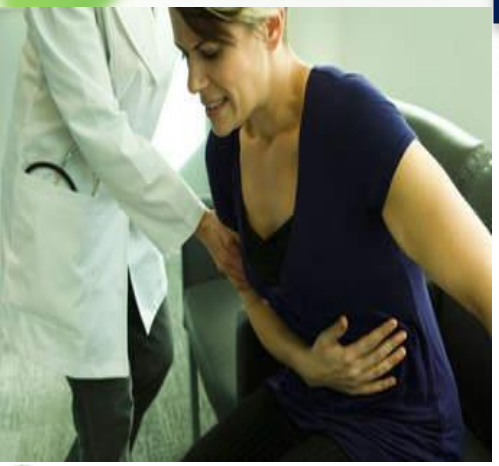
Physiology of Pain



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Learning Objectives

1- What is pain and its significance

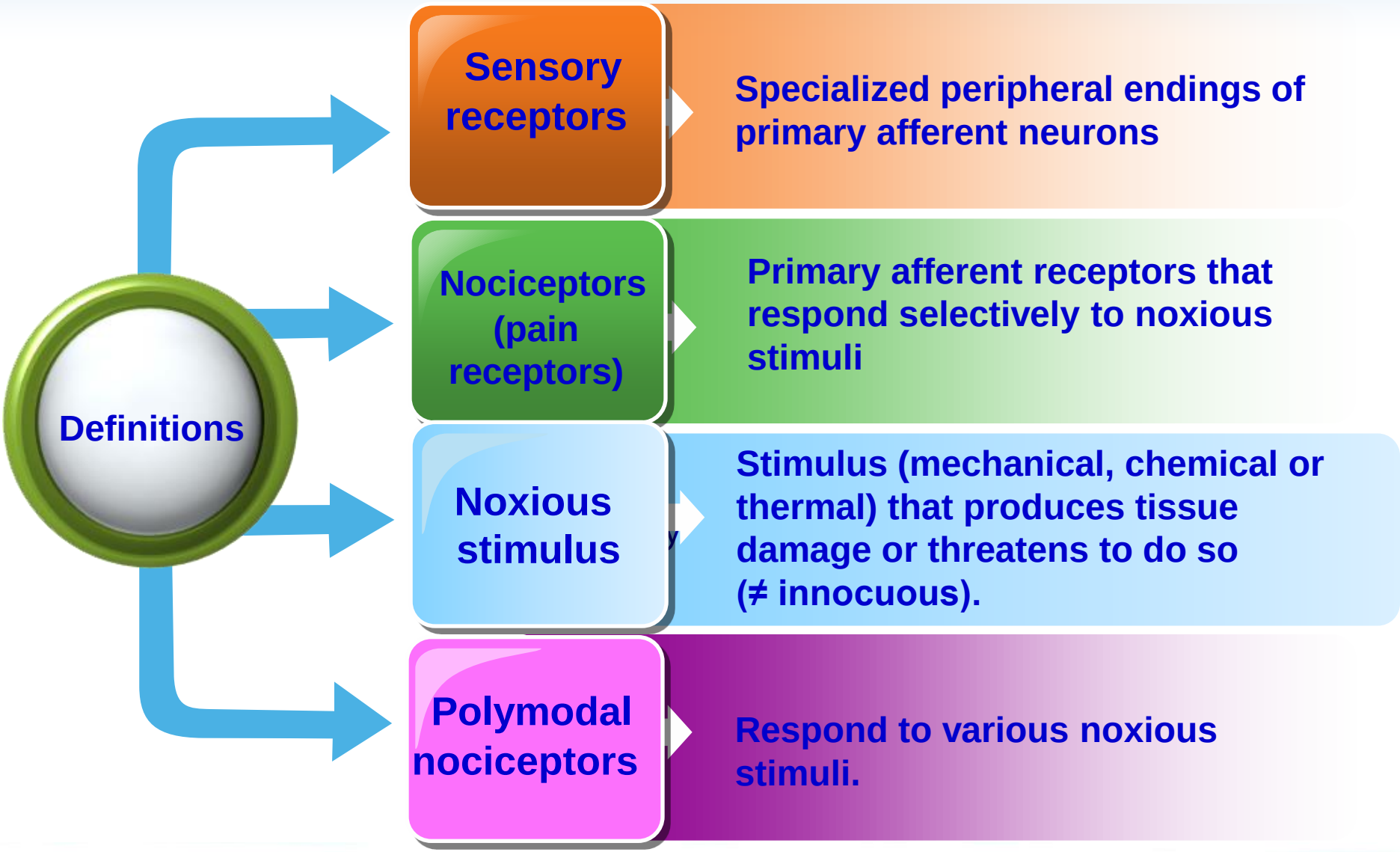
2-Pain receptors & mechanism of stimulation

3- Qualities & Types of pain

6- Role of thalamus and cerebral cortex in pain perception

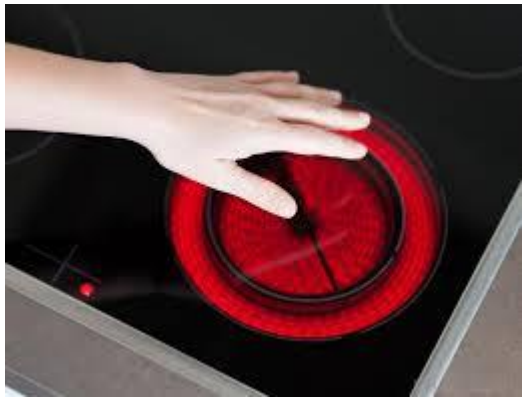
5- Pathway of pain

4- Referred pain


Definitions
Sensory receptors
Specialized peripheral endings of primary afferent neurons
Nociceptors (pain receptors)
Primary afferent receptors that respond selectively to noxious stimuli
Noxious stimulus
Stimulus (mechanical, chemical or thermal) that produces tissue damage or threatens to do so (≠ innocuous).
Polymodal nociceptors
Respond to various noxious stimuli.

Significance of Pain: Why do we feel pain?

- It is a protective mechanism meant to make us aware that tissue damage is occurring or is about to occur:-
  - Avoid noxious stimuli
  - Remove body parts from danger
  - Promote healing by preventing further damage
  - Storage of painful experiences in memory to avoid potentially harmful event in the future



- The sensation of pain may be accompanied by behavioral responses (withdrawal, defense) as well as emotional responses (crying, anxiety or fear).
- Pain is perceived at both the cortical & thalamic levels.

Pain Reception and Perception

Reception
الإستقبال

- **Response of nerve receptors in the skin and tissues to stimuli resulting from actual or potential tissue damage**

Perception
الإدراك

- **The process by which pain is recognized and interpreted by the brain**

Pain & Nociception

	Nociception	Pain
What is?	Transmission of signals evoked by activation of nociceptors from periphery to the CNS.	Perception of unpleasant sensation that originates from a specific body region
Pain is	an unpleasant sensory and emotional experience associated with actual or potential tissue damage.	

Pain Receptors `Nociceptors`?

“ Are special receptors that respond only to noxious stimuli and generate nerve impulses which the brain interprets as "pain". (Sherrington 1906)

Sir Charles Scott Sherrington

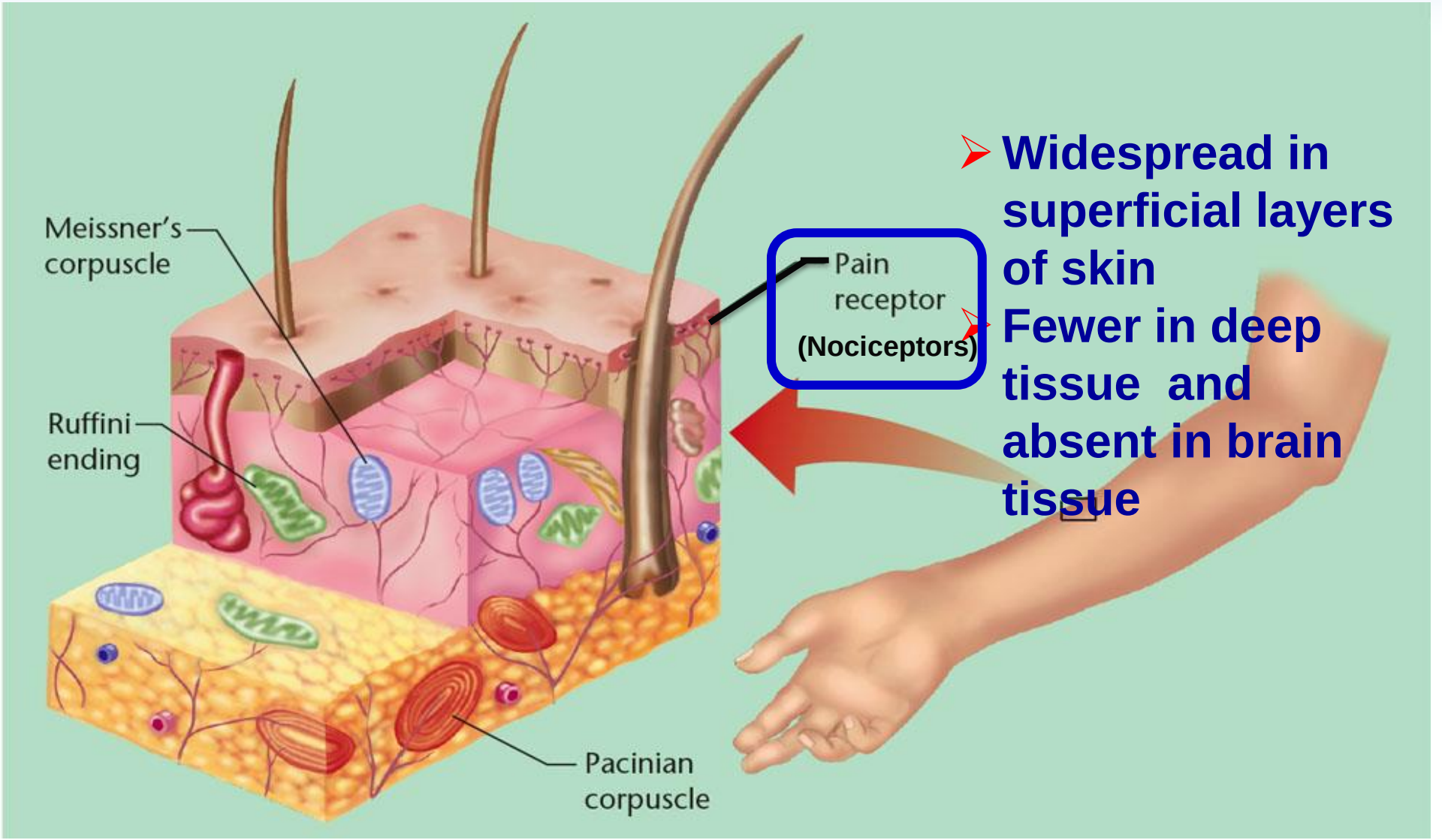
What are the Characteristics of Nociceptors?

- They are the most widely distributed.
- They are specific (have adequate stimulus), pain is not produced by overstimulation of other receptors.
- They are high threshold receptors i.e. painful stimuli must be strong & noxious to produce tissue damage.
- They do not adapt (or very little) to repetitive stimulation

Why?

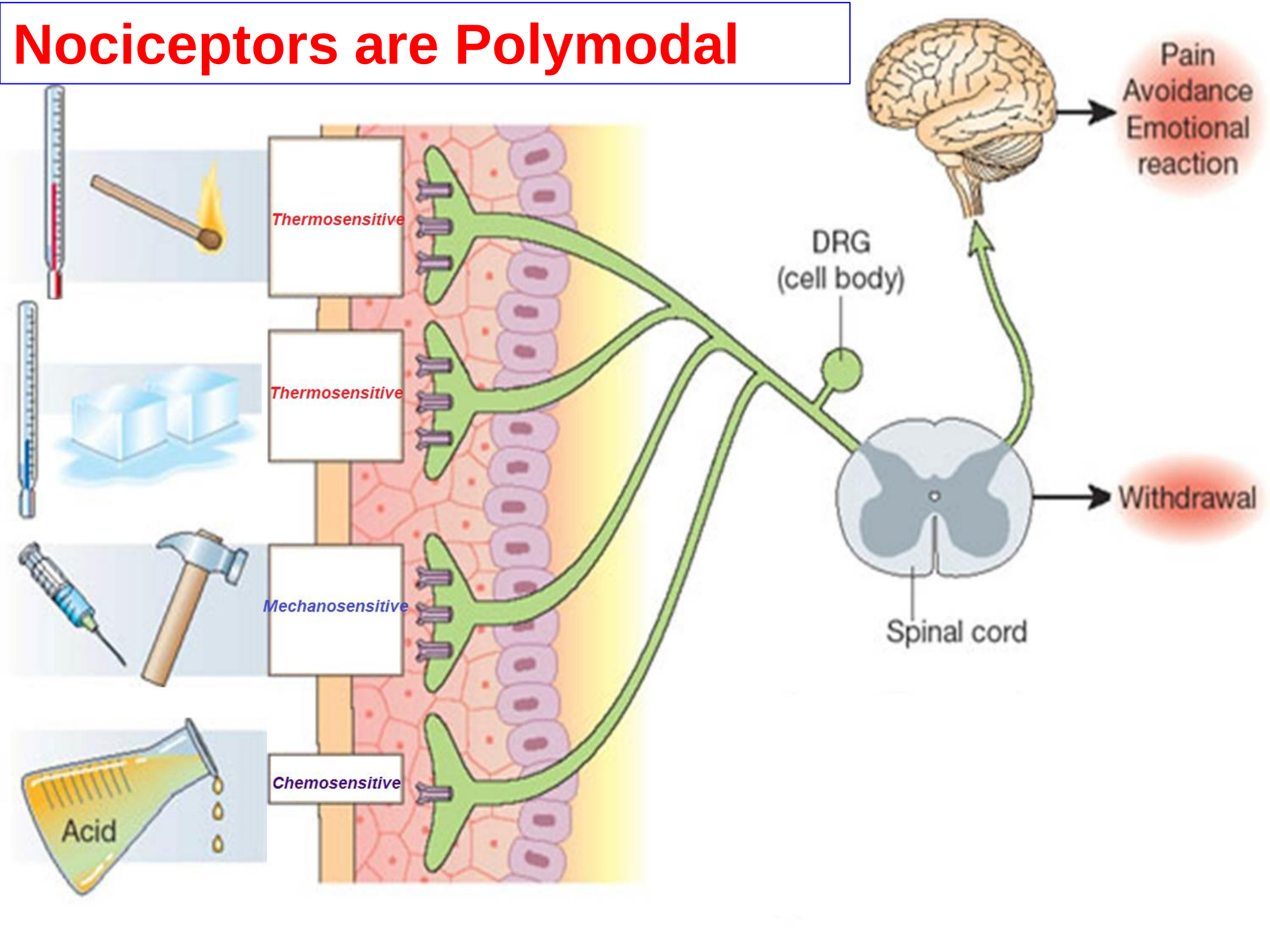
It allows the pain to keep the person apprised of a tissue-damaging stimulus as long as it persists.

Distribution of Pain Receptor (Nociceptors)

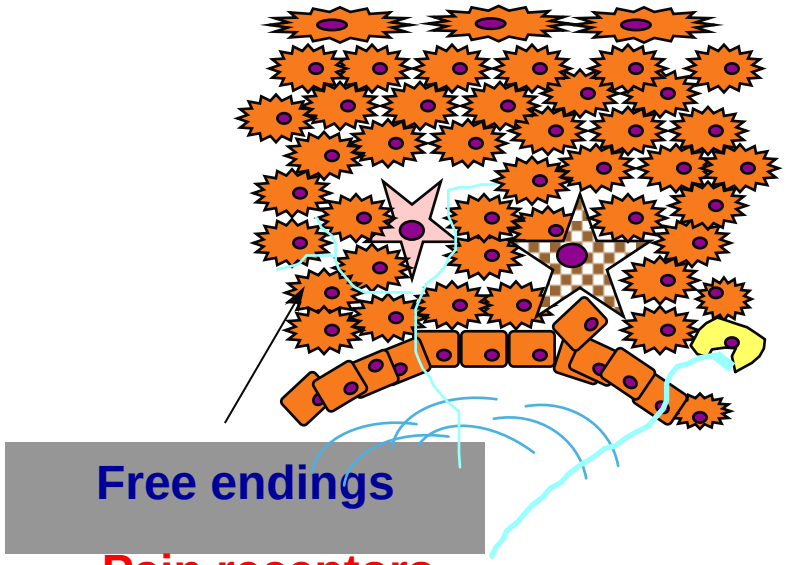


- **Widespread in superficial layers of skin**
- **Fewer in deep tissue and absent in brain tissue**

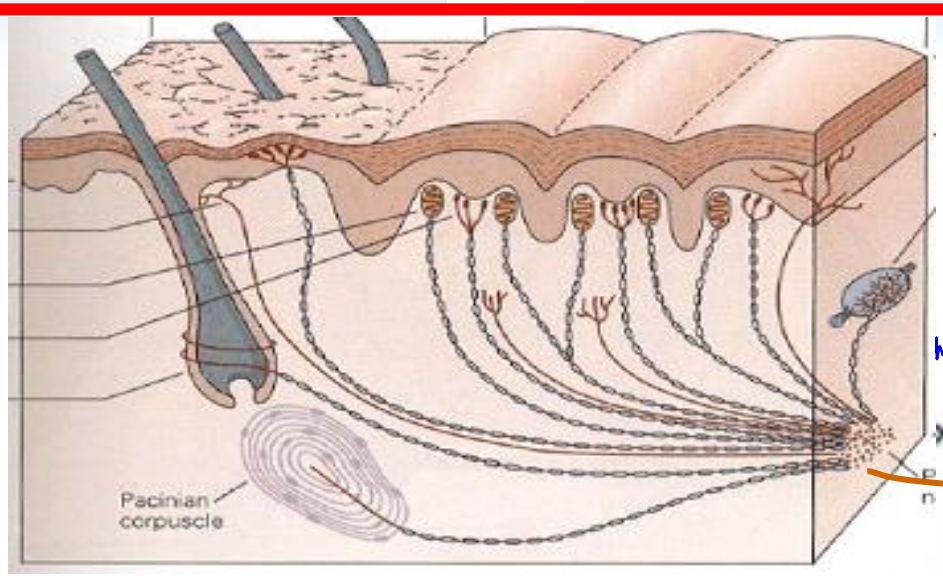
Nociceptors are Polymodal

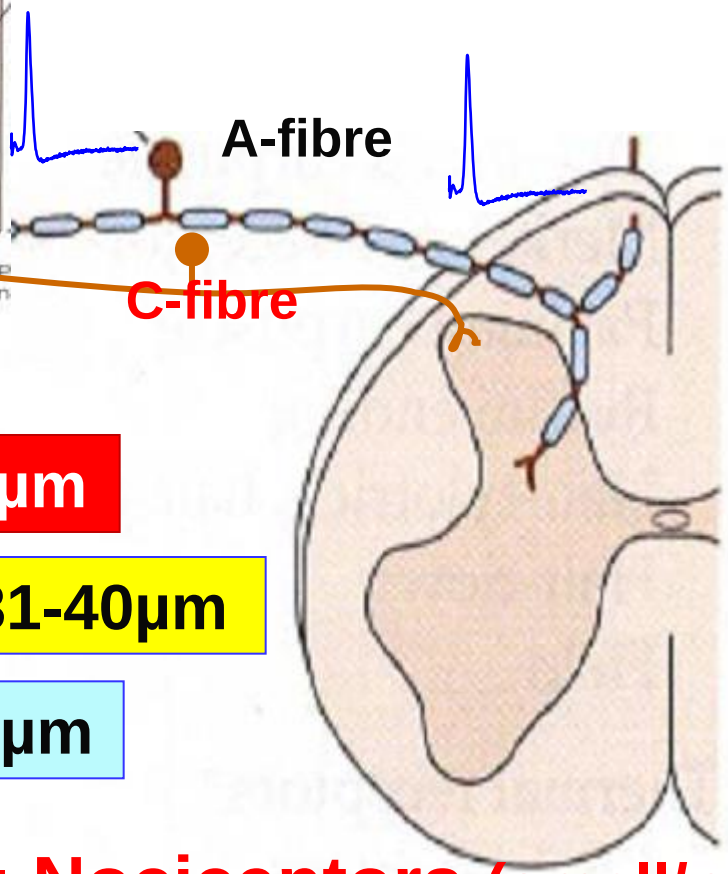


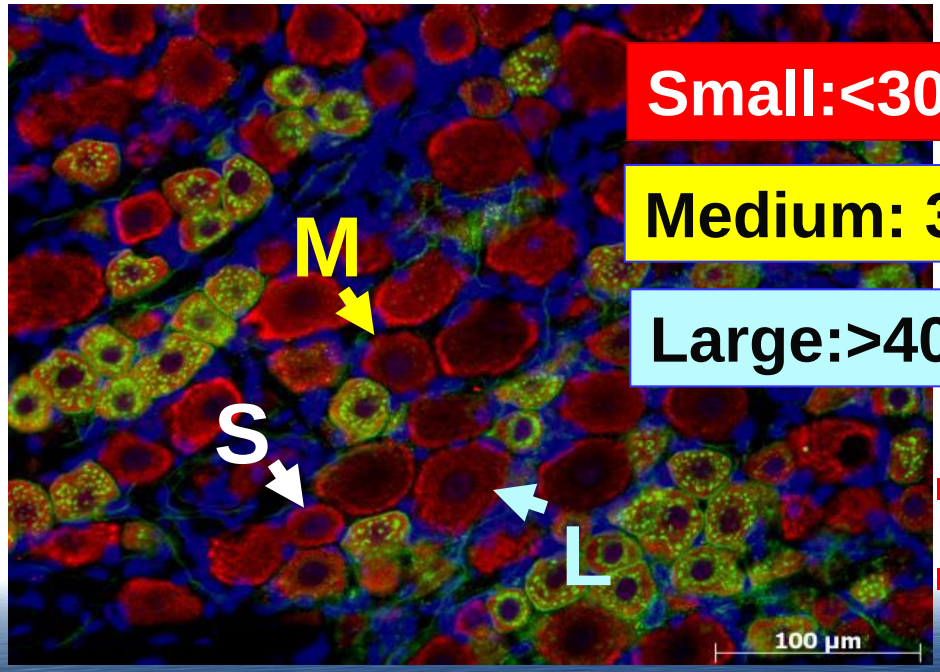
- All pain receptors are **free nerve endings** of:
  1-Unmyelinated C fibers (diameter 0.4 – 1.2 µm with conduction velocity 0.5 - 2 m/s
  2- Small diameter myelinated Aδ fibers (diameter fine 2 - 5 µm with conduction velocity 12 - 30 m/sec.



Type-A & Type-C Fibers







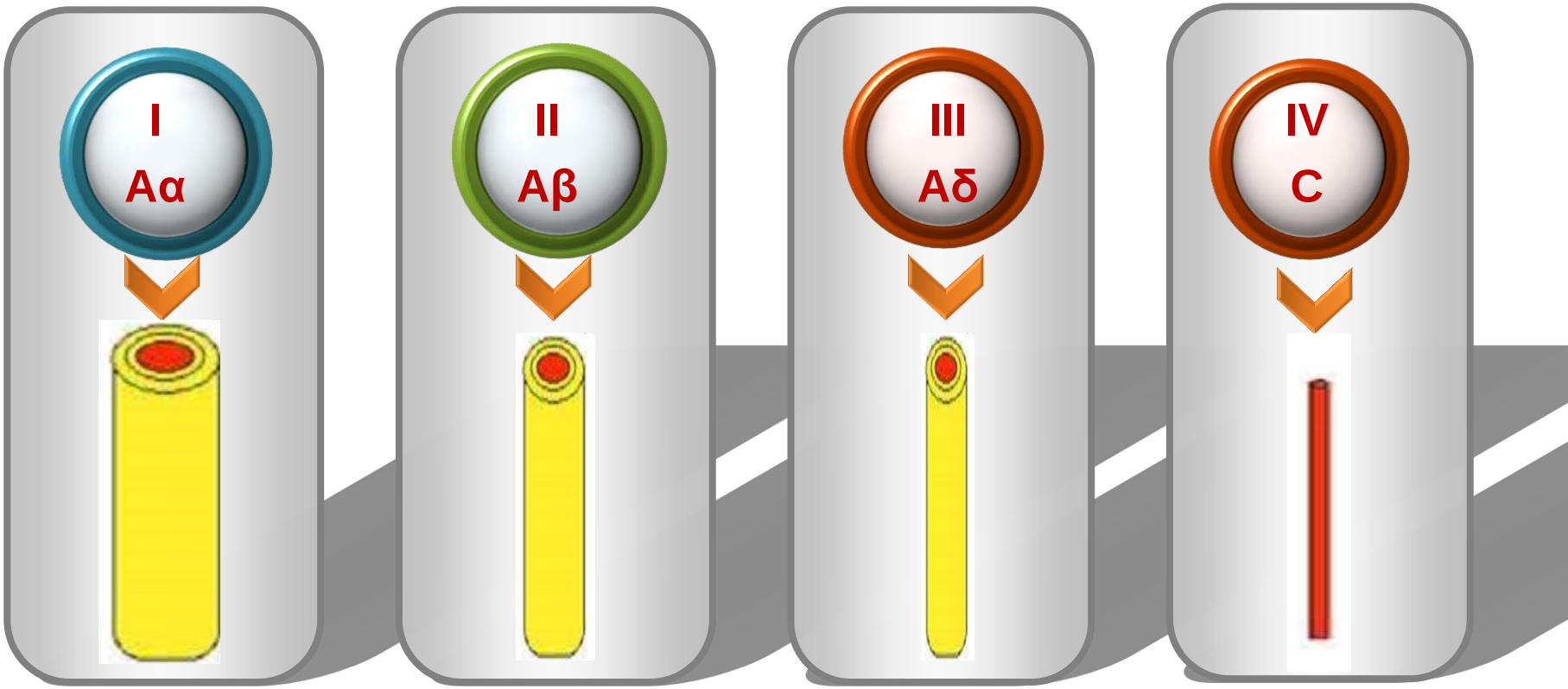
Small:<30µm

Medium: 31-40µm

Large:>40µm

- **Nociceptors (small/medium)**
- **Non-nociceptors (large)**

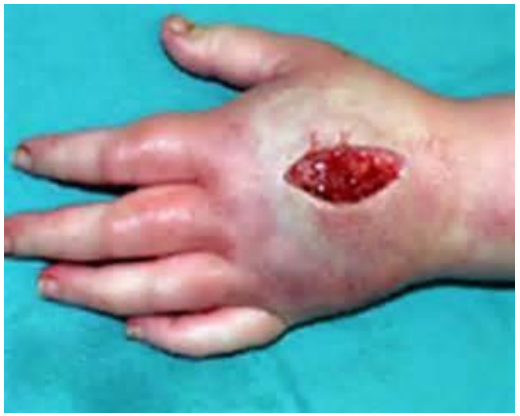
Classification of Nerve fibres

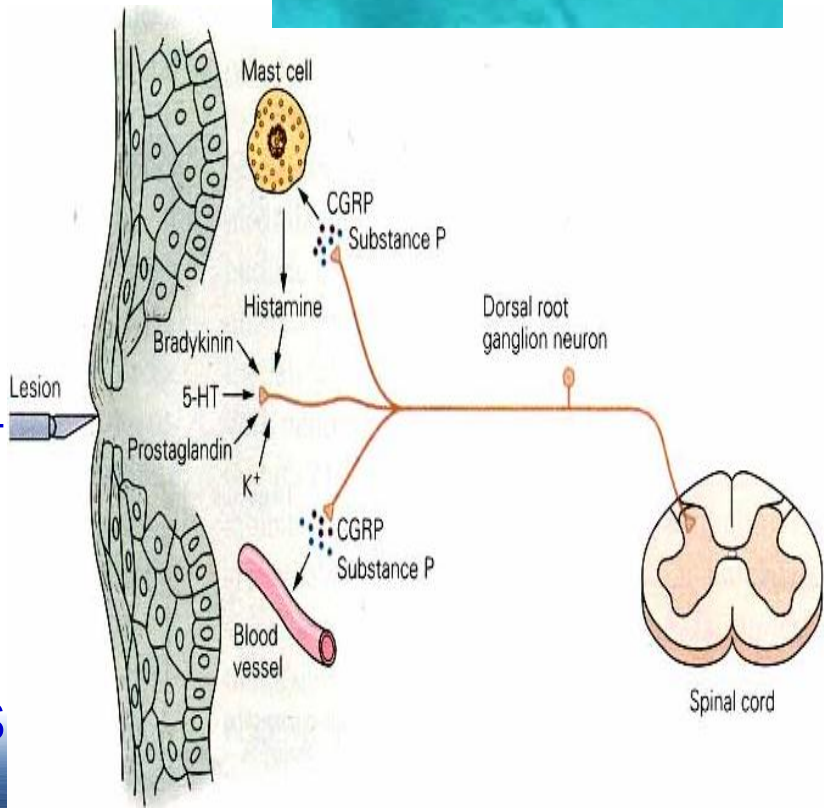


	I	II	III	IV
Diameter (μm)	10-20	5-10	2-5	0.5-2
Conduction Velocity (m/s)	70-120	30-70	5-30	0.5-2

Mechanism of Stimulation of Nociceptors

- Pain receptors are depolarized either directly or through the production of pain producing substances (inflammatory mediators) from damaged tissues
- e.g. bradykinin, histamine, substance P, calcitonin gene-related peptide (CGRP), interleukins, prostaglandins, K^+ Ach, proteolytic enzymes.
- PGs & substance-P enhance the sensitivity of pain receptors

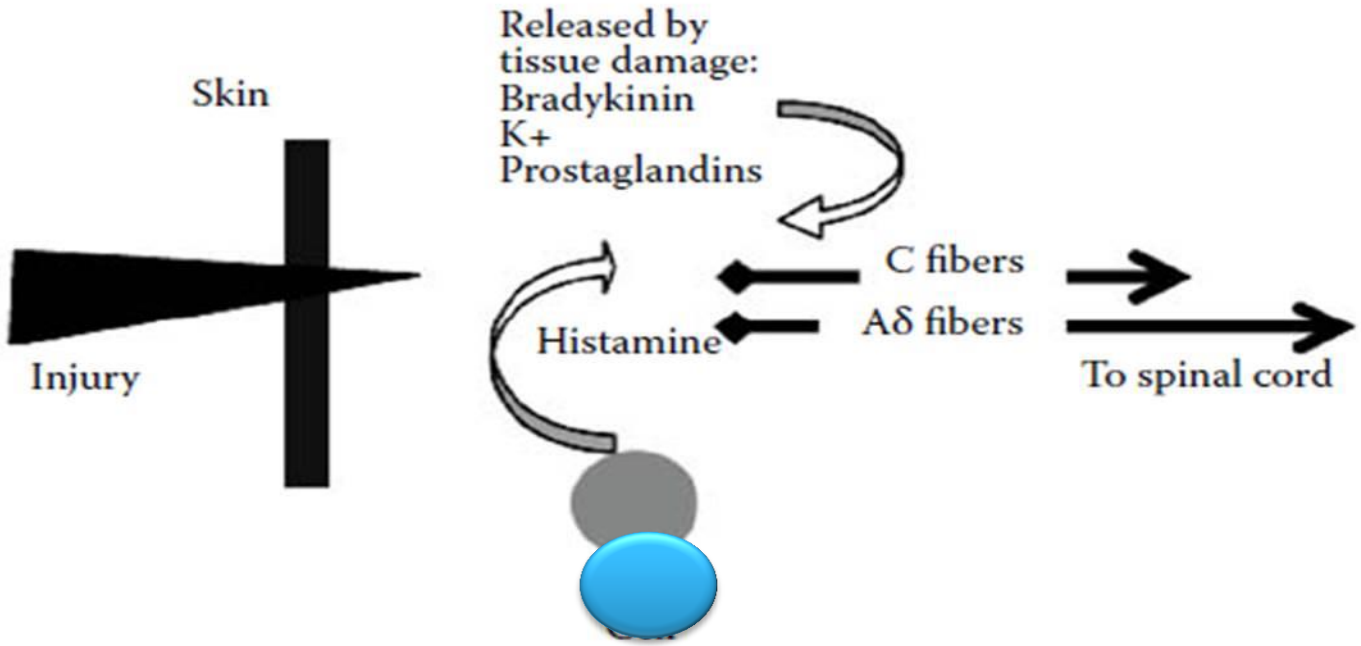




Chemical Substances Released During Tissue Damage

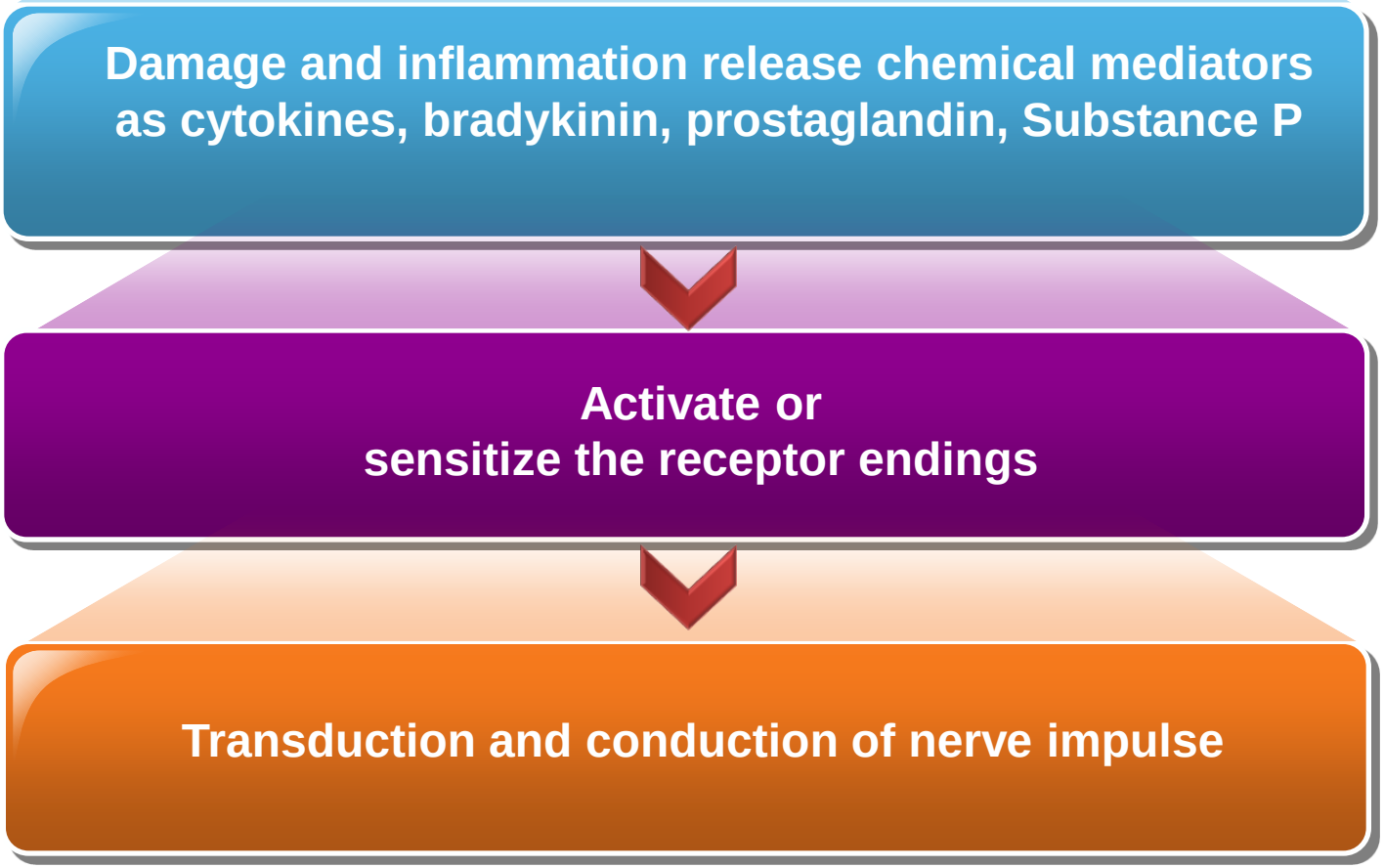
Substance	Source
Potassium	Damaged cells
Serotonin	Platelets
Bradykinin	Plasma
Histamine	Mast cells
Prostaglandins	Damaged cells
Leukotrienes	Damaged cells
Substance P	Primary nerve afferents

Pain Mechanism

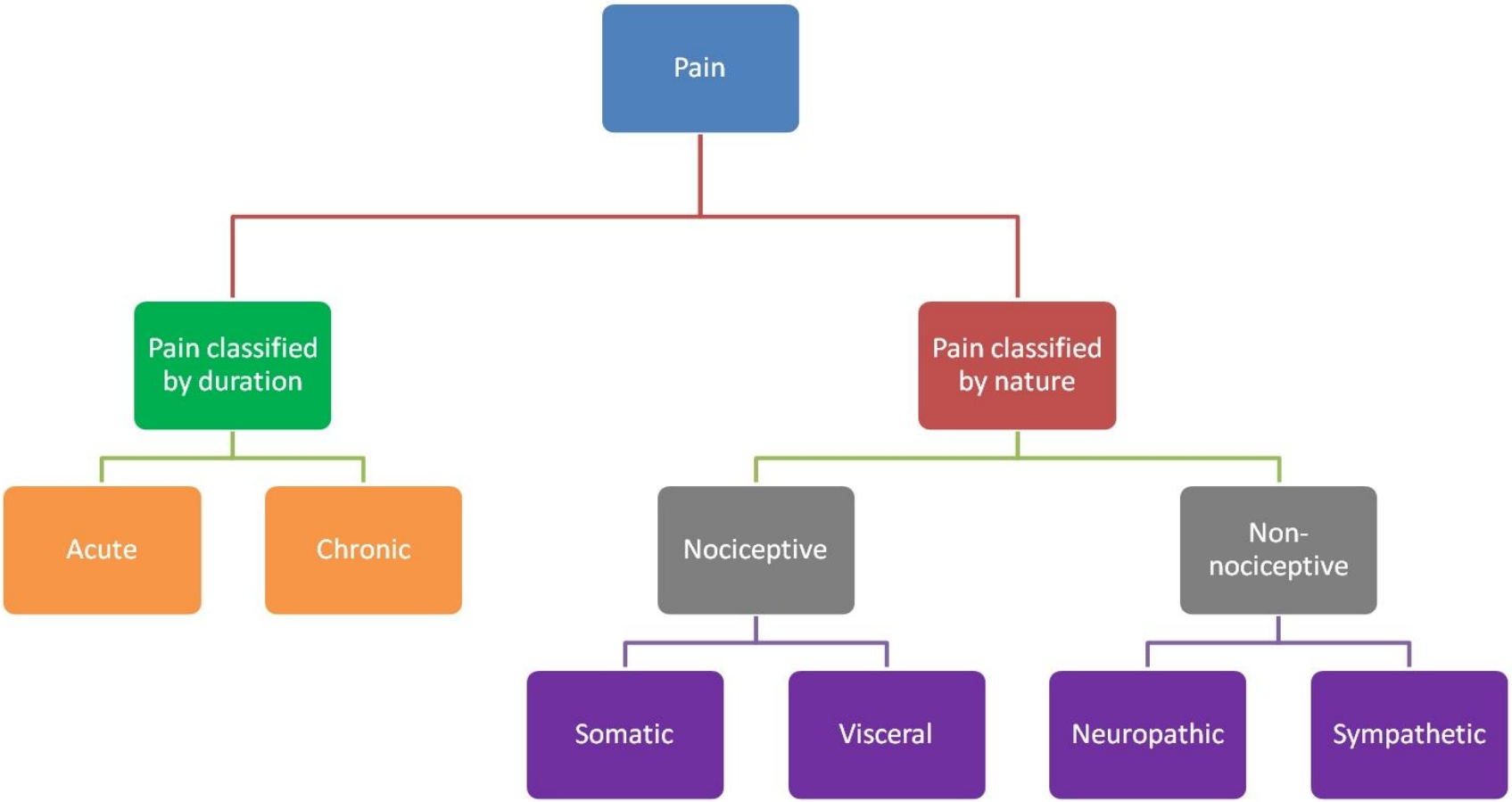


Some chemicals released by tissue damage that stimulates nociceptors. In addition release of substance-P, along with histamine, produce vasodilation and swelling.

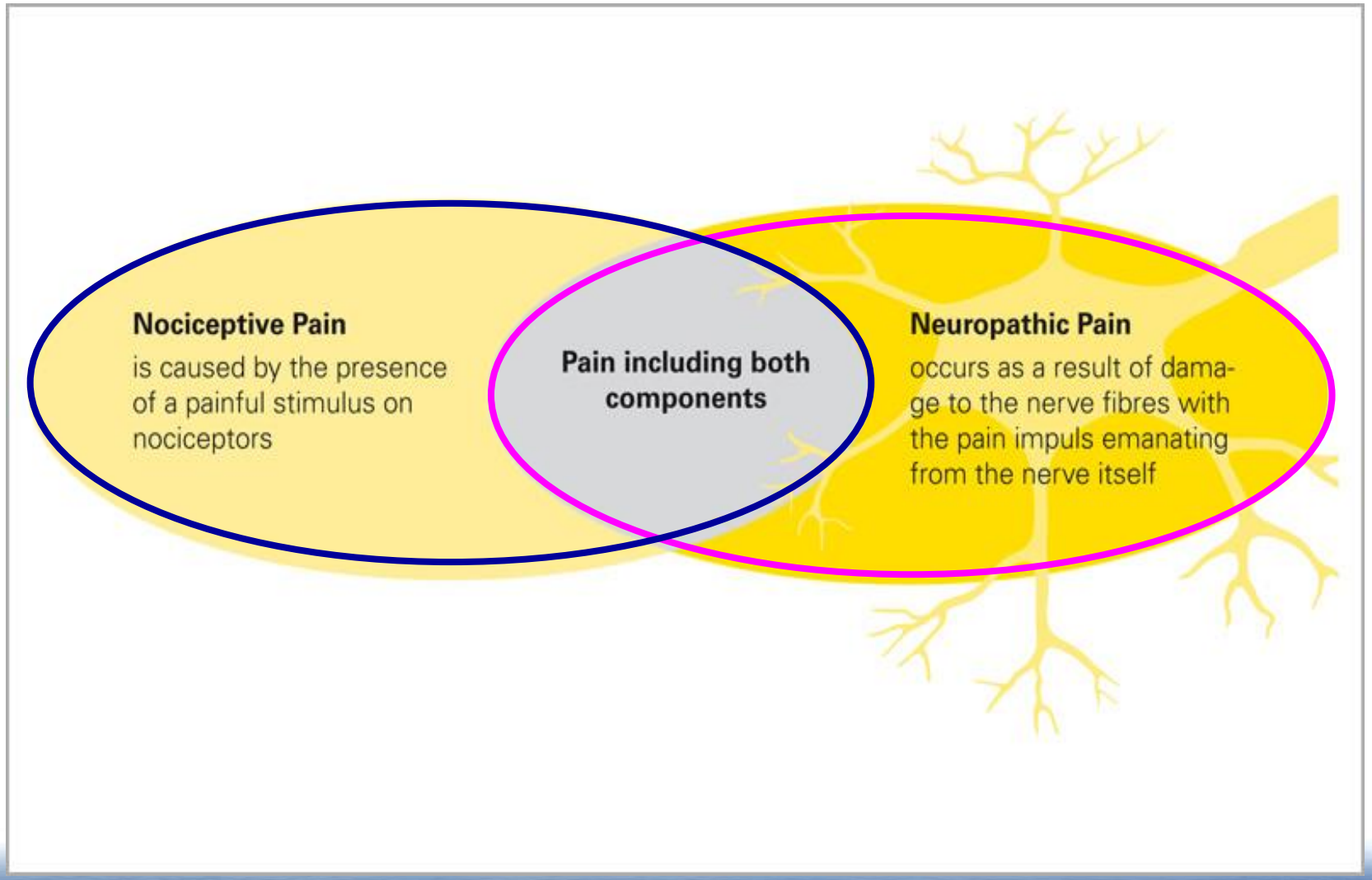
Pain Mechanism



Classification of Pain



Nociceptive & Neuropathic Pain



Differences Between Nociception & Neuropathic Pain

Nociception	Neuropathic pain
Sustained primarily by the nociceptive system	Sustained by aberrant processes in PNC or CNS
Proportionate to stimulation of the nociceptors when acute	Disproportionate to stimulation of the nociceptors
Serve as a protective function, normal pain when acute	Serve no protective function
Pathological when chronic	Pathological pain
Respond to common analgesics	Resistant to common analgesics
E.g.: acute burn, bone fracture and other similar somatic & visceral pain	E.g.: painful diabetic & peripheral neuropathies, sympathetic-mediated pain, nerve inflammation, compression

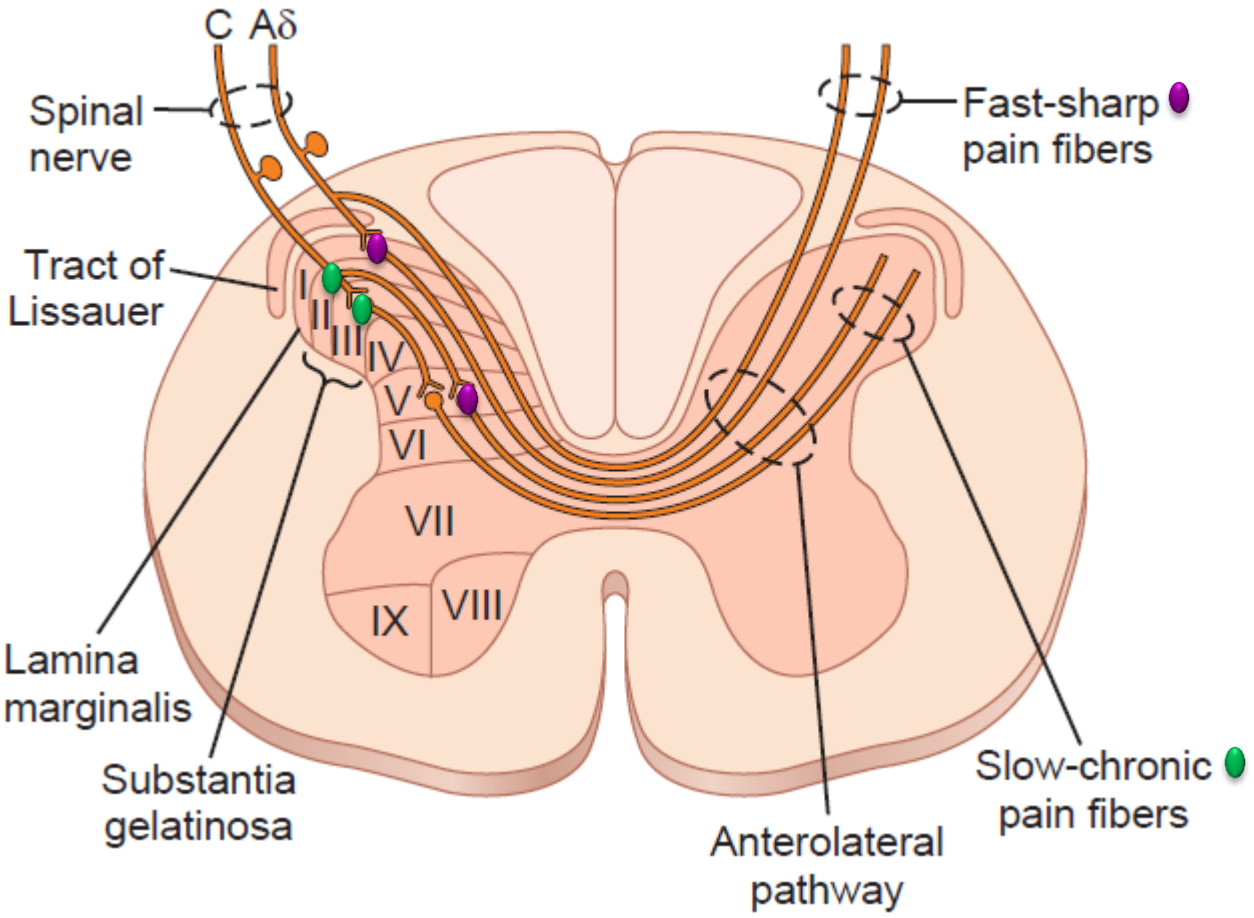
Qualities of Pain

(Phenomenon of double-pain)

Fast/immediate (1st) pain vs slow/delayed (2nd) pain

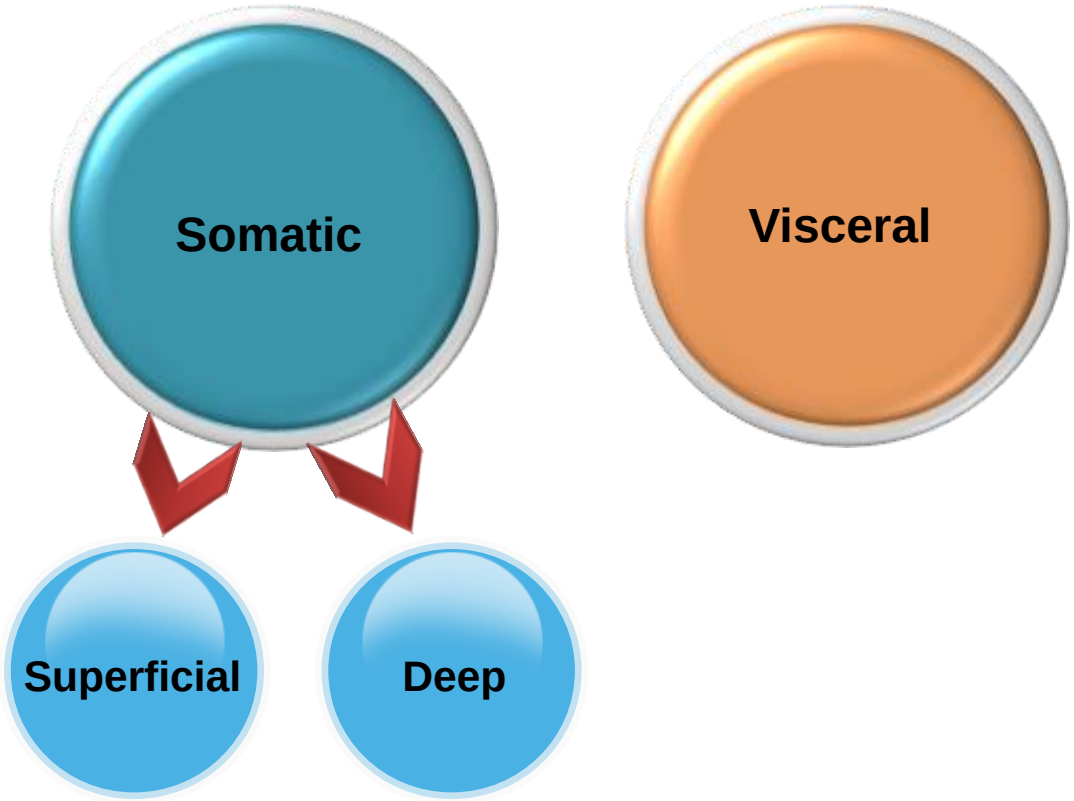
Fast (immediate) pain	Slow (second) pain
▪Sharp, intense, pricking, well localized	▪Burning, aching, throbbing "unbearable" diffuse, dull, chronic pain, poorly localized
▪Felt within **0.1 sec** on stimulation of Mechanical & Thermal nociceptors	▪Felt after **1 sec** or more on stimulation of Polymodal receptors
▪Associated with reflex withdrawal	▪Associated with destruction of tissue
▪ Usually somatic not visceral	▪Can occur in skin or internal organ/tissue
▪Transmitted by **Aδ- fibers** in the peripheral nerves & centrally by **Neospinothalamic Tract**	▪Transmitted by **C fibers** peripherally & centrally by **paleospinothalamic Tract**
▪ Terminate at I and V laminas	▪Terminate at II and III laminas
▪ Neurotransmitter – Glutamate	▪Neurotransmitter – Substance-P
▪20% pain conduction	▪80% of pain conduction

Transmission of both "fast-sharp" and "slow-chronic" pain signal into and through the spinal cord on their way to the brain.

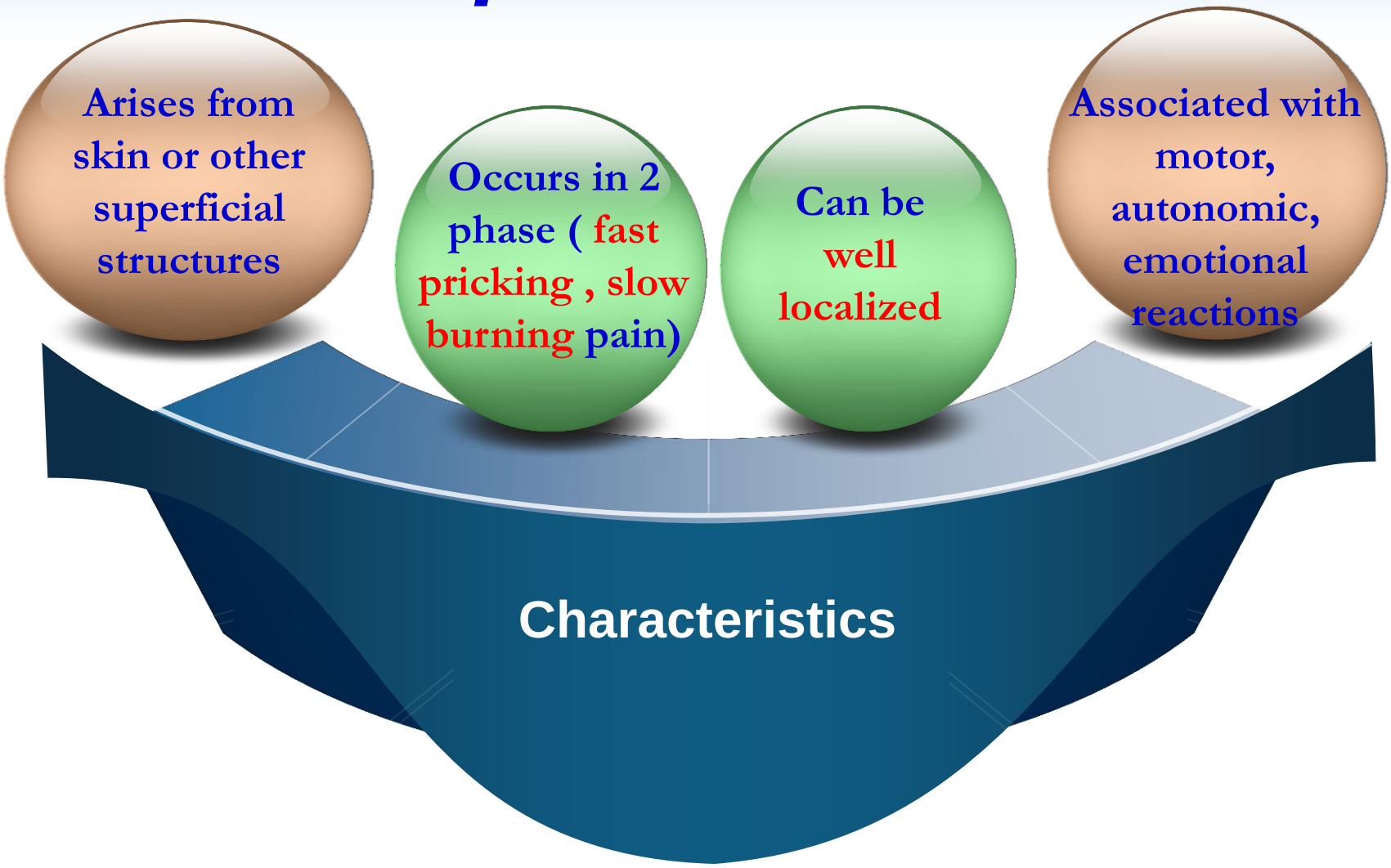


Types of Pain

- Pain can be classified according to the site of stimulation into:-



Superficial Pain



Deep Pain

Arises from muscles, joints, periosteum, tendons & ligaments

Diffuse, slow prolonged conducted by type C fibers

May be referred , initiate reflex contraction of nearby muscles

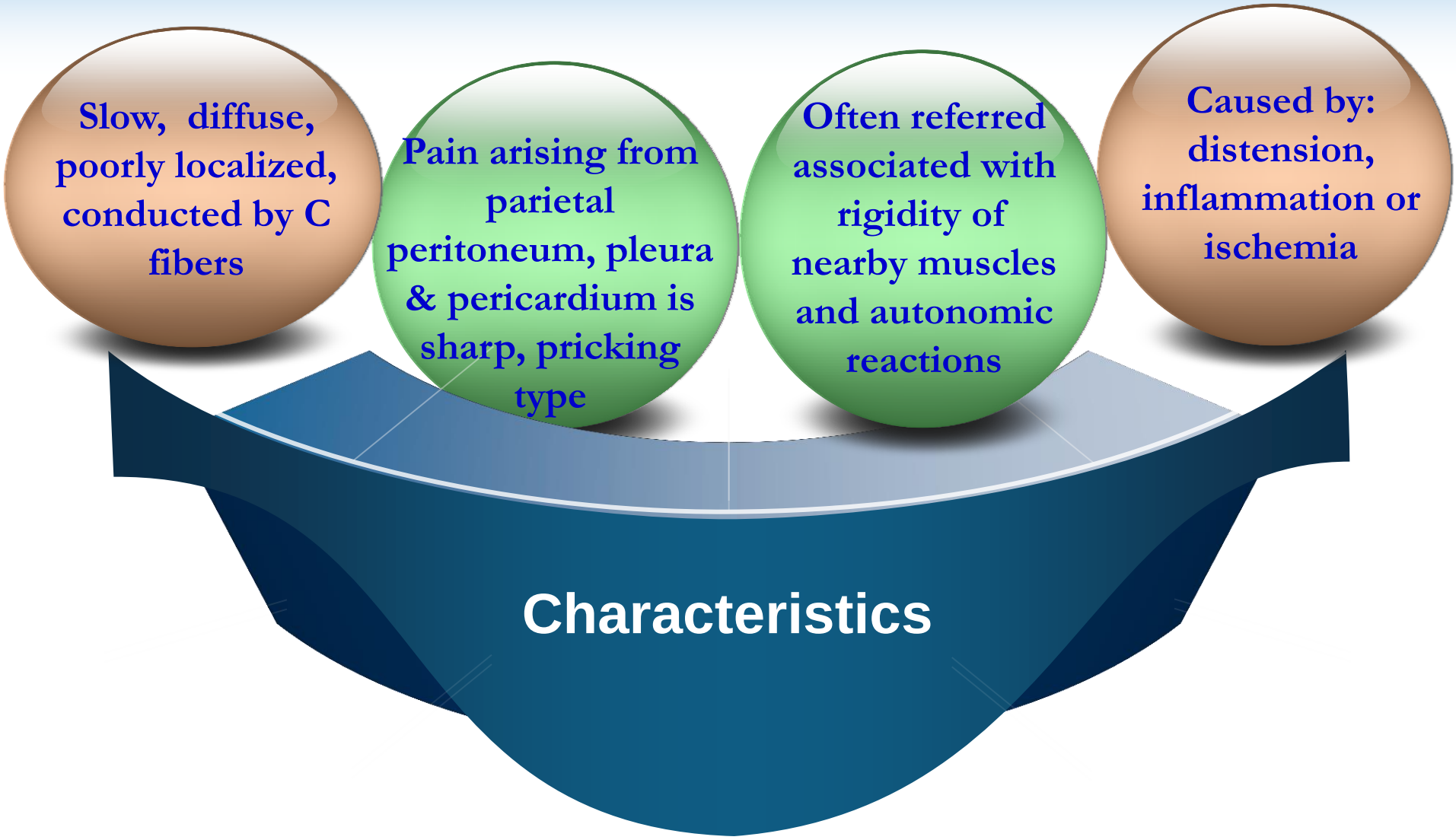
Caused by: trauma, bone fracture, inflammation, arthritis, muscle spasm & ischemia

Characteristics

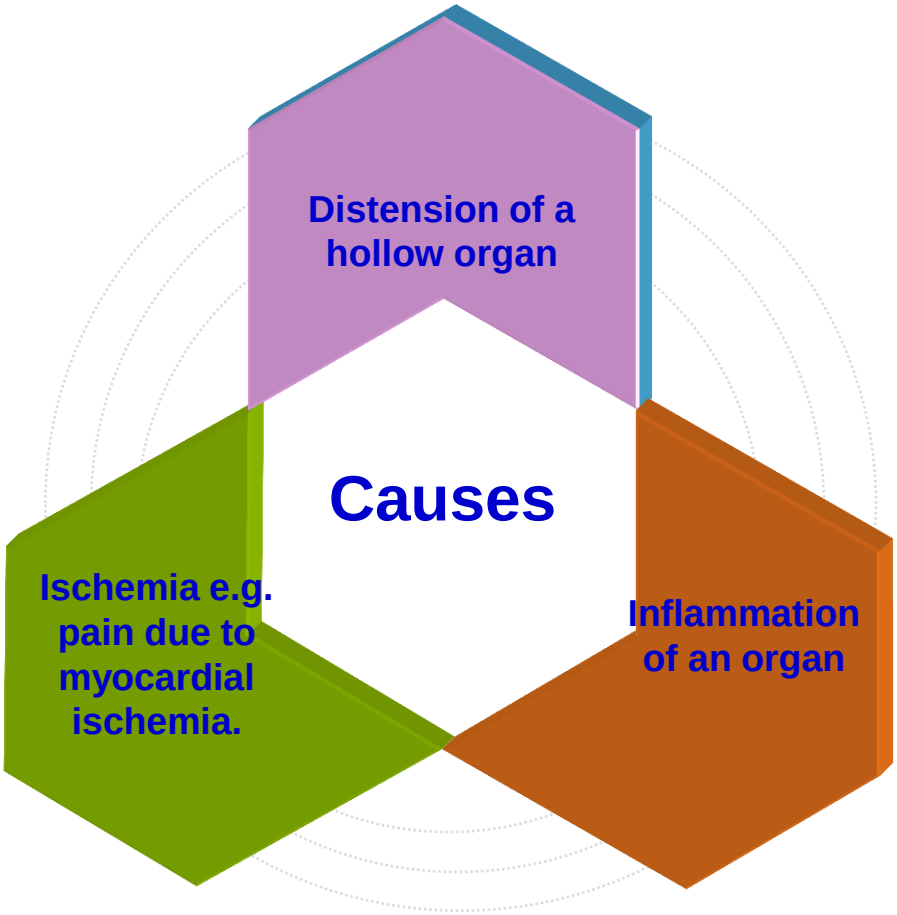
Visceral Pain

- There are few pain receptors in most viscera
- Some viscera are pain insensitive e.g. **liver parenchyma**, **lung alveoli**, **brain tissue**, **visceral layer of peritoneum, pleura and pericardium**.

Visceral Pain….Cont.



Causes of Visceral Pain



N.B: Cutting, crushing are not painful when applied to viscera

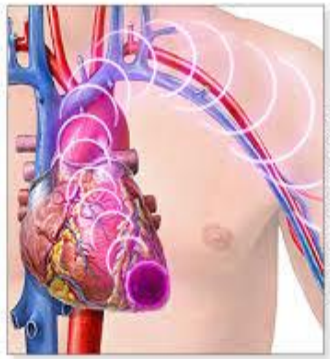
Referred Pain

- This is pain that is felt away from its original site.
- It is most frequent with visceral pain & deep somatic pain but cutaneous pain is not referred.
- Pain is referred according to dermatomal rule i.e. the person generally localizes pain in the dermatomal segment from which the visceral organ originated in the embryo, not necessarily where the visceral organ now lies.
- When pain is both localized and referred it is called radiating pain

Examples of Referred Pain

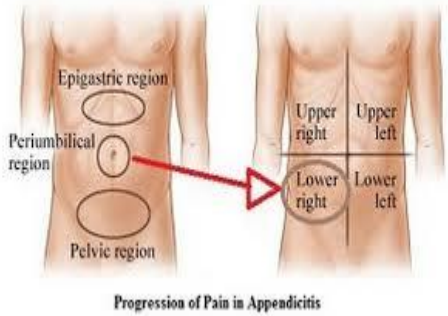
Examples

- **Cardiac pain** → Is referred to the jaw, left shoulder & inner side of left arm



Pain in the chest radiating up to the jaw or down the left (or, less often, right) arm might signal a heart attack

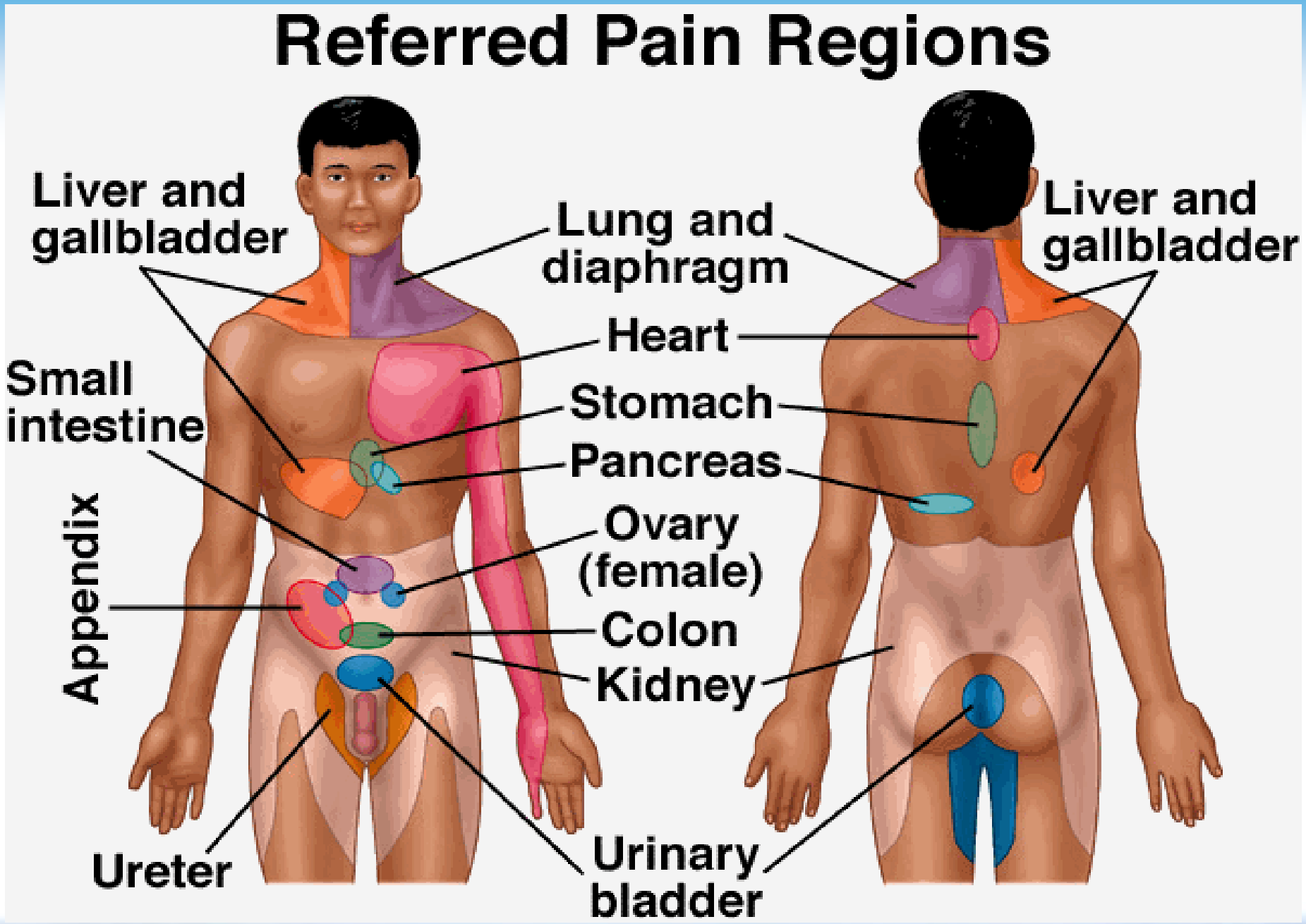
- **Pain of appendicitis** → Is referred to periumbilical region



Progression of Pain in Appendicitis

- **Pain from ureter** → Is referred to testicular region

Referred Pain Regions

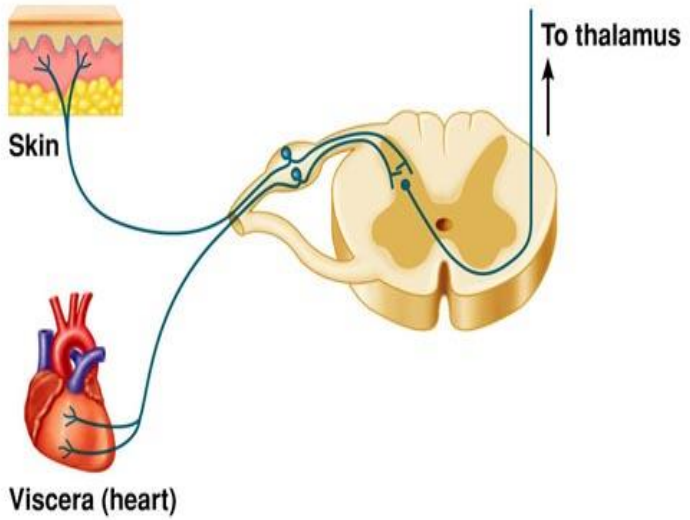


Organ	Site of referred pain
Meninges	Back of head &neck
Heart	Central chest, left arm
Diaphragm	Shoulder tip
Esophagus	Behind sternum
Stomach, duodenum	Epigastrium
Small bowel, pancreas	Around umbilicus
Large bowel, bladder	Lower abdomen
Kidney	Loin
Ureter	Testicles
Trigon of bladder	Tip of penis
Hip	Knee
Appendix	Umbilicus
Uterus	Low back

Mechanism of Referred Pain

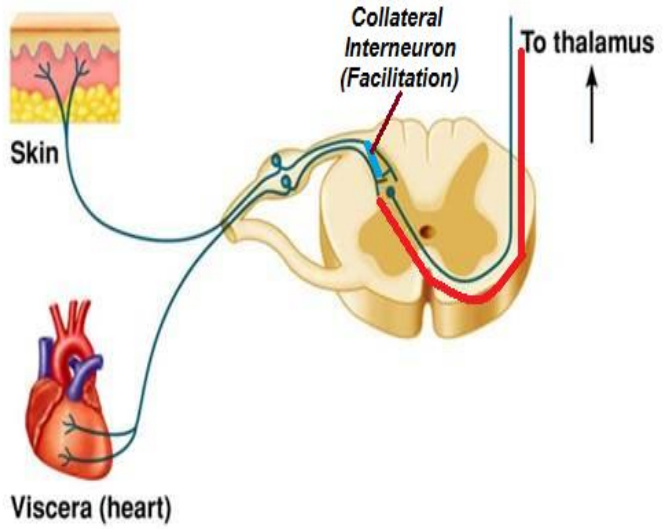
Convergence theory

- Afferent pain fibers from skin area & diseased viscera that develop from same embryonic segment converge on same 2nd order neuron and finally stimulate the same cortical neuron.
- The brain interprets the information coming from visceral nociceptors as having arisen from cutaneous nociceptors, because this is where nociceptive stimuli originate more frequently



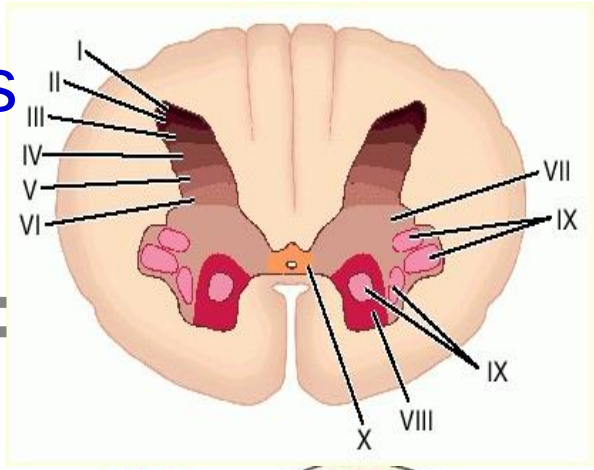
Facilitation theory

- Pain fibers from skin are always carrying impulses, not enough to produce pain.
- Impulses from diseased viscus pass through afferents which give collaterals to ST neurons receiving pain fibers from skin.
- As a result, ST neurons' excitability is raised (they are facilitated) to reach a threshold level.
- The signals reaching the brain are projected to skin area and pain is felt in skin dermatome



Pathway of Pain

Pain sensation is carried by **lateral spinothalamic tracts** which includes 2 separate pathways:-



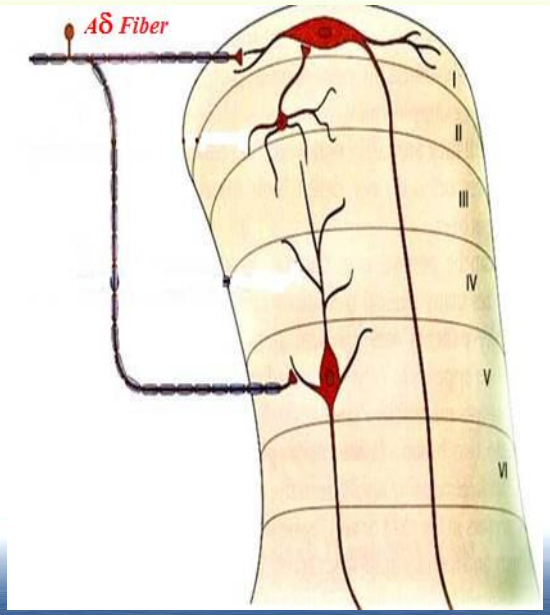
A) <u>The neospinothalamic pathway</u>:

This transmits fast pain.

- **<u>First order neurons</u>**

  Are mainly **Aδ** afferent nerves.

  They terminate at lamina I & V of dorsal horn.

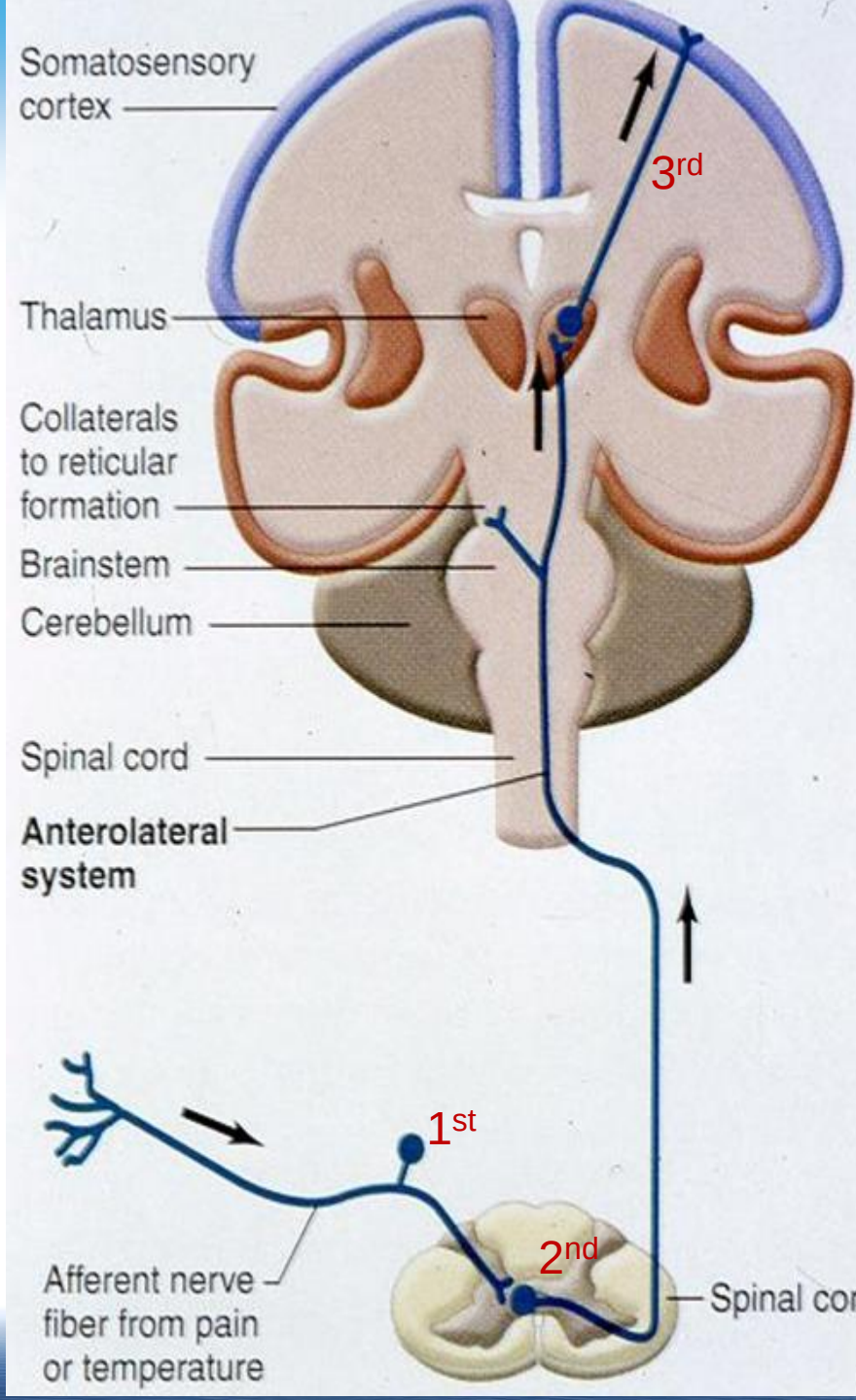


- **Second order neurons**

  These constitute the tract. They start at dorsal horn, cross to opposite side and ascend in lateral column of spinal cord. The fibers ascend in brain stem to terminate in ventrobasal complex of thalamus.

- **Third order neurons**

  These start at thalamus & most fibers project to somatosensory cortex.



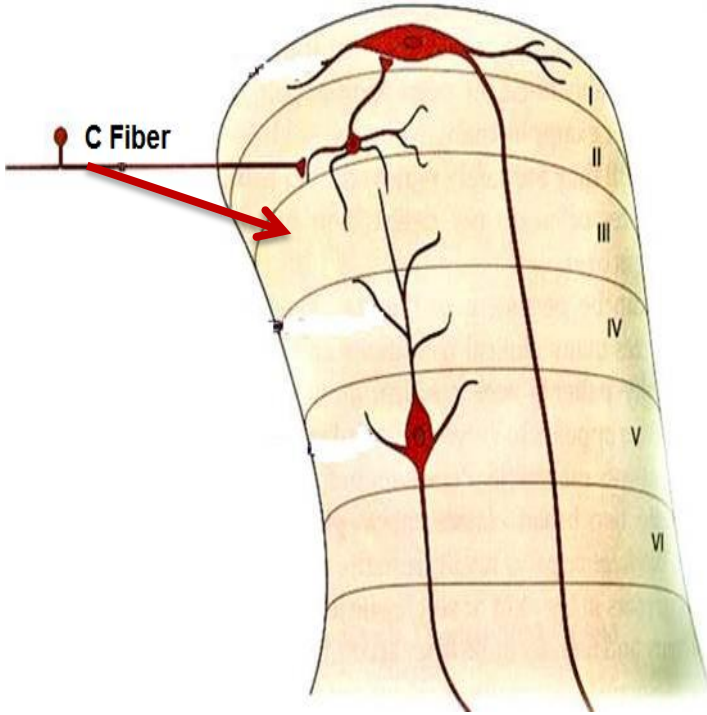
B) The paleospinothalamic pathway:

This transmit slow pain sensation.

- **First order neurons**

  They are mainly **type C fibers**.

  They enter spinal cord via dorsal roots, terminate at substantia gelatinosa in laminae II & III of dorsal horn(substantia gelatinosa).



Second order neurons

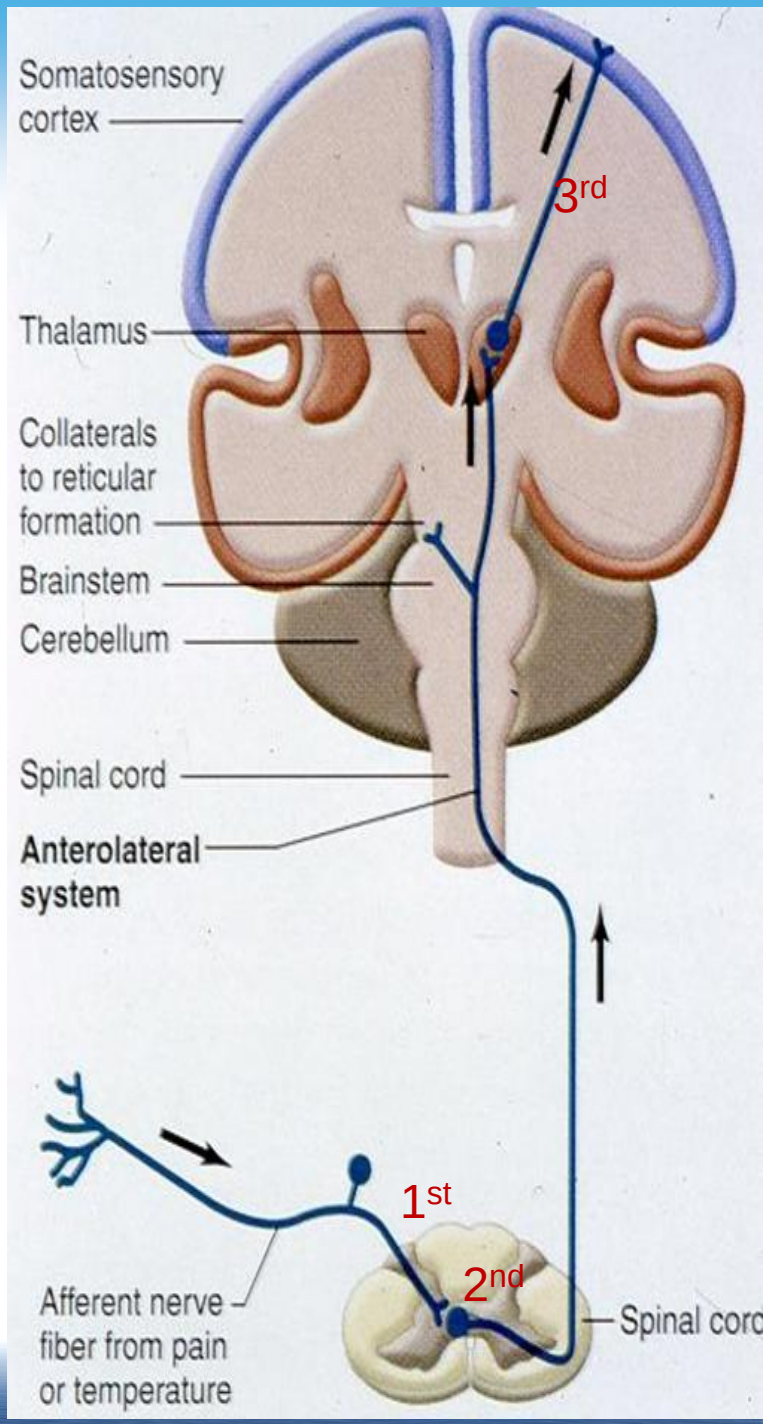
They start at SGR, cross to opposite side in front of central canal, ascend in lateral column of SC & terminate at:-

- Reticular formation of brain stem.
- Intralaminar nuclei of thalamus.
- Hypothalamus & adjacent region of basal brain.

Impulses arriving these regions have strong arousal effects and can be perceived.

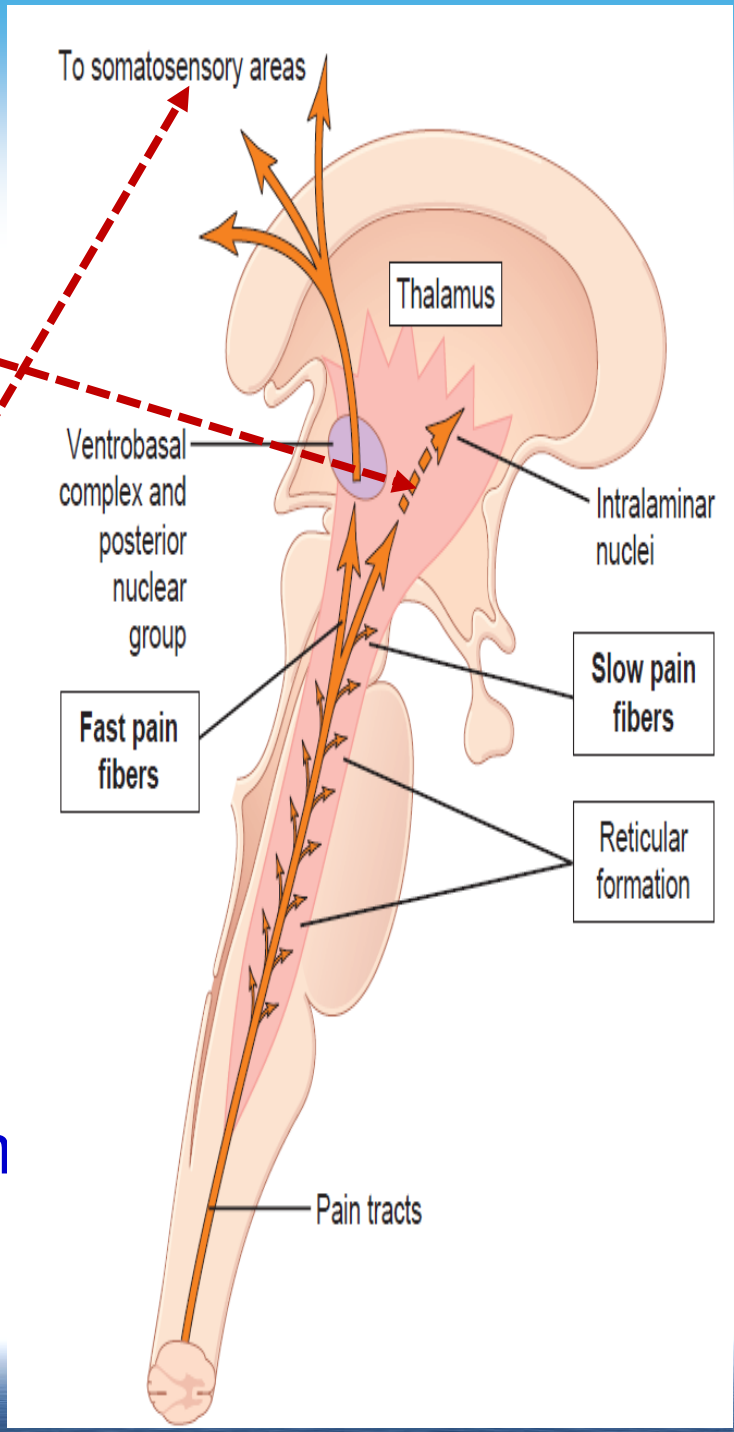
Third order neurons

- These start at thalamus,
- Few fibers project to cerebral cortex.



Role of Cerebral Cortex in

- Full perception of pain occurs when signals enter RF of brain stem, thalamus & basal regions.
- Somatosensory cortex plays important role in topognosis i.e. **localization & interpretation of pain quality.**
- Fast pain is localized better than slow pain because signals carried in neospinothalamic tract reach somatosensory cortex, while a small proportion of paleospinothalamic pathway reach there.




Thank You!