

Neurophysiology

Pain

Fatima Ryalat, MD, PhD

Assistant Professor, Department of Physiology and Biochemistry

School of Medicine, University of Jordan

Pain

- According to the International Association for the Study of Pain, pain is defined as:

Unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.

Pain

- Pain is more than a direct response to a stimulus. It is a personal, multidimensional experience.
- It is accompanied by motivated behavioral responses and emotional reactions.
- Also, the subjective perception of pain can be influenced by other past or present experiences.

Pain Stimuli

- Pain can be elicited by multiple types of stimuli, classified as mechanical, thermal, and chemical.
- Some of the chemicals that excite the chemical type of pain are bradykinin, potassium ions, and proteolytic enzymes.

Prostaglandins

- All nociceptors can be sensitized by prostaglandins, which greatly enhance the receptor response to noxious stimuli.
- Tissue injury, among other things, can lead to local release of prostaglandins, which act on nearby nociceptors' peripheral endings to lower their threshold for activation.
- NSAIDs inhibit the synthesis of prostaglandins, accounting at least in part for the pain-relieving properties of these drugs.

Hyperalgesia

- A pain nervous pathway sometimes becomes excessively excitable, which gives rise to hyperalgesia.
- Possible causes of hyperalgesia are the following:
 - (1) excessive sensitivity of the pain receptors, called primary hyperalgesia (e.g. sunburn).
 - (2) facilitation of sensory transmission, called secondary hyperalgesia.

Fast (acute) Pain

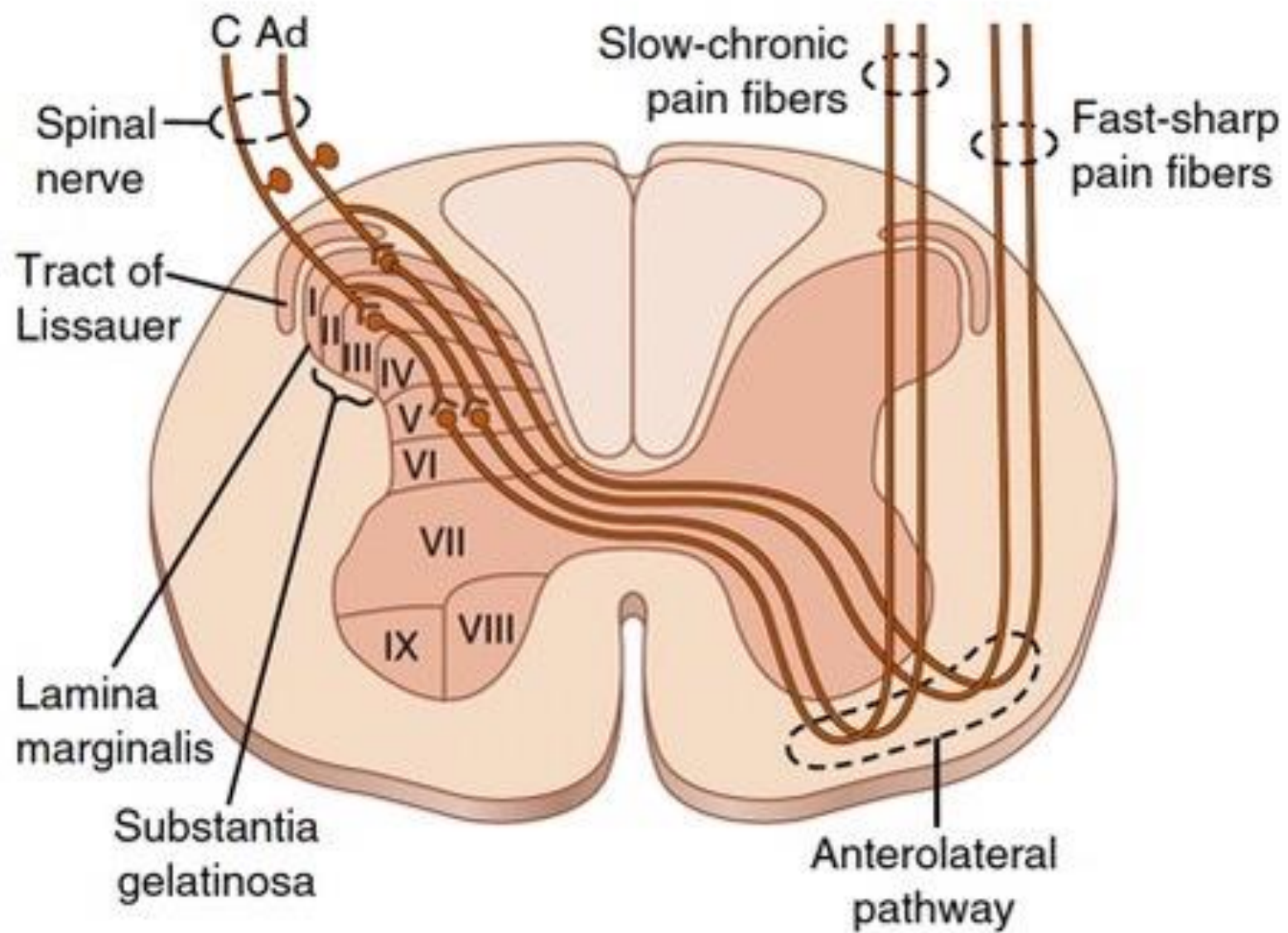
- The fast-sharp pain signals are elicited by either mechanical or thermal pain stimuli.
- Fast-sharp pain is not felt in most deep tissues of the body.
- They are transmitted in the peripheral nerves to the spinal cord by small type A δ fibers at velocities between 6 and 30 m/sec.
- a fast-sharp pain is followed a second or so later by a slow pain.
- The sharp pain plays an important role in making the person react immediately to remove himself or herself from the stimulus.

Chronic (slow) Pain

- Slow pain can occur in the skin and in almost any deep tissue or organ.
- this type of pain is elicited mostly by chemical types of pain stimuli.
- It is transmitted to the spinal cord by type C fibers at velocities between 0.5 and 2 m/sec.
- This feeling is a dull, aching, poorly localized sensation that persists for a longer time and is more unpleasant.

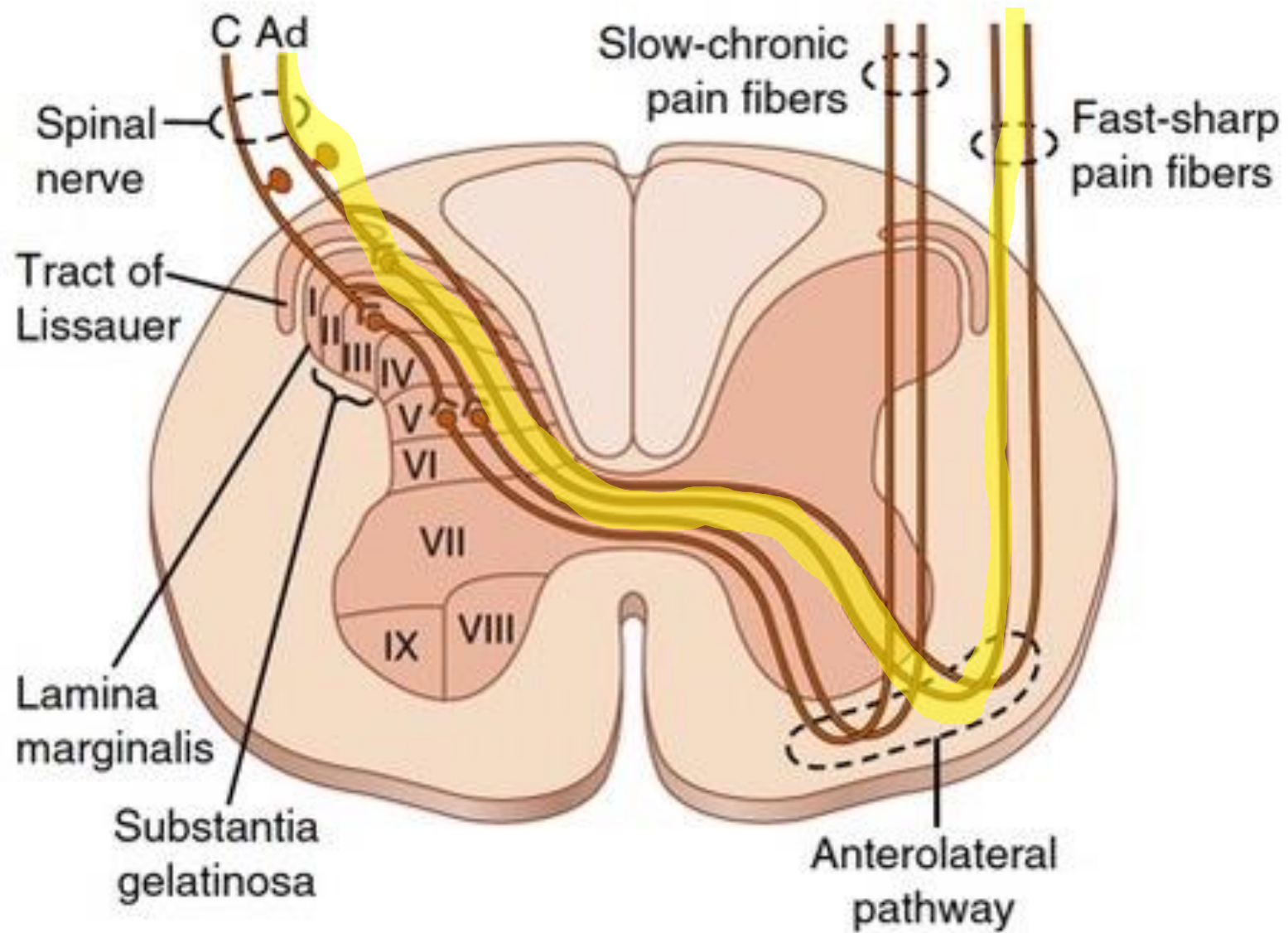
Pain

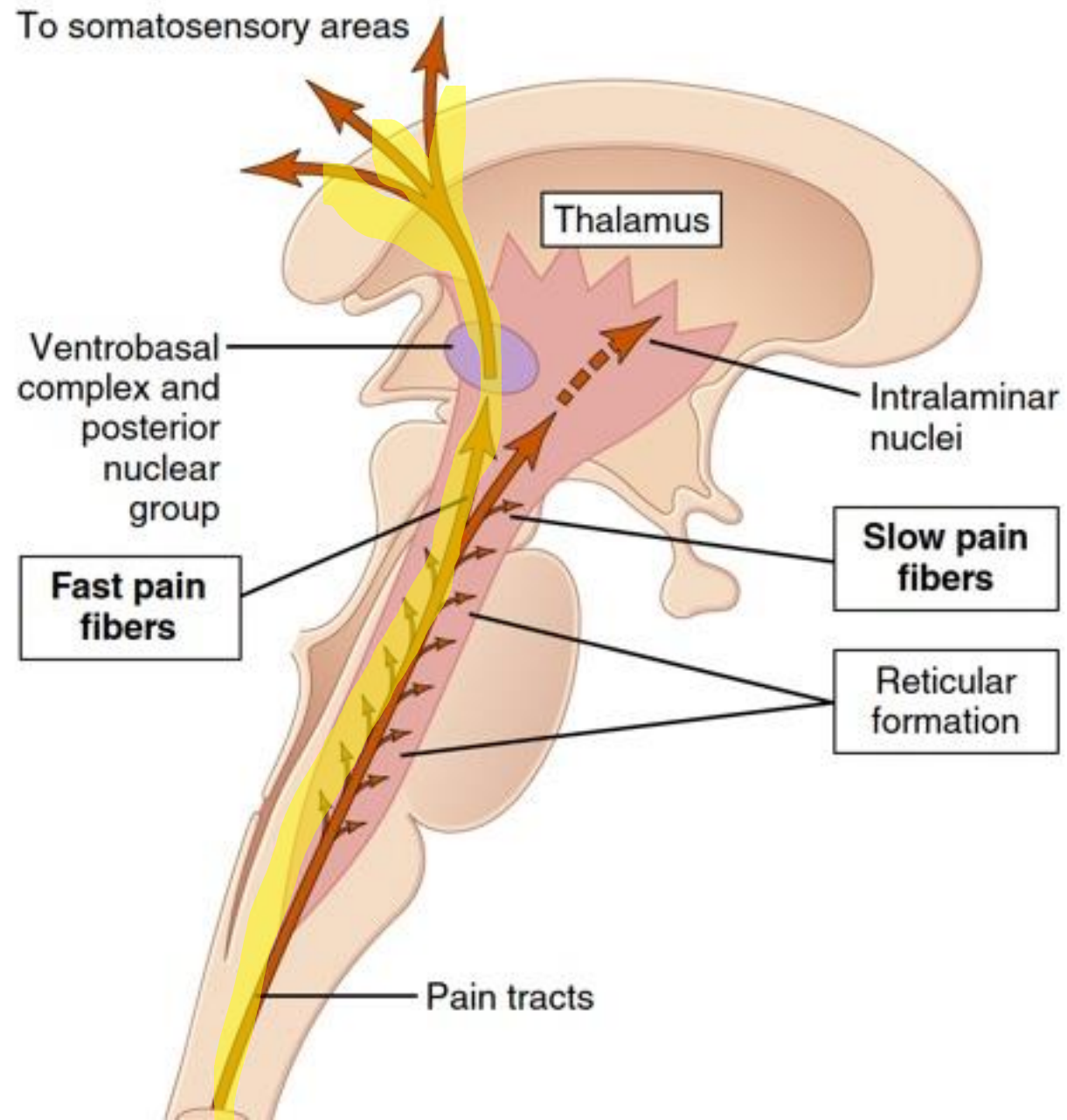
- Even though all pain receptors are free nerve endings, these endings use two separate pathways for transmitting pain signals into the central nervous system.
- The two pathways mainly correspond to the two types of pain:
 - a fast-sharp pain pathway.
 - a slow-chronic pain pathway.



Neospinothalamic tract

- A few fibers of the neospinothalamic tract terminate in the reticular areas of the brain stem, but most pass all the way to the thalamus without interruption, terminating in the ventrobasal complex along with the dorsal column–medial lemniscal tract for tactile sensations.
- A few fibers also terminate in the posterior nuclear group of the thalamus. From these thalamic areas, the signals are transmitted to other basal areas of the brain, as well as to the somatosensory cortex.



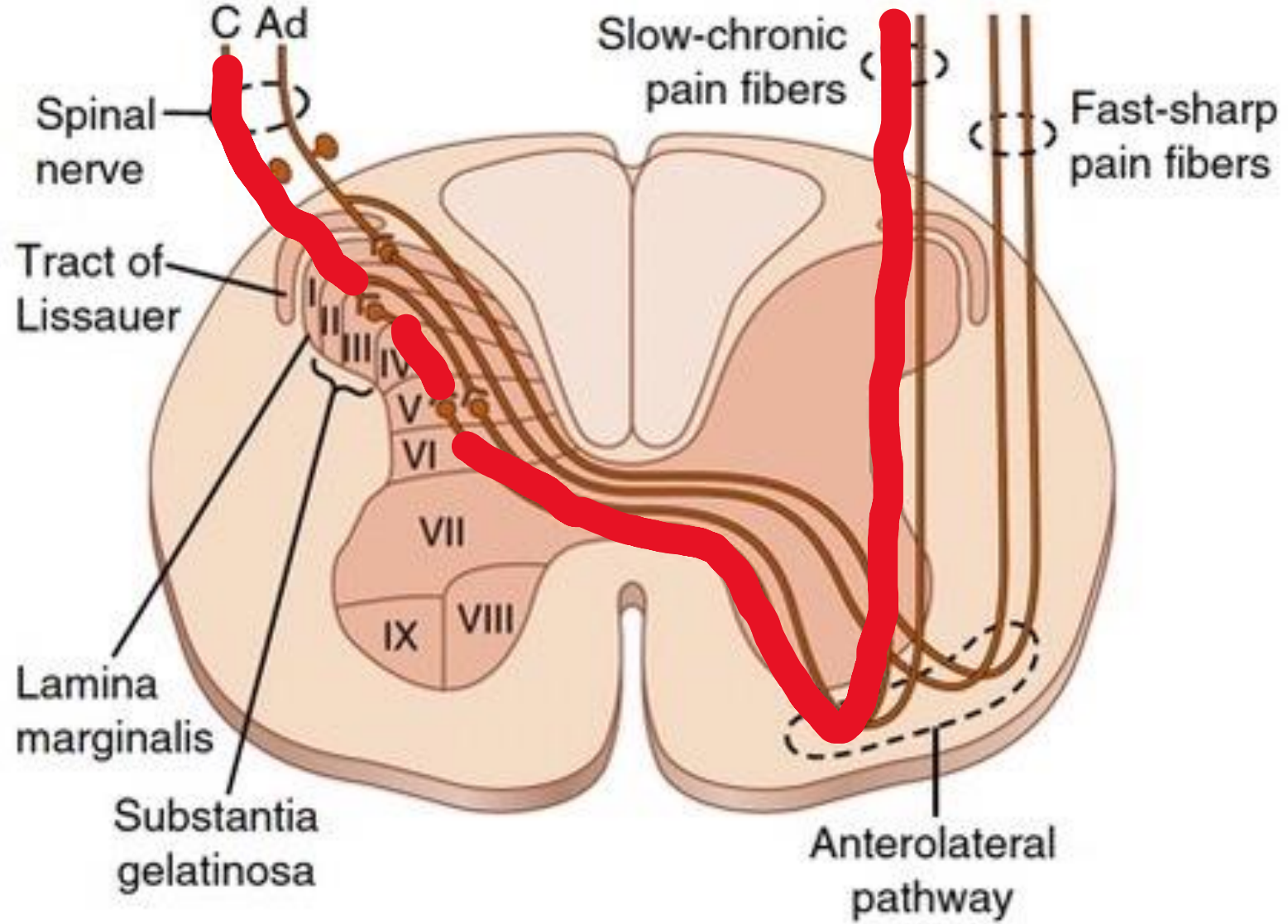


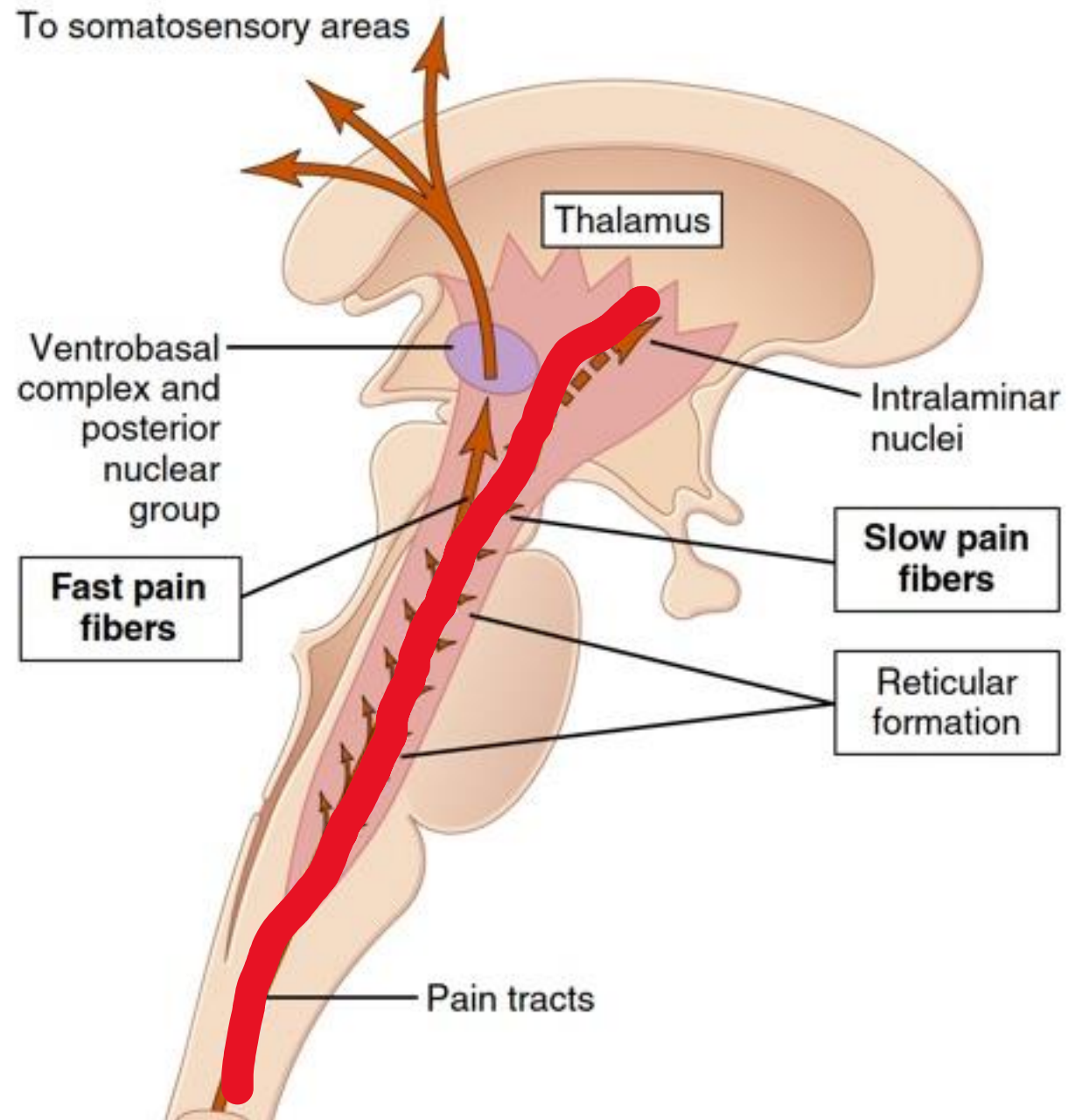
Localization of fast pain

- The fast-sharp type of pain can be localized much more exactly in the different parts of the body than can slow-chronic pain.
- When tactile receptors that excite the dorsal column–medial lemniscal system are simultaneously stimulated, the localization can be nearly exact.
- It is believed that glutamate is the neurotransmitter substance secreted in the spinal cord at the type $A\delta$ pain nerve fiber endings.

Paleospinothalamic pathway

- Most of the signals then pass through one or more additional short fiber neurons within the dorsal horns before entering mainly lamina V, also in the dorsal horn.
- Here, the last neurons in the series give rise to long axons that mostly join the fibers from the fast pain pathway, passing to the opposite side of the cord and then upward to the brain in the anterolateral pathway.





Paleospinothalamic pathway

- Type C pain fiber terminals entering the spinal cord release both glutamate transmitter and substance P transmitter.
- The glutamate transmitter acts instantaneously and lasts for only a few milliseconds.
- **Substance P** is released much more slowly, building up in concentration over a period of seconds or even minutes.

Paleospinothalamic pathway

- The slow-chronic paleospinothalamic pathway terminates widely in the brain stem.
- Only 10% to 25% of the fibers pass all the way to the thalamus. Instead, most terminate in one of three areas:
 - (1) the reticular nuclei of the medulla, pons, and mesencephalon.
 - (2) the tectal area of the mesencephalon deep to the superior and inferior colliculi.
 - (3) the periaqueductal gray region surrounding the aqueduct of Sylvius.

Paleospinothalamic pathway

- These **lower regions of the brain** appear to be important for feeling the **suffering types of pain**.
- From the brain stem pain areas, multiple short-fiber neurons relay the pain signals upward into the intralaminar and ventrolateral nuclei of the thalamus and into certain portions of the hypothalamus and other basal regions of the brain.

Paleospinothalamic pathway

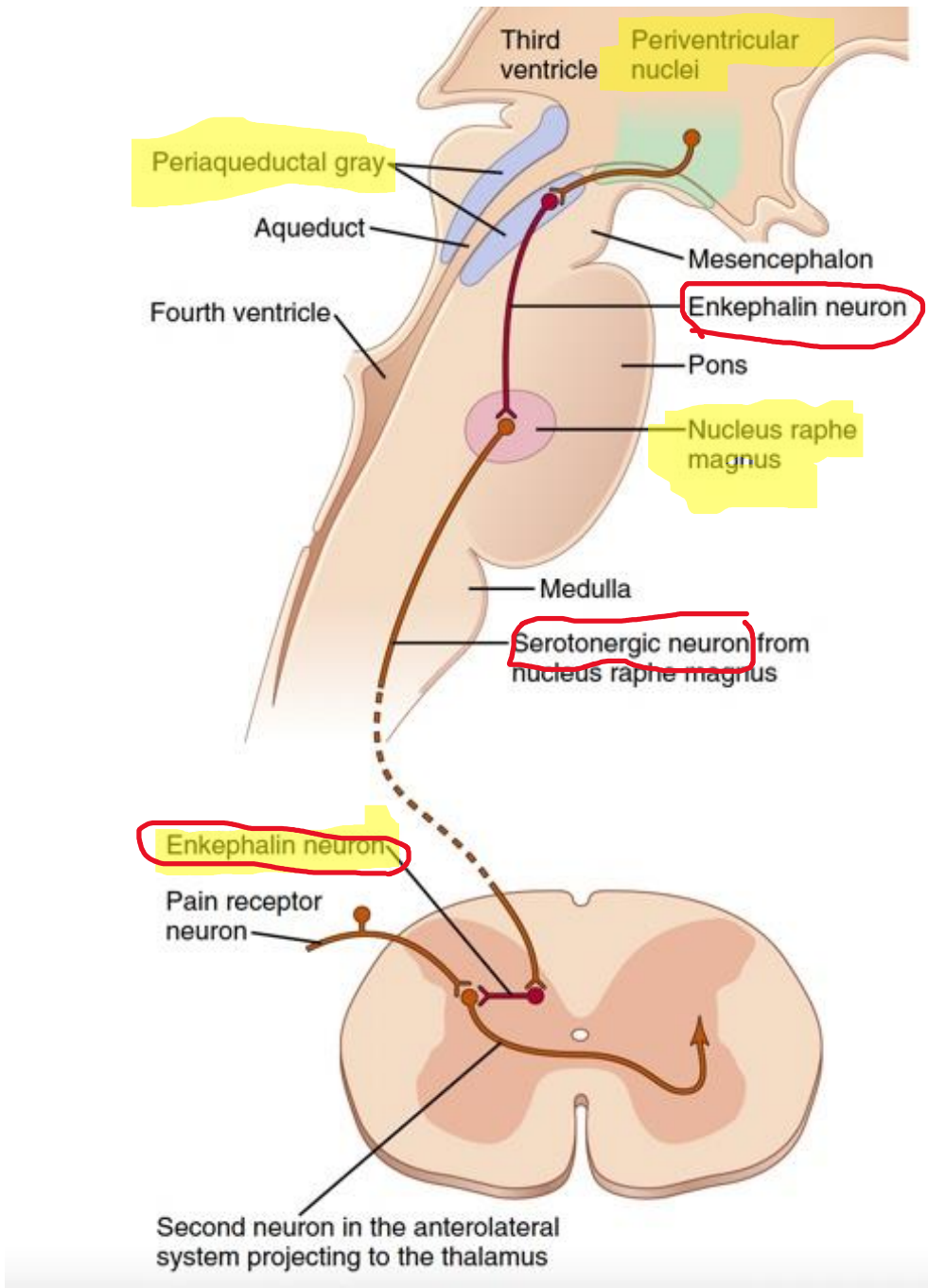
- Electrical stimulation in the reticular areas of the brain stem and in the intralaminar nuclei of the thalamus, the areas where the slow-suffering type of pain terminates, has a strong **arousal effect** on nervous activity throughout the entire brain.
- This explains why it is almost impossible for a person to sleep when in severe pain.

Paleospinothalamic pathway

- **Localization** of pain transmitted via the paleospinothalamic pathway is **imprecise**.
- For example, slow-chronic pain can usually be localized only to a major part of the body, such as to one arm or leg but not to a specific point on the arm or leg.
- This phenomenon is in keeping with the **multisynaptic, diffuse connectivity of this pathway**. It explains why patients often have serious difficulty in localizing the source of some chronic types of pain.

Pain suppression

- The degree to which different **people react to pain varies** tremendously.
- This variation results partly from a capability of the brain itself to suppress input of pain signals to the nervous system by activating a pain control system, called an **analgesia system**.



The endogenous analgesia system

- (1) The periaqueductal gray and periventricular areas of the mesencephalon and upper pons. Neurons from these areas send signals to
- (2) the raphe magnus nucleus, located in the lower pons and upper medulla, and the nucleus reticularis paragigantocellularis, located laterally in the medulla. From these nuclei, second order signals are transmitted down the dorsolateral columns in the spinal cord to
- (3) a pain inhibitory complex located in the dorsal horns of the spinal cord. At this point, the analgesia signals can block the pain before it is relayed to the brain.

The endogenous analgesia system

- Several transmitter substances, especially **enkephalin and serotonin**, are involved in the analgesia system.
- The enkephalin is believed to cause both **presynaptic and postsynaptic inhibition** of incoming type C and type A δ pain fibers where they synapse in the dorsal horns.

Pain control

- Electrical stimulation either in the periaqueductal gray area or in the raphe magnus nucleus can suppress many strong pain signals entering via the dorsal spinal roots.
- Also, stimulation of areas at higher levels of the brain that excite the periaqueductal gray area can also suppress pain. Such as the periventricular nuclei in the hypothalamus.

Pain control

- Stimulation of large-type $A\beta$ sensory fibers from peripheral tactile receptors can depress transmission of pain signals from the same body area.
- This effect presumably results from local lateral inhibition in the spinal cord.

Pain control

- Acupuncture is based on the idea that vital energy called qi (pronounced chee) flows through the body along pathways called meridians.
- According to one theory, acupuncture relieves pain by activating sensory neurons that ultimately trigger the release of neurotransmitters that function as analgesics such as endorphins, enkephalins, and dynorphins.

Pain control

- Exercise
- Distraction
- Deep breathing

Pain Assessment

Mnemonic :- SOCRATES

- S - Site**
- O - Onset**
- C - Character**
- R - Radiates**
- A - Associated Symt**
- T - Time/duration**
- E - Exacerbating**
- S - Severity**



Visceral pain

- Essentially all visceral pain that originates in the thoracic and abdominal cavities is transmitted through small type C pain fibers and, therefore, can transmit only the chronic, aching, suffering type of pain.
- One of the most important differences between surface pain and visceral pain is that highly localized types of damage to the viscera seldom cause severe pain.
- Conversely, any stimulus that causes diffuse stimulation of pain nerve endings throughout a viscus causes pain that can be severe.

Visceral pain

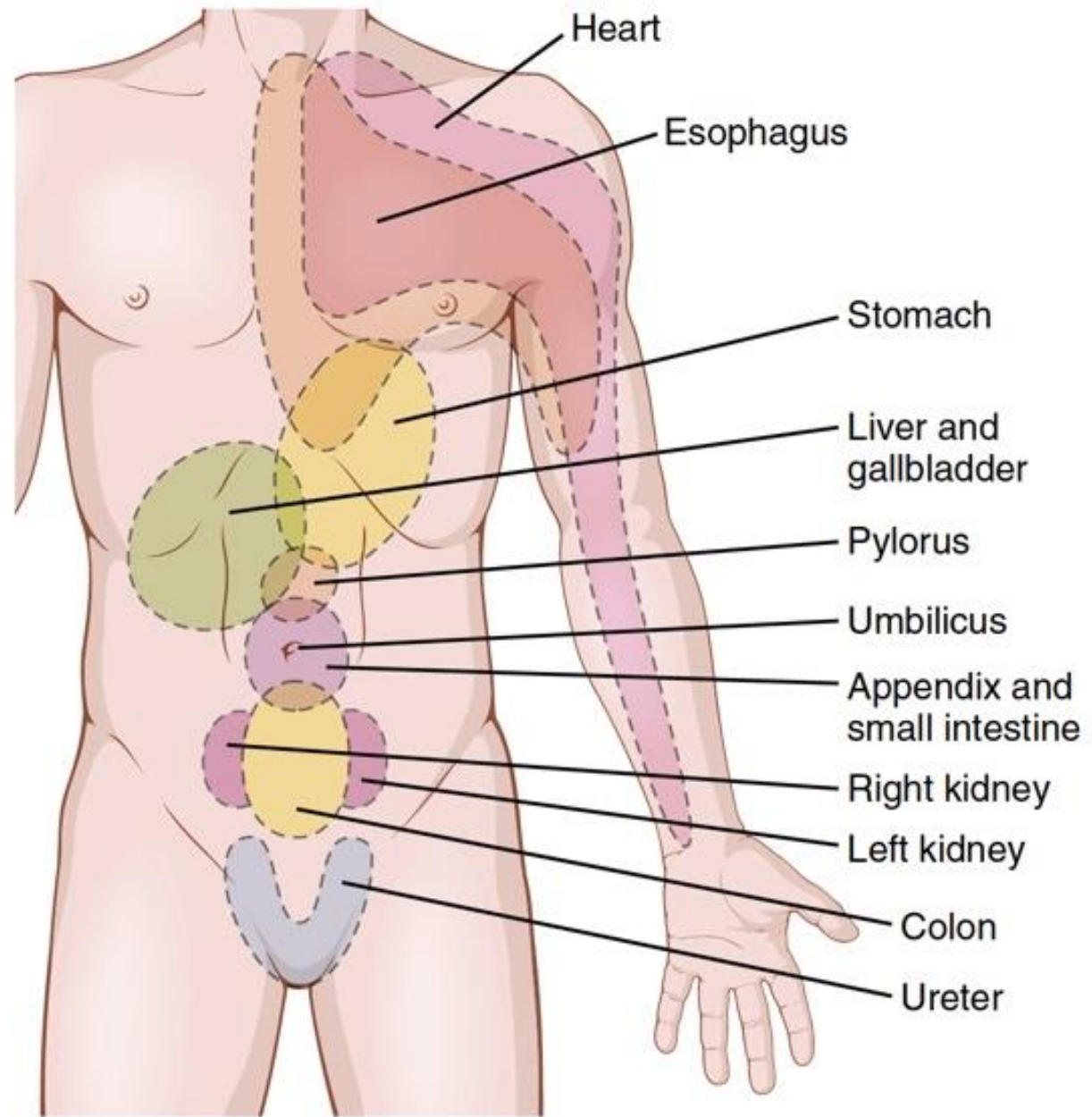
- Any stimulus that excites pain nerve endings in diffuse areas of the viscera can cause visceral pain.
- Such stimuli include ischemia of visceral tissue, chemical damage to the surfaces of the viscera, spasm of the smooth muscle of a hollow viscus, excess distention of a hollow viscus, and stretching of the connective tissue surrounding or within the viscus.

Visceral pain

- A few visceral areas are almost completely insensitive to pain of any type.
- These areas include the parenchyma of the liver and the alveoli of the lungs
- Yet, the liver capsule is extremely sensitive to both direct trauma and stretch, and the bile ducts are also sensitive to pain. In the lungs, even though the alveoli are insensitive, both the bronchi and the parietal pleura are very sensitive to pain.

Visceral Pain

- True visceral pain is transmitted via pain sensory fibers in the autonomic nerve bundles, and the sensations are referred to surface areas of the body that are often far from the painful organ.
- Pain from the viscera is frequently localized to two surface areas of the body at the same time because of the dual transmission of pain through the referred visceral pathway and the direct parietal pathway.

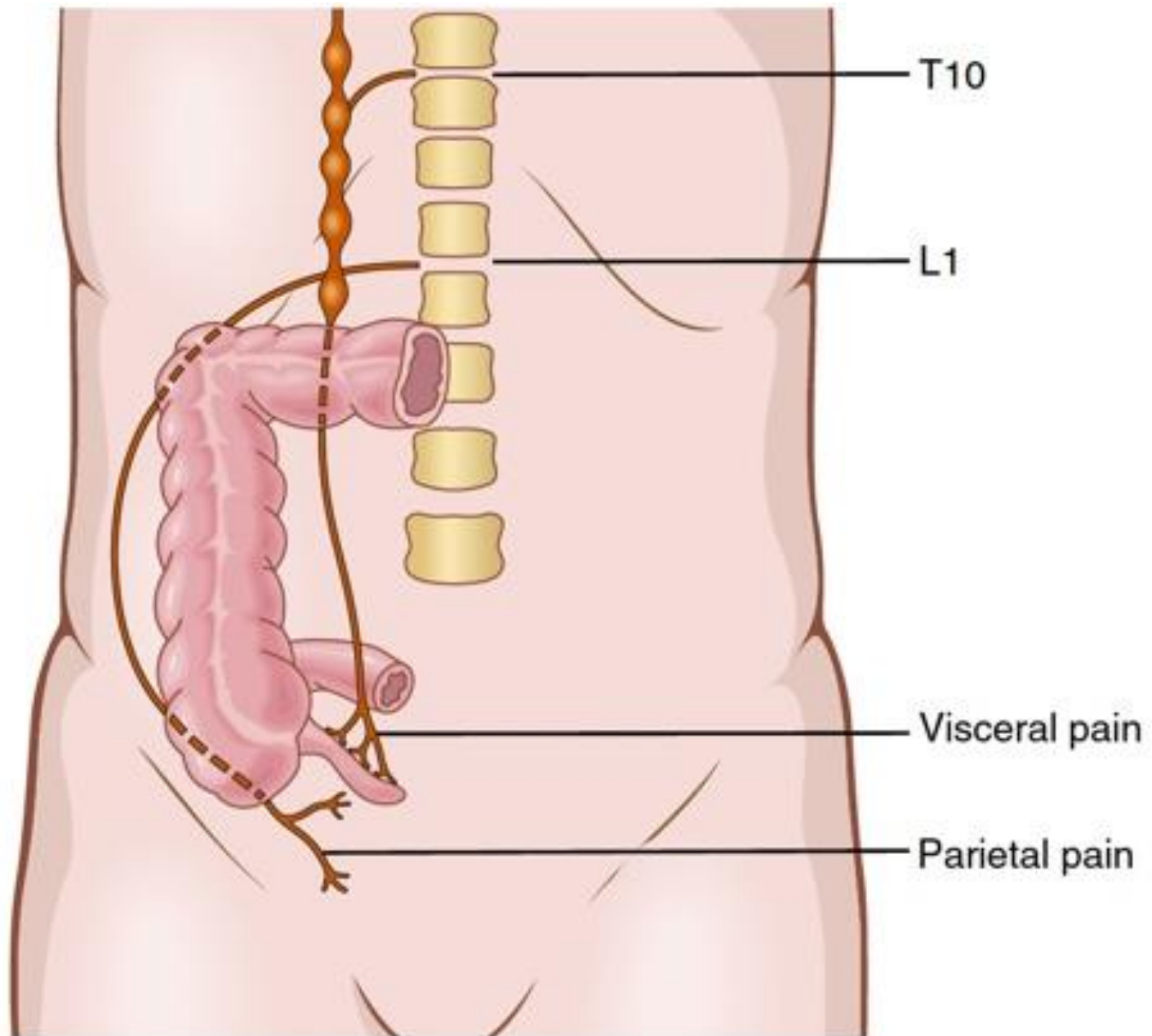


Parietal pain

- When a disease affects a viscus, the disease process often spreads to the parietal peritoneum, pleura, or pericardium.
- These parietal surfaces, like the skin, are supplied with extensive pain innervation from the peripheral spinal nerves.
- parietal sensations are conducted directly into local spinal nerves from the parietal peritoneum, pleura, or pericardium, and these sensations are usually localized directly over the painful area and sharp.

Localization of visceral and parietal pain

- Sensations from the abdomen and thorax are transmitted through two pathways to the central nervous system, the true visceral pathway and the parietal pathway.
- True visceral pain is transmitted via pain sensory fibers in the autonomic nerve bundles, and the sensations are referred to surface areas of the body that are often far from the painful organ.
- Conversely, parietal sensations are usually localized directly over the painful area.

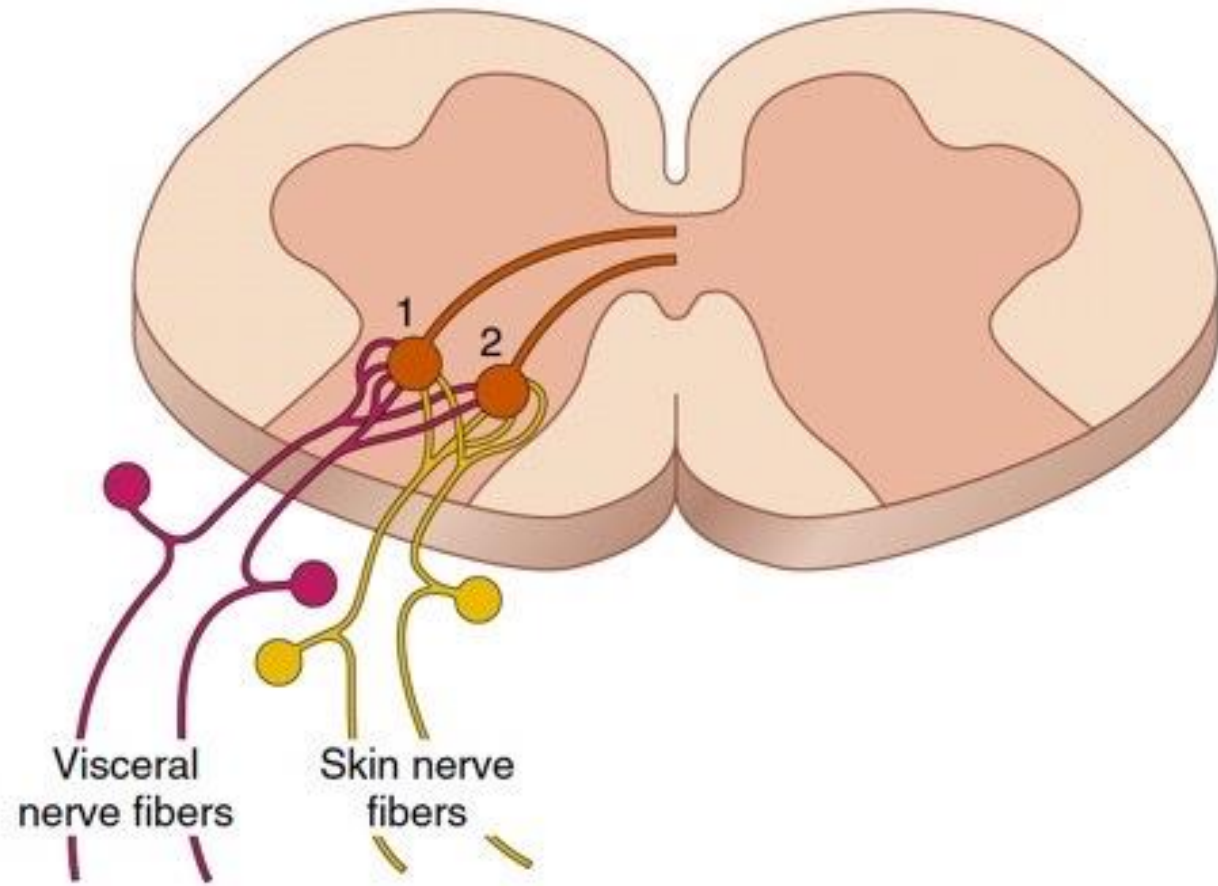


Referred pain

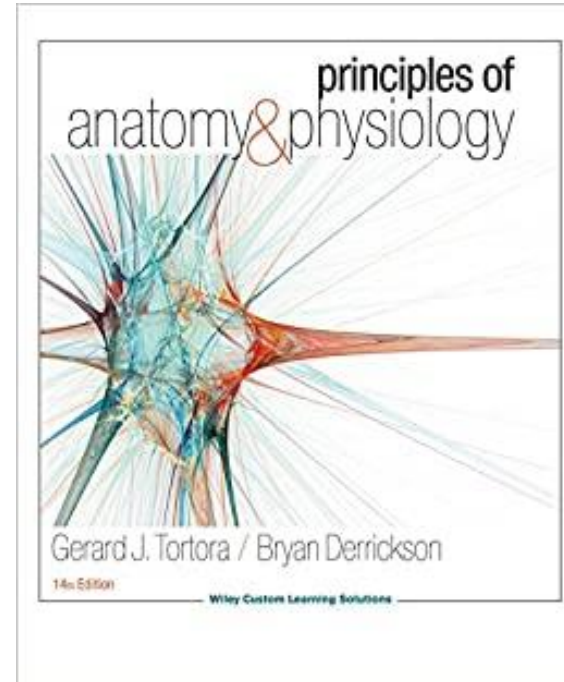
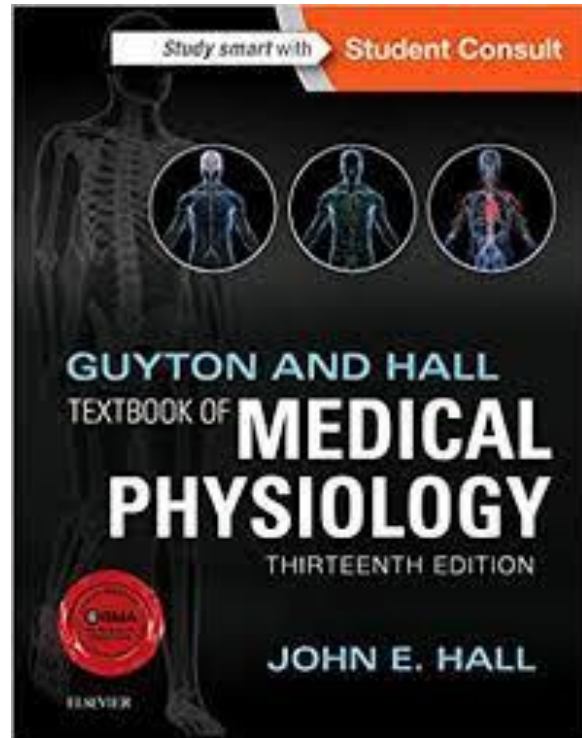
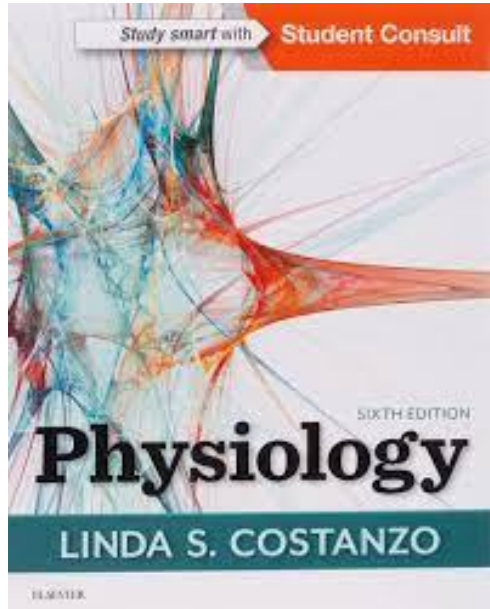
- When visceral pain is referred to the surface of the body, the person generally localizes it in the **dermatomal** segment from which the visceral organ originated in the embryo, not necessarily where the visceral organ now lies.
- For example, the heart originated in the neck and upper thorax, so the heart's visceral pain fibers pass upward along the sympathetic sensory

Mechanism of referred pain

- branches of visceral pain fibers are shown to synapse in the spinal cord on the same second-order neurons that receive pain signals from the skin.
- When the visceral pain fibers are stimulated, pain signals from the viscera are conducted through at least some of the same neurons that conduct pain signals from the skin, and the person has the feeling that the sensations originate in the skin.



References



9TH
Edition

Human Physiology From Cells to Systems

Lauralee Sherwood
Department of Physiology and Pharmacology
School of Medicine
West Virginia University

CENGAGE
Learning

Australia • Brazil • Mexico • Singapore • United Kingdom • United States

Copyright 2011 Cengage Learning. All Rights Reserved. May not be copied, scanned, or duplicated, in whole or in part. This no-distribution rights, even if you are permitted to reproduce the text for personal or internal use, or the internal or external use of specific clients, is granted by Cengage Learning for users registered with the Cengage Learning system. Cengage Learning reserves the right to remove additional content at any time if subsequent rights restrictions require it.

Thank you

Treatment of Pain by Electrical Stimulation

- Several clinical procedures have been developed for suppressing pain with use of electrical stimulation.
- Stimulating electrodes are placed on selected areas of the skin or, on occasion, implanted over the spinal cord, supposedly to stimulate the dorsal sensory columns.
- In some patients, electrodes have been placed stereotaxically in appropriate intralaminar nuclei of the thalamus or in the periventricular or periaqueductal area of the diencephalon. The patient can then personally control the degree of stimulation.

Phantom Pain

- A

Thalamus

- A

Corticofugal signals

- A

Somatosensory cortex

- A

Somatosensory cortex

- A

Somatosensory cortex

- A

Pain

- A

- **Complete removal of the somatic sensory areas of the cerebral cortex does not prevent pain perception.** Therefore, it is likely that pain impulses entering the brain stem reticular formation, the thalamus, and other lower brain centers cause conscious perception of pain.
- This does not mean that the cerebral cortex has nothing to do with normal pain appreciation; it is believed that the cortex plays an especially important role in **interpreting pain quality.**