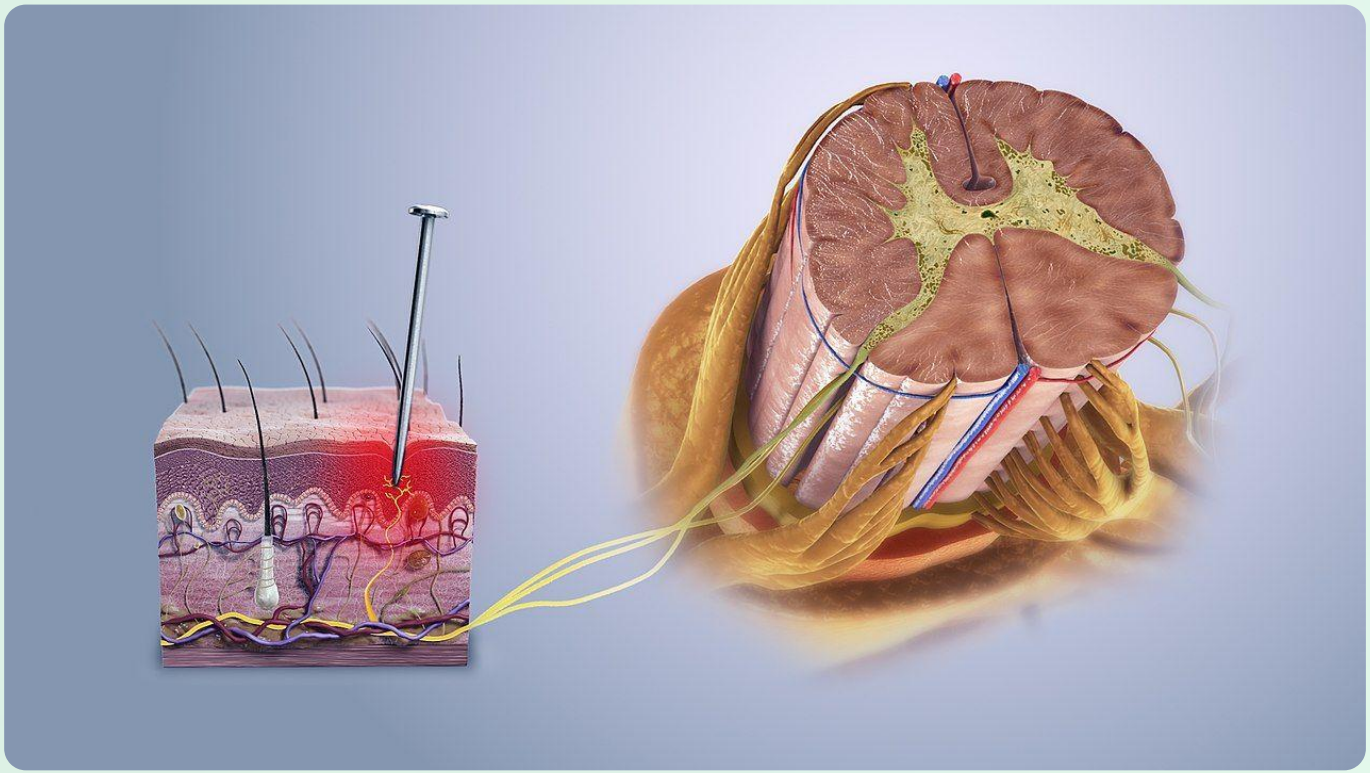


Pain

Pathological Physiology · Dental Medicine

STOMATOLÓGIA · PATOFYZIOLÓGIA

Definition of Pain

> "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."
>
> *— IASP (International Association for the Study of Pain), 1979*

Damage Signal

Pain serves as a warning signal alerting the organism to actual or potential tissue damage.

Localization

Pain helps identify and localize the site of injury or pathology within the body.

Protection

Pain drives protective behaviors that prevent further or more serious damage to tissues.

Non-Biological Pain

Psychogenic pain and phantom pain occur without a clear biological substrate or tissue damage.

Classification by Duration

Acute Pain

A protective mechanism that alerts the individual to an immediately harmful condition. Onset is usually sudden.

Physiological responses:

- Increased heart rate and respiratory rate
- Elevated blood pressure
- Pallor or flushing, dilated pupils
- Nausea, elevated blood sugar
- Increased gastric acid secretion, reduced gastric motility
- Altered blood flow to viscera, kidney, and skin

Psychological responses: fear, anxiety, general unpleasantness

Chronic Pain

Persistent or intermittent pain, typically defined as lasting **at least 6 months**. The cause is often unknown and may develop insidiously.

Psychological responses:

- Depression and hopelessness
- Sleep disorders
- Preoccupation with pain
- Attempt to minimize pain-related behavior
- Tendency to deny pain

Persistent pain allows for physiological **adaptation** — body functions may normalize, yet pain is not relieved.

Chronic Pain: Clinical Profile

Chronic pain produces significant behavioral and psychological changes that distinguish it fundamentally from acute pain.

Definition

Persistent or intermittent pain lasting **≥ 6 months**. Cause often unknown or the result of longstanding disease where treatment has failed.

Psychological Mechanisms

Chronic pain has different underlying psychological mechanisms than acute pain — often involving central sensitization rather than peripheral nociception.

Key Behavioral Changes

- Depression and hopelessness
- Sleeping disorders
- Preoccupation with the pain
- Tendency to deny pain
- Attempts to minimize pain-related behavior

Secondary Nature

Chronic pain is likely not in direct relationship with initial damage, but rather a consequence of secondary neuroplastic and psychosocial changes.

Pain Threshold vs. Pain Tolerance

Pain Threshold

The point at which a stimulus is first perceived as painful. It does **not vary significantly** among healthy individuals or within the same person over time.

Perceptual dominance: Intense pain at one location may paradoxically *increase* the pain threshold at another location, temporarily raising the perception barrier.

Pain Tolerance

The duration or intensity of pain an individual will endure before initiating overt pain responses. Varies greatly among individuals and in the same person over time.

Influenced by:

- Cultural prescriptions and expectations
- Role behaviors
- Physical and mental health status

Factors Modifying Pain Tolerance

Decreased Tolerance

- Repeated exposure to pain
- Fatigue, anger, boredom, apprehension
- Sleep deprivation
- Elderly patients show decreased tolerance

Increased Tolerance

- Alcohol consumption
- Medication and hypnosis
- Warmth and distracting activities
- Strong beliefs or faith

Women appear to be generally more tolerant of pain than men. Pain tolerance varies greatly between individuals and within the same individual across time.

Pain Assessment	
	Restful face, neutral expression
	Tight facial muscles; furrowed brow, chin, jaw (negati expression – nose, mouth brow)
	Quiet, not crying
	Mild moaning, intermittent
	Loud scream; rising, shrill, continuous (Note: Silent cry scored if baby is intubated as evidenced by obvious mo facial movement
	Usual pattern for this infant
;	Indrawing, irregular, faster than usual; gagging, breat
l	No Muscular rigidity; occasional random movement
	Tense, straight arms; rigid and/or rapid extension, f
l	No Muscular rigidity; occasional random moveme
	Tense, straight legs; rigid and/or rapid extension
	Quiet, peaceful, sleeping or alert, random le
	Alert, restless and thrashing

Age and Perception of Pain

1. **Neonates (0–2 days)**

   Less sensitive to pain or lack the ability to verbalize the pain experience.

2. **Infants (3–12 months)**

   A full behavioral response to pain becomes apparent — crying, motor withdrawal, facial grimacing.

3. **Older Children (15–18 yrs)**

   Tend to have a **lower** pain threshold than adults.

4. **Adults & Elderly**

   Pain threshold tends to **increase with aging**, likely due to peripheral neuropathies and changes in skin thickness.

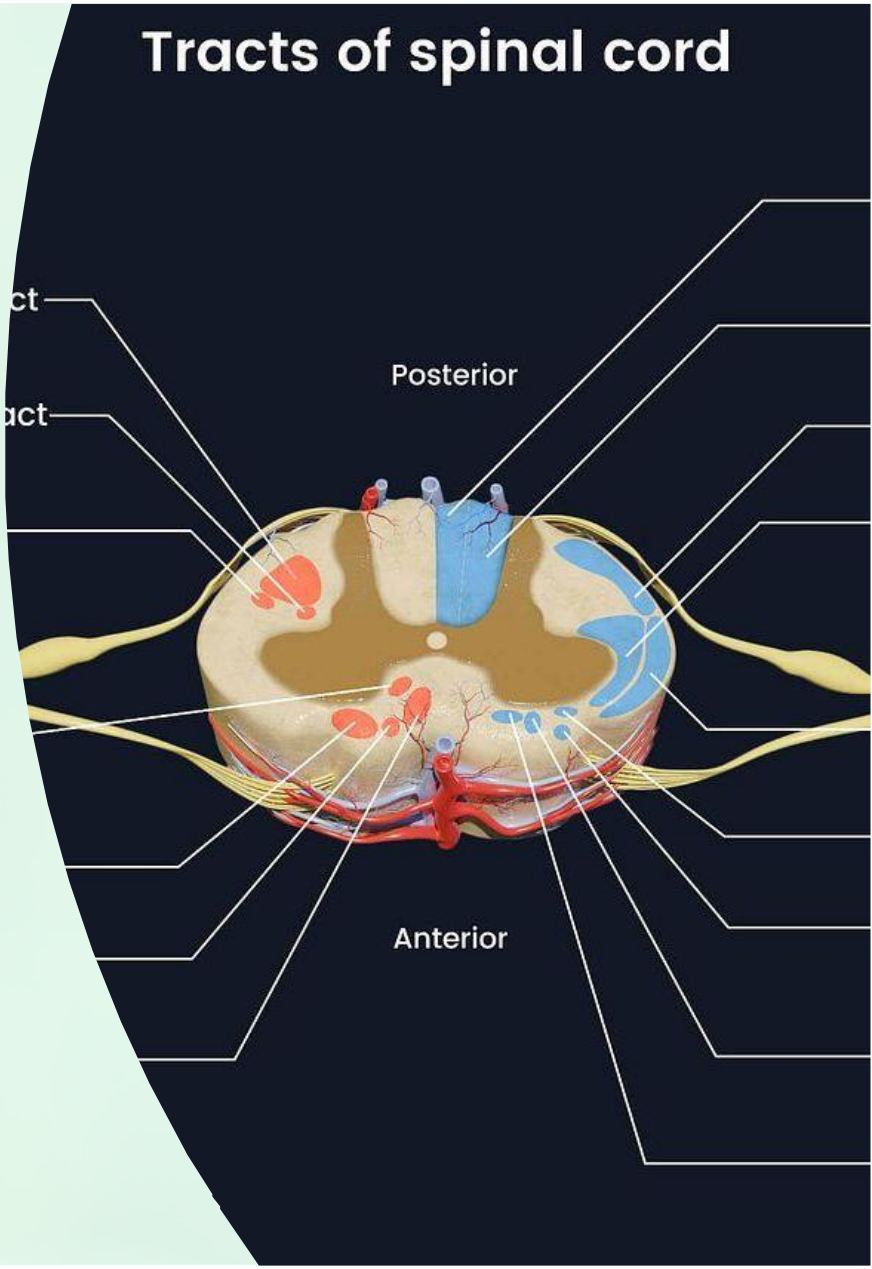
Classification by Origin

Peripheral Origin

Arising from muscles, tendons, joints, and visceral organs due to trauma or inflammation. Also includes peripheral nerve damage giving rise to **neurogenic pain**.

Central Origin

Arising from the CNS — brain or spinal cord damage, stroke, or epilepsy. Central pain syndromes are often difficult to treat and may be refractory to standard analgesics.



Classification by Localization: Somatic vs. Visceral

Feature	Somatic Pain	Visceral Pain
Localization	Superficial (skin) or deep (muscles, bones, joints)	Inner organs
Cause	Mechanical or thermal damage	Inflammation, ischemia
Transmission	Somatic afferent fibers	Sympathetic afferent fibers
Character	Sharp, well-localized	Diffuse, generalized
Accessory Signs	Rare	Nausea, vomiting, sweating

Classification: Somatogenic vs. Psychogenic

1. Somatogenic Pain

Pain with a known physical cause localized in body tissue. Subdivided into:

- **Nociceptive pain** — activation of peripheral nociceptors
- **Neuropathic pain** — damage or dysfunction of the somatosensory nervous system

2. Psychogenic Pain

Pain for which no known physical cause exists. The processing of sensory information within the CNS is disturbed, leading to pain perception without identifiable tissue pathology.

Examples include somatoform pain disorders and certain functional pain syndromes.

Nociception: Key Concepts



Noxa

Any factor capable of causing tissue damage and thereby activating the pain response.



Nociceptors

Polymodal pain receptors — morphologically represented by **free nerve endings**. They respond to multiple stimulus types.



Mechanical Stimuli

Tissue deformation, pressure, or stretch beyond normal physiological range.



Thermal Stimuli

Extreme heat or cold activating specific thermosensitive nociceptor subtypes.

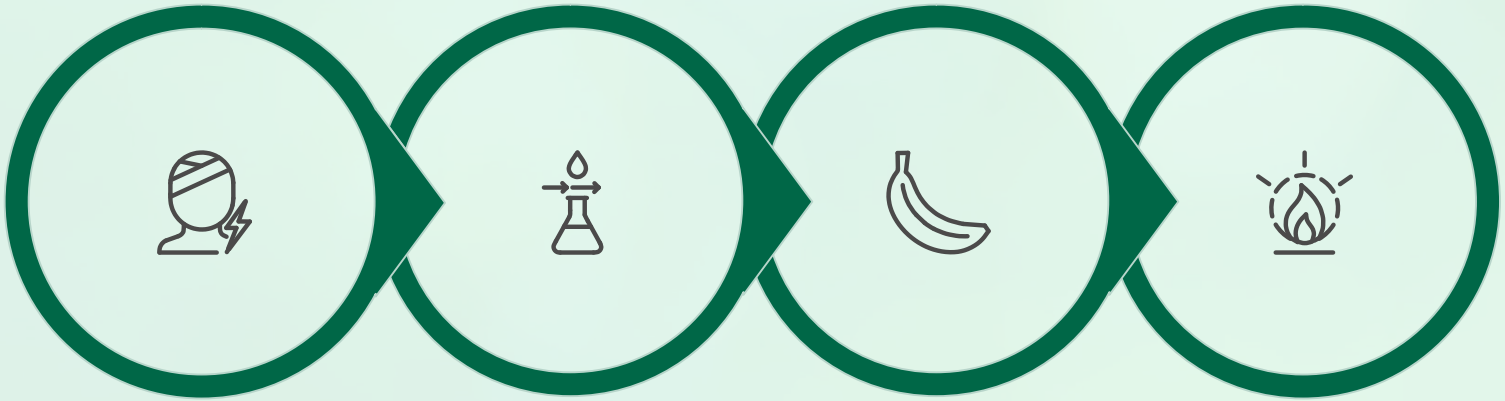


Chemical Stimuli

Bradykinin, histamine, prostaglandins; pH changes (acidosis); altered ion concentrations (Ca^{2+}, K^{+}).

Activation of Nociceptors During Tissue Damage

The precise mechanism initiating depolarization via chemical, mechanical, or thermal stimuli is not yet fully understood. However, the sequence of events during **tissue damage** is better characterized:



This cascade amplifies and sustains the nociceptive signal, contributing to peripheral sensitization and the development of inflammatory pain.

Pain Mediators and Their Effects

Upon tissue damage, a variety of chemical mediators are released that either **activate** or **sensitize** primary afferent nociceptive fibers.

Mediator	Source	Effect on Primary Afferent Fibers
Potassium (K^+)	Damaged cells	Activation
Serotonin	Thrombocytes	Activation
Bradykinin	Plasma kininogen	Activation
Histamine	Mast cells	Activation
Prostaglandins	Damaged cells	Sensitization
Leukotrienes	Damaged cells	Sensitization
Substance P	Primary afferent fibers	Sensitization

Stimuli That Activate Nociceptors

This reference table (Box 16-1) summarizes the full spectrum of inflammatory mediators, excitatory transmitters, and inhibitory transmitters involved in nociceptor activation and modulation. Note that endogenous opioids (endorphins, enkephalins, dynorphins) released from the PAG and NRM represent a key component of the descending analgesic system.

BOX 16-1 STIMULI THAT ACTIVATE NOCICEPTORS

Inflammatory Mediators (Excitatory)
- Bradykinin
- Leukotrienes
- Prostaglandins
- Serotonin
- Substance P
- Interleukins
- Tumor necrosis factor-alpha
- Nitric oxide
- ATP
- Neurokinins
- Calcitonin gene–related peptide

Excitatory Transmitters
- Glutamate (fast pain)
- NMDA
- AMPA
- Tachykinins
- Neurokinin A
- Neurokinin B
- Substance P
- Other receptors
- Calcitonin gene–related peptides
- Somatostatins
- Bombesins
- Cholecystokinins

Inhibitory Transmitters
- Gamma-aminobutyric acid (GABA)
- Glycine
- Descending pain modulators
- Norepinephrine–α_2-receptors
- Serotonin (5-hydroxytryptamine)
- Opioids (μ, δ, κ receptors)
  - Endorphins, Enkephalins, Dynorphins } Released from PAG and NRM and other areas of the brain

Sensitization and Hyperalgesia

Mediators act as long as the stimulus persists. Depolarization is initiated through activation, sensitization, or inflammation. Kallikrein is among the strongest activators.

Sensitization Manifests As:

- **Decreased excitation threshold** — stimuli that normally do not cause pain become painful (allodynia)
- **Increased excitation threshold** — stimuli that are normally painful become non-painful (e.g., fight-or-flight injury suppression)

Hyperalgesia

When peripheral tissues are damaged, there is increased sensitivity of the surrounding tissue:

- **Primary hyperalgesia** — occurs directly at the site of tissue damage
- **Secondary hyperalgesia** — occurs in surrounding, non-damaged tissue due to central sensitization

Platypus: A Unique Pain Model





The platypus is notable in pain research: male platypuses possess **crural spurs** on their hind limbs that deliver venom. This venom activates specific nociceptor subtypes, making the platypus a valuable animal model for studying pain signaling mechanisms and nociceptor pharmacology.

Afferent Nerve Fibers and Dorsal Horn Connections

Nociceptive fibers form direct or indirect connections with three main groups of dorsal horn neurons:

Projection Neurons

Transfer sensory (nociceptive) information to higher brain centers via ascending pathways.

Local Excitatory Interneurons

Transfer sensory information from primary afferents to projection neurons, amplifying the nociceptive signal.

Inhibitory Neurons

Regulate and modulate the transfer of nociceptive information to higher centers — a key target of analgesic strategies.

Irritation of nociceptors during tissue damage results from both direct local damage and the release of a cascade of chemical mediators acting on these fiber groups.

Referred Pain and Head Zones

Visceral pain can be **projected to skin areas** — specifically the dermatomes (area radicularis) served by the same spinal cord segment that receives signals from the damaged or inflamed organ.

Head Zones

Defined skin areas where visceral pain is felt. Each organ projects to a specific dermatomal region. For example:

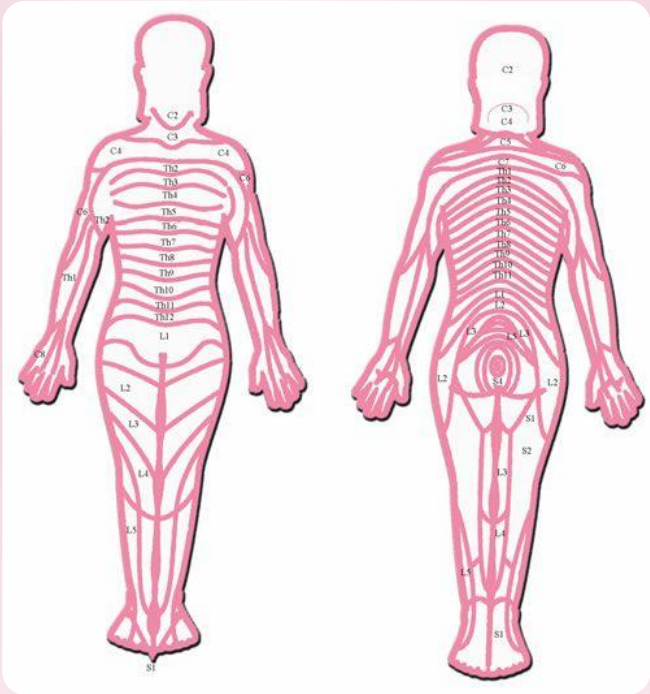
- Cardiac pain → left arm / jaw
- Hepatic pain → right shoulder
- Appendix → periumbilical region (McBurney's point)

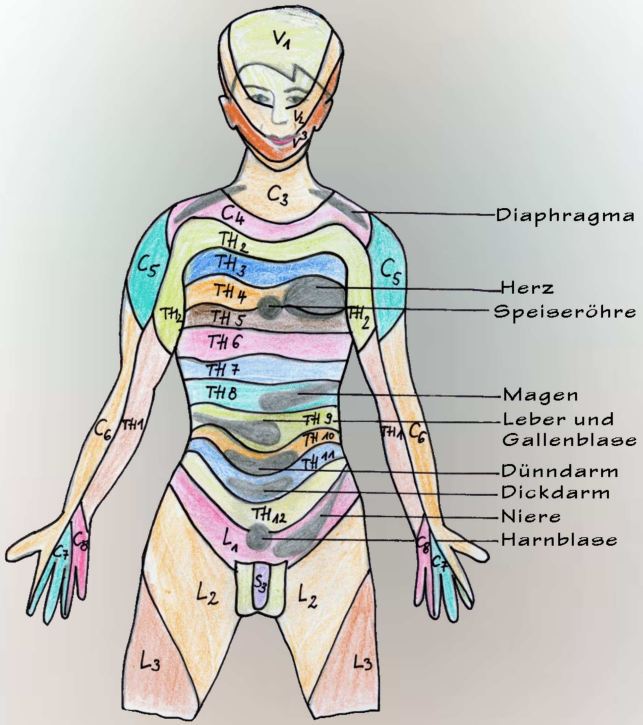
Irradiation Pain

So-called **irradiation (referred) pain** occurs during organ diseases when afferent signals from visceral organs converge on dorsal horn neurons that also receive input from somatic structures, leading the brain to mislocalize the source of pain.

Dermatomes: Spinal Segmental Map

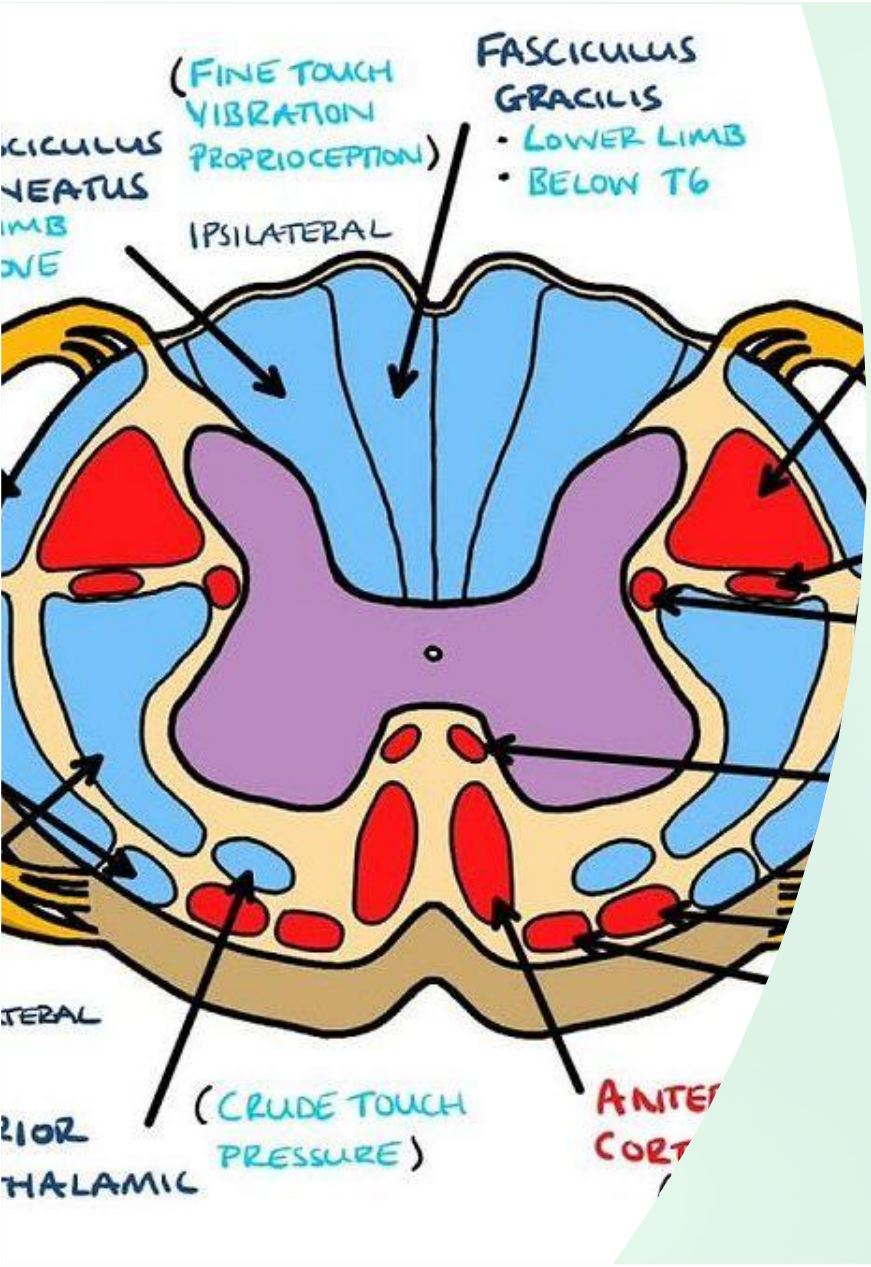
The dermatome map shows the cutaneous distribution of each spinal nerve root (C2–S1), anterior and posterior views. Understanding dermatomes is essential for localizing spinal pathology and interpreting referred pain patterns in clinical practice.





Head Zones: Visceral Referred Pain Areas

This diagram illustrates the Head zones for major internal organs: diaphragm (C3–C5), heart and esophagus (Th2–Th5), stomach (Th6–Th9), liver and gallbladder (Th7–Th10), small intestine (Th9–Th11), large intestine (Th11–L1), kidney (Th11–L2), and urinary bladder (Th11–L2, S2–S4).



CHAPTER

Ascending Pain Pathways

How nociceptive signals travel from the periphery to the brain — the anatomical and functional organization of pain transmission.

Afferent Nociceptive Fibers: Aδ and C

Aδ Fibers — "First Pain"

- Thicker, **myelinated** fibers
- Conduction velocity: **5–30 m/s**
- Respond to mechanical and thermal stimuli
- Produce **sharp, well-localized** pain
- Responsible for the initial, immediate pain sensation upon injury

C Fibers — "Second Pain"

- **Unmyelinated** fibers
- Conduction velocity: **0.5–2 m/s**
- Respond primarily to chemical stimuli; also mechanical and thermal
- Produce **deep, dull, burning** pain
- Responsible for the sustained, diffuse aching that follows initial injury

Pain Ascending Pathways

1

Spinothalamic Pathway

Transmits nociception to the **ventral posterolateral nucleus of the thalamus**, then to the somatosensory cortex. Primary role: **pain localization**.

2

Spinoreticular Pathway

Ascends bilaterally to the **reticular formation and thalamus**. Involved in the emotional and memory dimensions of pain experience.

3

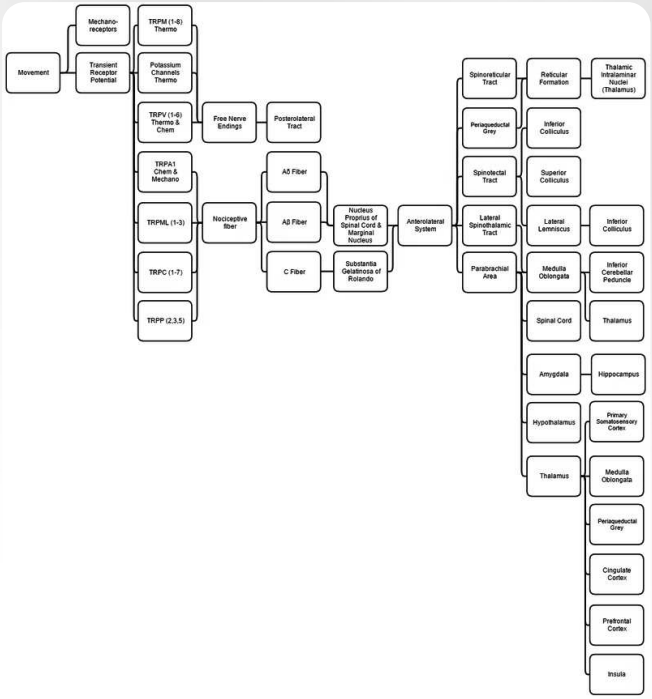
Spinomesencephalic Pathway

Connected with activation of the **limbic system**. Mediates autonomic nervous system responses and behavioral effects of pain.

4

Spinohypothalamic Pathway

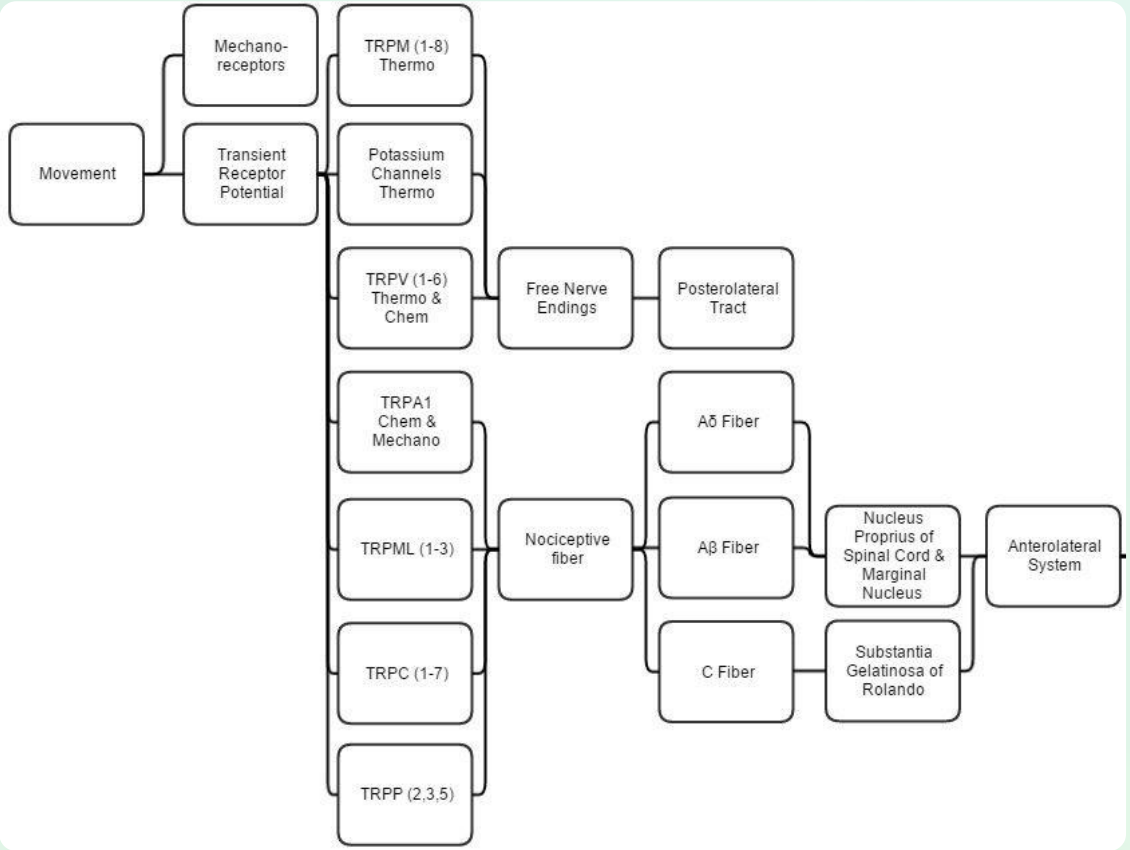
Projects to the **hypothalamus**. Carries information from lips, skin, sex organs, GIT, intracranial blood vessels, tongue, and cornea.



Nociceptive Pathway Diagram (Afferent)

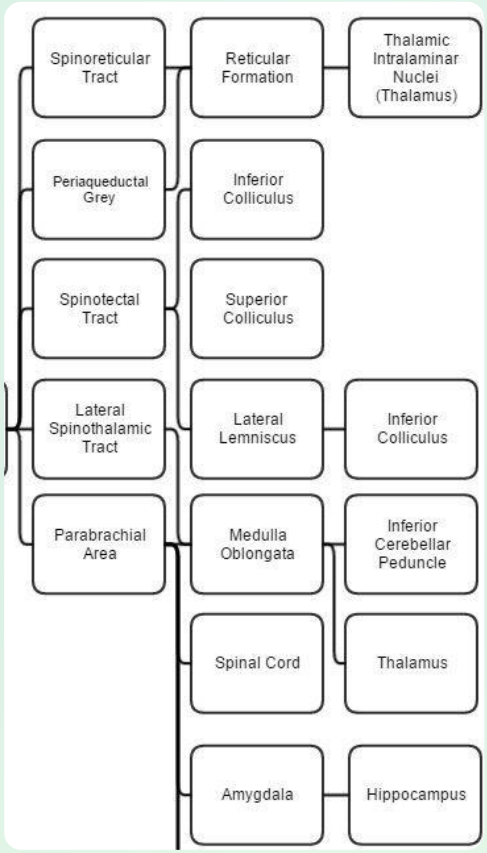
This flowchart maps how sensory input (from mechanoreceptors, temperature, and chemical stimuli) converges on nociceptive fibers (Aδ, Aβ, C), synapses in the dorsal horn, then propagates via the anterolateral system to multiple brain regions including the thalamus, periaqueductal grey, amygdala, hypothalamus, and cortex.

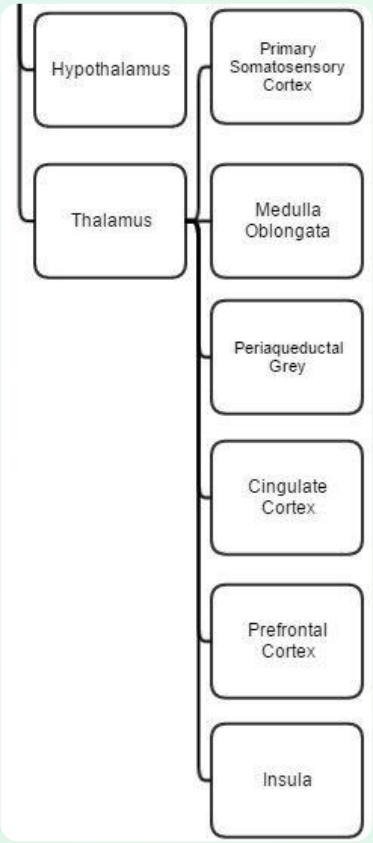
Nociceptive Pathway: Receptor to Spinal Cord



Detailed schematic showing the receptor-to-spinal cord segment of the nociceptive pathway. TRP channel subtypes (TRPM, TRPV, TRPA1, TRPML, TRPC, TRPP) funnel nociceptive input through free nerve endings into the posterolateral tract and spinal cord dorsal horn nuclei.

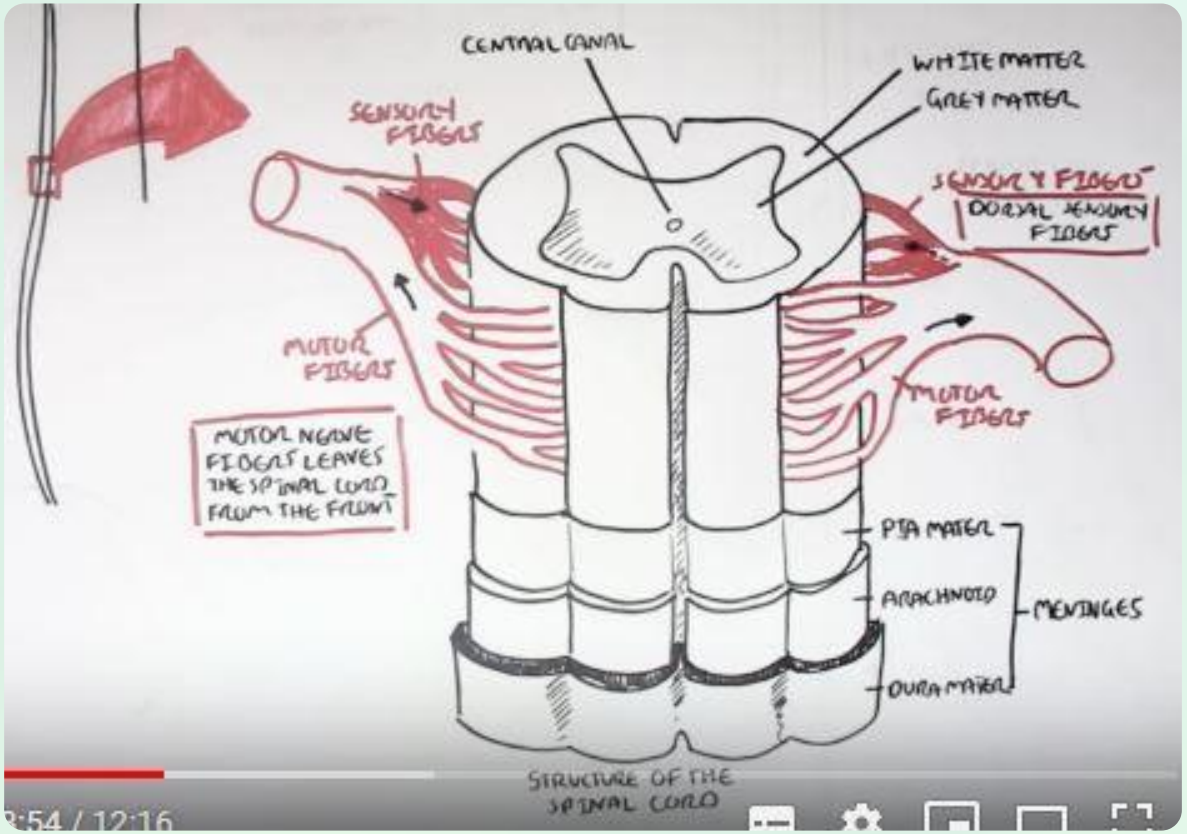
Ascending Pathways: Spinal Cord to Brain





Left: Spinal tracts (spinoreticular, spinotectal, lateral spinothalamic, parabrachial area) projecting to reticular formation, colliculi, lateral lemniscus, medulla, amygdala, and hippocampus. Right: Thalamic and hypothalamic projections reaching the primary somatosensory cortex, cingulate cortex, prefrontal cortex, and insula.

Nociception — Video Resource



Video reference: **https://www.youtube.com/watch?v=fUKlpuz2VTs** — An animated overview of nociception from peripheral receptor activation through spinal cord transmission to cortical perception.

Nociception — Peripheral Sensitization

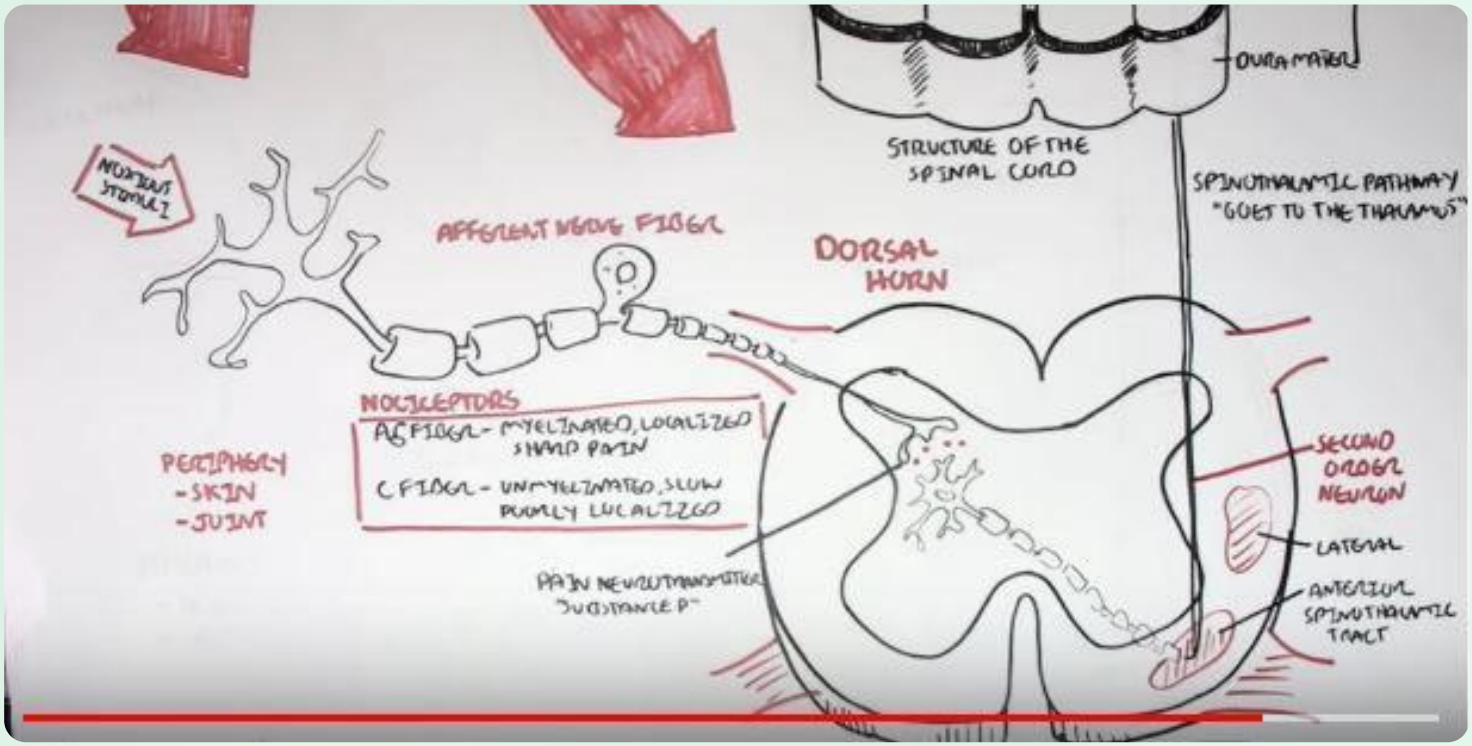
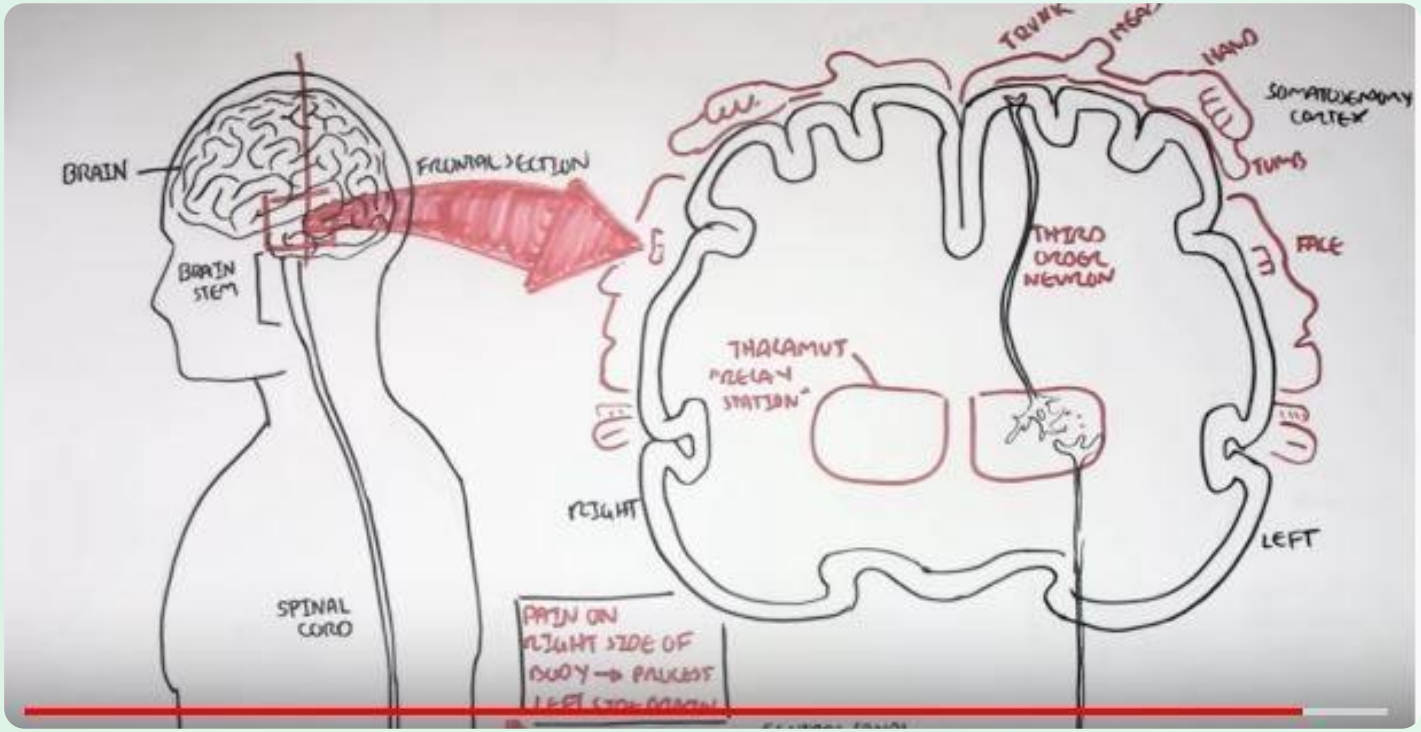


Illustration of peripheral sensitization mechanisms. Following tissue injury, inflammatory mediators lower the activation threshold of nociceptors, contributing to primary hyperalgesia at the site of damage.

Video: Nociception

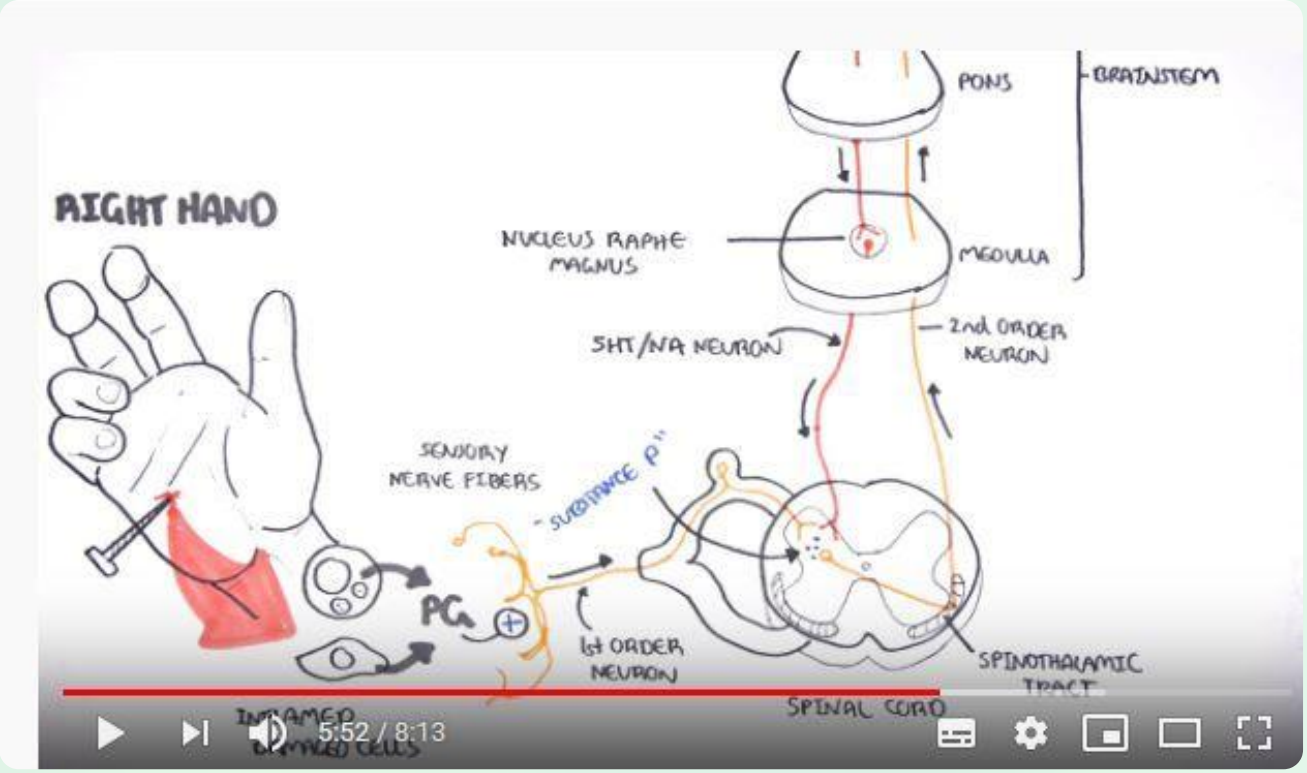
Nociception — Central Sensitization



Central sensitization refers to increased responsiveness of nociceptive neurons in the CNS to normal or sub-threshold afferent input. This mechanism underlies secondary hyperalgesia and many chronic pain states.

Video: Nociception

Pain — Neurotransmission Overview



Overview of neurotransmitter systems involved in pain modulation. Key players include glutamate (fast excitatory transmission), substance P, CGRP, GABA (inhibitory), and endogenous opioids. Understanding these systems underpins pharmacological pain management.

Video: Pain Neurotransmission

Pain — Spinal Cord Modulation

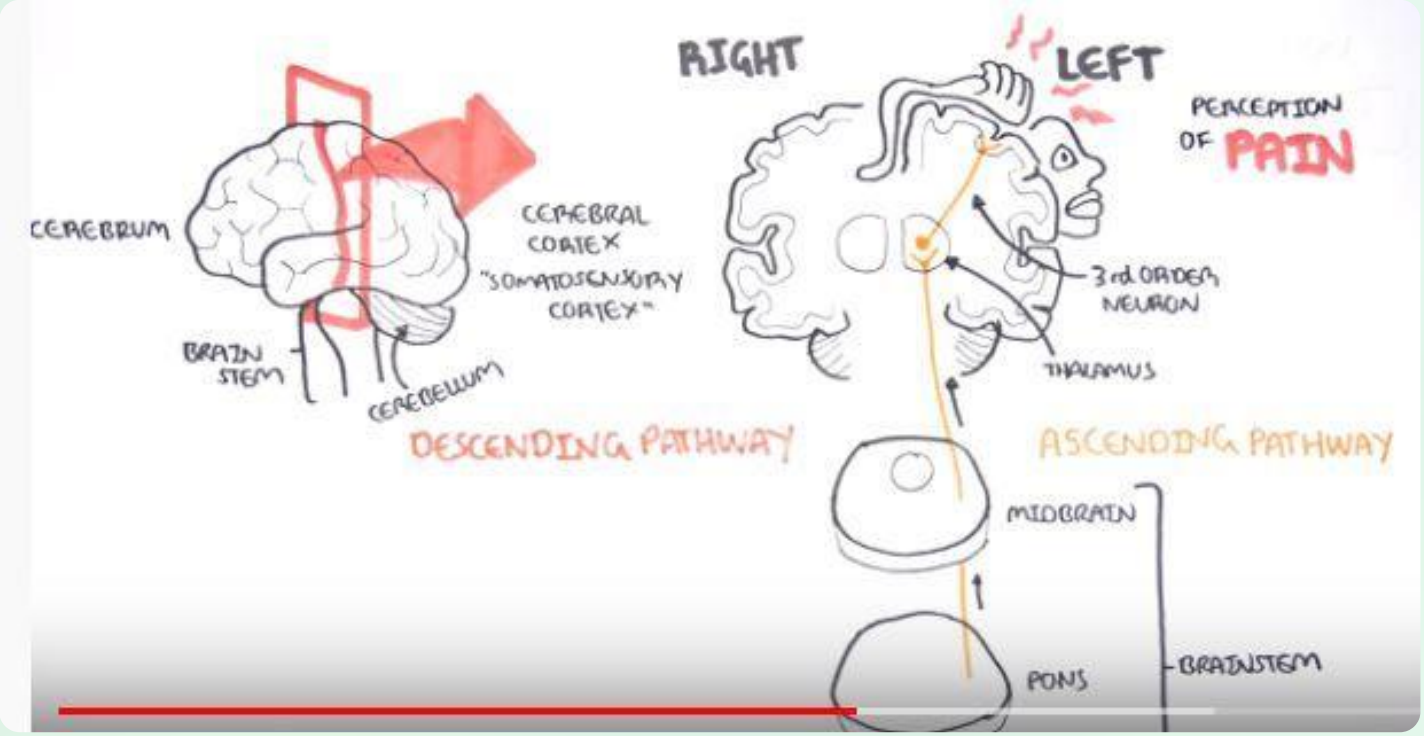
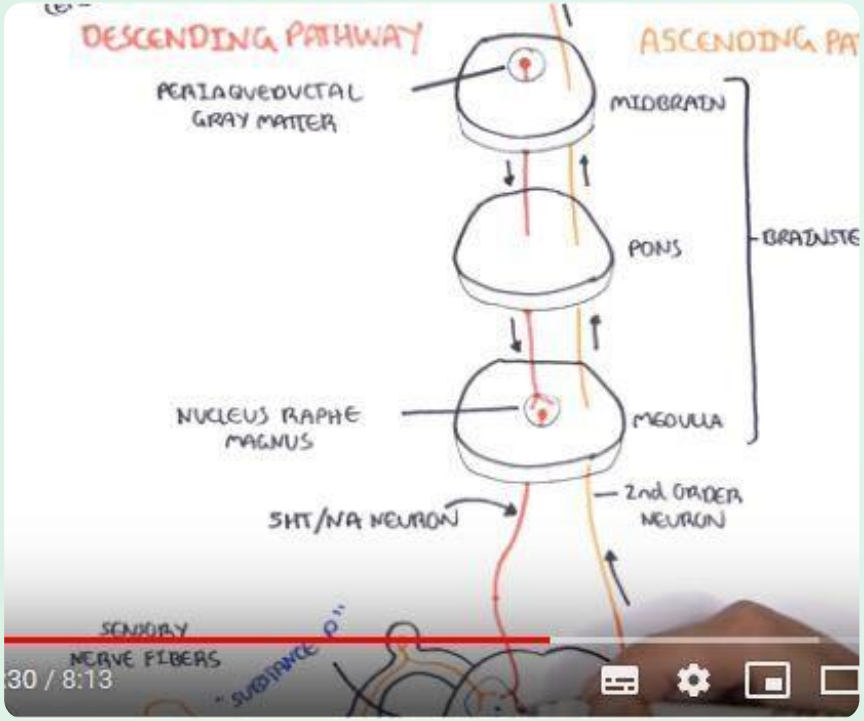


Illustration of dorsal horn circuitry showing interaction between Aδ, C, and Aβ fibers with projection neurons and inhibitory interneurons. This circuit is the anatomical substrate for the gate control theory of pain modulation.

Video: Nociception

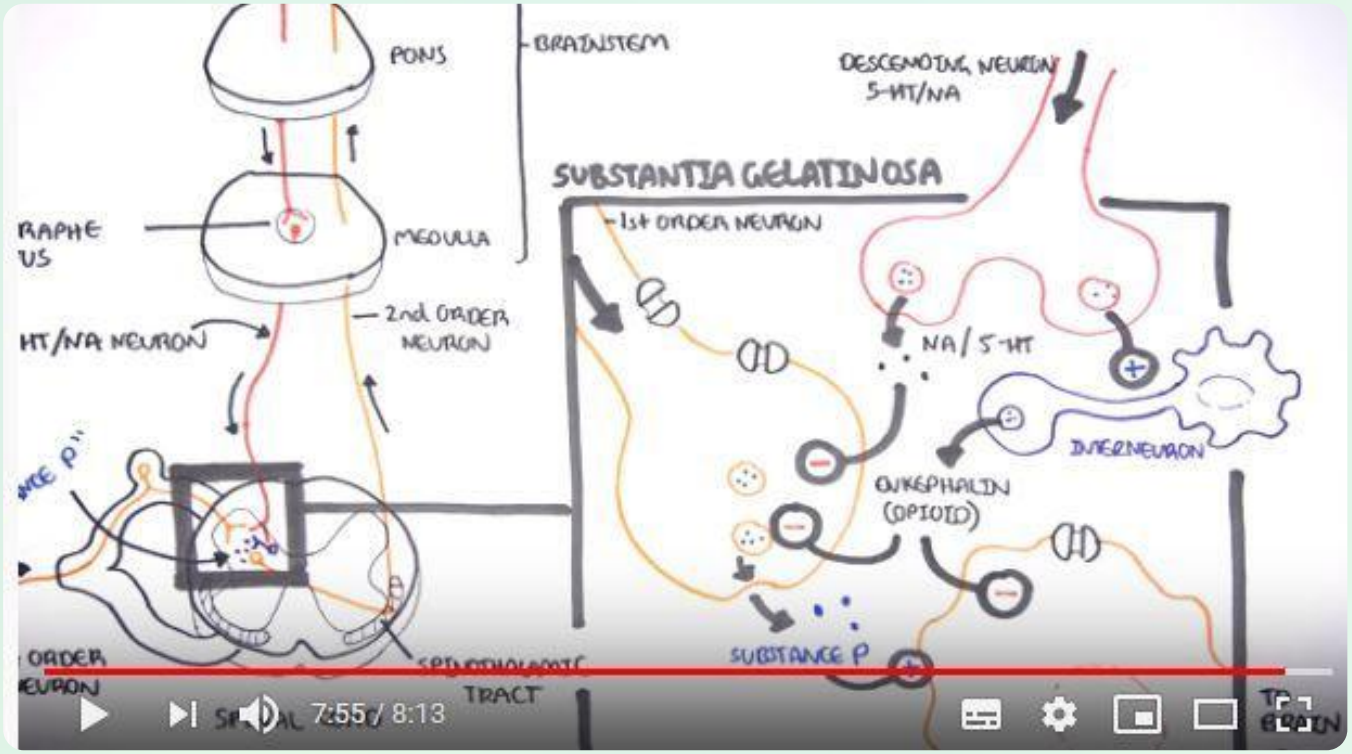
Pain — Cortical Processing



The "pain neuromatrix" encompasses multiple cortical regions: primary and secondary somatosensory cortex (sensory-discriminative dimension), anterior cingulate cortex (affective-motivational dimension), and prefrontal cortex (cognitive-evaluative dimension).

Video: Pain

Descending Analgesic System



The descending analgesic system originates primarily in the **periaqueductal grey (PAG)** and **nucleus raphe magnus (NRM)**. It modulates dorsal horn nociceptive transmission via serotonin, norepinephrine, and endogenous opioids, providing top-down pain suppression.

Video: Descending Analgesia

Gate Control Theory — Principles

Proposed by **Melzack and Wall (1965)**, the gate control theory was the first to explain pain modulation at the spinal cord level.

1 Site of Action

Cells of the **substantia gelatinosa Rolandi** and Lissauer's tract in the posterior horns of the spinal cord.

2 Gate Mechanism

Myelinated fibers (Aα, Aβ) activate inhibitory interneurons — closing the gate. Unmyelinated C-fibers inhibit those interneurons — opening the gate to pain.

3 CNS Control

The CNS controls gate opening/closing via efferent fibers. Voluntary, mechanical, and sensory systems interact to determine the individual's pain response.

Gate Control Theory — Mechanisms

Gate Open → Pain Perceived

- Inhibitory interneurons are **suppressed** by C-fiber activity
- Projection neurons are directly activated by both myelinated and unmyelinated fibers
- Increased transfer of nociceptive inputs to higher centers
- Increased pain perception

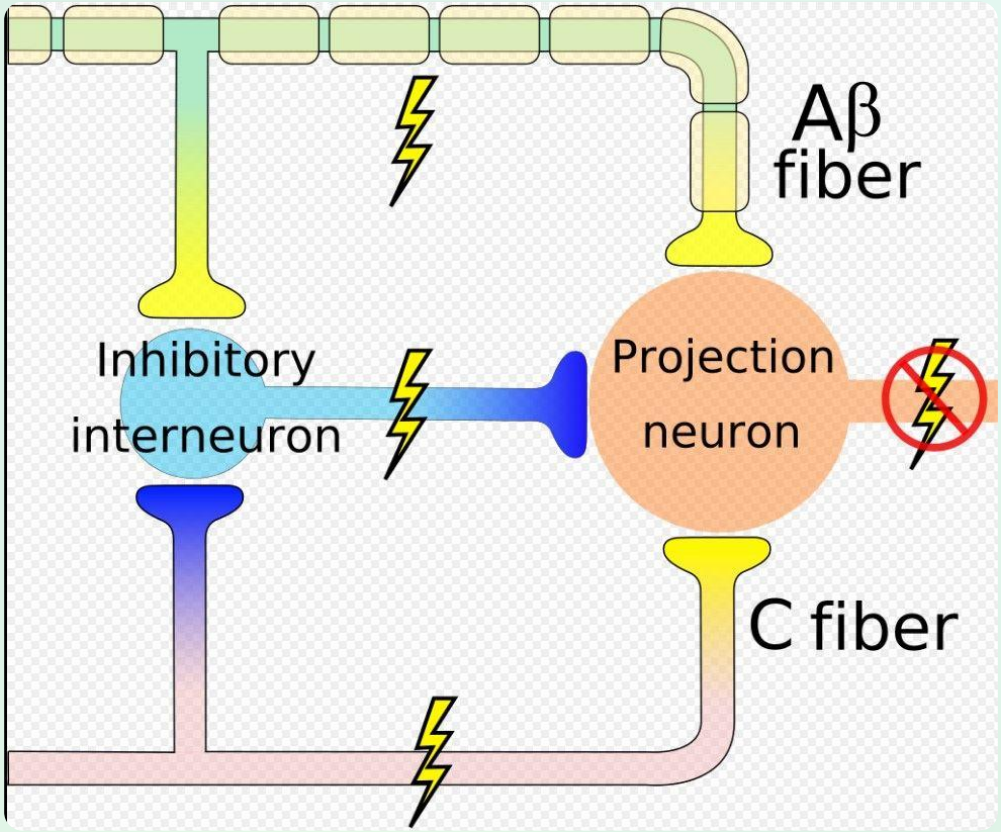
Gate Closed → Pain Suppressed

- Inhibitory interneurons are **activated** by Aβ fiber activity
- Projection neuron activity is inhibited
- Reduced transfer of inputs to higher centers
- Decreased pain perception

Clinical Evidence

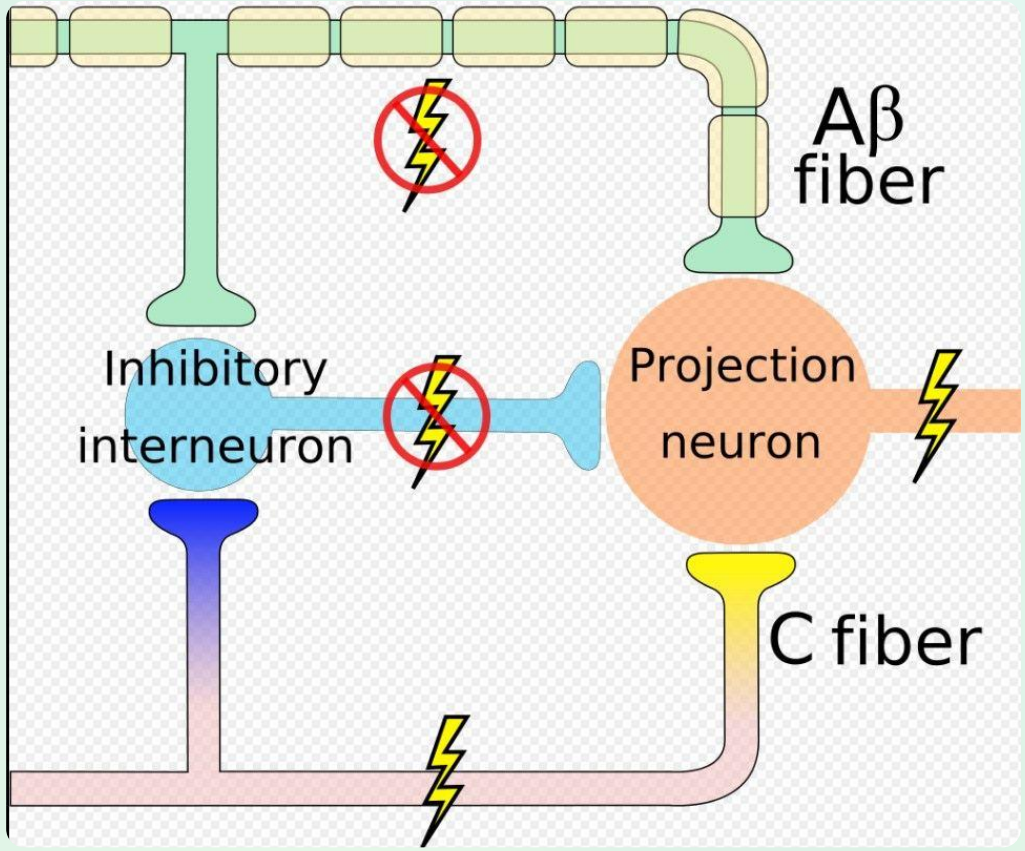
TENS (transcutaneous electrical nerve stimulation) exploits this mechanism by activating large Aβ fibers to close the gate and reduce chronic pain.

Gate Control Theory — Illustration I



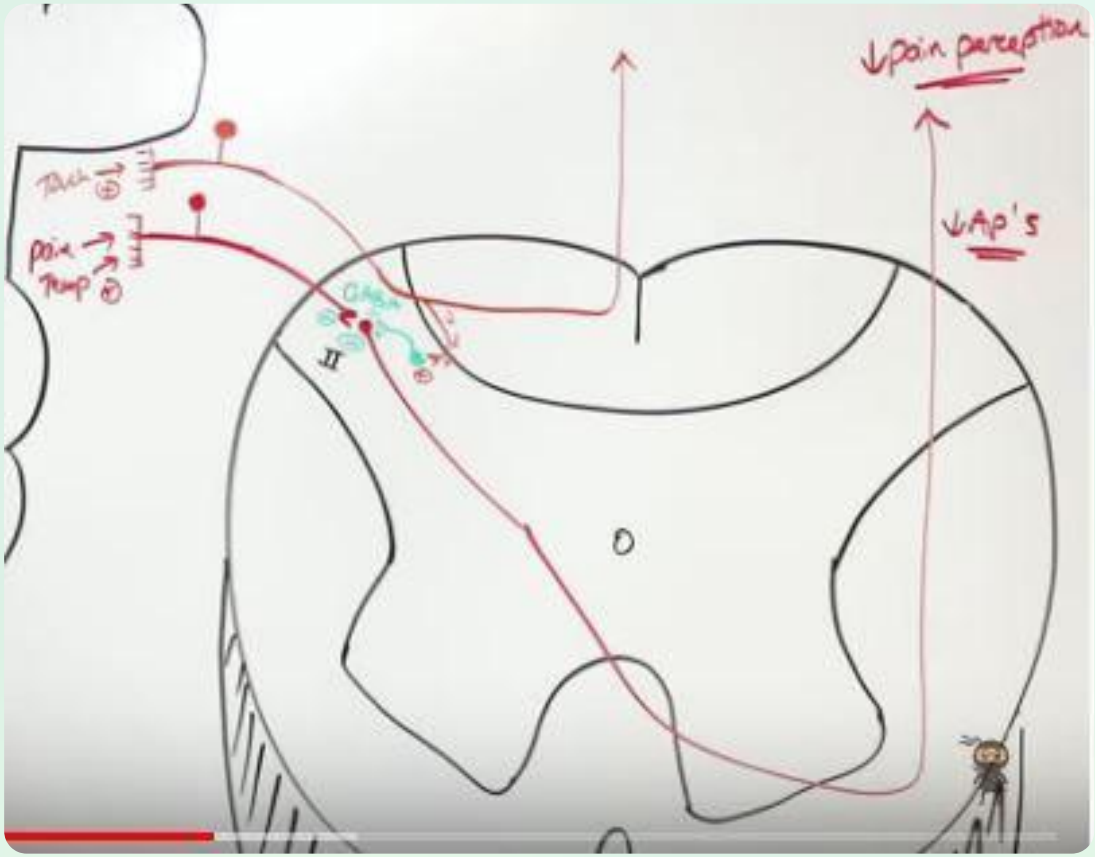
Schematic of dorsal horn circuitry underpinning the gate control theory, showing the interaction between large-diameter Aβ fibers, small-diameter C fibers, substantia gelatinosa interneurons, and transmission (T) cells.

Gate Control Theory — Illustration II

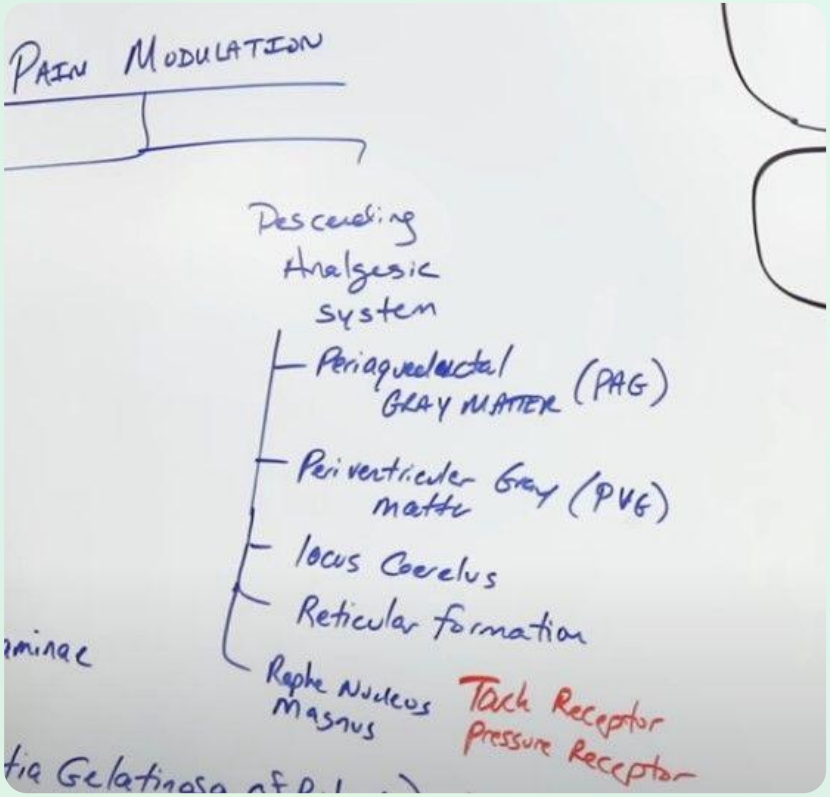


Expanded gate control model incorporating descending CNS control. Higher brain centers (cognitive and emotional) modulate the spinal gate, explaining why psychological state, attention, and expectation profoundly influence pain perception.

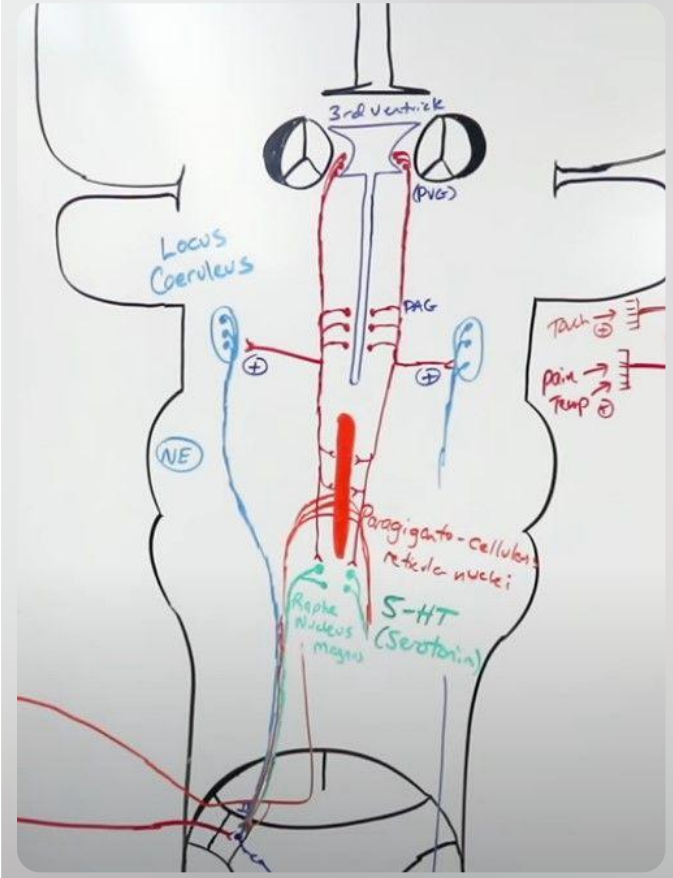
Gate Control Theory — Video Reference



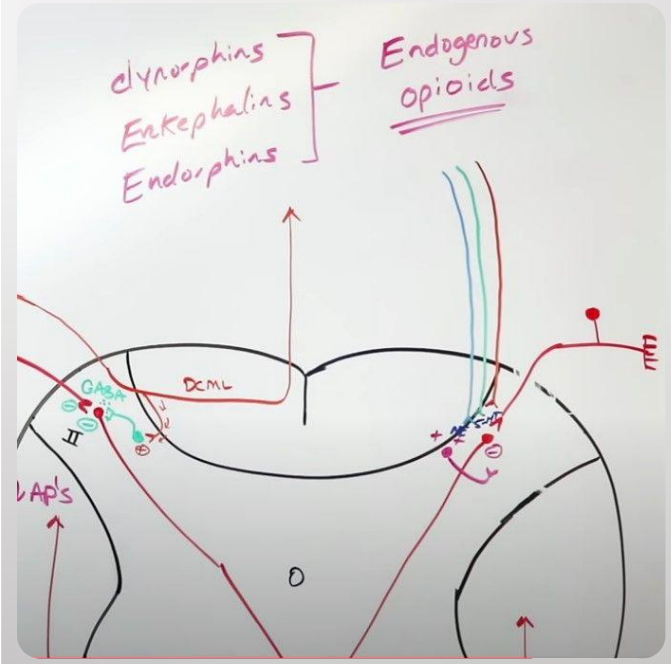
Animated explanation of the gate control theory of pain: **https://www.youtube.com/watch?v=8IhN6T3mT04**



Gate open state: C-fiber activity dominates, inhibitory interneurons are suppressed, and nociceptive signals pass freely to projection neurons and ascend to the brain.

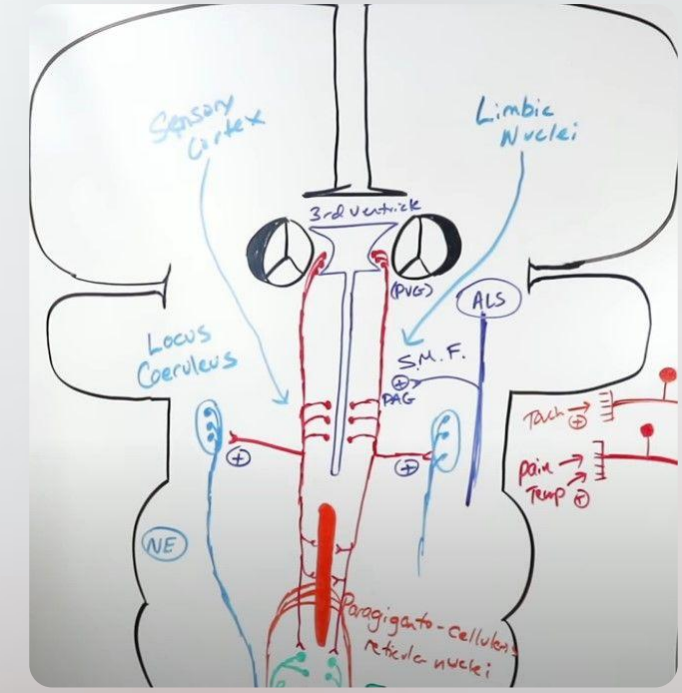


Gate closed state: Aβ fiber activity activates inhibitory interneurons, reducing transmission through projection neurons and limiting pain perception — the physiological basis of TENS and massage analgesia.



Descending CNS control of the spinal gate: cortical and subcortical structures (prefrontal cortex, PAG, NRM) send efferent signals to the dorsal horn to modulate gate status — explaining cognitive, emotional, and placebo influences on pain.

Summary schematic of the complete gate control model integrating peripheral afferent fibers, spinal cord interneuron circuitry, ascending pain pathways, and descending cortical modulation — illustrating pain as a dynamic, multidimensional experience.



Specific Types of Pain

Causalgia

Dull, irradiating, burning pain following traumatic nerve damage. Associated with sympathetically maintained pain syndromes.

Neuralgia

Pain without stimulation of pain receptors. Caused by a change in neurological structure (ion channels) or function — not by receptor excitation.

Radicular Pain

Irritation of spinal roots — most commonly due to spinal disc herniation causing dermatomal radiation.

Nociceptive Pain

Direct stimulation of peripheral nociceptors by trauma — the most common and well-understood form of pain.

Neuropathic Pain

Damage or disease affecting any part of the somatosensory nervous system — often chronic, burning, or shooting in character.

Phantom Pain

Pain perceived in amputated parts of the body. Reflects persistent cortical representation of the missing limb.

Phantom Pain and Mirror Therapy



Mirror Therapy



Mirror therapy uses visual feedback to "trick" the brain into perceiving movement of the phantom limb, reducing cortical reorganization and alleviating phantom pain.
Video reference

Additional Pain Types: Central & Headache

Psychogenic Pain

Pain caused, increased, or prolonged by mental, emotional, or behavioral factors — without identifiable organic pathology.

Thalamic (Central) Pain

Results from lesions of the thalamus — often severe, spontaneous, and refractory to analgesics.

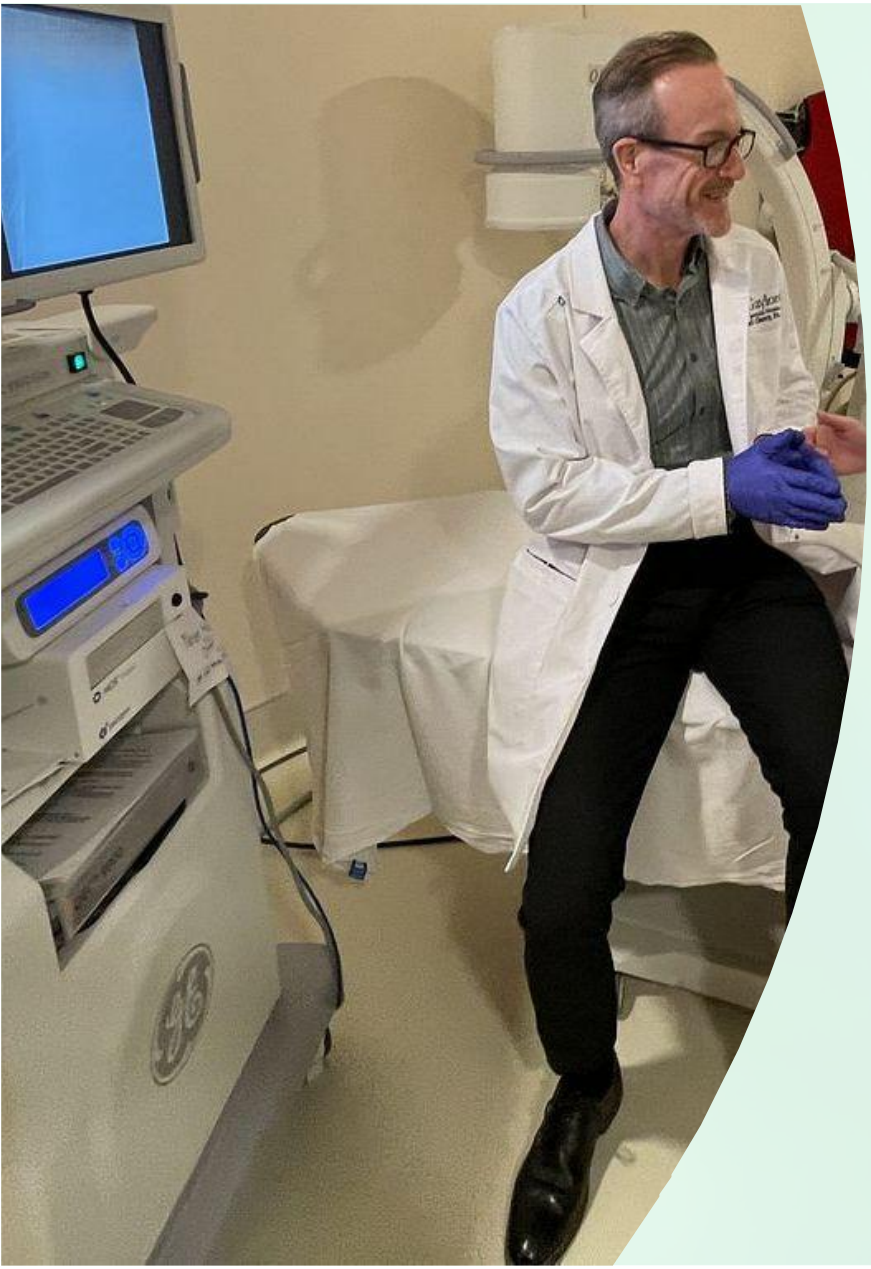


Headache

- **Cluster headache** — unilateral, extreme intensity, rapid onset, 15 min to 3+ hrs; no migraine aura
- **Migraine** — recurrent attacks, often with aura, nausea, photo- and phonophobia

Acute vs. Chronic Pain: Comparative Overview

Feature	Acute Pain	Chronic Pain
Course	Sudden incident	Long-term
Cause	External noxa	Internal disease; often unknown or failed long-term therapy
Onset	Sudden	Sudden or gradual and prolonged
Duration	Short	Months to years
Localization	Well-localized	Difficult to localize
Significance	Important diagnostic information	Often without clear biological sense
Prognosis	Usually resolves	Tends to persist or worsen



Chronic Pain: Clinical Significance

The number of patients suffering from chronic pain is increasing worldwide. Chronic pain is now recognized as a disease in its own right, not merely a symptom.

Definition

Pain lasting longer than the expected course of an acute disease, or beyond the expected healing time following treatment.

Mechanism

Likely not in direct relationship with the initial damage. It is more a consequence of secondary neuroplastic and psychosocial changes in the nervous system.

Psychological Profile

Different psychological mechanisms operate in chronic pain compared to acute pain — involving maladaptive central processing rather than peripheral tissue signaling.

Chronic Pain: Epidemiology and Common Conditions

Incidence

50%

Adults

Up to 50% of adults suffer from one or more chronic pain conditions

50%

Oncology

Approximately 50% of oncology patients experience significant pain

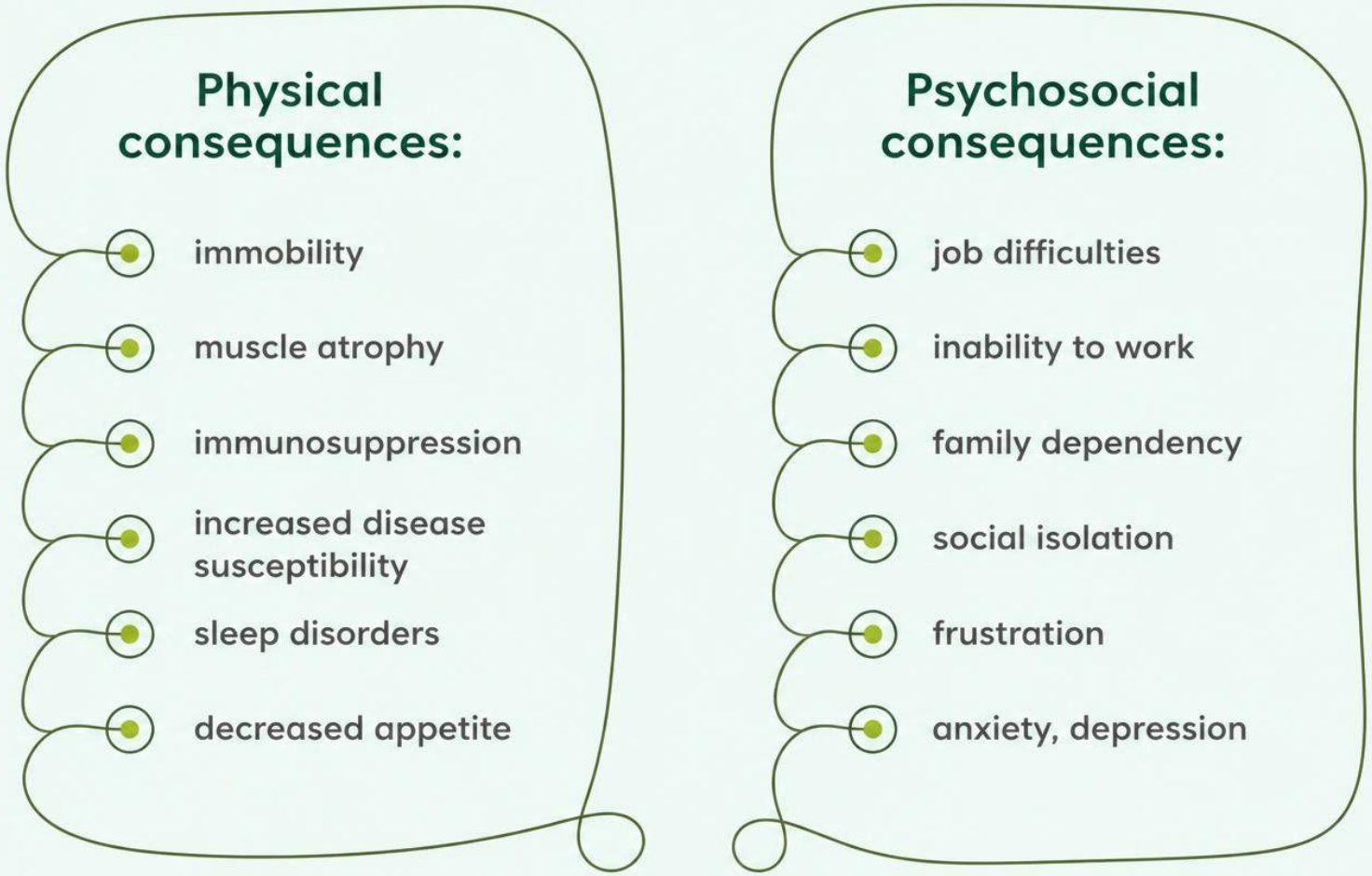
Incidence of strong chronic pain is higher in older age groups.

Common Conditions Associated with Chronic Pain

- Osteoarthritis and rheumatoid arthritis
- Low back pain and neck pain
- Arm and shoulder pain
- Chronic headache
- Myofascial pain syndromes
- Phantom limb pain

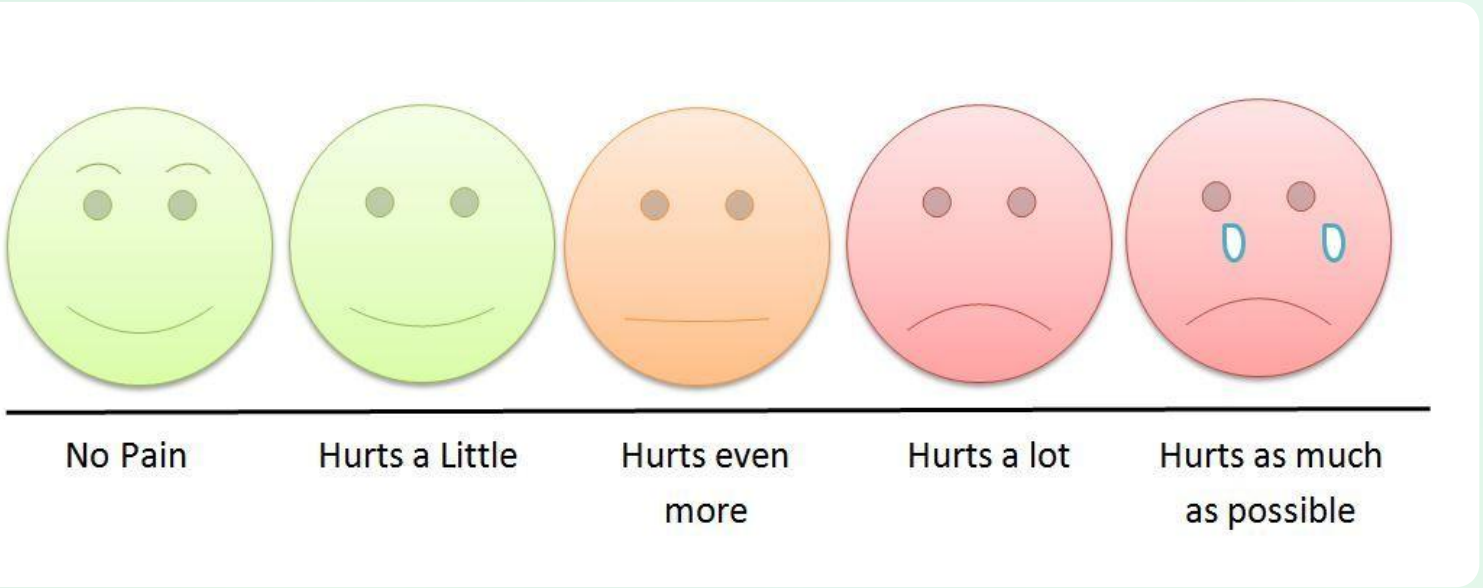
Chronic pain has become a major public health challenge with complex physical and psychosocial dimensions.

Consequences of Chronic Pain



How do we measure pain intensity? → Requires validated clinical tools — see pain assessment scales.

Pain Assessment Scales



Pain assessment scales are essential clinical tools for quantifying subjective pain experience. The most commonly used include the **Visual Analog Scale (VAS)**, the **Numerical Rating Scale (NRS, 0–10)**, and the **Wong-Baker FACES scale** for children or patients with communication difficulties. Regular, standardized pain assessment is a fundamental component of pain management in clinical practice.

Headache — Overview



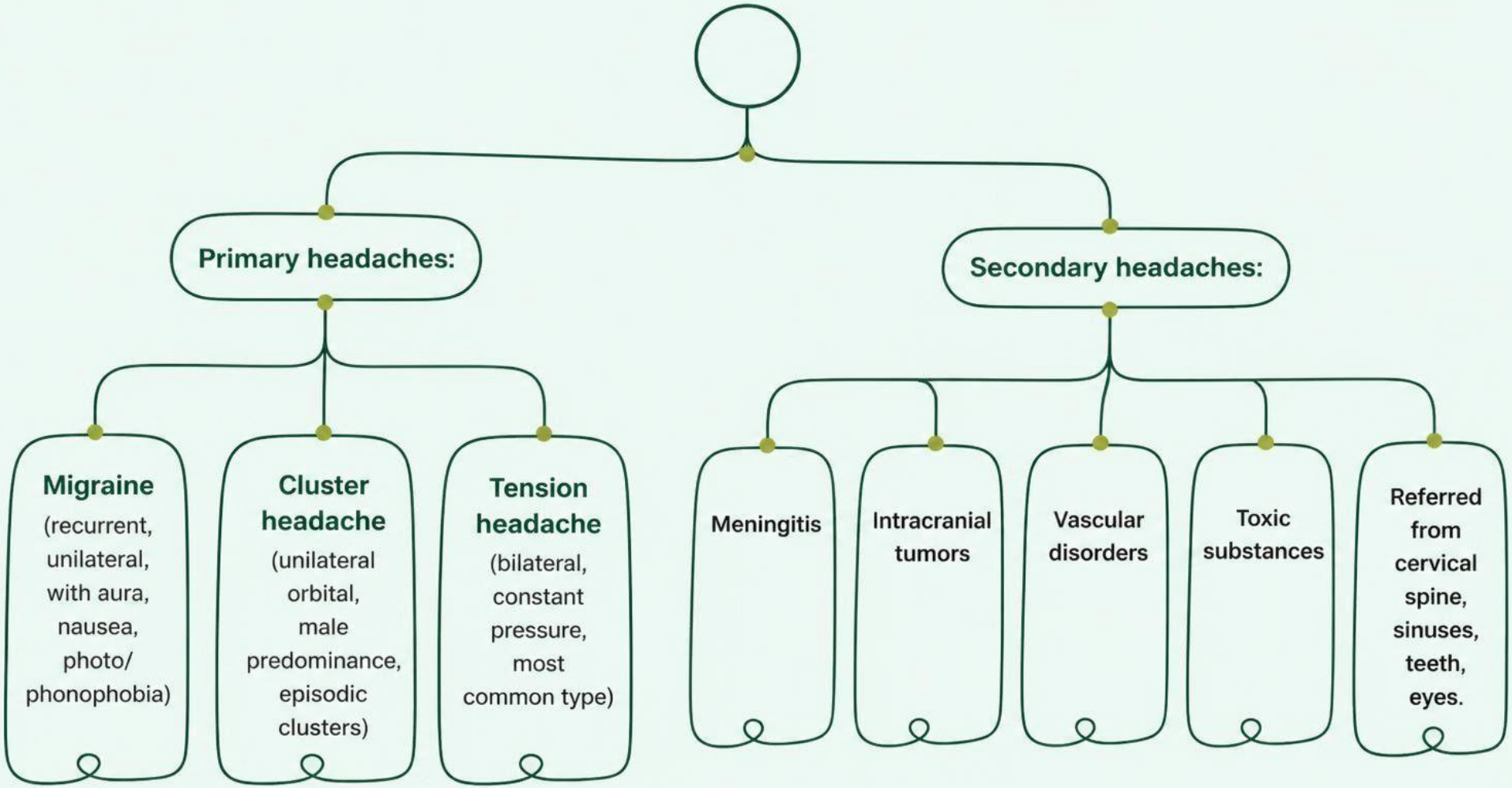
One of the most common types of pain

Headache affects the vast majority of the population at some point in their lives and represents a leading cause of disability worldwide.

Classification:

- **Primary (functional)** — migraine, cluster headache, tension headache
- **Secondary (organic)** — caused by meningitis, intracranial tumors, intracranial hypo-/hypertension, vascular disorders, toxic substances, cervical spine disorders, splanchnocranium, ear, or larynx pathology

Headache Classification



Extracranial Headache Sources

Sinusitis

Entrances of paranasal sinuses are richly innervated. Pain occurs when nasal mucosa around sinus openings is irritated — highly relevant in dental practice.

Otitis Media

The tympanic cavity is an extremely sensitive area. Its irritation produces very intense pain, often radiating to the jaw and temporal region.

Tension Headache

Most common type; affects both genders equally. Constant, bilateral (rarely unilateral) pressure sensation. Caused by neck/head muscle contraction, often psychogenic. Pathogenesis involves muscle hypoxia and K^+ shift to extracellular fluid.

Vertebrogenic Pain

Cervical spine disorders can produce referred headache. Muscle contraction leads to hypoxia, extracellular K^+ elevation, and relative decrease in calcium — triggering pain.

Extracranial Headache: Dental & Ocular Sources

These sources are of particular relevance in dental medicine and must be considered in the differential diagnosis of orofacial pain.

Toothache (Odontogenic Pain)

A major source of orofacial pain. Causes include:

- Dental caries
- Pulpitis (reversible and irreversible)
- Tooth fracture
- Periapical abscess

Odontogenic pain can radiate and be confused with sinusitis, neuralgias, or migraine.

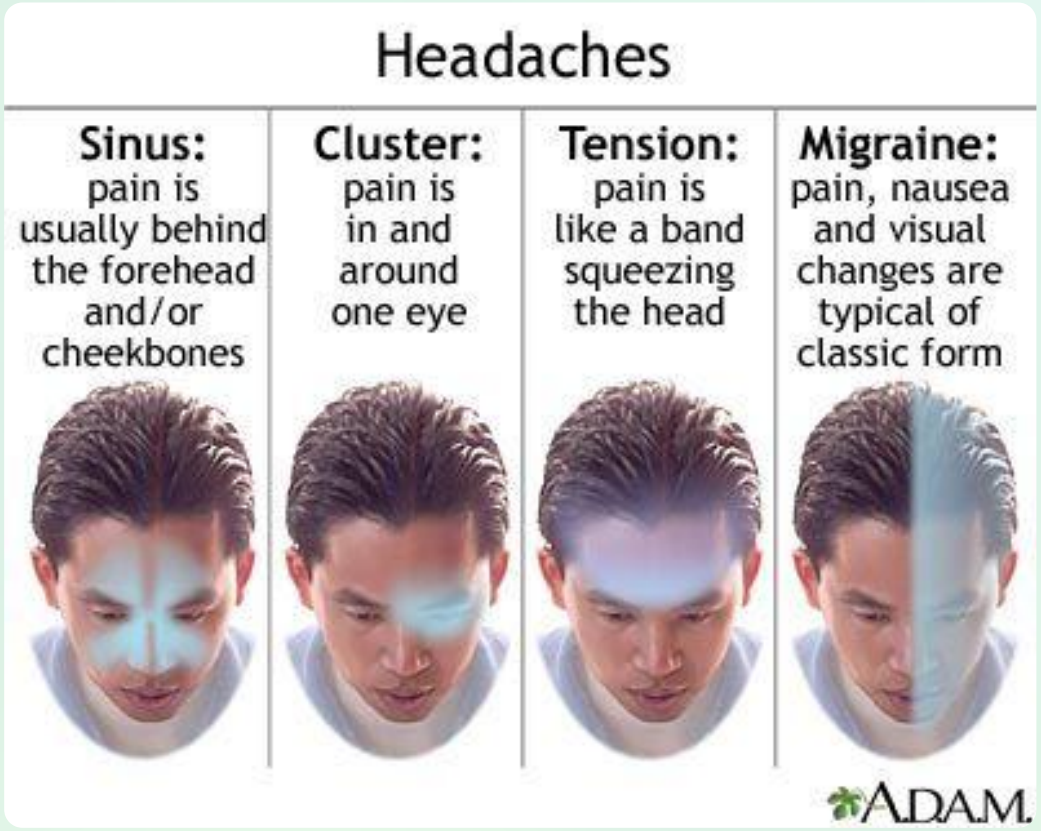
Ocular and Orbital Sources

- Conjunctiva is sensitive to mechanical and chemical stimuli
- Extraocular muscles and meninges covering the optic nerve can be sources of pain
- Bulbus is sensitive to changes in intraocular pressure (glaucoma)

Arteries, Muscles & Periosteum

Muscle contraction (especially temporalis, masseter) and the richly innervated periosteum are common extracranial pain generators in dental patients.

Intracranial Structures Sensitive to Pain



Pain-sensitive intracranial structures include the meninges, dural veins and arteries, and subarachnoid blood vessels — especially in areas innervated by the trigeminal nerve (n. trigeminus). Importantly, **brain parenchyma and intraparenchymal blood vessels do not contain nociceptors** and are therefore insensitive to direct stimulation.

Migraine: Pathophysiology and Clinical Features

Clinical Profile

- Recurrent attacks of mostly unilateral pain
- Associated nausea, vomiting, photo- and phonophobia
- Attacks last hours to days; side can alternate
- Affects **15–30% of women** and **3–13% of men**
- 70% of cases onset before age 30
- ~5% of prepubertal children; equal sex ratio pre-puberty
- **Aura** precedes attack: visual flashes, field defects

Pathophysiology

- Combination of **CNS changes** (cortical spreading depression) and **craniovascular disorders**
- CNS manifestations: visual symptoms, transient hemiparesis, aphasia, sensory deficits
- Pain related to trigeminal innervation of the craniovascular system (subarachnoid space)
- Afferent fibers release **Substance P, neurokinin, CGRP**, serotonin, and bradykinin onto vessel walls

Cluster Headache

Cluster headache is one of the most painful conditions known to medicine, often described by patients as worse than childbirth or kidney stones.

Epidemiology

More common in men than women (**4–5:1 ratio**), typically onset between 20–30 years of age. Patients report pain cycles occurring around the same period each year.

Pain Characteristics

Stereotypical, always unilateral, localized in the orbit. Spreads to the suboccipital area or shoulders. Onset is sudden, reaching maximum intensity rapidly.

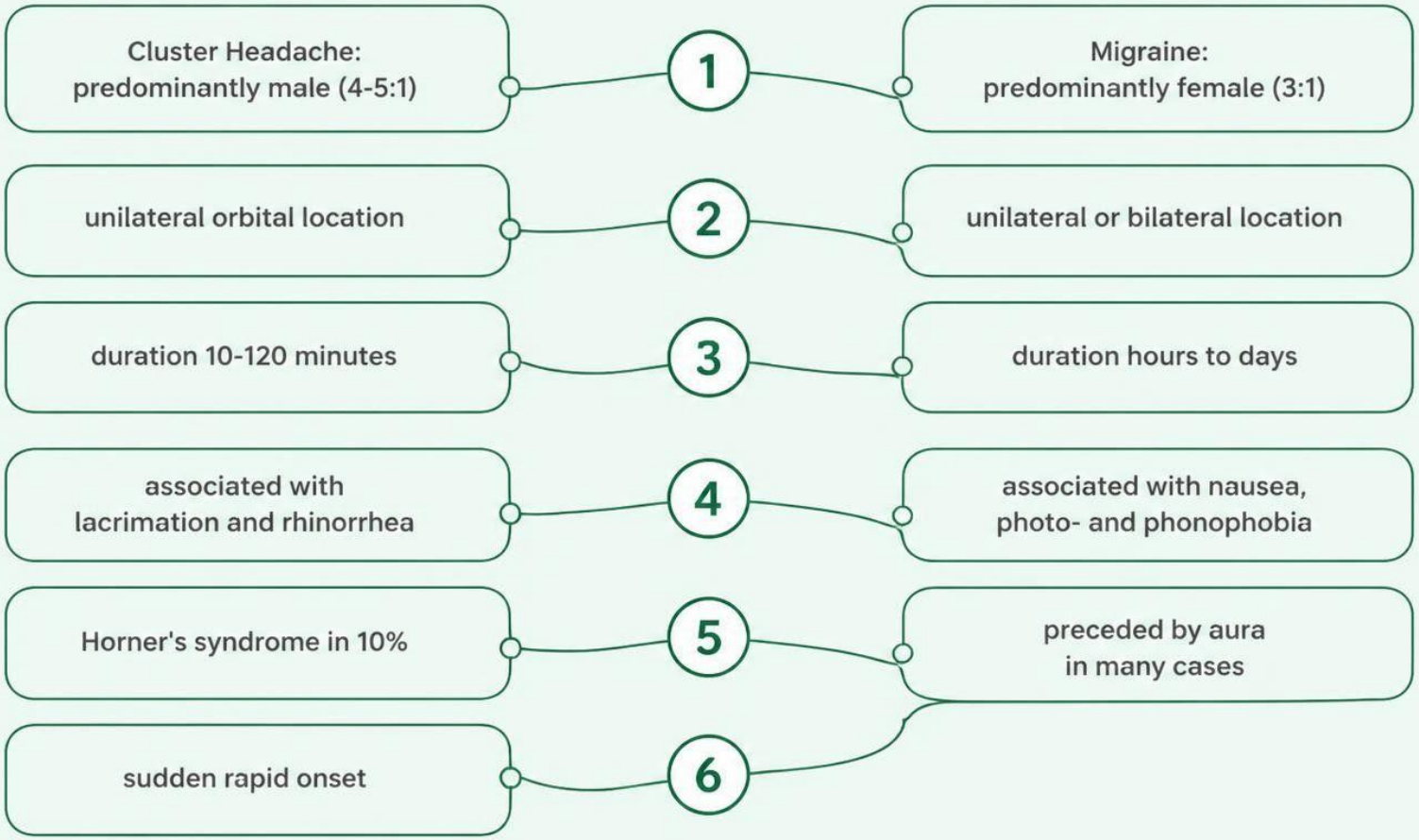
Duration & Pattern

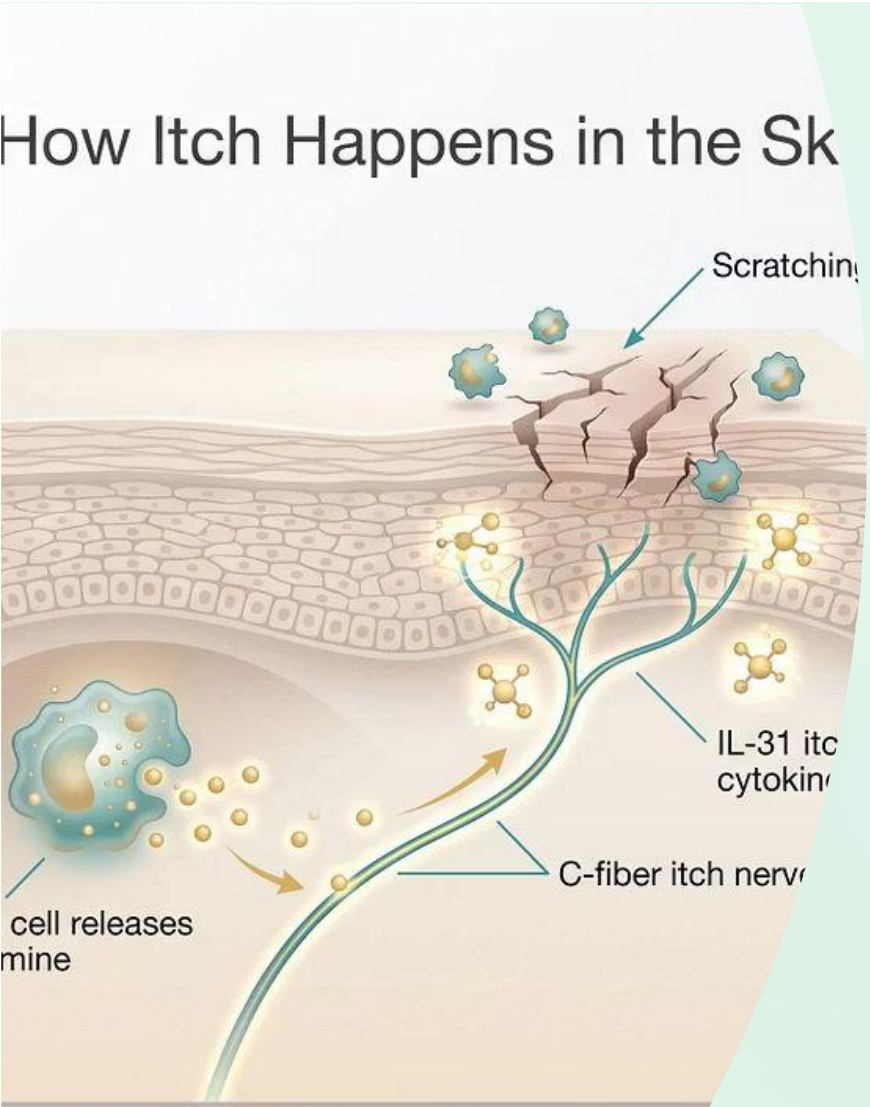
Attacks last 10–120 minutes, ending rapidly without residual pain. Can recur in "clusters" — 2–3 attacks per day for weeks.

Associated Features

Lacrimation, rhinorrhea, conjunctival hyperemia, unilateral photophobia. ~10% have **Horner's syndrome** (miosis + ptosis). 25–30% experience nausea and vomiting. Etiology remains unclear.

Cluster Headache vs. Migraine: Key Differences





Itching (Pruritus)

Definition & Classification

An uncomfortable sensation causing the need to scratch. Can be induced in skin or mucosa, or by central nervous system mechanisms.

Itching is **not a subtype of pain** — it is a **separate sensory category**:

- Does not transform to pain at high intensity
- Causes scratching reflex, not withdrawal
- Central opioids suppress pain but *cause* itching

Peripheral Mediators

- Histamine, acetylcholine, serotonin in skin
- Indirectly: neuropeptides, cytokines, proteases (via histamine release)
- Opioid receptor agonists in CNS cause itching centrally

Clinical Associations

Atopic eczema, urticaria, insect bites. Systemic: primary biliary cirrhosis, cholestasis, renal failure — explained by accumulation of **endogenous opioids**.

Pruritus: Mechanisms and Clinical Significance

Peripheral Receptors

Not fully characterized. Likely involve free nerve endings of **unmyelinated C fibers** — a subset distinct from pain-mediating C fibers.

Counter-inhibition by Scratching

Touch, pressure, and pain stimuli from scratching **decrease itching sensation** — via gate control mechanisms similar to pain modulation.

Systemic Causes

Pruritus without skin lesions occurs in **primary biliary cirrhosis**, other cholestatic liver diseases, and **renal failure**. The mechanism is thought to involve accumulation of endogenous opioids acting centrally.

For dental students: opioid analgesics used in pain management frequently cause pruritus as a side effect — an important consideration in clinical prescribing.

PATHOPHYSIOLOGY · DENTAL MEDICINE

Pain in the Oral Cavity: Diagnostic Considerations

A comprehensive guide to orofacial pain classification, pathways, and differential diagnosis — designed for students of dental medicine studying pathophysiology.



Course Overview

What We Will Cover

01

Definition & Classification

IASP definition of pain, acute vs. chronic, nociceptive vs. neuropathic orofacial pain categories

02

Pain Pathways

Orofacial nociceptive transmission from peripheral nociceptors through the trigeminal system to cortical perception

03

Differential Diagnosis

Dental and non-dental etiologies, referred pain mechanisms, and characteristic clinical patterns

04

Specific Syndromes

Trigeminal neuralgia, headache subtypes, neck pain etiologies, and temporomandibular disorders



CHAPTER 1

Defining Orofacial Pain

Primary Dental Etiologies

- Dental caries (cavities)
- Cracked or fractured tooth
- Exposed tooth root
- Periodontal (gum) disease
- Failed dental implants

Non-Dental Causes

- Temporomandibular joint disorders
- Masticatory muscle spasms
- Oral cancers
- Implant complications

"Toothache" refers to pain localized around a tooth, multiple teeth, or the jaws. Pain characteristics vary widely and may be aggravated by chewing, temperature extremes, or sweet foods.

CHAPTER 1

Referred Pain: Beyond the Oral Cavity

Clinical Pearl: Not all orofacial pain originates from dental structures. A thorough differential diagnosis must always consider systemic and regional pathology.

Cardiac Origins

Angina pectoris and myocardial infarction can present with referred pain to the jaw, particularly the left mandible — a potentially life-threatening presentation requiring immediate recognition.

Otologic Disorders

Inner and external ear infections refer pain to the temporomandibular region via shared neural pathways, particularly through the auriculotemporal nerve.

Sinus Pathology

Maxillary sinusitis produces pain in the upper teeth and jaw due to anatomical proximity and shared innervation, closely mimicking dental pain.

Neurological Conditions

Neuralgias and neuropathic pain syndromes — particularly trigeminal neuralgia — can manifest as severe orofacial pain with no identifiable dental pathology.

CHAPTER 1

Differential Diagnosis: Temperature Sensitivity Patterns

Sensitivity Without Recent Dental Work

Characteristics: Transient sharp pain to hot or cold stimuli

Possible causes: Loose filling, dental caries, enamel fracture, or minimal gum recession exposing dentinal tubules and root surfaces, allowing thermal stimuli to reach sensitive pulp tissue.

Prolonged Sensitivity Without Recent Work

Characteristics: Lingering pain after thermal stimulus removal

Possible causes: Irreversible pulpitis from deep decay, significant crack or fracture, advanced periodontal disease, or traumatic injury — suggesting permanent pulp damage requiring endodontic intervention.

Sensitivity After Recent Treatment

Characteristics: New sensitivity following dental procedures

Possible causes: Transient pulp inflammation (reversible pulpitis). The pulp tissue becomes temporarily hypersensitive but typically resolves within days to weeks.

CHAPTER 1

Additional Orofacial Pain Syndromes

Post-Treatment Discomfort

Dull ache and biting sensitivity after recent dental work indicates inflammatory response in the periodontal ligament, typically resolving spontaneously.

Abscess Formation

Constant, severe pain with pressure sensitivity, gum swelling, and tenderness indicates periapical or periodontal abscess — a dental emergency requiring prompt treatment.

Trigeminal Neuralgia

Sharp, jabbing pain triggered by touching specific areas or talking suggests trigeminal neuralgia — a neuropathic condition requiring neurological management.

Sharp Biting Pain

Acute pain when biting suggests structural compromise: loose filling, active decay, cracked tooth, cuspal fracture, or vertical root fracture requiring immediate evaluation.

Sinus-Related Pain

Dull ache in upper teeth and jaw may indicate maxillary sinusitis rather than dental pathology. Bruxism (teeth grinding) can produce similar symptoms.

TMJ Dysfunction

Clicking, popping sounds with painful jaw movement indicate temporomandibular joint disorder, requiring specialized evaluation and individualized treatment.

Accurate diagnosis requires careful history-taking, thorough clinical examination, and often imaging studies.

CHAPTER 2

Definition of Pain

> "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."
>
> — IASP, International Association for the Study of Pain, 1979

Damage (Danger) Signal

Pain alerts the organism to actual or potential tissue injury, initiating protective behavioral responses.

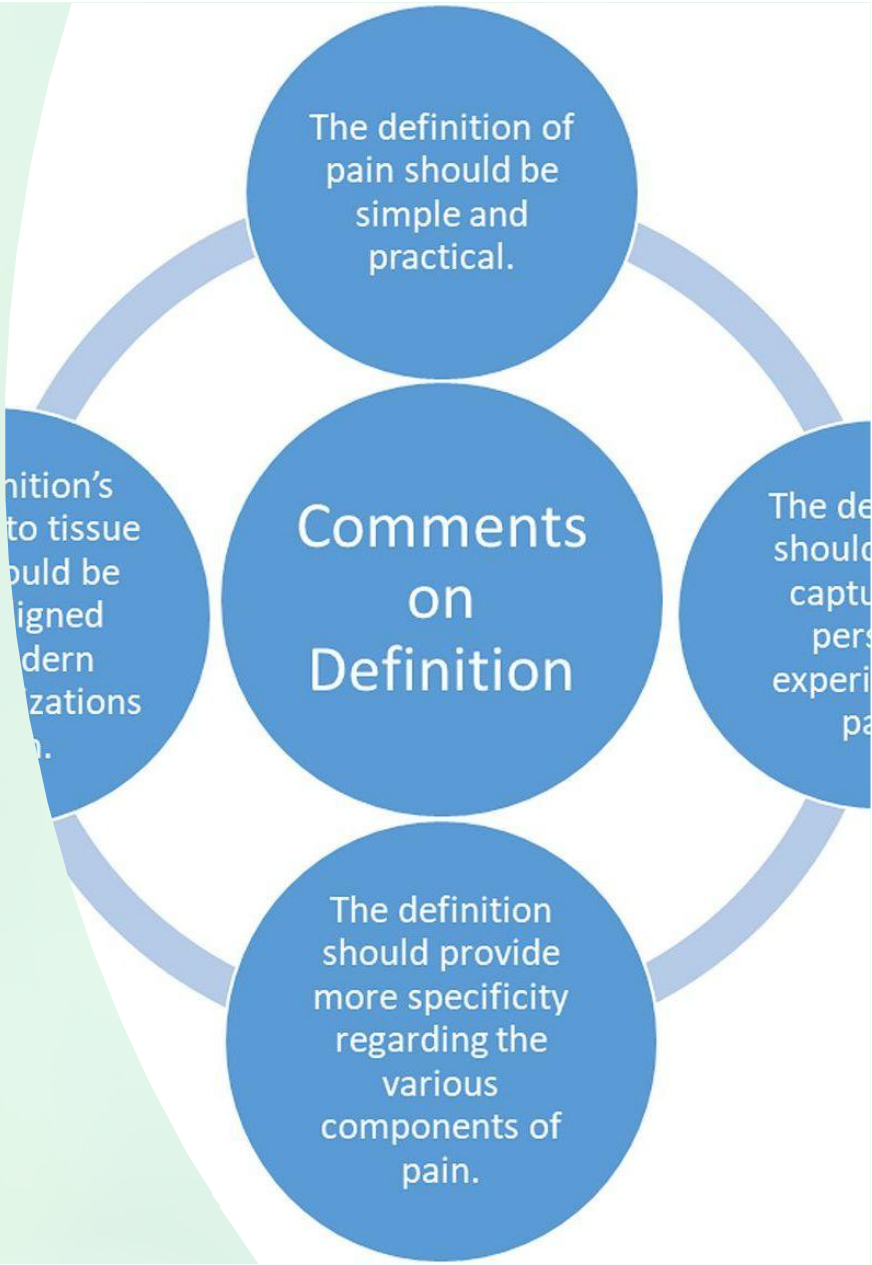
Indication & Localization

Pain helps identify the site and nature of tissue damage, guiding both the patient's and clinician's attention to the affected region.

Prevention of Further Damage

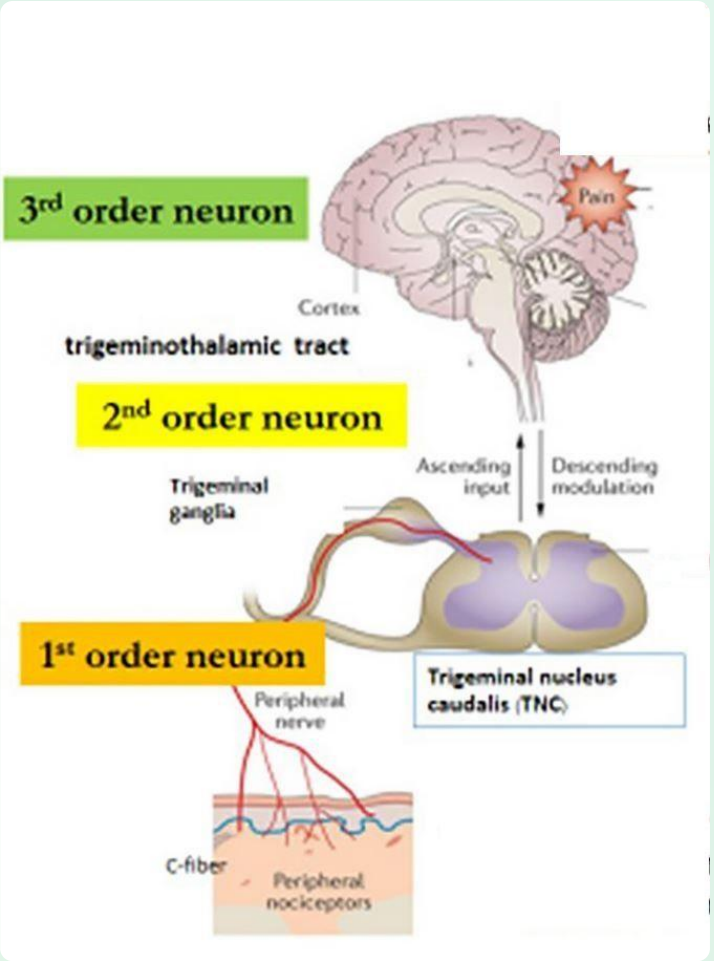
By generating aversive experiences, pain promotes avoidance behaviors that protect damaged tissues from further injury.

Orofacial pain encompasses pain arising in the oral cavity (teeth, gingiva, oral mucosa), face, jaw bones, and temporomandibular joint.



CHAPTER 2

Orofacial Pain Pathway



Orofacial pain pathways include primary afferent neurons, the trigeminal ganglion, brainstem nociceptive neurons, and higher brain centers regulating orofacial nociception.

1 1st Order Neuron

Nociceptors in the orofacial region transmit signals via the trigeminal (peripheral) nerve

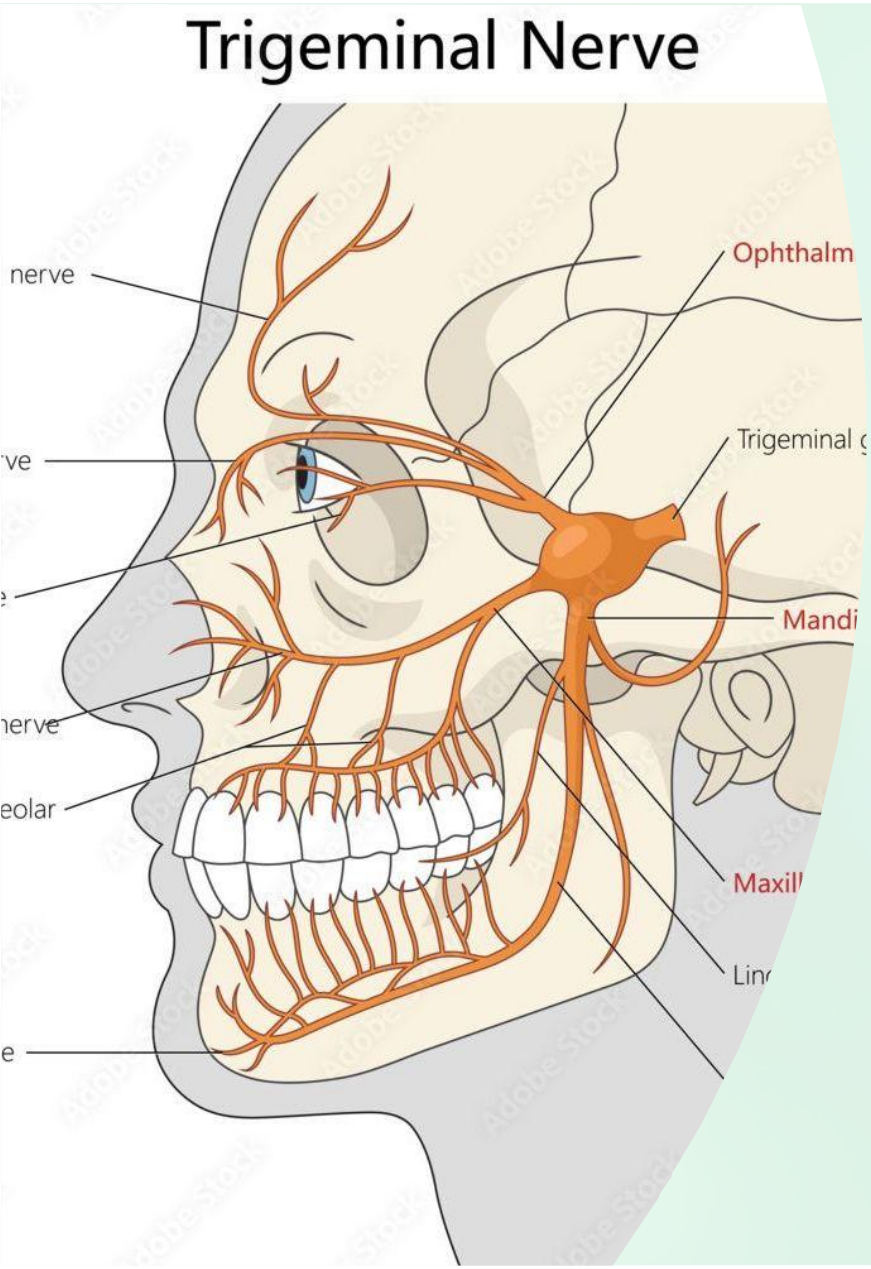
2 2nd Order Neuron

Synapse occurs at the trigeminal nucleus caudalis (TNC) in the brainstem

3 3rd Order Neuron

Signal ascends via the ventral trigeminothalamic tract to the thalamus and somatosensory cortex

The **descending modulatory pathway** releases serotonin, norepinephrine, and opioid peptides at the TNC, leading to pain reduction and central modulation.



CHAPTER 2

The Trigeminal Nerve: Gateway of Orofacial Sensation

The trigeminal nerve (CN V) is the primary sensory nerve of the face and oral cavity. It is composed of three main divisions — ophthalmic (V1), maxillary (V2), and mandibular (V3) — each responsible for distinct areas of sensation. Nociceptive signals from the entire orofacial region are funneled through this nerve, making it central to the understanding of orofacial pain pathophysiology.

V1 — Ophthalmic

Forehead, upper eyelid, dorsum of nose, cornea

V2 — Maxillary

Lower eyelid, cheek, upper lip, upper teeth, nasal mucosa, maxillary sinus

V3 — Mandibular

Lower lip, lower teeth, chin, jaw, anterior two-thirds of tongue, muscles of mastication

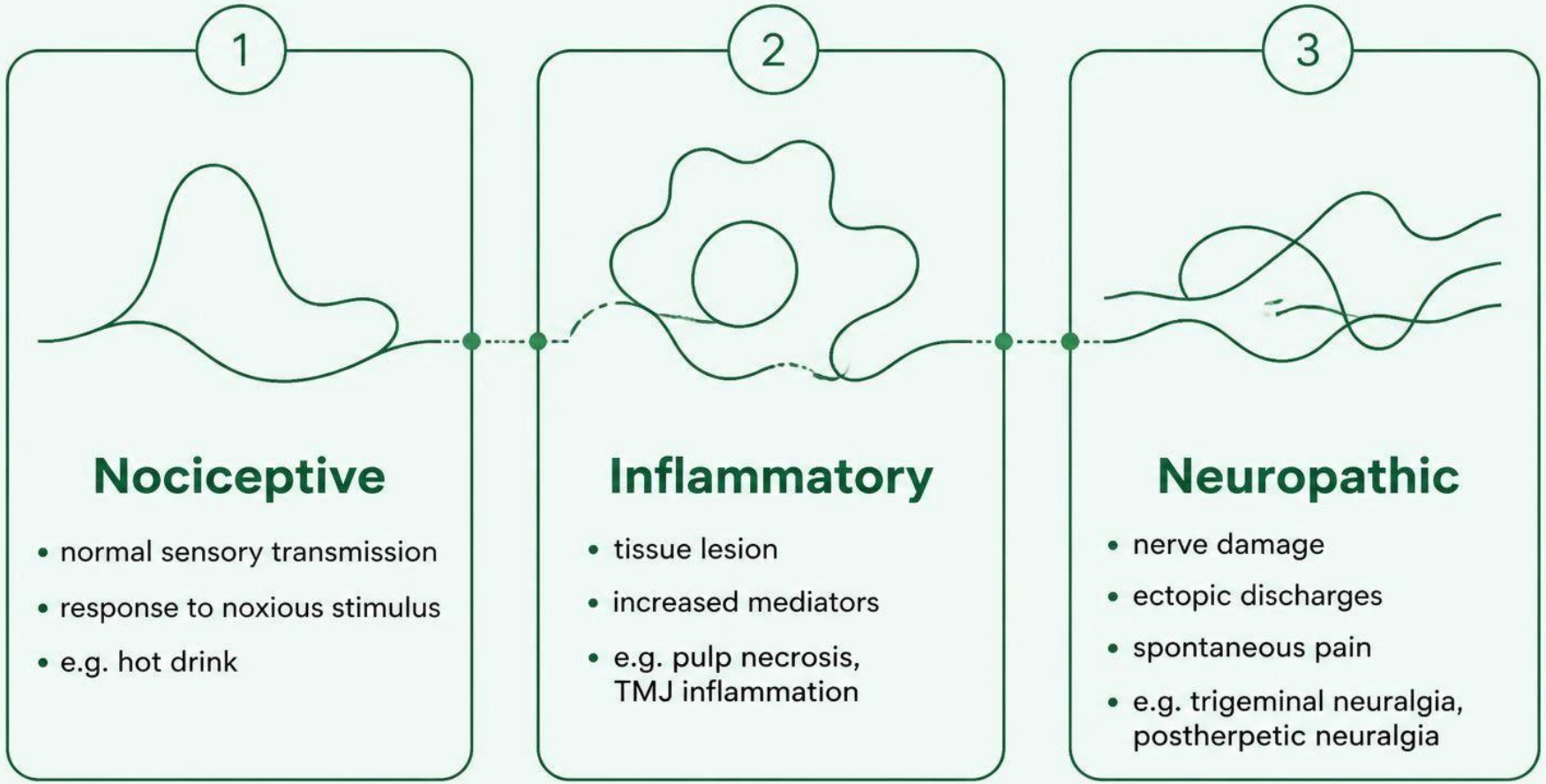
CHAPTER 3

Classification of Orofacial Pain: Acute vs. Chronic

Parameter	Acute Orofacial Pain	Chronic Orofacial Pain
Duration	Short-lived, resolves with healing	Sustained, persistent >3 months
Cause	Inflammation or acute tissue injury	Inflammation, nerve damage, central sensitization
Physiologic Response	Elevated BP, tachycardia via sympathetic response	Adaptation behaviors; depression, anxiety, psychological responses
Examples	Dental pulpitis, mucogingival pain	Trigeminal neuralgia, chronic pulpitis, temporomandibular disorder, postherpetic neuralgia, migraines

CHAPTER 3

Classification by Mechanism: Three Pain Types



Understanding the underlying mechanism is essential for selecting appropriate treatment strategies. Neuropathic pain, in particular, may persist even after the original injury has resolved, due to permanent changes in the somatosensory nervous system.

CHAPTER 3

Nociceptive vs. Inflammatory vs. Neuropathic Pain

Nociceptive Orofacial Pain

Mechanism: Noxious stimulation activates peripheral nociceptors; signal transmitted by normal components of the sensory trigeminal nerve.

Stimulation: Response to noxious stimulus only.
Example: Pain on drinking a very hot beverage.

Inflammatory Orofacial Pain

Mechanism: Strong noxious stimulus causes tissue lesions leading to local inflammatory responses and increased inflammatory mediators (prostaglandins, bradykinin, substance P).

Examples: Pulp necrosis, temporomandibular joint inflammation.

Neuropathic Orofacial Pain

Mechanism: Caused by nerve damage or injury — increased peripheral sensitization, altered sodium/calcium channel activity, ectopic discharges, and glial cell activation.

Stimulation: Response to both non-noxious and noxious stimulation; spontaneous pain may also occur in damaged nerves.

Example: Peripheral trigeminal nerve injury from facial trauma or trigeminal neuralgia.



CHAPTER 4

Pain in the Oral Cavity: Clinical Presentation

"Toothache" is pain typically localized around a tooth, multiple teeth, or the jaws. The severity can range from chronic and mild to sharp and excruciating — presenting as either a dull ache or intense, disabling pain.

Primary Dental Causes

- Dental caries (cavity)
- Cracked or fractured tooth
- Exposed tooth root
- Gum (periodontal) disease
- Failed dental implants

Non-Dental Causes

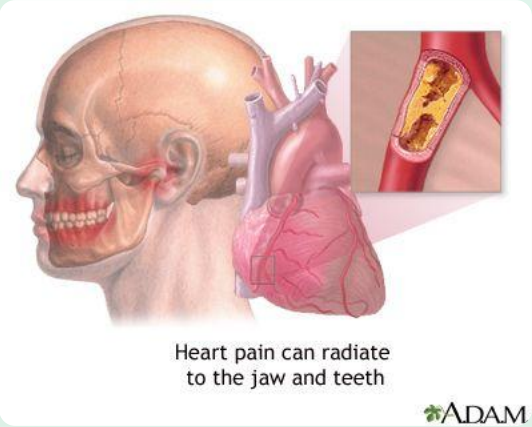
- Temporomandibular joint disease
- Masticatory muscle spasms
- Oral or jaw cancers
- Implant complications

Aggravating Factors

Pain may be worsened by chewing, temperature extremes (hot or cold), or sweet foods — all of which are important diagnostic clues during history-taking.

CHAPTER 4

Referred Pain to the Oral Cavity



Pain in the teeth and jaws does not always originate from local dental pathology. Clinicians must remain vigilant for systemic conditions that refer pain to the orofacial region.

Heart Disease

Angina pectoris and myocardial infarction — referred pain to the mandible and jaw (especially left-sided). Must be recognized as a potential life-threatening emergency.

Ear Infections

Inner and external otitis can refer pain to the temporomandibular region via the auriculotemporal nerve (branch of CN V3).

Sinusitis

Maxillary sinusitis produces pain and pressure that radiates to the upper teeth and jaw, mimicking dental pulpitis or periapical disease.

Neuralgias

Trigeminal neuralgia and other neuropathic conditions can produce severe orofacial pain with no identifiable dental source, requiring neurological workup.

CHAPTER 4

Diagnostic Patterns: Temperature Sensitivity

1

Sensitivity Without Recent Dental Work

Transient sharp pain to thermal stimuli — consider loose filling, caries, enamel fracture, or gingival recession exposing root surfaces and dentinal tubules.

2

Prolonged Sensitivity Without Recent Work

Lingering pain after thermal exposure suggests irreversible pulpitis from deep decay, fracture, advanced periodontal disease, or trauma — endodontic intervention likely required.

3

Post-Treatment Sensitivity

New sensitivity following dental procedures suggests reversible pulpitis — temporary pulp hypersensitivity that typically resolves within days to a few weeks without further treatment.

CHAPTER 4

Diagnostic Patterns: Biting Pain, Abscess & Referred Symptoms

Dull Ache After Treatment

Post-procedural biting sensitivity indicates transient periodontal ligament inflammation — typically self-limiting and resolves without additional intervention.

Sharp Pain When Biting

Acute biting pain points to structural compromise: loose filling, active decay, cracked tooth, cuspal fracture, or vertical root fracture. Warrants immediate clinical evaluation.

Abscess Formation

Constant, severe pain with swelling, purulent discharge, and sensitivity to touch indicates periapical or periodontal abscess — a dental emergency. Prompt drainage and antibiotics are required.

Upper Teeth Dull Ache

Pressure-like dull pain in upper posterior teeth may reflect maxillary sinusitis or bruxism rather than primary dental disease. Cross-referral to ENT or sleep medicine may be appropriate.

CHAPTER 4

Diagnostic Patterns: Neurological & Joint-Mediated Pain

Trigeminal Neuralgia

Touching a specific spot in or near the mouth triggers a sharp, jabbing pain lasting seconds. Talking, eating, or even a breeze may also trigger attacks. This is a hallmark presentation of trigeminal neuralgia, requiring neurological workup and specialized management.

Temporomandibular Dysfunction

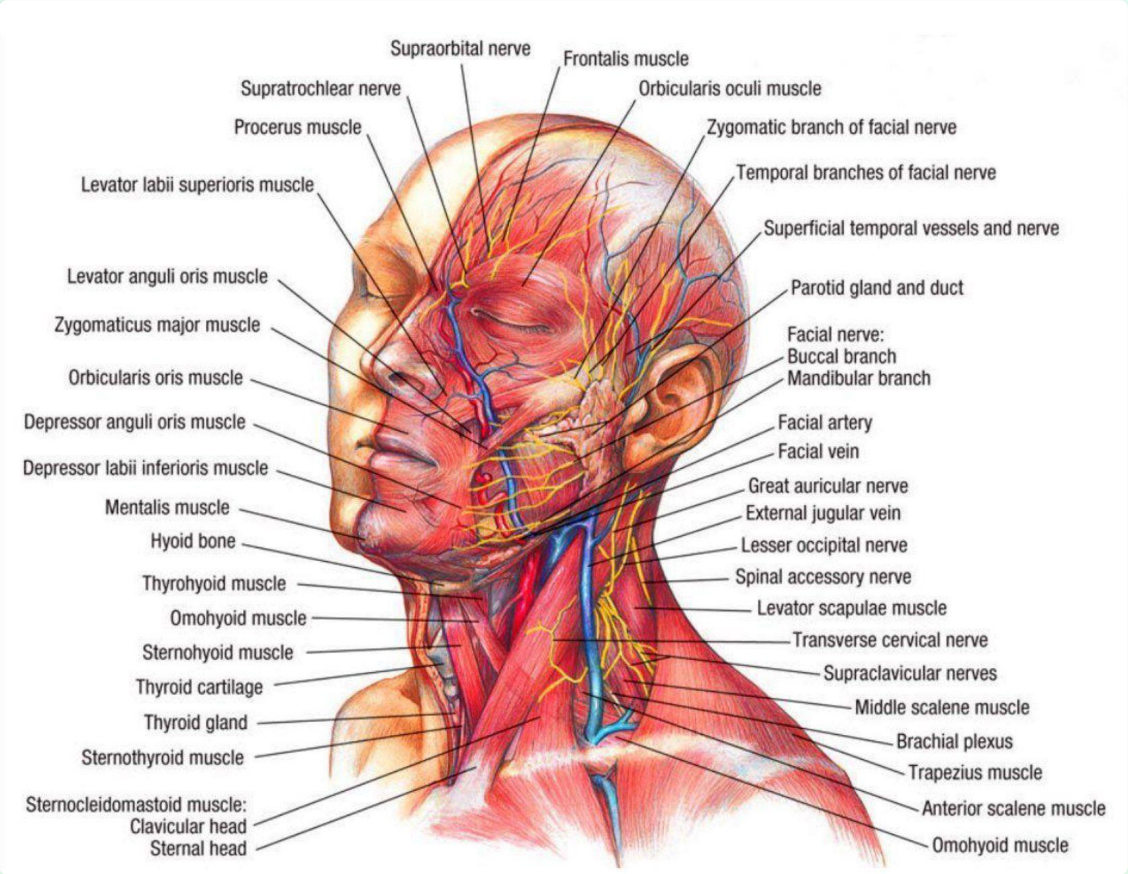
Clicking or popping sounds when opening or closing the mouth — often accompanied by pain during jaw movement — indicates temporomandibular joint (TMJ) dysfunction. Requires specialized musculoskeletal or orofacial pain evaluation.

Chronic Head, Neck, or Ear Pain

Persistent pain in the head, neck, or ear may originate from pulp-damaged teeth, but other dental or systemic medical etiologies must be systematically excluded before attributing pain to odontogenic sources.

CHAPTER 5

Pain in the Head and Neck Region



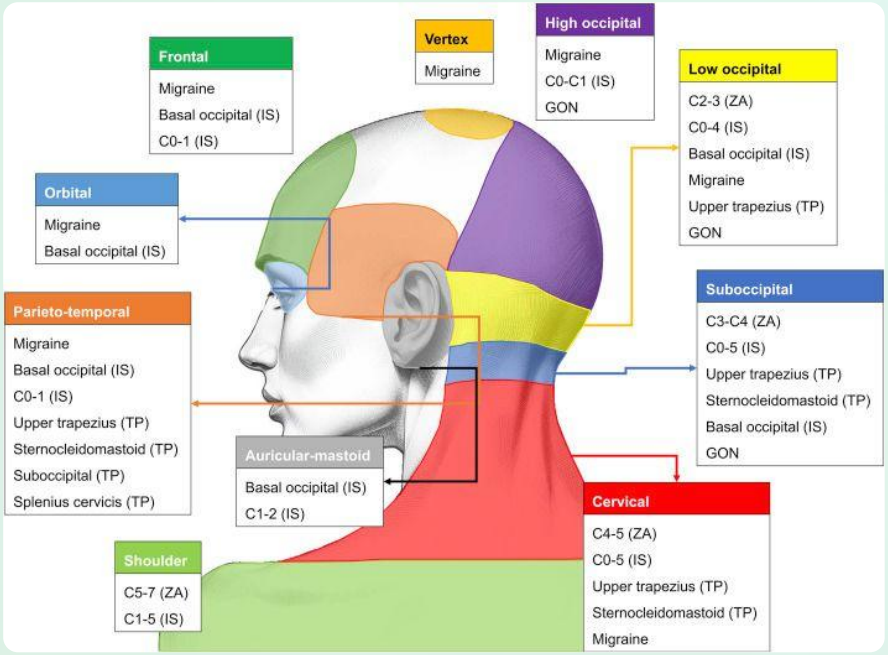
Head and neck pain is **multifactorial**, arising from a diverse range of anatomical structures. Accurate diagnosis requires distinguishing between odontogenic and non-odontogenic sources.

Muscles	Nerves	Vessels	Joints
Masticatory muscles, pericranial, cervical myofascial	Trigeminal, facial, occipital, cervical nerve roots	Carotid artery, vertebral artery, intracranial vasculature	TMJ, cervical zygapophyseal joints, atlanto-axial joint

Viscera
Cardiac, esophageal, thyroid, salivary glands

CHAPTER 5

Classification: Head and Neck Pain



Head Pain

Primary headaches: Migraine, Tension-type, Cluster

Secondary headaches: Vascular (hemorrhage, dissection), Infectious (meningitis, sinusitis), Traumatic, Neoplastic, or Metabolic causes — these arise from an identifiable underlying condition.

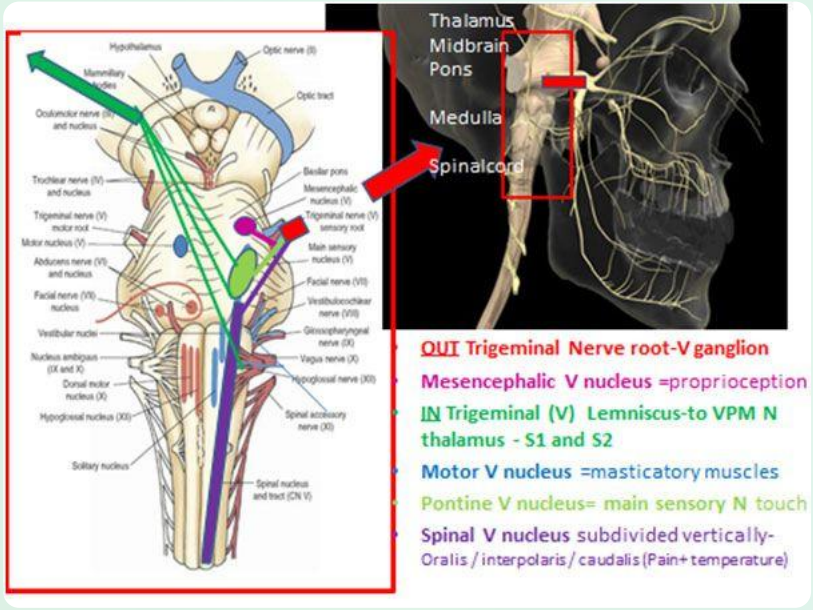
Neck Pain

Neck pain is classified by etiology:

- **Mechanical** — spondylosis, disc degeneration
- **Neurological** — radiculopathy, occipital neuralgia
- **Inflammatory** — rheumatoid arthritis, polymyalgia
- **Vascular** — vertebral artery dissection
- **Traumatic** — whiplash, fractures
- **Neoplastic** — primary or metastatic tumors
- **Referred** — from cardiac, esophageal sources

CHAPTER 5

Etiology: Primary Headache Syndromes



Migraine

Caused by activation of the **trigeminovascular system**, with release of CGRP (calcitonin gene-related peptide) causing neurogenic inflammation. Typically unilateral, pulsating, with photophobia and nausea.

Tension-Type Headache

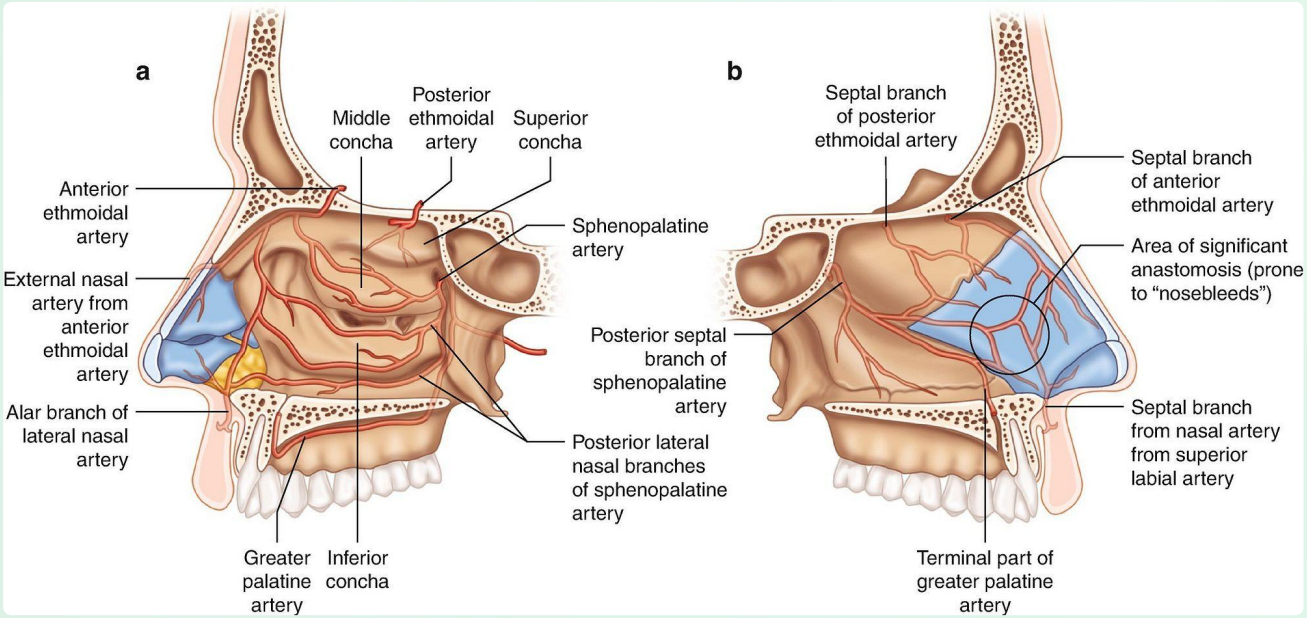
Associated with **pericranial muscle contraction**, myofascial trigger points, and psychosocial stress. Bilateral pressing/tightening pain, non-pulsating, without significant autonomic features.

Cluster Headache

Linked to **hypothalamic dysfunction** and trigeminal-autonomic activation. Severe unilateral orbital pain with ipsilateral autonomic features (lacrimation, rhinorrhea, ptosis). Occurs in episodic clusters.

CHAPTER 5

Etiology: Secondary Headache Syndromes



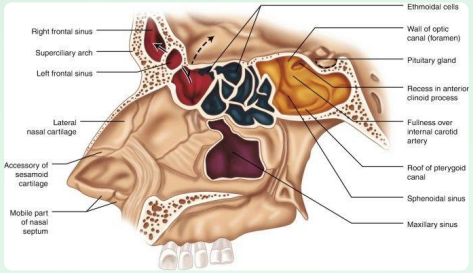
⚠ Secondary headaches always have an identifiable underlying etiology and require targeted medical management of the primary cause.

Vascular
Carotid dissection, intracranial hemorrhage, hypertension. Often presents as sudden severe "thunderclap" headache — requires urgent neuroimaging.

Infectious
Sinusitis, meningitis, encephalitis. Accompanied by fever, neck stiffness, or altered consciousness. Meningismus is a key clinical sign.

Structural
Intracranial tumors, raised intracranial pressure. Progressive headache that is worse in the morning or on Valsalva maneuver is a red flag.

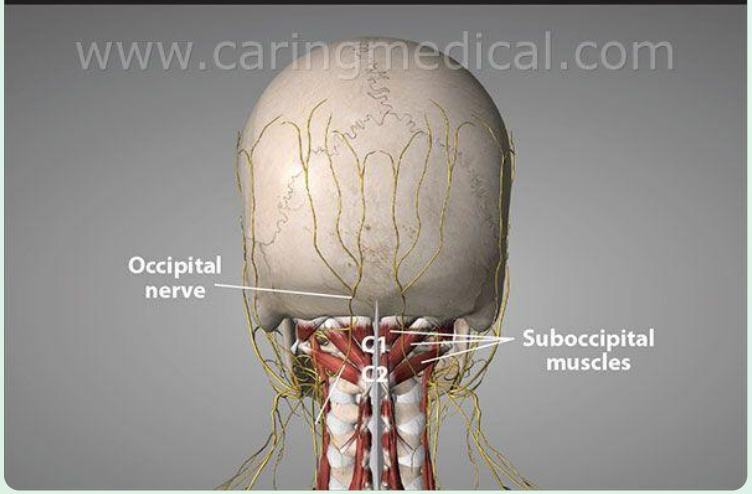
Drug/Toxin
Caffeine withdrawal, nitroglycerin-induced headache, carbon monoxide exposure. A thorough medication history is essential.



CHAPTER 5

Etiology: Posterior Neck Pain

Anatomical relation of suboccipital muscles to atlas (C1) and axis (C2) and occipital nerve. Upper (C1-C2) cervical instability can cause the suboccipital muscles to contract causing migraine headaches or occipital neuralgia.



Mechanical

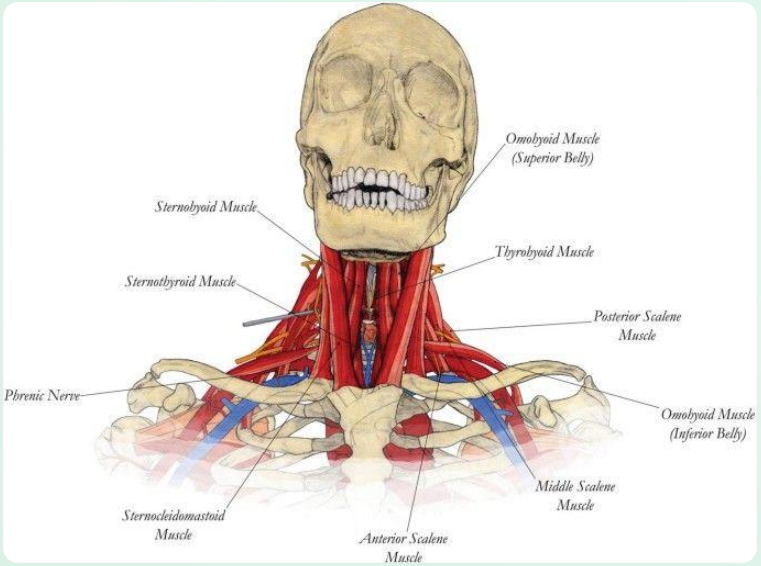
Cervical spondylosis, disc degeneration, and myofascial pain are the most common causes. Pain is typically dull and worsens with movement. Postural factors play a significant role.

Neurological: Occipital Neuralgia

Cervical radiculopathy and occipital neuralgia can produce pain that radiates from the posterior neck to the occiput and even to the face. Upper cervical spine instability at C1–C2 may cause pressure at the base of the skull, leading to contraction and spasm of the suboccipital muscles — resulting in headaches, migraines, and occipital neuralgia. The relationship between suboccipital muscles and C1–C2 vertebrae is of key anatomical importance.

CHAPTER 5

Etiology: Inflammatory, Vascular & Traumatic Neck Pain



Inflammatory

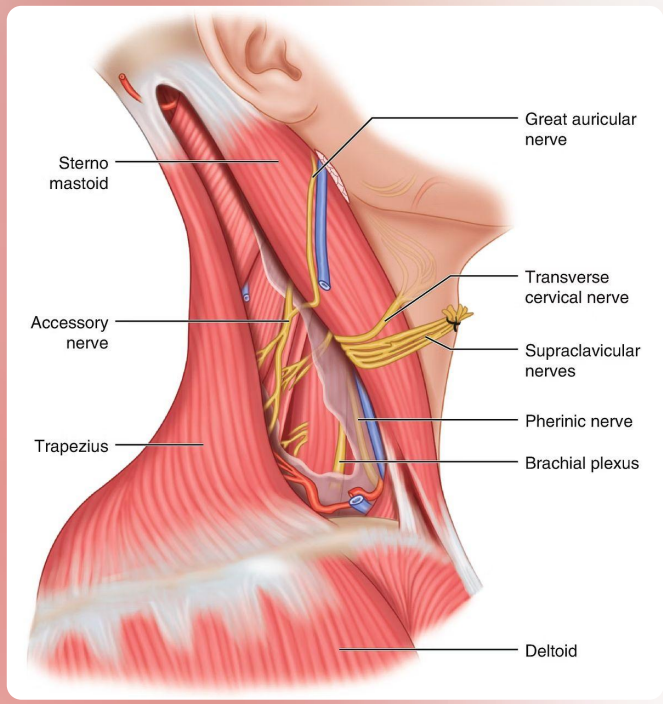
Rheumatoid arthritis affects the atlanto-axial joint, risking subluxation. **Polymyalgia rheumatica** causes bilateral shoulder and neck stiffness with elevated inflammatory markers.

Vascular

Vertebral artery dissection presents with sudden posterior neck pain and neurological symptoms. **Subarachnoid hemorrhage** causes a classic "thunderclap" occipital headache — a neurological emergency.

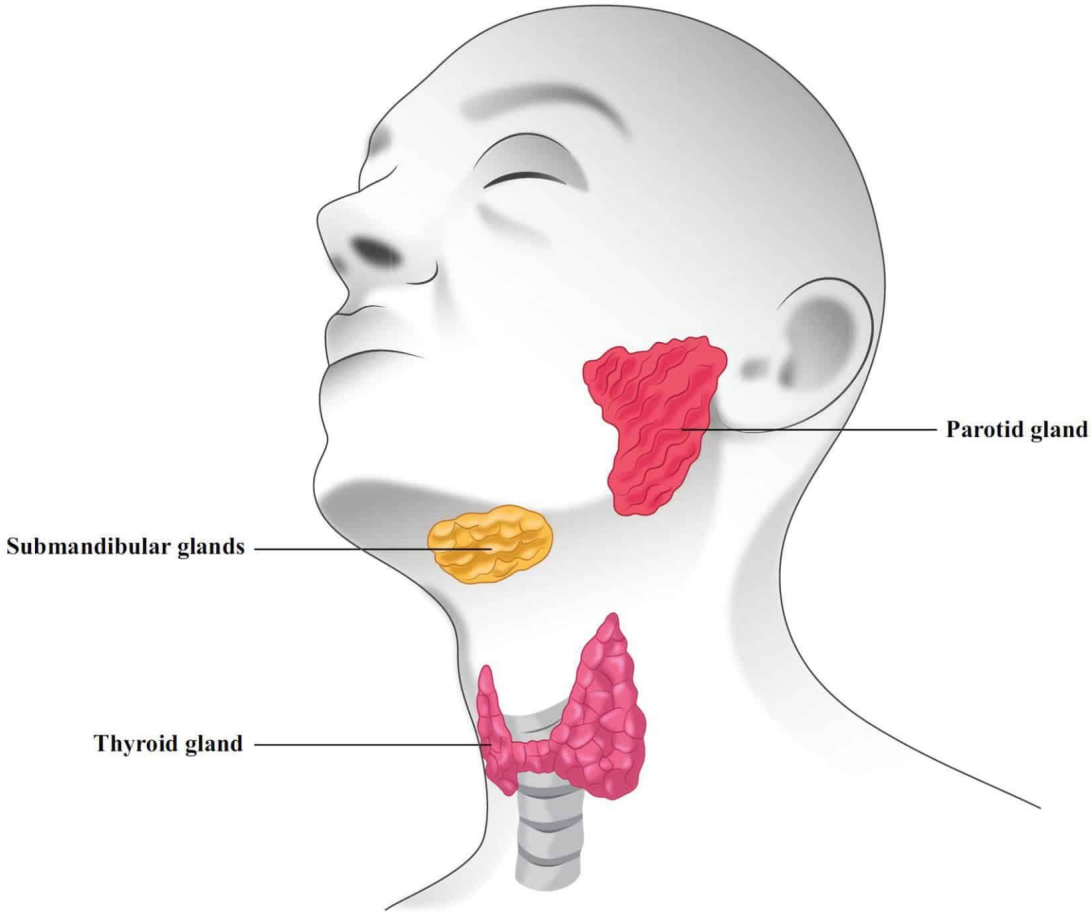
Traumatic

Whiplash injuries produce posterior neck pain and stiffness following hyperflexion-hyperextension. **Vertebral fractures** and muscle strains may also occur, particularly in contact sports or traffic accidents.



CHAPTER 5

Etiology: Anterior Neck Pain



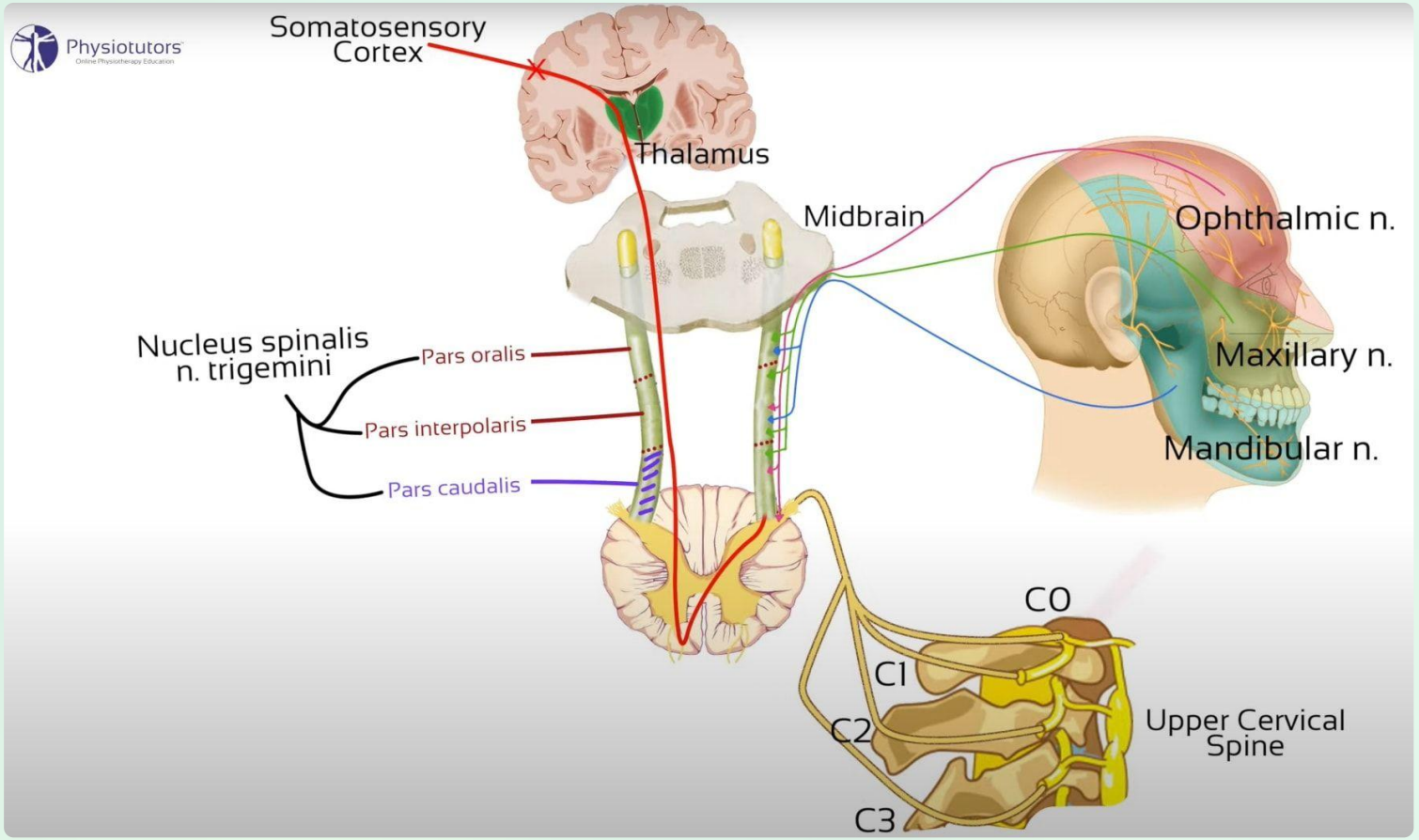
Infectious
Pharyngitis, sialadenitis, and deep neck space infections (e.g., Ludwig's angina — a rapidly spreading cellulitis of the floor of the mouth that is a dental emergency requiring airway management and IV antibiotics).

Neoplastic
Thyroid and salivary gland tumors present as a neck mass, often painless initially but progressive. Cervical lymphadenopathy from oral or pharyngeal malignancy must be excluded.

Referred
Anterior neck pain may be referred from cardiac sources (myocardial ischemia) or esophageal pathology (esophagitis, spasm). A thorough systemic review is essential when dental causes are absent.

CHAPTER 5

Referred Head and Neck Pain: Mechanism



Mechanism of Referred Pain

Convergence of visceral and somatic afferents onto shared second-order neurons in the dorsal horn explains why pain is perceived at a site distant from its true origin.

Common sources: Cardiac, sinus, TMJ, gastrointestinal, cervical spine.

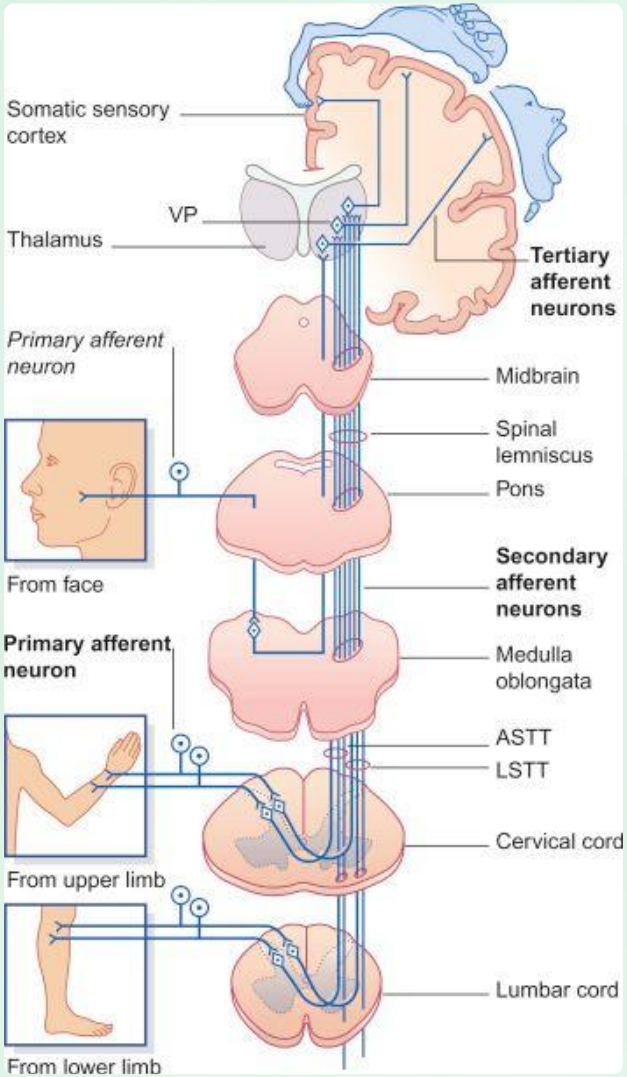
Classic example: Myocardial ischemia → jaw or neck pain

The Projection Error

When afferent nociceptive signals from the neck travel to the second-order neuron at the C1/C2 dorsal horn and reach the somatosensory cortex, the brain must determine their origin. Because the face has far denser nociceptive innervation than the upper cervical region, the cortex makes a **projection error** — attributing the stimulus to the fronto-orbital area of the face rather than the actual cervical source. This is the pathophysiological basis of **cervicogenic facial pain**.

CHAPTER 5

Pathogenesis of Orofacial Pain



Peripheral Mechanisms

Tissue injury activates peripheral nociceptors, triggering release of inflammatory mediators — prostaglandins, bradykinin, substance P, histamine — causing peripheral sensitization and lowered pain threshold.

Central Sensitization

Persistent nociceptive input leads to hyperexcitability within the trigeminal nucleus caudalis, amplifying pain perception — a key mechanism in chronic orofacial pain.

Convergence Theory

Shared afferent inputs of CN V (trigeminal) and upper cervical nerves (C1–C3) at the same second-order neurons explain why pain from one structure is perceived in the territory of another — the anatomical basis for referred pain in the orofacial region.

CHAPTER 5

Headache Subtypes: Clinical Overview

Type	Characteristics	Associated Features
Migraine	Pulsatile, unilateral	Nausea, photophobia, aura
Tension	Bilateral, dull	Mild photophobia
Cluster	Severe, orbital	Lacrimation, nasal congestion
Cervicogenic	Occipital, neck-origin	Triggered by movement

Migraine

Neurogenic inflammation mediated by CGRP release from trigeminovascular fibers. Unilateral pulsating pain with nausea, photophobia, and phonophobia. May be preceded by aura.

Tension-Type

Myofascial trigger points and pericranial muscle tension — often exacerbated by stress and poor posture. Bilateral non-pulsating pressure, without autonomic features.

Cluster

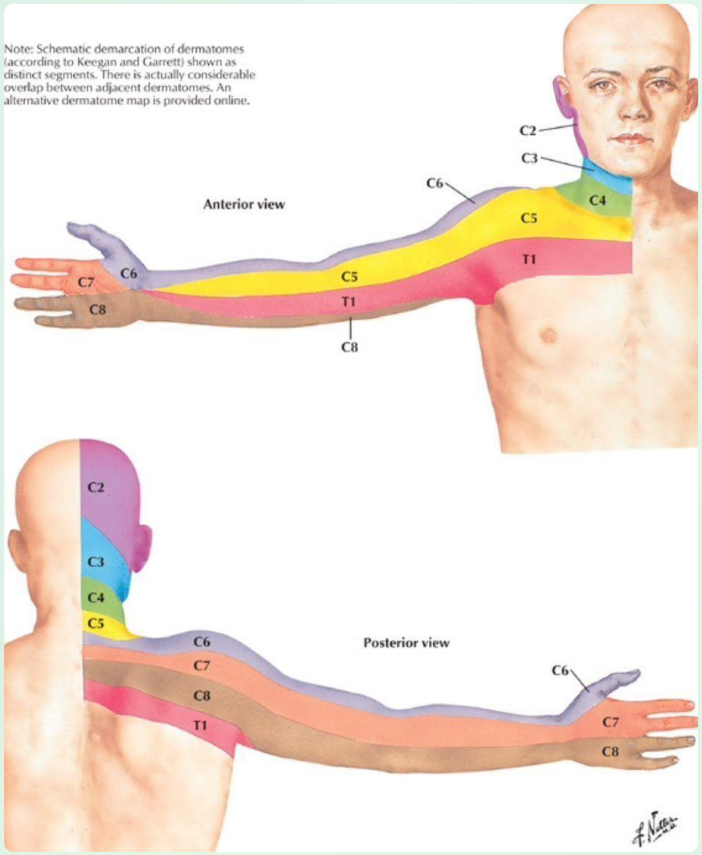
Hypothalamic activation with trigeminal-autonomic outflow. Strictly unilateral severe orbital pain with ipsilateral rhinorrhea, lacrimation, and Horner syndrome.

Cervicogenic

Secondary to cervical joint or myofascial dysfunction. Pain referred from upper cervical structures to the fronto-orbital region — often unilateral and precipitated by neck movements.

CHAPTER 5

Symptomatology: Neck Pain by Etiology

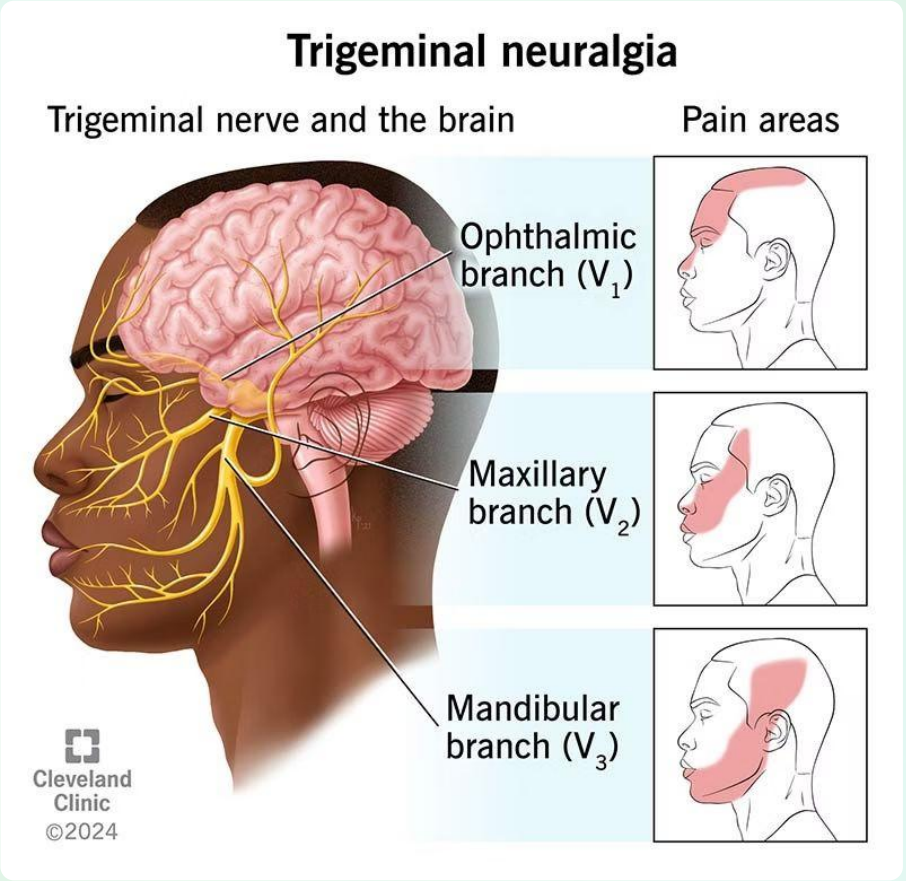


Type	Clinical Characteristics	Key Diagnostic Clues
Mechanical	Dull ache, worsens with movement	Postural history, occupational factors
Radiculopathy	Sharp, radiating pain to arm or jaw	Dermatomal distribution, motor/sensory deficit
Inflammatory	Morning stiffness, systemic symptoms	Elevated ESR, CRP; bilateral presentation
Vascular	Sudden, severe, neurologic deficits	Urgent neuroimaging; stroke workup
Neoplastic	Progressive, constant, nocturnal pain	Unexplained weight loss, lymphadenopathy

CHAPTER 6

Trigeminal Neuralgia: Overview



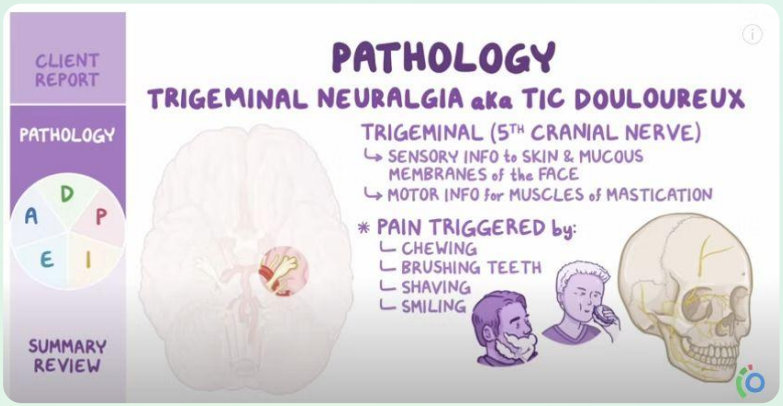


Trigeminal neuralgia (TN) is considered one of the most painful conditions known in medicine. It is characterized by recurrent, unilateral, brief electric shock-like pain in the distribution of the trigeminal nerve. Recognition of its clinical features is essential for dental professionals, as patients frequently present to dental clinics before receiving a correct diagnosis.

CHAPTER 6

Trigeminal Neuralgia: Pathophysiology & Causes





Trigeminal neuralgia is a long-term neuropathic pain disorder affecting the trigeminal nerve — responsible for conveying pain, touch, and temperature from the face. It is classified as a **neuropathic pain** condition caused by a lesion or disease of the somatosensory nervous system.

Two Clinical Types

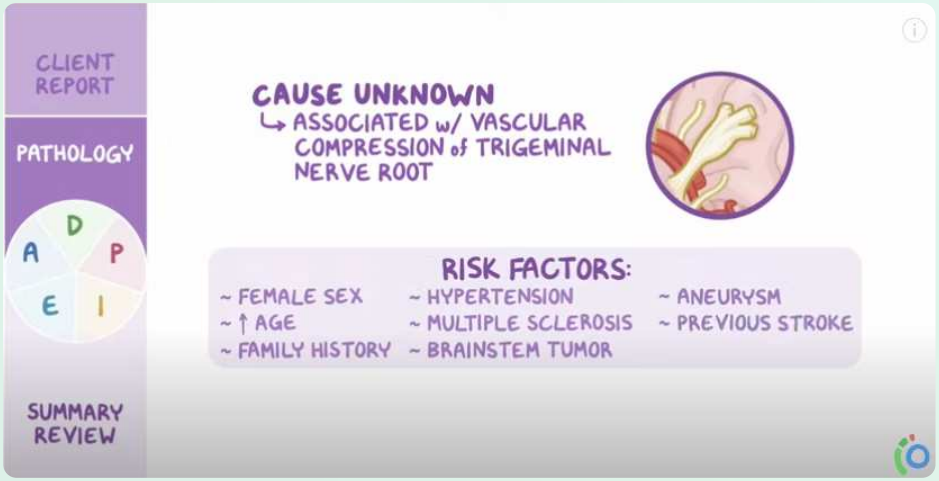
- **Typical (Classic/Paroxysmal):** Episodic attacks separated by pain-free intervals
- **Atypical:** Continuous background pain with less severe attacks

Primary Cause

Compression of the trigeminal nerve root by a tortuous or enlarged blood vessel (most commonly the superior cerebellar artery) causes focal demyelination. This results in erratic and hyperactive nerve firing — triggering severe pain attacks with the slightest stimulation of innervated facial regions.

CHAPTER 6

Trigeminal Neuralgia: Secondary & Idiopathic Causes

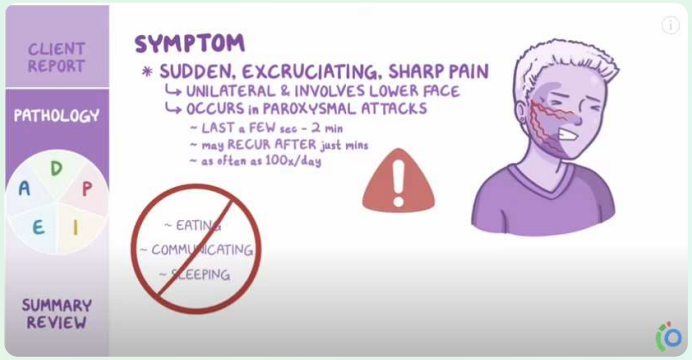


Secondary Causes (Identifiable Lesions)

- Intracranial aneurysm
- Arteriovenous malformation (AVM)
- Intracranial tumor (e.g., meningioma)
- Arachnoid cyst
- Multiple sclerosis (3–4% of MS patients develop TN)
- Trauma to the spinal trigeminal complex
- Postherpetic neuralgia (post-VZV reactivation)

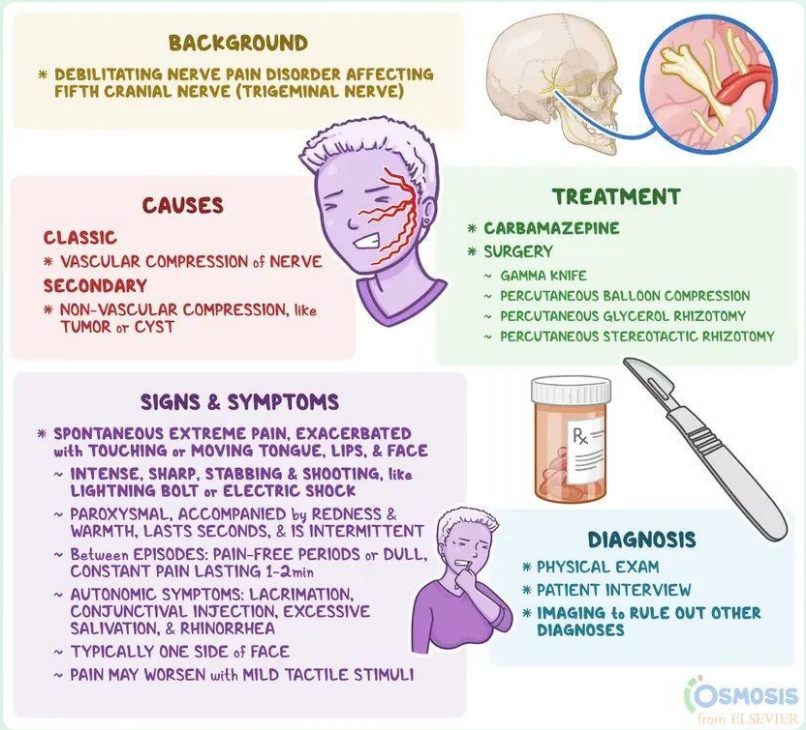
Idiopathic

When no structural cause can be identified on clinical examination or neuroimaging, the condition is classified as idiopathic trigeminal neuralgia. The diagnosis of exclusion requires thorough MRI evaluation to rule out secondary causes before this classification is applied.



CHAPTER 6

Trigeminal Neuralgia: Symptoms & Triggers



Symptom Profile

- Sudden paroxysmal attacks lasting seconds to several minutes
- 4–10 or more attacks daily during active phases
- Described as stabbing, electric shock-like, burning, crushing, or shooting
- Strictly **unilateral** in distribution
- Can migrate between branches of CN V
- Pain-free intervals between attacks (classic type)

Common Triggers

- Light touch to trigger zones (cheek, lip, gum)
- Chewing, eating, swallowing
- Talking, smiling
- Shaving or applying makeup
- Blowing wind or cold air
- Spontaneous (without identifiable stimulus)

Atypical TN

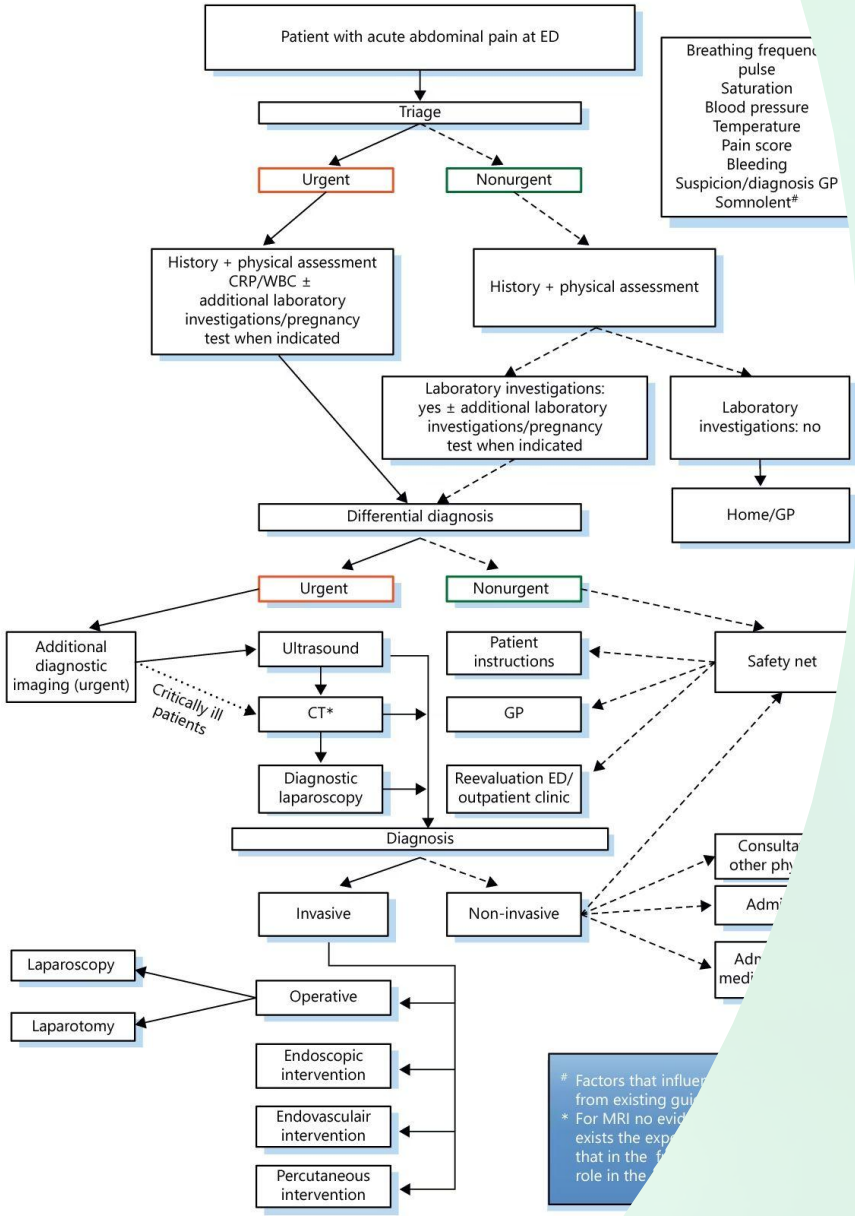
Continuous background pain, less severe than classic attacks but present >50% of the time. Described as burning or prickling. More difficult to treat.

CHAPTER 6

Trigeminal Neuralgia: Differential Diagnosis from Dental Pain

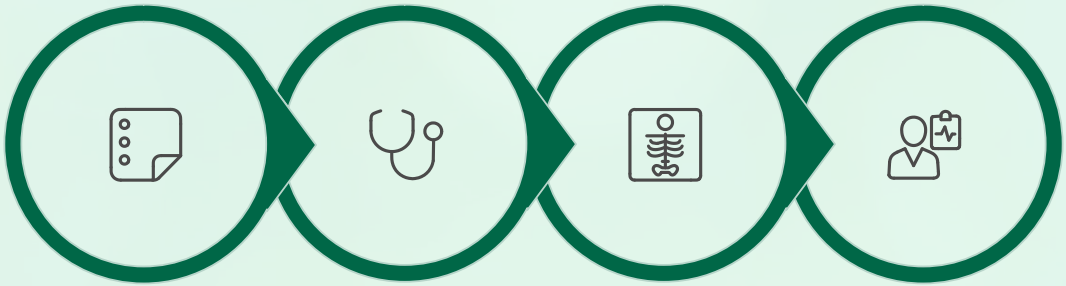
Trigeminal neuralgia is frequently misdiagnosed as dental pain, leading to unnecessary extractions or root canal treatments. Dental students must recognize its distinguishing features.

Feature	Trigeminal Neuralgia	Dental (Pulpal) Pain
Duration	Seconds to minutes; episodic	Continuous or prolonged
Quality	Electric shock, stabbing	Throbbing, aching, dull
Trigger	Touch, talking, wind	Temperature, chewing, sweets
Dental Findings	None on examination	Caries, fracture, perio lesion
Response to Dental Tx	No improvement	Resolves with treatment



REVIEW

Diagnostic Approach: Key Clinical Framework



History **Exam** **Imaging** **Differential**

A systematic diagnostic approach is essential when evaluating orofacial pain. The clinician must consider dental, musculoskeletal, neurological, vascular, and systemic etiologies before arriving at a diagnosis and treatment plan.

SUMMARY

Key Takeaways

Pain is Multidimensional

Both a sensory and emotional experience — orofacial pain encompasses nociceptive, inflammatory, and neuropathic mechanisms with distinct pathophysiological bases.

Referred Pain is Real

Cardiac, sinus, otologic, and cervical pathology can all present as apparent dental pain. Never treat without excluding systemic sources.

Know the Trigeminal System

The trigeminal nerve is central to all orofacial pain. Understanding its three divisions, pathways, and neuroplasticity is foundational to diagnosis and treatment.

Classify Before You Treat

Distinguish acute from chronic, nociceptive from neuropathic, and odontogenic from non-odontogenic pain — each category demands a different therapeutic approach.

Accurate diagnosis of orofacial pain requires a thorough history, clinical examination, appropriate imaging, and willingness to refer when systemic or neurological causes are suspected.

Local Anesthesia in Dentistry

Mechanism and Clinical Perspective — A guide for stomatology students in pathophysiology



The Objective of Local Anesthesia

1 Interrupt at the Source

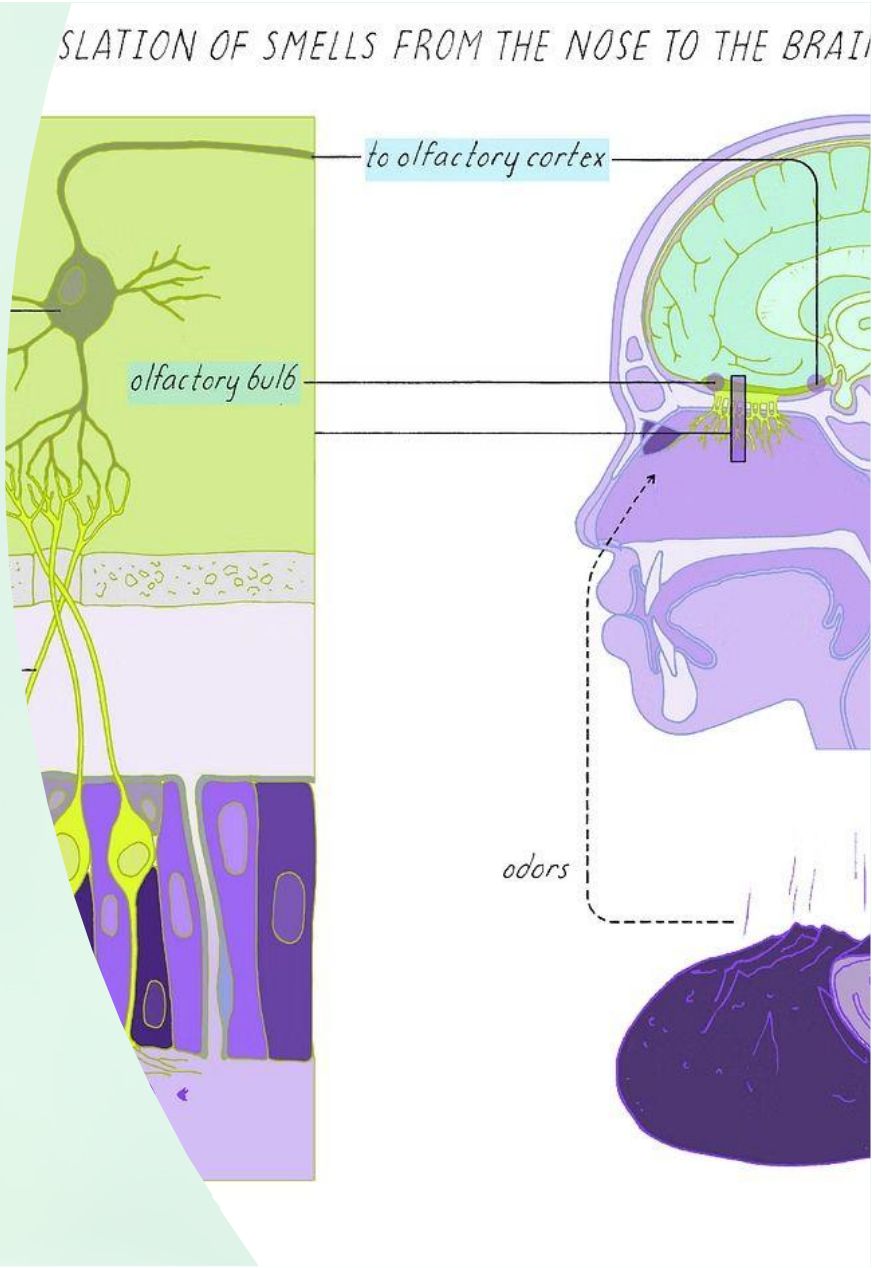
Block the pain pathway before nociceptive signals can travel centrally — stopping transmission at the peripheral nerve level.

2 Prevent Electrical Propagation

Halt the action potential before it reaches the brain, eliminating conscious perception of pain entirely.

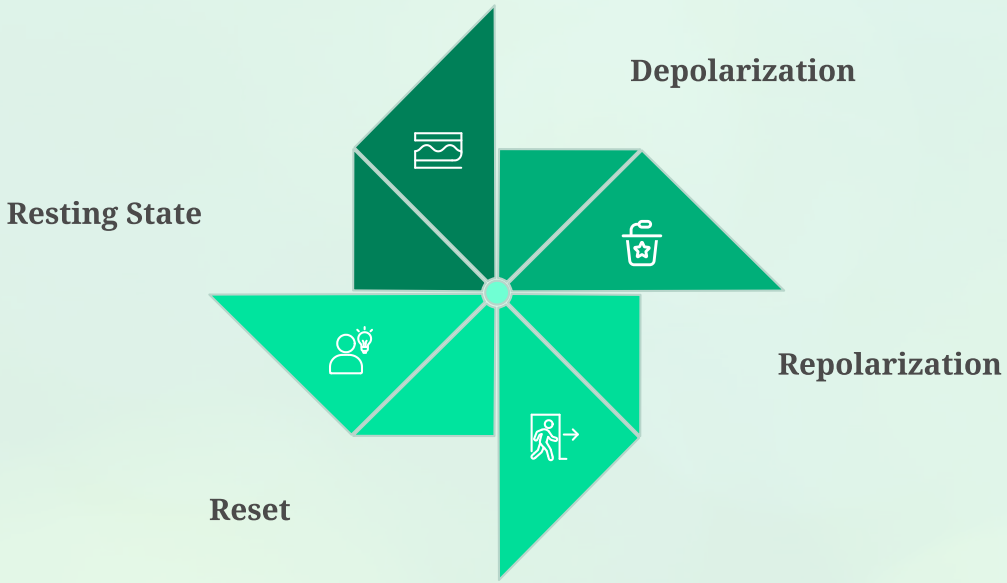
3 Localized, Not Systemic

Achieve complete operative comfort without disrupting consciousness, reflexes, or systemic homeostasis.



CHAPTER 1

The Anatomy of a Nerve Impulse



Resting State

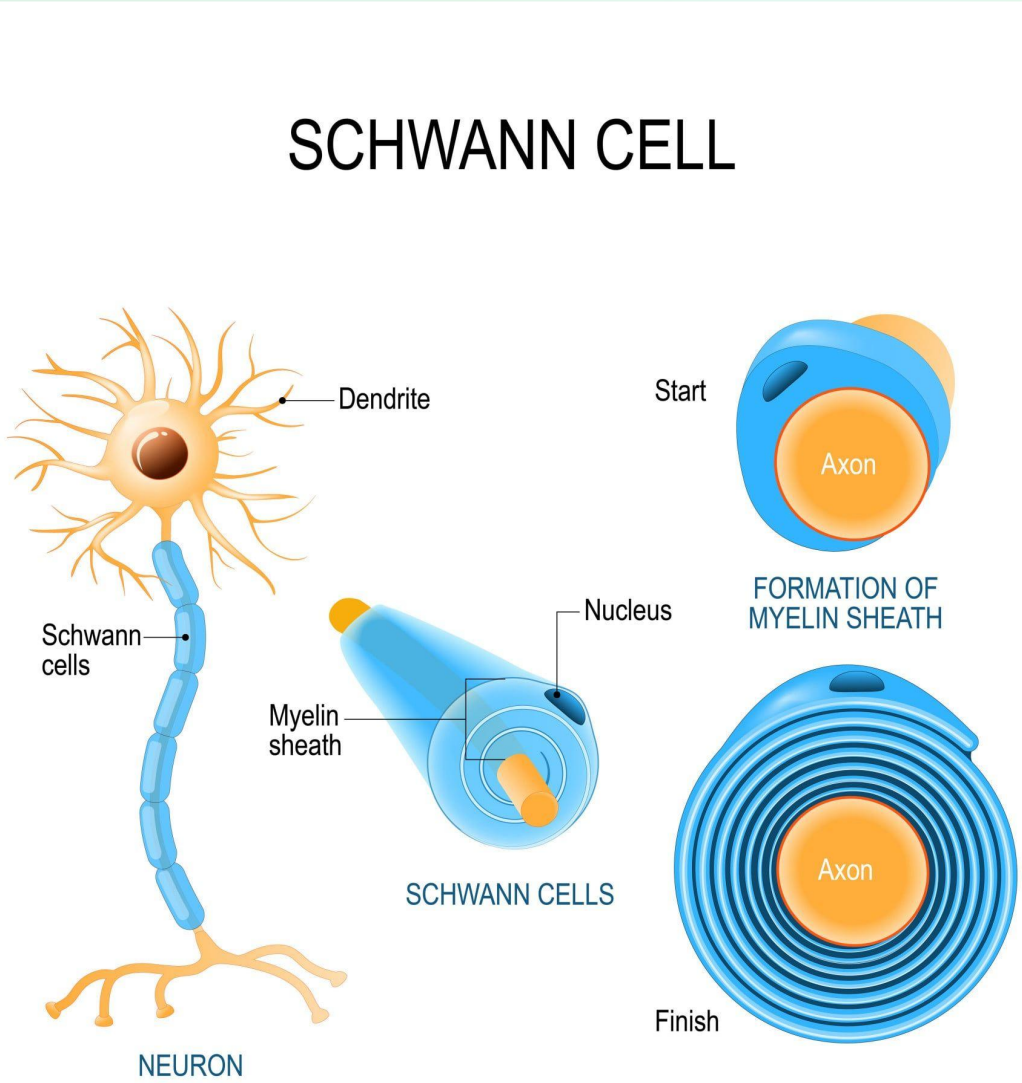
The nerve membrane is **polarized**: sodium ions (Na^+) concentrate outside, potassium ions (K^+) remain inside. The membrane is impermeable to Na^+ at rest.

Action Potential

A stimulus opens voltage-gated Na^+ channels → rapid influx creates the electrical signal. K^+ then exits to restore the resting negative potential — the cycle resets.

CHAPTER 1

Myelin & Nodes of Ranvier

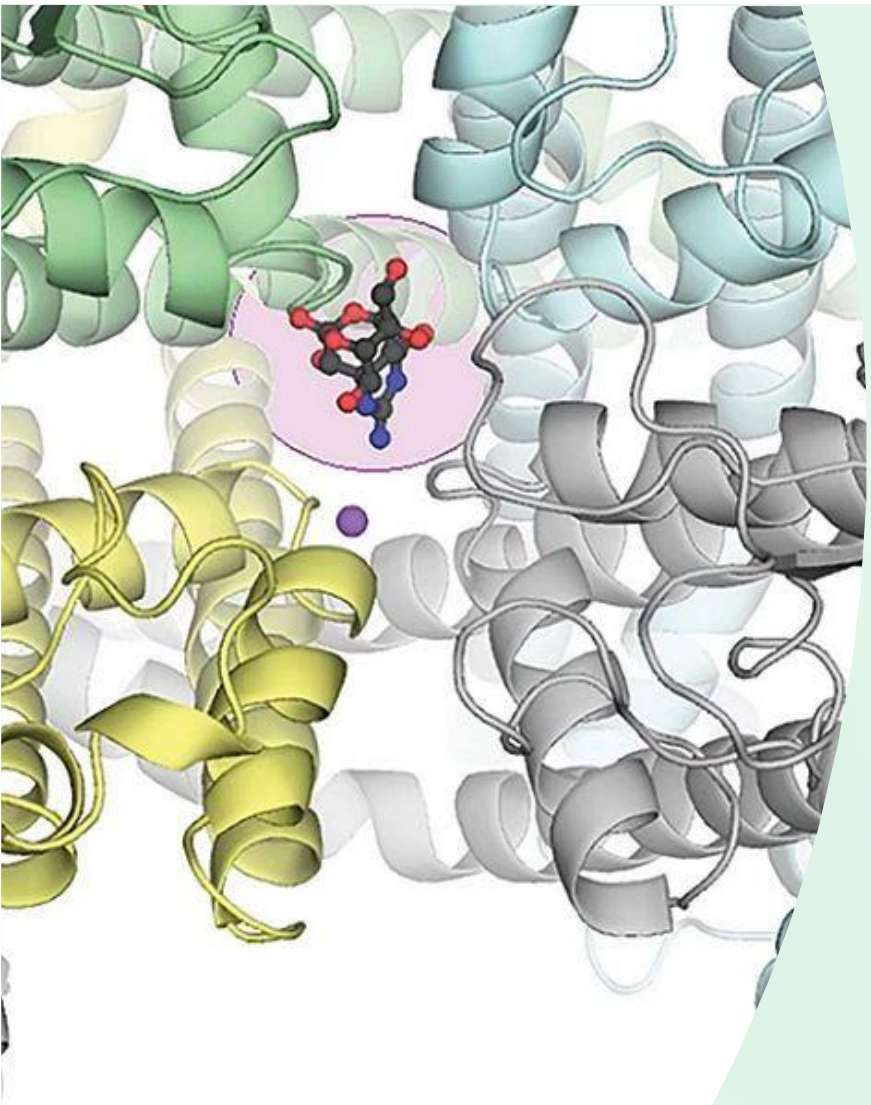


Myelin as Insulator

The myelin sheath wraps the axon, forcing the action potential to **jump** between gaps rather than travel continuously — enabling rapid saltatory conduction.

The 3-Node Rule

Voltage-gated sodium channels cluster at the **Nodes of Ranvier**. For conduction block, the anesthetic must saturate at least **three adjacent nodes** (~10 mm of nerve length). Blocking fewer nodes allows the impulse to skip over the blocked region.



CHAPTER 2

The Molecular Mechanism of Action

Specific Receptor Theory

The accepted gold standard — anesthetic molecules bind to a **specific receptor site** on the inner face of the Na^+ channel protein.

Physical Channel Block

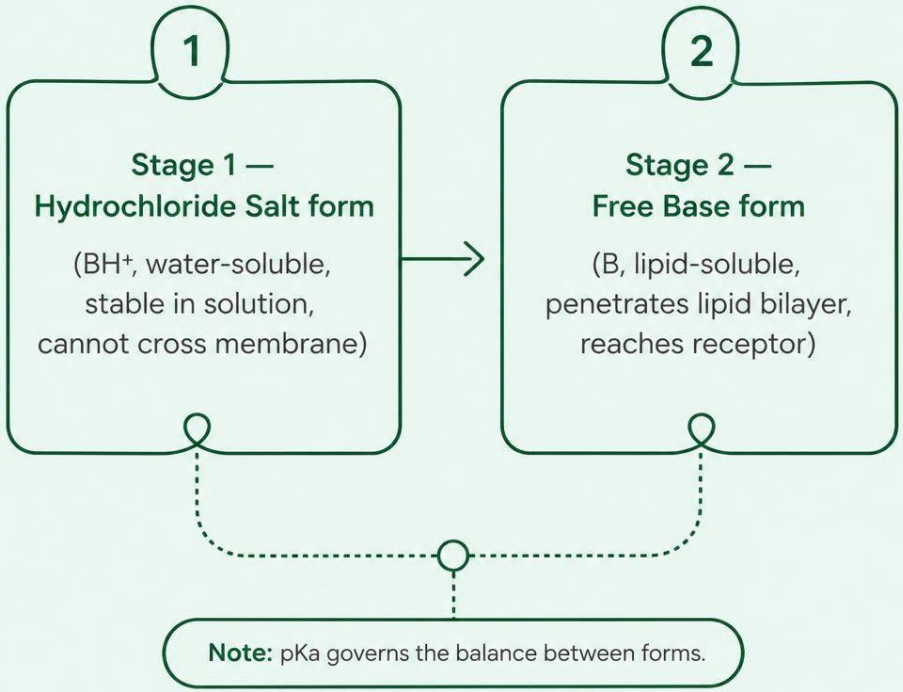
Bound anesthetic **physically occludes** the channel pore, preventing sodium influx regardless of membrane stimulation.

Use-Dependent Block

Channels in an **open or inactivated state** bind anesthetic more readily — repeated stimulation deepens the block progressively.

CHAPTER 2

From Water-Soluble to Lipid-Soluble



Dual Chemical Identity

Local anesthetics exist as **hydrochloride salts** in the cartridge — stable and water-soluble for storage. After injection into tissue, they must convert to their **free base (lipid-soluble)** form to cross the nerve membrane.

The pKa Factor

The **pKa** determines what fraction converts at physiological pH 7.4. A lower pKa (closer to 7.4) means more free base available → **faster onset**. Lidocaine (pKa 7.9) acts faster than bupivacaine (pKa 8.1) for this reason.

CHAPTER 2

The pH Challenge: Why Infection Changes Everything

Acidic Environment

Infected tissue has a pH of approximately **5.2** — significantly below the physiological 7.4. This acidic shift forces virtually all anesthetic molecules into their **ionized, water-soluble (BH^+)** form.

Clinical Consequence

With almost no free base available, the drug **cannot penetrate** the lipid nerve membrane. The result is **incomplete or failed anesthesia** — a frequent frustration when treating acute dentoalveolar abscesses.

⚠ Never attempt to compensate simply by injecting more volume into infected tissue — the pH remains hostile. Consider nerve blocks proximal to the inflamed zone.

Healthy Tissue

pH ~7.4 → equilibrium favors free base → membrane penetration → effective block

Infected Tissue

pH ~5.2 → equilibrium heavily favors ionized form → membrane barrier intact → anesthesia failure

CHAPTER 2

Potency and Duration

Lipid Solubility → Potency

Higher lipid solubility allows deeper membrane penetration and stronger channel binding. **Bupivacaine** is 4× more lipid-soluble than lidocaine — and 4× more potent.

Protein Binding → Duration

Anesthetics bind to protein components of the Na^+ channel. Higher affinity = slower dissociation = **longer blockade**. Bupivacaine (95% protein-bound) outlasts lidocaine (65% bound) significantly.

Diffusion → Termination

The block ends as molecules diffuse away from the injection site, are absorbed into local vasculature, and undergo hepatic metabolism. **Vasoconstrictors slow this diffusion.**



CHAPTER 3

Vasoconstrictors: Essential Partners

The Vasodilation Problem

All local anesthetics cause **vasodilation** at the injection site. This accelerates vascular absorption, shortening duration and reducing effective concentration at the nerve.

The Vasoconstrictor Solution

Epinephrine (1:100,000 or 1:200,000) counteracts this by constricting local vessels — keeping the drug concentrated at the target nerve for longer, reducing systemic absorption and total dose needed.

CHAPTER 3

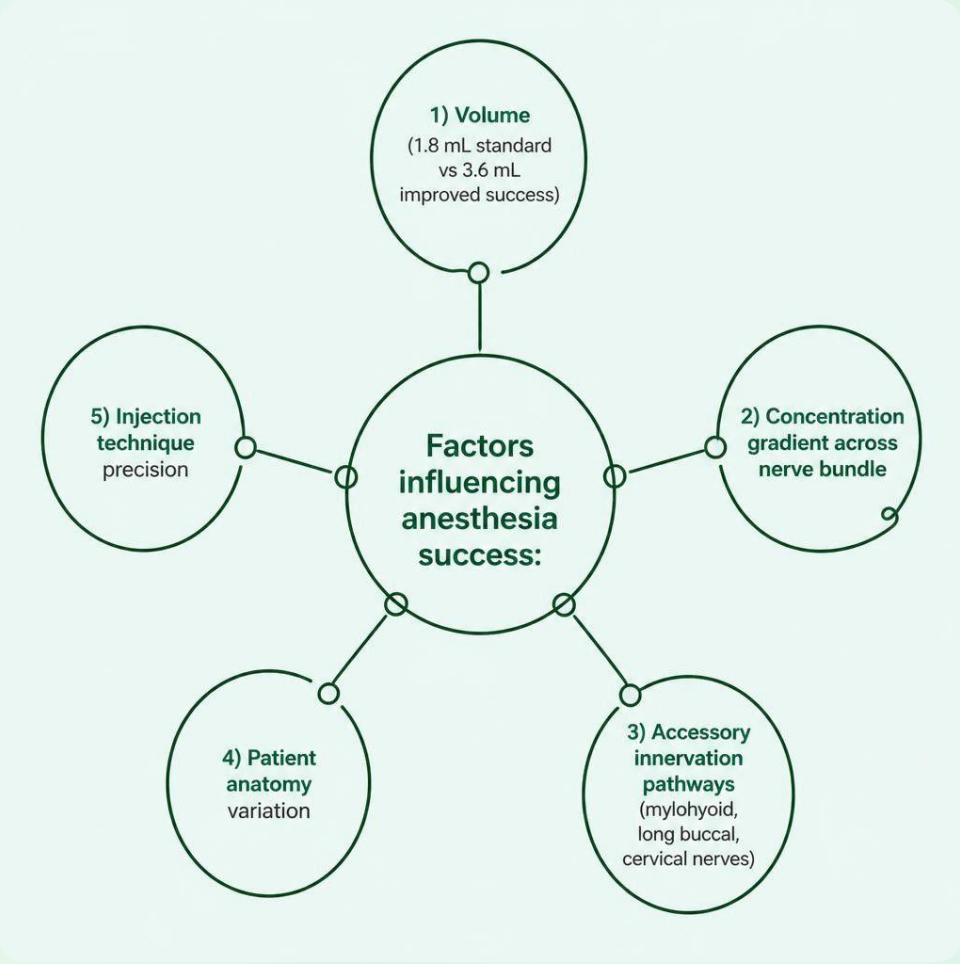
Managing Individual Variation

Volume Matters

Success depends on achieving a sufficient **concentration gradient** across the nerve bundle. Clinical evidence demonstrates that **3.6 mL** significantly improves success rates in mandibular molar anesthesia compared to the standard 1.8 mL — particularly for the inferior alveolar nerve block.

Accessory Innervation

Mylohyoid, long buccal, or cervical nerve branches may provide **cross-innervation** to mandibular molars. Apparent "failure" may reflect anatomy, not technique — supplemental infiltration is often the solution.





CHAPTER 3

Pros for the Practitioner

Precise Operative Control

A bloodless, pain-free, immobile field allows meticulous technique — critical for restorations, extractions, and surgical procedures.

Patient Cooperation

A comfortable patient is a still patient. Reduced anxiety means fewer interruptions, better procedural outcomes, and shorter chair time.

Expanded Clinical Capability

Enables complex, time-sensitive procedures that would be impossible without reliable pain suppression — from apicoectomies to full-arch extractions.

CHAPTER 3

Pros and Cons for the Patient

✅ Benefits

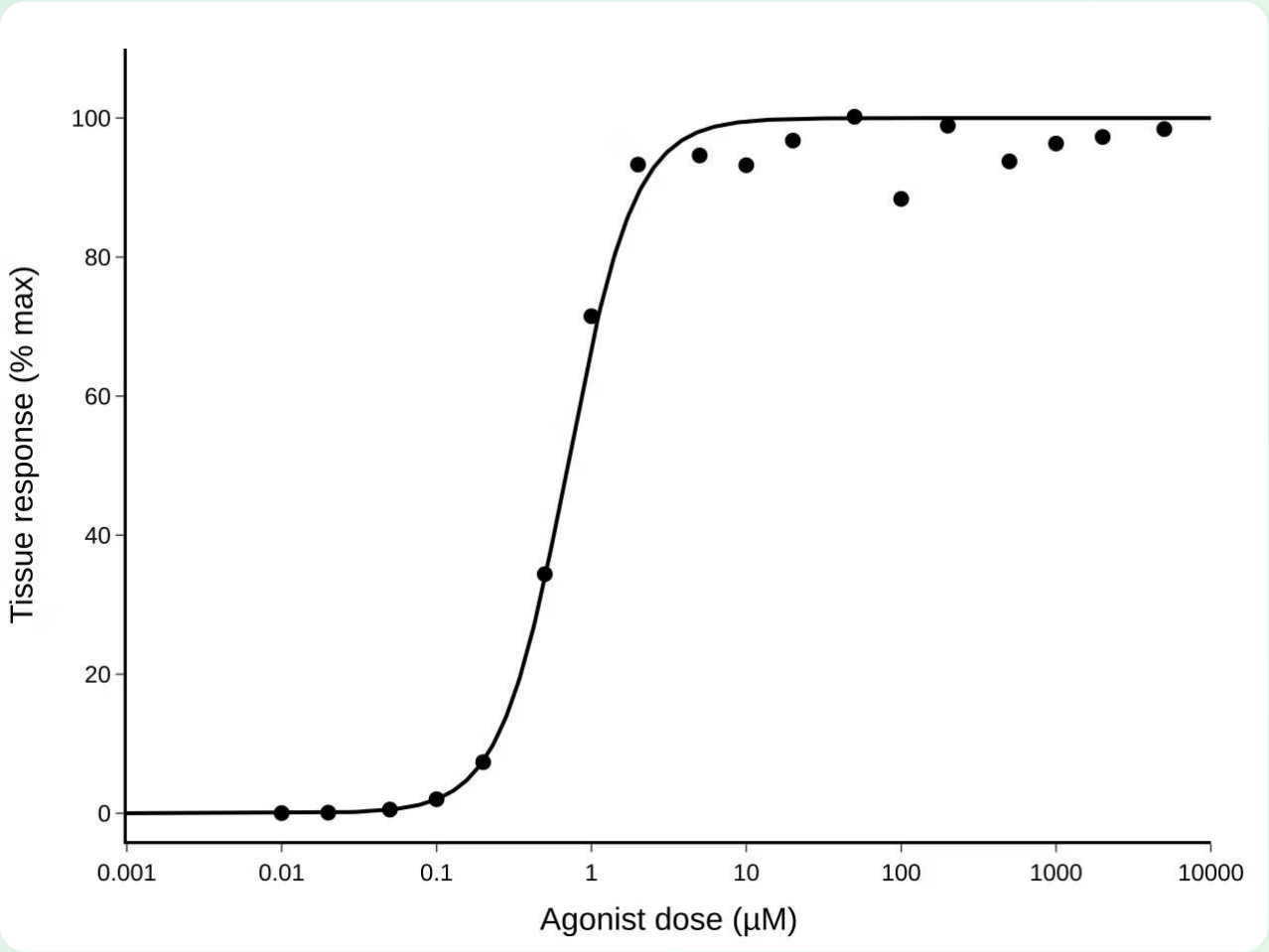
- **Complete absence of pain** during the procedure — the primary therapeutic goal
- Reduced procedural anxiety and psychological comfort
- Faster, more confident treatment by the clinician
- Enables longer, more comprehensive appointments

⚠️ Drawbacks

- **Residual numbness** lasting 2–4 hours post-procedure
- Risk of **accidental self-injury** (cheek/lip/tongue biting, especially in children)
- Unpleasant taste from the solution or cartridge
- Discomfort and anxiety from the injection itself
- Temporary speech and eating difficulty

CHAPTER 4

Safety and Toxicology



Paracelsus Principle

"The dose makes the poison." Local anesthetics are safe within recommended maximum doses — exceeded doses cause predictable systemic toxicity.

Primary Safety Rule

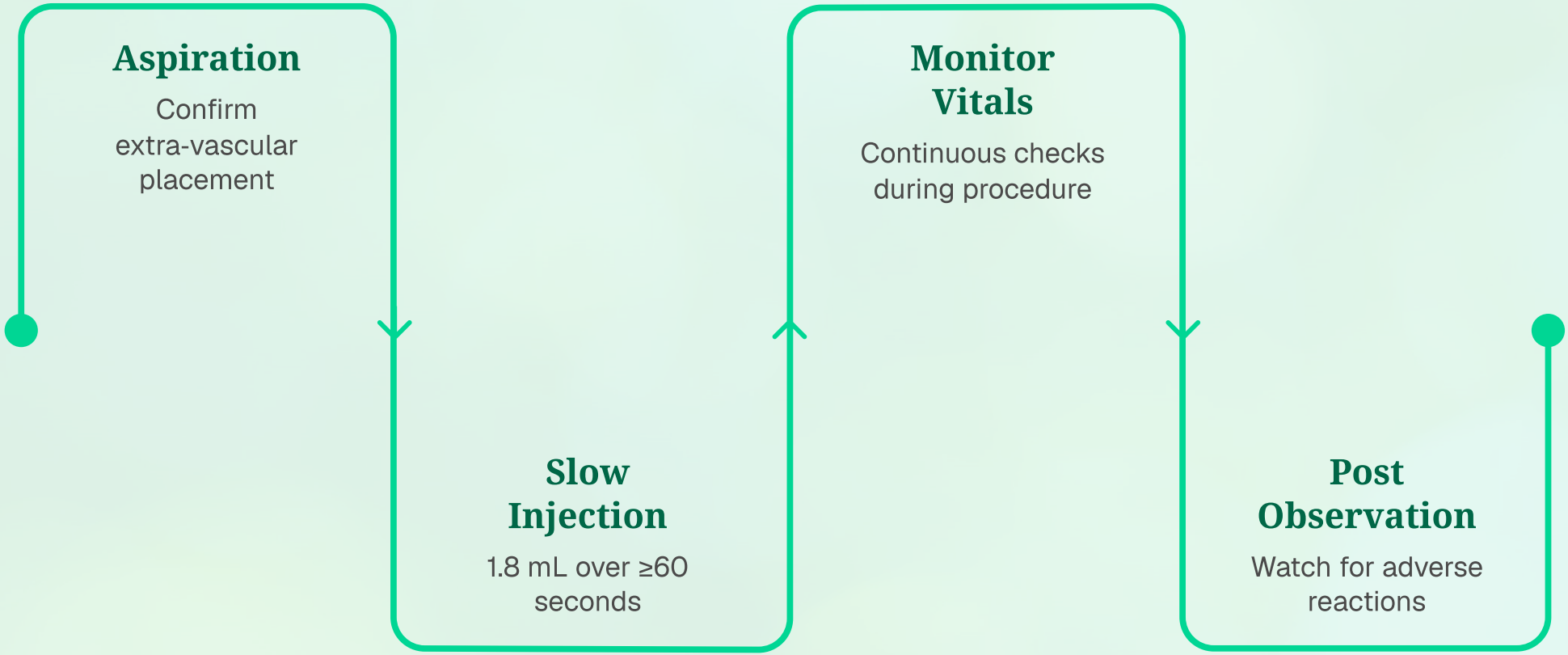
Avoid intravascular injection — always aspirate before depositing solution. Accidental IV bolus bypasses local buffering entirely.

Toxicity Spectrum

Systemic toxicity is **biphasic**: initial CNS excitation (tinnitus, metallic taste, seizures) followed by CNS/cardiovascular depression (arrhythmia, respiratory arrest) at higher plasma levels.

CHAPTER 4

Modern Clinical Protocols



Adhering to these protocols reduces the risk of systemic toxicity to near-zero in healthy patients — technique is as important as pharmacology.

Conclusion: The Mastery of Pain Control

The Molecular Key

Understanding the **sodium channel** — its states, its receptor sites, and the conditions that govern drug access — is the foundation of clinical efficacy.

Science Meets Technique

Pharmacological knowledge of pKa, lipid solubility, and protein binding must be paired with precise **injection technique** and anatomical understanding.

Patient-Centered Care

Local anesthesia is where **molecular science and human care intersect** — transforming what was once a feared procedure into a comfortable clinical experience.

