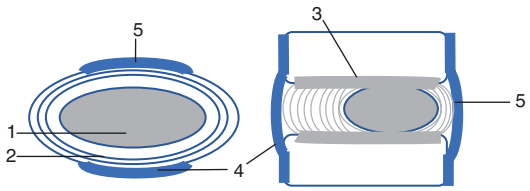

Fig. 46.1 The intervertebral disc: (1) nucleus pulposus, (2) annulus fibrosus, (3) cartilaginous endplate, (4) anterior longitudinal ligament, (5) posterior longitudinal ligament

- This joint consists of the **nucleus pulposus, annulus fibrosus** and the **cartilaginous endplates** (Fig. 46.1).
- The innermost layer, the **nucleus pulposus**, is semifluid, consisting of water, collagen, elastin and aggrecan.
  - Aggrecan helps the disc to retain water.
  - The fluid nature of the nucleus allows it to deform in the setting of pressure and transmit the force in all directions.
- The nucleus is surrounded by concentric rings of collagen fibers known as the **annulus fibrosus**.
- Degeneration within the intervertebral disc, often combined with localized mechanical stress, can result in tears within the annulus.
- Tears (Fig. 46.2) are classified as:
  - Concentric- if parallel to the layers of collagen
  - Radial- if perpendicular to the layers of collagen

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- A tear which extends from the nucleus through the outer edge of the annulus is known as a **full thickness tear**. This type of tear can result in herniation of the semifluid nucleus pulposus to the outer portion of the disc.
- The **innervation of the intervertebral disc** is complex and varied based on location (Fig. 46.3) [2].
  - The posterior aspect of the disc is innervated by the **sinuvertebral nerve**.
  - The posterolateral aspect is innervated by the **rami communicans or the ventral ramus**.
  - The lateral disc is innervated by branches of the **grey ramus communicans.**
  - The anterior disc is innervated by the **sympathetic plexus** surrounding the anterior longitudinal ligament.
- Nerve fibers of the disc are mainly nociceptive.
- The nerves have a close association with postganglionic efferent and sympathetic afferent fibers, similar to the pattern seen in certain visceral organs.

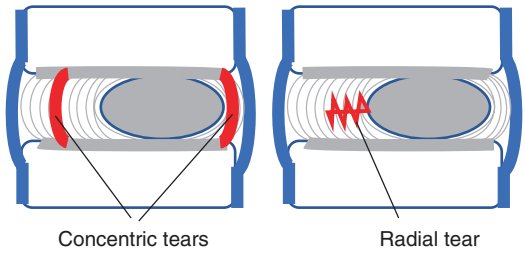
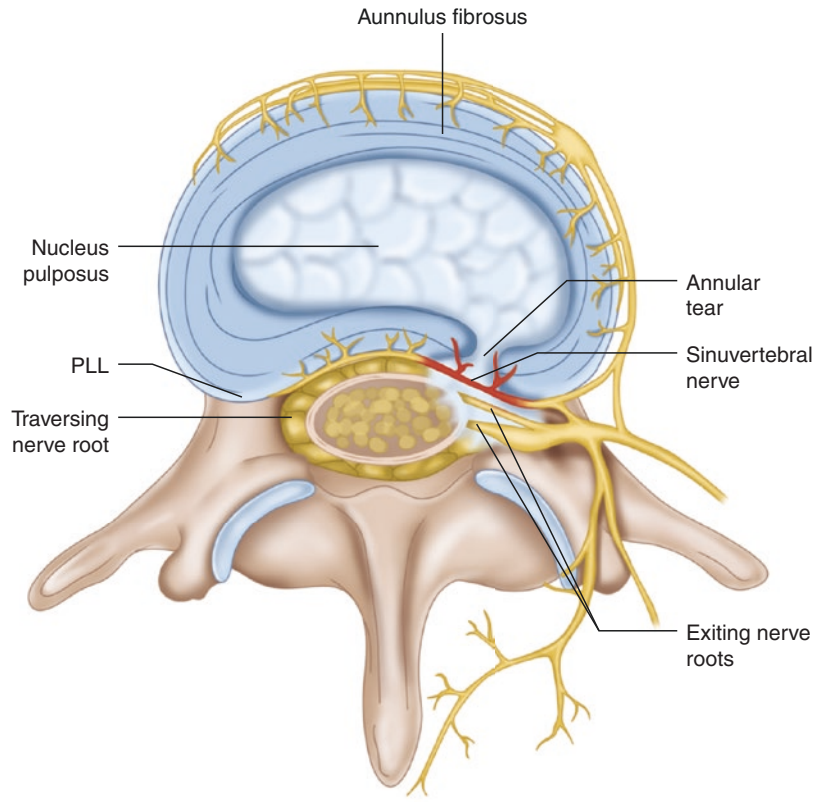


Fig. 46.2 Subtypes of annular tears

Pathophysiology

- Throughout the intervertebral disc, degradative enzymes (matrix metalloproteases and ADAMS) and growth stimulating factors (BMP-2, BMP-7, GDF-5, TGF-ß, IGF-1) result in an orchestrated process of matrix breakdown and formation [3].
- An imbalance of catabolic and anabolic processes can result in excessive degeneration within the disc.

Fig. 46.3 Innervation of the intervertebral disc



- A net **loss of proteoglycan and water from the nucleus** decreases the discs overall ability to transfer axial stress.
  - Tears in the annulus can develop as a result.
  - Patients can develop a nociceptive response when additional stress is applied to the damaged disc tissue.
- In cases of herniated nucleus pulposus, nerve root compression can result in concurrent **radiculopathy** in addition to discogenic pain.
- **Risk factors for DLBP** include increased age, genetic predisposition, nutritional factors and repetitive mechanical loading.

Clinical Characteristics

- Patients with DLBP typically present with **axial pain with prolonged standing or sitting**, occasionally radiating into the buttock and leg.
- Pain can be uni- or bilateral, and **does not follow** specific dermatomal pattern.
- These patients can also experience a sitting intolerance.
- On exam, there may be **paraspinal and midline tenderness**.
- As the pain is originating from the disc itself, symptoms are exacerbated by activities that **increase intradiscal pressure** (prolonged sitting or standing, coughing, sneezing, Valsalva maneuver).
- With regards to physical examination, the presence of **centralization phenomenon** or a positive **bony vibration test** can help to identify DLBP.
  - Centralization phenomenon- pain along the central line of the spine, brought on by **lateral movement**, which results in displacement of the nucleus.
  - Bony vibration test reproduces discogenic pain by **attaching electric vibrators** to the spinous processes.

Imaging

- **MRI** is the imaging **modality of choice** for evaluating a patient with suspected DLBP.
- **Characteristic MRI findings**:
  - Low intra-discal signal intensity on T2 weighted images (affected discs look darker compared to other discs)
  - **High-intensity zone (HIZ)** in the posterior aspect of the disc (bright white signal)
  - End plate **Modic changes**.
  - Healed annular tears will often enhance in the presence of **gadolinium** (contrast can also highlight continued swelling/granulation tissue within a disc after surgery)
- **Modic changes** refer to characteristic signal changes seen in the vertebral endplates and adjacent bone marrow [4].
  - **Type I changes**, also described as the **"inflammatory phase"** are characterized by **low signal intensity on T1 and high signal intensity on T2**.
  - **Type II changes** (commonly associated with discogenic pain) are due to fatty replacement of bone marrow and are characterized by **increased signal intensity on T1 and normal to high intensity on T2**.
  - **Type III changes** are due to subchondral sclerosis.

    Below the hardened endplate, **low signal intensity is seen on T1 and T2 images**.

Discography

- **Provocative discography** is an image-guided technique used to identify painful discs.
  - This procedure has been utilized to assist surgeons with identifying appropriate levels to fuse.
  - After accessing the disc with a needle, contrast is administered (with continuous pressure monitoring) into the disc of interest, as well as at least 1 adjacent 'healthy' disc for comparison.
  - The volume of contrast as well as the intradiscal pressures are recorded. Post-injection CT scan is performed to evaluate disc disruption.
  - **Positive discography** is noted when (1) Patient's pain is reproduced by stimulating the affected disc (2) Evoked pain has

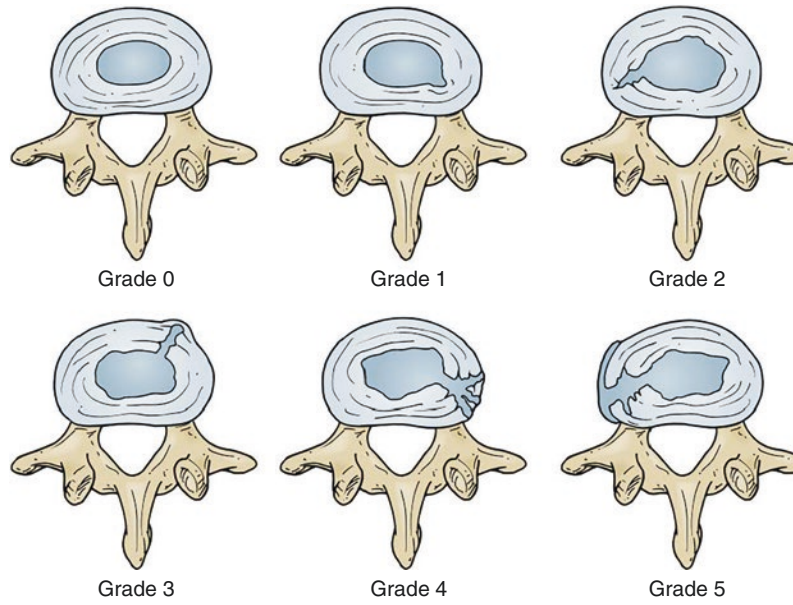


Fig. 46.4 Classification of annular tears based on CT-discography

an intensity of at least 7 on a 10-point scale (3) Pain is reproduced at a low pressure of stimulation: ≤50 psi above opening pressure (4) adjacent discs do not reproduce pain, and postdiscography CT demonstrates a grade III or IV fissure (Fig. 46.4) [5]

– Discography **is now out of favor** due to many false positives.

Treatment

- Management of DLBP often begins with **conservative treatment strategies** including physical therapy, exercise, and soft tissue mobilization.
- **Pharmacotherapy** with **nonsteroidal anti-inflammatory drugs, muscle relaxants and analgesics** are also considered.
- **Epidural steroid injections** are frequently utilized in the setting of failed conservative therapy, though the overall **effectiveness of this therapy for DLBP has been debated.**
  - Steroids have been shown to reduce production and release of pro-inflammatory cytokines, interrupting nociceptive signal transduction.
- Surgery

Clinical Pearls

- Discogenic lower back pain (DLBP) is the most common type of chronic lower back pain. While the external outline of the disc may remain intact, multiple processes (degeneration, end plate injury, inflammation, etc.) can internally stimulate **pain receptors inside the disc** without nerve root symptoms
- The most commonly used method for diagnosing DLBP is non-invasive MRI technology. An MRI of DLBP shows **low signal intensity of the disc** on T2W, a high-intensity zone (HIZ) at the rear of the disc, and end plate Modic changes.
- In the past decade, the most common surgical treatment for discogenic lower back pain has been disc excision with interbody fusions. Conservative therapies include physical therapy, anti-inflammatory drugs and epidural steroid injection.

4 MCQ Questions

1. Innervation to the lumbar intervertebral disc are provided by all of the following EXCEPT:
   A. Sympathetic afferent nerves
   B. Ventral rami

C. Sinuvertebral nerves
D. *Lumbar spinal nerves*

2. Which of the following is the characteristic MRI appearance for type 2 Modic changes?
   A. Decreased T1 signal, decreased T2 signal
   B. Decreased T1 signal, increased T2 signal
   C. Increased T1 signal, decreased T2 signal
   D. *Increased T1 signal, increased T2 signal*
3. All of the following are typical physical exam findings in a patient with discogenic low back pain EXCEPT:
   A. Pain with Valsalva
   B. Midline tenderness
   C. *Diminished patellar reflex*
   D. Pain relief when lying supine
4. Which of the following is true for discography?
   A. Involves the injection of normal saline into the potential culprit disc
   B. Is generally well tolerated by patients with low pain thresholds
   C. Utilizes post-procedure MRI for evaluation of the annulus
   D. Is diagnostic for DLBP when pain occurs at a pressure ≥50 psi above opening pressure

Answers to Review Questions

1. D, 2. D, 3. C, 4. D

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Craniofacial Pain: Headache and Botulinum Neurotoxins

47

Jay Karri and Eellan Sivanesan

Introduction

- **Chronic headache disorders are a leading cause of disability** and affected persons can have a greater burden on quality of life, including occupational, societal, and familial burden [1, 2].
- Focal interventions for headache management have gained much popularity in recent years and **injection of botulinum neurotoxin** has some promising supportive evidence for use in certain chronic headache disorders [1–3].

Mechanism of Action

- Botulinum neurotoxin acts at the neuronal presynaptic terminal to **inhibit acetylcholine release** by cleaving Soluble N-ethlymaleimide Attachment-Protein 25 (SNAP-25), which helps coordinate vesicle fusion and exocytosis [3–5].
- Decreased acetylcholine in the synaptic cleft leads to muscle relaxation and subsequent vasogenic and neurogenic decompression. However, this cannot fully explain botulinum neurotoxin mechanisms since many patients experience relief without any known compressive pathology [3–5].
- Recent studies have also suggested that **botulinum neurotoxin may inhibit release of noxious neurotransmitters including substance P and calcitonin gene-related peptide** and thereby dampen dysregulated inflammation [4].
- Others suggest that retrograde transport of botulinum neurotoxin from cutaneous sensory afferent neurons (following injection into key dermatomal landmarks) to the trigeminal ganglia occurs to further attenuate noxious **neurotransmitter release** [4].

Headache Indications

- While **only onabotulinum toxin (Botox®) is FDA approved for migraines**, the off label use of other botulinum neurotoxin formulations for varying chronic headache disorders has been reported [1–3].
- Per the International Headache Society, a definition of chronic migraines is met by the presence of headaches on **15 or more days per month** with migraines occurring on **8 or** more of these days across a span of **3 or more months (5)**.
- Appropriately identifying chronic migraines also requires practitioners to exclude other

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Table 47.1 Key features associated with chronic headache presentations

Headache type	Epidemiology	Location, description	Timing	Associated symptoms
Tension	Slightly more prevalent in women than men, all ages	**Across forehead**, can radiate to occiput	Starts gradually and lasts for minutes to hours, can vary extensively	Rare photophobia and phonophobia
Migraine	Typically women, usually in reproductive age	**Unilateral,** throbbing headache	4–72 hours, often with sudden onset	Photophobia, phonophobia, nausea, possible visual auras or focal neurological deficits
Cluster	Men in adolescence and early adulthood	Unilateral and retro-orbital, reported as a stabbing sensation	Up to 3 hours, but often occurs in clusters across a period of weeks to months	Ipsilateral eye symptoms including **lacrimation**, rhinorrhea, conjunctival redness, miosis, and/or ptosis

Table 47.2 Botulinum neurotoxin formulations and their associated FDA approved indications

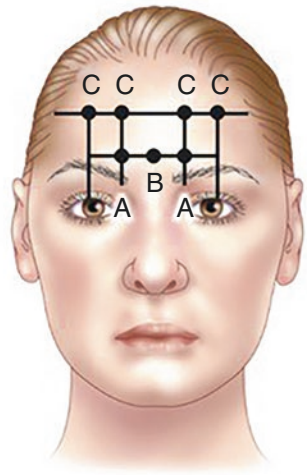
Botulinum neurotoxin formulation	FDA approved indications
BoNT Type A	
Abobotulinum (Dysport)	Cervical dystonia, glabellar lines
Incobotulinum (Xeomin)	Cervical dystonia, blepharospasm
Onabotulinum (Botox)	Blepharospasm, glabellar lines, cervical dystonia, upper limb spasticity, axillary hyperhidrosis, urinary incontinence, **chronic migraines**
BoNT Type B	
Rimabotulinum (Myobloc)	Cervical dystonia

common **chronic headache conditions** (Table 47.1) [6].

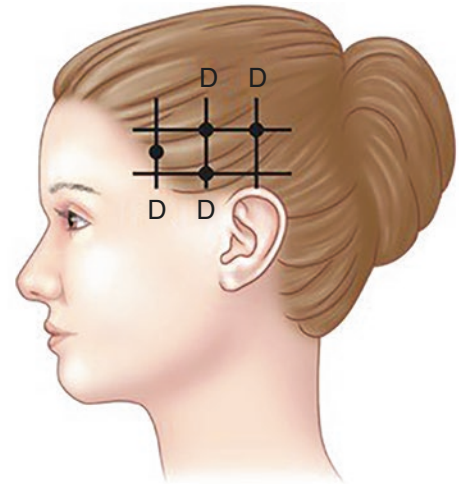
- The use of botulinum neurotoxin Type A, relative to placebo, is associated with a modest reduction of chronic migraine frequency and severity [1].
- Botulinum neurotoxin Type A has not been shown to be effective in reducing frequency or severity of episodic migraines or tension type headaches [1].
- There exists no high quality evidence supportive of botulinum neurotoxin use for cluster headache prophylaxis [1, 2].

Clinical Considerations

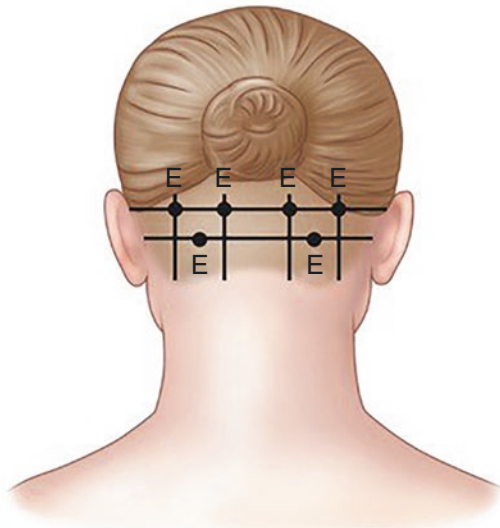
- While there exist various formulations of botulinum neurotoxin; Type A and Type B toxins, which correspond to the *Clostridium Botulinum* serotype isolates, are the most clinically utilized (Table 47.2) [3].
- Each botulinum neurotoxin formulation varies extensively in regards to **reconstitution and dilution** [3]. Additionally, the **unit dosing varies for the differing formulations**, largely owing to differences in molecular size i.e. efficacy of 100 units of abobotulinum is not equivalent to 100 units of onabotulinum.
- The current protocol for injection landmarks is provided by manufacturer recommendations and is intended for migraines (Fig. 47.1) [5]. The suggested dosing involves placement of botulinum neurotoxin intramuscularly within **seven key head and neck muscles** as follows:
  - forehead: corrugator, procerus (one site only), and frontalis
  - lateral pericranium: temporalis
  - posterior pericranium: occipitalis
  - posterior neck: cervical paraspinals and trapezius
- The clinical benefit with botulinum neurotoxin injections is thought to **start in 3 days** and, on average, is **sustained for 12 weeks** [3, 5].



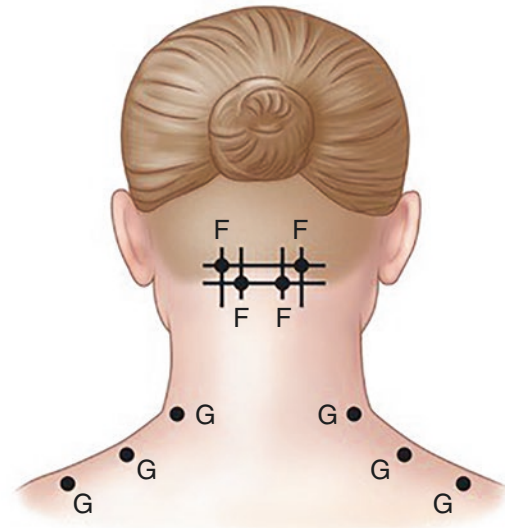
A. Corrugator: 5 U each side
B. procerus: 5 U (one site)
C,. Frontalis: 10 U each side



D. Temporalis: 20 U each side



E. Occipitalis: 15 U each side



F. Cervical paraspinal:
10 U each side
G. Trapezius: 15 U each side

Fig. 47.1 Schematic depicting the target injection sites across the seven key head and neck muscles in the forehead, lateral pericranium, posterior pericranium, and posterior neck

- **Resistance** to repeat botulinum neurotoxin injections in the context of the same dosing and targets may be secondary to **antibody formation** [3, 5]. While antibody formation as a whole and botulinum neurotoxin resistance may be mitigated by use of **smaller doses and decreased injection frequencies**, benefit of these practices and formulation specific risks have not be clearly explored.

Adverse Effects

- **Minimal to absent systemic absorption of** botulinum neurotoxin **is thought to occur** with intramuscular administration of therapeutic dosages, particularly for migraine applications [5].
- In 2009, the FDA released a **black box warning** delineating **rare but potential lethal complications of** botulinum neurotoxin **spread far beyond the injection site** [3, 5]. This warning followed reports of lethal cases of dysphagia and respiratory compromise possibly secondary to botulinum neurotoxin mediated chemo-denervation of swallowing and respiratory musculature, respectively.
- Other adverse effects include local pain, inflammation, and muscle weakness [5].

Contraindications and Considerations

- Absolute contraindications to botulinum neurotoxin administration include allergy or hypersensitivity or active infection overlying the injection targets [2, 5].
- **Relative contraindications that warrant careful consideration include neuromuscular disorders** given the risk of further acetylcholine depletion and subsequent exacerbated weakness in this population [5]. The most common neuromuscular disorders include:
  - Lambert-Eaton syndrome
  - botulism
  - myasthenia gravis
- Similarly, exacerbated weakness may also be manifested in patients in scenarios of **concomitant aminoglycoside use**, which itself may potentiate neuromuscular blockade [5].
- The supportive evidence for botulinum neurotoxin use in pregnant and breastfeeding mothers is **limited and inadequate** [5]. Botulinum neurotoxin is listed as a **pregnancy category C** medication for fetal risk.

Clinical Pearls

- The highest level supportive evidence for botulinum neurotoxin use in headache management is for the **reduction of frequency and severity of chronic migraines**.
- Chronic migraines are defined by the presence of **headaches on ≥15 days per month with migraines occurring on ≥8 of these days across ≥3 months**.
- **Onabotulinum toxin** is the only botulinum neurotoxin that is approved by the FDA for use in migraines.
- Relative contraindications exist for using botulinum neurotoxin injections in **persons with neuromuscular disorders** or those using aminoglycosides for fear that they may develop profound weakness.

Questions

1. **What is the mechanism of action of botulinum neurotoxin?**
   A. acts at the pre-synaptic terminal to inhibit acetylcholine release
   B. inhibits post-synaptic opening of potassium channels
   C. increases glutamate in the neuromuscular junction
   D. increases endogenous opioid release
2. **What is a potentially lethal complication associated with use of botulinum neurotoxin?**
   A. localized erythema at the injection site
   B. respiratory distress in a patient who received botulinum injections in his neck muscles
   C. post-procedural weakness in facial muscles
   D. intermittent abdominal cramping
3. **The strongest evidence for botulinum neurotoxin exists for which headache type?**
   A. Tension headache
   B. Cluster headache
   C. Migraine headache
   D. Medication overuse headache

4. **Per the International Headache Society, chronic migraine disorder is defined by the presence of headaches for __ days per months, with migraines occurring of __ or more of these days across a span of __ or more months?**
   A. 15, 8, 3
   B. 20, 10, 6
   C. 7, 4, 4
   D. 20, 10, 3
5. **What are the benefits of botulinum neurotoxin in persons with migraine disorders?**
   A. decreased chronic migraine frequency
   B. decreased chronic migraine severity
   C. no benefit in reducing episodic migraine frequency
   D. all of the above

Answers

1. A, 2. B, 3. C, 4. A, 5. D

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48 Craniofacial Pain: Supraorbital, Infraorbital, Auriculotemporal Nerve Block

Douglas W. Rybar and Dalia H. Elmofty

Introduction

- The supraorbital, infraorbital, and auriculotemporal nerve are superficial/peripheral branches of the trigeminal nerve [1]
- Local anesthetic injection near terminal superficial branches of the trigeminal nerve can provide significant analgesia for both acute and chronic craniofacial pain
- Landmark and ultrasound-guided techniques have been described when performing these blocks
- Divisions of the trigeminal nerve include the ophthalmic nerve (V1), the maxillary nerve (V2), and the mandibular nerve (V3)
- Supraorbital nerve originates from the frontal nerve which is a branch from V1 (Fig. 48.1). It is accompanied by the supraorbital artery. The supraorbital nerve exits the orbit lateral to the supratrochlear nerve
- Supraorbital nerve provides sensory innervation to the lateral forehead, upper eyelid and anterior part of the scalp
- Infraorbital nerve originates from V2 (Fig. 48.1). It is accompanied by the infraorbital artery. The infraorbital nerve leaves its foramen in a medial and caudal trajectory.
- Infraorbital nerve provides sensory innervation to the lower eye lid, lateral part of the nose, and upper lip
- Auriculotemporal nerve originates from V3 (Fig. 48.1) and is accompanied by the temporal artery
- Auriculotemporal nerve provides sensory innervation to the lateral scalp

Indications

Regional Anesthesia for Surgical Procedures

- Awake craniotomies and post-operative pain management
- Sinus and ear procedures to minimize anesthetic delivered and post-operative pain management

Supraorbital Nerve Block

- Supraorbital Neuralgia: a rarely diagnosed disease that has only recently been included in the International Headache Society classification. The majority of cases are post-traumatic in nature or related to entrapment neuropathy. Patients present with chronic frontal head-

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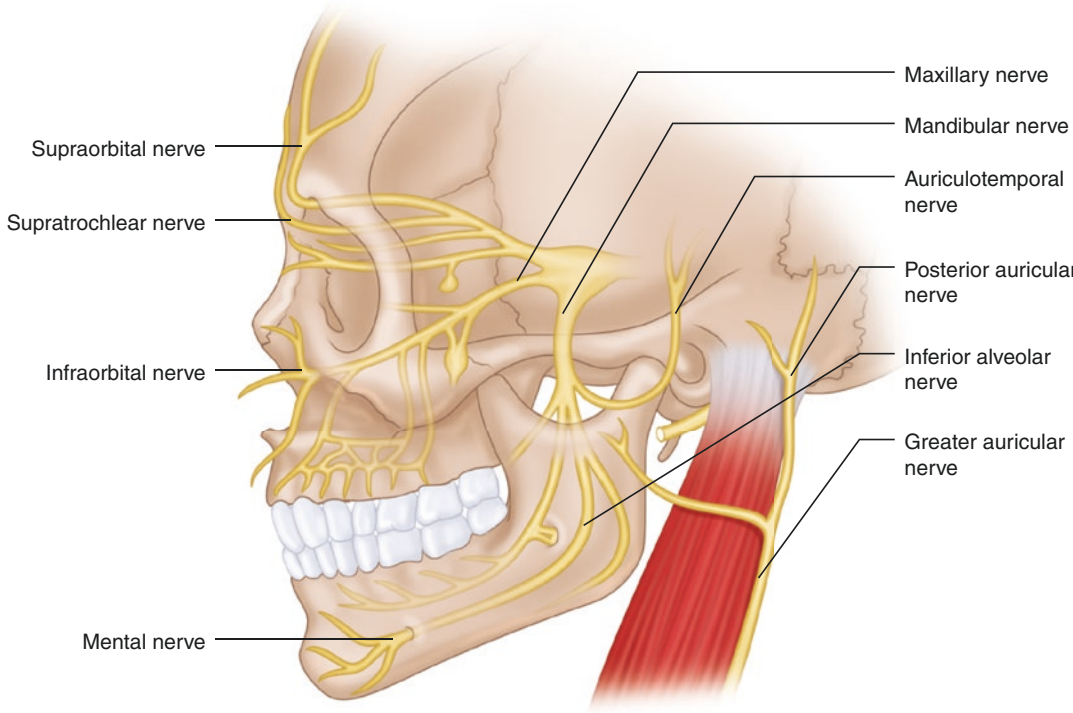

Fig. 48.1 Anatomical distribution of the supraorbital, infraorbital, and auriculotemporal nerves

aches and supraorbital notch tenderness. If a patient gets good pain relief with diagnostic supraorbital nerve block, peripheral nerve stimulation may be offered.
- Pain secondary to malignancy
- Herpes Zoster in V1 distribution
- Migraine headaches or Frontal headaches [2]

Infraorbital Nerve Block

- Infraorbital Neuralgia
- Pain secondary to malignancy
- Herpes Zoster in V2 distribution

Auriculotemporal Nerve Block

- Temporomandibular joint pain
- Atypical facial pain
- Pain secondary to malignancy
- Herpes Zoster

Contraindications

- Distortion of anatomical landmarks
- Overlying infection
- Local anesthetic allergies
- Inability of patient to tolerate performance regional anesthesia

Technique

Supraorbital Nerve Block

- *Landmark Technique (*Fig. 48.2*)*
  - Identify supraorbital notch:
    Palpation of the of superficial orbital ridge
    Moving from midline to lateral, approximately 2 cm from medial border, a step-off is felt to identify supraorbital notch
  - 25-gauge 1.5-inch needle (30-gauge for children) is introduced above the supraor-

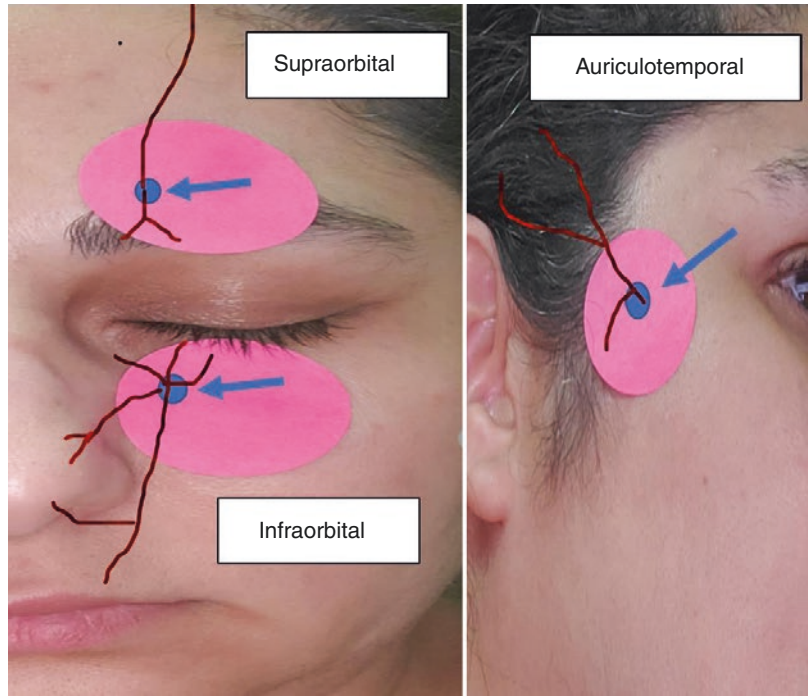

Fig. 48.2 Landmark technique for supraorbital, infraorbital, and auriculotemporal nerve block. Blue arrow points to site of needle insertion

bital notch and advanced in a slightly medial path until periosteum is contacted. 2–4 mL of anesthetic solution of choice is administered.

- *Ultrasound technique*
  - High frequency linear transducer placed transversely with a slight oblique tilt above orbital ridge
  - Sonoanatomy (Fig. 48.3)
    Orbital ridge appears as a hyperechoic linear structure
    Supraorbital notch is identified as a defect in the orbital ridge
    Color doppler should be used to visualize supraorbital artery and avoid intravascular injections
  - 25-gauge 1.5-inch needle (30-gauge for children) is introduced above the ultrasound probe in an out-of-plane approach towards the supraorbital foramen but not into the foramen in a medial and cephalad direction
  - Real-time view of needle tip during injection can help avoid intravascular or intraforaminal injection of local anesthetic
  - 1–2 mL of anesthetic solution of choice is administered

Infraorbital Nerve Block

- *Landmark Technique* (Fig. 48.2)
  - Infraorbital foramen is palpated inferior to the orbit
  - 25-gauge 1.5-inch needle introduced inferior and lateral to identified foramen
  - Needle advanced until contacting periosteum, avoid entering foramen
  - 1–2 mL of anesthetic of choice is administered
- *Ultrasound Technique*
  - High frequency linear transducer placed transversely with a slight oblique tilt below orbital on the zygomatic bone
  - Sonoanatomy (Fig. 48.4)
    Zygomatic bone appears as a hyperechoic structure. The infraorbital foramen appears as a defect in the bone
    Color doppler should be used to visualize infraorbital artery and avoid intravascular injections
  - 25-gauge 1.5-inch needle (30-gauge for children) is introduced inferior to the probe towards the infraorbital foramen until periosteum is contacted. 1–2 mL of anesthetic solution of choice is administered

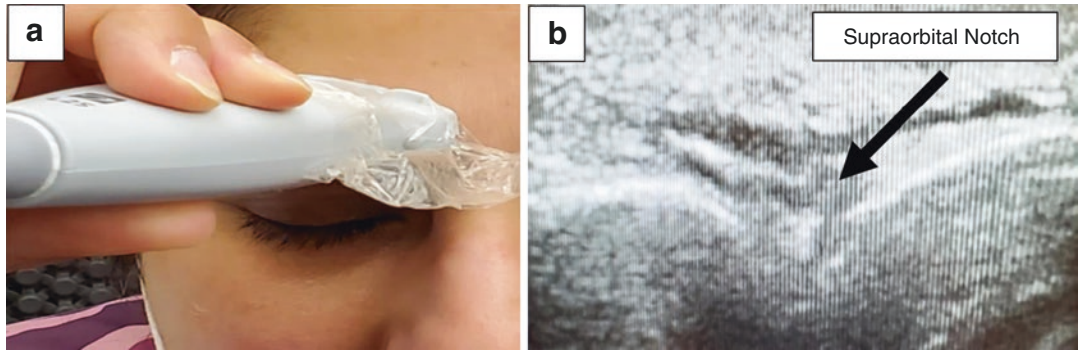

Fig. 48.3 Ultrasound image and probe orientation for supraorbital nerve block. (**a**) High frequency probe is oriented transversely with slight oblique tilt over the orbital ridge. (**b**) Supraorbital notch is visualized (black arrow)

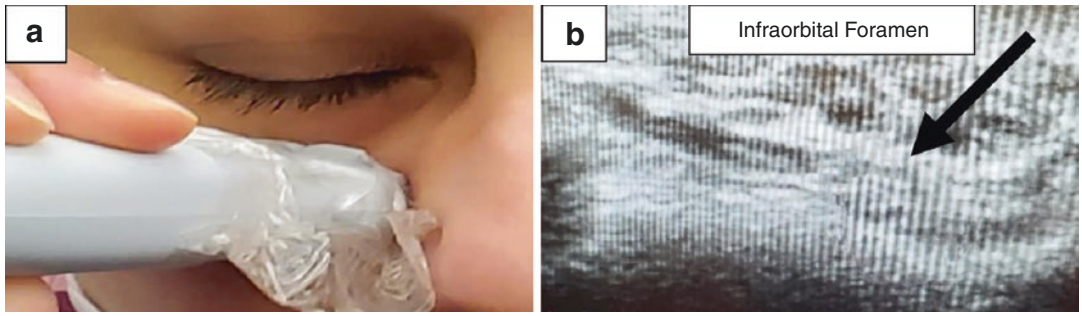

Fig. 48.4 Ultrasound image and probe orientation for infraorbital nerve block. (**a**) High frequency probe is oriented transversely below the orbit. (**b**) Infraorbital foramen is visualized (black arrow)

Auriculotemporal Nerve Block

- *Landmark Technique (*Fig. 48.2*)*
  - The temporal artery is palpated.
  - 27-guage needle is inserted approximately 1.5 cm anterior and 1 cm superior to tragus and advanced perpendicular to direction of nerve until periosteum is contacted. 1–2 mL of anesthetic solution of choice is administered

Complications

- Local anesthetic systemic toxicity (LAST)
  - Can occur with as little as 0.5 mL intravascular injection due to direct transfer of vasculature to the brain
- Persistent paresthesia
- Frey's syndrome
- The auriculotemporal nerve block can cause transient facial nerve paralysis, which is self-limited and resolve as the block wears off.

Clinical Pearls

- Supraorbital nerve emerges from the supraorbital foramen and travels deep beneath the corrugator supercilii, then penetrates the frontalis muscle to provide sensation to the upper eyelid and mid forehead.
- Infraorbital nerve block provides anesthesia to the upper lip, lateral nose, lower eyelid, and medial cheek [3].
- Temporal artery biopsy involves **injury to the auriculotemporal nerve**. The auriculotemporal nerve block can cause transient facial nerve paralysis.

- Auriculotemporal **(Frey) syndrome** characterized by recurrent episodes of gustatory flushing or sweating along the distribution of auriculotemporal nerve.

Questions

1. When performing an infraorbital nerve block, what direction of needle insertion is most effective to prevent penetration of infraorbital foramen?
   A. Lateral to medial and inferior to superior trajectory
   B. Lateral to medial and superior to inferior trajectory
   C. Medial to lateral and inferior to superior trajectory
   D. Medial to lateral and superior to inferior trajectory
2. What is the minimal volume of local anesthetic, if injected intraarterial during superficial trigeminal nerve block, can lead to generalized seizures?
   A. 5.0 mL
   B. 1.0 mL
   C. 0.5 mL
   D. 0.1 mL
3. Trigeminal neuralgia most commonly affects which nerve distribution of the trigeminal nerve?
   A. Mandibular
   B. Maxillary
   C. Ophthalmic
   D. All branches
4. The auriculotemporal nerve is a branch of which division of the trigeminal nerve?
   A. V1
   B. V2
   C. V3
   D. None of the above
5. Which of the following nerve is not branch of a cranial nerve?
   A. Great auricular
   B. Infraorbital
   C. auriculotemporal
   D. Supraorbital

Correct Answers

1. A. The infraorbital nerve leaves its foramen in a medial and caudal trajectory, therefore introducing the needle in a lateral to medial and cephalad approach minimizes the chance of inserting the needle through the foramen causing direct nerve or orbit damage.
2. C. Local anesthetic injection directly into the vasculature of the face can lead to seizure with as little as 0.5 mL due to the direct transfer of vasculature into the brain.
3. B. Trigeminal neuralgia generally affects its nerve branches unilaterally. Most common affected branches maxillary (35%), Mandibular (30%), Mandibular and Maxillary (20%), Ophthalmic and Maxillary (10%), ophthalmic (4%), all branches (1%)
4. C. The auriculotemporal nerve is a branch of the V3 division of the trigeminal nerve.
5. A. All of the nerves listed are derived from the trigeminal nerve (fifth cranial nerve) except the great auricular nerve.

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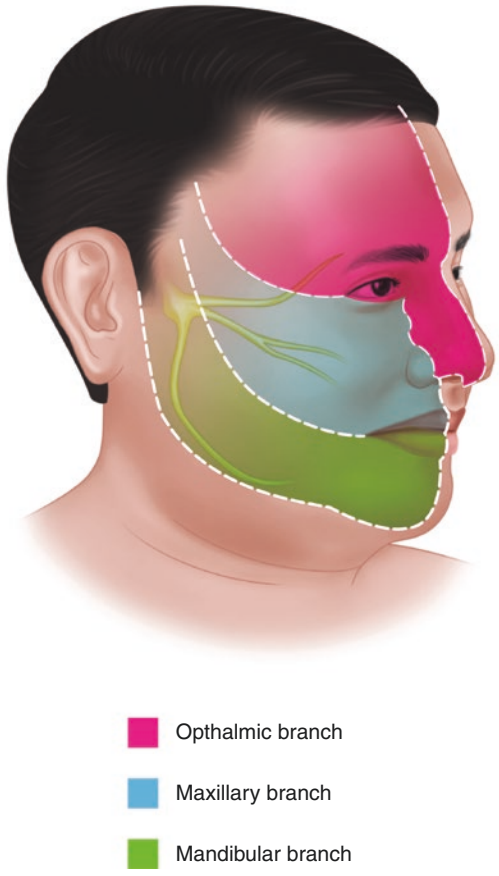
Craniofacial Pain: Trigeminal Neuralgia

49

Behnum A. Habibi and Chong Kim

Introduction

- Trigeminal neuralgia is a neuropathic pain in the face and characterized by recurrent **brief episodes of unilateral electric shock-like** [1] pains along the distribution of one or more divisions of the trigeminal nerve. Pain is usually triggered by innocuous stimuli.



- **Trigeminal nerve**: provides sensory supply to the face and the sensory and motor supply to the muscles of mastication. It has three major

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divisions: Ophthalmic (V1), Maxillary (V2), and Mandibular (V3) branches
  - These three peripheral branches join at the **Gasserian ganglion** (a.k.a. trigeminal ganglion, semilunar ganglion, or Gasser's ganglion) ⇒ trigeminal nerve root ⇒ trigeminal nerve nucleus in the pons

Clinical Manifestations

- Most common cause of chronic facial pain after age 50
- Incidence: females > males
- Usually **unilateral**, if bilateral, exclude multiple sclerosis
- Ophthalmic branch is **least affected**
- Pain is paroxysmal, **electric shock** like, stabbing, lasts few seconds to few minutes, and occurs repetitively up to 50–60 times a day. Pain can also present as continuous dull pain with paroxysms of pain. Pain can be reproduced by light touch on the affected area (trigger zone), chewing, talking, contact with a brush, cold air, smile etc. Pain may be accompanied by salivation, lacrimation or rhinorrhea.
- Primary Trigeminal Neuralgia
  - Usually due to compression of the trigeminal nerve root during its entry into the pons by an aberrant loop of an artery or vein, most commonly the **superior cerebellar artery**
- Secondary Trigeminal Neuralgia
  - vestibular schwannoma (acoustic neuroma), meningioma, multiple sclerosis, brain stem lesions or AV malformation.
- Differential diagnosis
  - Postherpetic neuralgia
  - Dental pain (usually continuous; **no paroxysm**)
  - Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)
  - Cluster headache
- Imaging (MRI head) identifies neurovascular compression or a structural brain lesion (eg, tumor in the cerebellopontine angle, demyelinating lesions including multiple sclerosis).

Treatment

- First line agents:
  - **Carbamazepine** [2]
    NNT = 4
    200–1200 mg/day
    SE: low Na, low WBC (agranulocytosis), aplastic anemia, high LFTs (hepatotoxicity)
  - Oxcarbazepine
    SE: similar to carbamazepine but less severe.
    600–1800 mg/day
- Second line agents:
  - Gabapentin/Pregabalin
  - Lamotrigine – need to titrate the dose over many weeks, given the risk of rash and other serious adverse effects
  - Baclofen –The starting dose of baclofen is 5 mg TID, with gradual titration to a maintenance dose of 50–60 mg per day. The drug should be discontinued slowly to avoid withdrawal.

Interventions

- Trigeminal nerve blocks
  - Target depends on pain distrbution, may include a single peripheral branch or Gasserian ganglion block
  - Targets for peripheral branch blocks
    Ophthalmic pain = **V1 = supraorbital foramen**
    Maxillary pain = **V2 = foramen infraorbitale**
    Mandibular pain = **V3 = mandibular notch or foramen mentale**
- Radiofrequency ablation
  - May be performed at Gasserian ganglion or over peripheral branches of Trigeminal nerve
  - SE: **anesthesia dolorosa** (or deafferentation pain) is neuropathic pain in an area

(usually in the face) that is numb to touch. Most commonly associated with treatment for trigeminal neuralgia.
  - Methods (approach for Gasserian ganglion block and RFA): patient supine, submento-vertex position, needle insertion ~3 cm from ipsilateral angle of the mouth, needle with 30-degree caudal incline, advance towards **foramen ovale**, confirm the position with fluoroscopy, motor testing, and sensory testing.
- Microvascular decompression: major neurosurgical procedure with craniotomy and the removal of various vascular structures, e.g., superior cerebellar artery, away from the trigeminal nerve.
- Gamma Knife radiosurgery: radiation beams are aimed at trigeminal nerves and the procedure is carried out with a stereotactic frame MRI. The beams cause axonal degeneration and necrosis.

Clinical Pearls

- The trigeminal nerve is a mostly sensory cranial nerve with motor innervation only to the muscles of mastication
- Trigeminal neuralgia is **usually unilateral**, affects females > males; bilateral symptoms should raise concern for MS
- MRI of the head is recommended to identify neurovascular compression or brain lesion
- First-line treatment is Carbamazepine (200–1200 mg/day). Know side effects.
- Trigeminal nerve branch blocks and ablation, as well as **Gasserian ganglion blocks** and ablation, are indicated for cases refractory to medical management
- Microvascular decompression at the Gasserian ganglion is the **most succesful** surgical treatment [3]
- Anesthesia dolorosa is a relatively rare side effect of trigeminal nerve trauma or surgery resulting in spontaneous pain signals without nociceptive stimuli

Questions

1. Which of the following branches of the trigeminal nerve is least likely to be affected in cases of Trigeminal Neuralgia?
   A. V1
   B. V2
   C. V3
   D. Each branch is equally affected
2. A 50-year-old woman presents reporting many weeks of short bursts of facial burning and tingling affecting the right face. She is unsure as to whether or not she has symptoms on the left side of her face as well. Her neurological exam is normal. What is the next best step?
   A. Refer for electrodiagnostic testing of the trigeminal nerve
   B. Order MRI of the head
   C. Trial of oral Carbamazepine
   D. Diagnostic block of the maxillary branch of the trigeminal nerve
3. The same woman returns to your clinic after a full work-up and has failed treatment with Carbamazepine. She elects for a trigeminal nerve branch block. Given the distribution of her symptoms, you recommend blocking only the maxillary branch. What is the anatomical target for this block?
   A. Supraorbital foramen
   B. Foramen infraorbitale
   C. Mandibular notch
   D. Foramen mentale
4. The same woman has not had any long-standing relief despite medical treatment and trigeminal nerve branch blocks. She elects for a surgical referral. Which surgical technique is most likely to confer the longest benefit in cases of idiopathic trigeminal neuralgia?
   A. Gamma-knife surgery
   B. Partial sensory rhizotomy
   C. Balloon compression
   D. Microvascular decompression
5. After successful surgical treatment of her symptoms, the same woman now presents with intermittent pain on the right side of her

face, though the skin itself is numb. What is the most likely diagnosis?

A. Post-herpetic neuralgia
B. Temporomandibular disorder
C. Anesthesia Dolorosa
D. Multiple Sclerosis

Correct Answers

1. A, 2. B, 3. B, 4. D, 5. C

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Craniofacial Pain: Occipital Neuralgia and Nerve Block

50

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Introduction: Occipital Neuralgia

- Occipital neuralgia is a type of headache characterized by piercing, throbbing, or electric-shock-like chronic pain in the upper neck, back of the head, and behind the ears, usually on one side of the head [1].
- The International Headache Society defines occipital neuralgia as a unilateral or bilateral paroxysmal shooting or stabbing pain in the posterior part of the scalp in the distribution of the greater, lesser, or third occipital nerve, sometimes accompanied by diminished sensation or dysesthesia in the affected area [2].
- Etiology of occipital neuralgia can include cervical instability, trauma, **compression** due to vascular abnormalities and mass lesions, due to arthrosis, sclerosis, osteolytic lesions, and Chiari I malformation. Surgeries at the cranio-cervical junction and upper cervical spine may also cause this syndrome.
- Diagnostic criteria: (1) **Occipital headache** associated with tenderness over the affected nerve branches. (2) **Trigger points** at the emergence of the greater occipital nerve or in the distribution of C2. (3) Pain improved by local anesthetic block of the affected nerve(s) (Fig. 50.1).

Treatment

- Conservative: non-pharmacologic options include heat/cold application, cognitive behavioral therapy, and massage. Pharmacologic options may be preferred by patients over injections or may be used in settings where practitioners are unable to provide occipital nerve blocks. Oral agents have not been systematically studied for their efficacy in occipital neuralgia. Gabapentinoids, tricyclic antidepressants, and baclofen have all been used given their efficacy in other craniocervical pain syndromes. Similarly, carbamazepine has been used for paroxysmal occipital pain.
- **Occipital nerve blocks** are often the treatment of choice. They may be diagnostic and therapeutic. Pain relief can last from days to months. They may be performed with or without steroid. The procedure can be repeated as needed, unless steroid is used.
- Botulinum toxin type A injections and peripheral nerve stimulation have been studied in small cases series.
- Surgical decompression of occipital nerve in refractory cases.

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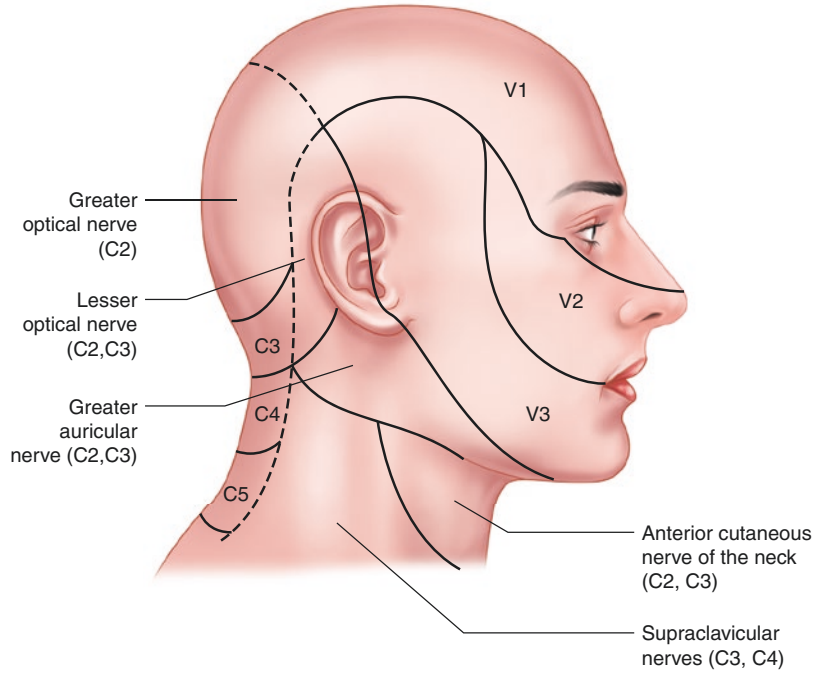

Fig. 50.1 Sensory innervation of scalp and neck. (Drawn by Sophia Haas, B. Arch)

Anatomy (Fig. 50.1)

- The greater occipital nerve (GON) arises from **dorsal primary rami of C2** (with occasional contribution from C3).
- GON passes through the semispinalis and trapezius musculature just inferior to the **superior nuchal line**, then continues alongside the occipital artery superiorly above the fascia and below the galea.
- The lesser occipital nerve (LON) arises from the **ventral primary rami of C2 and C3**.
- LON passes superiorly and laterally from the occiput to the lateral edge of the sternocleidomastoid muscle.
- LON innervates the scalp in the lateral area of the head posterior to the ear.
- The third occipital nerve originates from the third cervical spinal nerve, perforates the trapezius muscle, and supplies sensation to the upper posterior neck and lower occipital region of the scalp, medial to the greater occipital nerve territory.

Greater and Lesser Occipital Nerve Block Indications

- Diagnostic and therapeutic purpose
- Occipital headaches (occipital neuralgia)
- Neck pain felt in the upper back of the neck, potentially referring to the occiput, temporal, forehead, and retrobulbar regions of the head.
- Can be considered in
  - Chronic headaches
  - Cervicogenic headaches

Greater and Lesser Occipital Nerve Block Contraindications

- Coagulopathy
- Allergies to any of the local anesthetics
- Infection of the scalp
- Cervical instability or acute fracture
- Arnold-Chiari syndrome

Greater and Lesser Occipital Nerve Block Technique

Landmark Based

Landmarks (Fig. 50.2) [3]

1. External occipital protuberance
   (a) Midline occipital highest point (inion) on the posterior-inferior occiput of the skull
   (b) Insertions for both the nuchal ligament and the trapezius
2. Mastoid process
   (a) Posterior to the external acoustic meatus
3. Draw a line between the external occipital protuberance and mastoid process
   (a) GON lies 2/3 along the line, close to the occiput
   (b) LON lies 1/3 along the line, closer to the mastoid process

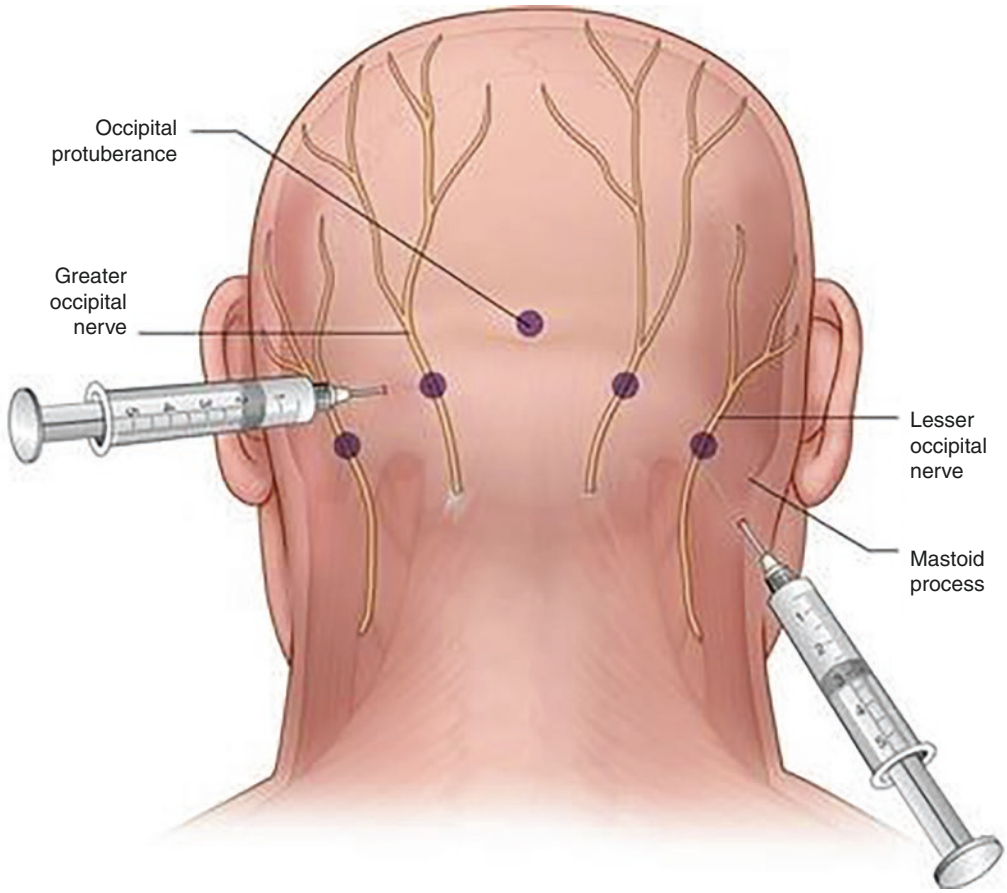

Fig. 50.2 shows landmarks, including occipital protuberance and mastoid process. The image outlines the targets for greater and lesser occipital nerves

Procedure

- Patient in seated or supine position, neck fully flexed
- Locate the external occipital protuberance (see above)
- For GON, injection site is often identified as a point of maximal tenderness and in approximately 2/3 along the line (close to occiput) between the external occipital protuberance and mastoid process.
- Slowly touch periosteum then slightly withdraw needle
- Aspirate to minimize intravascular injection
- Inject 1–2 mL of local anesthetic (steroid can be added)
- For LON, injection site is often identified as a point of maximal tenderness and located 1/3 along the line (closer to the mastoid process) between the external occipital protuberance and mastoid process.
- Slowly touch periosteum then slightly withdraw needle
- Aspirate to minimize intravascular injection
- Injection 1–2 mL of local anesthetic (steroid can be added)

Risks/Complications

- The most common complications include bleeding, bruising, swelling, and soreness at the site of injection
- Infection, local anesthetic toxicity
- Allergic reaction to the medication
- Nerve injury
- Seizure from intravascular injection of local anesthetic
- Headache exacerbation

Clinical Pearls

1. Occipital nerve block (ONB) can be diagnostic and therapeutic
2. ONB is a simple and safe treatment option for occipital neuralgia.
3. Landmark based ONB is simple and safe, though ultrasound guidance can be used (See references [3, 4])
4. In refractory cases, other treatment options include, botulinum toxin injections, radiofrequency ablation, occipital nerve decompression, occipital or spinal cord stimulation

Questions

1. Greater occipital nerve originates primarily from what cervical nerve root
   A. C2 ventral rami
   B. C2 dorsal rami
   C. C3 ventral rami
   D. C3 dorsal rami
2. Occipital neuralgia typically presents with the following features, except
   A. Tenderness over the posterior scalp
   B. Aura prior to the pain
   C. Pain behind the ear
   D. Recurring paroxysmal attacks
3. Which of the following is most likely to respond to occipital nerve blocks
   A. Migraines
   B. Post herpetic neuralgia
   C. Cervicogenic headaches
   D. Myofascial cervical pain
4. Lesser occipital nerves originates primarily from what cervical nerve roots
   A. C2 ventral rami
   B. C2 dorsal rami
   C. C3 dorsal rami
   D. none of the above
5. The occipital portion of the skull receives sensory innervation from
   A. Spinal accessory nerve (nerve XI)
   B. Facial nerve (nerve VII)
   C. Maxillary branch of trigeminal nerve (nerve V)
   D. None of the above

Answers

1. B, 2. B, 3. C, 4. A, 5. D

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Complex Regional Pain Syndrome

51

Amre Aboul-Fettouh and Johnathan Goree

Introduction

- Complex regional pain syndrome (CRPS) is characterized by severe, chronic pain following injury or surgical insult **disproportionate** to the expected clinical course of the inciting event [1].
- While pain is the hallmark of this illness, it is typically accompanied by hyperalgesia, allodynia, trophic changes, sudomotor changes, and vasomotor abnormalities in the involved limb or limbs.
- CRPS treatment is challenging due to its varying clinical course that ranges from mild and self-limiting to chronic and debilitating pain.
- The pathophysiology is **multifactorial** and believed to involve both **peripheral and central sensitization**. There are also genetic, inflammatory and psychological contributions.
- Incidence per person-years at risk for the disease ranges from 5.46 to 26.6 per 100,000 patient years. CPRS occurs more commonly in females, upper extremities, and in older adults with a peak incidence of 50–70 years of age. The most common presenting injury, that occurs in >40% of CRPS cases, is an antebrachial fracture. Other common inciting injuries or insults include sprains, contusions, crush injuries, and surgery.
- The incidence of job injury related CRPS is high. Many believe this is indicative of a psychosocial or **secondary gain** component to the disease.

Definition

- CRPS is subdivided into type I and II.
- Type I is formerly known as reflex sympathetic dystrophy (RSD) while Type II is formerly known as causalgia.
- Both types share the same core diagnostic features and the choice of treatment, with **type II demonstrating evidence of a known peripheral nerve injury** (high yield).
- Recent data suggests CRPS can be further subdivided into three stages based on timeline: acute, dystrophic, and atrophic. (See Table 51.1).
- **Most patients** present with warm CRPS; **increased** temperature of the affected limb. Patients with longer duration of disease normally progress to **cold CRPS** which is characterized by **decreased** temperature and poor cutaneous blood flow. Cold CRPS are thought to have **an unfavorable course of the** disease.

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Pathophysiology

- The pathophysiology of CRPS is not yet completely understood. One important trigger seems to be at the site of injury, eliciting a pro-inflammatory and immunological response which includes B-cell activation, **increased interleukins and substance P signaling**, and raised concentrations of osteoprotegerin (an osteo-clastogenesis inhibitor factor) [2].
- Pro-inflammatory mediators drive peripheral nervous system (PNS) sensitization resulting in **central sensitization and "wind up"** due to ongoing noxious primary afferent traffic into the dorsal horn.
- Peripheral nociceptive nerves have been shown to develop **catecholamine sensitivity and increased expression of adrenergic receptors,** which may explain the presence of autonomic features.
- Genetic and immune-related factors are also believed to contribute to the pathogenesis of CRPS and are currently under investigation.
- Dysfunction within the sympathetic nervous system → **excessive sympathetic outflow** → **vasoconstriction** → cooler temperature, **discoloration** (blue), and pain in the affected limb

Clinical Symptoms

- Patients with CPRS may exhibit a wide array of symptoms but can be classified as a triad compromising of sensory abnormalities, autonomic signs, and motor dysfunction. The vasomotor and sudomotor dysfunctions may manifest as **changes in skin color, temperature, and sweating patterns [5].**
- Trophic changes may also be present in the hair, nails, or skin. Symptoms can be classified into the three CRPS subtypes in Table 51.1.
- The initial characteristic symptom is sudden onset penetrating, burning pain associated with allodynia and hyperalgesia. This pain can spread regionally **without specific dermatomal distribution** from the site of initial trauma (usually triggered mechanically, thermal and psychological factors can exacerbate the pain). Over time, symptoms can emerge proximally and **even in the contralateral limb.**

Table 51.1 Stages of CRPS with corresponding clinical signs and symptoms

Stages	Duration	Signs & symptoms
Acute	Starts 2–6 weeks after initial injury up to 6 months	Skin changes: initially **warm and dry**, later cold and cyanotic. Mottling of the skin Sweat changes: hyperhidrosis Edema: non-pitting Pain: usually **not significant**, tenderness and hyperesthesia may happen
Dystrophic	Starts 2–6 weeks after initial injury up to 6 months	Skin changes: **cool, pale, mottled** cyanotic and a shiny appearance Mottling of the skin Sweat changes: hyperhidrosis Edema: extensive edema with an indurated and brawny character Pain: diffuse, constant, **burning**, and increased by stimuli hyperesthesia, hyperalgesia and allodynia may also be present
Atrophic	Starts 6–8 months after the initial injury	Skin changes: **irreversible atrophy, cold** Fat and muscle changes: irreversible atrophy Joint changes: decrease range of motion and decrease strength Pain: **intractable**, hyperesthesia, hyperalgesia and allodynia may also be present

Diagnostic Modalities

Radiology Testing

- No diagnostic test has been proven to be definitive. Clinical findings remain the **gold standard** for the diagnosis.

- Bone scintigraphy and x-ray bone densitometry are common imaging tools used to detect **bone abnormalities** reported to occur within the first year of the disease.

Diagnosis

- Currently, the standard for clinical CRPS diagnosis is based on criteria from the **Budapest clinical diagnostic criteria** by the International Association of the Study of Pain (IASP) (Table 51.2).
- **CRPS prediction score (CPS)** (Table 51.3) has shown better sensitivity and specificity when compared to the Budapest criteria.

Table 51.2 Budapest clinical diagnostic criteria for CRPS

Budapest clinical diagnostic criteria for CRPS	
1	Continuing pain, which is disproportionate to any inciting event.
2	Must report at least one symptom in all four of the following categories: *Sensory* – reports of hyperesthesia and/or allodynia. *Vasomotor* – reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry. *Sudomotor/edema* – reports of edema and/or sweating changes and/or sweating asymmetry. *Motor/trophic* – reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin).
3	Must display at least one sign at time of evaluation in two or more of the following categories: *Sensory* – evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or temperature sensation and/or deep somatic pressure and/or joint movement). *Vasomotor* – evidence of temperature asymmetry (>1 °C) and/or skin color changes and/or asymmetry. *Sudomotor/edema* – evidence of edema and/or sweating changes and/or sweating asymmetry. *Motor/trophic* – evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin).
4	There is no other diagnosis that better explains the signs and symptoms.

Table 51.3 CRPS predictive score

Predictor	*Value*
Negative predictors	
Spontaneous/uncertain cause or miscellaneous cause (i.e., not fractures, blunt traumatic injuries, surgery, CTS, sharp traumas, palmar or plantar fascial fibromatosis, inflammation, animal bites, local infections, or burns)	−4
Location	<1
No trophic changes	−4
Indifferent skin color	−1
Indifferent sweating	−1
No temperature difference (subjective)	−1
Tendon reflexes increased	−1
No sensitivity disorders at all	−3
No altered sensitivity during pinprick	Additional −1
No altered sensitivity during slight touch	Additional −1
Positive predictors	
Spontaneous pain sensations	+1
Augmentation of pain (any cause)	+1
Augmentation during night, orthostasis, nonpainful touch or cold	Additional +1
Increased growth of hair/nails	+3
Skin color livid or hyperemic	+3
Increased sweating	+4
Edema	+1
Swelling	+1
Tendon reflexes decreased	+3
Reduction of complex strength (handgrip/tiptoe-standing)	+4
Tremor (any kind)	+3
Focal (myoclonic) dystonia	+3
Movement initiation disorders	+4
Allodynia	+1
Sum (Minimum = −18, Maximum = +33)	
Diagnostic threshold for CRPS	≥+4 points

Treatment

- Treatment for CRPS is multimodal and includes **medical, psychological, physical and occupational** therapy components.
- Mirror therapy and graded motor imagery are shown to improve clinical outcome.
- Medications include NSAIDs, **gabapentin, pregabalin, or a tricyclic antidepressant**,

bisphosphonate treatment in patients with abnormal bone scan, and topicals (eg lidocaine patch or capsaicin), ketamine oral or IV infusion

- Serial sympathetic ganglion blocks are routinely employed by interventional pain physicians as a means of decreasing pain either with local anesthetic or chemical/thermal neurolysis. Traditionally, lumbar sympathetic blocks are performed in patients with **CRPS in the lower extremity** and stellate ganglion blocks performed in patients with **CRPS in the upper extremity**.
- Neuromodulation is usually considered after failed conservative management. Recent studies have shown that dorsal column stimulation (DCS) as a tertiary option may be effective for short term pain reduction.
- The ACCURATE Study published in 2017, found that DRG stimulation provided consistent pain relief than DCS at 3 months and 12 months [3].
- Another novel treatment for CRPS I & 2 is wireless peripheral nerve stimulation (permanent or temporary placement on a peripheral nerve by ultrasound) [4].

Clinical Pearls

1. CRPS types I and II differ etiologically by the presence (type II) or absence (type I) of **evidence of nerve injury**
2. Pain is the hallmark of the condition, with associated triad allodynia, autonomic signs, and motor dysfunction.
3. The pathophysiology of CRPS is still not well understood. Peripheral and central sensitization and neuroimmune mechanisms are thought to play important roles in CRPS.
4. **CRPS is a clinical diagnosis**. There is no diagnostic test considered to be a gold standard. Diagnostic criteria can help narrow diagnosis.
5. Treatment involves a multimodal approach that includes pharmacologic, interventional and neuromodulation therapy with treatment centered around physical therapy.

Five MCQ Questions

1. **Which of the following accounts for the difference between complex regional pain syndrome (CRPS) Type II and CRPS Type I?**
   A. Immobility of joint
   B. Temperature changes
   C. Nerve trauma
   D. Absence of pain
2. A 42 -year old male presents with burning pain, allodynia, swelling, and intermittent blue discoloration in his left hand with all fingers and most of the forearm to the elbow. This occurred 4 months ago when he suffered a biking accident and fell onto his left arm. Which procedural intervention is MOST appropriate for pain control to help the patient tolerate physical therapy?
   A. Left median block
   B. Left Ulnar block
   C. Left stellate ganglion block
   D. Left musculocutaneous block
3. Concerning the treatment of CRPS:
   A. Physical therapy and normalization is essential.
   B. Sympathetic blocks alone have been shown beneficial late in the disease course.
   C. Imaging modalities are the gold standard for diagnosing CRPS.
   D. None of the above
4. What is the most common precipitating event for complex regional pain syndrome (type I)?
   A. Surgery
   B. Burn
   C. Crush injury
   D. Fracture
5. Which is a late feature of complex regional pain syndrome?
   A. Tingling
   B. Skin flushing
   C. Muscle atrophy
   D. Mottling of the skin

Answers

1. C, 2. C, 3. A, 4. D, 5. C

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Sympathetic Blocks: Stellate Ganglion Block

52

Mayson Callaway and Boris Spektor

Introduction

- In general it is difficult to perform isolated sympathetic blocks without concomitantly blocking associated somatic nerves but the stellate ganglion, lumbar sympathetic trunk, celiac plexus, superior hypogastric plexus, and ganglion impar are anatomically separated from somatic nerves. Therefore, they are common sites for sympathetic blockade [2]
- Stellate ganglion is a sympathetic ganglion formed by fusion of the inferior cervical and first thoracic ganglia, present in approximately 80% of the population (stellate = star-shaped) [1]
- It is a confluence of preganglionic fibers that continue cephalad to the cervical sympathetic chain and postganglionic fibers that provide sympathetic innervation of the ipsilateral upper extremity, head, neck and heart [1, 4]

Anatomy

- The ganglion is located at the anterior border of the first rib extending to the C7 transverse process, posterolateral to prevertebral fascia along the anterior surface of the longus colli muscle [1]

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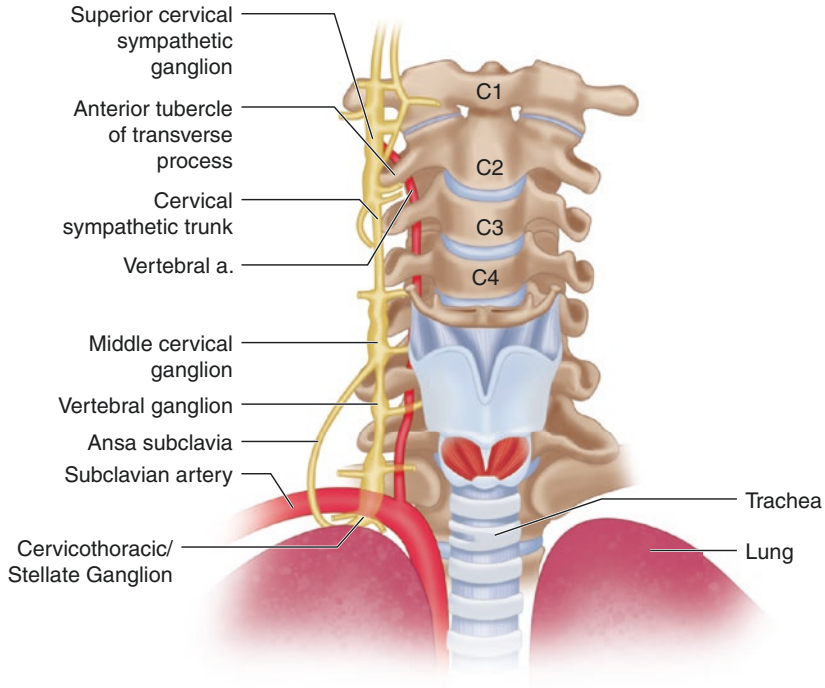

Anatomy of the cervical sympathetic chain

- At C7 level it is in close proximity to the dome of the pleura and directly medial or posterior to the vertebral artery (anatomical variation). The vertebral artery, inferior thyroidal artery and esophagus are relatively more exposed and vulnerable at the **C7 level compared to C6 [1, 4]**
- Block is typically performed at **C6 transverse process** (Chassaignac's tubercle) with injectate migrating caudally along the prevertebral fascia
- At C6 level sympathetic chain lies posterior to carotid artery and anterior to longus colli muscle, deep to the prevertebral fascia

Indications

- Complex Regional Pain Syndrome (CRPS)
- Postherpetic neuralgia (early)
- Refractory ventricular tachycardia or ventricular electrical storm (significant decrease in number of arrhythmia episodes and defibrillations after **left-sided block**) [3]
- Intractable angina
- Intractable peripheral vascular disease of the upper extremity
- Hyperhidrosis
- Raynaud's disease
- Phantom limb pain

Contraindications

- Severe COPD
- contralateral phrenic or recurrent laryngeal nerve palsy
- glaucoma
- coagulopathy or anticoagulation (relative)

Technique

- *Landmark*
  - palpate C6 transverse process anteriorly, retract SCM/carotid laterally, puncture skin lateral to cricoid aimed laterally (may perforate thyroid), touch needle down on anterior surface of transverse process, withdraw

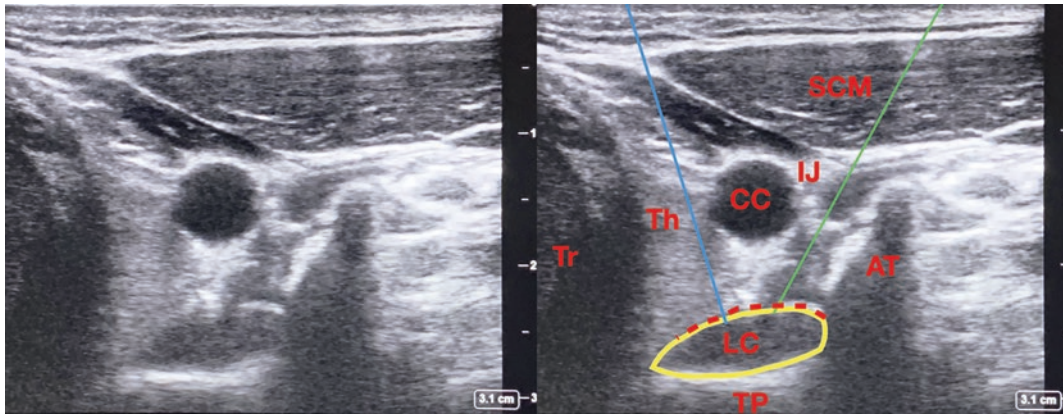

Fig. 52.1 Ultrasound at right-sided C6 level: paratracheal anterior (blue arrow) and lateral (green arrow) needle trajectories demonstrated. Prevertebral fascia- red dotted line. SCM sternocleidomastoid, IJ internal jugular vein (collapsed), CC common carotid artery, Th thyroid, Tr trachea, AT anterior tubercle, TP transverse process of C6

2–3 mm, aspirate and deposit local anesthetic injectate [1, 4]

- *Ultrasound* (Fig. 52.1)
  - locate C6 and C7 transverse processes (generally no anterior tubercle is visible at C7), longus colli muscle, internal jugular vein, common carotid artery and thyroid with linear array ultrasound probe**. Blockade at C6 level preferred** to decrease risk of complications. Identify best needle trajectory to prevertebral fascia on anterior border of longus colli muscle, insert needle either paratracheally or laterally to deposit local anesthetic at target location just deep to prevertebral fascia (the medial paratracheal approach has increased risk of thyroid hematoma and injury); appreciate injectate spread in real time; if no spread seen, intravascular injection likely [1, 4]
- *Fluoroscopic*
  - locate **C6 transverse process**, direct needle towards anterior tubercle just inferior to uncinate process and advance until contact with bone made; withdraw needle about 3 mm; after negative aspiration, inject contrast dye looking for craniocaudal spread; subsequently deposit local anesthetic

Complications

- **Intravascular injection** and seizures
- **Vertebral artery dissection- stroke** (Fig. 52.2)
- Neuraxial block (high spinal or epidural)
- Hematoma
- Difficulty swallowing (Vagus nerve blockade)
- Vocal cord paralysis and hoarseness (**RLN blockade**)
- Shortness of breath (**Phrenic nerve blockade**)
- Brachial plexus blockade or injury
- Tracheal or esophageal puncture
- Pneumothorax

Preventive Measures to Avoid Complications

- Use of ultrasound
- Lateral needle approach
- **C6 level for injection**
- Holding of anticoagulants if possible (intermediate risk procedure per American Society of Regional Anesthesia 2018 interventional pain guidelines)

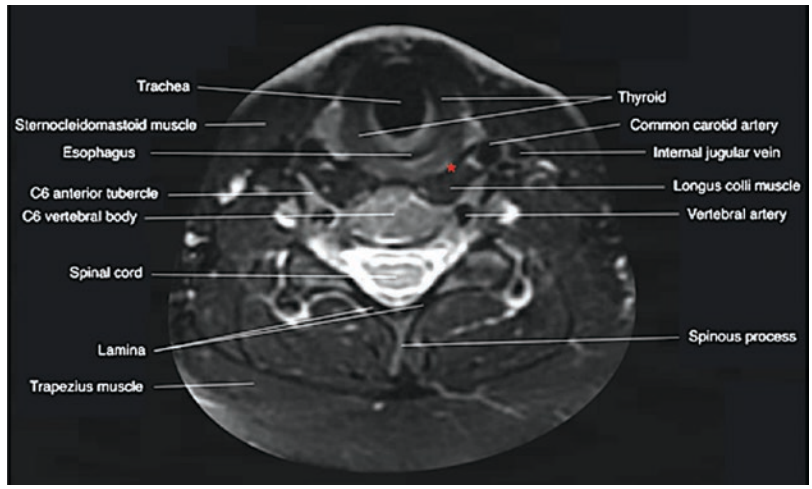

Fig. 52.2 Axial CT image at C6 demonstracting proximity of sympathetic chain, labeled with a red asterisk, to other anatomical structures

Clinical Pearls

- Stellate ganglion is located anterior to the longus colli muscle near the transverse **process of C7**
- It is commonly **blocked at C6** (Chassaignac's tubercle) to avoid proximity of the ganglion to vertebral artery and pleura at C7
- Retraction of SCM/carotid laterally is crucial for landmark technique due to relation to common carotid artery
- **Phrenic and recurrent laryngeal nerves** often blocked
- Blockade commonly used to treat sympathetically-mediated pain syndromes including CRPS, peripheral vascular disease, and refractory cardiac tachyarrhythmias
- Horner's syndrome (sympathetic block of the head and neck with miosis, ptosis, anhidrosis), nasal congestion, and ipsilateral arm warmth secondary to vascular dilation confirmatory of blockade (in a small population of patients, **may not be blocked with stellate** as upper extremity sympathetic fibers may arise from T1 and T2 ganglia)

Questions

1. Which of the following correctly describes the location of the stellate ganglion?
   A. Anterior to C7 transverse process
   B. Lateral to C6 transverse process
   C. Superior to carotid body
   D. Posterior to longus coli muscle
2. Where is the most common site to block the stellate ganglion?
   A. C4 transverse process
   B. C5 transverse process
   C. C6 transverse process
   D. Anterior border of first rib
3. Which of the following is not an indication for stellate ganglion blockade?
   A. CRPS
   B. Refractory VT
   C. Peripheral vascular disease of the arm
   D. Thyroid storm
4. Which of the following is not common following stellate ganglion blockade?
   A. Ptosis and miosis
   B. Hoarseness
   C. Warmth of ipsilateral arm
   D. Tachycardia
5. Blockade of the stellate ganglion at the C6 level compared to the C7 level reduces the risk of all of the following except?
   A. Vascular injury
   B. Transient phrenic nerve blockade
   C. Esophageal injury
   D. Pneumothorax
6. Ten minutes after a stellate ganglion block, a patient becomes apneic. The most likely cause is

A. Paratracheal hematoma
B. Phrenic nerve block
C. Subarachnoid injection
D. Vertebral artery injection

Answers

1. A, 2. C, 3. D, 4. D, 5. B, 6. C

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Sympathetic Blocks: Celiac Plexus Nerve Block and Neurolysis

53

Priscilla Agbenyefia, Russell Stuart, and Grace Chen

Introduction

- The celiac plexus block and neurolysis have been used successfully to treat cancer pain originating from the **stomach, distal esophagus, biliary tree and the pancreas** [1–3]. In addition, the **kidney, pancreas, adrenals and omentum** derive at least partial innervation from the celiac plexus. The descending colon, sigmoid colon, rectum, and pelvic viscera are excluded.
- The celiac plexus consists of a collection of nerve fibers lying over the anterolateral surface of the aorta at the level of the celiac artery, superior mesenteric artery and renal arteries [1, 2]. Many of these nerve fibers are preganglionic sympathetic fibers originating from the **greater (T5-T9, lesser (T10-T11), and least splanchnic (T12) nerves** [1, 2] (Fig. 53.1). The posterior trunk of the vagus nerve supplies parasympathetic efferent fibers to this plexus [1, 2].
- It is important to note that the celiac plexus is located anterior to the crura of the diaphragm and often **anterior to the aorta**, sometimes necessitating a transaortic approach [1]. The greater, lesser and least splanchnic nerves are located **posterior to the diaphragm and aorta** [1]. For pancreatic cancer pain, neurolysis of splanchnic nerves appears to provide comparable analgesic benefit that may cause fewer complications.

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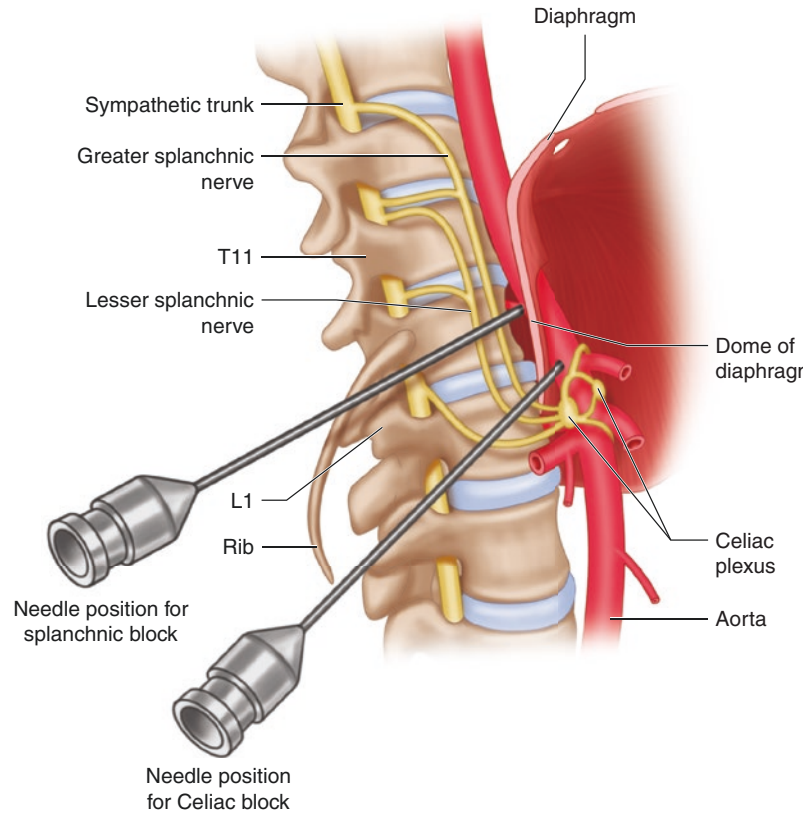

Fig. 53.1 Illustration of needle position difference between a celiac plexus block and a splanchnic block. The celiac plexus block is the lower needle, at L1, commonly transcrural or transaortic. The splanchinic needle is the high needle, at T12, more posterior than the aorta

Indications

- Celiac plexus block and neurolysis are most often studied for **pancreatic cancer pain**. The procedure may also be useful for managing pain in the setting of other upper abdominal malignancies [1–3] (gastric cancer, cancer of the distal esophagus, and cancer involving the biliary tree) [1–3].
- Proper patient selection necessitates evaluation of the source of pain; i.e. pain localized to a visceral structure such as the pancreas (commonly presents with "**pain wraps around**" or "**piercing from front to back**"), versus musculoskeletal pain originating from the abdominal wall (localized, non-radiating pain, which **will not respond** to this block) [2].
- Primary pain from metastatic cancer **invasion of the abdominal wall** is not amenable to celiac plexus or splanchnic neurolysis [2] since afferent nerve fibers responsible for somatic pain do not relay in the celiac plexus [2].
- Celiac plexus block and neurolysis have also been effective to treat chronic abdominal pain conditions such as chronic pancreatitis. Neurolysis is not usually done for non-cancer pain due to the possibility of deafferentation pain and fibrosis with worsened recurrent pain and outcomes.

Contraindications Specific to this Block

- Abdominal aortic aneurysm or aortic mural thrombosis [2, 3].
- celiac plexus block → unopposed parasympathetic dominance → increase in gut motility. Therefore, **bowel obstruction or any intra-**

abdominal perfusion deficits from vascular obstruction or compromise is also a relative contraindication [2].

- Given the hypotension which can be associated with this procedure from **mesenteric vasodilation resulting from decreased sympathetic tone**, it is important to ensure that patients are not severely hypotensive prior to the procedure [1, 2].

Block Technique

- There are various percutaneous, endoscopic as well as open approaches to block nociceptive fibers for visceral pain from the upper abdomen [2, 4, 5]. Percutaneous approaches include the classic retrocrural approach for neurolysis of the splanchinic nerves that feeds into the celiac plexus, anterocrural approach, transaortic approach, transintervertebral disc approach, and anterior approach [2, 4, 5].
- Celiac block: Starting at left-sided, after infiltration of 1% lidocaine over the upper margin of the L1 vertebral body (T12 or T11 for splanchnic nerve block, See Fig. 53.2), a 22G 5 or 8 inch spinal needle is advanced in a coaxial view to anterior to the L1 vertebral body. Multiple AP and lateral imaging are performed to confirm coaxial needle position. Once the needle is at the anterolateral margin of the L1 vertebral body, contrast dye is injected under live fluoroscopy. After negative aspiration, a 10–15 mL of 0.25% bupivacaine in injected.
- Optimal contrast spread in a retrocrural approach is noted along the anterolateral edge of the target vertebral body in the retrocrural space with no posterior spread [2, 4] to avoid affecting spinal nerves.
- If contrast spread crosses midline in the PA view in celiac plexus block, a unilateral approach can be employed [4, 5]. However, a bilateral block, if possible, is recommended to achieve a denser block [4, 5].
- Digital subtraction angiography can be used to rule out intravascular uptake of contrast. A test dose with 2% lidocaine and 1:200,000 epinephrine may also be used to identify intravascular needle placement.
- If the patient obtains significant pain relief with the block, 5–10 ml of 50–100% ethyl alcohol or 10–12% phenol are injected for neurolysis on each side [2.4,5].
- In addition to pain relief after the celiac plexus block, an increase in heart rate and decrease in blood pressure from **mesenteric vasodilation** confirms successful sympathetic blockade.
- Ethyl alcohol, unlike phenol, causes intense pain on injection. This is mitigated by alcohol injection **after a satisfactory celiac plexus block** [2, 4, 5].

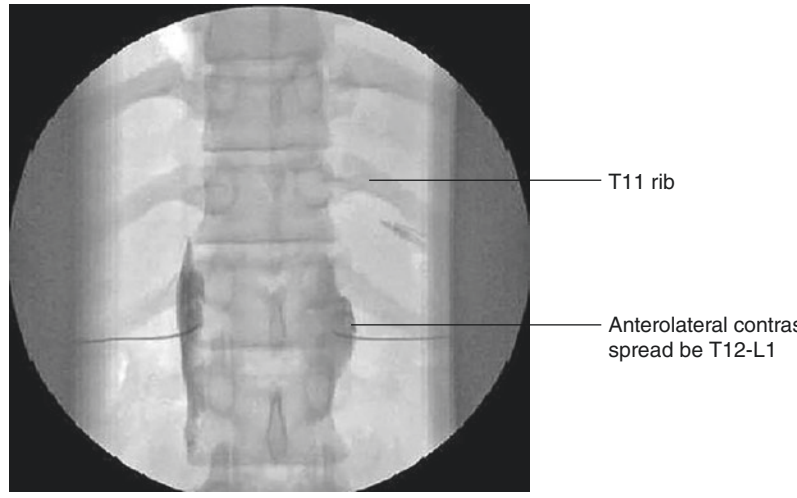

Fig. 53.2 Anterior-posterior view of radiographic contrast spread in a splanchnic nerve block. (Reproduced and modified with permission. Lawrence et al. [6])

Complications Specific to this Block

- Celiac plexus block and neurolysis confer less than a **2% risk of serious complications** and **0.15% risk of paralysis** [2, 5]. Procedurally, the most common complication is localized pain on injection.
- Aortic perforation and dissection have also been reported, along with retroperitoneal hematoma, intraperitoneal perforation and injury to intra-abdominal viscus (Fig. 53.3), hematuria and acute renal injury from renal laceration, pneumothorax, paraplegia from direct injury to spinal cord or vasospasm of spinal segmental arteries including the artery of adamkiewicz may occur [4, 5]. For these reasons, **injection against high pressure**, signifying dense tissue, is discouraged.
- Expected side effects from unopposed parasympathetic innervation of the gastrointestinal tract and concomitant mesenteric vasodilation often results in **abdominal cramps** from peristalsis, diarrhea and orthostatic hypotension [2, 4, 5]. These are usually transient, but could last for several days [4, 5].
- Orthostatic hypotension can be attenuated by preoperative intravenous hydration [2, 4, 5]. Judicious intravenous and oral hydration is advised post-procedurally as dehydration can worsen orthostatic hypotension and result in presyncope, syncope and falls.

Clinical Pearls

- The location of the celiac plexus is the largest autonomic plexus and lies anterolateral to the aorta at the level of the celiac artery, superior mesenteric artery and renal arteries at the **T12/L1** vertebral level in 94% of individuals [2, 4].
- The sympathectomy produced by a celiac or splanchnic block causes hypotension by decreasing preload to the heart. Other complications include: subarachnoid injection, seizure from an intravascular injection,

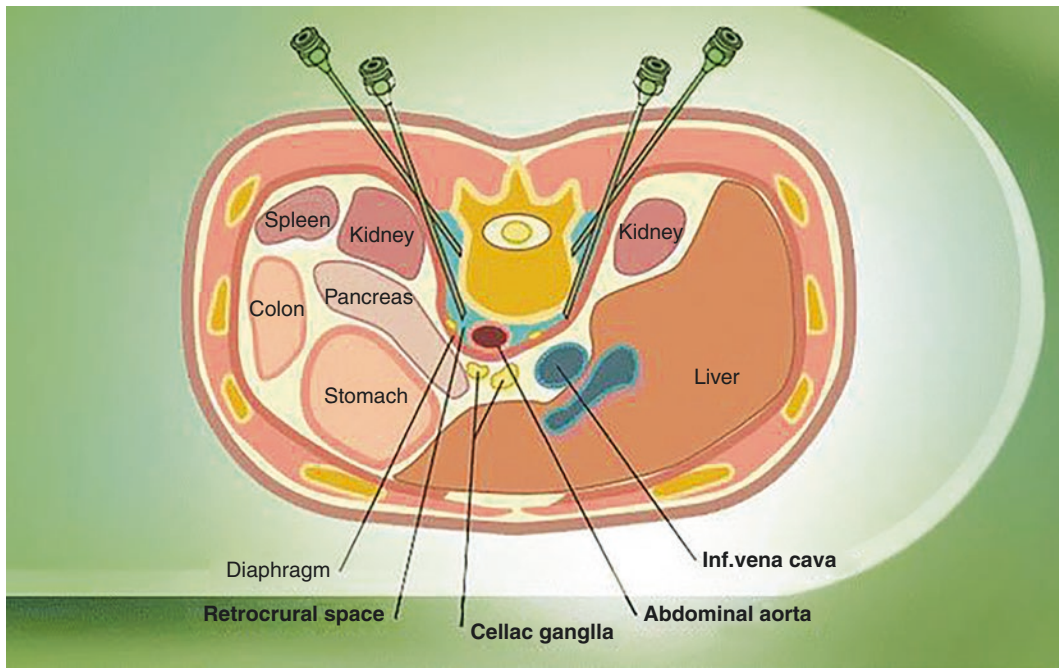

Fig. 53.3 Cross section of structure surrounding celiac block. (Reproduced with permission. Nedeljkovic and Ali [7])

retroperitoneal hematoma from aortic puncture, and diarrhea.

- Celiac plexus neurolysis with **ethyl alcohol can cause severe pain on injection**. Achieving a successful blockade before neurolysis will help decrease the pain on injection [4, 5].
- A test dose with about 3 mL of 2% lidocaine and 1:200,000 epinephrine on each side of a celiac plexus block along with **digital subtraction angiography** can help confirm intravascular needle placement and prevent inadvertent intravascular injection of injectate [2, 4, 5].

Questions

1. Which of the following patients would be unlikely to have significant pain relief from a celiac plexus block?
   A. 34 year old male construction worker with pancreatic cancer on high dose opioids and severe nausea.
   B. 45 year old female mother of three with rectal cancer which has spread to the sacroiliac joint.
   C. 80 year old female retired computer engineer with gastric cancer who is being discharged to hospice care.
   D. 40 year old male stock broker with chronic pancreatitis.
2. What are the spinal levels that contribute to the celiac plexus by way of the greater, lesser and least splanchnic nerves?
   A. T5-T12
   B. T5-L2
   C. T8-L2
   D. D.T8-T12
3. The celiac plexus is typically located on the anterolateral border of the aorta at the level of the celiac artery, superior mesenteric artery and renal arteries at which vertebral levels in most individuals?
   A. L1/L2
   B. T11/T12
   C. L2/L3
   D. T12/L1
4. Anterior spinal cord syndrome from celiac plexus block is typically the result of which of the following?
   A. Direct needle penetration of the spinal cord
   B. Vasospasm of the artery of Adamkiewicz
   C. Ethyl alcohol injection into epidural venous plexus
   D. Needle advancement into Inferior vena cava
5. A celiac-plexus block would treat pain which of the following organs?
   A. Uterus
   B. Adrenal gland
   C. Descending colon
   D. Prostate

Answers

1. B: this patient likely has a complex multifocal pain complaint with components of her pain coming from the somatic involvement of the sacroiliac joint, but also from the involvement of pelvic organs which would be supplied by the superior hypogastric plexus, and not celiac plexus.
2. A: The celiac plexus is supplied by preganglionic fibers from the Greater (T5-T9), Lesser (T10-T11) and Least (T12) splanchnic nerves.
3. D: The celiac plexus is the biggest autonomic plexus in humans and located anterolateral to the aorta at the T12/L2 vertebral level in 94% of individuals in cadaveric and MRI studies [2].
4. B: The artery of Adamkiewicz is the largest segmental artery that feeds into the anterior spinal artery. It enters the spinal canal from the left side between T9 and L1 in 80% of individuals. Injury or vasospasm of the artery is rare but possible with the retrocrural technique for celiac plexus blocks. Vasospasm of the artery can result in anterior spinal cord syndrome.

5. B: The pelvic organs (e.g., uterus, ovaries, prostate, distal colon) are supplied by the hypogastric plexus

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Sympathetic Blocks: Lumbar Sympathetic Block

54

Ruchir Gupta and Natalie Strand

Introduction

- The sympathetic nervous system (SNS) has shown to be implicated in neuropathic pain, pain due to vascular insufficiency, and visceral pain.
- Lumbar sympathetic blocks (LSB) are used to assess the role of the SNS in neuropathic pain.

Anatomy

– Sympathetic nervous system is an **efferent system,** which transmits the impulses from the spinal cord to the effector cells. Under normal conditions, they have **no influence on sensory neuronal activity** but it exhibits interactions with sensory system during acute or chronic tissue damage and painful stimuli as a part of the defense strategy (fight and flight)
– Sympathetic activity on nociceptive neurons may generate a state **of central sensitization** which produces spontaneous pain (termed as 'sympathetically maintained pain')
– The lumbar sympathetic block is commonly performed at the densest portion of lumbar sympathetic ganglia at **L2 and L3** [3]. (Fig. 54.1)
– Figure 54.2 shows a cross sectional view of the spinal cord and where neurons from the sympathetic chain terminate and communicate with the spinal cord

Indications [1, 2]

- Sympathetically maintained neuropathic pain; Complex Regional Pain Syndrome of the Lower Extremities (Chap. 16, chronic pain), Phantom limb pain,
- Peripheral Vascular Disease, Raynaud's Phenomenon, Ischemic Leg Pain, thromboangiitis obliterans (Burger's disease) and atherosclerosis (sympathectomy → vasodilation)

Diagnostic vs Therapeutic Lumbar Sympathetic Block

Diagnostic Blocks

- Pure sympathetic block without any accompanying somatic block
- Objective signs of sympathetic block can be identified using **changes in skin tempera-**

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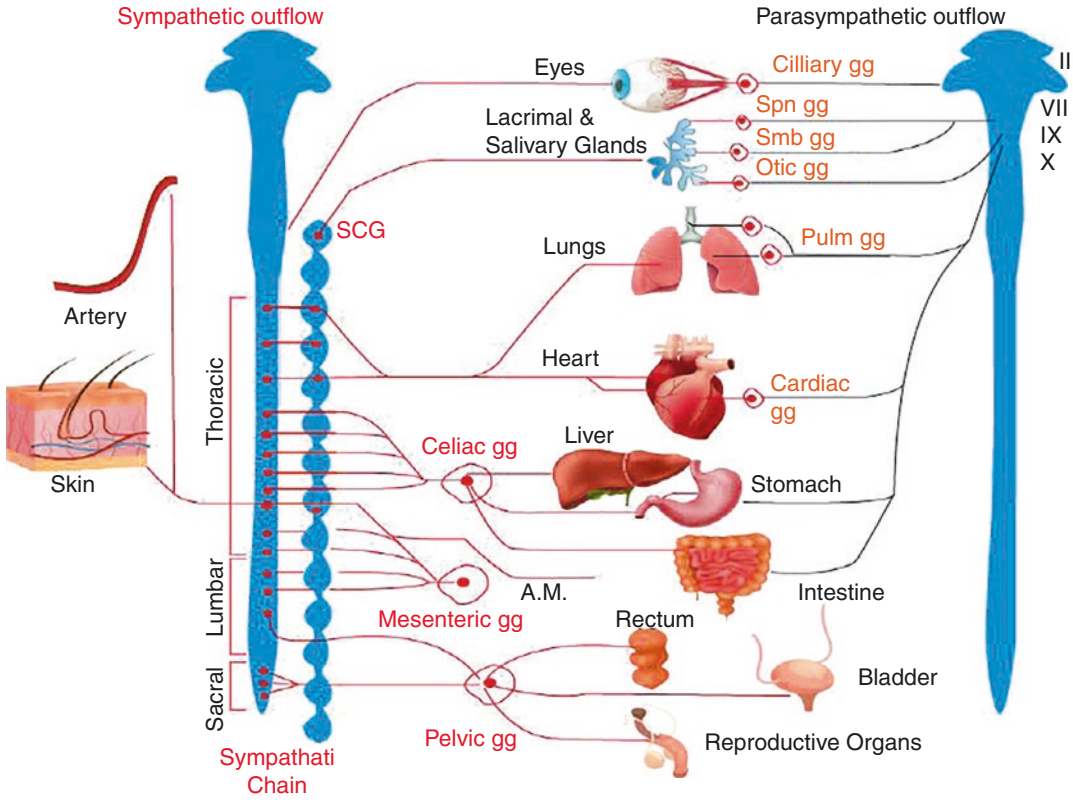

Fig. 54.1 Lumbar sympathetic chain located along the anterolateral aspect of the first through fourth lumbar vertebral bodies

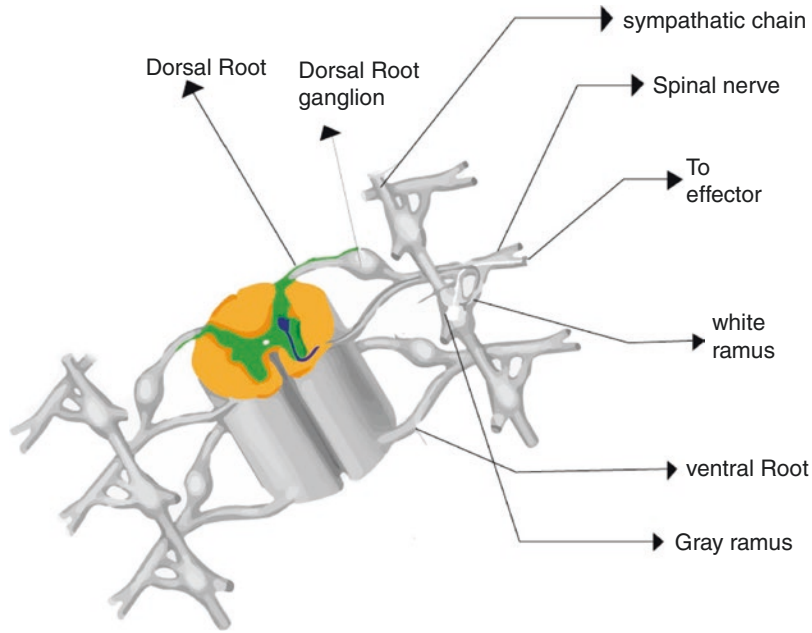

Fig. 54.2 The preganglionic neurons exit the spinal cord via white rami of the ventral roots of spinal nerves L1–L4 and then synapse at the corresponding lumbar sympathetic ganglion. The postganglionic neurons extend distally and innervate organs

ture, decreasing pain, and anhidrosis in the distal extremity
- False-positive results can occur due to spread of solution to adjacent somatic nerves or **into the epidural space**, systemic effects of absorbed local anesthetic, or a placebo response

Therapeutic Blocks

- LSB with use of neurolytic chemicals such as phenol or alcohol, neuroablative techniques such as radiofrequency lesioning for long lasting effects.
- Neurolytic blocks are indicated primarily for cancer and peripheral vascular disease, and should be used with great caution

Technique

- Place patient prone with a pillow under the abdomen
- Recommended needle: 22 gauge 5–7 inch spinal needle
- Under AP view, identify L2 or L3 and square the endplates of the vertebral body. Next, rotate the C-arm ipsilateral to the injection site until the tip of the transverse process lines up with the anterior border of the vertebral body
- After injecting local anesthetic over skin and subcutaneous tissue, needle should be advanced toward the anterolateral surface of L3 vertebral body under direct fluoroscopic guidance
- Advanced until needle contacts bone of the lateral margin of the vertebral body
- Rotate c-arm to obtain both AP and lateral views to verify needle position
- Advance needle under lateral view until needle tip is approximately 3 millimeters dorsal to the anterior border of the vertebral body
- After negative aspiration, inject 1–2 cm of contrast under live fluoroscopy. Contrast should spread **anterior to vertebral body** in a thin line with no evidence of vascular uptake
- Rotate C-arm in the AP position. Contrast should be in paramedian area with spread toward the midline during washout views
- After negative aspiration for blood or CSF, inject 10–20 ml of 0.25% bupivacaine with frequent aspiration every 1–2 ml
- Monitor skin temperature for changes to assess for successful sympathetic block

Potential Complications

- Intravascular injection into vena cava, aorta resulting local anesthetic toxicity
- Dural puncture and post dural puncture headache
- Genitofemoral neuralgia.
- Ejaculatory failure
- Inadvertent spinal or epidural injection

Techniques to Avoid Complications

- Though blind injection techniques have been reported, the standard of care is to perform this procedure under fluoroscopy
- Fluoroscopic guidance along with use of contrast agents can prevent injury to blood vessels and or avoidance of spinal/epidural injection

Clinical Pearls

- CRPS → dysfunction within the sympathetic nervous system → excessive sympathetic outflow → vasoconstriction, cooler temperature, discoloration (blue), and pain in the affected limb.
- Blockade of the sympathetic fibers via the LSB provides relief from pain arising from CRPS, phantom limb, ischemic disease, and neuropathic pain of the lower extremities.
- Block is performed at **L2 or L3** under fluoroscopic guidance.
- Change in temperature or blood flow (measured by a Doppler flowmeter) on the ipsilateral side is objective evidence of successful blockade

MCQ (5)

1. Which of the following conditions is treatable by a lumbar sympathetic block?
   A. CRPS of the left upper extremity
   B. CRPS of the left lower extremity
   C. Intractable pain from pancreatic cancer
   D. Phantom limb pain of the right upper extremity
2. Which of the following landmarks are commonly used for lumbar sympathetic block?
   A. T12
   B. L3
   C. L4
   D. L5
3. Confirmation of a successful lumbar sympathetic block is accomplished via demonstration of
   A. Loss of complete sensation over the ipsilateral limb
   B. Change in color over the contralateral limb
   C. Change in temperature over the ipsilateral limb
   D. Loss of motor function over the ipsilateral limb
4. A patient with a long history of burning pain in the right lower extremity had spinal block at L4/5 level. He is unable to lift his leg but pain remained unchanged. What is the most likely cause?
   A. Pain in the head
   B. Myofascial pain dysfunction syndrome
   C. Failed epidural
   D. Complex regional pain syndrome
5. Which of the following is not a potential complication of lumbar sympathetic blocks
   A. post dural puncture headache
   B. aorta puncture
   C. pneumothorax
   D. apnea

Answers to MCQs

1. B, 2. B, 3. C, 4. D, 5. C

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55 Sympathetic Blocks: Superior Hypogastric Block and Neurolysis

Pete C. Schmidt

Introduction

- Visceral pain located **below the umbilicus** generally responds to superior hypogastric plexus block.
- The superior hypogastric plexus is located in the retro-peritoneum and extends from the **anterior aspect of L5 and sacrum**. It mediates most of the nociceptive afferents from the pelvic organs (**uterus, ovaries, prostate, bladder, distal colon, vulva, penis, upper rectum)**.
- The plexus contains coalescence of sympathetic postganglionic fibers formed from pelvic sympathetic fibers of the aortic plexus and **L2 and L3 splanchnic nerves**.
- As these fibers descend, at a level of L5, they begin to divide into the **hypogastric nerves.** From the plexus, the right and left hypogastric nerves follow in close proximity to the iliac vessels and pass into the pelvic plexuses, which are situated on either side of the rectum, seminal vesicles, bladder, and prostate. Afferent fibers from the pelvic viscera pass through the plexus.
- Neurolytic blocks should be reserved for **cancer-related pain** or debilitating non-malignant pain due to the risk of complications

Anatomy

- The superior hypogastric plexus is located in the retroperitoneum
- The plexus is located anterolaterally on the vertebral bodies and provides visceral innervation to most of the pelvic organs (excluding ovaries and fallopian tubes) (Fig. 55.1)
- The block is traditionally performed using bilateral needles directed towards the anterior portion of L5, with needle tips eventually **anterolateral to the L5/S1 disc** [1]
- This block is technically difficult due to the iliac crests and L5 transverse processes
- Additional techniques have been described using anterior-approach ultrasound, anterior-approach fluoroscopy, intradiscal approach, and CT guidance [2].

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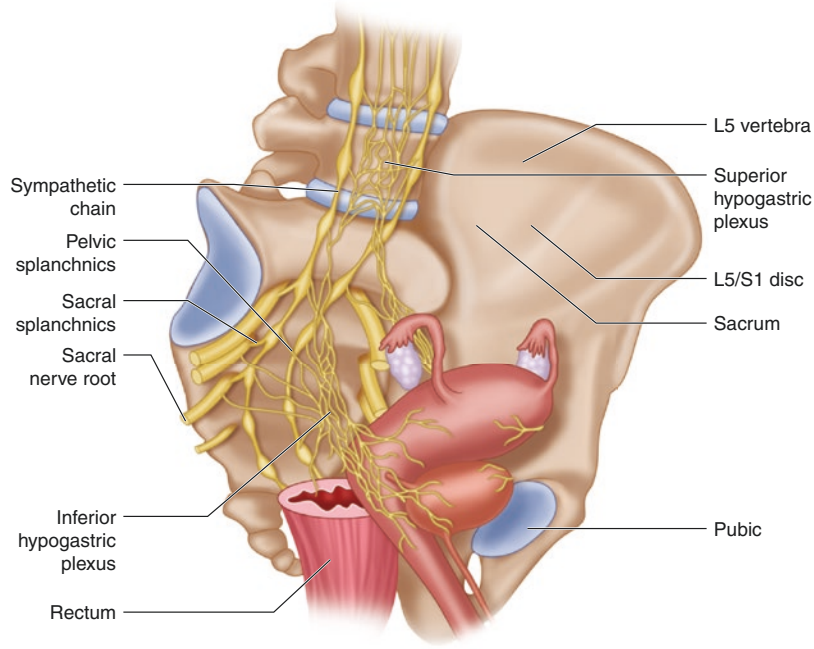
Fig. 55.1 Anatomy



Indications [3, 4]

- Cancer pain affecting the pelvic organs
- Postoperative pain relief after hysterectomy
- Chronic post-prostatectomy pain
- Gynecologic pain from endometriosis, adhesion, and chronic inflammation
- Interstitial cystitis
- Penile pain

Contraindications

- Anticoagulation
- Poorly-controlled diabetes (if steroid is to be used)
- Severe scoliosis or spondylosis
- Heart disease that would not tolerate hypotension

Types of Block

Diagnostic (Temporary) Blocks

- Performed as detailed above but with medications limited to local anesthetic, with or without steroid or clonidine
- Contrast dye injection should always be used to confirm needle tip location prior to injection
- If the patient has constant baseline pain in the block target area, it is logical to minimize analgesia immediately prior to the procedure to maximize diagnostic sensitivity
- If the diagnostic block is positive (patient has a meaningful reduction in pain), the practitioner may opt to proceed the neurolytic block immediately

Therapeutic Blocks

- Identical to diagnostic blocks but injection of local anesthetic is followed by the injection of either phenol (10–15%) or pure ethyl alcohol
- Both neurolytic agents work by denaturing neural proteins, leading to Wallerian degeneration (See chapter Table 21.1, Chap. 21)
- Duration of effect is widely variable but it is not uncommon to repeat neurolysis after 6–12 months if there is a return of pain (Fig. 55.2)

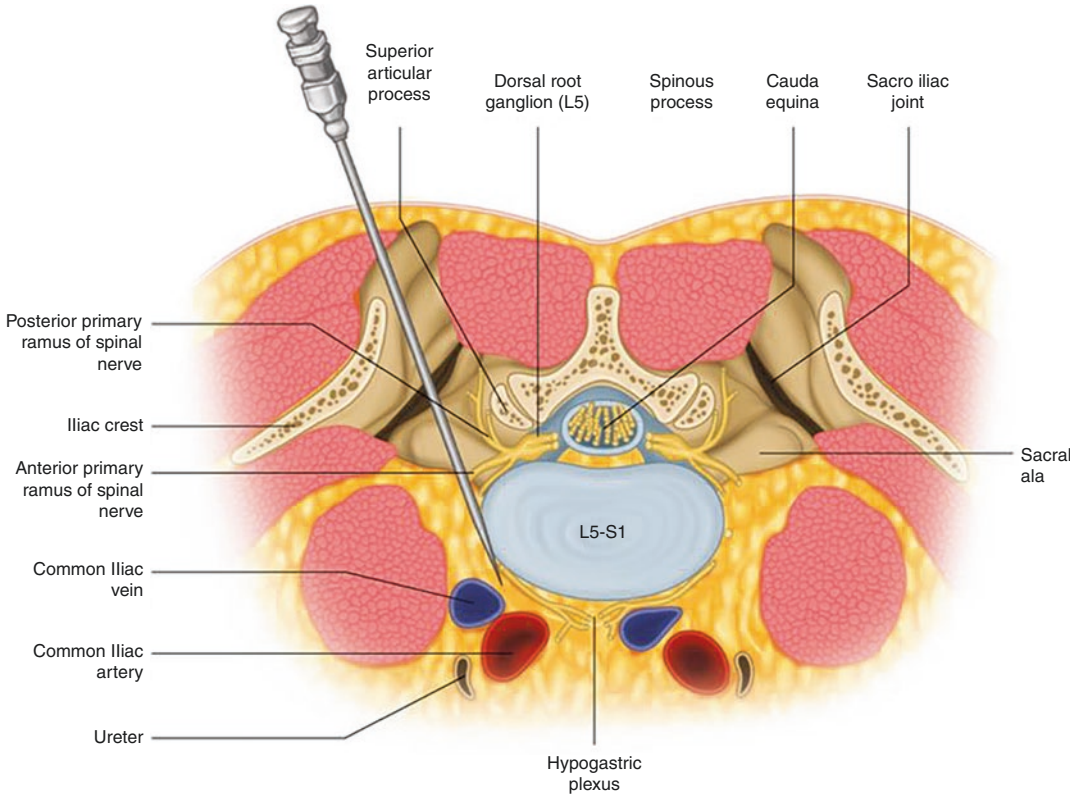


Fig. 55.2 Needle approach

Complications

- Minor: bleeding, bruising or pain at the injection site, transient hypotension
- Major: infection, iliac vessel damage, local anesthetic toxicity, ureter damage, nerve root damage or destruction

Clinical Pearls

1. Superior hypogastric blocks are technically challenging and often reserved for **cancer-related pain** [5]
2. The blocks provide pain relief to organs of the pelvis
3. These blocks must be performed under fluoroscopic guidance by an experienced practitioner because of adjacent structures
4. The targeted anatomical landmark is **L5/S1**

Questions

1. Which of the following structure is unlikely to be damaged by the superior hypogastric block?
   A. Aorta
   B. Spinal nerve roots
   C. Urinary bladder
   D. Pancreas
2. Visceral pain from which of the following organs might be responsive to a superior hypogastric block?
   A. Bladder
   B. Liver
   C. Duodenum
   D. Pancreas
3. Across which two vertebral levels is the superior hypogastric plexus located?
   A. L2/3
   B. L3/4

C. L4/5
D. L5/S1

4. Which of the following structures make superior hypogastric plexus blocks uniquely challenging?
   A. Iliac crests
   B. Spinous process of L4
   C. Diaphragm
   D. Psoas muscle

Answers

1. D, 2. A, 3. D, 4. A

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Sympathetic Blocks: Ganglion Impar Block and Neurolysis

56

May Chin, James Evan Fenska, and Magdalena Anitescu

Introduction

- Ganglion impar (ganglion of Walther) is the ganglion located **most caudally** in the sympathetic chain and is the **only unpaired ganglion** of sympathetic chain [1].
- The ganglion impar block was first described in 1990 for use in perineal pain from malignancy.
- The use of the ganglion impar block has now expanded to include other chronic pelvic pain syndromes such as Complex Regional Pain Syndrome (CRPS), postherpetic neuralgia, **coccydynia** as well as cancer pain from the pain **from distal rectum, distal urethrae, perineum**, distal 1/3 of vagina, and vulva.

Anatomy (Fig. 56.1)

- Paired paravertebral sympathetic trunks rise from thoracolumbar roots and travel the length of the spinal column.
- At the level of the coccyx, the paired trunks merge at the midline, forming a **solitary ganglion** called the **ganglion impar** (*Impar*- Latin for "odd"). It is also known as Ganglion of Walther [1].
- The Ganglion Impar is typically found in the **midline**.
- **Retroperitoneal** structure, it is anterior to sacrum and posterior to rectum.
- Ganglion impar extends from sacrococcygeal line to the first or second coccygeal vertebra.
- It contains both visceral afferent nerves and postganglionic sympathetic fibers that supply the perineum and visceral pelvic organs, including the **perianal region, distal portion of rectum, distal urethra, scrotum, vulva, and distal 1/3 of vagina**.

Indications for Performing the Ganglion Impar Block [1, 2]

- **Malignant Pain** arising from metastatic or local invasion of:
  - Anus
  - Distal rectum
  - Perineum
  - Distal urethra and Bladder
  - Uterine Cervix
  - Distal vagina
  - Scrotum

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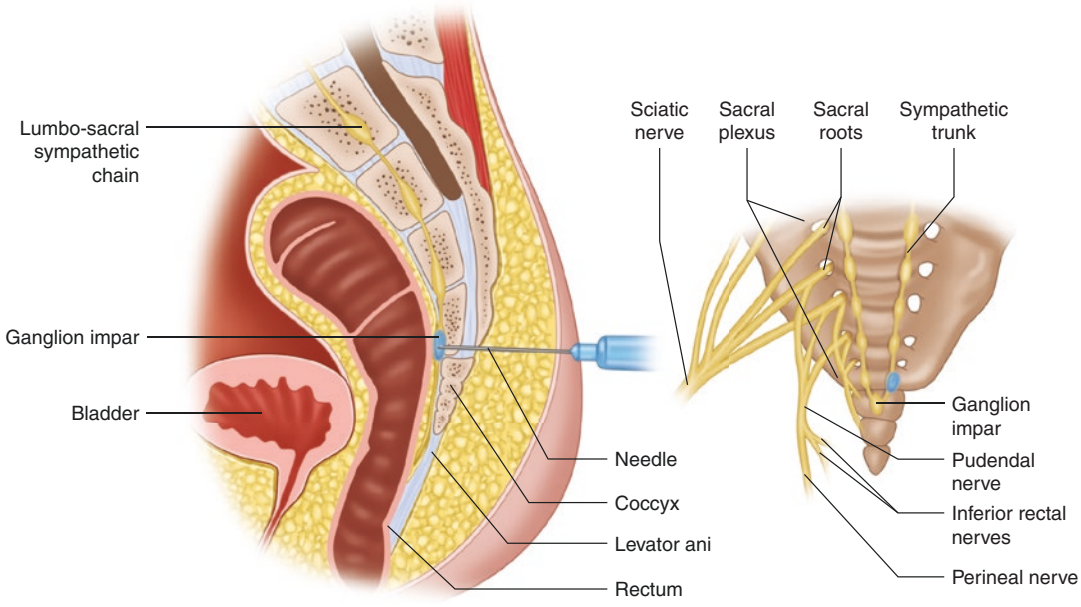

Fig. 56.1 Ganglion impar: coronal and sagittal section

- **Nonmalignant Pain**
  - Coccydynia
  - Sacrococcygeal pain
  - Perianal pain
  - Chronic Pelvic Pain

Contraindications to Performing the Block

- **Absolute Contraindications**
  - Anticoagulation
  - Infection near injection site
  - Local Anesthetic Allergy
  - Patient Refusal
- **Relative Contraindications**
  - Prior Failed Block
  - Presence of local bony metastasis due to risk of tumor seeding
  - Thrombocytopenia

Technique

- The patient is placed in a prone position with a pillow under their abdomen to minimize lordosis.
- The fluoroscope is placed in the A-P axis to ascertain the midline for needle insertion.
- The C-Arm is then rotated to the lateral view to visualize the sacrococcygeal joint or the intracoccygeal joint as well as the **anterior sacro-coccygeal line**.
- A spinal needle is advanced until the tip of the needle is visualized **just anterior to the sacrum** and posterior to the rectum.
- Iodinated contrast is injected to confirm placement of the needle. This may appear as a curved shaped image, hence the name, the **"comma sign"** (Fig. 56.2).
- The fluoroscope can then be returned to A-P axis to confirm midline spread of contrast without vascular uptake.
- Typically, a **diagnostic block is first performed** with local anesthetic with the optional addition of a corticosteroid.
- Following a successful diagnostic block with pain relief, a **neurolytic block using phenol or ethanol (alcohol)** may be considered (Table 56.1).
- For noncancer pain, a neurolytic block is generally avoided due to **risk of denervation pain**. Conservative treatments with NSAIDs, pelvic physical therapy, and ergonomic cush-

Table 56.1 Characteristics of ethanol and phenol for neurolysis [4, 5]

	Phenol	Ethanol
Common concentrations	4–6%	Commercially available 95% or higher. Lower concentrations used when mixed with local anesthetic
Pain on injection	Painless	Painful
Onset	15 minutes	Immediate
Duration	8–12 weeks	12–24 weeks
Baricity to CSF	Hyperbaric	Hypobaric
Mechanism of neurolysis	Denatures proteins, microvascular thrombosis	Disrupts myelin sheath, Wallerian degeneration
Mechanism of healing	Nerve roots regenerate, then Schwann cells and myelin	Schwann cells provide structure for axonal regrowth (Wallerian regeneration)
Adverse effects/risks	Painless burns, neuroma formation, neuritis, hypotension, flaccid paralysis	Neuritis, vasospasm, paralysis, painful injection

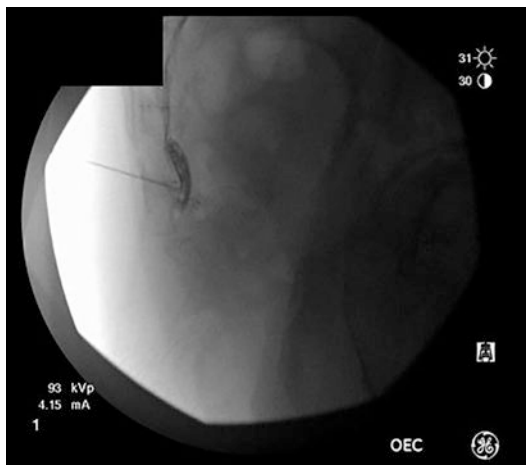

Fig. 56.2 Comma sign. Spread of contrast for ganglion impar block shows a distinctive comma shape in lateral fluoroscopy

ions remain the mainstay of management of these etiologies.
- Radiofrequency ablation may be considered to prolong relief in cancer and noncancer pain if conservative treatments are ineffective [3].

Neurolysis

- Indicated for pain from primary or metastatic cancer of **perineum, anus, distal rectum, or vulva**.
- May use phenol or alcohol for neuroablation after a successful prognostic block with local anesthetic (Table 56.1).
- Phenol and Ethanol have different mechanisms of action, treatment profiles, and adverse effects which can guide selection (Table 56.1).
- Regeneration: Healing occurs via **Wallerian regeneration** in which Schwann cells re-align to provide structure for regrowth of axon
- Ethanol is **hypobaric to CSF**; if it diffuses into CSF, it may cause paralysis
- Injection of ethanol causes **severe pain on injection** and therefore is frequently administered following or with a local anesthetic
- It has a **faster onset** and a **longer duration of effect** compared to phenol

Complications (Uncommon) of Ganglion Impar Block

- Local cellulitis around injection site
- **Perforation of rectum**
- Neuritis if using neurolytic agents
- Sciatic nerve impingement
- Block Failure
- Rare risk of bladder, bowel, sexual dysfunction

Clinical Pearls

- Ganglion Impar Block is commonly indicated for visceral pain associated with cancer in the **perianal and pelvic area**. It may also be useful in a variety of chronic pain syndromes such as **coccydynia.**
- In patients with malignant pain, successful **prognostic block with local anesthetic** may be followed by a **neurolytic block**.
- **Ethanol** and **Phenol** are the two most common agents used for neurolysis. They each have different mechanisms of action, side effect profiles, and pharmacodynamics.
- Complications are rare, although there is a potential for **rectal trauma**, and neuritis with neurolytic blocks.

Questions

1. Which of the following best describes the Ganglion Impar?
   A. A paired sympathetic ganglion at the sacral level
   B. A retroperitoneal structure at the L5 level
   C. A retroperitoneal solitary ganglion close to the sacrococcygeal junction
   D. A solitary ganglion anterior to the rectum at the sacrococcygeal junction
2. The following conditions may benefit from a ganglion impar block EXCEPT:
   A. Pain from cancer of the cecum
   B. Vulvodynia
   C. Pain from cancer of the bladder
   D. Coccydynia
3. Which of the following is true regarding neurolysis with ethanol compared to phenol?
   A. Injection of Ethanol alone is typically painless
   B. Ethanol has a longer duration of action than phenol
   C. Ethanol is hyperbaric to cerebrospinal fluid
   D. Ethanol is more potent than phenol
4. Which of the following is a may be an adverse effect from neurolysis using Phenol?
   A. Neuritis
   B. Vasospasm
   C. Hypoglycemia
   D. Cephalad Intrathecal Spread
5. The Ganglion Impar conveys sympathetic nerve fibers arising from which two vertebral levels?
   A. Cervical and Sacral
   B. Cervical and Thoracic
   C. Thoracic and Lumbar
   D. Lumbar and Sacral

Answers

1. *C*. The Ganglion Impar is a solitary sympathetic ganglion located retroperitoneally on the midline. It is found anterior to the sacrococcygeal junction and posterior to the rectum.
2. *A*. The ganglion impar block is indicated for malignant and nonmalignant pain from pelvic viscera and perineal structures, including the anus, rectum, bladder, cervix, vagina, and scrotum. Pain sensation from the cecum is typically transmitted via the lesser thoracic splanchnic nerves of T5-T12, and thus pain from cancer of the cecum would not be treated by a ganglion impar block.
3. *B*. Compared to Phenol, Ethanol has a faster onset and longer duration, typically 8–12 weeks. Ethanol is also less potent than phenol, as 100% ethanol is typically used for neurolysis whereas the concentration of phenol commonly used is 6%. Ethanol causes neurolysis via myelin destruction and Wallerian degeneration, whereas phenol causes protein denaturation and axonal destruction. Pure ethanol causes severe pain on injection, so it is frequently given with local anesthetic. Ethanol is hypobaric to CSF, and may cause unwanted neurolysis of cephalad nerves if it diffuses into the CSF.

4. *A*. Neuritis may be associated with phenol injection affecting peripheral nerves although this risk may be more common with alcohol. Other adverse effects of neurolysis with phenol include hypotension from vascular uptake, flaccid paralysis, neuroma formation, and painless burns in the event of skin contact. Injection of phenol is painless due to its local anesthetic activity, whereas ethanol injection would be severely painful.
5. *C*. The ganglion Impar is the caudal termination of the paired sympathetic trunks which lie anterolateral to the vertebral bodies throughout the length of the spine. These sympathetic trunks arise from the lateral horn of the thoracic and lumbar spinal cord, and exit the spinal cord via the thoracic and lumbar ventral roots.

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Neuropathic Pain: Postherpetic Neuralgia

57

Chikezie N. Okeagu, Alex D. Pham, and Alan D. Kaye

Introduction

- **Chronic neuropathic pain** condition that persists 3 months or more following an outbreak of **shingles (herpes zoster)** [1]
- Shingles is caused by the **varicella zoster virus (VZV)**, the same virus that causes chicken pox [1]
- More than 95% of adults have been exposed to VZV. Exposure typically occurs in childhood [1]
- **1 out of 3 people** in the United States will develop shingles in their lifetime. Increased incidence in the **elderly and immunocompromised** [1, 2]
- Characteristic **painful dermatomal rash** follows initial nonspecific symptoms (fever, headache, malaise)
  - Pain often precedes rash [2]
- Rash initially maculopapular similar to hives and progresses to **blistering vesicular rash** [3]
  - Possible to have shingles pain without rash/lesions - *Zoster sine herpete* [2]
- **Thoracic dermatomes** most commonly affected, followed by **trigeminal dermatomes** (most frequently ophthalmic division) [2]
- Neurological disease with the highest incidence in the US; approximately 1 million cases yearly [1]
- **10–20%** of people with shingles (herpes zoster) will go on to develop PHN [1]
- Risk factors for development of PHN [1]
  - Female gender
  - Advanced age
  - Severe shingles prodrome (i.e particularly painful case, presence of significant rash)
  - Elevated fever in the acute phase of shingles episode
  - Sensory dysfunction in the affected dermatome

Signs and Symptoms

- Pain that persists in the affected dermatome **≥3 months** following the healing of the shingles rash [1]
- Pain is **neuropathic** in quality. Itching of lesions also causes distress [3]

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- Common characteristics of PHN associated pain include [3]:
  - Constant aching or burning pain
  - Paroxysmal electric shock-like pain
  - **Allodynia**- exaggerated pain response to typically innocuous stimuli
  - **Hyperalgesia**- amplification of pain response to noxious stimuli
- Loss of sensory function may occur [3]
- Perturbation of motor function occurs in rare cases (muscle weakness, tremor, paralysis) [4]

Pathophysiology

- After resolution of primary infection, VZV lies dormant in the **dorsal root ganglia** (Fig. 57.1) [3]
- VZV reactivates and replicates within the ganglia of susceptible patients traveling **anterograde** through 1 or more spinal nerves [5]
  - Results in characteristic vesicular rash in one or two unilateral dermatomes [5]
- Virus triggers **inflammatory immune response** capable of damaging peripheral and central neurons [3]
- Damaged neurons **lose ability to inhibit nociceptive pain signals** [3]
  - Lowers threshold for nociceptive pain activation causing disproportionate response to stimulus
- Also results in **lower threshold for action potential** causing spontaneous discharge of neurons [3]

Diagnosis and Treatment

- Diagnosis is made through **history and physical** [3]
- Staples of treatment include (first line) [3]:
  - **alpha-2 delta ligands (i.e., gabapentin preparations, pregablin)**
    And/or
  - **Tricyclic antidepressants**
- Tramadol or opioids generally considered as second line treatments [3]
- Topical medications may also be used as adjunct treatments (capsaicin, lidocaine patches) [3]
- No role for anti-viral medication in PHN treatment, although they may prevent progression of acute herpes zoster to PHN
- Treatment can be challenging in elderly patients in the setting of multiple comorbidities and polypharmacy [3]
- Prevention of shingles through vaccination against VZV is the most effective means of preventing PHN [1, 2]

Prognosis

- Even with optimal treatment, only ~50% of patients achieve clinically significant pain relief.
- Pain typically lessens or resolves over time [1]
- Some patients experience persistence pain for months, years, or life [1]

Clinical Pearls

- The Varicella Zoster Virus (VZV) is responsible for both chicken pox and shingles.
- After primary infection (chicken pox), VZV lies dormant in the dorsal root ganglia. The virus may reactivate in susceptible patients with weakened immunity leading to secondary infection known as Herpes Zoster (shingles)
- Post herpetic neuralgia is an agonizing potential complication of Shingles that occurs when pain persists for a prolonged duration of time (>3 months)
- The pathophysiology is thought to involve immune mediated inflammatory damage to central and peripheral neurons leading to aberrant functioning
- First line treatments include alpha-2 delta ligands, TCAs, and opioids/tramadol. Topical capsaicin and local anesthetics may be used as adjuncts
- Even with treatment, clinically significant pain relief is difficult to achieve

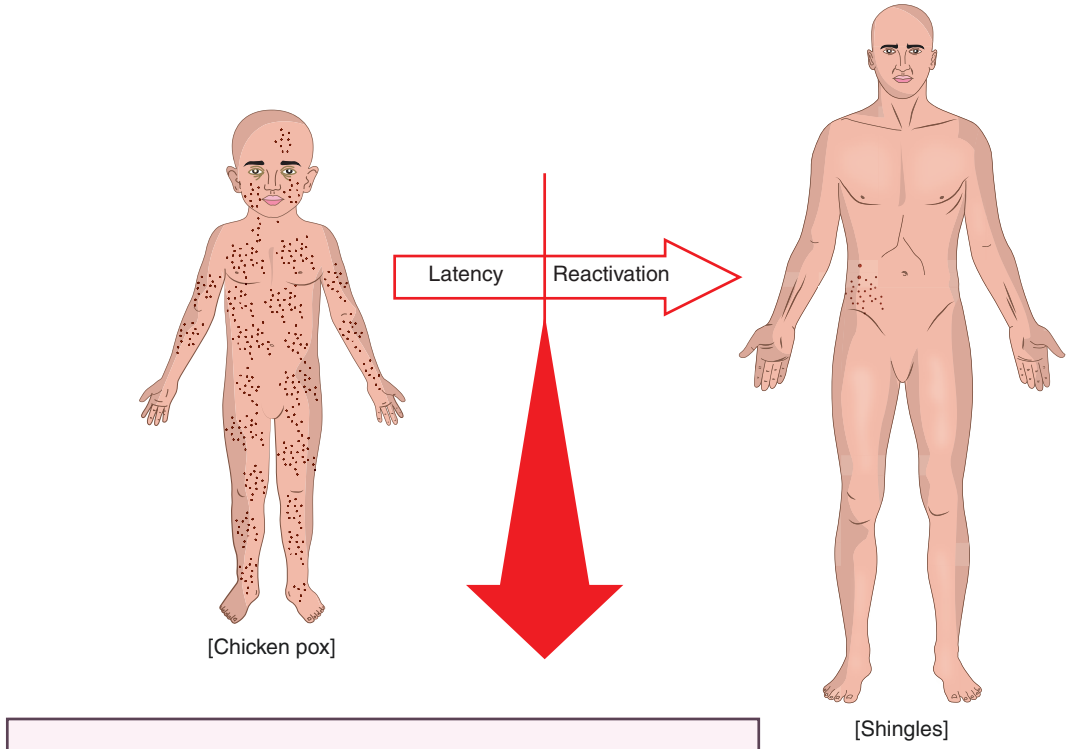

Fig. 57.1 After primary infection, VZV remains latent in the DRG. As immunity wanes due to age or immunosuppression, VZV can reactivate and manifest as shingles

- Prevention of chickenpox and/or shingles through vaccination is the most reliable means of preventing PHN

MCQ

1. **During the latency period, the Varicella Zoster Virus lies inactive in the _____?**
   A. Dorsal root ganglia
   B. Mastoid air cell
   C. Alpha-motor neuron
   D. Glossopharyngeal nerve
   E. None of the above
2. **What is the mechanism by which VZV causes neuropathic pain?**
   A. VZV increases the action potential threshold for peripheral and central neurons
   B. VZV lowers the action potential threshold for peripheral and central neurons
   C. A and B
   D. VZV causes a reduction of nociceptor proliferation
   E. None of the above
3. **A 74-year old man presents to your office complaining of pain in a band like distribution on his right flank. He reports no past medical history and tells you that his PCP told him that his health is "astonishingly excellent". The patient notes that he has been taking hydroxychloroquine prophylactically in order to protect himself from SARS-CoV-2 infection. On further questioning, you learn that the patient previously had a vesicular rash that was confined to the T8 dermatome on the right side. While the rash healed more than 3 months ago, the pain has persisted. Which of the following medications would NOT be effective in treating the patient's condition?**
   A. Gabapentin
   B. Topical Lidocaine Patches
   C. Amitriptyline
   D. Valacyclovir
   E. Tramadol
4. **A 68-year old woman presents to your office for a routine visit. She tells you that a friend of hers recently had shingles and is now struggling with post herpetic neuralgia pain. She asks you what, if anything, could have been done to prevent the development of PHN. How would you educate this patient?**
   A. Vaccination against VZV is the most effective method of preventing shingles and the subsequent episode of PHN
   B. Early treatment with high dose opioids can shorten the duration of PHN pain
   C. There is no role for capsaicin cream in the treatment of PHN
   D. SSRI anti-depressants are widely considered as the first line treatment for PHN pain
5. **Which of the following dermatomes is most commonly afflicted by herpes zoster and PHN?**
   A. Coccygeal
   B. Lumbar
   C. Thoracic
   D. Sacral
   E. Saphenous

Answers

1. A, 2. B, 3. D, 4. A, 5. C

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Further Reading

See references.

Neuropathic Pain: Phantom Limb Pain and Central Post-Stroke Pain

58

Daniel Rothstein and William Grubb

Introduction

Phantom Limb Pain

- Phantom limb pain is a painful sensation in a missing limb after amputation.
- Stump pain is pain in the residual portion of the limb after amputation.
- Phantom limb sensations are abnormal sensations such as paresthesia, dysesthesia, and hyperpathia of the missing limb that are not painful.
- Phantom limb pain is a neuropathic pain (pain in the absence of a clear nociceptive stimulus) and a poorly understood pain syndrome. It is a diagnosis of exclusion after other causes of stump pain including ischemia, infection, neuroma, and pressure-related wounds are eliminated.

Phantom limb sensation	Phantom limb pain	Stump pain
Acute to chronic	Typically present in the first week after amputation but can persist up to several years.	Acute pain that gradually subsides in 1–3 weeks. Pain may become chronic due to poor wound healing or neuroma.

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Phantom limb sensation	Phantom limb pain	Stump pain
Symptoms in the missing limb	Symptoms in the missing limb	Symptoms in residual limb
Painless	Neuropathic pain	Nociceptive pain

Inadequate control of preoperative and postoperative pain may increase the risk of phantom limb pain.

- The incidence of phantom limb pain in patients post-amputation is 50–80% [1].
- Persistence of phantom limb pain beyond 6 months after amputation is associated with a poor prognosis.
- Phantom limb pain typically will present in the first week after amputation but can persist for up to several years.
- Risk factors for phantom limb pain include:
  - Females
  - Upper limb amputations
  - Presence of pre-amputation pain
  - Poor pain control perioperatively
  - Poor pain control postoperatively
  - Presence of stump pain
  - Presence of emotional factors such as depression and anxiety

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Central Post-Stroke Pain

- Central pain is defined as pain stemming from a lesion or dysfunction of the central nervous system (spinal cord, brainstem, or cerebral) [2].
- Central post-stroke pain is a neuropathic pain syndrome that results from a cerebral vascular accident and occurs in 1–8% of patients post-stroke.
- Strokes involving structures within the **spinothalamocortico-tract** are associated with the highest incidence of central post-stroke pain.
- Other types of chronic pain syndromes may also occur in patients post-stroke, such as musculoskeletal pain, hemiplegic shoulder pain, headache, and painful spasms.

Symptoms and Signs

Phantom Limb Pain

- Typical pain descriptors include **burning, stabbing, tingling, electric-type**, and **numbing** [1].
- The pain is usually intermittent and moderate to severe in intensity.
- The distal portion of the phantom limb (i.e. hand or foot) is typically the most painful.
- **Telescoping** occurs in some patients. It is a phenomenon where the middle portion of the phantom limb is perceived to be shortened (i.e. the foot is perceived to be close to the stump).
  - Telescoping is associated with a **poor prognosis.**
- Chronic stump pain (also known as residual limb pain) occurs in 5–10% of patients post amputation and may co-exist with phantom limb pain.
  - Hyperalgesia and allodynia may be present at the stump with subcutaneous **neuromas** contributing to the pain.

Central Post-Stroke Pain

- Central post-stoke pain is often debilitating and can be difficult to diagnose, especially in the setting of cognitive or speech dysfunction that may exist post-stoke [2].
- Pain may be constant or intermittent.
- Typical descriptions of pain are related to thermal sensory changes, such as burning, freezing, and shooting.
- Common signs include allodynia, hyperalgesia, dysesthesia.
- Depression often coexists due to debilitating pain and functional limitations post-stroke.

Pathophysiology

Phantom Limb Pain

- The specific pathophysiology of phantom limb pain is not well understood but can be broadly described by three mechanisms: peripheral, spinal, and supraspinal [3].
  - Peripheral

    Peripheral sensitization results from upregulation of voltage gated sodium channels in the peripheral nervous system and dorsal root ganglion resulting in hyperexcitability.
  - Spinal

    Lamina reorganization: crosslinking between afferent non-noxious neurons with afferent noxious neurons from different lamina.

    Central sensitization: increase of noxious stimuli from the peripheral nervous system leads to upregulation of N-methyl-D-aspartate (NMDA) receptors in the central nervous system.
    - Mediated by substance P, tachykinins and neurokinins

There is a decrease in activity of the descending inhibiting spinal tracts. This leads to the phenomenon known as "**windup**" and is associated with changes in the firing of central nociceptive neurons.

– Supraspinal

Cortical reorganization: restructuring of the somatosensory and motor cortex whereby the area that corresponded to the amputated limb is replaced by neighboring body areas.

Central Post-Stroke Pain

- The pathophysiology of central post-stroke pain remains unclear and likely involves multiple interacting mechanisms.
- **Central sensitization** plays a key role in the development of central post-stroke pain and other types of chronic neuropathic pain [4].
  - Decreased synaptic thresholds lead to increased neuronal firing.
  - Augmented activation of NMDA and sodium channels.
  - Heightened excitability of neurons in central pain pathways.

Treatment

Phantom Limb Pain

- Effective perioperative pain control (e.g. epidural**,** peripheral nerve block, or patient controlled analgesia) is associated with decreased incidence of phantom limb pain.
- Phantom limb pain is often refractory to treatment. A multimodal approach is important to achieving optimal outcomes.
- Treatment options include non-pharmacologic, pharmacologic, interventional, and surgical techniques [5].
  - Non-pharmacologic

    TENS unit, biofeedback, cognitive therapy, and acupuncture have shown mild to moderate benefit.

    Mirror therapy has shown significant benefit [6].
    - Non-invasive modality in which a patient sees a mirror reflection of the non-amputated limb in place of the amputated limb.
  - Prosthesis: well-fitting prosthesis or the use of an assistive device can reduce phantom pain.
  - Pharmacologic

    Acetaminophen and NSAIDs can be used as first line oral analgesics.

    Adjuvant analgesics such as anticonvulsants (gabapentin, pregabalin, carbamazepine, etc.), antidepressants (duloxetine, nortriptyline, amitriptyline, etc.), muscle relaxants (cyclobenzaprine, baclofen, tizanidine, etc.), local anesthetic (mexelitine), and NMDA blockers (ketamine, methadone) may be helpful in chronic phantom limb pain.

    Opioid analgesics (tramadol, oxycodone, morphine, methadone, etc.) should be considered for severe or refractory pain.
  - Interventional

    Injection therapy: limited benefit has been shown from epidural, sympathetic, or peripheral nerve blocks.

    Neuromodulation techniques such as spinal cord stimulation and deep brain stimulation have shown variable outcomes.
    - A systematic review of 12 studies on spinal cord stimulation in the treatment of phantom limb pain showed mixed results [7].

    Percutaneous peripheral nerve stimulation of femoral and/or sciatic nerves achieved significant pain relief and improvement in quality of life in small studies [8].
  - Surgical

    Dorsal root entry zone lesioning has shown benefit in upper phantom limb pain but studies are lacking in lower phantom limb pain.

Stump revision surgery may be considered for patients with neuromas resulting in chronic intractable stump pain.

Given the lack of evidence and level of invasiveness, surgical modalities are limited to the most refractory patients.

Central Post-Stoke Pain

- Treatment options for central post-stroke pain are limited.
- Specific targeted treatments are lacking due to poorly understood pathophysiology and heterogeneity of the disease processes in stroke patients.
- Adjuvant pain medications used in neuropathic pain syndromes are the preferred treatment modality [4].
  - Antidepressants

    Tricyclic antidepressants amitriptyline and nortriptyline are first line treatments.

    Selective serotonergic receptor inhibitors venlafaxine and duloxetine may also be considered.
  - Antiepileptics

    Lamotrigine and gabapentin have shown moderate effectiveness.
- Interventional treatments
  - Spinal cord stimulation and deep brain stimulation **are not effective**.
  - **Motor cortex stimulation** may be considered for refractory central post-stroke pain.

Questions

1. Which of the following is *not* a risk factor for developing phantom limb pain post-amputation?
   A. Presence of pre-amputation pain
   B. Lower limb amputation
   C. Poor perioperative pain control
   D. Presents for stump pain
2. Telescoping is a phenomenon of phantom limb pain in which:
   A. The middle portion of the phantom limb is perceived to be shortened and is associated with a poor prognosis
   B. The middle portion of the phantom limb is perceived to be elongated and is associated with a poor prognosis
   C. The middle portion of the phantom limb is perceived to be shortened and is associated with a good prognosis
   D. The middle portion of the phantom limb is perceived to be elongated and is associated with a good prognosis
3. The following treatment has *not* been shown to significantly reduce pain in patients with phantom limb pain:
   A. Good perioperative pain control at time of amputation surgery
   B. Mirror therapy
   C. Epidural steroid injections
   D. Appropriately fitted prosthesis
4. The following medication has shown significant benefit in the treatment of central post stroke pain:
   A. Topiramate
   B. Oxycodone
   C. Pregabalin
   D. Amitriptyline
5. The following neuromodulation modality is likely to be most effective in treating central post-stroke pain:
   A. Spinal cord stimulation
   B. Deep brain stimulation
   C. Dorsal root ganglion stimulation
   D. Motor cortex stimulation

Answers

1. B, 2. A, 3. C, 4. D, 5. D

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59 Neuropathic Pain: Peripheral Neuropathies

Anna Irwin and Christian Renwick

Introduction [1]

- Neuropathy refers to pathology affecting one (mono-neuropathy) or many (polyneuropathy) peripheral nerves, with the **distal nerves** usually affected commonly.
- Mono-neuropathy includes trauma or compression of a single nerve such as carpal tunnel syndrome or meralgia paresthetica (Table 59.1, Fig. 59.1e).
- Multiple mono-neuropathy (mono-neuritis multiplex) is caused by vascular pathology and presents with peripheral neuropathy in two or more nerves. The history is important in distinguishing between **polyneuropathy and mono-neuropathy multiplex**.
- The peripheral nerves are susceptible to toxic, infectious, hereditary and inflammatory factors that can impair their function and lead to polyneuropathy (Table 59.1).
- Polyneuropathy is caused by a wide variety of disease: DM, alcohol abuse, and HIV, Charcot-Marie-Tooth disease, ESRD/uremia, Lyme's disease, Vitamin B12 or folate deficiency, porphyria, amyloidosis, Guillain-Barré syndrome, chemotherapy, and idiopathic (up to 50% of cases).
- Polyneuropathies are classified further into neuropathies of large fiber (A-alpha and A-beta) and small fiber (A-delta and C) neuropathy (Fig. 59.1a, b).

Table 59.1 Classification of neuropathy

Mononeuropathy	Polyneuropathy
Carpal tunnel syndrome	Hereditary disorders Charcot marie tooth Hereditary sensory neuropathy
Radial nerve palsy	Inflammatory disease Guillian Barre syndrome Vasculitis Chronic inflammatory demyelinating Polyneuropathy (cidp)
Lateral femoral cutaneous neuralgia	Systemic disease Diabetes Paraneoplastic syndrome
Piriformis syndrome (sciatic nerve)	Toxins INH Alcohol Chemotherapy
Tarsal tunnel syndrome (tibial nerve)	

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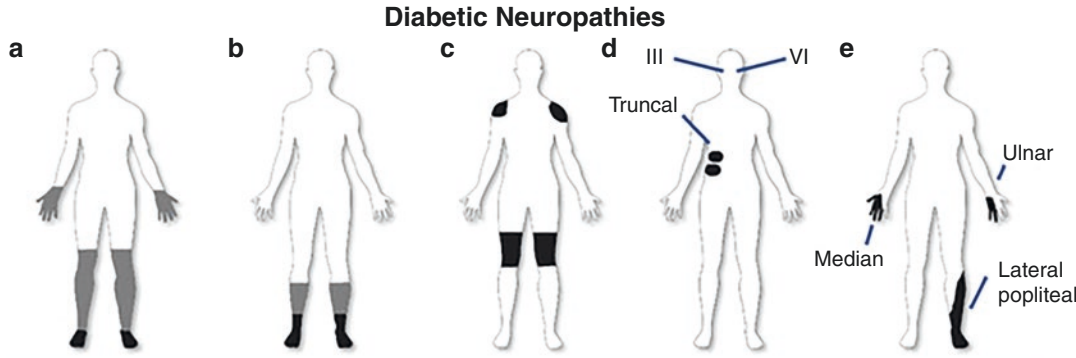
Mechanism

- The general mechanism of neuropathy relates to inflammatory, metabolic, and ischemic effects on the peripheral nerves.
- In autoimmune neuropathies such as Guillain-Barré syndrome the **damage to the myelin and schwann cells** is caused by immune complex. Often inflammatory cells invade the axons to cause damage.
- Alcohol, chemotherapy, and toxic chemicals (eg. INH), primarily cause **axonal damage** and occasionally demyelination as in the case of n-hexane exposure.
- Hereditary diseases such as Charcot-Marie-Tooth disease and Krabbe disease are predominately **demyelinating** in nature however substantial coexistent axonal loss can also be present. Mitochondrial disorders most often exhibit an axonal pattern.
- Up to 50% patients have no identifiable cause of the neuropathy. This is referred to as **idiopathic neuropathy**. It typically begins **in adults over 50 years old** and progresses over months to years. Electrodiagnostic studies show a primarily axonal polyneuropathy. Proposed but unproven causes include impaired glucose tolerance, hypertension, dyslipidemia, and increased **oxidative stress**.

Diagnosis

- Large fiber neuropathies (Fig. 59.1a) present with **aching pain, weakness, poor balance, and history of fall,** while painful small fiber neuropathies (Fig. 59.1b) present with **stabbing, electric shock like pain, allodynia, hyperalgesia, affecting distal extremities** symmetrically (distal to proximal pattern).
- Loss of proprioception, sensation to touch, vibration, impaired reflexes, abnormal nerve conduction study are **hallmark of large fiber neuropathy**. On the other hand, small fiber neuropathies present with impaired response to **pin prick and temperature**, normal strength and reflexes, and **abnormal skin biopsy** (loss of epidermal nerves).



Large-fiber neuropathy	Small-fiber neuropathy	Proximal motor neuropathy	Acute mono neuropathies	Entrapment
Sensory loss: 0 – +++ (touch vibration)	Sensory loss: 0 – + (thermal allodynia)	Sensory loss: 0 – +	Sensory loss: 0 – +	Sensory loss in nerve distribution: + – +++
Pain: + – +++	Pain: + – +++	Pain: + – +++	Pain: + – +++	Pain: + – +++
Tendon reflex: N - ↓↓↓	Tendon reflex: N – ↓	Tendon reflex: ↓↓	Tendon reflex: N	Tendon reflex: N
Motor deficit: 0 – +++	Motor deficit: 0	Proximal motor deficit: + – +++	Motor deficit: + – +++	Motor deficit: + – +++

N, normal

Vinik A et al. Clin Geriatr Med. 2008;24:407.

Fig. 59.1 Clinical presentation of the different types of neuropathy [5]

EMG/NCS/Skin Biopsy/QST [2]

- Patients with mild symptoms who have a known reason for neuropathy **do not** need extensive work up.
- When history and physical is not conclusive other testing may be warranted.
- Nerve conduction studies (NCS) and electromyography (EMG) help determine neuroanatomic localization, severity, chronicity, and physiology (**demyelinating vs axonal**). **NCS will be normal in small fiber neuropathies.**
- NCS are carried out by applying an electrical stimulus to the skin overlying a nerve trunk, followed by the recording of the generated electrical response over either the nerve trunk or muscle innervated by it, at some distance from the stimulation.
- NCS are useful in the assessment of the degree of axonal damage but **they evaluate large myelinated fiber functions.**
- EMG records the electrical potentials generated in a muscle belly through a needle electrode inserted in the muscle. It records **activity during needle insertion**, during **periods of rest** (spontaneous activity), and **during periods of voluntary muscle contraction.**
- In EMG, needle insertion is accompanied by brief bursts of electrical activity. Continued burst firing of potentials well after needle placement is **abnormal.** Muscles are electrically silent at rest; thus **spontaneous electrical activity** at rest may be pathologic. **Myopathy vs neuropathy** can be distinguished with EMG.
- While nerve conduction studies are best for large fiber neuropathies, **most painful peripheral neuropathies are small fiber** in nature. Skin biopsy help in diagnosis of small fiber neuropathy.

Management [3]

- Priority treatment is management of underlying processes, such as glycemic control for diabetic neuropathy.
- Pharmacotherapy includes antidepressants, such as tricyclic antidepressants (**TCAs**) and SNRIs (including duloxetine or venlafaxine), and gabapentinoid drugs, such as gabapentin and pregabalin.
- Topical agents can prove useful, such as lidocaine patches, capsaicin creams, and TENS units.
- Chronic inflammatory demyelinating polyneuropathy requires a different treatment eg glucocorticoids, IVIG, or plasma exchange.
- For toxic drug induced neuropathy eg chemotherapy or drug induced neuropathy, **discontinuation of causative agent** is the first step.

Diabetic Neuropathy

- Distal symmetrical polyneuropathy is the most common form of diabetic neuropathy and presents as pain in the toes and distal foot but eventually progresses until it affects the foot and legs per a **stocking distribution** (Fig. 59.1b)
- Affects both type 1 and type 2 diabetics mellitus
- 4–8% of patient with DM have neuropathy by the time of diagnosis
- Burning and/or shooting pain presentation

Clinical Pearls [4]

- In diabetic neuropathy, hyperglycemia is responsible for damaging the nerves
- Medications beneficial for treating peripheral neuropathic pain include TCAs, SNRIs, Gabapentin, and Lyrica
- Diabetic neuropathy typically presents as pain in the toes and distal foot, but eventually progresses to affect the foot and legs per a **stocking distribution** (Fig. 59.1b)
- EMG/NCS are usually more informative with identifying large fiber neuropathies, however, most peripheral neuropathies **affect small fiber nerves.** Skin biopsy help in diagnosis of small fiber neuropathy.

Questions

1. What is the most common distribution of diabetic neuropathy?
   A. distal to proximal distribution
   B. Burning in the knees
   C. Unilateral arm pain
   D. Jaw Pain
2. Painful small fiber neuropathy typical presents with:
   A. Deep-throbbing pain
   B. Electric, stabbing, shooting pain
   C. Pulsatile pain
   D. Aching sensation
3. Small fiber neuropathy can be diagnosed with which of the following test?
   A. Nerve conduction study
   B. Electromyography
   C. Deep tendon reflex
   D. skin biopsy
4. Most painful neuropathies are
   A. Small fiber neuropathy
   B. Mononeuropathy multiplex
   C. Carpal tunnel syndrome
   D. Large fiber neuropathy

Answers

1. A, 2. B, 3, D, 4. A

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Neuropathic Pain: Genitofemoral Nerve Block

60

Xiaoying Zhu and Dmitri Souza

Introduction

Genitofemoral nerve block (GFNB) is used to diagnose and treat pain from genitofemoral neuralgia [1, 2].

- Genitofemoral neuralgia is a chronic pain condition usually caused by nerve damage from trauma or surgeries in the inguinal or pelvic region, such as inguinal hernia repair, C section, appendectomy, and laparoscopic surgeries [3].
- Combined with ilioinguinal nerve block, GFNB can be used for surgical anesthesia or postoperative pain for inguinal herniorrhaphy or testicular surgery.

Anatomy

- Genitofemoral nerve (GFN) is a branch of lumbar plexus (Fig. 60.1).
- It consists mainly of sensory fibers, from L1 and L2 spinal nerves [3, 4].
- GFN passes downward in retroperitoneal space, pierces the psoas muscle to descend along the anterior surface of the muscle.
- It divides into a genital and femoral branch at a variable distance above the level of the inguinal ligament.
- The genital branch travels downward medially (just lateral to the pubic tubercle),
  - in males, together with the spermatic cord, supplying motor fibers to the cremaster muscle and sensation to the scrotum [3].
  - in females, accompanying the round ligament, innervating the mons pubis and the labia majora [3].
- The femoral branch travels alongside the external iliac artery to the femoral sheath (lateral and superficial to the femoral artery).
- It innervates a small area of the skin of the anterior superior part of the thigh (the femoral triangle) [3] (Fig. 60.1).
- The relation between the genital branch and the spermatic cord varies considerably; it can travel outside the spermatic cord dorsally, ventrally, or inferiorly.

Indications

- Diagnose and treat chronic genitofemoral neuralgia.
- Surgical anesthesia/postoperative pain for inguinal hernia repair and testicular surgery

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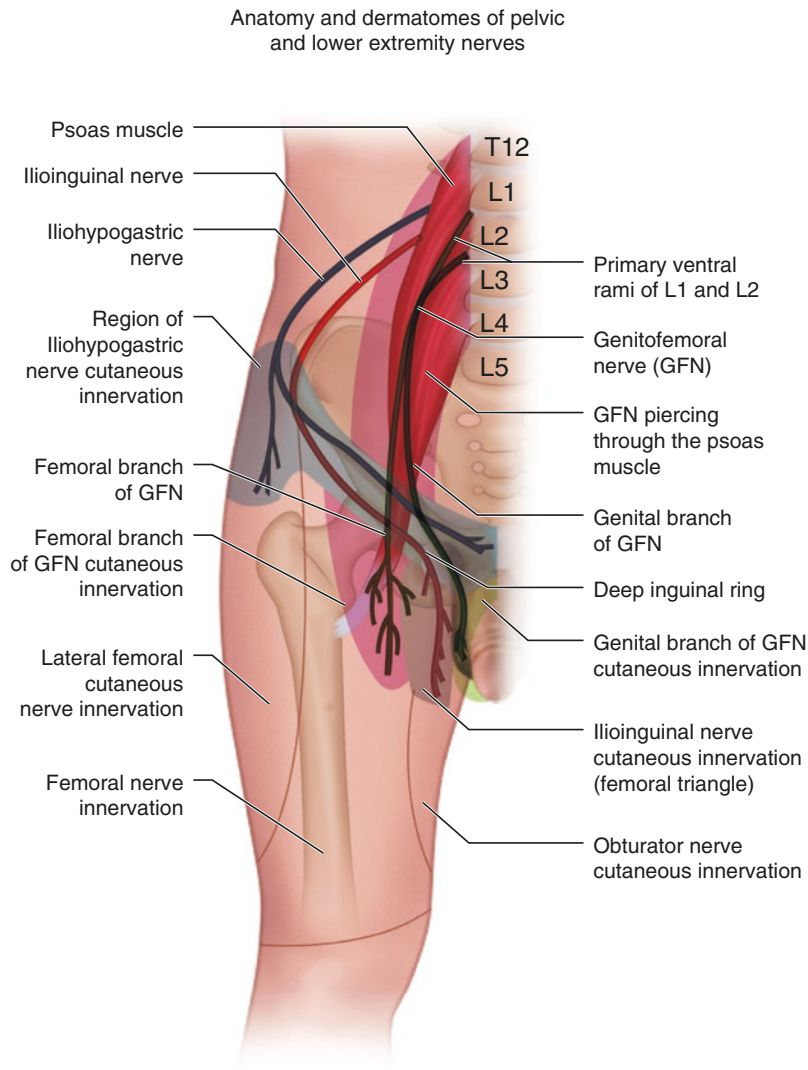

Fig. 60.1 The genitofemoral nerve arises from the fusion of the ventral primary rami of L1 and L2 and pierces the psoas muscle, then descends along its anterior surface and splits into the genital branch and the femoral branch proximal to the inguinal ligament. The genital branch supplies sensation to the spermatic cord, scrotum, and adjacent thigh in males and the labia majora, mons pubis, and adjacent thigh in females. It is shown passing through the deep inguinal ring. The femoral branch supplies sensation to the anterior proximal thigh just lateral to the femoral triangle

when combined with ilioinguinal and iliohypogastric nerve blocks.

Techniques

US Guided: Genital Branch Block

- A high-frequency linear probe is placed perpendicular to the inguinal ligament, about 1 to 2 cm lateral to the pubic tubercle [1].
- When the probe is moved cephalad, the femoral artery (longitudinal section) is visualized penetrating deep to become the external iliac artery. At this point, an oval or round structure (the cremaster in males, the round ligament in females) superficial to the femoral artery can easily be visualized (Fig. 60.2). The probe is then moved in the medial direction, slowly, moving away from the femoral artery. The needle is inserted in-plane, injecting local anesthetic only for diagnosis, or local anesthetic plus steroid for therapeutic effect, for a total of 10 ml.
- Because of the anatomical variability, it is recommended to inject half of the injectate inside the spermatic cord, but outside the vessels and vas deferens [4].

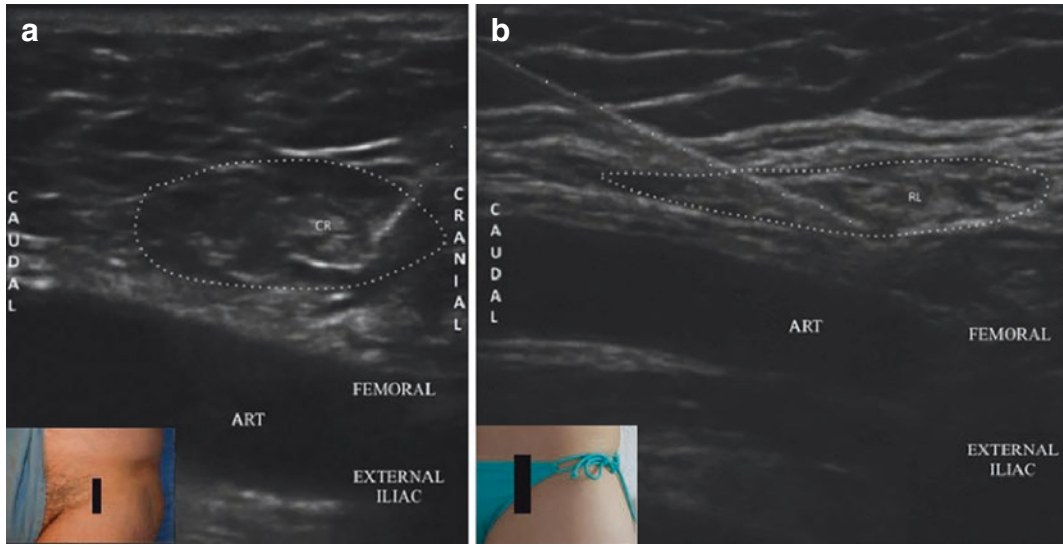

Fig. 60.2 Cross-sectional ultrasound image of the internal inguinal ring filled with local anesthetic and needle tip near the cremaster or round ligament. Dotted line represents the internal inguinal ring; (**a**) male, (**b**) female, CR cremaster, RL round ligament, ART femoral artery (superficial) and external iliac artery (deep). (Image courtesy of Thiago Nouer Frederico, MD)

US Guided: Femoral Branch Block

- A high-frequency linear probe, approximately a third of the distance between the pubic tubercle and the anterior superior iliac spine, caudal to the inguinal ligament [1].
- The femoral branch is superficial and lateral to the femoral artery, above the space between the femoral artery and femoral nerve (Fig. 60.3).
- A needle inserted in-plane, inject 10 ml of injectate around the nerve.

Complications Specific to GFNB

- Spermatic cord structures (testicular artery and vas deferens) damage
- Inadvertent femoral nerve block
- Peritoneal cavity transgression

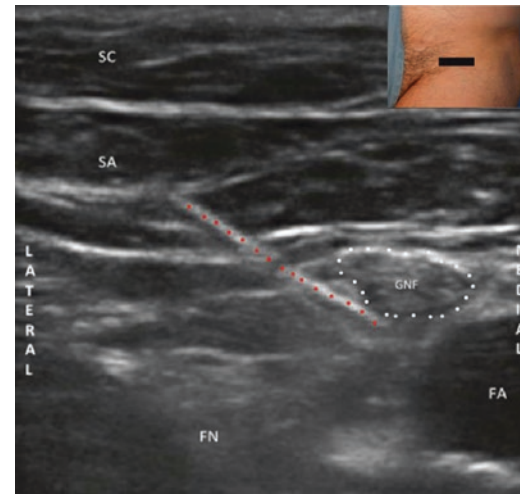

Fig. 60.3 Ultrasound image taken transversely below the inguinal ligament, showing injection of the femoral branch of the genitofemoral nerve. Note the needle (red dots) and the space distension by the local anesthetic (white dots). FA femoral artery, FN femoral nerve, GNF femoral branch of genitofemoral nerve, SC subcutaneous tissue, SA sartorius muscle. (Image courtesy of Thiago Nouer Frederico, MD)

Preventive Measures to Avoid Complications

- No vasoconstrictors in the injectate to avoid testicular artery vasoconstriction.
- No particulate steroid

Clinical Pearls

1. GFNB is commonly used to diagnose and treat pain from genitofemoral neuralgia (groin pain, genital pain, suprapubic pain).
2. Pain may be misdiagnosed as interstitial cystitis, endometriosis, inguinal or femoral hernias, hip joint pathologies.
3. There is usually point of tenderness just lateral to the pubic tubercle.
4. Numbness in GFN distribution is confirmatory for successful GFNB.
5. GFN, ilioinguinal and iliohypogastric nerves originate from similar levels of spinal nerve roots, and innervate adjacent areas. Therefore, it is often clinically difficult to determine which nerve is causing the pain.
6. If a patient reports pain suggestive of genitofemoral neuralgia that does not respond to GFNB, a lesion more proximal in the lumbar plexus or an L1 radiculopathy should be considered.

Questions

1. What spinals nerves give rise to the GFN?
   A. T10 T11
   B. L1 L2
   C. L3 L4 L5
   D. S1 S2
2. What anatomical structures/areas does GFN innervate?
   A. Groin
   B. Scrotum, vagina, labia majora
   C. Anterior proximal thigh
   D. All of above
3. Which of the following medications can not be used for blocking the genital branch of GFN?
   A. Dexamethasone
   B. Bupivacaine
   C. Epinephrine
   D. Clonidine
4. What are the possible complications of GFNB?
   A. Intravascular injection
   B. Femoral nerve block
   C. Peritoneal penetration
   D. All of above
5. Genitofemoral neuralgia can be caused by
   A. Inguinal hernia repair
   B. C section
   C. Blunt trauma
   D. All of above

Answers

1. B, 2. D, 3, C, 4. D, 5. D

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Neuropathic Pain: Pudendal Nerve Block

61

Rahul Chaturvedi, Rajiv Reddy,
and Krishnan Chakravarthy

Introduction

The second stage of labor is related to both uterine pain (T10-L1), as well as birth canal pain which is supplied by the pudendal nerves (S2-S4). Prior it epidural anesthesia, the block was preferred for second stage of delivery to relieve pain from introital distension and perineal repair. (when fetus is in birth canal it is mostly somatic pain supplied by pudendal nerve).

- Used for chronic pelvic pain secondary to pudendal neuralgia

Anatomy

- The pudendal nerve is a mixed sensory-motor nerve, which originates from the spinal rami of spinal nerves, **S2-S4** (Fig. 61.1).
- The nerve exits through the greater sciatic foramen, below the sacrospinous ligament. It reenters the pelvic cavity through the lesser sciatic foramen, coursing above the sacrotuberous ligament.
- The pudendal nerve courses intimately with the pudendal artery and vein and lies medially to the pudendal vessels.
- After entering the pudendal or "Alcock's" canal, the nerve gives off two branches—the **inferior rectal nerve** and the **perineal nerve.** The pudendal nerve then continues to course through the perineum as the **dorsal nerve**, which provides sensory innervation to the **penis** and **clitoris**.
- The inferior rectal nerve provides sensory input to the **perianal skin** and motor input to the **external anal sphincter.**
- The perineal nerve branches off into the superficial perineal and deep perineal branches. The perineal nerve provides motor input to the **levator ani, bulbospongiosus and ischiocavernous** muscles and provides sensory innervation to the **scrotum** in males and **labia majora** in females.

Indications

- Obstetric procedures
  - Second stage of labor
  - Perineal laceration or episiotomy
  - Hemorrhoidectomy

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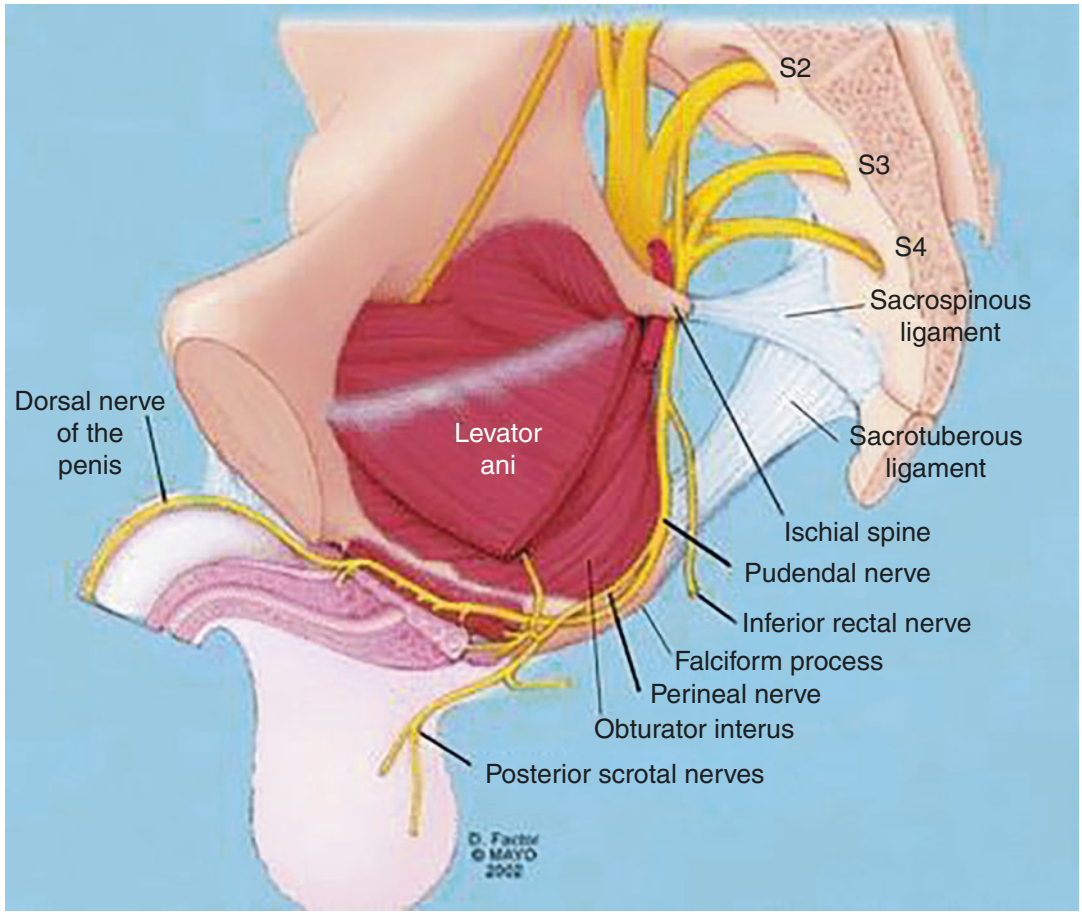

Fig. 61.1 Schematic anatomy of the intrapelvic path of the pudendal nerve. (From Popeney et al. [6]. Reprinted with permission from John Wiley and Sons and used with permission of Mayo Foundation for Medical Education and Research. All rights reserved; Reproduced with permission from Mayo Clinic foundation)

- Urologic procedures
  - Transurethral prostatectomy
  - Transrectal prostate biopsy
- Pudendal neuralgia: characterized by [1] pain in the anatomical territory of the pudendal nerve; [2] worsened by sitting; [3] the patient is not woken at night by the pain; [4] no objective sensory loss on clinical examination; [5] positive anesthetic pudendal nerve block.

Approaches to the Pudendal Nerve Block

Transvaginal Approach

- This is the most common approach for obstetric procedures, with the patient in the **lithotomy** position.

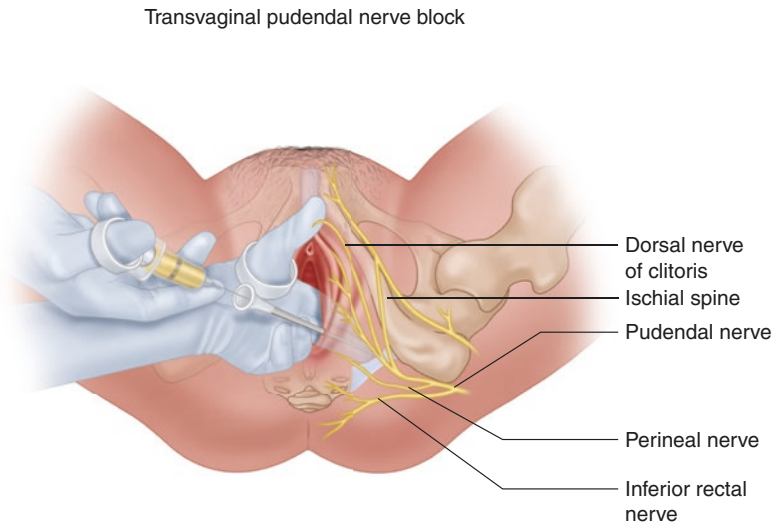

Fig. 61.2 Transvaginal pudendal nerve block. (Reference: Rapkin [3]. Additional helpful images for illustrator: 1. https://www.aafp.org/afp/2012/0301/p447.html. 2. https://www.familygp.online/pudendal-block-2/)

- The first step involves identifying the **ischial spine** through the lateral vaginal wall (Fig. 61.2).
- Using a long needle, the sacrospinous ligament is punctured, and advanced 1 cm below the ischial spine.
- Following negative aspiration, the anesthestic (**lidocaine 1%** or **bupivacaine 0.25%**) is injected posterior to the ischial spine.
- Perform a sensory test (**pinprick**) in the ano-genital region to ensure adequate coverage.

Xray Guidance

- The patient is placed in the prone position on the procedure room table.
- AP fluoroscopic guidance was used to visualize pelvic inlet (at the level of the two femoral heads). The falciform process (the ischial spine) is then highlighted by 5- to 15-degree ipsilateral oblique angulation of the fluoroscope.

After 1% lidocaine infiltration using a 25 gauge 1.5 inch needle, a 25-gauge 3.5 inch needle is advanced to the tip of the ischial spine, where the pudendal nerve transiently leaves the pelvis (Fig. 61.3). After negative aspiration for heme, 5 mL of bupivacaine 0.25% is injected. (Pain Physician. 2004;7:319-322).

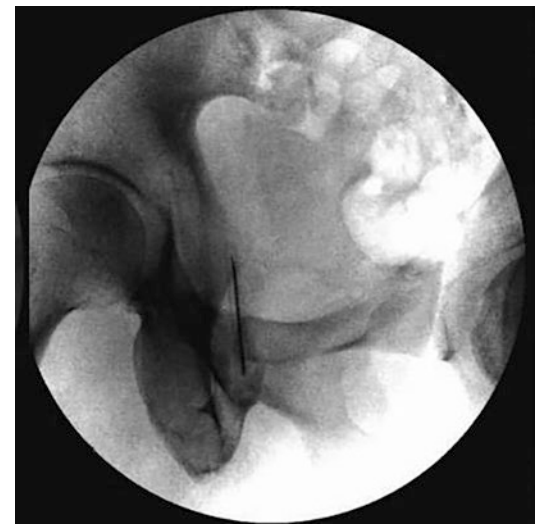

Fig. 61.3 Xray guided pudendal nerve block. (Reproduced with permission from: A novel technique for pudendal nerve block. Pain Physician. 2004;7(3): 319–22. (PMID: 16858468))

Clinical Pearls

1. Pudendal nerve block can be used for patients with pudendal neuralgia, gynecological procedures (second stage of labor, perineal laceration, episiotomy), hemorrhoidectomy, and various urological procedures (e.g, transurethral biopsy).
2. The pudendal nerve is a mixed sensory-motor nerve, which originates from the spinal rami

of spinal nerves, S2-S4. It provides sensory innervation to the skin of the perineum and mucosa of the anal canal and motor function of external anal sphincter, urethral sphincter, and perineal musculature.

3. knowledge of the nerve's close **proximity to ischial spine** is important when performing blocks either blind or image-guided approaches.
4. Nantes criteria have been proposed for diagnoses of pudendal neuralgia. Pudendal nerve block satisfy one of the nantes criteria.

Questions

1. Which of the following indications warrants a pudendal nerve block?
   A. First stage of labor
   B. Cesarean delivery
   C. Cystectomy
   D. Episiotomy
2. The pudendal nerve arises from which of the following nerve roots?
   A. L2-L4
   B. L4-L5
   C. S1-S2
   D. S2-S4
3. A 12-month-old boy presents for revision circumcision in the urology office. As the anesthesia resident, you plan on placing a nerve block for adequate anesthesia. Which of the following correctly describe the innervation of the penis?
   A. The iliohypogastric provides sensory innervation to the root of the penis.
   B. The dorsal penile nerve separates into two branches at the level of the pubic symphysis
   C. The dorsal penile nerve arises from the perineal nerve branch of the pudendal nerve.
   D. The pudendal nerve arises from the L2-L4 nerve roots
4. Twenty-four hours following vaginal delivery, a patient begins to report tingling around the lateral aspect of her thigh. Which of the following most likely led to this complication:
   A. Pudendal nerve block
   B. Epidural anesthesia
   C. Lithotomy Positioning
   D. Spinal anesthesia
5. One of your patients is extremely anxious about her upcoming pudendal nerve block and asks you for the most common symptoms. You let her know that the most common complication is:
   A. Bladder laceration
   B. Injection site infection
   C. Vaginal discomfort
   D. Bleeding

Answers

1. D, 2. D, 3. B, 4. C, 5. C

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Further Reading

Atlas of pain medicine procedures, Chapter 62: Pudendal nerve block; OB/GYN Hospital medicine, Chapter 69: Pudendal nerve blocks.

Cancer Pain: Overview

62

David Cassagnol and Magdalena Anitescu

Introduction

- **Chronic pain is common in the cancer population** with prevalence ranging between 15% and over 70% depending on the type and stage of disease [1].
- Cancer pain can be described as:
  - **Nociceptive**: somatic or visceral pain that is caused by tissue injury or mass effect
  - **Neuropathic**: a result of nervous system dysfunction or damage
  - **Mixed pain syndrome**: combination of nociceptive and neuropathic pain
- Cancer pain can further be categorized as **tumor vs non-tumor related**:
  - Tumor-related pain exists as a direct result of the neoplasm (e.g., vertebral compression fracture, DVT, pain from tumor invasion, etc.). About 75% of these patients have recognized chronic cancer pain syndromes [1]
  - Non-tumor related pain is usually associated with cancer treatment eg chemotherapy induced neuropathy, oral mucositis, pain from radiation therapy(e.g. Bone pain, plexopathy, enteritis etc) or surgical procedures.

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Cancer Pain Assessment

- The **description of the quality of the pain can point to its etiology**:
  - Cramping, sharp, aching, diffuse ➔ visceral pain
  - Throbbing, pressure, aching ➔ somatic
  - Stabbing, shooting, tingling, burning, electrical ➔ neuropathic
  - Transient, sudden, severe, flare-up ➔ breakthrough
- The quality of life and functional status assessments can be used as indicators of the impact of pain in the patient's life, prognosis and efficacy of treatment. Performance status scales such as the Eastern Cooperative Oncology Group (ECOG) or Karnofsky scales derive scores that estimate patients' ability to perform activities of daily living on their own. **The ECOG score** ranges from 0 to 5, with 0 being asymptomatic and fully functional and 5 being death [3].
- Elucidate medical and psychiatric comorbidities including anxiety, mood, personality and substance-use disorders.
- **identify needs for palliative care** Elucidate medical and psychiatric comorbidities including anxiety, mood, personality and substance-use disorders.
- while encouraging patients to take an active role in their pain management.

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Treatment of Cancer Pain

- **Primary treatment of malignancy** through various modalities such as: external beam radiation, surgical resection, chemotherapy and targeted therapies such as immunotherapy [1, 2].
- **Pharmacological management of cancer pain should adhere to the 3-step WHO analgesic ladder** algorithm (See details in Chap. 30) [4].
  1. Opioids
     - **Mainstay of cancer pain treatment**. They have the ability to significantly improve quality of life [1].
     - Drug selection should **match potency with intensity of pain** (weak opioids for mild to moderate pain and stronger opioids for severe pain) [4].
     - Dosing principles include rapid titration to effect, starting with the minimum recommended dose. As cancer pain is continuous, **immediate and slow-release** doses should be scheduled at regular intervals [2].
     - For opioid naïve patients, transdermal buprenorphine, tramadol, tapentadol or hydrocodone may be the initial drug of choice.
     - For patients with **kidney impairment**, hydromorphone or fentanyl are preferred rather than morphine or oxycodone
     - For intractable cancer pain with neuropathic component when other opioid therapy provides inadequate analgesia or required a high dose, trial of methadone may be initiated (40 mg/day maximum dose)
     - Consider **opioid rotation** in the absence of adequate analgesia or unacceptable side-effects. Typically, the new opioid is started at a **dose 25–50% lower than** the calculated equianalgesic dose (Fig. 62.1) [1].
     - **Oral administration of opioids is preferred**. However, with disease progression, other routes of administration may become necessary. Other modes of delivery include intrathecal drug delivery if patient's life expectancy **is >3 months**. If the life expectancy is **<3 months** tunneled epidural drug delivery or home PCA may be considered [2].

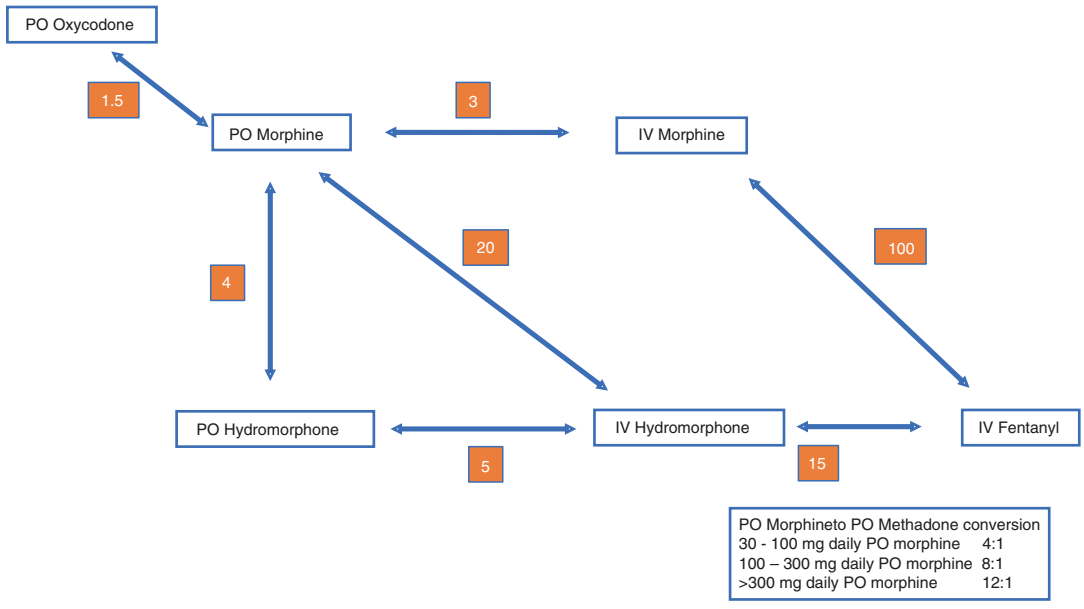

Fig. 62.1 Opioid analgesic conversion chart (also see Chap. 34)

2. Non-opioid analgesics/adjuvants
   - **Acetaminophen and NSAIDs are routinely used for all stages of cancer pain** although there is no significant evidence to support or oppose their use alone or in combination with opioids [2]. Their use is restricted during chemotherapy due to concern **for masking neutropenic fever**.
   - **Adjuvant analgesics can be co-administered at any step of the ladder** [4]. They are particular useful when opioids alone provide inadequate relief. These include many types of drugs: antidepressants, gabapentanoids, anticonvulsants, anxiolytics, hypnotics, local anesthetics, NMDA receptor antagonists and cannabinoids (Chaps. 32, 33, 34, 35, and 36, Chronic pain) [1, 2].
   - Gabapentin, pregabalin, duloxetine and TCAs are first-line treatments for neuropathic pain [2]. If the patient cannot tolerate these medication**, duloxetine** can be started as a third line agent for neuropathic pain (Chap. 32, Chronic pain).
   - Oral ketamine trouches or IV ketamine infusion have been shown some efficacy in cancer related neuropathic pain; the drug is likely helpful in cases of central sensitization or wind up (Chap. 35, Chronic pain) [2].

- Interventional therapies
  - Interventional techniques are appropriate **when conventional treatments do not provide adequate relief**. They can be used alone or in combination with systemic therapy. These techniques are discussed in more details in Chaps. 17, 18, 19, 20, 21, 26 and 27, Chronic pain.

Neurolytic Blocks/Spinal Neurolytic Blocks

- Neurolytic blocks are typically reserved for patients with **short life expectancy** as their effects typically last 3–6 months [1].
- Neurolysis modalities include dehydrated alcohol, phenol, radiofrequency ablation and cryoablation (Chap. 26, Chronic pain).
- The celiac plexus block is safe and effective in the **treatment of pain associated with pancreatic cancer and other upper intraabdominal malignancies**, providing several months of pain relief [2, 5]. It is routinely performed under fluoroscopic guidance at the **T12-L1** level. (See Chap. 18, Chronic pain)
- The superior hypogastric plexus block can relieve **pain in the pelvic region** related to malignancy of ovaries, uterus, cervix, bladder, rectum or prostate [5].
- It is performed under fluoroscopic guidance at the level of L5; technique can be trans-discal (one needle placement) or bilateral, under the L5 transverse process. (See Chap. 20, Chronic pain)
- Spinal neurolysis, although less frequently used than in the past, is useful for **focal pain in limited number of dermatomes as well as in deafferentation pain.** Duration of relief tends to be limited while neurological deficits are elevated [5].

1. Intrathecal drug delivery (Chap. 27, Chronic pain)
   - Intrathecal delivery of opioids and local anesthetics can be achieved through **implanted pumps** or tunneled catheters [1, 5].
   - This type of delivery generally allows for smaller doses and less side effects. Catheter is routinely placed around T8-T10 (Fig. 62.2); intrathecal medication used include opioids, local anesthetic, clonidine, ziconotide, alone or in various combinations.
   - **It is useful in pain refractory to escalating doses of systemic opioids, opioid rotation and switching of route of administration.**
   - IT pump placement is appropriate in patients with a **life expectancy greater than 3 months** [2].
2. Spinal cord stimulation (Please see Chap. 27 for details)

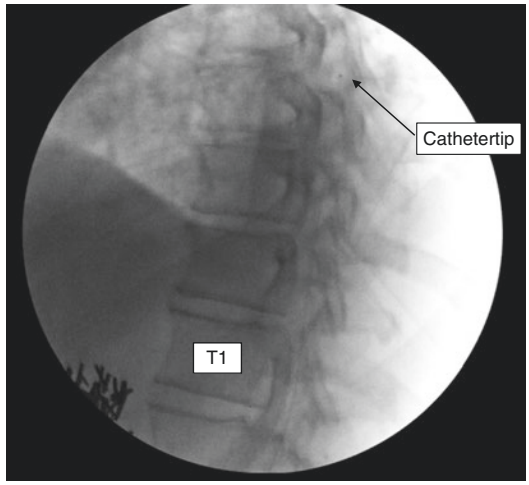

Fig. 62.2 Intrathecal catheter tip placed at T8-T9 interspace (also see Chap. 27)

- Spinal cord stimulation is a neuromodulation technique which can be applicable to cancer-related cases, especially when **slow-growing** [2].
- There exists a concern of inadequate pain control when tumor growth extends beyond the area covered by the stimulator.
- SCS can also be used in treating pain in cancer survivors. It has been described as a good treatment option in **chemotherapy induced peripheral neuropathy** of the lower extremities.

3. Peripheral nerve blocks/stimulation
   - Peripheral nerve and plexus blocks are used in combination with systemic agents when pain is distributed along one or more peripheral nerves such as pain associated to pathological fractures. Their effect is **short lasting** and the role limited in the cancer pain arena [2, 5].

- Integrative and rehabilitative therapies (Chap. 36, Chronic pain): Various therapies such as acupuncture, relaxation, biofeedback, hypnosis and guided imagery provide cancer pain patients with strategies that **increase coping, reduce pain and anxiety** [1, 5].

Clinical Pearls

- Chronic cancer pain can be nociceptive, neuropathic, tumor-related or non-tumor-related
- Adequate initial and ongoing assessments are instrumental to determine appropriate treatment
- Pharmacological treatment should be guided by the **WHO 3-step ladder** (Chap. 30, Chronic pain)
- Oral route and scheduled doses are preferred as cancer pain is continuous
- Best therapy is achieved with **longer acting analgesics** while immediate release agents are used for breakthrough pain
- Interventional techniques are appropriate when conventional treatments do not provide adequate relief or when patients have significant side effects from medications
- There is an increasing role for integrative and rehabilitative therapies in anxiety and pain reduction

Questions

1. A 17-year-old male with no past medical history is newly diagnosed with left femur Ewing sarcoma. He complains of intermittent mild pain with ambulation. According to the WHO analgesic ladder guidelines, which agent is the most appropriate therapy for this patient?
   A. Oral methadone
   B. Fentanyl patch
   C. Oral acetaminophen
   D. Oral morphine
2. A 64-year-old patient with severe chronic upper abdominal pain from pancreatic cancer uses 24 mg of IV morphine through a PCA pump. An allergy to morphine is suspected after development of a rash. Her physician wishes to convert IV PCA morphine to scheduled IV hydromorphone. What dose of IV hydromorphone should the patient be prescribed if administered every 4 hours?
   A. 1 mg

B. 0.6 mg
C. 0.8 mg
D. 0.4 mg

3. Which of the following would most likely benefit from a neurolytic block?
   A. Pelvic pain from prostate cancer
   B. Lower leg pain from tibial fracture
   C. Incisional pain from hernia repair
   D. Acute pain from chemical burn
4. A 56-year-old male with non-Hodgkin's lymphoma has been undergoing treatment with multiple chemotherapeutic agents including vincristine. He presents with bilateral moderate foot pain described as burning, tingling and pins-and needles. Select the correct type of pain experienced by the patient and the associated treatment.
   A. Nociceptive pain/Duloxetine
   B. Neuropathic pain/lidocaine patch
   C. Nociceptive pain/oral oxycodone
   D. Neuropathic pain/gabapentin
5. A 54-year-old female was diagnosed with multiple myeloma 18 months ago. Her course was complicated by a lumbar compression fracture 12 months ago, requiring escalating doses of oral morphine. She complains that her pain is no longer adequately treated and requests more pain medication. What is the next best step in management?
   A. Increase oral morphine dose
   B. Refer to addiction specialist
   C. Discontinue morphine and start oral hydromorphone at 70% of equianalgesic dose
   D. Continue oral morphine and add oral hydromorphone

Answers

1. C: the WHO analgesic ladder recommends non-opioids such as oral acetaminophen or oral ibuprofen +/− adjuvants for patients experiencing mild pain. Opioids are reserved for moderate or severe pain.
2. B: the first step consists of converting the patient's daily IV morphine dose to its oral equivalent:

$$\text{PO morphine} = \text{IV morphine} \times 3 = 24\ \text{mg} \times 3 = 72\ \text{mg PO morphine.}$$

In the second step, convert oral morphine dose to IV hydromorphone:

$$\text{IV hydromorphone} = \text{PO morphine} / 20 = 72\ \text{mg} / 20 = 3.6\ \text{mg IV hydromorphone per day}$$

In the third step, divide the daily IV hydromorphone dose by 6 (q4h = 6 doses/day):

$$3.6\ \text{mg} / 6 = 0.6\ \text{mg IV hydromorphone q4h.}$$

3. A: a neurolytic block can destroy a nerve or a plexus with chemicals, radio frequency ablation or cryoablation. Indications for neurolytic blocks include recalcitrant pain syndrome of malignant or benign etiologies. These include visceral pain from cancer, neuropathic pain (CRPS, herpes zoster, diabetes) or chest pain from chronic angina. Neurolytic blocks are usually not appropriate in the setting of acute pain.
4. D: this patient is likely experiencing neuropathic pain from peripheral neuropathy, a

known side effect of vincristine. Neuropathic pain typically presents with sensations of burning, tingling or shooting pain. It is commonly treated with gabapentin, pregabalin, duloxetine or TCAs.

5. C: this patient has developed tolerance to morphine as evidenced by increased pain intensity despite escalating dosing of opioids. In the absence of adequate analgesia or unacceptable side effects, opioid rotation should be considered. The new opioid should be started at a dose 20–50% lower than the equianalgesic dose. In this case, continuing morphine or adding adjuvants is unlikely to yield good relief. Addiction to opioids is rare in cancer patients.

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Neuroablation Techniques for Pain Management

63

Anita Gupta and Brent Earls

Introduction

- Neuroablation refers to any type of treatment used to reduce or disrupt (ablate) nerve signals or transmit pain signals [1].
- In general, it is considered a safe procedure involving a section of nerve tissue that is removed or destroyed either by heat, cold (**cryoablation**), radiofrequency (**rhizotomy**), or chemical application to a focused well demarcated area based upon a thorough history and physical examination [1].
- The treatment goal is to deter pain signals and reduce pain in that particular area with the neuroablation therapeutic intervention [1, 2].

Anatomy

- The targeted anatomy for the intervention is dependent on the targeted peripheral nerve or nerve plexus, and careful needle advancement is employed with guidance through ultrasonography, fluoroscopy, and in combination with techniques for sensory and motor nerve stimulation [1, 2].
- The anatomic locations for neuroablation differ depending on the type of pain and site of the specific symptoms in patients [1, 2].
- In general, most procedures performed along the peripheral sensory nerves should avoid the motor nerves to prevent long term complications [1, 2].
- Most commonly performed procedures include the **cervical and lumbar facet radiofrequency ablation** procedures for neck and lower back, respectively, which applies radiofrequency ablative pulses along the dorsolateral sensory medial branches of the nerves of the spine [2].
- For cancer pain, celiac plexus blocks and chemical neurolysis are commonly performed for pancreatic cancer-related pain in the area of anterolateral to the vertebral body of L1-L2 (See Chap. 18, chronic pain) [2].

Types of Interventional Neuroablation Procedures

Neuroablation can be divided into chemical and physical radiofrequency neurolysis. Both methods produce nerve injury and result in degeneration of the nerve fiber from the distal to the lesion, which causes a temporary interference in nerve cell transmission. Schwann cells are preserved which potentially allows for axonal regeneration

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with reconnection to the proximal end of the nerve fiber.

Radiofrequency Ablation

- Radiofrequency ablation (RFA) techniques are often used for nerve ablation of the medial branch nerve, percutaneous cordotomy, percutaneous rhizotomy, and percutaneous radiofrequency sympathectomy [4, 5] and a variety of other painful conditions and their treatments.
- Conventional RFA creates a current with an oscillating frequency, generating heat that makes circumscriptive lesions used for selective nerve lesioning.
- In most RFA procedures, heat is generated 60–80 C for 90 to 120 seconds to form well-localized in clinical procedures. RF thermal lesions produce irreversible protein denaturation when the tissue temperature rises above 60 °C.

Pulsed and Cooled Radiofrequency Ablation

Compared with thermal conventional RFA, pulsed RFA **at less than 42 °C** can avoid complications eg neuralgia, and deafferentation pain. It uses a 500 KHz current, applying 2 bursts/s with each pulse lasting 20 ms over a 120 second interval [3]. After pulsed RFA, the internal ultrastructural components of the axons show microscopic damage, including abnormal mitochondrial membranes and morphologic changes of the mitochondria, and disruption/disorganization of the microfilaments and microtubules. The damage is more pronounced in C-fibers than A-delta and A-beta fibers.

Chemical Ablation

Usually, alcohol or phenol are used for chemical ablation for cancer-related conditions. Alcohol is the most commonly used for intractable visceral cancer pain to produce damage to the unmyelinated sympathetic chains and ganglia. Chemical denervations are not recommened to use in the non-cancer patients with chronic pain.

Surgical Neurolysis

- Surgical neurolysis or neurectomy involves directly severing a nerve and is usually reserved for rare cases with a poor prognosis with a surgical specialist involved in collaboration to determine best course of action.
- This modality carries a high risk of **deafferentation pain**, which could be a complication due to loss of neuronal input, resulting in spontaneous firing within the spinothalamic tract [6].

Peripheral nerve injury induced by neuroablation (**high yield**)

- Neuroablation is basically iatrogenic peripheral nerve injury. A peripheral nerve is composed of the myelin, axon, endoneurium, fascicle, perineurium, and epineurium.
- Each axon is covered by **endoneurium**; fascicles are collection of axons, which are covered by **perineurium**. **The epineurium** surrounds the nerve trunk (Fig. 63.1).
- Peripheral nerve injury by neuroablation can be one of the three different stages of injury as described by Seddon (3,4): “Neurapraxia”, or first degree PNI (Fig. 63.1). Axons are anatomically intact, but nonfunctional. Full recovery is expected without any intervention can be expected within 3–6 months.
- “Axonotmesis”, the second degree PNI, involves damage to the nerve fibers but sheath and its supporting connective tissues still remain. “Neurotmesis (complete transection)”, the third degree PNI. Most of the connective tissue framework is lost and distorted including the epineurium (Fig. 63.1)

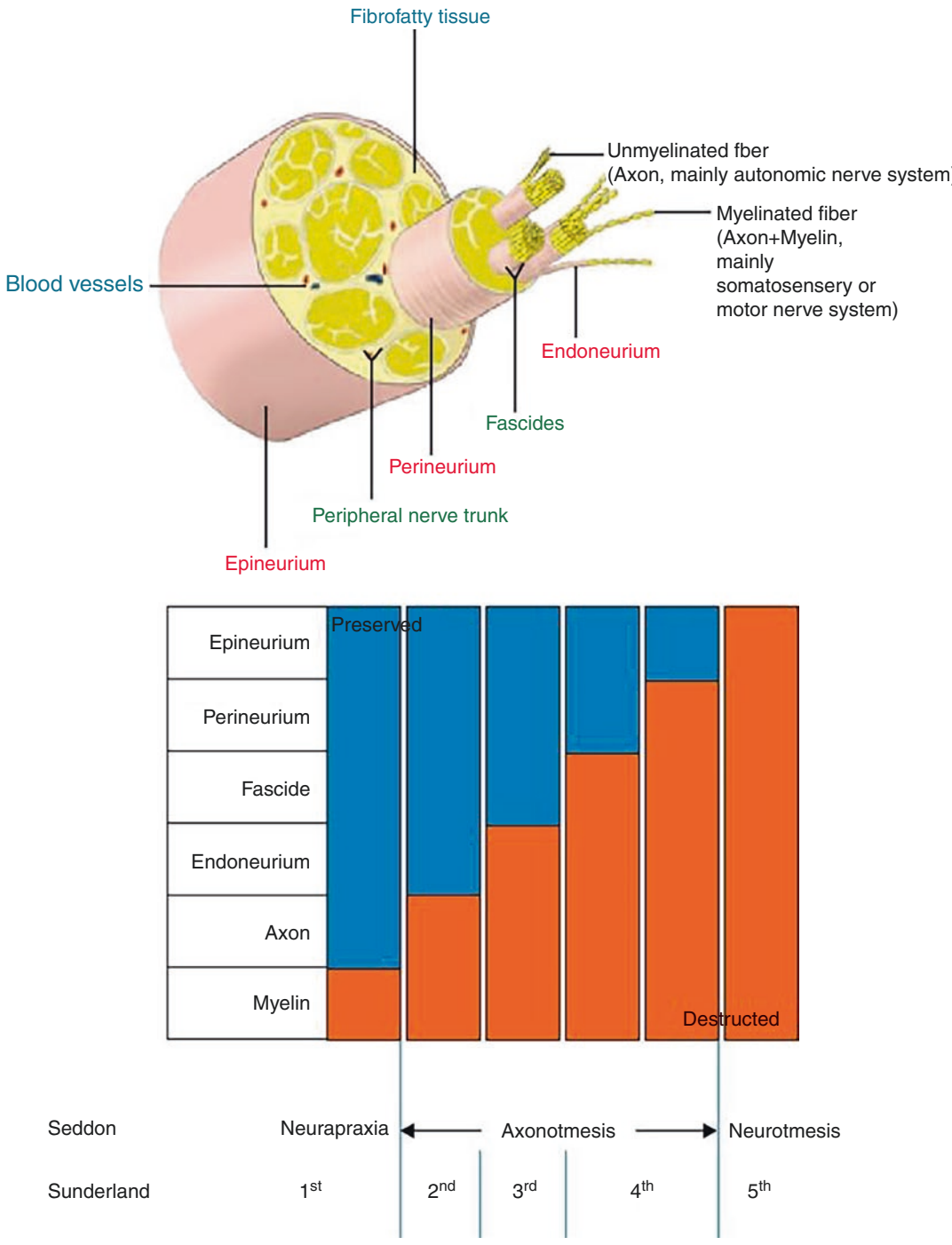

Fig. 63.1 Classification of peripheral nerve injury. (Source: The Korean Journal of Pain, 03 Jan 2016, 29(1):3–11: Reproduced with permission)

Regeneration of Neurons after Neuroablation

The process starts immediately after the injury with following steps: (1) remyelination, (2) axonal sprouting (3) regeneration (Fig. 63.2).

Macrophages migrate into injured site Schwann cell proliferation increase synthesis of surface cell adhesion molecules, laminin and fibronectin, and nerve growth factor.

activation of trophic factors, neurpoietic cytokines, insulin-like growth factors (IGFs), and glial cell line derived neurotrophic factors (GDNFs) regeneration.

Clinical Pearls

- It is recommended to perform under fluoroscopic guidance with or without ultrasound guidance based on type and site of block.
- This procedure is usually completed in a sterile surgical suite and takes between 30 minutes to 1 hour, depending on the number and which nerves are being blocked.
- If the nerve that's blocked isn't the nerve causing the pain, it will likely not be reduced during a neuroablation technique.
- Nerve ablation isn't sufficient for all scenarios. If the outcomes aren't favorable to other

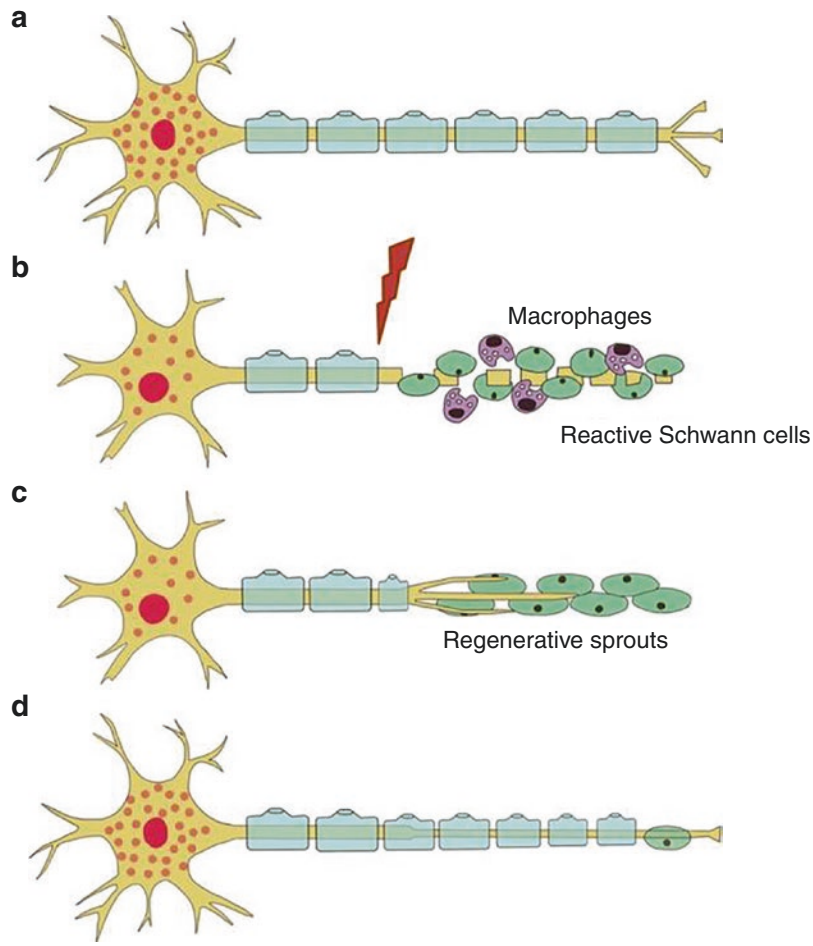

Fig. 63.2 Degeneration and regeneration after peripheral nerve injury. (**a**) Normal neuron and nerve fiber. (**b**) The axotomy results in fragmentation of the distal axon and myelin sheaths. Schwann cells proliferate. Macrophages invade the distal nerve segment, and phagocytize degrading materials. (**c**) Axonal sprouts advance embedded in the Schwann cells and are attracted by gradients of neurotrophic factors. (**d**) Axonal reconnection with end organs and maturation and remyelination of the nerve fiber. (Source: The Korean Journal of Pain, 03 Jan 2016, 29(1):3–11: Reproduced with permission)

treatments, like diagnostic anesthesia nerve blocks, nerve ablation might not be a correct treatment choice to consider [7].

- Know classification of peripheral nerve injury: neuropraxia, axotemesis, and neurotemesis (Fig. 63.1)

Questions

1. All of the following factors increase lesion size during conventional radiofrequency ablation except:
   A. Use a 16-gauge cannula instead of a 20-gauge cannula
   B. Extend lesion time from 3 min to 5 min
   C. Pre-lesion dexamethasone injection through a cannula
   D. Increasing heating temperature from 80C to 90C
2. Pulsed radiofrequency differs from traditional radiofrequency in all the following ways except for:
   A. The current is delivered in short bursts to target tissues.
   B. Lower risk of deafferentation pain
   C. Less risk of neuro-destruction
   D. Longer duration of effect
3. The most common side effect following radiofrequency ablation is:
   A. Dysesthesia of skin over the operative area
   B. Neuritis
   C. Damage to surrounding non-targeted spinal nerves
   D. Nausea
4. A patient is scheduled for a celiac plexus neurolytic block. Which of the following is true of phenol compared to alcohol?
   A. More hyperbaric
   B. Permanent neurolysis
   C. Causes more pain on injection
   D. Causes more dysesthesia
5. In a lower limb, which of the following is correct regarding the reduction of ankle-plantar flexor spasticity with a phenol injection into the tibialis posterior:
   A. Can facilitate correction of ankle flexion abnormality
   B. Can abolish ankle clonus
   C. Has a period of effectiveness of at least six months
   D. All of the above

Answers

1. C: The size of an RF lesion can be affected by many factors, including manipulating cannula tip sizes, generator settings, heating temperature, and lesion time within practical limits. Lesion size can also be further enhanced by pre-injection with >3% sodium chloride. However, there is some research suggesting that steroids injected before ablation may result in a decrease in lesion size.
2. D: Pulsed radiofrequency offers many advantages over traditional ablation techniques, including reduced risk of deafferentation pain, less risk of neuro-destruction, and lower rise in tissue temperature by delivering short bursts of 50 kHz current to target nerves. Despite these benefits, pulsed radiofrequency has the downside of more expensive equipment and shorter duration of therapeutic effect, leading to the need for more frequent repeat procedures.
3. B: Although radiofrequency can be associated with both major and minor complications, there is limiting data documenting the occurrence of these complications. Some patients may experience transient dysesthesias of the skin over the operative area and have been shown to be more common in cervical medial branch and sacroiliac joint lateral branch procedures. The most feared, but fortunately much rare, the complication is damage to surrounding, non-targeted spinal nerves. Multiple methods have been implemented to prevent this complication, including fluoroscopy in various views and motor testing. The most common side effect of treatment is neuritis secondary to an inflammatory response either of the heated nerves or the surrounding tissue, lasting from several days to 2 weeks.

4. A: Neurolysis can be chemical, thermal, or surgical. The injection of alcohol is often painful and has a wide distribution of spread, attributed to its hypobaric. Alcohol neurolysis also has a higher chance of causing dysesthesia, so it is usually limited to end-stage cancer or sympathetic fibers. Local anesthetic should be injected before neurolysis with alcohol. Phenol is capable of acting as a local anesthetic, so the injection is not as painful. Some literature suggests that phenol may have a higher affinity for vascular tissues, making it not as well suited for highly vascular regions. Neither, however, create a permanent blockade.
5. D: Tibialis posterior nerve blocks may be used for spasticity reduction and may ameliorate increased muscle tone. They are especially indicated in abnormalities of the lower limb. Botulinum toxin A (BTA) injections have also been studied for similar applications and found to have comparable results, however, through different mechanisms of action.

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Spinal Cord Stimulation and Intrathecal Pumps

64

Sarah Rogers, Tony El-Hayek, and Jianguo Cheng

Spinal Cord Stimulation

Introduction

· Spinal Cord Stimulation (SCS) is clinically used to manage chronic pain conditions that are not well controlled by conservative treatment [1]. Strong levels of evidence support the efficacy of SCS in select patients with specific indications, such as bailed back pain syndrome [2, 3] and complex regional pain syndrome [4].

. The technique requires percutaneous or surgical implantation of electrodes in the epidural space. The selection of candidates for SCS is based on specific indications, psychological evaluation, and physical and mental comorbidities. It's a two-stage process. A trial is performed, followed by permanent implantation after successful trials (≥50% pain relief and functional improvement).

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Mechanism of Action

· The SCS technology was developed based on the gate control theory of pain transmission, which postulates that the input of large diameter nerve fibers (A-beta) can inhibit the input of small diameter, pain conducting afferent fibers (A-delta and C). However, the true mechanisms of neuromodulation are much more complex and remain to be determined. Preclinical and human mechanistic studies suggest that SCS techniques likely modulate the conduction, transmission, and perception of pain signals, as well as processes involving non-neuronal cells in the spinal cord that contribute to central sensitization and chronification of pain.

. The mechanism of action for paresthesia stimulation, or conventional stimulation, is WDR (wide-dynamic-range) neuron suppression by gabaergic (GABA) and other inhibitory interneurons.

. The mechanism of action for paresthesia-free stimulation, or high frequency/burst stimulation, has no involvement of the gabaergic system and does not generate action potentials. The burst spinal cord stimulation appears to modulate the activity of C fibers terminating on dorsal horn neurons in the superficial laminae of spinal cord.

Indications: Neuropathic: CRPS, DM neuropathy, failed back surgery syndrome.

Ischemic: Angina, PVD.

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Contraindications

- Absolute: patient refusal, major psychological disorders, systemic or local site of infection, spinal stenosis at the level of electrode placement, loss of spinal canal due to surgery/trauma, trial failure, spina bifida.
- Relative: Coagulopathy, immunosuppression, pregnancy, ICD/pacer [5], increased ICP.

Technique

- SCS electrodes are placed in the dorsal aspect of the epidural space via a Touhy needle at a shallow angle of entry under fluoroscopy guidance.
- Temporary leads are placed percutaneously for trials and are connected to an external generator while testing the efficacy of SCS. After a successful trial, the trial leads are removed. For implant surgery, an incision is made to create a space for placing and anchoring the electrode and another incision is made for the IPG, which is connected to the electrodes tunneled under the skin.
- The usual levels for lead position for pain in anatomic regions are as follows: Neck – Above C3, Shoulder – Above C5, Hand – C5–6, Abdomen T5–7; Thigh – Anterior thigh T7, T8, posterior thigh T11 to L1, Foot – L1, Low back – T9 to T10
- SCS trial: Conscious sedation/MAC + local; SCS implant: MAC or general (rare).
- Complications: nerve and spinal cord injury, infection, hematoma, lead breakages or migration, hardware malfunction, CSF leakages, pain at implanted pulse generator site.

Anesthetic Considerations for MRI in Patients with SCS

- Preoperative management→ Decrease amplitude (stimulus intensity) to the lowest possible setting. The anesthesia team is responsible and must be prepared to manage the SCS in the perioperative period.
- Intraoperative management→ Turn off the SCS prior to induction and be sure that it remains off throughout the case with plans to have the SCS interrogated post-operatively.
  - If the SCS were to be accidently turned back on, the device should have been at the lowest stimulus intensity possible and will hopefully have minimal interference.
- Postoperative management→ It is imperative to interrogate the device after a procedure before it can be safely turned back on for patient treatment.
- ECG → If left on, the SCS can result in high frequency artifacts in multiple leads [6]
- Electrocautery→ Bipolar electrocautery is recommended over monopolar cautery due to the creation of current that is relayed from the wound, to the grounding pad and possibly the device.
  - If monopolar cautery must be used, it must be at the lowest effective setting and the grounding pad must be placed as far away from the SCS device as possible and on the contralateral side of the pulse generator [6].
- Pacemaker/defibrillators→ It is recommended that SCS and cardiovascular implanted electronic devices should not be used simultaneously, but there are many examples of safe use [5] and the final decision is up to the patient and medical provider.
  - Obtain a baseline ECG to rule out any new interference/artifact, place the CIED into bipolar mode.
  - Ensure that the plantable pulse generator (IPG) for the SCS is contralateral to the CIED [6].
  - Defibrillation can cause damage to the SCS device. But if necessary, place the paddles perpendicular to the SCS with the lowest energy that will result in therapeutic intervention [6].
- Obstetric Anesthesia→ It is recommended that SCS should be turned off at the time pregnancy is diagnosed and for it to remain off until delivery [7].

  - Epidural solutions are unlikely to result in lead migration, but they are more likely to result in patchy distribution due to fibrous deposits around the SCS leads [6].
  - Spinal anesthesia has been safely administered in this patient population [7].
  - Prior to any labor analgesia/neuraxial technique, it is necessary to review radiographic and implant records to know lead location and decrease the risk of SCS dislodgement [6].
- Regional Anesthesia→ There is no recommendation against the use of neuraxial techniques for patients with SCS in place, but caution should be applied to technique and location.
- Ultrasound and Lithotripsy→ It is recommended that patients do not undergo this intervention. But if necessary, it is imperative to turn off the SCS and to keep the focus of the beam 15 cm away from the device [6].
  - Post-operatively, the device can be turned back on slowly titrated up to therapeutic effect for the patient.
- Microwave Ablation and Diagnostic Ultrasound→ There is a risk of potential disruption of cords or heating of the SCS device. If possible, it is recommended to keep the patient conscious so they are able to verbally report abnormal sensations.
- MRI → Compatibility is all based on the manufacturer of the SCS. It is extremely important that the anesthesia provider looks up the specific manufactured device and its MRI compatibility [6].
- Radiation Medicine→ It is recommended to turn off the SCS, to limit the total dose to 5 gray (Gy), and that the IPG of the SCS must be at least 1 cm away from the beam [6].
- CT Scan→ Preferred method of imaging for patients with SCS in place. It is recommended that the device be turned off prior to undergoing the scan and the lowest dosage of radiation to be used.

Intrathecal Pumps

Introduction

- The intrathecal drug delivery system (IDDS) allows drugs to be infused directly into the cerebral spinal fluid (CSF) surrounding the spinal cord, thus bypassing the blood-brain barrier.
- Drugs, such as local anesthetics, opioids, and ziconotide alone or in combinations can be infused by this system to treat cancer pain and other refractory pain conditions.
- Typically, very lower doses of drugs are required by this approach due to direct access of the therapeutic targets, such as opioid receptors and specific ion channels, resulting in a decrease in side effects and adverse events [8].

Indications: Cancer pain, moderate to severe non-cancer pain that is refractory to conventional opioid pharmacotherapy, or in patient who is intolerant of opioid therapy but they have shown to improve symptoms.

Contraindications

- Absolute: Systemic infection, allergies to materials of implant/catheter, active IV drug abuse, infection at implantation site, unsuccessful IT trial, major psychological disorders.
- Relative: Severe spinal abnormalities, anticoagulation therapy, hemodynamic instability, high opioid tolerance, increased ICP, lack of social or family support.

Technique

- Discussion is made with surgeon regarding the location of the pump pocket; abdominal

location requires lateral decubitus position and buttock location requires prone position.
- Fluoroscopy is used to guide access to intrathecal space via a Touhy needle. Flow of CSF confirms the tip of the needle in the intrathecal space.
- A radiopaque intrathecal catheter is threaded through the Touhy needle and to verify appropriate placement of the catheter (dorsal to the spinal cord at a desired level).
- A purse string suture is placed around the Touhy needle. The needle is then removed and the catheter is left and held in place by tieing the purse string suture, which is intended to prevent CSF leakage.
- A horizontal incision of about 12 cm is made in the abdomen (about 15 cm lateral to the umbilicus) to create a pocket for the pump.
- The catheter is connected to the pump through tunneling under the skin, and pump is then securely sutured, wounds are closed, and then the patient is taken to recovery.

Complications: Infection, bleeding, respiratory depression, pump malfunction/catheter failure, inflammatory mass formation surrounding the catheter tip, hormonal dysfunction, hygroma or seroma formation, peripheral edema.

Anesthetic Consideration for Patients with Intrathecal Pumps

- Preoperatively
  - The patient's pain physician should be included in the perioperative pain management plan.
  - Intrathecal medication doses should be known by the Anesthesia providers, and there should not be escalation of IT dosing nor oral opioids [9].
  - Regional anesthesia should be used if applicable.
- Intraoperatively
  - Opioids may be used, but it is encouraged to use multi-modal approach with ketamine, acetaminophen, steroids, and NSAIDs when indicated [10].
  - Extra caution should be used with applying continuous opioid infusions due to risk of prolonged side effects.
  - If the intrathecal pump has been damaged and unable to be fixed immediately, it should be turned off and the patient should be transitioned to IV opioids for the duration of the case.
- Postoperatively
  - Short- acting opioids are appropriate as indicated, but long-acting opioids should be avoided.
  - Continuous pulse oximetry and apnea monitors should be continued in the post anesthesia care unit and on the general floor.
  - For continuous catheter infusions, local anesthetics should be combined with epinephrine and/or clonidine instead of opioids [9].
  - PCAs are appropriate but basal rates should be avoided [10].
  - The patient should follow up postoperatively no more than 2 weeks after surgery for continued management.

Opioid Conversion Table [8].

	Intravenous	Epidural	Intrathecal
Morphine	10 mg	1 mg	0.1 mg
Hydromorphone	1 mg	0.2 mg	0.04 mg
Fentanyl	100mcg	33mcg	6-10mcg

Clinical Pearls

- Perioperative concerns for patients with spinal cord stimulators who undergo surgery with cautery: Bipolar should be used; SCS should be turned off.
- Lumbar neuraxial anesthesia may be difficult with SCS or IT pump. Need to know location of the leads/catheter from X-Ray images.
- MRI compatibility should be confirmed and manufacturer's recommendations should be followed before going for MRI.
- Spinal anesthesia with IT pump: medication may be delivered through catheter port after aspiration with strict sterile technique.
- Drugs approved for IT pump include baclofen, morphine, and ziconotide.

Questions

1. Which of the following is the most common complication that occurs with malfunctioning of spinal cord stimulators?
   A. Infection
   B. Pain at pulse generator site
   C. Lead migration
   D. Spinal cord injury
2. A 67-year-old male with a PMHx of pancreatic adenocarcinoma, HTN, and COPD presents to your pain clinic for management of his chronic pain. He is interested in changing his management to an intrathecal pump, rather than taking oral morphine. His current oral morphine dose is 120 mg /daily. What would be the most appropriate initial ITP dose of morphine/day?
   A. 0.2 mg
   B. 2.0 mg
   C. 5.0 mg
   D. 10.0 mg
3. Which of the following dose conversions is correct?
   A. Hydromorphone (1 mg IV = 0.04 mg Intrathecal)
   B. Fentanyl (100mcg IV = 33mcg intrathecal)
   C. Morphine (10 mg IV = 1 mg Intrathecal)
   D. Morphine (1 mg Epidural = 0.5 mg Intrathecal)
4. What is the most important factor that determines the success of SCS?
   A. Patient selection
   B. Type of stimulator
   C. Physicians surgical skills
   D. Duration of chronic pain
5. You are paged to a code blue on the general medicine floor. As you arrive, the patient is in ventricular fibrillation and the nurse reports that the patient has a history of chronic pain and a spinal cord stimulator for T8-L1 with the impulse generator (IPG) located in the left low back. Where do you place the defibrillator paddles and what settings do you use?
   A. Perpendicular to the IPG; lowest therapeutic energy setting
   B. Perpendicular to the IPG; highest therapeutic energy setting
   C. Parallel to the IPG; lowest therapeutic energy setting
   D. Parallel to the IPG; highest therapeutic energy setting

Answers

1. C
2. A
3. A
4. A
5. A

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Multimodal Analgesia for Chronic Pain

65

Jacob Deweerth and Ratan K. Banik

Introduction

- The perception of pain depends upon neural signals that are processed at **multiple levels** from the periphery through the neuraxis to multiple areas within the cerebral cortex (Fig. 65.1, Chap. 1, chronic pain).
- Changes can occur at transcriptional, translational and posttranslational levels in both peripheral and central neurons. Peripheral neuronal sensitization is mainly mediated by inflammatory mediators whereas central sensitization results from repetitive discharges of C fibers (wind-up phenomenon, see Chap. 1, chronic pain).
- The descending pathways can modulate pain transmission via neurotransmitters including **endogenous opioids, serotonin, and norepinephrine**. Because of such complexities in the pathophysiology of chronic pain **multimodal treatment strategies** may be required (Fig. 65.1).
- Chronic pain is associated with disturbances in mood, sleep, energy, and daily activities which can affect the patient's mental, social, sexual, and general physical health (Chap. 3, chronic pain). In addition to pharmacologic therapy, chronic pain patients may benefit from **education** about their condition and **psychotherapy** to improve coping skills and reduce anxiety, fear, and stress (Table 65.1).
- Multidisciplinary therapy can be offered in a gradual fashion as needed or in a formalized setting such as a structured **pain rehabilitation program**.

Multimodal Treatment Paradigms

1. Psychological comorbidities, if present, can be addressed with pain psychotherapy for mindfulness-based stress reduction, relaxation training, biofeedback, and CBT
2. Physical Therapy: graded exercise (land and aquatic), pacing, addressing fear avoidance and guarding
3. Mechanical treatments: Ice/heat, TENS, massage therapy
4. Integrated medicine: acupuncture, yoga, Tai Chi, chiropractic treatments
5. Lifestyle modification: Tobacco cessation, sleep hygiene, dietary counseling, weight loss
6. Interventional treatments: Steroid injections, nerve blocks, trigger point injections, neuromodulation
7. Multimodal medication therapies: Acetaminophen, NSAIDs, TCAs, SNRIs, muscle relaxants, topical medication, anti-convulsant

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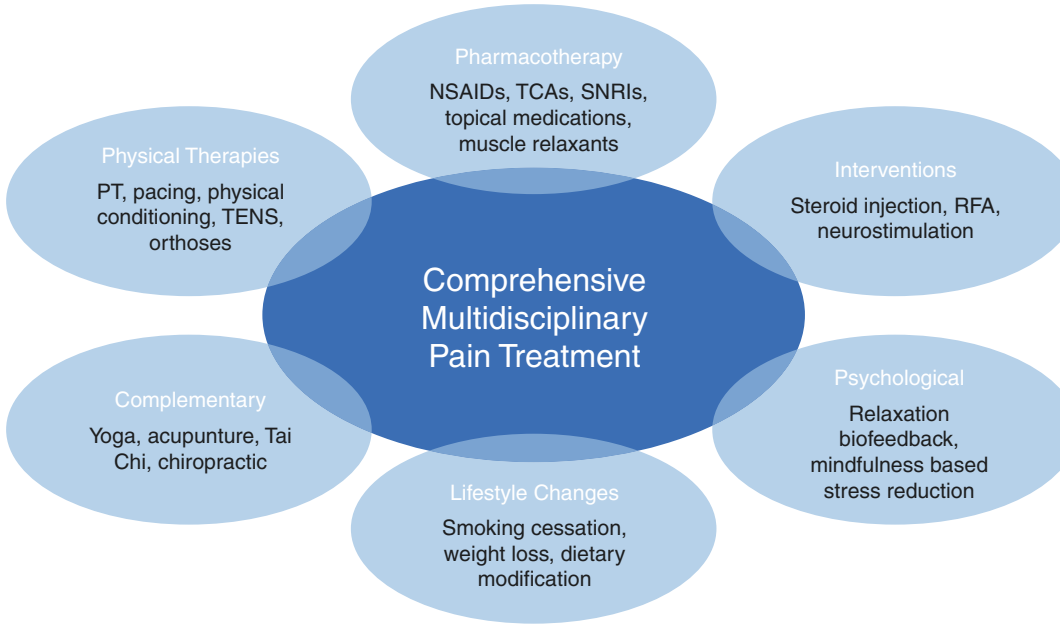

Fig. 65.1 Comprehensive multidisciplinary pain treatment**.** (Need to be drawn by a Springer illustrator)

Table 65.1 Behavioral interventions for chronic pain

Biofeedback	Patients are trained to influence physiologic processes—such as blood pressure, skin temperature—with the aid of visual or auditory devices that amplify these processes. Examples include electromyographic biofeedback, which measures tension in the frontalis muscle, and EEG biofeedback, which has been found effective in treating some chronic pain
CBT	Cognitive strategies and skills are taught so that maladaptive processes and irrational thinking, which directly affect perceptions and experiences, can be overcome
Hypnosis and guided imagery	With visualization and one's imagination, patients can obtain a hypnotic state that is essentially aroused yet has little or no peripheral awareness. In guided imagery, patients focus on something (e.g., their chronic pain) that they would like to alter or eliminate. Suggestibility is an important element of both hypnosis and guided imagery
Meditation	In the health care setting, the forms of meditation that have been best researched include transcendental meditation and mindfulness meditation. In the former, the patient repeats a silent word or mantra to reduce and eventually transcend one's internal dialogue. In the latter, the patient maintains a nonjudgmental state of awareness in which emotions, judgments, beliefs, and so on are addressed
Patient education	Teaching patients about common symptoms, possible adverse effects, appropriate treatments, self-care strategies, and the likely course of the discomfort has been found to reduce the anxiety that may be heightened in the uninformed, which in turn may prolong symptoms. Psychoeducational approaches broaden the scope of the training to include adaptive psychological strategies such as CBT
Relaxation techniques	Hypoarousal may be obtained from several relaxation procedures, the most studied of which is progressive muscle relaxation, which aims to reduce muscular tension by alternately tensing and relaxing muscles. Hypometabolic states in which sympathetic arousal is reduced—As in Benson's relaxation response—Also may be achieved. These techniques can ameliorate symptoms that are associated with chronic pain, such as anxiety, fatigue, and sleep disturbance

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Drug Therapy

- Due to complex pathophysiology of chronic pain, a combination of medications is often required. Multimodal medication therapies are well established for the treatment of other diseases such as hypertension, diabetes, and depression [1, 2].
- The common classes of medication in the treatment of chronic pain include acetaminophen, NSAIDs, TCAs, SNRIs, muscle relaxants, topical medication, and anticonvulsants**.** Most analgesic and adjuvant drugs have sedative side effects and a 'low and slow' strategy (starting with low dose with slow upward titration) is suggested to balance effective treatment and acceptable side effects.
- Neuropathic pain (pain caused by nerve injury) such as spinal cord injury, multiple sclerosis, central post-stroke pain, diabetic neuropathy, postherpetic neuralgia, radiculopathy, and intercostal neuralgia are more likely to respond to gabapentenoids, tricyclic antidepressant, and duloxetine (See Chap. 32, Chronic pain).
- Inflammatory pain (rheumatoid arthritis, osteoarthritis, etc.) pain typically responds to the combination of oral and topical NSAIDs (Chap. 31, chronic pain). Chronic low back pain has been shown to have both inflammatory and neuropathic component, which may require a combination of multiple medication classes to achieve optimal improvement.
- Management of patients with widespread pain will likely require multidisciplinary treatment including medications (NSAID medications, muscle relaxants, anti-neuropathic agents, and others), **group therapy, targeted physical therapy, social support, and pain psychotherapy** (Fig. 65.1).
- The prescription of opioids should be limited to **acute flare** of chronic pain conditions; starting with the lowest effective dose of immediate-release opioids (Table 33.3, Chap. 33, chronic pain) and at no greater quantity than needed for the expected duration of pain; **3 days or less** often is sufficient; more than **7 days** is rarely needed.

Psychotherapy

- Cognitive Behavioral Therapy (CBT) with **a pain psychologist** may be beneficial for patients with comorbid anxiety, depression, PTSD, bipolar affective disorder, and others (Table 65.1).
- Additional evidence based pain psychology therapies include neurocognitive education, biofeedback, mindfulness based stress reduction, and relaxation strategies.
- Engagement in CBT and other pain psychology therapies is dependent on **patient motivation and engagement**, and benefit may be variable depending on the extent to which the patient is able or willing to engage with therapy
- In a population of patients with co-morbid pain and depression, those received treatment of depression (medications, therapies, or combination) were significantly less likely to report pain interference with work (OR 0.57) and a trend toward fewer limitations in their activities of daily living [5].
- The use of psychological modalities for the treatment of chronic pain predates many of our current interventional techniques, with the successful use of **operant conditioning** to achieve reductions in medication usage, improvements in self-reported pain, and improvements in physical function [6].
- For specific pain pathologies including phantom limb pain and complex regional pain syndrome, graded **motor imagery** has been shown to have long term benefit.

Physical Therapy

- Pain based physical therapy is guided by a physical therapist to provide therapeutic exercise, a home exercise program (HEP), and to

address **maladaptive pain behaviors** including fear avoidance and guarding.
- Therapeutic exercise involves physical movements, postures, or activities designed to ameliorate impairment, improve function, and enhance overall wellbeing of the patient. Manual stretching, myofascial therapy, dry needling, passive mobilization, and active exercises are also utilized.
- While the aggregate of studies evaluating the effectiveness of a wide range of physical activity and exercise programs across a myriad of painful conditions shows mixed value, there is little to no evidence of risk of harm [8].
- More focal studies evaluating the effect on low back pain have shown as much as 30% improvement in **Oswestry Disability Index** scores in as little as 4 weeks of treatment [9].

Orthoses or Prosthesis

- Patients with movement evoked pain or an antalgic gait may benefit from short term use of orthotics (braces, splints, etc.) to limit motions that incite pain. Long term use, however, is not recommended as the goal is to use PT to improve function.
- Appropriately fitted orthoses can also help treat and prevent the progression of **phantom limb** and residual limb pain.

Mechanical Modalities

- The application of heat or cold, and TENS unit to localized area of pain can provide short term pain relief. These modalities are particularly useful when pain is mild or moderate.
- Transcutaneous electrical nerve stimulation (TENS) is a widely available modality for the treatment of myofascial and superficial neuropathic pain. TENS can be tried as a supervised trial when working with a physical therapist.
- Cold application with cold packs and/or menthol based topical products may reduce myofascial pain. Possible mechanism include initial vasoconstriction, followed by vasodilation, however patients should be advised about the risks of prolonged or excessive exposure.
- Heat application increases blood flow and has soothing effect. Superficial heating with hot packs, heating pads, or baths can improve chronic pain in the joints and muscles, however like with cold application, patients should be advised about the risks of prolonged exposure.

Interventions

- Injections of local anesthetic and/or steroid medication are intended to provide **temporary pain relief** by stopping the pain cycle. One of the most common pain injections is an epidural steroid injection (Chap. 10, chronic pain) and other common procedures include facet joint injections, selective nerve root blocks, sacroiliac joint injections, and peripheral nerve blocks.
- Some injections are primarily for diagnostic purposes and can be used to isolate pain generating structures for further intervention such as **radiofrequency ablation** or surgery.
- Although most pain procedures are short lasting with pain relief pain for 1 to 12 months, they enable patients to be **engaged in physical therapy** and help in addressing underlying physical problems causing pain.
- Intrathecal pain pump or spinal cord stimulation may offer long lasting pain relief in select patients (Chap. 27, chronic pain).
- Although interventional procedures have an excellent safety profile, they are **rarely indicated** as stand alone first-line treatments.

Complementary and Alternative Medicine

The complementary and alternative medicine strategies such as acupuncture, yoga, massage therapy, and Tai-chi have been widely used, but there is not enough high-quality research to make a recommendation to include them in the multimodal integrative therapies for chronic pain. In

most cases, the risks associated with these treatments are **low** and they can be included in a multidisciplinary treatment program if patients **express interest in them**.

Emerging Modalities

- Transcranial Magnetic Stimulation (TMS): The application of an electromagnetic field exterior to the skull which produces changes in cell signaling in targeted areas of the brain. The treatment is currently being evaluated for efficacy in chronic pain, depression, PTSD, and other conditions [10].
- Platelet Rich Plasma (PRP): Isolated plasma concentrates of a patient's own blood containing growth factors to stimulate tissues **regeneration**. These are commonly injected into joints to facilitate enhanced recovery of tissues with low baseline perfusion (eg. Tendinitis) [11].
- Stem cell therapies: The basis of this therapy is to inject undifferentiated cells to promote the repair response of diseased, dysfunctional, or damaged tissues. In addition, stem cells release neurotrophic factors, which helps in replacing the injured neural cells, making them good candidates for neuropathic pain. However, the use of stem cells is still in the early stages due to various ethical problems.

Clinical Pearls

- In summary, the optimal treatment of chronic pain will often require the employment of multiple domains of treatment including **interventional, pharmacologic, physical, and psychological**.
- It is also important to remember that greater progress can be achieved in the treatment of patients with chronic pain when multiple domains of life, including pain severity, physical function, well-being, and mental wellness are used to assess progress.
- While the moonshot goal of the elimination of pain should never be abandoned, seeking improvements across multiple domains of the patient's pain experience will help to improve overall patient satisfaction, adherence, and outcomes [7].

Questions

1. A 30 year old male diagnosed with post amputation pain 6 weeks after a left BKA should be treated with all of the following as initial therapy **EXCEPT**:
   A. Opioids
   B. Tricyclic antidepressant medications
   C. Physical therapy and orthotics
   D. Graded motor imagery
2. A 56 year old male is POD 3 from spine surgery. He reports incomplete analgesia with 10 mg of oxycodone Q4 hours. Which medication change is most appropriate?
   A. Increase oxycodone to 20 mg Q4 hours
   B. Initiate IV ketamine infusion
   C. Restart patient controlled analgesia (PCA) with morphine
   D. Start Acetaminophen 1000 mg Q8h
3. Which of the following side effects is **least** likely to occur in association with increases in opioid medications?
   A. Diarrhea
   B. Respiratory depression
   C. Pruritis
   D. Sedation
4. A 35 year old female presents to her PCP with new onset low back pain that occurred while exercising. Neurological examination is unremarkable and physical examination only reveals lumbar paraspinal tenderness. Which of the following is an appropriate initial recommendation?
   A. Lumbar MRI
   B. Referral for lumbar epidural steroid
   C. NSAID medications and physical therapy referral
   D. All of the above

Answers

1. A: Tricyclic Antidepressant medications, graded motor imagery, physical therapy, and orthotic use have all been shown to provide relief at by various mechanisms of action for patients with post amputation pain. Opioid medications are not contraindicated, but are not considered first line therapy outside of the immediate post-operative period.
2. D: The addition of non-opioid medication to an opioid regimen is more likely to produce improvements in analgesia than an increase in opioid medication [3, 4]. IV ketamine infusion and opioid PCA are appropriate therapies for poorly controlled pain, however this should be limited to the post-operative period, and should be only be initiated after the initiation of a multimodal medication regimen.
3. A: Constipation is a common side effect from opioid medications, as are the remaining choices.
4. C: In the absence of neurological findings or radicular pain, the initial treatment for mechanical low back pain in low risk individuals is includes non-opioid analgesics and physical therapy. If the pain fails to resolve, is accompanied by radicular pain or neurologic findings, or is accompanied by other constitutional symptoms such as weight loss or fever, additional work up and/or procedures may be indicated.

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Transcutaneous Electrical Nerve Stimulation

66

Rohit Aiyer, Ellen Johnson, and Joseph Poli

Introduction

Transcutaneous electrical nerve stimulation (TENS)

- TENS is low-intensity electrical stimuli (2 and 100 Hz,) that produces a tingling or vibratory sensation. It is believed to be an effective, safe, and non-invasive intervention for pain.
- The intervention is based on Melzack and Wall's 'gate control theory' that there is a gateway in the **substantia gelatinosa of the dorsal horn** of the spinal cord, which controls or regulates the flow of pain signals. The non-painful input closes the "gates" to painful input, which prevents pain sensation from traveling to the central nervous system. Therefore, stimulation by non-noxious input is able to **suppress pain.**
- It is thought that pain may be alleviated by using peripheral stimulation, such as rubbing, vibration, heat or cold, or, as in the case of TENS, electrical stimulation directly over the area of pain. This peripheral stimulation activates large myelinated A-beta nerve fibers and **local inhibitory circuits** (small unmyelinated 'C' fibers) within the dorsal horn of the spinal cord.
- It is delivered from a hand-held battery-powered generator to the skin via surface electrodes.
  - TENS is an enticing option for pain management because it is inexpensive, readily available, has few adverse effects, no risk of overdose, and patients can self-administer the treatment as well as optimize their dosing independently [1].

The International Association for the Study of Pain (IASP) defines three types of TENS Units:

- Conventional TENS – high frequency (50–100 Hz), low intensity, short pulse width (50–200 μs)
  - analgesia onset in <15 min, analgesia lasts a few hours at best [2]
- Acupuncture-like TENS – low frequency (2–4 Hz), high intensity, long pulse width (100–400 μs)
  - lower frequency yields slower onset time (20-30 min) but longer duration of action (hours to days) [2]
- Intense TENS –high frequency, high intensity, short pulse width
  - most useful for short-term analgesia (ex. during joint mobilization) [2]

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Mechanism

- At the anatomical location of stimulation, TENS provides analgesia by **reducing substance P production** and acting as a peripheral alpha-2 receptor antagonist [3].
- Conventional (high frequency, low intensity) TENS is thought to generate analgesia via the gate theory of pain. It activates large, myelinated A-beta fibers which inhibit transmission of nociceptive information from C fibers. Patients experience paresthesia below the electrodes [1].
- Acupuncture-like TENS (low frequency, high intensity) TENS activates small, myelinated A-delta fibers which increase the activity of descending pain inhibitory pathways. Patients experience muscle twitches below the electrodes rather than paresthesia [1].
- Low frequency TENS also decreases hyperalgesia via antagonism of GABA-A, serotonin 5-HT2A and 5-HT3, muscarinic M1 and M3 receptors [3].
- High frequency TENS (including both conventional and intense TENS) is thought to work by increasing the concentration of beta endorphins in the bloodstream and methionine-enkephalin in the cerebrospinal fluid [3].
- High frequency TENS also decreases hyperalgesia by blocking muscarinic receptors (M1 and M3) and GABA-A receptors in the spinal cord [3].
- Low frequency TENS does not provide pain relief in opioid tolerant patients but high frequency TENS does.

Indications

- Myofascial Pain
- Neuropathic Pain
- Radiculopathies
- Arthritic Pain
- Acute Pain

Current Evidence on Efficacy

- A review by Vance *et al* analyzed various studies that examined the use of TENS to treat chronic pain conditions. The review concluded that TENS is effective for **postoperative pain, painful diabetic neuropathy and osteoarthritis**. TENS can also be considered in patients with **fibromyalgi**a and **spinal cord injury** [3].
- A retrospective review investigated 110 patients in the ED with acute pain. 83% of patients reported functional improvement after using TENS. Investigators concluded that in 99% of cases it was useful to combine TENS with other treatment modalities to treat acute pain [4].
- Meta-analysis evaluating use of TENS for chronic musculoskeletal pain showed a statistically significant **decrease** in pain, based on 38 studies that were reviewed [5].
- Cochrane review stated that quality of evidence in the literature for TENS was quite low. The authors were not able to recommend TENS for chronic pain or determine if the intervention is harmful or beneficial in regards to analgesia, disability, and quality of life [6].

Contraindications

- First trimester pregnancy
- Epilepsy
- Demand-type pacemaker
- Placement over eyes, neck, mucosa, areas of malignancy, broken or damaged skin

Complications

- Can potentially impact transdermal drug delivery systems if applied nearby
- Allergic reactions to the electrode pads or contact dermatitis
- Syncope
- Nausea

Clinical Pearls

- The TENS unit applies electrical current on the skin at frequencies that range from low (<10 Hz) to high (>50 Hz).
  - High frequency TENS activates large, myelinated A-beta fibers which inhibit transmission of nociceptive information from C fibers. Low frequency TENS activates small, myelinated A-delta fibers which increases the activity of descending pain inhibitory pathways.
  - High frequency TENS decreases hyperalgesia by increasing the concentration of beta endorphins and methionine-enkephalin. Low frequency TENS decreases hyperalgesia by blocking GABA-A, serotonin 5-HT2A and 5-HT3 and muscarinic M1 and M3 receptors.
  - There is mixed evidence for the efficacy of TENS in chronic pain conditions, with larger studies needed to better evaluate treatment.

Five MCQ Questions

1. In low frequency TENS, which of the following receptors are not antagonized?
   (a) Muscarinic receptors
   (b) Serotonin receptors
   (c) GABA-A receptors
   (d) Nicotinic receptors
   (e) None of the above
2. Which of the following is an absolute contraindication to using a TENS unit?
   (a) History cerebrovascular injury
   (b) History of myocardial infarction
   (c) Diabetic Neuropathy
   (d) Epilepsy
   (e) None of the Above
3. What are the parameters of Acupuncture-Like TENS?
   (a) Low frequency, high intensity, long pulse width
   (b) Low frequency, high intensity, short pulse width
   (c) High frequency, high intensity, short pulse width
   (d) High frequency, high intensity, long pulse width
   (e) Low frequency, low intensity, long pulse width
4. Which fibers are stimulated in conventional TENS?
   (a) A-Alpha
   (b) A-Beta
   (c) A-Delta
   (d) C-Fiber
   (e) A-Gamma
5. What is considered the starting point of high frequency TENS therapy?
   (a) 10 Hertz
   (b) 50 Hertz
   (c) 100 Hertz
   (d) 150 Hertz
   (e) 200 Hertz

Answers

1. d
2. d
3. a
4. b
5. b

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World Health Organization Analgesic Ladder

67

Jonathan M. Hagedorn

Introduction

- The World Health Organization (WHO) cancer pain analgesic ladder was developed in 1986 as a **three-step ladder** of increasingly strong pain-relieving medications [1].
- In 1996, the WHO updated the ladder to include new interventional options for those patients struggling with pain despite following the laddered approach or those individuals that experienced intolerable side effects during medication titration [2].

Structure

- **WHO Cancer Pain Analgesic Ladder Structure:**
  - A three-step ladder (Fig. 67.1) [1].

    Step 1: non-opioid medications ± adjuvants
    - Examples: acetaminophen, nonsteroidal anti-inflammatory medications (NSAIDs), aspirin, paracetamol

    Step 2: weak opioids and non-opioids ± adjuvants
    - Examples: codeine, tramadol

    Step 3: strong opioids and non-opioids ± adjuvants
    - Examples: morphine, hydromorphone, fentanyl, methadone, oxycodone
- Every step of the ladder should integrate **adjuvant medications** to address pain and other confounding factors (Table 67.1) [1].
- *Modified WHO Analgesic Ladder for Chronic Non-Cancer Pain* **(1996):**
- A four-step modified analgesic ladder (Fig. 67.2) [3]
- **Step 1: non-opioid medications ± adjuvants**
- **Step 2: weak opioids and non-opioids ± adjuvants**
- **Step 3: minimally invasive interventions and non-opioids ± weak opioids and adjuvants**
  - Including nerve blocks, radiofrequency ablation, spinal cord stimulation, and spinal (epidural and subarachnoid) administration of local anesthetics.
- **Step 4: strong opioids ± adjuvants**

Integrative medicine therapies can also be instituted at each step.

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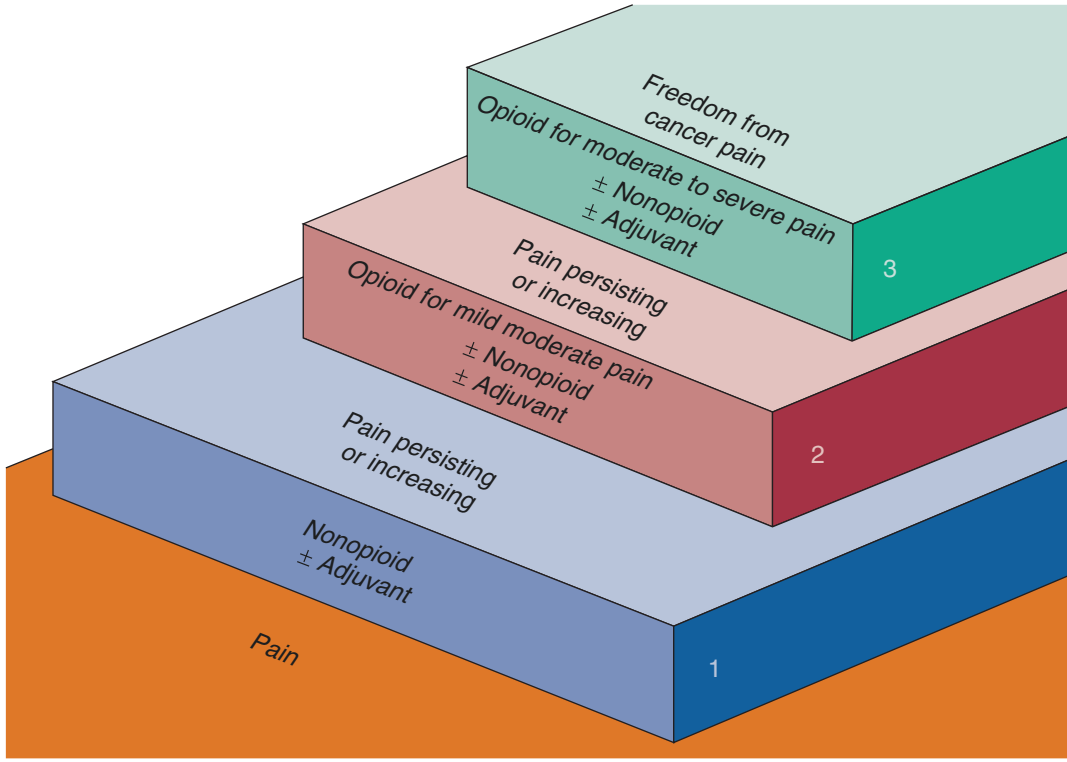

Fig. 67.1 World Health Organization cancer pain three-step ladder. Used with permission from Wolters Kluwer Health publishing

Table 67.1 Adjuvant medication classes, specific drugs, and indications (See Chap. 32, chronic pain)

Medication Class	Specific Drugs	Indication
Tricyclic antidepressants (TCA)	Nortriptyline, amitriptyline	Neuropathic pain, depression
Serotonin-norepinephrine reuptake inhibitors (SNRI)	Duloxetine, venlafaxine	Intractable pain, depression
Gabapentinoids	Gabapentin, Pregabalin	Neuropathic pain
Topical medications	Lidocaine patch, capsaicin	Neuropathic pain
Cannabinoids	Medical cannabis	Intractable pain, nausea, loss of appetite
Bisphosphonates	Clodronate, Pamidronate, Zoledronic acid	Metastatic bone pain
Corticosteroids	Dexamethasone, methylprednisolone	Fatigue, nausea, loss of appetite

- These may include acupuncture, massage, yoga, relaxation, tai chi, and spinal manipulation.

Advantages and Disadvantages:

- Advantages of the WHO analgesic three-step ladder:
  - **Simple** and concise layout
  - Clear diagram for easy use
  - Flexibility is provided to work within local regulations
  - **Proven** to achieve pain relief in 70–90% of patients [4, 5]
- Disadvantages of the WHO analgesic three-step ladder:
  - Lack of evolution

    Does not introduce new medications and interventions

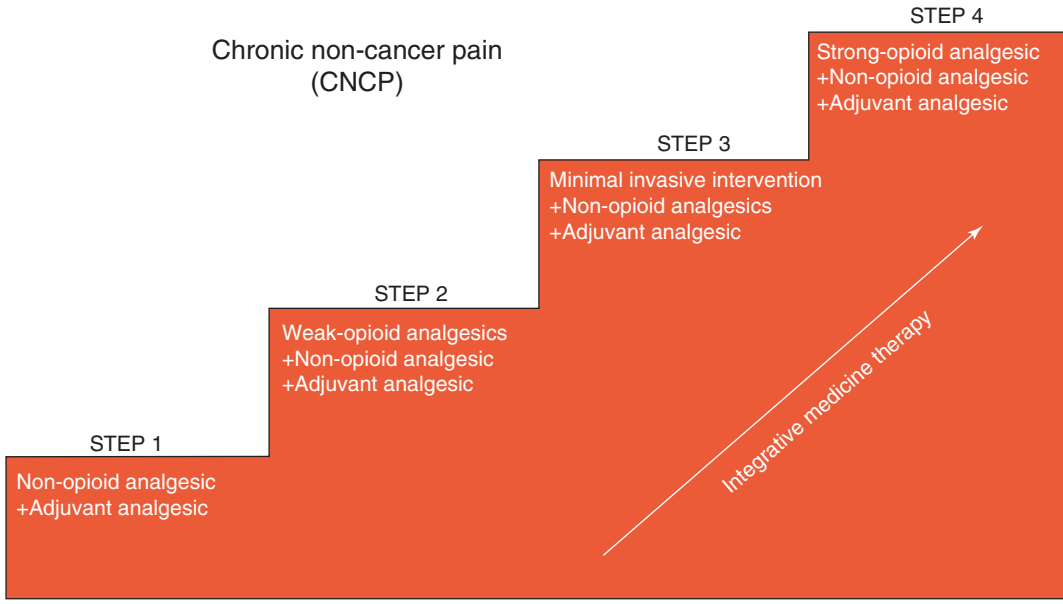

Fig. 67.2 Proposed chronic non-cancer pain four-step ladder. Used with permission from Dove Medical Press Limited

- Lack of guidance on different formulations
  For example, extended release versus immediate release opioids
- Lack of guidance on different medications for different symptomatology
  For example, no mention of a specific adjuvant for a certain complaint
- Wide range of non-pharmacological approaches are not incorporated. This includes yoga, acupuncture, psychotherapy, occupational therapy, and physical therapy.
- The laddered approach is not appropriate for all patients. Some patients may require initiation of medications at Step 2 or Step 3, but the recommendations do not provide guidance in this scenario.

Clinical Pearls

1. The WHO Analgesic Ladder was introduced in 1986 and modified in 1996 with the overall goal of providing a systematic approach for appropriate pain care in **cancer patients** [1, 2].
2. The organizational structure of the ladder involves **three-steps** of increasingly strong medications with adjuvant medications and procedural interventions as needed if the traditional medications are not providing adequate pain control.
3. Step 1 starts with non-opioids, such as NSAIDs and acetaminophen. If pain persists, step 2 involves starting a weak opioid (i.e. codeine or tramadol). If analgesia remains inadequate, step 3 introduces a strong opioid (i.e. morphine or hydromorphone) with titration to effect [1]. Lastly, it has been proposed to introduce step 4 to the original ladder. This step includes minimally invasive therapies (interventional pain procedures), although some experts would suggest these **procedures may be offered at any step along the treatment** continuum.
4. **Adjuvant medications that can be added at any step** to improve pain control include antidepressants, gabapentinoids, topical medications, corticosteroids, and cannabinoids [2].
5. All medications should be titrated to pain relieving dosages on an **individual basis** and may need to be rotated to other medications if side effects occur without sufficient pain control [1].

Questions

1. A 56-year-old male presents to your clinic with uncontrolled low back pain associated with renal cell carcinoma metastatic to the lumbar spine. He has tried acetaminophen without relief and avoids NSAIDs due to the renal effects of these medications. Which medication would be appropriate if you are following the WHO analgesic ladder?
   A. Ibuprofen
   B. Morphine
   C. Codeine
   D. Hydromorphone
2. A 44-year-old female presents for follow-up at pain clinic. She has been using oral morphine for the past six months for pelvic pain related to ovarian cancer. She has tried multiple adjuvant medications in addition to the opioid medications. What is the most reasonable next step?
   A. Decrease morphine dose by 20% OME
   B. Continue morphine at the same OME
   C. Increase morphine dose by 20% OME
   D. Discontinue morphine and initiate hydromorphone at 20% less OME
3. With the patient above, you make the decision to discontinue morphine and initiate hydromorphone at 20% less OME. She initially does well, but again requires progressive increases in OME and experiences side effects with the higher dosages. What is the most appropriate next step in the patient's pain treatment?
   A. Consideration of an intrathecal drug delivery system (IDDS)
   B. Decrease hydromorphone dose by 20% OME
   C. Continue hydromorphone at the same OME
   D. Increase hydromorphone dose by 20% OME
4. Per the WHO modified analgesic ladder, acupuncture therapy may be added at which step?
   A. first step
   B. second step
   C. third step
   D. Any step

Answers

1. C
2. D
3. A
4. D

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NSAIDs and Acetaminophen for Acute and Chronic Pain

68

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Introduction

- NSAIDs function through their inhibition of the cyclooxygenase enzymes (**COX-1 and COX-2**)—the main enzymes responsible for the production of key elements in the inflammatory cascade. However, the COX enzymes are present throughout the human body, and the inhibition of these enzymes is responsible for many of the main deleterious side effects of NSAIDs, including **GI irritation/ulcers**, **bleeding**, and **renal injury**.
- NSAIDs and acetaminophen alone have been shown to be efficient in managing mild pain and are often used as an adjunct to the management of moderate to severe pain.
- The preoperative use of COX-2 selective NSAIDs has been shown to reduce cerebrospinal fluid **prostaglandin and IL-6** levels, as well as decrease surgical site prostaglandin levels during the perioperative period.
- The use of NSAIDs leads to diminished inflammation in these regions, decreased pain, and an opioid-sparing quality.
- Results of a recent meta-analysis suggested that the addition of an NSAID or acetaminophen to an opioid PCA diminished post-operative nausea/vomiting, decreased sedation, and provided an opioid sparing-effect

Pharmacology

- Interrupts the inflammatory cascade by inhibiting cyclooxygenase enzymes, block prostaglandin synthesis in the periphery and central nervous system
- Two isoforms of cyclooxygenase enzymes: COX-1, COX-2 (Fig. 68.1). COX-2 selective inhibitors cause less side effects.
- Local tissue injury leads to:
  - disruption of the cell membrane phospholipids
  - release of arachidonic acid. (Fig. 68.1)
- COX enzymes catalyze the conversion of arachidonic acid into: (Fig. 68.1). COX-**1 expressed in most tissues** and responsible for maintaining normal function of GI tract, kidney and platelet; on the other hand, COX-2 is an inducible form, **almost undetectable in most cells** but expressed during inflammation.
  - Prostaglandin E2➔ pain, bone formation, fever
  - Prostacyclin I2➔ stomach: increase mucus production. Decrease HCL secretion; kidney: cytoprotective vasodilation
  - Thromboxane➔ enhances platelet aggregation

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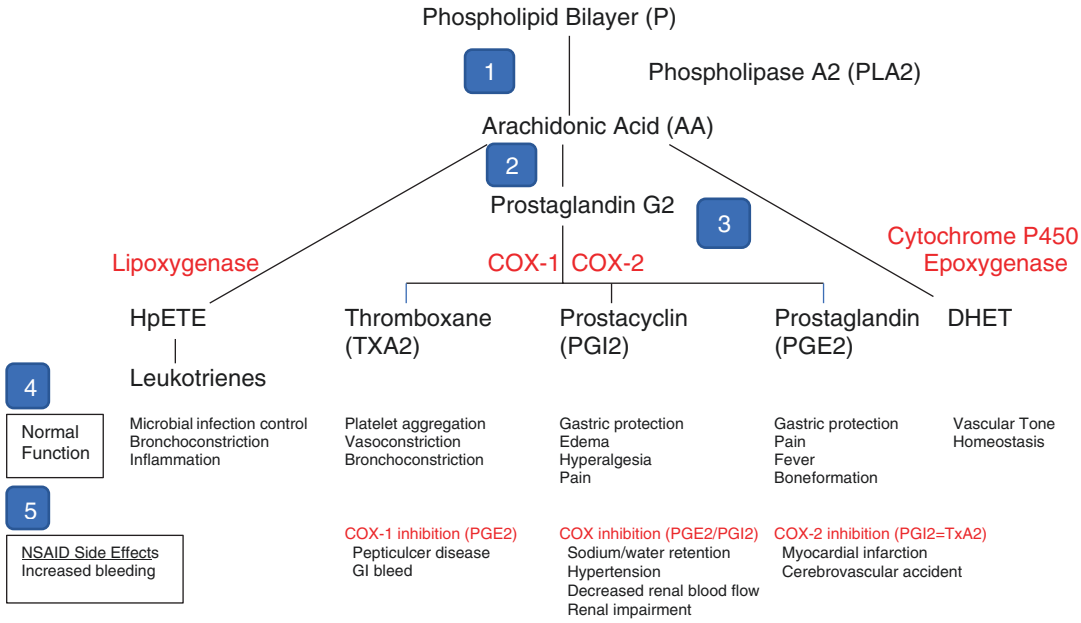

Fig. 68.1 (1) Tissue trauma causes phospholipid release. PLA2 converts phospholipid to AA (2) Cyclooxygenase (COX-1&2) convert AA to TXA2, PGI2 and PGE2 (3) NSAIDS/acetaminophen impair COX-1&2 preventing TXA2, PGI2 and PGE2 formation (4) Normal function (5) NSAID changes—COX-2 decreases PGI2 which then allows a greater impact of TXA2 causing strokes or MIs [6]

Classes of NSAIDS

- Six main pharmacological classes of NSAIDS—differing chemical structures: Acetic Acid Derivatives, COX-2 Selective, Enolic Acid Derivatives, Fenamates, Propionic Acid Derivatives, and Salicylates (aspirin). See the table above.

Pharmacokinetics

- Half-lives vary; rapid absorption following oral administration. Peak plasma concentrations--generally 2–3 hours.
- Weak acids with usual pKa values <5; ionized at physiologic pH; highly protein bound [1]
- Metabolism
  - hepatic biotransformation via cytochrome p450 mediated oxidation
  - glucuronide conjugation, followed by renal excretion
  - 10% excreted unchanged in urine [1]
- Common metabolic pathway; therapeutic decision for the appropriate drug determined by:
  - route of delivery
  - patient comorbidities
  - specific half-life/COX sensitivity
- Most NSAIDs administered orally; some rectally, parenterally, or topically.
- NSAIDs available parenterally in the US: ketorolac, ibuprofen

Adverse Effects

- Nonspecific: rash, dyspepsia, abdominal pain, diarrhea.
- Cardiovascular: myocardial infarction, strokes, hypertension—reduced prostaglandin I2 (PGI2 or prostacyclin) production by vascular endothelium ➔unopposed action of prothrombotic platelet thromboxane A2 (Fig. 68.1) ➔ endothelial injury➔ stroke, MI, HTN [3].

Table 68.1 Summary of the Common Nonsteroidal Anti-inflammatory Drugs and Acetaminophen [1, 5]

Drug	Trade Name	Half-Life (hr)	Daily Dose Range	Dosing Schedule	Pediatric Dose
Acetaminophen	Tylenol Ofirmev (IV)	2	2–4 g	325–650 mg q4h	10–15 mg/kg q6-8hr prn
Acetic acid derivatives					
Etodolac	N/A	7	400–1200 mg	200–400 mg tid/qid, XR 400–1000 mg qd	15–20 mg/kg/24 hr
Indomethacin	Indocin	2–5	100–200 mg	25–50 mg tid/qid XR 75–150 mg qd	1–4 mg/kg/24 hr. oral 0.1–.25 mg/kg qd-bid IV
Sulindac	N/A	8–16	400 mg	150–200 mg bid/tid	NA
Enolic acid derivatives					
Meloxicam	Mobic	15–20	7.5–15 mg	7.5–15 mg daily	NA
Nabumetone	N/A	24	1000–2000 mg	1000 mg bid or 2000 mg qd	NA
Piroxicam	Feldene	40–50	20 mg	10–20 mg daily	NA
Fenamates					
Diclofenac	Voltaren	1–2	150–200 mg	50 mg tid/75 mg bid	2–3 mg/kg/24 hr
Ketorolac	Toradol	4–6	IV: 120 mg/day	30 mg first dose; then 15 mg q6hr	IV: 0.5 mg/kg/day, single dose only
Tolmetin	Tolectin	5	600–1800 mg	200–600 mg tid	20–30 mg/kg/24 hr. Split over 3–4 doses
Propionic acid derivatives					
Fenoprofen	Nalfon	2–3	1.2–2.4 g	300–600 mg qid	NA
Flurbiprofen	Ansaid	2	200 mg	100 mg bid	NA
Ibuprofen	Motrin, Advil, Brufen Caldolor (IV)	6	1.2–2.4 g 3200 mg	400–800 mg qid 400–800 mg qid	7.5–10 mg/kg qid 10 mg/kg qid
Ketoprofen	N/A	2–4	225 mg	75 mg tid	NA
Naproxen	Naprosyn, Aleve, Anaprox	14	550–1100 mg	250–550 mg bid	5–10 mg/kg bid
COX-2 selective					
Celecoxib	Celebrex	6–12	200 mg	100–200 mg qd/bid	3 mg/kg bid
Salicylates					
Acetyl salicylic acid	Aspirin	.25	325 mg-4 g qd	300–600 q4–6 h	N/A
Salsalate	N/A	7–8	3000 mg	1000 mg tid	NA

  - Short-term use, little CV risk [3]
- Renal: reduction in prostaglandin PG synthesis ➔decline in glomerular hydrostatic pressure (the driving force for GFR, Fig. 68.1)➔acute kidney injury. In healthy patients, PGs play little role in renal hemodynamics, however, PG synthesis is increased in the setting of patients with preexisting renal disease and use of NSAID precipitate kidney injury. Therefore, use of NSAID is not recommended in patient CKD (GFR < 60 mL), dehydration, volume depleted states e.g. heart failure, nephrotic syndrome, cirrhosis, elderly, hypercalcemic states, etc.
- Bone healing: controversial, probably no significant effect.
  - Bone healing needs an inflammatory response (IL-1, IL-6, tumor necrosis factor, fibroblast growth factor).
  - NSAIDs inhibit inflammatory/healing response—leading to decreased bone healing
  - Due to this assumption—pushback on perioperative NSAID use from orthopedic surgeons.

- Allergy/hypersensitivity: urticaria, angioedema from decreasing prostaglandin (destabilizes histamine), asthma, vasomotor rhinitis, and nasal polyps from inhibiting bronchodilator PGE2.
- GI: irritation and erosion of the GI mucosa.
  - COX-1 inhibition—decreases prostaglandins and results in decreases in mucous production. It also decreases HCL production (Fig. 68.1)
  - With erosion/ulceration—hemostasis compromised by the inhibition of COX-1, leads to GI bleed
  - Risk factors for GI issues: prolonged use, advanced age, h/o ulcers, co-administration of steroids, and higher doses of NSAIDS [4].
- Bleeding: Inhibition of COX-1 dependent platelet aggregation.
  - Aspirin (ASA): irreversible inhibition of platelets through COX-1 acetylation.
  - Platelets—no nucleus; actions of aspirin last the entire 10–14 day lifecycle of the platelet.

NSAID Selection: Analogous analgesic efficacy. Match patient co-morbidities with differences in: (1) half-life, (2) route of delivery, (3) COX specificity, and (4) cost

- **Aspirin:** The "original" NSAID. Antipyretic and analgesic; used for its cardioprotective COX-1 mediated anti-platelet function in adults. Low dose (<100 mg daily) suppresses **COX-1 mediated expression of thromboxane** for the life of the platelet. (10–14 days)
- **Meloxicam:** Blocks COX-2 > COX-1. Action between true COX-1 and COX-2 inhibitors. Inhibits COX-2 at low doses (7.5 mg), while there is greater effect upon COX-1 at higher doses (15 mg). **Better GI tolerability** profile than nonselective NSAIDs.
- **Ketorolac:** Pyrrolo-pyrrole subtype. IV or PO. Used perioperatively. Opioid-sparing effect. Analogous to morphine effects. Renal function and perioperative bleeding limit the dose in patients >65 or those weighing <50 kg (15 mg q6h and not more than 60 mg in 24 hours).
- **Naproxen:** Weak COX inhibitor; equal COX-1 and COX-2 binding throughout its long half-life (9–26 hours).
- **Ibuprofen:** Traditional NSAID for acute and chronic pain. Inhibits both COX enzymes; shorter half-life (2–4 hours). Weak COX inhibitor = high doses required.
- **Diclofenac: Potent COX inhibiter**; greater than ibuprofen or naproxen. Inhibits both COX isoenzymes; equal selectivity for COX-2 as celecoxib. Short half-life (1–2 hours). **Only approved topical NSAID in the United States**: gel, patch, or ointment. Efficacious analgesia without the systemic side effects. Side effects of topical = application site reactions.
- **Celecoxib:** Decreased GI side-effects, **increased thrombotic risk** from decreased production of COX-2 derived prostacyclin. Longer half-life (6–12 hours). Contraindicated if sulfa allergy present.
- **Acetaminophen: Antipyretic** and weak anti-inflammatory effects
  - **Mechanism unknown**; analgesic effects correlate with a reduction in levels of PGE2.
  - The antipyretic effects from COX-1
  - No significant peripheral prostaglandin synthesis inhibition; **drug acts centrally**; not effective for inflammatory disorders.
  - Routes of administration = oral, rectal, parenteral.
  - Metabolized to sulfate and glucuronide conjugates in the liver; small amount secreted unchanged in urine.
  - Few side-effects with normal dose. Minor metabolite (NADPI) very potent and fatal in overdose.
  - NADPI = fulminant hepatic failure, renal tubular acidosis, and hypoglycemia. Treat with N-acetylcysteine therapy [2].
  - The addition of acetaminophen to multimodal analgesic regimens can improve pain control.
  - It is contraindicated in patients having severe hepatic insufficiency or severe active liver disease.

Questions

1. Which of the following NSAIDs is most likely to increase bleeding risk?
   A. Salsalate
   B. Choline magnesium trisalicylate
   C. Acetaminophen
   D. Acetyl salicyclic acid
2. Myocardial infarction from NSAID use is likely a result of which of the following?:
   A. Decreased prostaglandin I2 production
   B. Unopposed thromboxane production
   C. Blockade of COX 1 and COX2
   D. All of the above
3. Ketorolac acts at which part of pain pathway?
   A. Peripheral sensory receptors
   B. Dorsal route ganglia
   C. Spinothalamic tract
   D. Periaqueductal gray
4. Which of the following NSAIDs would LEAST likely to inhibit platelet activation?
   A. Ibuprofen
   B. Naproxen
   C. Aspirin
   D. Celecoxib
5. An 83-year-old male with past medical history significant for chronic renal insufficiency and hypertension, presents to the clinic with right knee pain due to osteoarthritis. What would be the best medication to prescribe?
   A. Hydrocodone/acetaminophen 5/325 q4h PRN
   B. Ibuprofen 600 mg q6h
   C. Tramadol 50 mg daily
   D. Diclofenac gel 50 mg BID to right knee.

Answers

1. D: Acetyl salicylic acid, commonly known as aspirin, is an acetylated salicylate vs. the other drugs listed are non-acetylated salsalates or acetaminophen. The acetylated form causes an irreversible 98% reduction in TxA2 for the life of the platelet and thus increases bleeding risk. The other salicylic derivatives cause increases in bleeding, but are short-lived over the life of the drug [1].
2. D.
3. A. Although there is some evidence for CNS activity, the primary action of NSAIDS is in decreasing peripheral inflammation [2].
4. D: Celecoxib is a Cox-2 selective NSAID. Hence, it would not be expected to inhibit Cox-1 mediated platelet activation. However, there is a small component of Cox-1 activity present, so there is some anti-platelet activity, albeit small and not likely clinically significant [1].
5. D: Diclofenac gel 50 mg BID to right knee. This patient has already tried treating his knee pain physical therapy and application of a knee brace without relief. Pharmacologic intervention is warranted. However, opioids (hydrocodone, tramadol) are not generally first line agents for pain. Furthermore, his age puts him at additional risk for opioid related side effects. Hence, the best initial treatment would be NSAIDS or acetaminophen. Yet, he has multiple medical conditions that put him at risk for complications of systemic NSAID use (ibuprofen), including advanced age, renal disease, and hypertension. So, the topical NSAID diclofenac is the best of the listed options for him at this time.

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69 Antidepressants and Anticonvulsants for Neuropathic Pain

Michael Lankhorst, Marshall Ladd, and Angie Rakes

The use of antidepressants and anticonvulsants in the treatment of neuropathic pain is common across a wide range of syndromes. While not all antidepressants and anticonvulsants are useful in management, there are some families that appear to show benefit. Understanding the use of these medications and the risks associated is a common area for board questions.

Antidepressants

TCA

- Inhibition of presynaptic neurotransmitter reuptake (norepinephrine and serotonin) is the primary mechanism for the therapeutic effects of tricyclic antidepressants.
- subdivided into two categories. (1) The tertiary amines eg amitriptyline, clomipramine, doxepin, imipramine, and trimipramine, which are more potent **in blocking reuptake of serotonin** than norepinephrine. (2) Secondary amines eg desipramine, nortriptyline, and protriptyline, which are more potent in blocking **reuptake of norepinephrine.**
- Tertiary amines cause **more side effects**
- patients must be **screened for cardiac disease and suicidality** before starting therapy. It has cardiac effects, anticholinergic effects and antihistaminic effects. Also it affects sexual dysfunction (decreased libido, delayed ejaculation).

This group is considered a multi-target drug class with effects on:

- Reuptake of serotonin and adenosine
- Noradrenergic effects
- Blockade of the NMDA receptor
- Blockade of sodium and calcium channels
- Opioidergic effect

- Pain relieving effective dose is significantly lower than antidepressant effective dose
- Lowest number needed to treat (NNT) of the neuropathic medication classes 3.6. Average number needed to harm (NNH): 9
- Are safe to use in those with impaired renal function
- TCAs are often associated with anticholinergic side effects including dry mouth, urinary retention, and constipation; also problematic is an increased risk of falls (not recommended for patients >65).
- Increase risk of serotonin syndrome with concurrent use of SSRI

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- Toxicity from TCA overdose can be fatal. Therefore not recommended for patients with suicidal ideation or severe depression. It **prolongs QT interval**, leading to arrhythmias. Overdose of cyclic antidepressants can also cause **anticholinergic toxicity** and seizures. Furthermore, these medications are **highly lipophilic** and protein bound and are therefore **not effectively removed** by hemodialysis.

SNRI

- Commonly used are venlafaxine (Effexor) and duloxetine (Cymbalta)
- Milnacipran (Savella) is primarily used for **fibromyalgia**
- Primary difference between the SNRI's is the level of serotonergic to noradrenergic effect
  - Venlafaxine **primarily serotonergic** at lower doses with increasing noradrenergic component as dose increases.
  - Duloxetine and milnacipran are **primarily noradrenergic** with the latter having the greatest noradrenergic effect of the group
- This class can also be used to treat non-neuropathic pain states like osteoarthritis and chronic back pain
- NNT is around 6.4 across all neuropathic pain groups, but number needed to harm was high at 11.8
- Slower time to effect at 4–6 weeks for this group vs TCA
- Concerns:
  - Renal failure or GFR less than 30
  - Liver dysfunction (duloxetine)
  - Use of other serotonergic drugs (think Parkinson's, tramadol, SSRI, antiemetics)
  - Duloxetine impairs CYP 2D6- may increase beta blockers-propranolol, some antiarrhythmics- propafenone and flecainide as well as others

Anticonvulsants

- For neuropathic pain primarily focus on alterations in sodium and calcium channels.

Gabapentin and Pregabalin

- Both drugs are widely used for neuropathic pain and their molecular structures are similar. There are differences in pharmacokinetics.
- Gabapentin is structurally related to GABA. However, **it does not bind** to GABA-A or GABA-B receptors, and it does not influence synthesis or uptake of GABA.
- Both gabapentin and pregabalin bind to the **alpha-2-delta subunit of voltage-gated calcium channels** (frequently asked) and modulates calcium currents. They also modulate the release of several neurotransmitters including glutamate, noradrenaline, and substance P. The net result is **inhibition of neuronal excitability**.
- pregabalin has **improved bioavailability** compared to gabapentin. It is **rapidly absorbed in an hour**. The rapid action of pregabalin has been linked to euphoria and abuse potential. Pregabalin is favorable to drug-addicts or patients in methadone treatment programs.
- Both are renally cleared, requiring dose adjustment according to **renal function** in renal failure and dialysis
- Pregabalin has specific FDA approval for **spinal cord injury and fibromyalgia**
- Both are first line therapy for the following:
  - Diabetic peripheral neuropathy (DPN)
  - Postherpetic Neuralgia (PHN)
  - Spinal Cord Injury Pain
- Gabapentin has specific indication for:
  - HIV Neuropathy
  - Cancer related neuropathic pain

  - Postamputation phantom limb pain
  - Neuropathic pain not otherwise specified
- Concerns:
  - Dizziness (falls)
  - Cognitive impairment (mental fogginess, word finding difficulty, fatigue, somnolence)
  - Weight gain (peripheral edema)

Topiramate and Sodium Valproate (SV)

- Topiramate is used in neuropathic pain, including postherpetic neuralgia, intercostal neuralgia, and CRPS. Also used in **migraine prophylaxis** and frequently as a mood stabilizer
- It has potential for development of **kidney stones** and **ocular glaucoma,** as topiramate is an inhibitor of the enzyme, carbonic anhydrase.
- Topiramate➔ metabolic acidosis➔ decreased urinary citrate excretion➔ increased urinary pH➔ propensity to form calcium phosphate stones.
- Weight loss associated with topiramate may be a benefit for obesity.
- Mechanism of action:
  - Topiramate- Sodium/calcium channel blockade, **enhances** the action of the GABA (inhibitory) neurotransmitter, and **inhibits** the AMPA-type glutamate (excitatory) receptor.
  - Sodium Valproate- Poorly understood, likely sodium channel blockade
- Concerns:
  - Weight loss, metabolic acidosis, past history of kidney stones are concerns with topiramate
  - Weight loss/gain, hyponatremia, rash, GI, thrombocytopenia, hepatotoxicity associated with SV
  - Birth defects (cleft palate, neural tube defects)
  - Hyponatremia more common with SV, metabolic acidosis with topiramate
  - Cognitive impairment similar and in some cases worse than gabapentinoids

Lamotrigine (Lamictal)

- It is an antiepileptic medication commonly prescribed for seizure control by neurologists and for mood stabilization by psychiatrists.
- Recommended for use in post stroke pain, trigeminal neuralgia, and HIV neuropathy and diabetic neuropathy. Prophylactic treatment for headache disorder specifically SUNCT: short-lasting unilateral neuralgiform headache with conjunctival injection and tearing
- Although generally well tolerated, rash may occur in up to 10% of individuals and **Steven-Johnson syndrome, also known as toxic epidermal necrolysis**, has been reported in 0.08% of individuals.

Carbamazepine and Oxcarbazepine

- The chemical structure of both compounds are similar to that of the tricyclic antidepressants, but mechanism of action is quite different.
- It binds to **voltage-dependent sodium channels**, after they change from the activated to the inactivated state. This binding extends the inactivated phase and inhibits the generation of rapid action potentials when the cell is experiencing incoming depolarizing trains.
- Other side effects include **pancytopenia** (necessitating a complete blood count and monitoring while on this therapy), Stevens Johnson syndrome, and toxic epidermal necrolysis.
- With a NNT of <2, carbamazepine is the most studied treatment for trigeminal neuralgia (common board question), and many studies have highlighted its usefulness.
- The usual initial starting dose of CBZ is 2 to 3 mg/kg per day orally (eg, 100 to 200 mg daily for most patients) given two, three, or four times daily; the dose is increased every five days to 10 mg/kg daily (eg, 800 to 1200 mg/day). Generally, three-times-daily dosing of the immediate-release formulation is recommended.
- Oxcarbazepine, **the keto-analog of carbamazepine**, was developed to preserve carbamazepine's membrane-stabilizing effects while

minimizing adverse effects. A major advantage of oxcarbazepine is that drug plasma level or CBC monitoring are **generally not necessary**.

- Significant **hyponatremia** (sodium <125 mmol/L) may develop during treatment with oxcarbazepine.
- Concerns:
  - Similar to other anticonvulsants for cognitive and balance issues
  - Hyponatremia
  - Rash can happen with both, but Stevens Johnson syndrome more likely with carbamazepine
  - Carbamazepine also associated with agranulocytosis, aplastic anemia

Clinical Pearls

- For almost all neuropathic pain conditions **gabapentin and pregabalin are first line therapy**.
- Tricyclic antidepressants have a narrower window for treatment **but are typically the lowest number needed to treat** for most neuropathic pain conditions.
- Signs of TCA poisoning include sedation, confusion (due to antihistaminic effects), delirium, or hallucinations, arrhythmia(sinus tachycardia to VT/VF), refractory hypotension, and anticholinergic effects (eg, hyperthermia, flushing, dilated pupils), Seizures (due to blockade of GABA A receptor.
- All the medications covered in this chapter may cause cognitive impairment, and selecting the correct drug or combination frequently requires addressing the patient's comorbidities and other current medications.
- Gabapentin is **more variably absorbed then pregabalin** and may be affected by GI changes like **gastric bypass.**

Questions

1. What is considered the first line pharmacological treatment for trigeminal neuralgia?
   A. Carbamazepine
   B. Oxcarbazepine
   C. Gabapentin
   D. Amitriptyline
2. The direct mechanism of action of the gabapentinoids is?
   A. Increasing the availability of serotonin and norepinephrine
   B. Binding to sodium type channels
   C. Binding to calcium type channels
   D. Binding to Mu type receptors
3. You have a patient with metastatic cancer currently being treated with multiple antiemetics (including Zofran) for chemotherapy associated nausea who is also on an antidepressant (fluoxetine) as well for depression related to her illness. Which of the following medications if added to treat her developing neuropathy could contribute to a severe metabolic derangement?
   A. Gabapentin
   B. Duloxetine
   C. Topiramate
   D. Pregabalin
4. A 40-year-old patient is referred to your clinic for management of overall body pain and has many myofascial tender points across the entire body and has associated issues with mental fogginess, daytime fatigue, waking unrefreshed and has a history of depression, multiple GI disturbances and bladder spams. Which of the below medications is currently FDA approved for treatment of the above condition?
   A. Fluoxetine
   B. Pregabalin
   C. Gabapentin
   D. Nortriptyline

5. Which of the following medications would not typically require adjustment for renal clearance?
   A. Gabapentin
   B. Pregabalin
   C. Duloxetine
   D. Nortriptyline

Answers

1. A
2. C
3. B
4. B
5. D

Suggested Reading

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Opioid Analgesics, Tolerance, Dependence and Addiction

70

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Introduction

- Opioid analgesics are commonly used alone or as parts of multimodal regimens for treating acute and chronic pain. Yet, their use in chronic non-cancer pain is controversial.
- In some patients they help alleviate pain and allow functional restoration, however, they also have the potential for serious risks including unintentional overdose, abuse, addiction, and diversion. The latter have contributed to the public health crisis and prescribing controversy in the United States.
- Professional societies and regulatory agencies have established guidelines regarding the rationale for opioid use and the safe initiation and management of patients on opioid therapy [1]. It is imperative for health professionals to understand the benefits and risks of these medication, and unintended consequences of opioid therapy, in order to yield safe and efficacious treatment endpoints.
- **Opioids** act on pre- and post-synaptic receptors in the CNS, in dorsal horn of the spinal cord, and on peripheral nerves.
- **Opioids are classified based on their receptor binding and activating profile** (agonists, partial agonists and antagonists), **as well as on their origin** (as natural, synthetic or semi-synthetic) [2].

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Classification of Opioids

Natural	Agonist
Morphine	Morphine
Codeine	Meperidine
Papaverine	Fentanyl analogs
Semisynthetic	Antagonists
Heroin	Naloxone
Hydromorphone	Naltrexone
Synthetic	Agonist- antagonists
Fentanyl related	Pentazocine
Methadone related	Butorphanol
Pentazocine related	Nalbuphine
	Buprenorphine

Morphine

- μ-receptor agonist, low oral bioavailability (24-40%) and hydrophilicity contribute to slower onset *vs* other opioids
- Longer analgesia (4-5 h) relative to its $t_{1/2}$ (2-5 h);
- analgesia is due to **parent drug** and to its metabolite **morphine 6-glucuronide** (M6G), (5-15%),

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- an μ- and δ- agonist that contributes to analgesia and side effects;
- the other metabolite **morphine 3-glucuronide** (M3G), (50%), lacks any μ- and δ- activity, but can cause **hyperalgesia**
- side effects: CNS excitability, seizures, and myoclonus;
- metabolites are renally excreted and the dose should be adjusted **in renal failure**; renal impairment may affect the M3G/M6G ratio and cause **neuroexcitatory effects**

Codeine

- weak μ-agonist; its effect depends on **its conversion to morphine in the liver**;
- the genetic polymorphism of CYP2D6 is responsible for the variable response to codeine;
- **poor metabolizers (5-10% of patients)** have insufficient pain relief;
- drugs that inhibit CYP2D6, such as paroxetine, fluoxetine, and bupropion decrease its effect. (Table 70.1)

Oxycodone

- a μ-agonist with oral bioavailability 55-70% and $t_{1/2}$ shorter that morphine's;
- its plasma levels reach steady state within 24 h (*vs* 2-5 d for morphine);
- undergoes **hepatic metabolism** via P450 2D6 into oxymorphone, an active metabolite, and via CYP3A4 to noroxycodone, an inactive metabolite (Table 70.1);
- P450 2D6 inhibiting drugs or genetically low levels of P450 2D6 (10% of population) reduce its efficacy (Table 70.1); in contrast drugs that inhibit the P450 3A4 enzyme (SSRI, TCA, neuroleptics) may enhance its efficacy. (Table 70.1)

Hydrocodone

- slightly less potent than oxycodone; converted by P450 2D6 to **hydromorphone** and CYP3A4 to **norhydrocodone** (both active metabolites) (Table 70.1);
- poor CYP2D6 metabolizers are at risk for accumulation and toxicity. (Table 70.1)

Hydromorphone

- hydrophilic, strong μ-agonist **~5–7x** more potent than morphine,
- oral bioavailability 20% to 80%, $t_{1/2}$ 1.5-3.5 h,
- duration of analgesia 3 to 4 h; undergoes hepatic biotransformation into **hydromorphone-3-glucuronide** (H3G), that lacks analgesic efficacy but may be neuroexcitatory;
- hydromorphone and H3G are both renally excreted, but are preferable to morphine in patients with renal insufficiency.

Methadone

- racemic mixture of d-methadone (blocks the NMDA receptor),
- inhibits serotonin and norepinephrine reuptake, and 1-methadone (μ- and δ- agonist);
- **no known neurotoxic or active metabolites**; high absorption with **variable** oral bioavailability (range 40–99%); lipophilic;
- **unpredictable bioavailability and pharmacokinetics** and high inter-individual variability ($t_{1/2}$ 10-60 hrs) make its effects **unpredictable**;
- commonly related to unintended overdose and deaths from respiratory depression and arrhythmias due to **QT prolongation**;
- may be helpful in opioid rotation from other opioids possibly due to its NMDA receptor blockade (**but should be used with caution**).

Table 70.1 Pharmacologic considerations of opioid effect – relevant drug or agent interactions

	CYP3A4	CYP2D6	Potential Effect
Substrate	Calcium channel blockers Statins Quinidine Benzodiazepines Sleep aids (*zolpidem, zopiclone*) Psychiatric drugs (*haloperidol, carbamazepine, mirtazapine*) Macrolide antibiotics HIV antivirals	Beta-blockers Anti-psychotic drugs (*haloperidol*) SNRIs Tricyclic antidepressants (*fluoxetine, bupropion*) Histamine H1 receptor antagonists metoclopramide Tamoxifen	May increase the parent opioid concentration leading to increased analgesic effect or toxicity
Inhibitor	Calcium channel blockers (*diltiazem, verapamil*) Macrolide antibiotics Azole antifungals Grapefruit juice Star fruit HIV antivirals	Antiarrhythmic agents SNRIs SSRIs Histamine H2 receptor antagonists Bupropion Cinacalcet	May increase the parent opioid concentration leading to increased analgesic effect or toxicity
Inducer	Anticonvulsants (*carbamazepine, phenytoin, barbiturates*) Rifampin St. John's wart	Rifampin Glucocorticoids (*dexamethasone*)	May reduce opioid levels and therefore may reduce analgesic effect

Buprenorphine

- lipophilic semisynthetic opioid; causes analgesia acutely, but also suppresses withdrawal and addiction;
- **high affinity** but **low intrinsic activity** at μ-receptor (partial agonist) results in acute analgesia, but maximal opioid effect is less than that of full agonists ("***ceiling effect***");
- it can displace full agonists from μ- receptors and block the other opioids' effects, but full agonists cannot displace it from the μ- receptors because of its higher affinity, so buprenorphine's receptor occupancy prevents the other opioids from exerting effects;
- it is used in treating **addiction** because its slow dissociation from the μ- receptors suppresses opioid withdrawal; hepatically metabolized via P450 3A4 into nonactive metabolites (80% to 90%).

Tramadol

- weak μ- agonist and **inhibitor of norepinephrine and serotonin reuptake**;
- metabolized via CYP2D6 to the active metabolite O-desmethyl tramadol (M1); poor CYP2D6 metabolizers (Table 70.1) form less M1 leading to inadequate pain relief;
- ultrarapid metabolizers produce increased M1 leading to higher analgesia, to higher risk of nausea, to over-sedation and respiratory depression;
- mostly renally excreted (30% unchanged and 60% as metabolites); its capacity to inhibit the reuptake of serotonin with concomitant serotonergic drugs (TCAs, SSRIs, SNRIs, triptans, MAOIs, antiparkinson medications)
- can result in **serotonin syndrome** that manifests as diarrhea, tremor, tachycardia, autonomic hyperactivity, altered mental state, and even death, when severe.

Fentanyl

- very lipophilic, synthetic potent μ-agonist **~100x** more potent than morphine;
- available for iv (rapid onset-short duration of 1-2 μg/kg- higher doses attenuate sympathetic responses), for neuraxial use, for transmucosal use, or for transdermal administration in patches (12 h onset of action; **steady state in 3-4d**; 24 h needed for clearance after patch removal);
- metabolized by CYP3A4 (Table 70.1) in the liver to **norfentanyl** which is inactive, and excreted renally; prescribed or illegally made fentanyl has recently emerged as a common drug of abuse.

Systemic effects of Opioids

- Constipation: it can be useful for patients with diarrhea (loperamide or opium tincture)
- Cough suppression: used for smooth anesthesia induction
- Hemodynamic stability in healthy patients (minimal effects)
- Hypotension due to histamine release by morphine, meperidine, venodilation (sympathectomy effect), arterial relaxation of smooth muscle
- CNS: pain relief by activation of receptors, sedation, EEG changes by normeperidine, pupillary constriction by Edinger-Westphal n., nausea/vomiting by stimulation of chemoreceptor trigger zone, vomiting center, vestibular center etc.
- Musculoskeletal: rigidity
- Biliary: sphincter of Oddi spasm, increased biliary pressure

Risks of Opioids and Risk Mitigation

The opioid risk tool (Table 70.2) is a screening tool based on self-report in adult patients to assess the risk for opioid abuse in adult patients prior to consideration of chronic opioid prescriptions. A score of 3 or lower indicates lower risk for future opioid abuse, a score of 4 to 7 indicates moderate risk for opioid abuse, and a score of **8 or higher** indicates a **high risk** for opioid abuse.

Prevention of Opioid Use Disorders

- Screen for family history (genetic predisposition) and for personal substance abuse.
- Assess risk using an opioid risk tool, such as **ORT** (Table 70.2) or **Screener and Opioid Assessment for Patients with Pain** (**SOAPP**).
- Avoid opioids in **current drug abusers**; prior drug abuse is a relative contraindication.
- Caution in bipolar disorders, depression, anxiety, ADD/ADHD, sociopathic, borderline disorders.
- Sign **opioid agreement** and monitor closely with: (1). Clinical assessments; (2). On line **Prescription Drug Monitoring Program (PDMP);** (3). Periodic random **urine drug testing;** (4). Periodic **pill counts.**

Trial Therapy and Ongoing Assessment

- when starting opioid therapy, start with the lowest effective dose (Table 70.3). **In elderly patients** or in those with severe **renal or liver disease** much lower initial doses are recommended.

Table 70.2 Opioid risk tool (ORT)

Risk factor	Female	Male
Family history of substance abuse		
Alcohol	1	3
Illegal drug	2	3
Prescription drugs	4	4
Personal history of substance abuse		
Alcohol	3	3
Illegal drugs	4	4
Prescription drugs	5	5
Age between 16 – 45 years old	1	1
History of pre-adolescent sexual abuse	3	0
Psychological disease		
ADD, OCD, bipolar disorder, schizophrenia	2	2
Depression	1	1
Scoring total		

Table 70.3 Equianalgesic doses of commonly used opioids and recommended starting doses

Drug	Equianalgesic dose		Conversion ratio to oral morphine	Recommended starting dose		Dosing interval
	Oral	(*iv*, *im*, *sbc*		Oral	*iv*, *im*, *sbc*	
Morphine	30 mg	10 mg	Parenteral (*iv*, *im*): 3 times	5 - 15 mg;	2 - 5 mg;	Q4 to 6 hours
Hydromorphone (dilaudid)	3 -7 mg	1 - 2 mg	7 times	1 - 2 mg	0.5 – 2 mg	Q4 to 6 hours
Codeine	200 - 300 mg	N/A	0.15 times	15–30 mg		Q4 to 6 hours
Oxycodone	10 – 20 mg	N/A	1.5 times	5 mg		Q4 to 6 hours
Hydrocodone	30 mg	N/A	1 to 1.5 times	5 mg		Q4 to 6 hours
Tramadol	300 mg		0.1 times	25 to 50 mg		Q6 hours
Fentanyl transdermal patch	~12 mcg/hr. patch	100 mcg	100 times	IV Q1 hours		Patch: Q48-72 hours

- Equianalgesic doses of opioids (see Chap. 34, chronic pain) have been calculated based on studies using typical, standard opioid doses for acute short-term pain. When switching from one opioid to another, it is recommended to use a lower dose than the exact "equianalgesic" dose, by reducing the calculated dose by 30-50% due to **incomplete cross tolerance** among different opioid agents.
- **Controlled substance agreement:** Necessary requirement for chronic opioid therapy.
- **Ongoing assessment with DIRE:** Patients on chronic opioid therapy should be monitored closely with a clinician-rated instrument, such as the DIRE, designed to predict the efficacy of analgesia and adherence with long-term opioid therapy. The DIRE score ranges from 7 to 21, with a score of 13 or below suggesting that a patient **is not a suitable candidate** for long-term opioid therapy.
- **Monitoring of adverse effect, misuse or abuse:** Prescription drug monitoring, urine drug screen, pill count, frequent follow up, identify patients with high risk of abuse (personal or family history of substance use disorder, younger age, mental health disorders, multiple prescriber, long term use, higher dose of opioids - for example hazard ratio **8 times higher in patients with > 100 MME**). The benefits and harms for patients on chronic opioid therapy should be assessed at least **every 2 months**.
- **Indication and strategy for discontinuation of opioid therapy:** ineffectiveness, side effects, abuse/misuse/diversion. For addiction, referral to addiction specialist or starting with buprenorphine/methadone therapy

Tolerance, Dependence and Addiction

- **Tolerance:** a physiologic phenomenon of reduced pharmacological effect to an opioid as a result of its chronic, repeated use; a patient who has developed tolerance to opioids needs **higher dose to feel the same effect**.
- **Dependence:** another physiologic state at which physical acclimatization to chronic opioid use ensues to the point that if opioid is discontinued, **withdrawal symptoms** (*dysphoria; nausea, vomiting, diarrhea; myalgia; tremor; lacrimation, rhinorrhea, sweating; mydriasis; piloerection; yawning; insomnia*) occur.
- **Addiction (Opioid Use Disorder or OUD)**:

  - in contrast to tolerance and dependence, OUD is an abnormal, pathological response.
  - this does not require physiological tolerance or dependence in order to be considered as OUD
  - OUD typically involves **harm** to the individual, together with strong **obsession to obtain** opioids, and **difficulty to control** their use.

Diagnosis of **Opioid Use Disorder:** Diagnosis is facilitated by the presence of **at least two** relevant DSM-V criteria, **within 12 months** [4]:

- Opioids used at **higher doses** and longer than intended.
- **Persistent desire** and/or unsuccessful efforts to cut down or quit opioid
- Craving for opioids
- Excessive amount of time spent in obtaining and/or using opioids
- Important social, occupational, recreational activities **neglected or reduced** because of opioid use
- Ongoing use of opioids despite work/school/home problems
- Ongoing use of opioids despite them causing significant interpersonal problems
- Ongoing use despite opioids having caused physical/psychological problems
- Recurrent use of opioids in hazardous situations
- Tolerance or withdrawal (doesn't apply if OUD is related to prescribed opioids)

Treatment of Opioid Use Disorder [5]

- If a patient develops behavioral manifestations indicative of OUD, the prescriber, should:
  - **discontinue opioids** (gradually) and **treat withdrawal symptoms** appropriately with **$\alpha_2\delta$ agonists** (clonidine), **buprenorphine, methadone.**
  - if opioids put a patient **at imminent risk** (overdose, addiction, etc.), or are being **diverted**, they should be immediately discontinued, and the patient should be treated for withdrawal.
  - ***exceptions to abrupt discontinuation***: patients with **unstable angina**, with **heart disease**, and **pregnant women (especially third semester)**: these patients should be weaned off in a gradual manner with close follow-up, preferably hospitalized
- Refer patient to **Medication Assisted Treatment Programs (MATP)**
  - MATPs usually combine substitution medications with behavioral therapy or counseling.
  - **substitution agents used in MATP include**: methadone; buprenorphine-based agents (suboxone*: buprenorphine/naloxone,* subutex*: sublingual buprenorphine*); injectable extended-release naltrexone (*vivitrol*).
  - addition of **behavioral therapy,** plus **community self-help group, improve outcome**
- If left untreated, addiction to opioids may lead to **serious and life-threatening** complications, including death.

Clinical Pearls

1. For acute pain, prescribe the lowest effective dose of immediate-release opioids (Table 70.3) and at no greater quantity than needed for the expected duration of pain; **3 days or less** often is sufficient; more than **7 days** is **rarely** needed.
2. **Nonpharmacologic therapy** and **nonopioid** drugs are **preferred** for chronic non-cancer pain.
3. Before starting opioids, assess risk (Table 70.2); continue opioids only if there is clinically meaningful improvement in **pain and function** that outweighs risks to patient safety.
4. Avoid increasing dosage to **≥50 MME/d**, and avoid exceeding **90 MME/d** for chronic non-cancer patients. Prescribe **prophylactic naloxone** nasal spray and educate family about its use.

5. Renal disease affects dosing, duration and intensity of effect of some opioids; codeine, hydrocodone (*its metabolite* ***hydromorhpone-3-glucuronide*** *may accumulate and lead to neuroexcitatory effects, such as agitation, confusion, hallucinations*) and morphine (*M6G can accumulate and cause* ***respiratory depression,*** *hypotension, and lethargy*) should be **avoided**. Oxycodone (*mainly metabolized by liver*) and hydromorphone (*mainly metabolized by liver but metabolite H3G can accumulate*) should be used **with caution**.

MCQ Questions

1. A 45 yo female patient with diffuse muscle pain from fibromyalgia has been on oxycodone 10 mg every 6 hrs as needed for her pain. Over the last several months she has experienced problems with her job, and had few car accidents. Her urine has been positive for hydrocodone, hydromorphone and tramadol. Correct actions at this point include:
   A. *Switch to morphine ER (MSContin) to mitigate the risk of addiction*
   B. *Discharge from practice for violation of opioid agreement*
   C. *c. Switch to fentanyl patches for more stable analgesia and less potential for abuse*
   D. *d. Refer to a Medication Assisted Treatment Program with behavioral therapy*
2. A 58 yo male patient with coronary artery disease and chest pain at rest and exertion, has been on hydrocodone/acetaminophen 10/325 mg qid prn for chronic back pain after failed back surgery. He has been frequently found sleepy and unresponsive by his spouse. His urine has tested positive for alprazolam and oxycodone. Appropriate management is:
   A. *B. Discharge from practice for violation of opioid agreement*
   B. *Switch to oxycodone, prescribe naloxone spray and provide instructions to spouse*
   C. *Discontinue medications immediately and start him on methadone in titrated doses*
   D. *Refer for hospital admission for gradual weaning in a controlled environment*
3. A 75 yo patient with metastatic prostate cancer and chronic kidney insufficiency has been on high doses of morphine extended release (*MSContin*) and immediate release morphine for breakthrough pain. He complains of inadequate pain relief, that -as he claims- results in stress, anxiety, agitation, tremors, sweating and muscle twitching. You will next:
   A. *Discontinue ms contin and add equipotent immediate release morphine*
   B. *Increase the dose of morphine further*
   C. *Switch to equipotent hydromorphone which is a much more potent analgesic*
   D. *Switch to methadone which may be preferable in this setting*
4. Which of the following statement of a patient gives you a clue that she has addiction but not physical dependence of a controlled substance:
   A. *A."I don't want to drink too much but once I start drinking with my friends I cannot stop until I pass out"*
   B. *"I must take this drug, if I stop using it I get crazy"*
   C. *"When I started using needle, I got a shot and I passed out; now I take 5–6 shots, nothing happens"*
   D. *"None of the above"*
5. John Glenn is a 80 year old male with prostate cancer. His pain had been well controlled on extended release oral morphine 60 mg every 12 hours. Today he came to your office for severe pain of intensity 8/10. You asked your resident to calculate the least dose of *iv* morphine he should get based on his current oral dose. The resident said that he should get at least:
   A. *2 mg IV morphine every 4 hours*
   B. *4 mg IV morphine every 4 hours*
   C. *6 mg IV morphine every 4 hours*
   D. *8 mg IV morphine every 4 hours*

Correct Answers of MCQs

1. E
2. E
3. D
4. A
5. C

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Equianalgesic Doses of Opioids

71

Aaron Cheung and Christine Oryhan

Introduction

- Opioids vary greatly in their relative potency.
- **Opioid rotation** is defined as a switch from one opioid to another or altering the administration route (PO, IV, etc) in an effort to provide better outcomes.
- Opioid rotation is commonly practiced in the management of refractory pain, development of tolerance and side effects.
- The **equianalgesic dose** is defined as the dose of a different drug that produces a similar level of analgesia.
- When switching from one opioid to another, the starting dose of the new drug must be adjusted according to its predicted equianalgesic dose; otherwise, the patient may develop **withdrawal or unintentional overdose**.
- **Incomplete cross tolerance** refers to tolerance at one opioid receptor that partially extends clinically to another, and therefore a dose reduction should be considered when changing opioids, particularly after chronic use.

Opioid Rotation Guidelines

- **Step 1: Identify indications** for switching opioids (adverse effects, poor analgesic efficacy, drug interactions, changes in clinical status, financial/social considerations).
- **Step 2: Equianalgesic dose** of new opioid should be calculated based on a standard equianalgesic dosing table and **reduced** by **25–50%** (Table 71.1)
  - Patient characteristics should be used to determine degree of reduction (i.e. elderly or frail patients should have dose **reductions closer to 50%)**
  - If switching to **methadone**, doses should be **reduced by 75–90%** and **starting doses** should **not exceed 30 mg/day**
- **Step 3:** Assess patient carefully after transition and determine if dose should be increased/decreased by 15–30% based on pain severity, withdrawal, and/or side effects.

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https://doi.org/10.1007/978-3-030-87266-3_71

Table 71.1 Opioid Equivalency Chart [1–3]

	EQUIANALGESIC DOSES				
OPIOID	Oral	Intravenous	Epidural	Intrathecal	Notes
Morphine	30 mg	10 mg	1 mg	0.1 mg	
Hydromorphone	7.5 mg	1.5–2 mg	0.3 mg	0.06 mg	5x morphine
Oxycodone	20 mg	–	–	–	1.5x morphine
Hydrocodone	30 mg	–	–	–	1x morphine
Tramadol	200 mg	–	–	–	
Fentanyl	–	100 mcg	33 mcg	6–10 mcg	5.5mcg/hr. (transdermal patch)
Methadone	10 mg	5 mg	–	–	Dose varies with non-opioid naive patients

Morphine

Reference standard in which all other opioids are compared to; total opioid doses commonly reported in morphine equivalent dose per day **(MEDD)**

- **Low lipophilicity → ↓ uptake** by blood-brain barrier
- Metabolized in liver → **morphine-3-glucuronide** (**inactive**) and **morphine-6-glucuronide** (**active**), both **renally** cleared→ caution with renal failure
- Associated with **histamine release**, clinically manifests as pruritus
- Common routes of administration include: oral, rectal, intramuscular, subcutaneous, intravenous, epidural, intrathecal

Fentanyl

- Highly **lipophilic → rapid onset**
- **100x** more **potent** than **morphine**
- **Minimal hemodynamic** effect, **no histamine** releasing properties
- Common routes of administration include: intravenous, intrathecal, submucosal, and transdermal (Table 71.2)

Methadone

- Very **potent** with **long, variable half-life** (13–50 hours) → requires careful **monitoring** [4]

Table 71.2 Initial Transdermal Fentanyl Dosing Based on Oral MEDs

Oral Morphine (mg/day)	Transdermal Fentanyl (mcg/hour)
60–134	25
135–224	50
225–314	75
315–404	100
405–494	125

[a]Should not be used to convert from transdermal fentanyl to other opioids

Adapted from Duragesic [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.:2009

- Check EKG prior to initiating and with increasing dose (**QTc prolonging**)
- Additional **NMDA-receptor antagonist** and **SSRI** activity
- **Non-linear** equianalgesic dosing relative to morphine.
- Common routes of administration include: oral and intravenous (**Oral to IV ratio 2:1**)

Buprenorphine

- **Partial opioid agonist** with strong receptor affinity
- **Very potent** (about **75–100x more potent** than oral morphine) with **long and variable half life**
- **Ceiling effect** for respiratory depression
- Common routes of administration include: sublingual, buccal, transdermal (Table 71.3)

Table 71.3 Initial Transdermal Buprenorphine Dosing Based on Oral MEDs

Oral Morphine (mg/day)	Transdermal Buprenorphine (mcg/hour)
Opioid-naïve	5
<30	5
30–80	10
>80	Consider alternative

Adapted from Butrans [package insert].Stamford, CT: Purdue Pharma, Inc.:2014

Other Common Opioids

- Oxycodone: widely used, 1.5x more potent than morphine, high oral bioavailability
- Hydromorphone: 5x more potent than morphine; moderate duration; used commonly PO, IV, and intrathecally; preferred opioid in patients with renal dysfunction
- Hydrocodone: equivalent potency to morphine, often taken in combo with acetaminophen, metabolites include hydromorphone
- Codeine: used cautiously in children (rapid **CYPD6** metabolizers can cause overdose)
- Tramadol: Synthetic codeine analog, has **SNRI** activity, **maximum** daily dose 400 mg.

Clinical Pearls

1. Opioid conversion charts should only be used as a guide due to large **variability** among patients [5]
2. **Incomplete cross tolerance** should be considered when changing from one opioid to another, and usually requires a dose reduction of 25–50%
3. **Patient safety** should be regarded as the most important factor when dosing opioids
4. Conversion ratios between opioids are not always **bidirectional**
5. In patients with **hepatic dysfunction/failure**, opioid clearance is decreased, and doses should be reduced
6. In patients with **renal dysfunction/failure**, avoid morphine and codeine, use hydromorphone/oxycodone with caution, and consider methadone/fentanyl preferentially
7. Morphine is considered the **reference standard** for comparing potency between opioids

Questions

1. A 75-year-old male with a history of chronic pain presents with a malfunctioning intrathecal morphine pump. The patient receives 8 mg/day of morphine intrathecally. What is the approximate equianalgesic dose of IV morphine?
   A. 800 mg/day
   B. 80 mg/day
   C. 8 mg/day
   D. 4 mg/day
2. All of the following statements about opioid rotation are true, **EXCEPT**:
   A. An additional dose reduction should be considered when switching from an equipotent PO dose to an IV dose of the same opioid
   B. When switching to another opioid, it is recommended to include a 25–50% dose increase to adjust for incomplete cross tolerance
   C. Transitioning from one opioid to another may reduce the severity of side effects
   D. Younger patients may not require as much of a dose reduction compared to elderly patients
3. A 67-year-old female with a history of fibromyalgia, chronic back pain, and opioid use disorder presents with refractory pain. She currently takes a daily morphine equivalent dose of 600 mg. The decision is made to transition her to methadone. In regards to methadone initiation, which of the following is **TRUE**?
   A. The initial dose of methadone should not exceed 60 mg/day
   B. The dose should be titrated to effect daily

C. Initial equianalgesic dose should be reduced by 75–90%
D. This patient is at an equal risk of overdose compared to an opioid-naive patient

4. A 78-year-old male with a history of chronic back pain is admitted with a small bowel obstruction. He is found to have an elevated creatinine of 3.54. He takes 20 mg of morphine three times a day at home. Which of the following is the best option to manage this patient's chronic pain?
   A. Continue patient's current oral morphine regimen
   B. Transition to IV morphine 3 mg q 8 hours PRN
   C. Transition to IV morphine 5 mg q 8 hours PRN
   D. Transition to IV hydromorphone 0.5 mg q 8 hours PRN
   E. Transition to IV HM 1 mg q 8 hours PRN
5. Which of the following statements about methadone is **INCORRECT**?
   A. Methadone has a linear dose conversion
   B. Methadone has a very long half life
   C. Methadone is an NMDA receptor antagonist
   D. Methadone requires close monitoring in patients with prolonged QTc

Answers

1. A
2. B
3. C
4. D
5. A

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Further Reading

Barash, Clinical Anesthesia, eighth Edition, pp. 3939–50.

NMDA Blockade

72

Austin H. Nguyen and Ariana M. Nelson

Ketamine

- Phencyclidine (PCP) structural analogue (see Fig. 72.1)
  - Does **NOT** modulate GABA receptor
  - Primary mechanism of action: **noncompetitive NMDA receptor antagonism** (Fig. 72.2)
- Preparations are available as an aqueous mixture of two optical isomers; the S(+)-ketamine isomer has greater anesthetic and analgesic potency than the R(−) isomer.
- Ketamine is extensively metabolized by hepatic **cytochrome P-450** primarily into the active metabolite **norketamine.**
- Norketamine is approximately **1/3 to 1/5 as potent as ketamine** and is excreted by the kidneys. It may lower seizure threshold when combined with other agents which lower seizure thresholds.
- Monoaminergic properties and interacts with **Na^+ and L-type Ca^+ voltage-gated channels**, cholinergic receptors, and opioid receptors.
- Ketamine **dissociates the thalamus** (sensory relay between reticular activating system and cerebral cortex) from the limbic cortex (awareness of sensation).

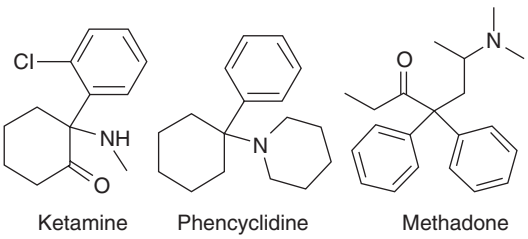

Fig. 72.1 Structural similarity between ketamine and phencyclidine

- At lower doses ketamine may produce analgesia **without inducing a dissociative state.** In the dissociative state, patients exhibit some aspects of consciousness (e.g. eye opening, swallowing) but are **unable to process** or recall sensory input [1].
- **Reduces acute tolerance to opioids,** though mixed evidence if ketamine use reduces total perioperative opioid requirement [3].
- Anesthesia: ketamine is close to being a **"complete" anesthetic**, offering analgesia, amnesia, and unconsciousness with relative hemodynamic stability.
- Analgesia: acute and chronic pain
  - **Minimal** respiratory depression
  - Systematic review and meta-analysis of perioperative ketamine demonstrates:
    - Decreased postoperative pain scores
    - Increased time to first analgesic request
    - Reduces opioid consumption up to 24-hours postoperatively [3]

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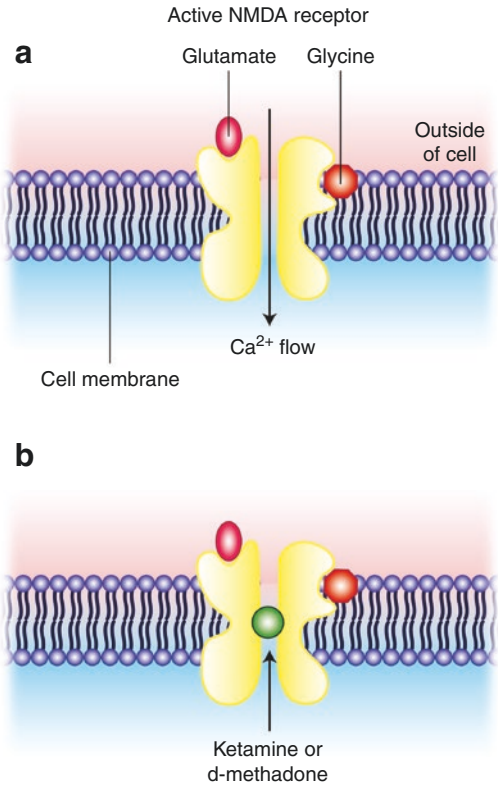

Fig. 72.2 (**a**) NMDA receptor and binding sites of neurotransmitters glutamate, glycine. (**b**) Ketamine and d-methadone act as noncompetitive antagonists whose binding sites are within the ion channel pore region

Pharmacokinetics

- Ketamine route (bioavailability): IV, IM (93%), oral (16–29%), nasal (8–50%), rectal (11–30%), subcutaneous (high), or epidural (77%).
- Peak plasma levels 10–15 minutes following IM administration.
- Lipid solubility of ketamine allows a rapid distribution half life.
- Dosing [4]:
  - Induction: IV 1–2 mg/kg; IM 3–5 mg/kg.
  - Sedation: (often in combination with propofol) IV 2.5–15 mcg/kg/min.
  - Acute postoperative pain: 0.1–0.5 mg/kg/hour by continuous infusion or 0.3–0.5 mg/kg by IV bolus.
  - Chronic pain: oral administration (note: low oral bioavailability, expensive since it needs to be **compounded**).
  - Ketamine IV infusion has been used in some centers for CRPS, neuropathic pain, cancer pain, and other intractable chronic pain states. Available data suggest that infusions given for 1–2 hours and repeated every 2–4 weeks have the potential to provide long term pain relief.

Systemic Effects

- CNS: Recent evidence in anesthetized and mechanically ventilated patients demonstrates **ketamine does *not* increase intracranial pressure** [2].
- The neuroexcitatory effects of ketamine historically have precluded use in patients with concerns for seizures and lowered seizure threshold (**there are case reports of ketamine induced seizure at ED).** Ketamine is also known as potent **antiepileptic** used in status epilepticus and emerging evidence demonstrates a neuroprotective effect of ketamine.
- Psychiatric: Known psychotomimetic effects of ketamine include dysphoria, disturbing dreams, hallucinations, and delirium. These effects during emergence are attenuated in patients **premedicated with benzodiazepines** or combined administration with propofol.
- Cardiovascular: Via CNS sympathetic stimulation, ketamine causes indirect **increases** in heart rate, arterial blood pressure, and cardiac output. However, the **direct myocardial depressant** effects of ketamine may be unveiled with sympathetic blockade and/or catecholamine depletion.

- Respiratory: Ketamine exhibits **minimal respiratory depression**. Racemic ketamine has potent **bronchodilatory** effects. Upper airway reflexes remain intact. Increased salivation is also associated with ketamine, but may be attenuated by an anticholinergic agent.

Methadone

- Long-acting synthetic opioid (see Fig. 72.1) with a long but variable half-life.
- Mechanism: acts on mu, delta, kappa opioid receptors, inhibitor of serotonin and NE reuptake, NMDA antagonist. Therefore it is a **broad spectrum** opioid.
- It is prepared as a racemic mixture of L and D isomers. L-isomer acts as mu receptor agonist and D isomer acts as NMDA antagonist. In addition, it acts as a **serotonin and norepinephrine reuptake inhibitor.**
- The effect of methadone reversed by 60% with naloxone, and other 40% effect mediated by the non-NMDA receptors.
- Indications: **chronic pain, acute postoperative pain**, opioid withdrawal and abuse treatment. The nonopioid activity of methadone make it a potentially useful treatment for neuropathic pain [5].

Pharmacokinetics

- Excellent oral bioavailability, approximately 80%. Can be detected in blood in 15–45 min. Peak plasma conc 2.5–4 hours. Highly bound to plasma protein.
- Methadone undergoes a biphasic pattern of elimination, with an **alpha-elimination phase persisting 8–12 hours** and a beta-elimination phase ranging from **30 to 60 hours**. The alpha elimination phase equates **to the period of analgesia**, which typically doesn't exceed 6–8 hours. This explains why methadone is used once daily dose for addiction therapy but **q6-q8 hours for analgesia.**
- Extensive cytochrome P450 metabolism to inactive metabolites and cleared by bile and urine. **Note drug interaction with CYP inducers and inhibitors**
- Dosing: pain management in opioid naive patient: Initiate **2.5 mg PO every 8 hours**, titrate no sooner than q 3–5 days. Pain management in opioid tolerant patient: high variability.
- Detoxification: **20–30 mg PO daily** or minimum dose to suppress withdrawal for 2–3 days then decrease 20% daily as tolerated

Systemic Effects

- Due to variable half-life of methadone that may increase with repeat dosing, adverse effects may be insidious and/or **delayed onset**. As such, close monitoring and slow titration are paramount
- Cardiovascular: Methadone is known to cause **QT prolongation** and *torsades de pointes* in dosing as low as 20 mg/day via blockade of the delayed rectifier potassium channel. **EKG should be performed prior to initiating therapy**, at 30 days, and annually thereafter

Clinical Pearls

- Ketamine is a unique drug providing **anesthesia as well as analgesia**
- The primary mechanism of action for ketamine is via NMDA antagonism, **distinct from most other anesthetics,** which provides GABA receptor modulation
- Ketamine is a versatile non-opioid adjuvant that offers significant analgesia while minimizing respiratory depression and offering relative hemodynamic stability
- Methadone is a synthetic opioid with a significantly **longer half-life**
- Methadone may cause QT prolongation and/or *torsades de pointes*. Prior to initiating

methadone, an EKG should be performed with **repeat at 1 month and annually**

Questions

1. A patient presents with a large pericardial effusion requiring emergent pericardial window. Which anesthetic is the most appropriate agent for induction of anesthesia?
   A. Fentanyl
   B. Ketamine
   C. Propofol
   D. Midazolam
2. Ketamine is chosen as the induction agent for a 25 year-old undergoing laparoscopic appendectomy. **All** of the following are likely to **increase** *except*:
   A. Heart rate
   B. Cerebral blood flow
   C. Mean arterial pressure
   D. Bronchomotor tone
3. A patient has taken methadone 30 mg PO methadone twice daily for one year due to cancer pain. Which of the following has likely *decreased* in this patient due to long term opioid use:
   A. Risk of respiratory depression
   B. Constipation
   C. Required dose for adequate analgesia
   D. Nausea and vomiting due to methadone
4. A patient recently diagnosed with metastatic colon cancer is being evaluated for pain control. Prior to starting methadone, which of the following would be most essential to perform:
   A. Electrocardiogram
   B. Urine drug screen
   C. Pulmonary function test
   D. Arterial blood gas for PaCO2
5. All of the following modulate the NMDA receptor except:
   A. Ketamine
   B. Phenobarbital
   C. Methadone
   D. Dextromethorphan

Answers

1. B
2. D
3. D
4. A
5. B

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Non-pharmacological Approaches to Chronic Pain Management

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Acupuncture/Acupressure

- Acupuncture, the art of needle penetration, has been widely use in the treatment of chronic pain for thousands of years.
- "Acus" is Latin for needle and "punctura" is Latin for penetration.
- Incorporates the use of needles to stimulate anatomical points which results in therapy.
- It is considered one of the **oldest medical procedures** and requires board certification to practice.
- Current working mechanism of action: acupuncture stimulation results **in the release of endorphins, interleukins, substance P, and adenosine** which helps to mitigate the pain relief response. Opioid antagonists **can block** the analgesic effects of acupuncture.
- A meta-analysis of RCTs of acupuncture found that the superiority of acupuncture over sham acupuncture, but the **effects are too small** to be clinically significant. It should be noted, however, that both acupuncture and sham acupuncture **have strong placebo effect**.
- Acupressure or Shiatsu, is **pressure with fingers or small beads** at acupuncture points. A meta-analysis of four randomized trials of acupressure found that pain intensity was significantly reduced in the acupressure group compared with a placebo control (light touch) or compared with a combined control (light touch or no treatment).

Techniques

- Acupuncture point locations are determined either by using anatomic structures and via theoretical framework of eastern medicine such as the five elements (fire, wood, earth, water, metal) and meridians.
- Once the location of pain is identified, fine point needles are inserted to desired location.
- The usual duration of treatment is twenty minutes per session.
- A transcutaneous electrical nerve stimulation unit maybe attached to the acupuncture needles to send electrical pulses which is thought to result in the release of endorphins.

Considerations

- Avoid the insertion of acupuncture needles at sites of **active malignancy and infection**.
- Patients with automatic implantable cardioverter-defibrillator (AICD) or pacemaker should **avoid electro-acupuncture**

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because of risk of electrical interference with the device, however, traditional acupuncture is safe in these patients.
- Pregnancy is not an absolute contraindication, but cautions should be observed since some points can induce labor.
- Use of anticoagulants and bleeding disorders **are not contraindications** to treatment but caution should be taken.

Meditative Movement Therapies: Tai chi/Qigong/Yoga

- Balance problems are common in elderly resulting frequent falls and significant morbidity.
- Balance exercises are recommended for individuals who have a history of falling, chronic pain setting for fibromyalgia, and joint pain and to help improve balance and stability. Research has shown participation in group classes of exercises such as tai chi improve balance and reduce falls risk.
- Tai Chi is a type of balance exercise of gentle flowing, low-impact, **slow-motion exercise** movement that incorporates mind-body practice. Series of motions are done without pausing and movements are circular but never forced.
- Qigong is the focused and specific **thoughtful breathing exercise** while doing activity.
- Yoga uses **interactions among the mind, body**, and behavior to improve different aspects of physical and mental health. Yoga includes physical postures, breathing control, and meditation along with cognitive strategies of mindfulness.
- The main goal of meditative movement therapies is to help restore function or **limit stresses of chronic pain** through balanced physically stimulating management.
- The benefits of yoga have been evaluated in >100 meta-analyses, which shows statistically **significant benefits of yoga** compared with no intervention. The benefits of yoga are similar to **other forms of light to moderate exercise**.
- Patients who are unable to perform intense exercise, yoga is a reasonable alternative. The patient who has cervical disc disease and glaucoma **should avoid yoga**. Yoga practice vary significantly, it is advised **to start at light levels** and increasing the intensity of practice over time as tolerated.

Group Therapy

- Incorporates the use cognitive behavioral therapy in group psychotherapy settings.
- Usually 8-weeks in length. May have multiple sessions based on progress.
- Skills taught: focused breathing, muscle relaxation, visualization of relaxing settings, and guided imagery.
- Therapeutic goal: to decrease anxiety associated with having pain, problem-solving techniques to approach pain care.
- Other benefits: finding a community that understands what living with 24/7 pain is and means reducing reduces patient isolation.
- Using positive peer pressure to improve coping mechanisms.

Clinical Pearls

1. RCTs have proven efficacy of acupuncture in chronic pain syndromes, specifically low back pain, knee osteoarthritis, and migraine. It is generally very safe if appropriate sterile techniques are utilized. Both acupuncture and sham acupuncture **had greater efficacy** than when patients are left untreated.
2. Group therapy is recommended especially when multiple interventions have been unsuccessful for pain control or if the patient has a history of poor compliance.

Questions

1. Current mechanism of action for acupuncture is:
   A. Placebo effect
   B. Release of interleukins
   C. Release of substance P
   D. All of the above
2. Which of the following is not a contraindication for acupuncture:
   A. History of surgery and presence of scar tissue
   B. Anemia
   C. Pregnancy
   D. Severe neutropenia
3. Using positive peer pressure to help with coping mechanisms is used in which of the following:
   A. Tai Chi
   B. Group therapy
   C. Physical therapy
   D. Acupuncture
4. Gentle flowing exercise that incorporates slow, not forced movement is known as:
   A. Acupuncture
   B. Quigong
   C. Meditation
   D. Tai Chi
5. Meditative Movement Therapies include which of the following:
   A. Tai Chi
   B. Quigong
   C. Yoga
   D. All of the above

Answers

1. D
2. C
3. B
4. D
5. D

Suggested Reading

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