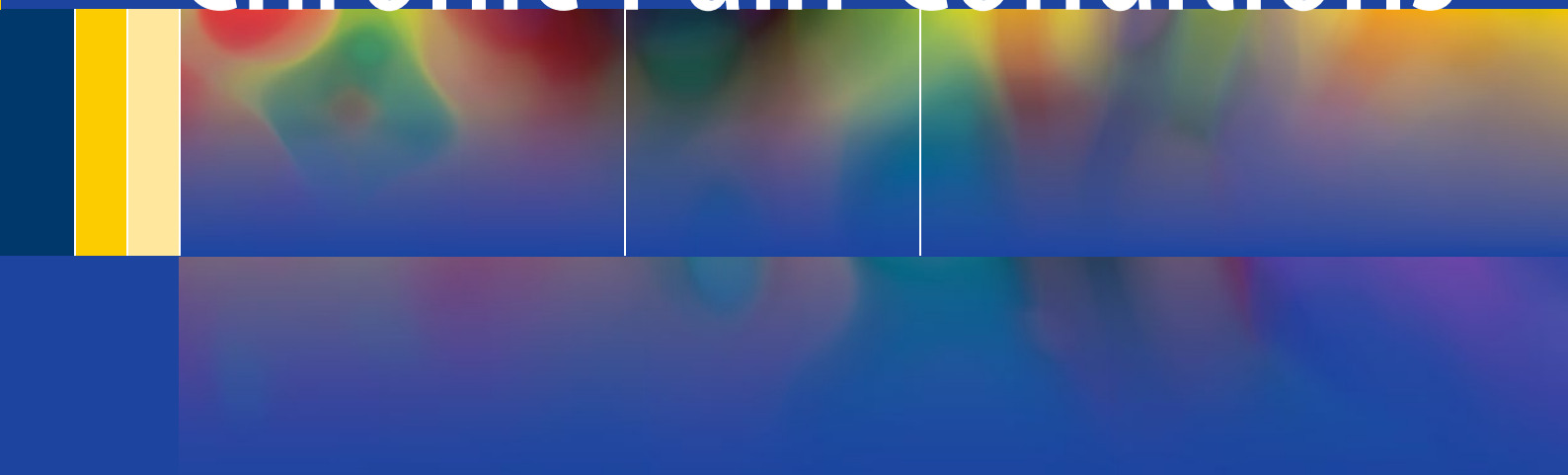
Jason E. Pope
Timothy R. Deer
Editors

Treatment of Chronic Pain Conditions



A Comprehensive Handbook

Springer

Jason E. Pope • Timothy R. Deer
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Treatment of Chronic Pain Conditions

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To my wife and partner in all things, Emily. Thank you for your steadfast support, grace, generosity, and heart. I am humbled and honored to share this life with you.

To my loving children, Liam, Olivia, and Vivienne. It is a joy to see you experience the world and I am so proud of you.

To my parents, thank you for your sound advice on navigating work–life balance and your unflinching support.

To Dianne and Paul, thank you for your love and support.

To my twin brother, Greg, thank you for your quiet intellect and demeanor.

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To my families at NANS, INS, ASRA, AAPM, and ASIPP. Looking forward to many more years of service.

To Timothy Deer, my mentor and friend, thank you for your support, advice, and partnership. We continue to not be victims of circumstance.

Finally, thank you to God, for making all things possible.

Jason E. Pope, MD

To my patients to whom I have dedicated this book and many hours of work to try to improve the quality of life and suffering of many.

To Missy my wonderful wife and partner in all things. Thank you so much for your support and love. To my children, it has been amazing watching your personal growth and success. Morgan, Taylor, Reed, and Bailie keep up the great work and strive for excellence.

To Jason Pope who has been a brother to me in our goal to improve the global footprint of patient care and excellence in treating the suffering. Brotherly love and friendship is a great thing which I cherish.

To my family in practice in the United States. Chris Kim (my Korean brother); Brian Yee, Warren Grace, Nick Bremmer, Chong Kim, and Doug Stewart; and my incredible clinical team.

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Most importantly my deepest gratitude to God from whom all blessings flow. I am humbled by the ability to continue to work at the wonderful field of medicine.

Timothy R. Deer, MD

Foreword

After over 25 years of working on a daily basis with pain medicine fellows, I came to realize the great privilege I have by working with bright, young doctors who chose the management of acute and chronic pain as their career.

The inquisitive minds of those intelligent and motivated trainees have kept us honest and allowed me personally to enhance my knowledge, as I had to examine the world's literature to be able to answer their intelligent and probing questions and satisfy their eagerness to learn.

To all those fellows in training or going to training as well as all pain management specialists who would like to get comprehensive and practical answers to their burning questions, I am delighted to forward this comprehensive handbook that covers all aspects of the acute and chronic pain management in a complete, easy-to-read manner.

This handbook has 51 chapters that address the basic anatomy and physiology of acute and chronic pain, the fundamentals of clinical examination, and full assessment of radiologic and neurologic studies. This handbook also emphasizes the interdisciplinary aspects of the management of pain from medication to physical restoration and psychological rehabilitation. Finally, there are several chapters that explain the most advanced state-of-the art interventional techniques in a very comprehensive and practical manner.

Congratulations to my friends Timothy Deer and Jason Pope for assembling a great line up of the best pain specialists to contribute to such great book.

Finally, this handbook will be a great asset to those starting their career in pain medicine.

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Part I

The Basics: I. Background Focus

Chronic Pain

1

George C. Chang Chien, Eduardo Jusino, and Armin Deroee

Key Concepts

- Chronic pain is defined as pain that persists beyond the normal tissue healing time and is at least 3–6 months in duration.
- Pain is categorized as being nociceptive or neuropathic. Nociceptive pain is subdivided into somatic and visceral pain. Neuropathic pain is subdivided into peripheral neuropathic pain and central neuropathic pain.
- The sequence of events by which a pain stimulus is perceived involves four processes: transduction, transmission, modulation, and perception.

Definition

The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage." Adaptive pain protects the body from injury and promotes healing when injured. Maladaptive or chronic pain represents pathologic operation of the nervous system.

Chronic pain is defined as pain that persists beyond the normal tissue healing time. This time interval is often indicated as 3 months, though some experts have identified the window as 6 months (Table 1.1).

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Types of pain

Pain is categorized as being nociceptive or neuropathic.

Nociceptive pain arises from a nerve fiber sensitive to a noxious stimulus or to a stimulus that may become noxious. Nociceptive pain is subdivided into somatic (skin, bones, and joints) and visceral (body organs) pain. Somatic pain originates from injury to body tissue and it is well localized, discrete, and intense. Visceral pain results from stimulation of the visceral stretch receptors, and it is diffused and poorly localized.

Neuropathic pain develops from abnormal neural activity due to disease, injury, or dysfunction of the peripheral nervous system (PNS) and/or central nervous system (CNS). It is associated with abnormal sensations (dysesthesia) and pain from normally non-painful stimuli (allodynia). Neuropathic pain may be continuous and/or episodic. The pain is usually described as burning, electric shock, numbness, tingling, and itching.

Neuropathic pain is subdivided into peripheral neuropathic pain and central neuropathic pain. Peripheral neuropathic pain is due to damage to a peripheral nerve with or without autonomic changes (postherpetic neuralgia, diabetic neuropathy, and complex regional pain syndrome). Central neuropathic pain results from abnormal central nervous system activity (thalamic pain syndrome, poststroke pain, and postspinal cord injury pain).

Mechanism

Pain sensation starts in the peripheral nerves through nociceptors. The nociceptor is a receptor of a sensory neuron that responds to potentially damaging stimuli by sending signals to the spinal cord and brain. The pain signal is transmitted from the peripheral nerve to the dorsal horn of the spinal cord and through the CNS where it is processed in the somatosensory cerebral cortex. Nociceptors are categorized as fast conducting myelinated A-delta fibers that signal

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Table 1.1 Definitions of some of the common terminology in pain medicine

Chronic pain	A pain that persists beyond the normal tissue healing time. This time interval is often indicated as 3 months, though some experts have identified the window as 6 months
Nociceptive pain	A pain that arises from a nerve fiber sensitive to a noxious stimulus or to a stimulus that may become noxious
Neuropathic pain	A pain from abnormal neural activity due to disease, injury, or dysfunction of the peripheral nervous system and/or central nervous system
Neurogenic pain	Pain initiated or caused by a primary lesion or dysfunction or by transitory perturbation in the peripheral or central nervous system
Central pain	Pain initiated or caused by a primary lesion or dysfunction in the central nervous system
Peripheral sensitization	Increased excitability in peripheral nociceptors because of peripheral injury that manifests as primary hyperalgesia
Central sensitization	Increased and prolonged excitability of CNS nociceptors because of peripheral injury that causes promoting increased sensitivity to painful stimuli (secondary hyperalgesia)

immediate, sharp pain and slow conducting unmyelinated C fibers that transmit delayed, longer-lasting dull pain. The five types of nociceptors include the following: thermal, mechanical, chemical, silent, and polymodal.

The sequence of events by which a pain stimulus is perceived involves four processes: transduction, transmission, modulation, and perception. Transduction occurs in the peripheral terminals of nociceptor sensory fibers where different forms of energy (thermal, mechanical, or chemical) are converted into electrical activity. Transmission is the process by which the electrical activity is conducted through the nervous system. This involves three major components: peripheral, synaptic, and central transmission. Nociceptive impulses travel along peripheral nerve fibers through first-order neurons (peripheral transmission) to the dorsal horn of the spinal cord where they synapse with the second-order neurons (synaptic transmission) and further transmit via neurons that cross the spinal cord and ascend to the thalamus and brainstem nuclei where third-order neuron synapsis occurs (central transmission). Modulation is the process where neural activity may be altered along the pain transmission pathway. Perception is the final stage of the pain-signaling process by which neural activity in the transmission pathway results in subjective sensation of pain at the level of the somatosensory cortex.

Chronicity

Many factors may contribute to the development of chronic pain. Peripheral injury leads to increased excitability in peripheral nociceptors (peripheral sensitization) that manifests as primary hyperalgesia. This leads to increased stimuli of the CNS that causes increased and prolonged excitability of CNS nociceptors (central sensitization) promoting increased sensitivity to painful stimuli (secondary hyperalgesia). At least three mechanisms are responsible for central sensitization in the spinal cord: (1) windup and sensitization of second-order wide dynamic range neurons, (2) dorsal horn neuron receptor field expansion, and (3) hyperexcitability of flexion reflexes. Also, peripheral injury is accompanied by many changes including new expression of sodium channels, adrenergic receptors, and cholinergic receptors that contribute to depolarization of injured nociceptors. This depolarization results in sodium and calcium flux that may cause spontaneous action potentials with or without stimulation. Derangements can occur in both the ascending and descending signaling systems at any level. All of these factors may contribute to the development of chronic pain following injury.

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Mechanisms of Chronic Pain

2

Eduardo Jusino, George C. Chang Chien, and Beth H. Minzter

Key Concepts

- Sensitization is a process in which repeated stimulus of a receptor results in the progressive amplification of a response.
- The key excitatory neuromodulators are glutamate, aspartate, and substance P.
- The main inhibitory neuromodulators are GABA, glycine, enkephalins, and somatostatin.
- Mechanisms of persistent pain include the following: peripheral sensitization, central sensitization, ectopic excitability of sensory neurons, physical rearrangement of neurons' circuitry, and disinhibition.
- Research into the mechanisms that generate and maintain chronic pain are necessary to develop new interventions and improved treatment outcomes.

Introduction

After inflammation or tissue injury, pain sensation may continue long after the withdrawal of the noxious stimuli. This transition from acute to chronic pain has been a long-standing medical enigma. Recent advances in the study of pain transmission and processing have begun to unravel the cellular mechanisms that underlie the maintenance of chronic pain. The term sensitization refers to the process in which a repeated stimulus results in the progressive amplification of a response. Sensitization is a key factor in the genesis of chronic pain and a demonstration of plasticity within the nervous system. As an example, repeated stimulation of nociceptive C fibers entering the dorsal root can elicit a progressive increase in the number of action potentials generated. The dorsal root ganglia may become hyperexcitable and display continuous spontaneous electrical activity. This activity results from the expression of many cell-specific molecules in modified cells, which alter the complex neuronal circuits of our nervous system. These neuronal changes are the mainstay of sensitization. Chronic pain sensation can result from such injury. Understanding the changes that follow in neural structures at a molecular level may help lead to new therapeutic interventions.

There are various primary excitatory and inhibitory neurotransmitters implicated in the propagation of chronic pain. The amino acids glutamate and aspartate are the key excitatory neurotransmitters in the somatosensory system. The four types of excitatory amino acid receptors are the N-methyl-D-aspartate (NMDA), alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA), kainite, and metabotropic receptors. Gamma-aminobutyric acid (GABA) and glycine are the key inhibitory neurotransmitters. Substance P is the key excitatory neuropeptide. The enkephalins and somatostatin are the key inhibitory neuropeptides.

Peripheral Sensitization

Nociceptive stimulation of tissue in a neuron's receptive field causes release of inflammatory mediators (prostaglandins, bradykinin, histamine, cytokines, growth factors) that may reduce the threshold for excitation of peripheral receptors. When changes occur in the response characteristics of the primary afferent fibers which transmit pain, the A-delta and C fibers, the peripheral nervous system is said to be sensitized. Peripheral sensitization causes the nerve to be responsive to benign, normally nonpainful stimuli, and this is termed allodynia. This may also provoke an exaggerated response to painful stimuli, known as hyperalgesia. Changes

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in cellular transduction such as increases in the cAMP-PKA mechanism may be involved in further sensitization. Inflammation leads to upregulation of nitric oxide synthase that can cause neuropeptides to be released from nociceptive nerve terminals, and these neuropeptides therein produce inflammatory hyperalgesia. The recruitment of previously silent nerve fibers which become sensitive to stimuli after exposure to inflammatory mediators is another mechanism of peripheral sensitization. The final common pathway for peripheral sensitization appears to involve an increase in intracellular calcium and protein kinase levels.

Central Sensitization

Central sensitization amplifies the synaptic transfer from the nociceptor terminal to the dorsal horn neurons. Initial sensitization is an activity, which is dependent on stimulated nociceptors, but subsequent transcriptional changes at the molecular level sustain the sensitization. Previously subthreshold synaptic input to nociceptive neurons will now generate an augmented action potential output. The NMDA receptor plays an important role as its responsiveness to glutamate is increased, leading to increased excitability of the dorsal horn cell. Inflammation may contribute to both peripheral and central sensitization. Neuroimmune interaction produced by peripheral inflammation causes changes in brain-derived neurotrophic factor, substance P, neurokinin, dynorphin, and cyclooxygenase 2 which may lead to transcription-dependent central sensitization. Also, neuroglial interactions contribute to sensitization by releasing cytokines and chemokines after nerve injury, altering gene transcription. The main causes of central sensitization-maintained pain include neuronal sensitization, reduction in inhibitory interneuron activity, and modulation of descending pathway activity.

Neuronal sensitization is triggered by intense electrical or noxious stimulation of C fibers which promote wide-dynamic-range (WDR) neuron hyperexcitability in the dorsal horn. Repetitive electrical stimulation provokes increased excitability leading to action potential "windup." Windup refers to slow, prolonged depolarization and ultimate burst of action potentials with stimulation. WDR neuron sensitization is associated with excitatory amino acids, tachykinins, and calcitonin gene-related peptide. These neuromodulators affect the dorsal horn neuron by increasing cation fluxes, impinging on intracellular transduction mechanisms, and modulating receptor and transmitter gene transcription. Synaptic transmission augmentation at NMDA receptors is the final common pathway. Adequate depolarization causes an increase in intracellular calcium level leading to protein kinase phosphorylation that antagonizes the magnesium blockade at the NMDA receptor.

Interneurons, as well as descending signals arising from the brain, may be excitatory or inhibitory. Stimulation of some cortical and subcortical areas may cause analgesia. Reduction in inhibitory interneuron activity results in increased WDR neuron excitability consistent with clinical hyperalgesia and allodynia. The loss of GABA and glycerine activity in the dorsal horn produces a state of neuronal hyperexcitability.

Modulation by supraspinal descending pathways is likely due to increases or decreases in several neurotransmitters causing descending facilitation or inhibition. The endogenous opioid, noradrenergic, and serotonergic systems are involved in descending control of nociceptive pain perception. There is evidence that serotonin receptors provoke the release of substance P from the spinal cord. This release of substance P correlates with the receptors' ability to increase nociception at the level of the neurons. Increases in noradrenaline in the dorsal horn may potentiate descending noradrenergic inhibitory circuits, thereby reducing nociceptor stimulation. Diminished cerebral GABA can lead to disinhibition of descending facilitation.

It has been demonstrated that the injured neurons within the DRG are markedly more sensitive to activation, creating the potential for a therapeutic window for treatment of chronic pain with electrical stimulation.

Conclusion

The major causes of hypersensitivity to pain after injury are peripheral and central sensitization. Substances released after tissue injury can be nociceptor sensitizers. NMDA receptor changes can increase dorsal horn excitability. Activated glial cells may produce cytokines that alter gene transcription and contribute to further sensitization. Other mechanisms for persistent pain include but are not limited to the following: ectopic excitability of sensory neurons due to upregulation of voltage-gated sodium channels or downregulation of potassium channels, physical rearrangement of neurons' circuitry in the dorsal horn, and disinhibition due to loss of GABA and glycine-mediated inhibition.

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Overview of Chronic Pain

3

Denis G. Patterson

Introduction

Chronic pain is a term that defines a set of specific medical conditions in which a patient suffers from pain for extended periods of time. While many interventional treatment options exist depending on the nature of the complaint and the patient's overall well-being, otherwise, many patients are given opioid therapy by primary care and ER physicians. This chapter addresses several key national factors that are currently tied to chronic pain: a growing epidemic of opioid use in the United States which is partially attributable to the lack of physicians who were effectively trained to treat pain, and the result is a significant economic burden on the country.

Opioid Epidemic

The use of using opioids to treat non-cancer pain began in 1986 when Portenoy and Foley published a seminal paper. They treated 38 patients with non-cancer pain for greater than 6 months with a median daily dose of less than 20 morphine milligram equivalents per day. The lack of clinically significant adverse events led them to conclude that physicians could safely and effectively prescribe opioid medications to patients without a history of substance abuse with "relatively little risk of producing maladaptive behaviors which define opioid abuse." The results of this paper began the push for physicians toward a greater acceptance of the use of opioid analgesics to treat non-cancer pain. The movement gained momentum in the 1990s when state medical boards curtailed restrictions on laws governing the prescribing of opioids for the treatment of chronic non-cancer pain. This led to new pain management standards for inpatient and outpatient medical care implemented by the Joint Commission on the Accreditation of Health Care Organizations (JCAHO) in 2000. These new standards lead to an increased awareness of the right to pain relief, which provided further justification for physicians to use opioids to treat non-cancer pain. Other factors that fueled the increase were aggressive marketing by the pharmaceutical industry and the promotion for increased use of opioids in the treatment of non-cancer pain by a myriad of medical organizations.

Unfortunately, the above positions were based on unsound science and blatant misinformation, accompanied by the dangerous assumptions that opioids are highly effective and safe and devoid of adverse events when prescribed by physicians. As a result, opioid use became an epidemic in the United States. The quantity of prescription painkillers (i.e., opioid medications) sold to pharmacies, hospitals, and doctors' offices was four times larger in 2010 than in 1999. Enough prescription painkillers were prescribed in 2010 to medicate every American adult around-the-clock for 5 months. According to the CDC, drug overdose death rates in the United States have more than tripled since 1990. In 2008, more than 36,000 people (approximately 100 people per day) died from drug overdoses, and nearly three-fourths of these deaths were caused by prescription drugs. The misuse and abuse of prescription painkillers was responsible for more than 475,000 emergency department visits in 2009, a number that nearly doubled from the previous 5 years. Almost all prescription drugs involved in overdoses come from prescriptions originally. Most prescription painkillers are prescribed by primary care and internal medicine doctors and dentists, not specialists. The 80/20 rule applies here: 20% of prescribers prescribe 80% of all prescription painkillers.

Lack of Physicians to Treat Pain

Unfortunately, legitimate chronic pain patients who need help have become collateral damage on the recent war on opioid prescribing. Patients who were previously stable on an

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effective low dose of painkillers have suddenly been cut off by their physicians for no apparent reason. These chronic pain patients are now paying the price because their physicians fear that law enforcement is "looking over their shoulder."

Meanwhile, public and medical misperceptions are widespread about the nature of pain, its causes, and the way it affects individual patients. Misinformation is fueled by the fact that comprehensive research is lacking, even on basic questions like how many people suffer from disabling chronic pain and how well-existing drugs like opioids treat long-term pain.

The problem is magnified by barriers that exist that allow legitimate chronic pain patients from being able to seek medical care. Traditionally, these patients would seek help from their primary care physicians, but access to primary care physicians in parts of the United States is shrinking due to the dwindling number of primary care physicians. Existing primary care physicians receive little medical education about treating chronic pain and are left to treat most pain with little specific guidance about effective care. In medical school, students receive only a few hours at most of education on pain treatment.

Primary care physicians seeking guidance on treating pain patients might find that they do not have resources to specialists who treat chronic pain. Currently, there are only about 3000–4000 pain specialists in the entire United States. That means that there is only one board-certified pain physician to treat every 25,000–33,000 patients that suffer from chronic pain. Many board- certified pain physicians struggle to keep up with the demand.

Economic Burden

Chronic pain affects 100 million Americans. Pain affects more Americans than diabetes, coronary heart disease, stroke, and cancer combined. The most common chronic pain conditions that patients suffer from are back pain (27%), severe headache or migraine pain (15%), neck pain (15%), and facial ache or pain (4%). Back pain is the leading cause of disability in Americans under 45 years old. More than 26 million Americans between the ages of 20–64 experience frequent back pain.

Chronic pain causes a tremendous cost on our country in health-care costs, rehabilitation, and lost worker productivity. The costs of unrelieved pain can result in longer hospital stays, increased rates of rehospitalization, increase outpatient visits, and decreased ability to function fully leading to lost income and insurance coverage. Chronic pain is a significant public health problem that costs society at least $560–$635 billion annually. This includes the total incremental cost of health care due to pain ranging between $261–$300 billion and $297–$336 billion due to lost productivity (based on days of work missed, hours of work lost, and lower wages).

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Part II

The Basics: II. Anatomy

Anatomy of the Spine

4

Harpreet Singh, George C. Chang Chien, and Robert Bolash

Key Concepts

- Keen understanding of spinal anatomy is necessary for accurate diagnosis of painful spine conditions and safe undertaking of interventional spine procedures.
- The spinal cord ends at the lower border of the L1 vertebra but may extend as far as the L3 vertebra in select individuals.
- The "safe triangle" approach for transforaminal epidural injections may minimize injury to the nerve root but does not guard against entering the segmental radiculomedullary artery.
- Bony architecture of the spine is best revealed by CT. MRI is the imaging modality of choice for details of bone marrow, ligaments, fascial planes, neural tissues, and soft tissue structures.

Introduction

The vertebral column consists of 33 bony elements joined together by joints and ligaments (Table 4.1). It houses and protects both the spinal cord and proximal portions of the spinal nerves. Detailed understanding of spinal anatomy is essential for accurate diagnosis of painful spine conditions and the safe performance of interventional pain procedures.

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Osteology

The vertebral column consists of seven cervical, 12 thoracic, and five lumbar vertebrae along with five fused sacral bones that form the sacrum and four fused bones to form the coccyx (Fig. 4.1). Each vertebra consists of a *vertebral body*, a cylindrical ventral mass made of cancellous bone, and a *dorsal vertebral arch* made mostly of cortical bone. The large *intervertebral vertebral foramen*, wherein the spinal cord traverses, is enclosed by the vertebral body and dorsal arch. The body is connected to the dorsal arch by two stout horizontal supports known as *pedicles*. The posterior arch is composed of two flat bones known as *laminae*, which join together in the midline and project posteriorly to form *spinous process*. Near the junction of pedicle and laminae, there are *superior* and i*nferior articular processes* which create a joint with the inferior and superior articular processes of the preceding and succeeding vertebrae, respectively, to form *synovial zygapophyseal joints* (Z-joints, facet joints). At the junction between superior and inferior articular processes, *transverse processes* project laterally on both sides of the vertebra. The junction between the two vertebral bodies consists of cartilaginous end plates of adjacent vertebra, an intervertebral disk, and anterior and posterior longitudinal ligaments.

The size, shape, and sectional contour of the body are variable throughout the spine. However, it is the characteristic elements in the dorsal arch, which gives vertebrae their distinct identity in different areas of the spine (Fig. 4.2).

Cervical Vertebrae

There are seven cervical vertebrae, the first two (*atlas*-C1 and *axis*-C2) and seventh cervical vertebra are unique in morphology. A typical cervical vertebra consists of a bean-shaped body which is relatively small in size. Unique to the cervical spine are the *uncovertebral joints* or the *joints of*

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Table 4.1 Ligaments supporting the vertebral column

Ligament	Attachment	Function
Anterior longitudinal ligament	Anterior tubercle of C1 to the sacrum, abutting the anterior surface of vertebral bodies	Limits extension
Posterior longitudinal ligament	From C2 to the sacrum, attached to posterior surface of intervertebral disk	Stabilization by limiting spinal flexion. Prevents posterior disk herniation
Supraspinous ligament	Superior to inferior along the tip of the spinous processes	Stabilization by limiting spinal flexion
Interspinous ligament	Connects inferior aspect of the cranial spinous process to the superior surface of the adjacent spinous process	Stabilization by limiting spinal flexion
Ligamentum flavum	Connects the lamina of adjacent vertebra	Stabilization by limiting spinal flexion
Inter-transverse ligament	Connects adjacent transverse processes	Limits lateral flexion

Luschka, formed by the hook-shaped processes of the superior surface of the vertebral bodies of the third to the seventh cervical vertebra and first thoracic vertebra. The transverse process of the cervical vertebra is perforated by the foramen transversarium which protects the vertebral artery. Part of the transverse process dorsal to the foramina creates the posterior tubercle, whereas the ventral end forms the anterior tubercle. The anterior tubercle is most prominent at C6 vertebra where it is also known as *Chassaignac tubercle*. The laminae enclose a relatively large vertebral foramen with a triangular cross section. The superior and inferior articular processes face obliquely superior/posteriorly and inferior/anteriorly, respectively. Notably, the *ligamentum flavum* may not be fused at midline in the cervical spine.

In total, the base of stability in the typical cervical spine vertebra is created by these five points of articulation: the bilateral facets, intervertebral disk, and the uncovertebral joints (above and below).

The atlas, or C1 vertebra Vertebrae, is shaped like a ring and lacks a definite body, consisting only of anterior and posterior arches connected by lateral masses. Lateral masses have superior and inferior articular surfaces. The superior articular surfaces are directed cranially and internally where they articulate with the occipital condyles. The inferior articular surfaces are positioned caudally with a slight medial and posterior tilt. The inferior articular surface of the atlas articulates with the superior articular processes of axis. The axis, or C2 cervical vertebra, is characterized by a prominent anterior odontoid process, which serves as a pivot allowing rotational movement of the atlas and serves to prevent horizontal displacement of the atlas over the axis (Fig. 4.3).

Thoracic Vertebrae

There are 12 thoracic vertebrae, which are characterized by both facet joints and costal articulations. The typical thoracic vertebra (T2–T8) is heart shaped and intermediate in size between the cervical and lumbar vertebra. They have two characteristic demifacets on each side of the body, which articulate with the ribs. The superior demifacet is larger and, in combination with smaller inferior demifacet of the preceding vertebra, articulates with the corresponding rib. Pedicles project from the superior aspect of the body; superior articular processes project from the junction of lamina and pedicle. They are coronal in their plane of articulation, bear an oval articular facet facing backward, and are slightly lateral. The two articular surfaces lie in the arc of a circle permitting limited rotation. Spinous process of thoracic vertebrae angulate downward, gradually increasing in angulation until reaching T7. At T8, their angulation begins to decrease such that the spinous process of T12 is near horizontal. Transverse processes are directed laterally and slight posteriorly. They contain an articular facet on the ventral aspect, which articulates with the tuberculum of the corresponding rib.

Lumbar Vertebrae

The bodies of the lumbar vertebrae become progressively larger to accommodate the increased weight of the trunk and upper body. Transverse processes in the lumbar region vary in length, with the longest at the L4 level and the thickest at the L5 level. True transverse elements are represented by accessory and mammillary processes which are joined by mamillo-accessory ligaments (which may be ossified). Notably, the medial branch of dorsal ramus passes beneath this ligament. The superior lumbar articular processes are widely situated and positioned medially, while the inferior articular processes are reciprocally directed laterally. Laminae in the lumbar region are shorter, and there is less dorsal overlap when compared to the thoracic region. Spinous processes are shorter and nearly horizontally oriented. The vertebral foramen in the lumbar region is triangular in shape and larger compared to thoracic levels but smaller compared to cervical levels (Fig. 4.4).

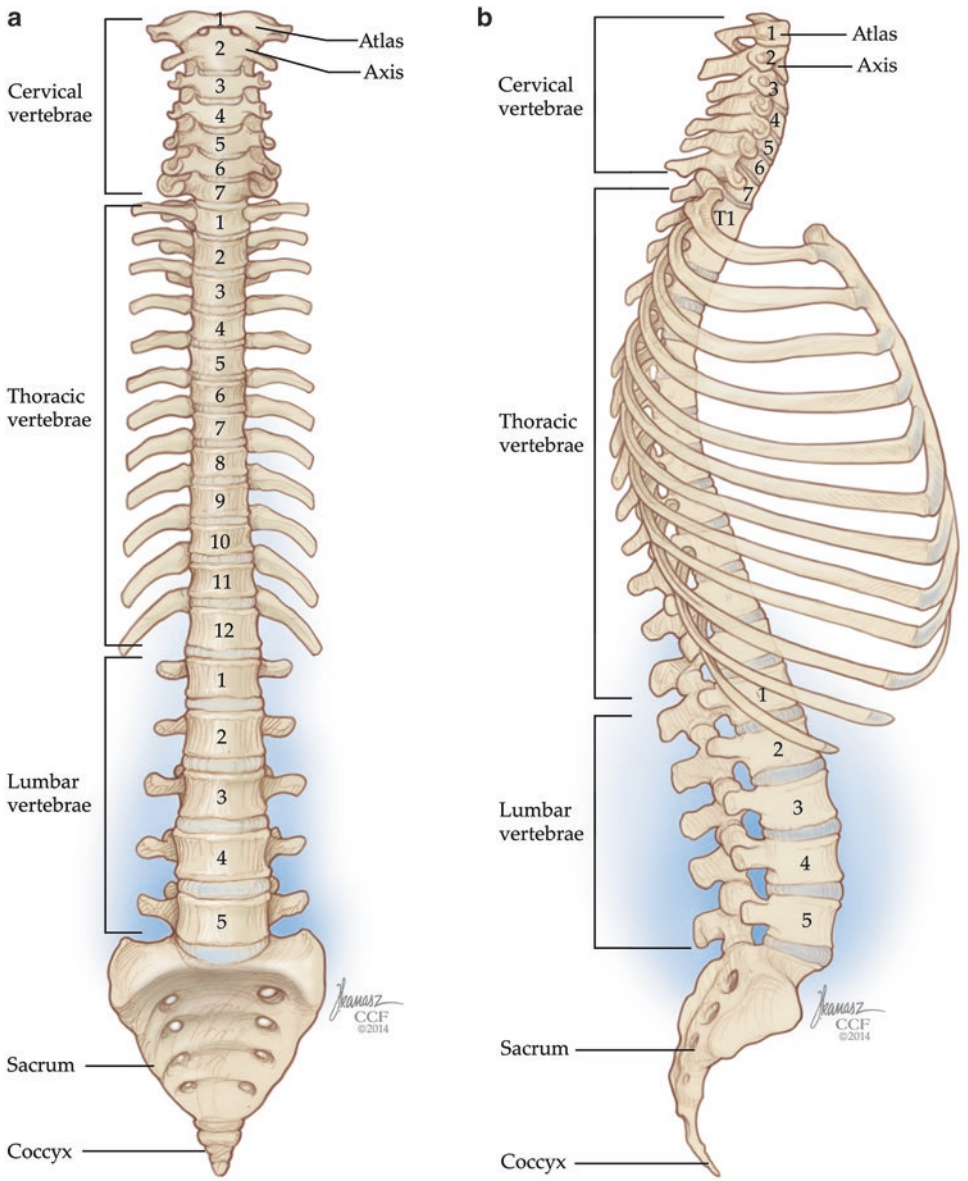

Fig. 4.1 Vertebral column lateral and anterior view (**a**) AP view and (**b**) lateral view (Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2014–2015. All Rights Reserved)

Sacrum and Coccyx

The sacrum is a wedge-shaped bone formed by the fusion of the five sacral vertebrae and their costal elements. The sacrum articulates with two pelvic bones posteriorly forming *sacroiliac joints* on either side.

The sacral canal is the caudal continuation of the vertebral canal. It extends the length of the sacrum and ends at the *sacral hiatus* where the coccyx, a small triangular bone formed by fusion of four coccygeal vertebrae, begins. The anterior and posterior walls of this canal are perforated by sacral foramina, through which the sacral spinal nerves pass. There are four pairs of dorsal and ventral sacral foramina. Sacral spinal nerves divide into dorsal and ventral rami within the sacral canal, and they exit the sacrum via the anterior and posterior sacral foramina, respectively.

Intervertebral Foramen and the Safe Triangle

On the lateral aspect of the posterior elements of the vertebral bodies are foramina created by two adjacent vertebrae. The anterior border of the foramen is formed by the bodies of the vertebrae and the intervertebral disk. The posterior border is marked by the superior and inferior articular processes and facet joints. The superior and inferior borders are formed by the pedicles of the superior and inferior vertebra, respectively. The structures passing through these foramina include the *spinal nerve root*; *dorsal root ganglion*; *segmental spinal artery*; communicating veins between the internal and external plexuses; and *sinu-vertebral nerves*.

The "safe triangle" was initially described by Bogduk and refers to a three-dimensional area lateral to the inferior

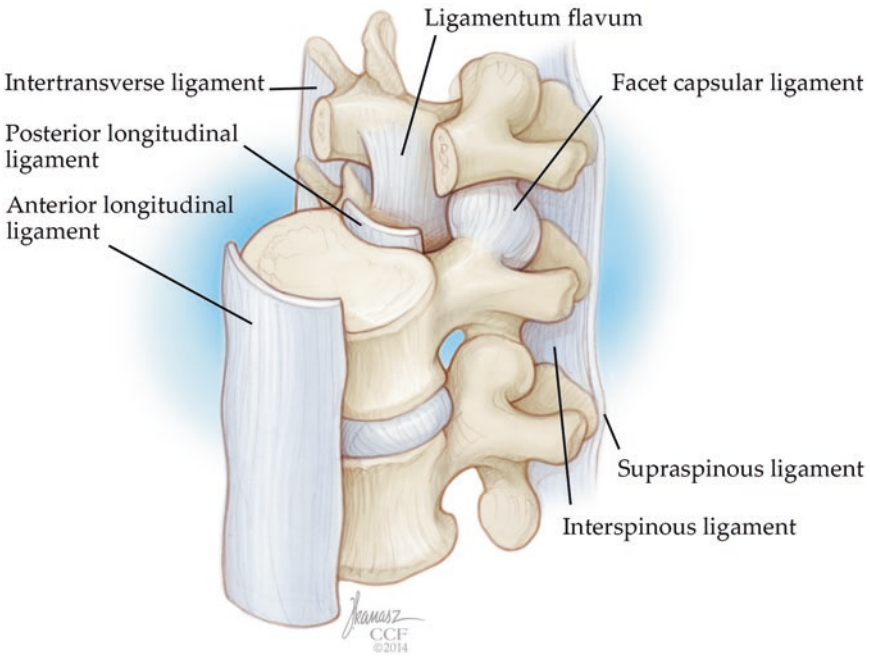

Fig. 4.2 Ligaments of the spine (Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2014–2015. All Rights Reserved)

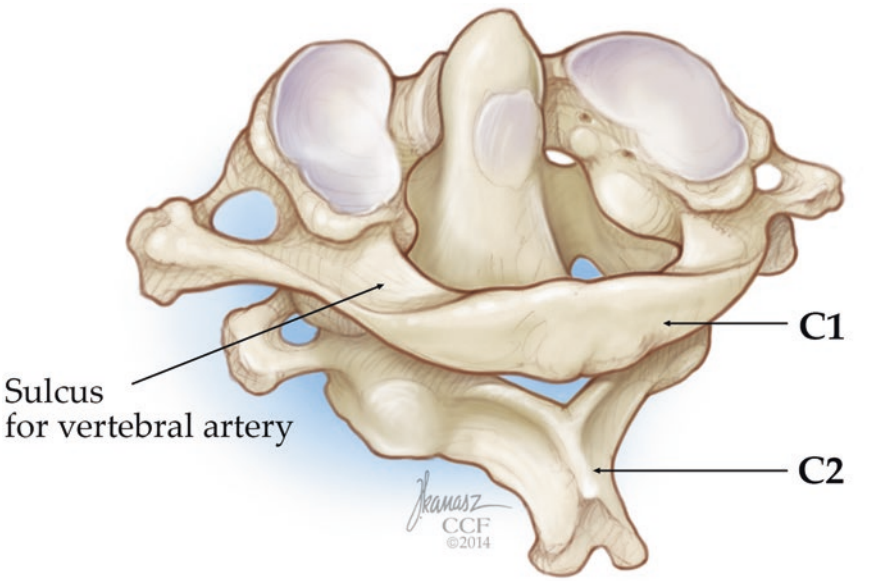

Fig. 4.3 Cervical vertebrae (Atlas and Axis) (Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2014–2015. All Rights Reserved)

margin of pedicle, dorsal to the vertebral body, and cephalad to presumed location of the nerve root (Fig. 4.5). Entering in this area for any interventional procedure (e.g., transforaminal epidural injection) reduces the risk of nerve root injury but does not preclude entering in to the segmental spinal arteries.

Intervertebral Disk

Approximately 80% of the vertebral column's length is due to vertebral bodies, and 20% consists of the intervertebral disk. The intervertebral disk is composed of the cartilaginous end plates, the central *nucleus pulposus*, and the circumferential *annulus fibrosus*. In the adult human, the intervertebral disk is mostly avascular.

Spinal Cord

The central nervous system consists of the brain and spinal cord. The spinal cord extends continuously from the medulla oblongata and terminates at the *conus medullaris*, which is connected by the *filum terminale* to the dorsum of the first coccygeal vertebra. The adult human spinal cord usually ends at the lower border of L1 but may extend as far as L3.

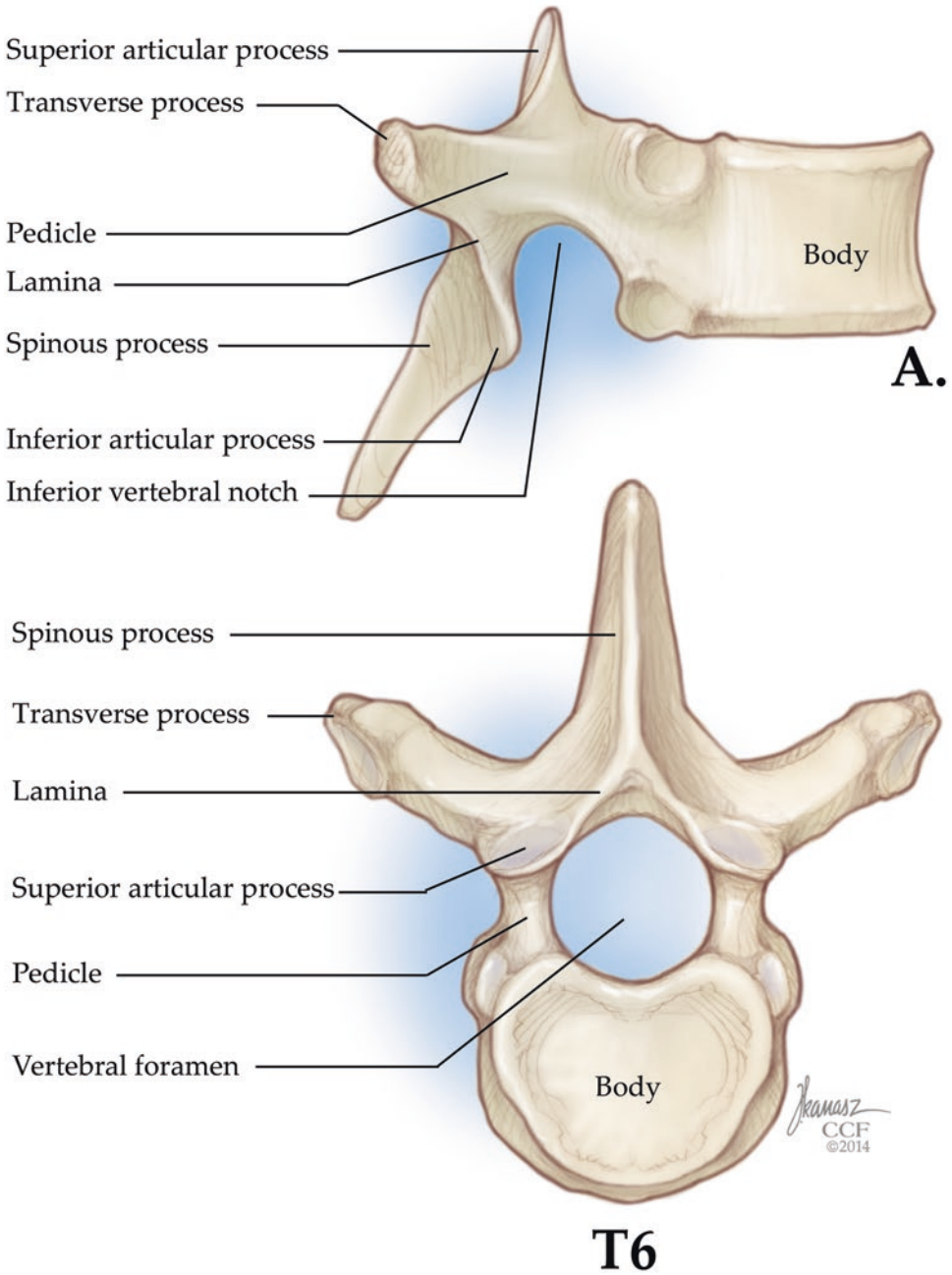

Fig. 4.4 Thoracic and lumbar vertebrae (**a**) AP view and (**b**) lateral view (Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2014–2015. All Rights Reserved)

The spinal cord is divided in half by a dorsal median sulcus and a ventral median fissure. It contains a central canal in the middle and continues cranially with the cerebral ventricular system. As is the case with the rest of the CNS, the spinal cord is composed of white and gray matter. White matter forms the bulk of the deep parts of the brain and the superficial parts of the spinal cord. It is composed of bundles of myelinated nerve cell processes, axons, which carry nerve impulses between the cell bodies of the neurons, which make up the gray matter. Large white matter tracts form descending motor fibers from the brain to the spine, whereas ascending sensory tracts transmit light touch, pressure, temperature, and pain from the spinal cord to the brain (Fig. 4.6).

Gray Matter

The gray matter of the spinal cord surrounding the central canal is "H-shaped," with two dorsal and two ventral horns. The *ventral horn* contains the cell bodies for motor neurons,

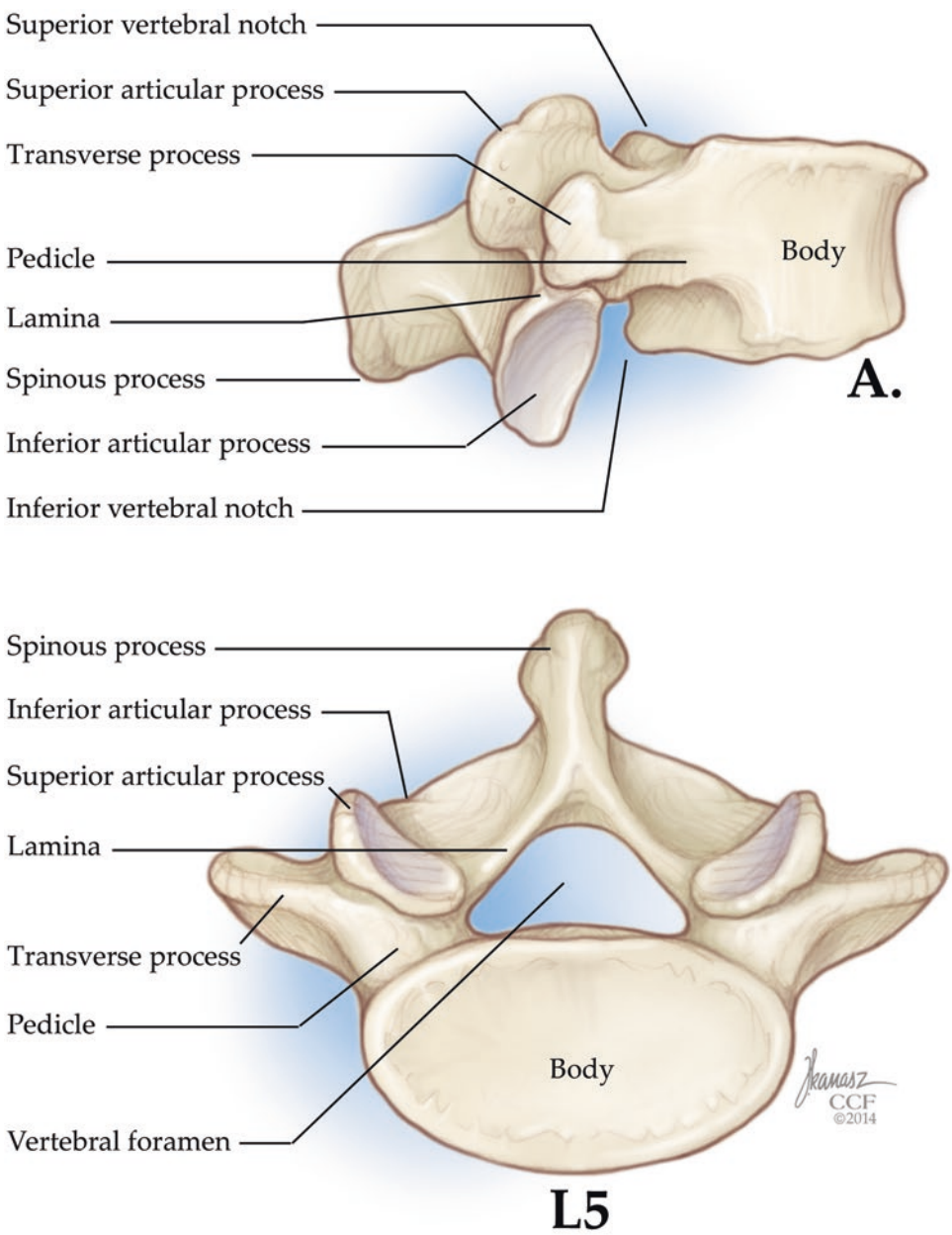

Fig. 4.4 (continued)

and afferent nerves from the dorsal rootlets terminate in the *dorsal horn*. In thoracic and upper lumbar areas, there are small projections in the middle of the dorsal and ventral horn, called *lateral horns*, which contain cell bodies for preganglionic sympathetic fibers. Cytoarchitecturally, the spinal cord gray matter is divided into ten distinct areas known as *Rexed laminae*.

Lamina I to VI is primarily involved with sensory functions and processing. Laminae I and II are the main targets for primary nociceptive afferents. Lamina II, also known as *substantia gelatinosa*, contains mostly interneurons involved with modulation of input from sensory neurons. Aß-fibers, which respond to fine touch, project in laminae III, IV, and V. Aδ nociceptors project to laminae I and V. Lamina V receives both non-noxious (Aß-fibers) and noxious input monosynaptically from Aδ nociceptors and indirectly (polysynaptically) from C fibers. These types of neurons that respond to multiple stimuli are known as WDR (wide dynamic range) neurons and are most abundantly found in lamina V. WDR neurons fire in graded fashion and exhibit phenomenon called windup, wherein repetitive stimulation leads to increased firing and post-discharge.

Rexed lamina VII consists of cell body of preganglionic sympathetic fibers in the lateral horn of the spinal cord. Laminae VIII and IX located in the ventral horn consist of cell bodies of motor fibers to the skeletal muscles.

White Matter

White matter surrounds the gray matter and is divided into ventral, lateral, and dorsal columns by the ventral and dorsal horn. It consists of ascending and descending tracts, consisting of nerve fibers connecting the brain and spinal cord. Their names usually refer to their origin and destination, e.g., corticospinal tract originating from cerebral motor cortex relaying motor signals to the ventral horn of the spinal cord.

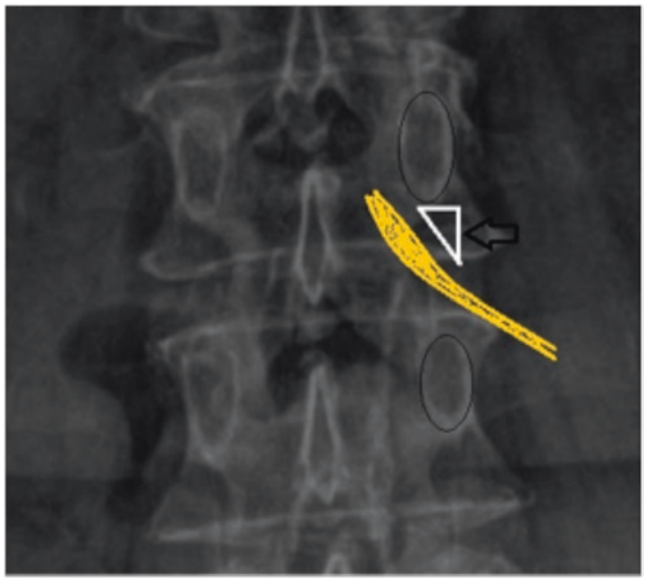

Fig. 4.5 The "safe triangle" – triangular area just superolateral to the nerve root, below the pedicle, and posterior to the vertebral body

Arterial Supply to the Spine

The spinal cord is supplied by three longitudinal arteries, one anterior spinal artery, which forms from the union of the two anterior spinal branches of each vertebral artery at the level of the foramen magnum, and two posterior spinal arteries which may either be direct branches of the vertebral artery or branches from posterior inferior cerebellar arteries (PICA). These longitudinal arteries receive collaterals from segmental arteries which originate from spinal branches of the vertebral, deep cervical, intercostal, and lumbar arteries. They transverse the intervertebral foramina at respective levels and supply anterior and posterior nerve roots, but most not reach the spinal cord. These smaller segmental arteries are called radicular arteries. However, larger segmental arteries primarily situated in the lower cervical, lower thoracic, and upper lumbar regions reach the dura where they divide to form ascending and descending arterioles and anastomose with anterior and posterior spinal arteries. These arteries are also known as *radiculomedullary arteries* to distinguish them from those radicular arteries that supply only the nerve roots. The largest radiculomedullary artery is called the

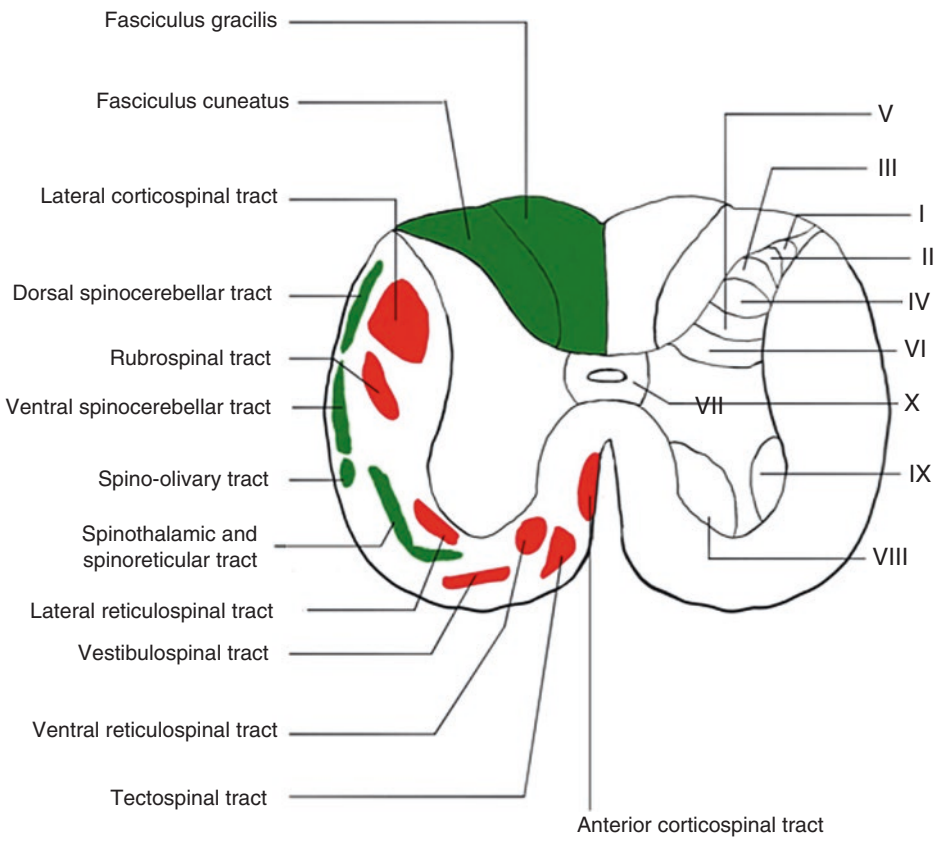

Fig. 4.6 Cross section of spinal cord demonstrating the Rexed laminae and ascending and descending tracts