



بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

اللهم صل على محمد وآل محمد

السلام عليكم ورحمة الله وبركاته

# *Physiology of*



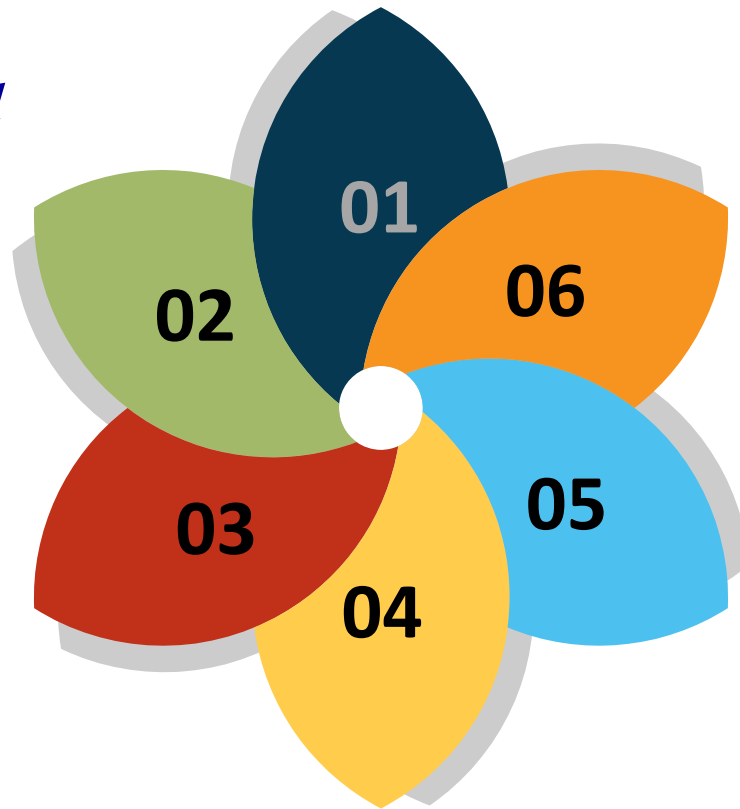
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College of Medicine, K S U*

# Learning Objectives

■ 1- *What is pain and its significance*

■ 2- *Pain receptors & mechanism of stimulation*

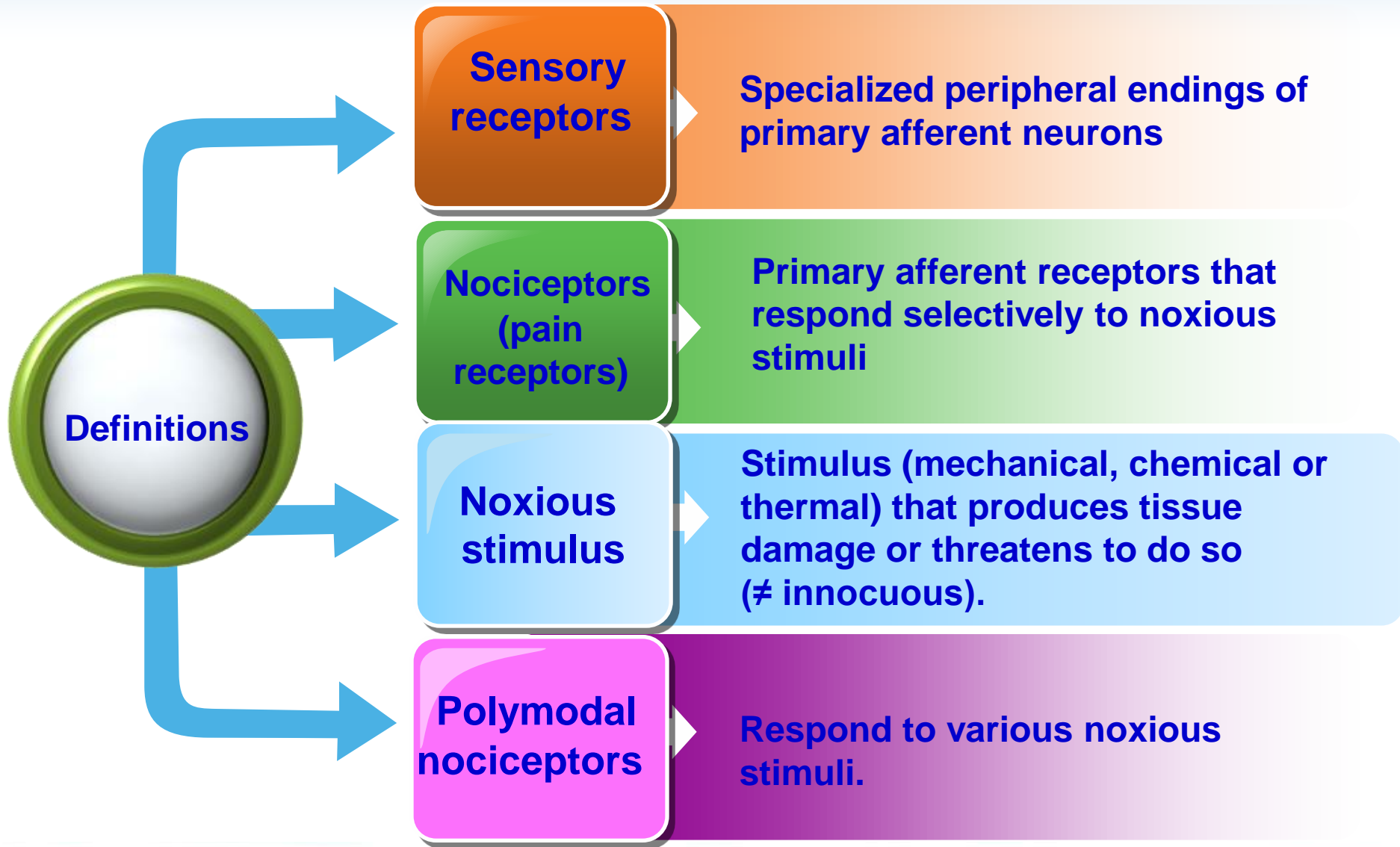
■ 3- *Qualities & Types of pain*



■ 6- *Role of thalamus and cerebral cortex in pain perception*

■ 5- *Pathway of pain*

■ 4- *Referred pain*

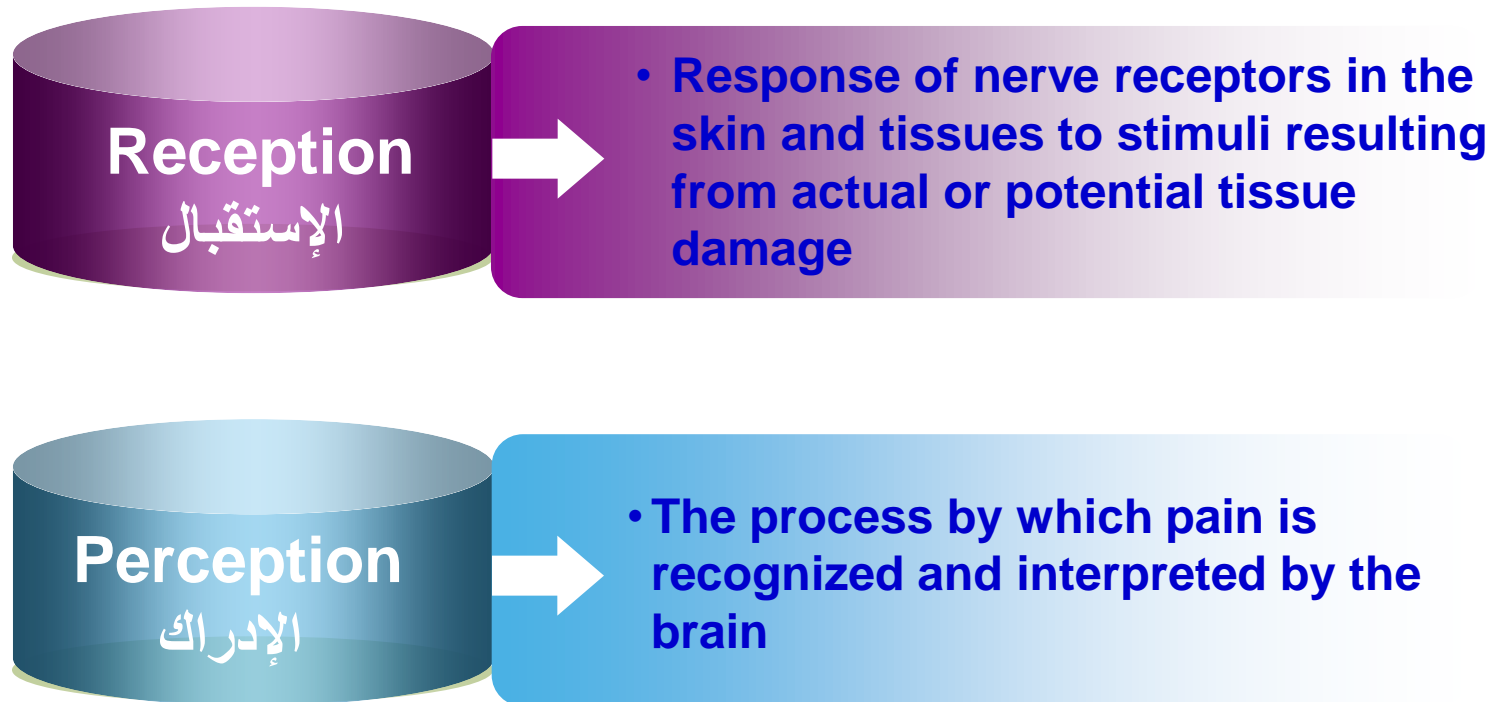


# Significance of Pain: Why do we feel pain?

- 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



# 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)*



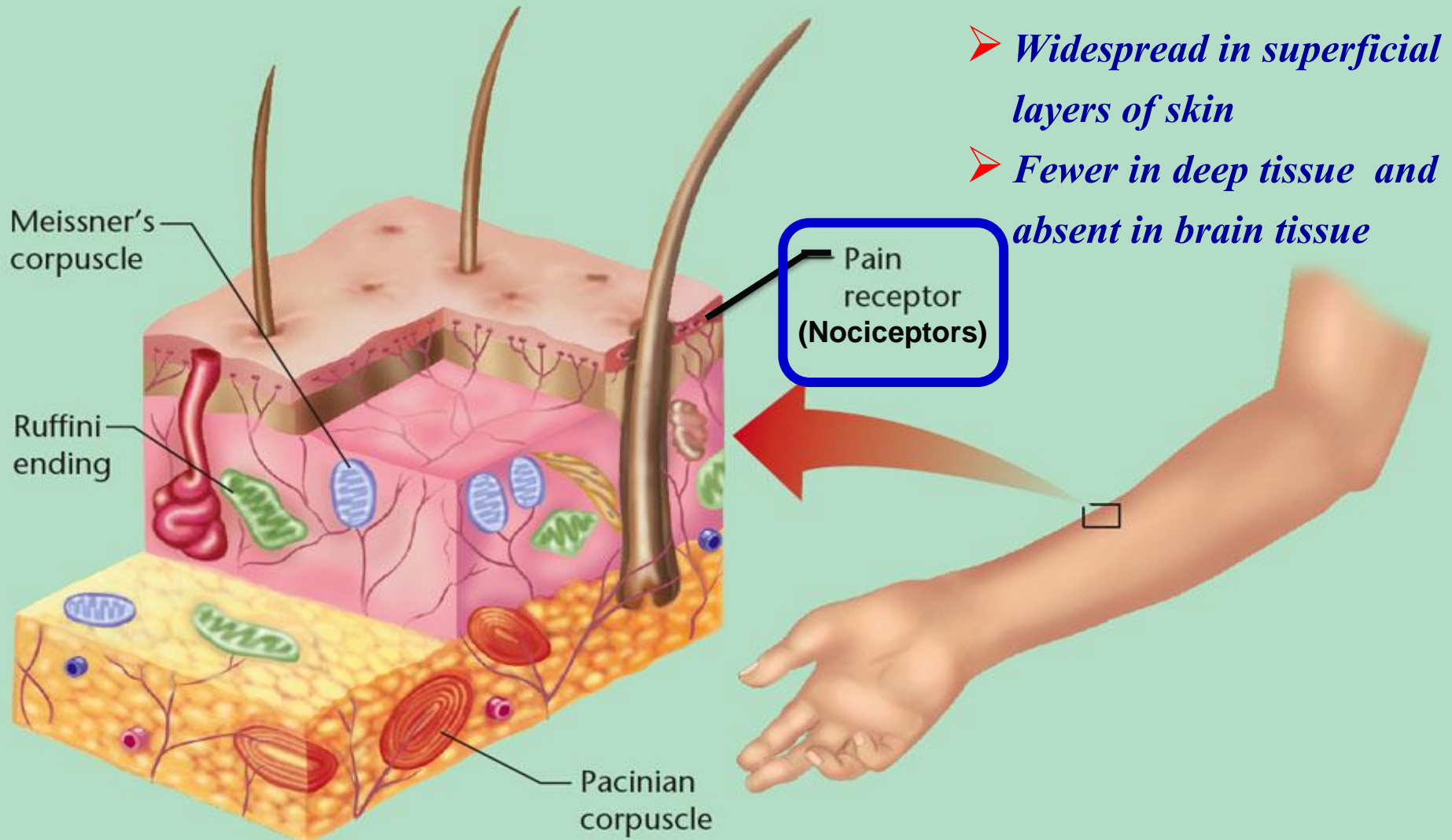
**Sir Charles Scott  
Sherrington**



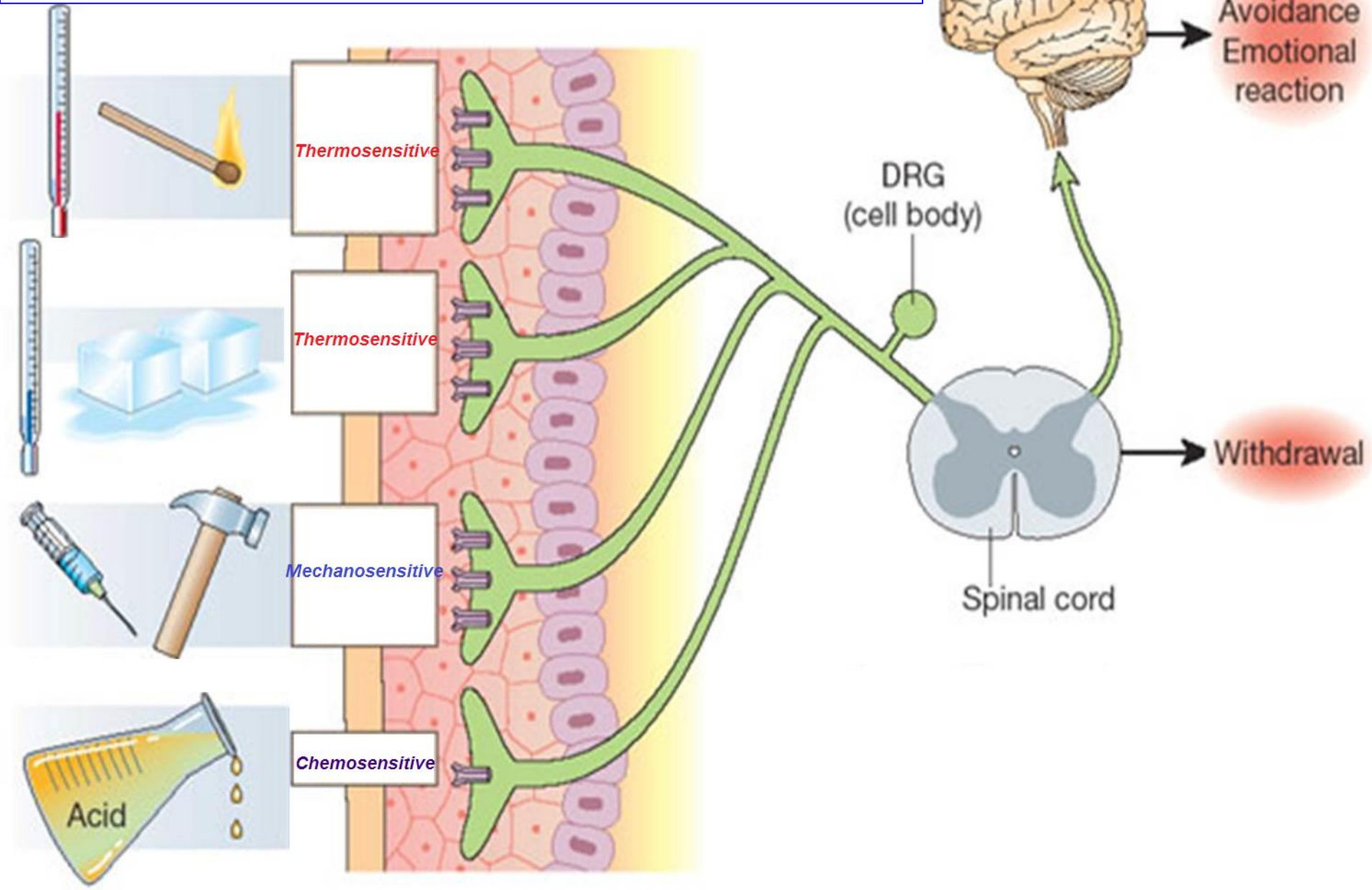
# What are the Characteristics of Nociceptors?

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

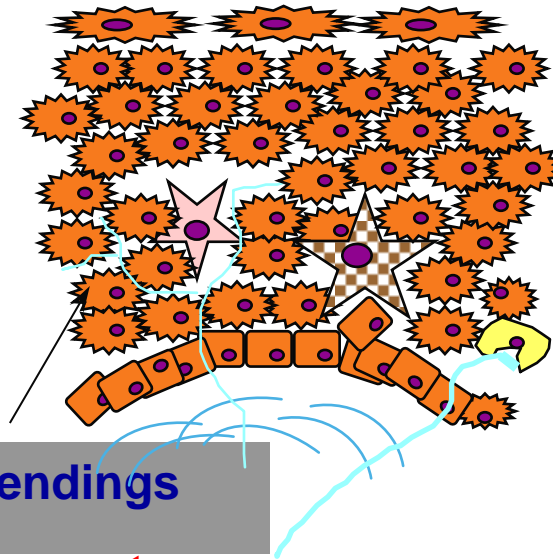
# Distribution of Pain Receptor(Nociceptors)



# Nociceptors are Polymodal



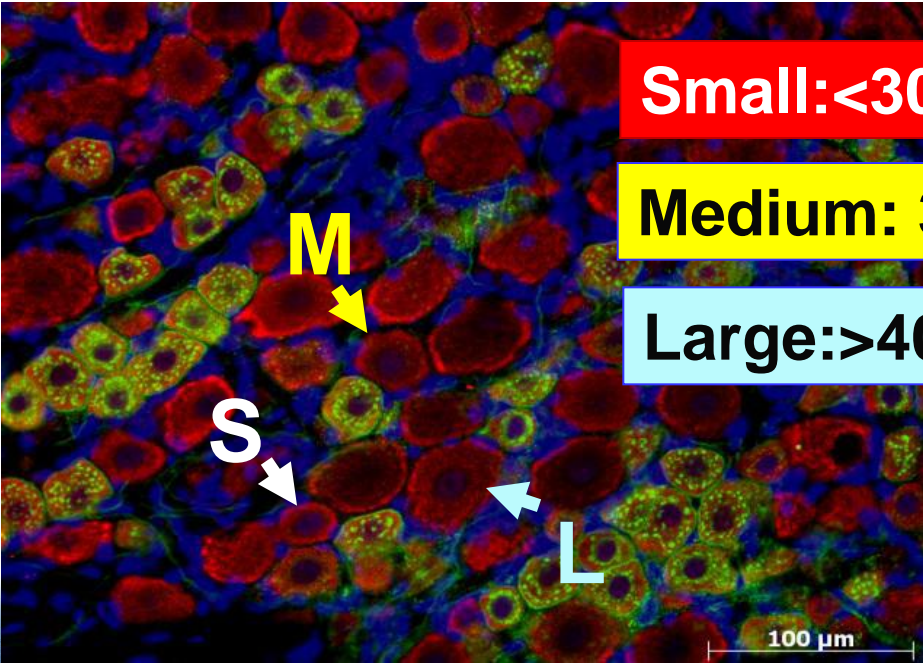
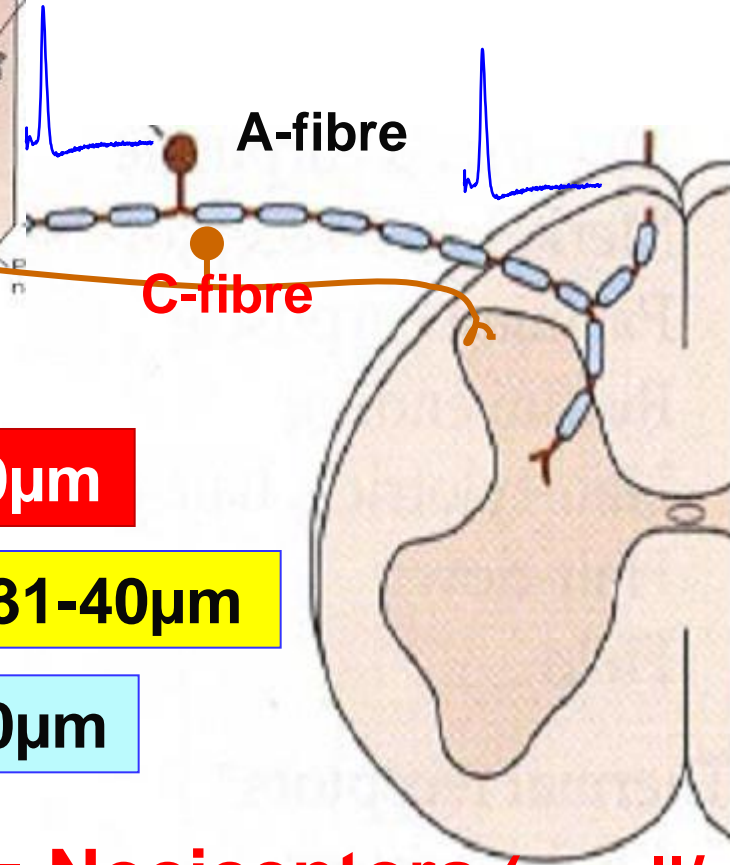
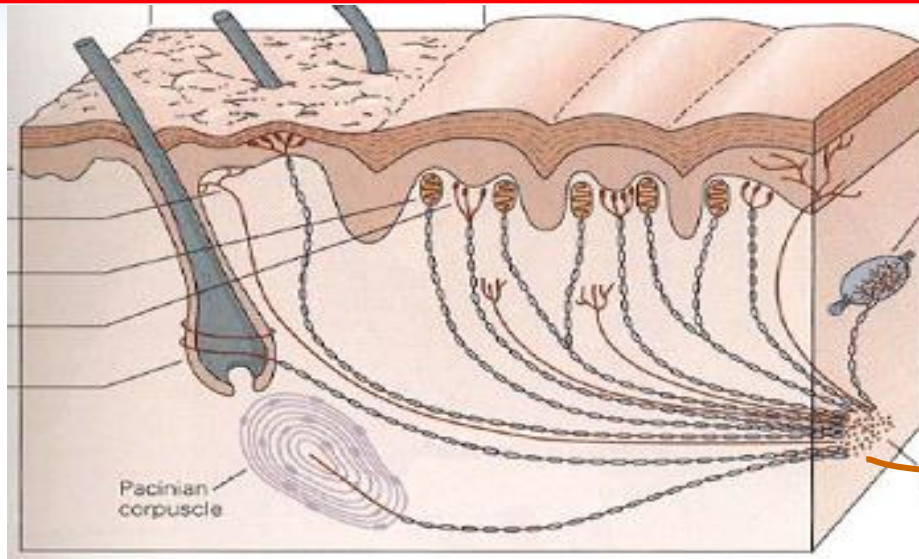
- All pain receptors are free nerve endings of :
  - 1- **Unmyelinated C fibers** (diameter 0.4 – 1.2  $\mu\text{m}$  with conduction velocity 0.5 - 2 m/s)
  - 2- **Small diameter myelinated  $A\delta$  fibers** (diameter fine 2 - 5  $\mu\text{m}$  with conduction velocity 12 - 30 m/sec..)



Free endings

Pain receptors

# Type-A & Type-C Fibers



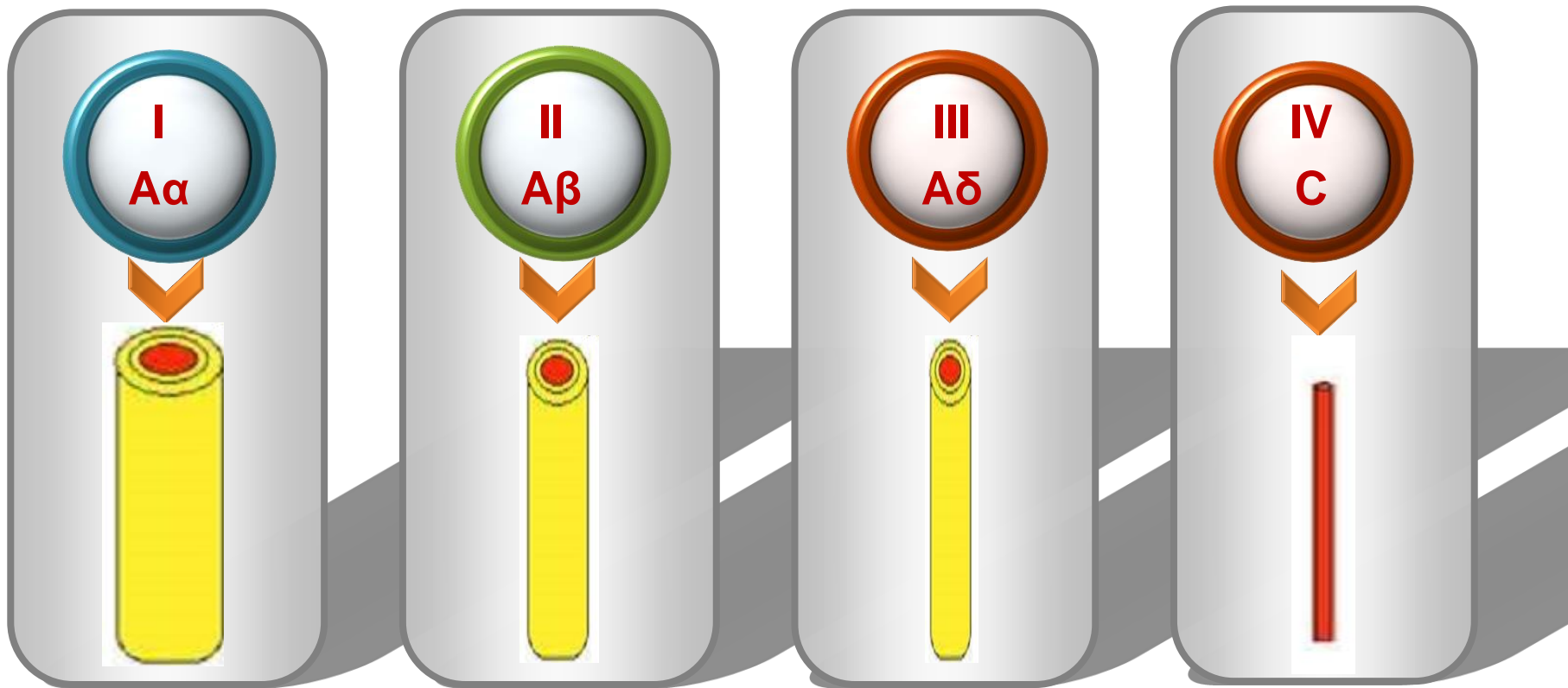
Small: <math>< 30\mu\text{m}</math>

Medium: 31-40µm

Large: >40µm

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

# Classification of Nerve fibres



Diameter ( $\mu\text{m}$ ) **10-20**  
Conduction  
Velocity (m/s) **70-120**

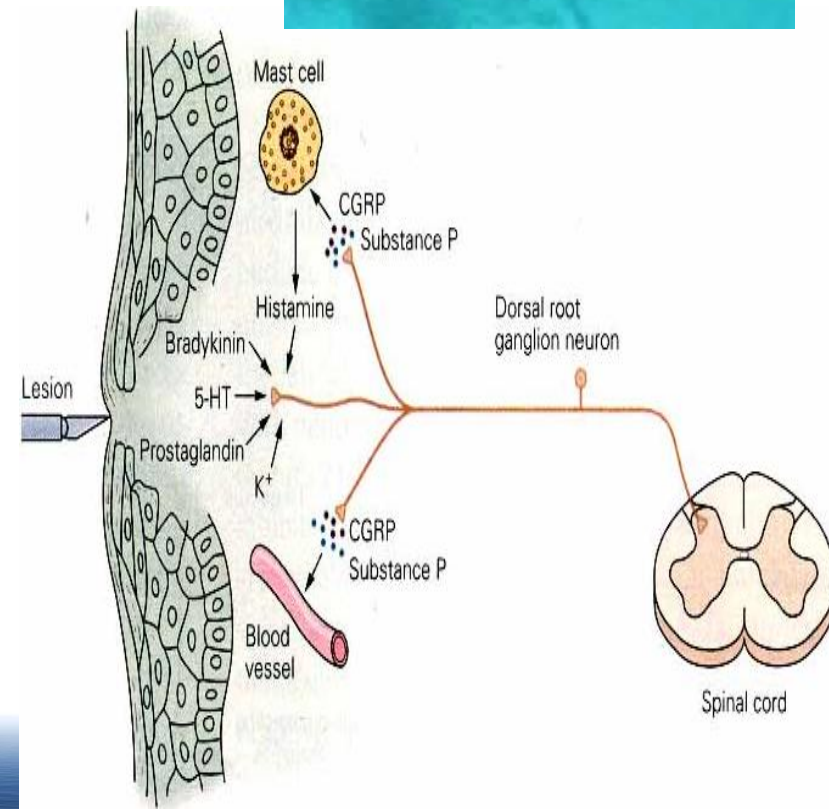
**5-10**  
**30-70**

**2-5**  
**5-30**

**0.5-2**  
**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.

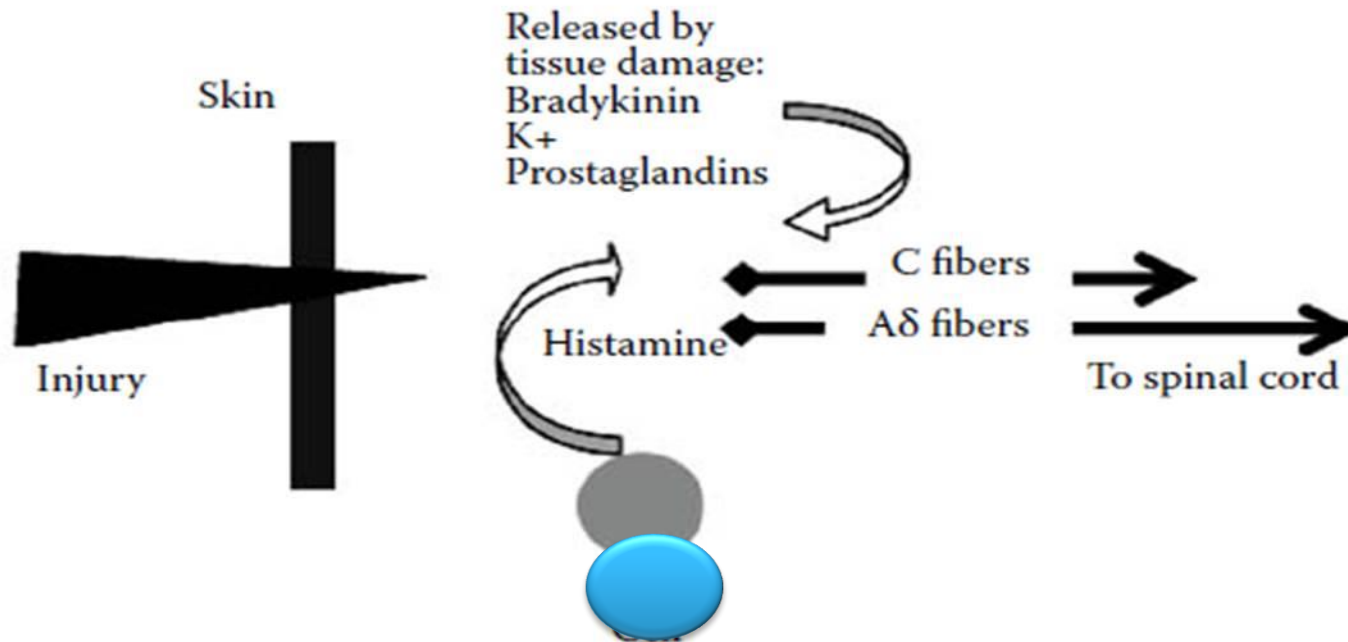


# Chemical Substances Released During Tissue Damage

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



# 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**

**Damage and inflammation release chemical mediators as cytokines, bradykinin, prostaglandin, Substance P**

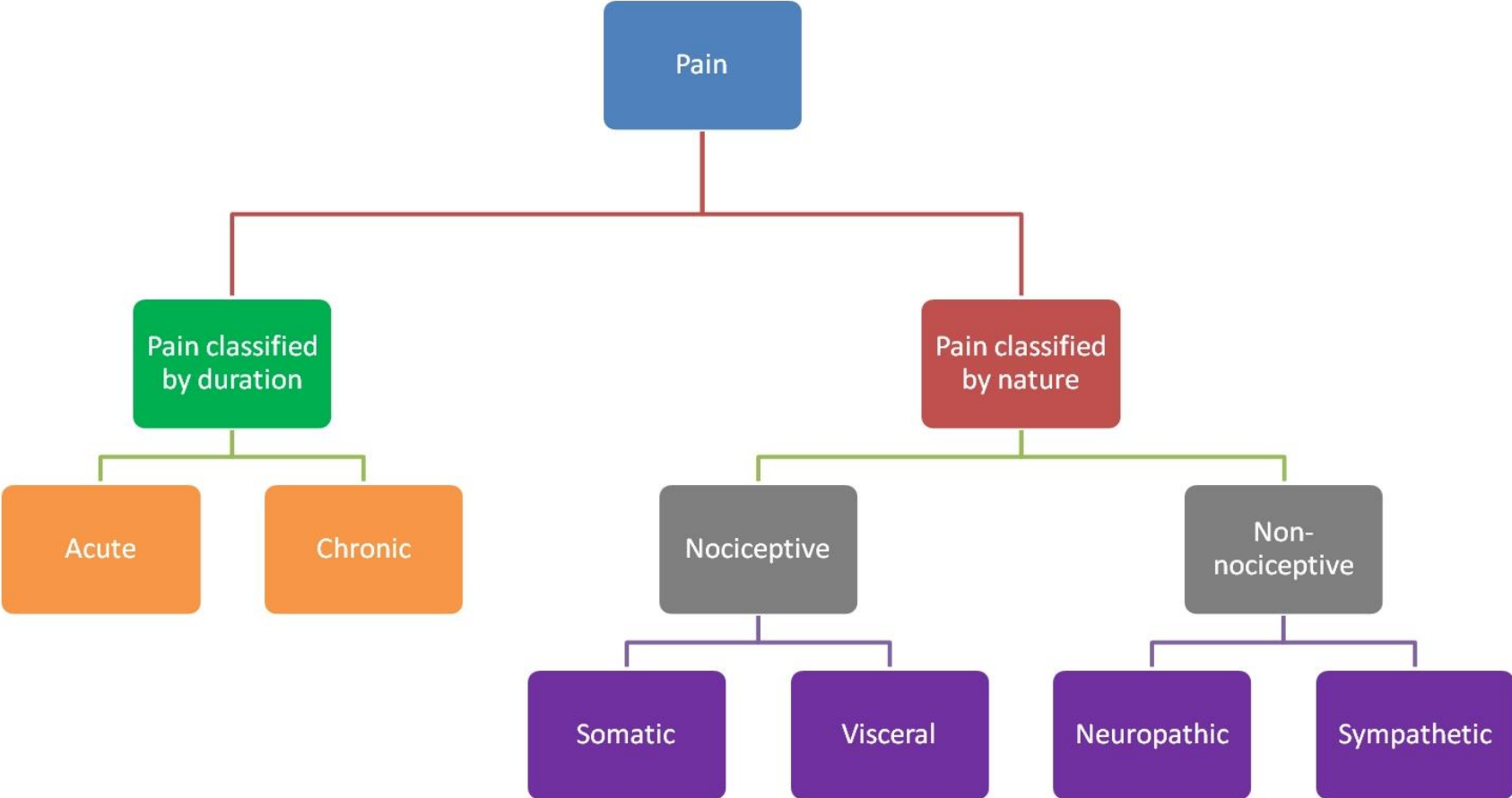


**Activate or sensitize the receptor endings**

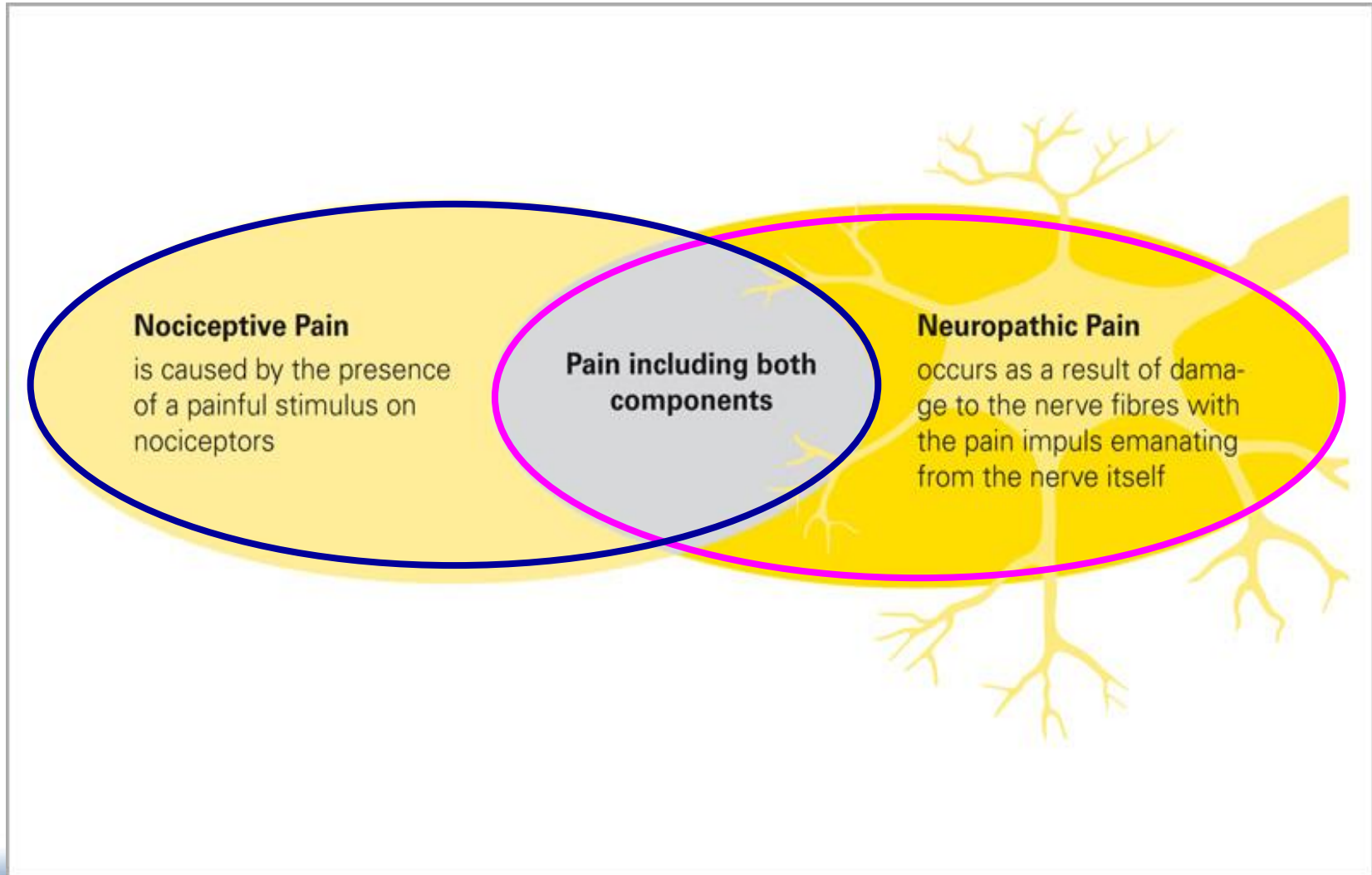


**Transduction and conduction of nerve impulse**

# Classification of Pain



# Nociceptive & Neuropathic Pain



# Differences Between Nociception & Neuropathic Pain

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

# Qualities of Pain

## (Phenomenon of double-pain)

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

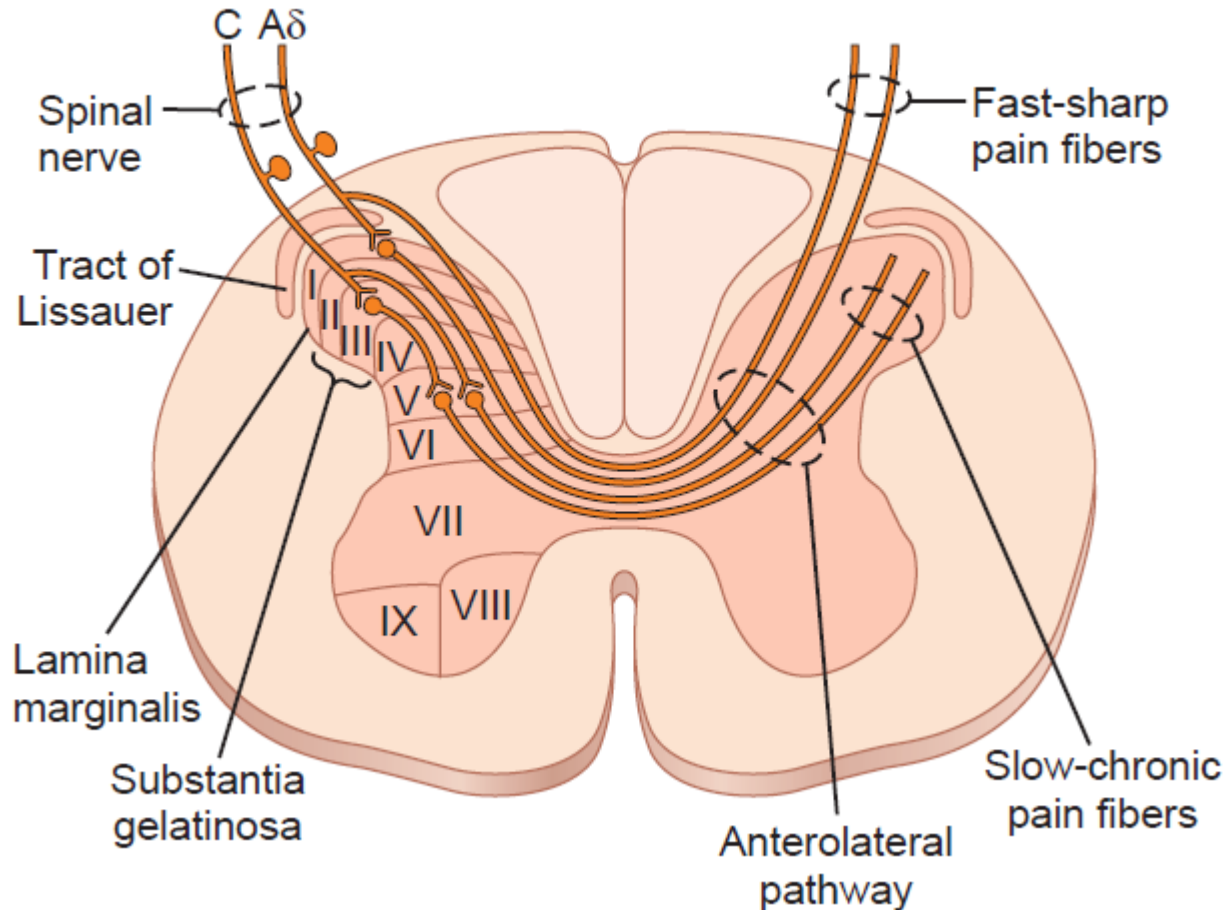
### *Fast (immediate) pain*

- Sharp, intense, pricking, well localized
- Felt within **0.1 sec** upon stimulation of Mechanical & Thermal nociceptors
- Associated with reflex withdrawal
- Usually somatic not visceral
- Transmitted by **A $\delta$ - fibers** in the peripheral nerves & centrally by **Neospinothalamic Tract**
- Terminate at I and V laminae
- Neurotransmitter – glutamate
- 20% pain conduction

### *Slow (second) pain*

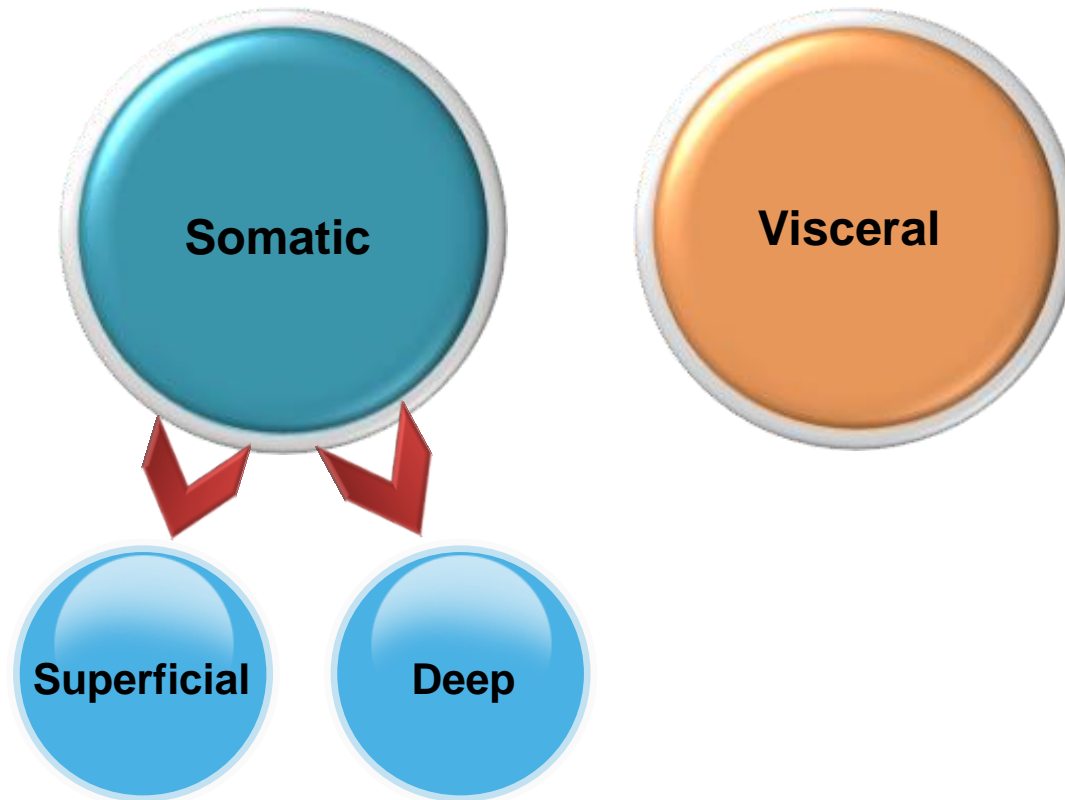
- Burning, aching, throbbing “unbearable” diffuse, dull, or chronic pain, poorly localized
- Felt after **1 sec** or more upon stimulation of Polymodal receptors
- Associated with destruction of tissue
- Can occur in skin or any internal organ/tissue
- transmitted by **C fibers** peripherally & centrally by **paleospinothalamic Tract**
- Terminate at II and III laminae
- Neurotransmitter – Substance-P
- 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*

*Arises from skin or other superficial structures*

*Occurs in 2 phase ( fast pricking , slow burning pain)*

*Can be well localized*

*Associated with motor, autonomic, emotional reactions*

**Characteristics**

# *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.*

*Slow, diffuse,  
poorly localized,  
conducted by C  
fibers*

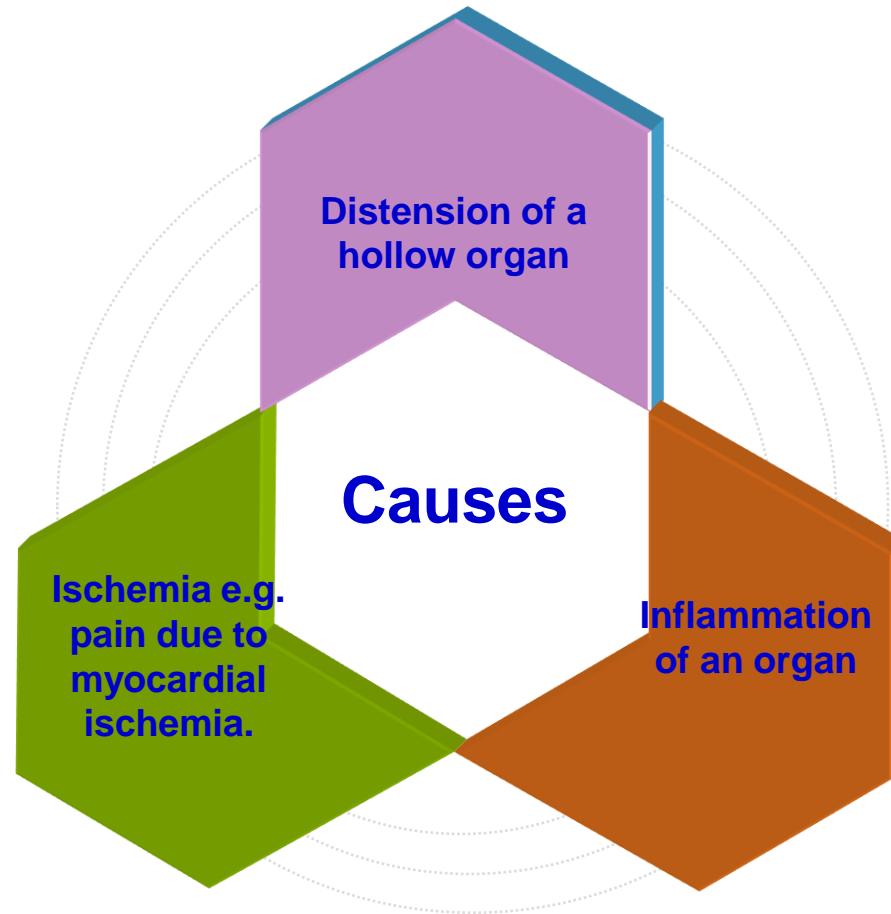
*Pain arising from  
parietal peritoneum,  
pleura & pericardium  
is sharp, pricking type*

*Often referred  
associated with  
rigidity of nearby  
muscles and  
autonomic reactions*

*Caused by:  
distension,  
inflammation or  
ischemia*

**Characteristics**

# Causes of Visceral Pain



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

# Referred Pain

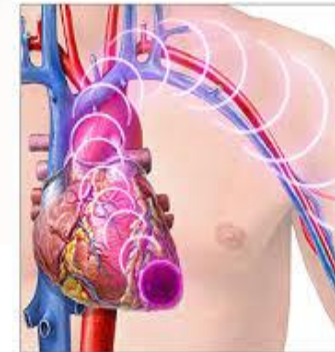
- *This is pain that is felt away from its original site.*
- *It is most frequent with visceral pain & deep somatic pain but **cutaneous pain is not referred.***
- *Pain is referred according to dermatomal rule i.e. the person generally localizes pain in the dermatomal segment from which the visceral 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



**Cardiac pain**

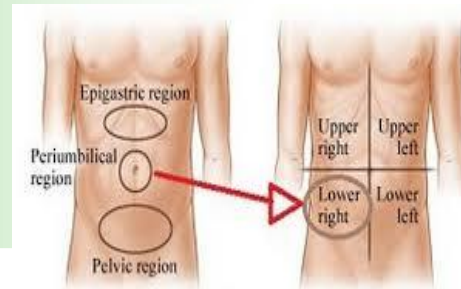
Is referred to the jaw, left shoulder & inner side of left arm



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**

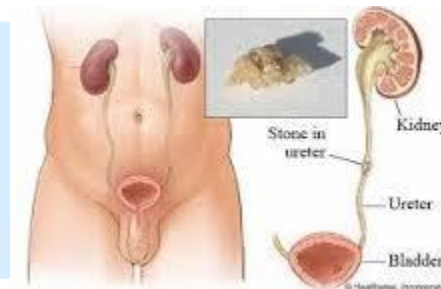
Is referred to periumbilical region



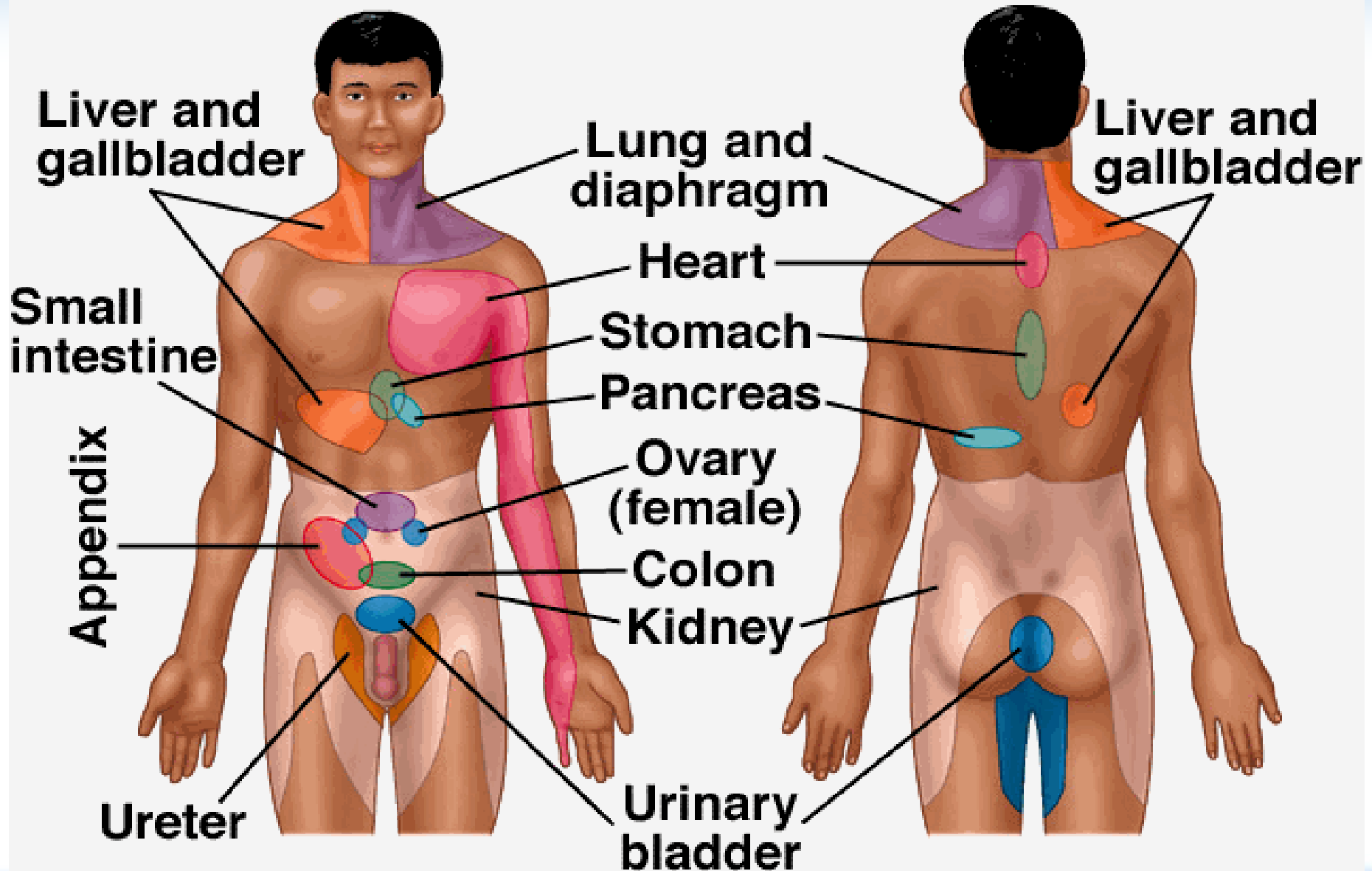
Progression of Pain in Appendicitis

**Pain from ureter**

Is referred to testicular region



# Referred Pain Regions



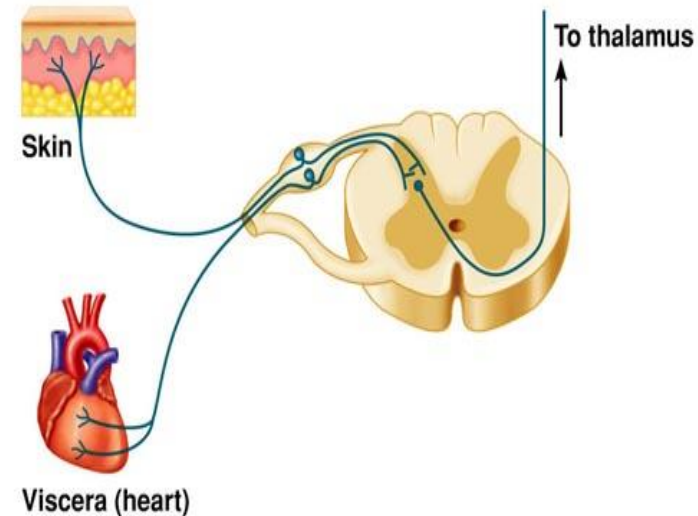


<i>Organ</i>	<i>Site of referred pain</i>
<i>Meninges</i>	<i>Back of head &amp; neck</i>
<i>Heart</i>	<i>Central chest, left arm</i>
<i>Diaphragm</i>	<i>Shoulder tip</i>
<i>Esophagus</i>	<i>Behind sternum</i>
<i>Stomach, duodenum</i>	<i>Epigastrium</i>
<i>Small bowel, pancreas</i>	<i>Around umbilicus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

# Mechanism of Referred Pain

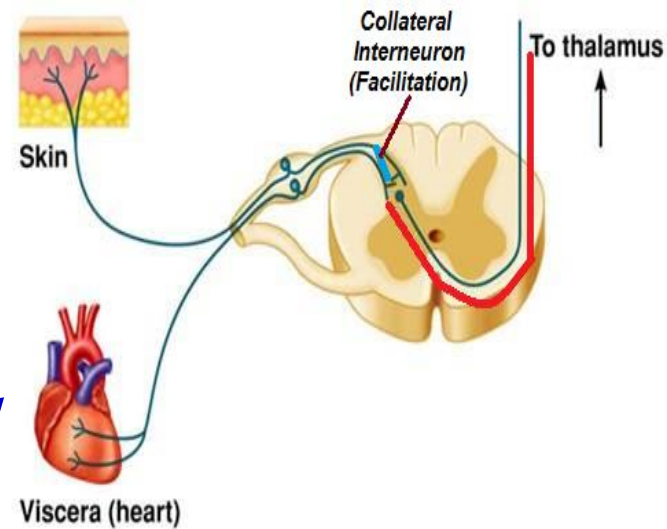
## Convergence theory

- *Afferent pain fibers from skin area & diseased viscera that develop from same embryonic segment converge on same 2<sup>nd</sup> 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:-*

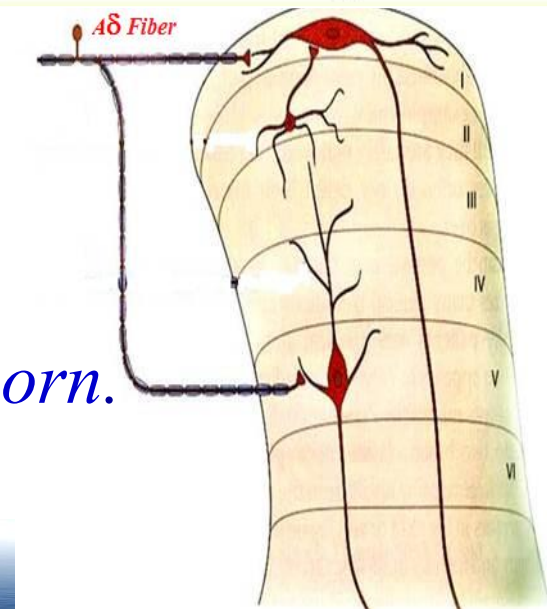
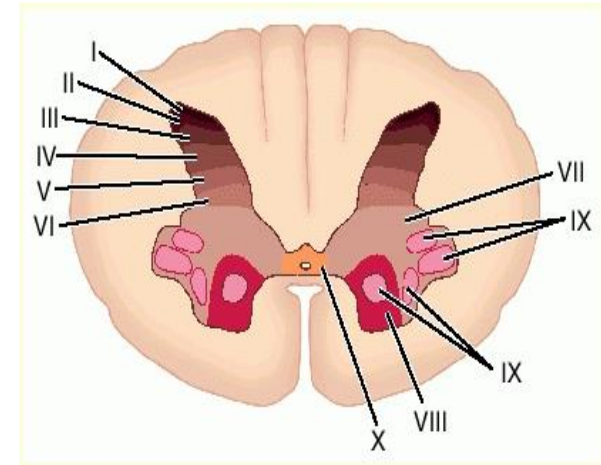
## *A) The neospinothalamic pathway:*

*This transmits fast pain.*

### *○ First order neurons*

*Are mainly  $A\delta$  afferent nerves.*

*They terminate at lamina I & V of dorsal horn.*

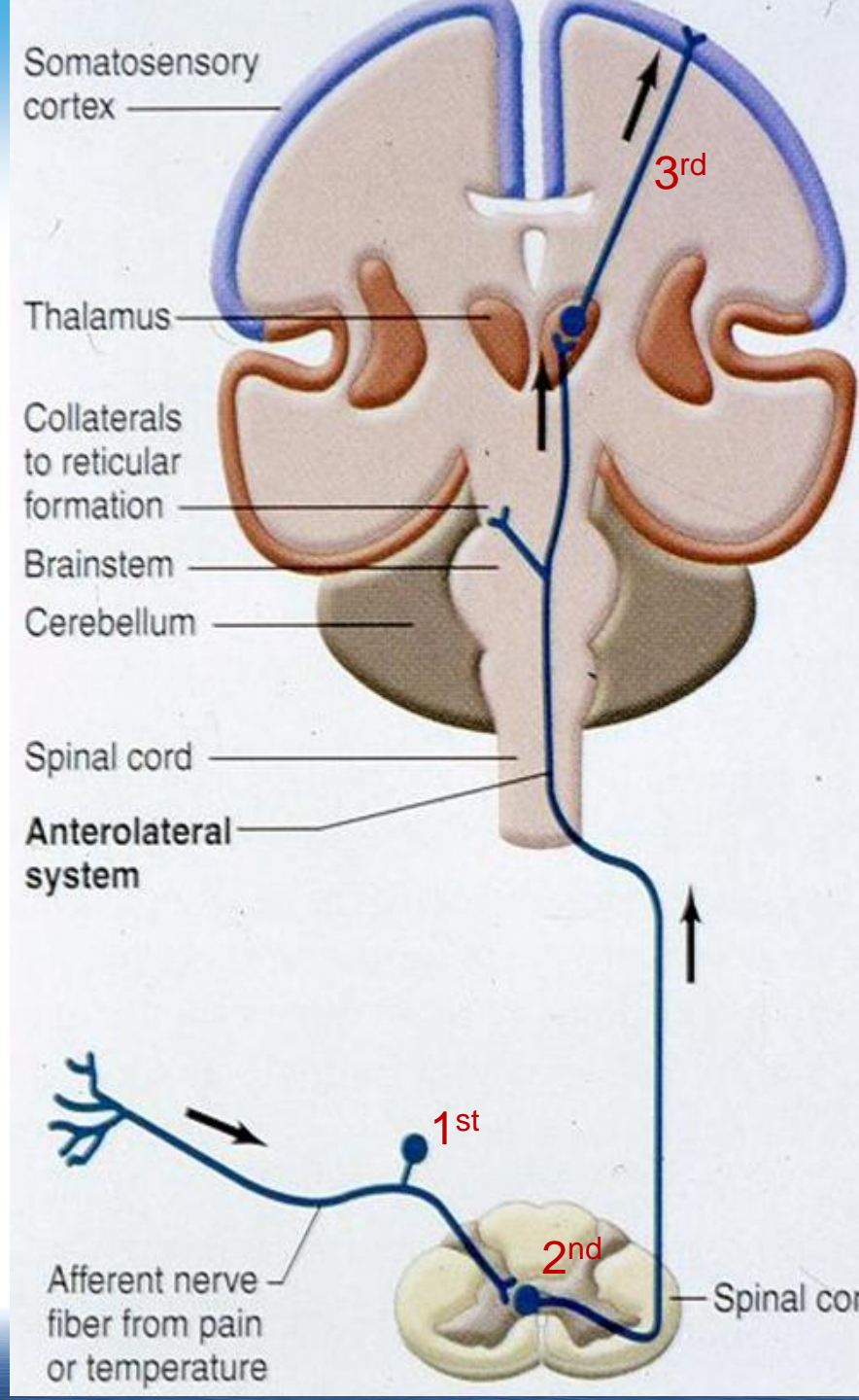


## ○ Second order neurons

*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.*



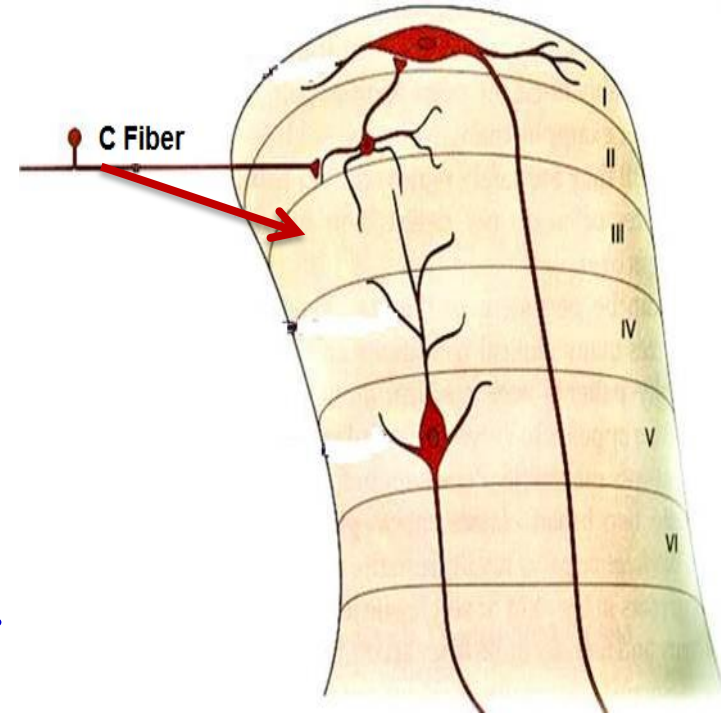
## **B) The paleospinothalamic pathway:**

*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

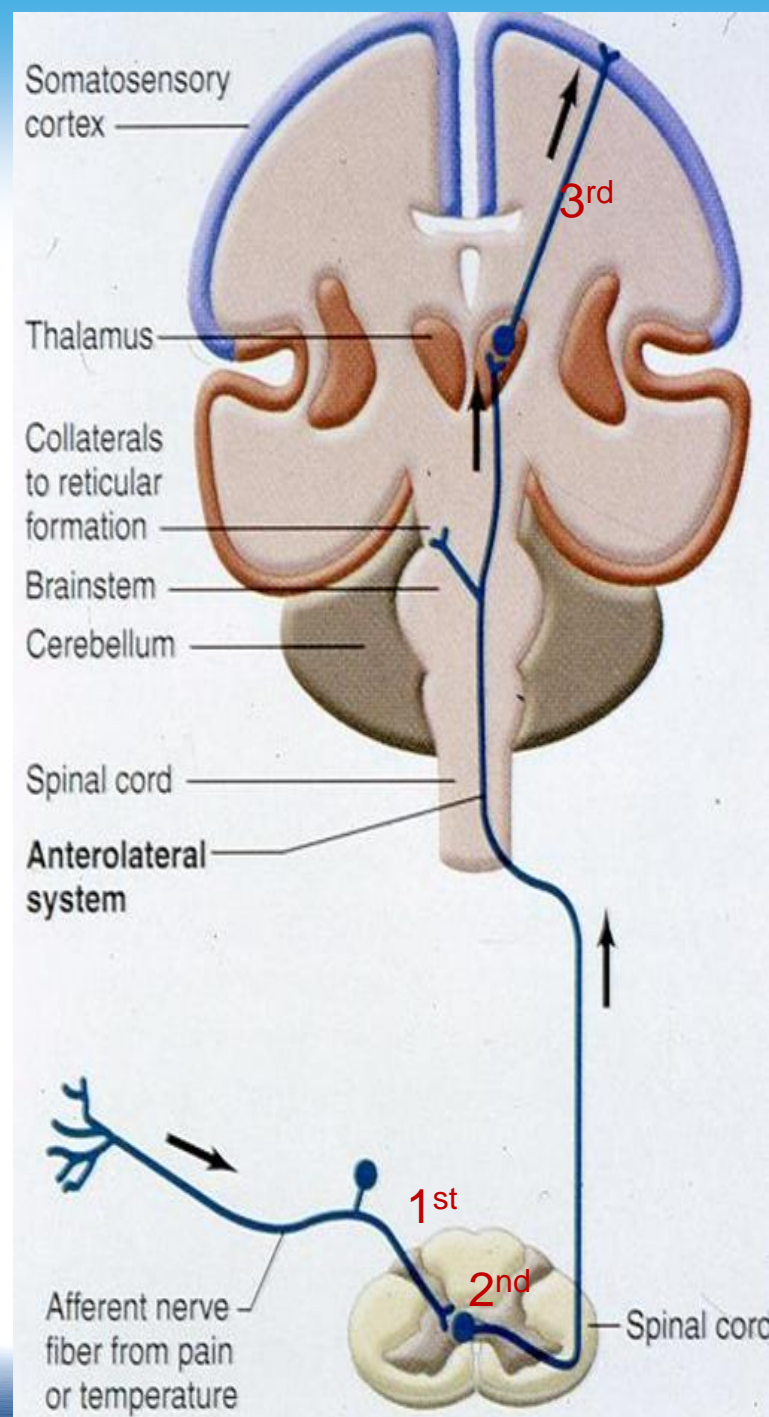
*They start at SGR, cross to opposite side in front of central canal, ascend in lateral column of SC & terminate at:-*

- *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.*

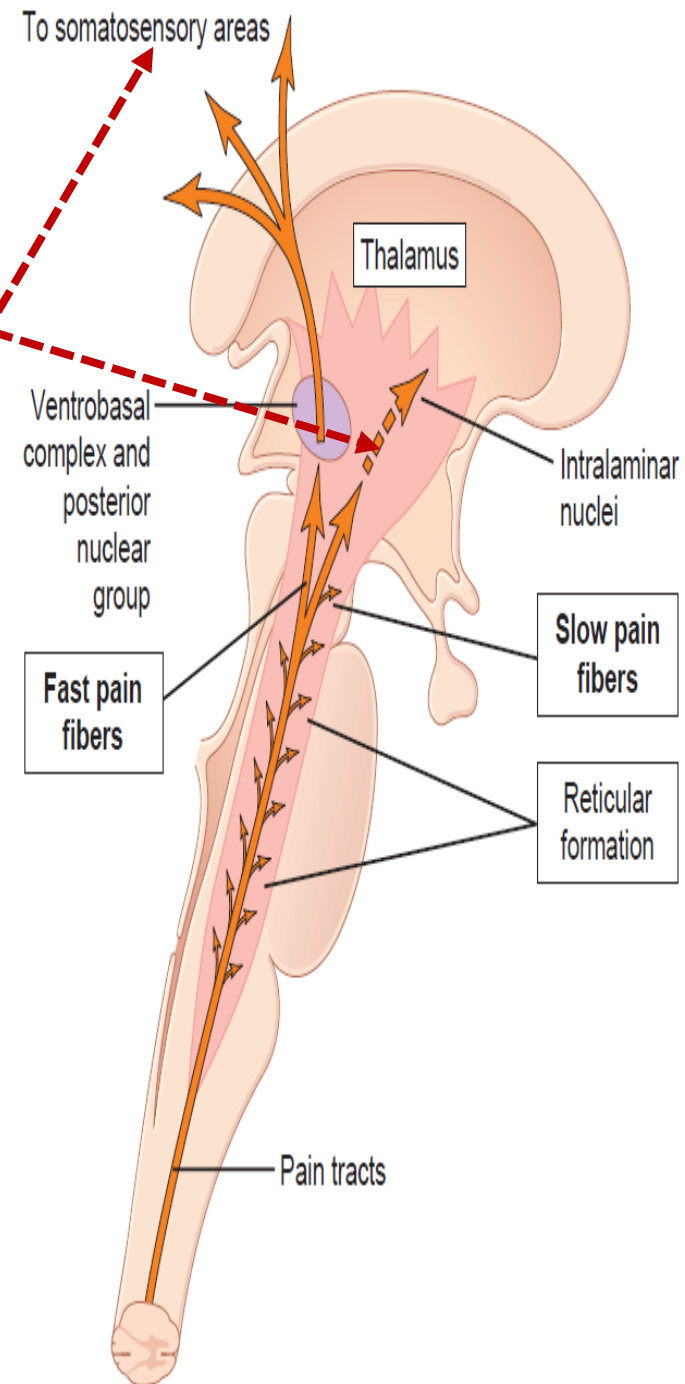
## ○ Third order neurons

- *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.*





The image features a bright, green landscape with a path leading to a horizon. The top of the image is framed by fresh green leaves with water droplets. The text "Thank You!" is centered in the middle of the image.

**Thank You!**