



بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

اللهم صل على محمد وآل محمد

السلام عليكم ورحمة الله وبركاته

# *Physiology of Pain*

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# Learning Objectives

- *Pain receptors (nociceptors)*
- *Reactions associated with pain sensation*
- *Mechanism of stimulation of pain receptors*
- *Qualities of pain*
- *Types of pain*
  - *Somatic pain ( superficial & deep pain).*
  - *Visceral pain.*
- *Referred pain*
- *Pathway of pain*
  - *The neospinothalamic pathway*
  - *The paleospinothalamic pathway*
- *Role of cerebral cortex in pain perception*

# Pain

*What is pain ?*

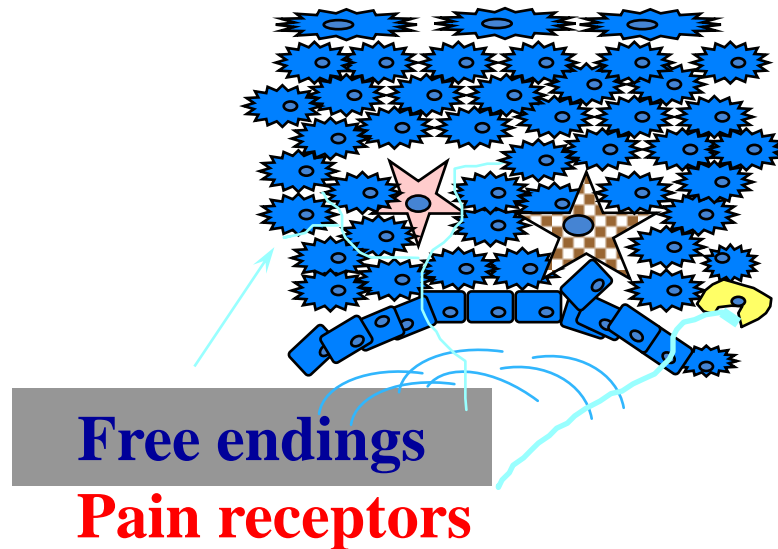
*Pain is unpleasant sensory and emotional experience associated with actual or potential tissue damage.*

# Pain is characterized by the following:

- *It has a **protective function**.*
- *Pain receptors are the most **widely distributed**.*



○ *All pain receptors are free nerve endings of unmyelinated **C fibers** & small diameter myelinated **A $\delta$  fibers**.*



Roman Numeral	Letter	Size ( $\mu\text{m}$ )	Conduction Velocity m/sec	Myelination
Ia	-	12-20	70-120	√√√√√
Ib	-	12-20	70-120	√√√√√
-	A $\alpha$	12-20	70-120	√√√√√
II	A $\beta$	6-12	30-70	√√√√
-	A $\gamma$	2-20	10-50	√√√
III	<b>A<math>\delta</math></b>	<b>1-6</b>	<b>5-30</b>	<b>√√</b>
-	B	< 3	3-15	√
IV	<b>C</b>	<b>&lt; 1.5</b>	<b>0.5-2</b>	<b>None</b>

- *Pain sensation can be produced by **various types of stimuli** i.e. mechanical, thermal & chemical.*
- *Pain receptors **adapt very little**, if not at all.*
- *Localization of pain stimuli is less exact than that of other modalities.*
- *Pain receptors are high threshold receptors i.e. painful stimuli must be strong & noxious to produce tissue damage.*
- *Pain is perceived at both the cortical & thalamic levels.*



# *Pain Reception and Perception*

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

***Perception:*** The point at which a person experiences pain.

# *Reactions associated with pain sensation*

**1- Motor reactions** may take the form of:-

- \* Reflexes e.g. withdrawal reflex.
- \* Muscle rigidity ( stiffness).

**2- Autonomic reactions**

- \* Mild pain stimulates post. hypothalamic N → sympathetic changes e.g. tachycardia.
- \* Severe pain stimulates ant. hypothalamic N → parasympathetic changes e.g. bradycardia.

**3- Emotional reactions** as anxiety, crying.....etc.

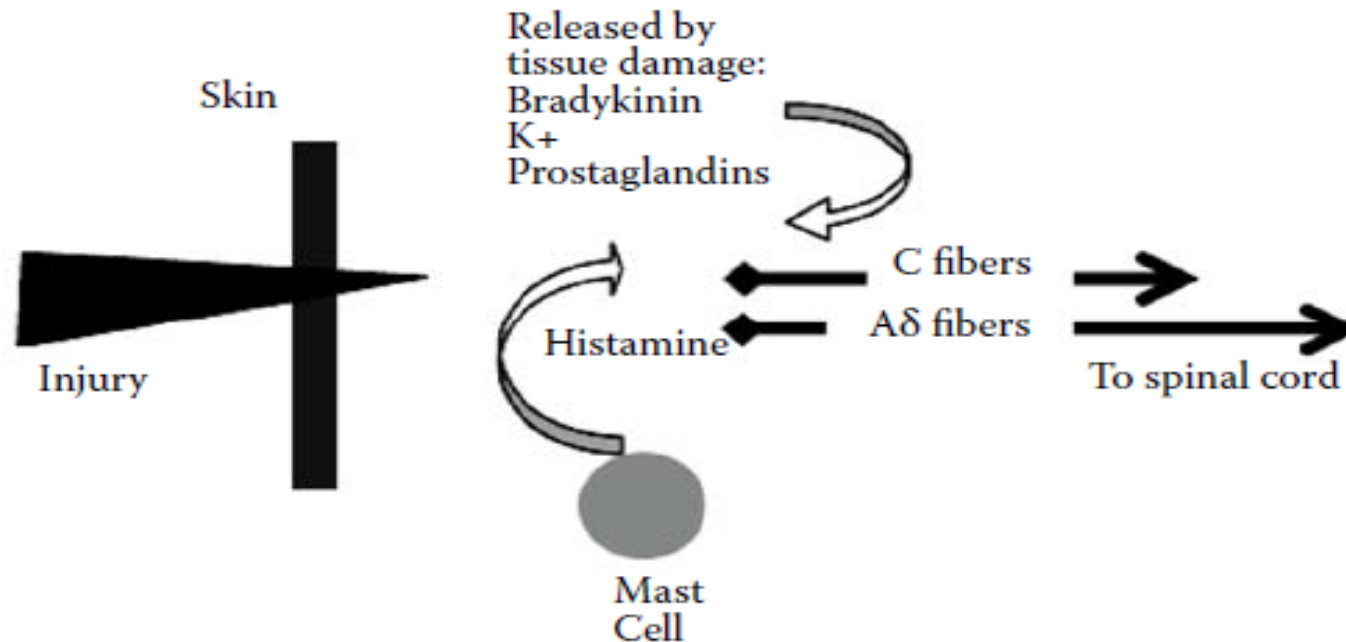
# *Mechanism of stimulation of nociceptors*

- \* Pain receptors are depolarized either directly or through the production of pain producing substances, produced from damaged tissues as a result of inflammation ( also called inflammatory mediators) e.g. bradykinin, serotonin, histamine, interleukins, substance P,  $K^+$ , Ach, proteolytic enzymes.*
- \* Prostaglandins & interleukins lower threshold 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



*Fig. 1.* 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*

A vertical flowchart illustrating the pain mechanism. It consists of five rectangular boxes connected by downward-pointing blue triangles. The boxes contain the following text from top to bottom: 'Damage and inflammation', 'Release chemical mediators activate or sensitize the receptor endings', 'Cytokines, bradykinin, prostaglandin, Substance p', 'Results in transduction', and 'Conduction of nerve impulse'.

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graph TD; A[Damage and inflammation] --> B[Release chemical mediators activate or sensitize the receptor endings]; B --> C[Cytokines, bradykinin, prostaglandin, Substance p]; C --> D[Results in transduction]; D --> E[Conduction of nerve impulse];
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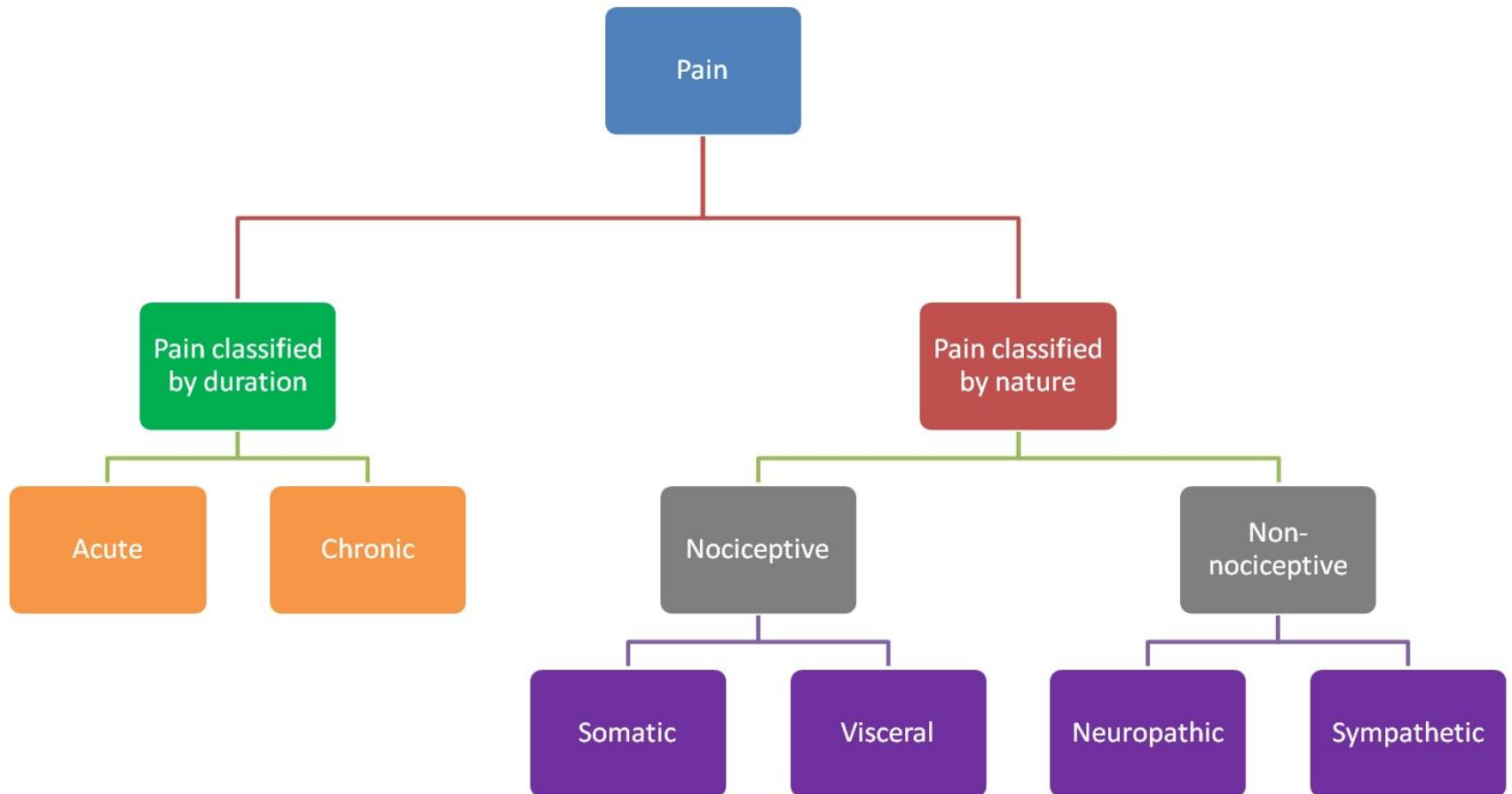
*Release chemical mediators activate or sensitize the receptor endings*

*Cytokines, bradykinin, prostaglandin, Substance p*

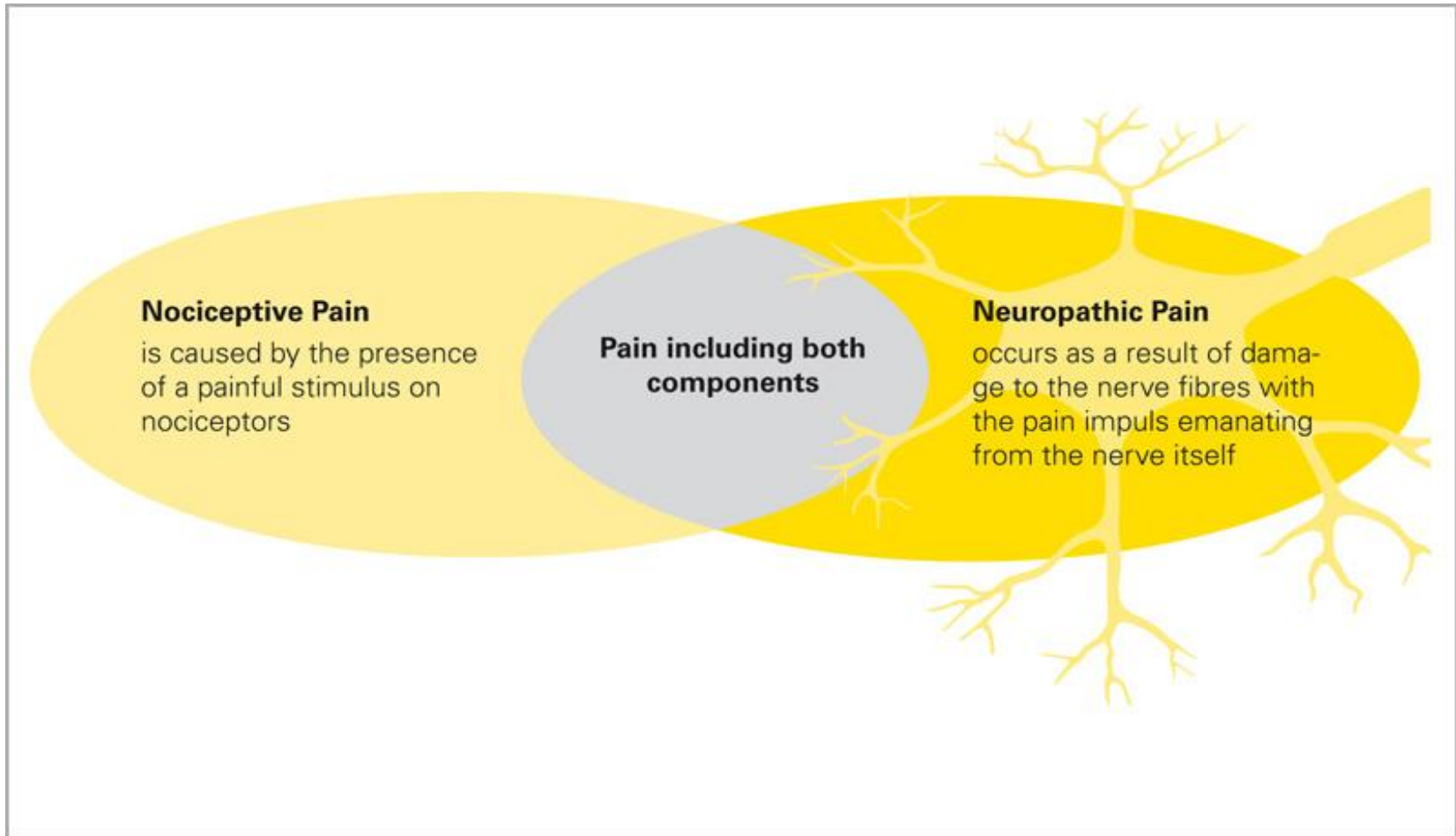
*Results in transduction*

*Conduction of nerve impulse*

# *Classification of Pain*



# *Nociceptive & Neuropathic Pain*





# *Qualities of pain*

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## *I. Fast pain (immediate, first)*

*e.g. The type of sensation felt when skin is cut with a knife.*

- It is also called pricking, acute, sharp or electric pain.*
- It occurs mainly in **skin** by mechanical or thermal stimuli.*
- It appears **very rapidly** within 0.1 sec., and lasts for short time.*
- It is usually **well localized**.*
- It is transmitted via type **A $\delta$**  fibers:*
  - Myelinated*
  - Diameter fine 1 - 6  $\mu\text{m}$*
  - 5 - 30 m/sec. conduction velocity*
  - Terminated in neurons at I and V laminae*
  - 20% pain conduction*
  - The neurotransmitter is glutamate*

# Slow pain (delayed or second)

- ❑ *It is also called **burning**, aching, diffuse, dull, or chronic pain.*
- ❑ *It occurs in **skin, deep tissues & viscera**.*
- ❑ *It appears **slowly**, after one sec. or more, and lasts for longer duration.*
- ❑ *It is diffused (**poorly localized**).*
- ❑ *It is transmitted via **type C** fibers:*
  - *Non-Myelinated*
  - *0.4-1.2  $\mu\text{m}$  in diameter*
  - *0.5 to 2 m/s conduction velocity*
  - *Terminate in neurons at II and III laminae*
  - *Neurotransmitter – Substance- P*
  - *80% of pain conduction*

# *Types of pain*

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

- 1. Somatic pain (superficial & deep pain).*
- 2. Visceral pain.*

# *Superficial pain*

- *It arises from skin or other superficial structures.*
- *It occurs in 2 phase of **fast pricking** followed by **slow burning** pain.*
- *It can be **well localized**.*
- *It may be associated with motor, autonomic, emotional reactions.*

# *Deep pain*

- *It originates from muscles, joints, periosteum, tendons & ligaments*
- *It is **slow prolonged** conducted by type **C fibers**.*
- *It is **diffuse** (i.e. poorly localized).*
- *It can initiate reflex contraction of nearby muscles.*
- *It may be referred to other sites.*
- *It is caused by: trauma, bone fracture & inflammation, arthritis, muscle spasm & ischemia.*

# *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**.*

# *Characters of visceral pain*

- It is **slow** pain conducted by **C fibers** (pain arising from parietal peritoneum, pleura and pericardium is sharp, pricking type).
- It is **diffuse**, poorly localized, the patient feels pain arising from inside but he cannot pinpoint it exactly.
- It is often associated with nausea and **autonomic reactions**.
- It can be associated with **rigidity** of nearby muscles.
- It often **referred** to other sites.

# *Causes of visceral pain*

- ☞ Distension of a hollow organs*
- ☞ Inflammation of an organ.*
- ☞ Ischemia e.g. pain due to myocardial ischemia.*
- ☞ Cutting, crushing are not painful when applied to viscera.*

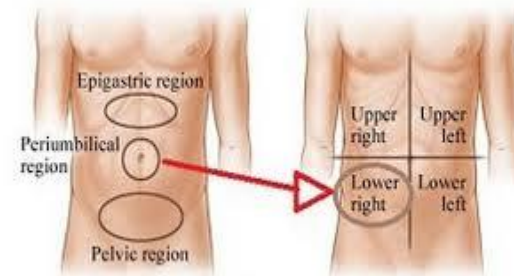
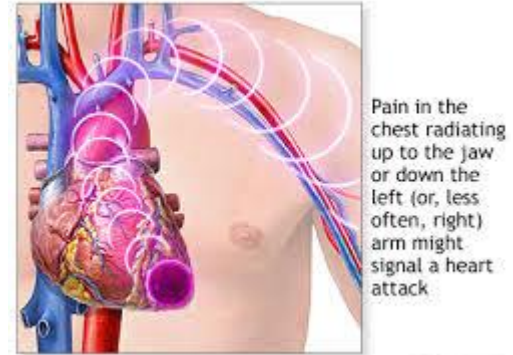


# *Referred pain*

- *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.*

# *Examples of referred pain:*

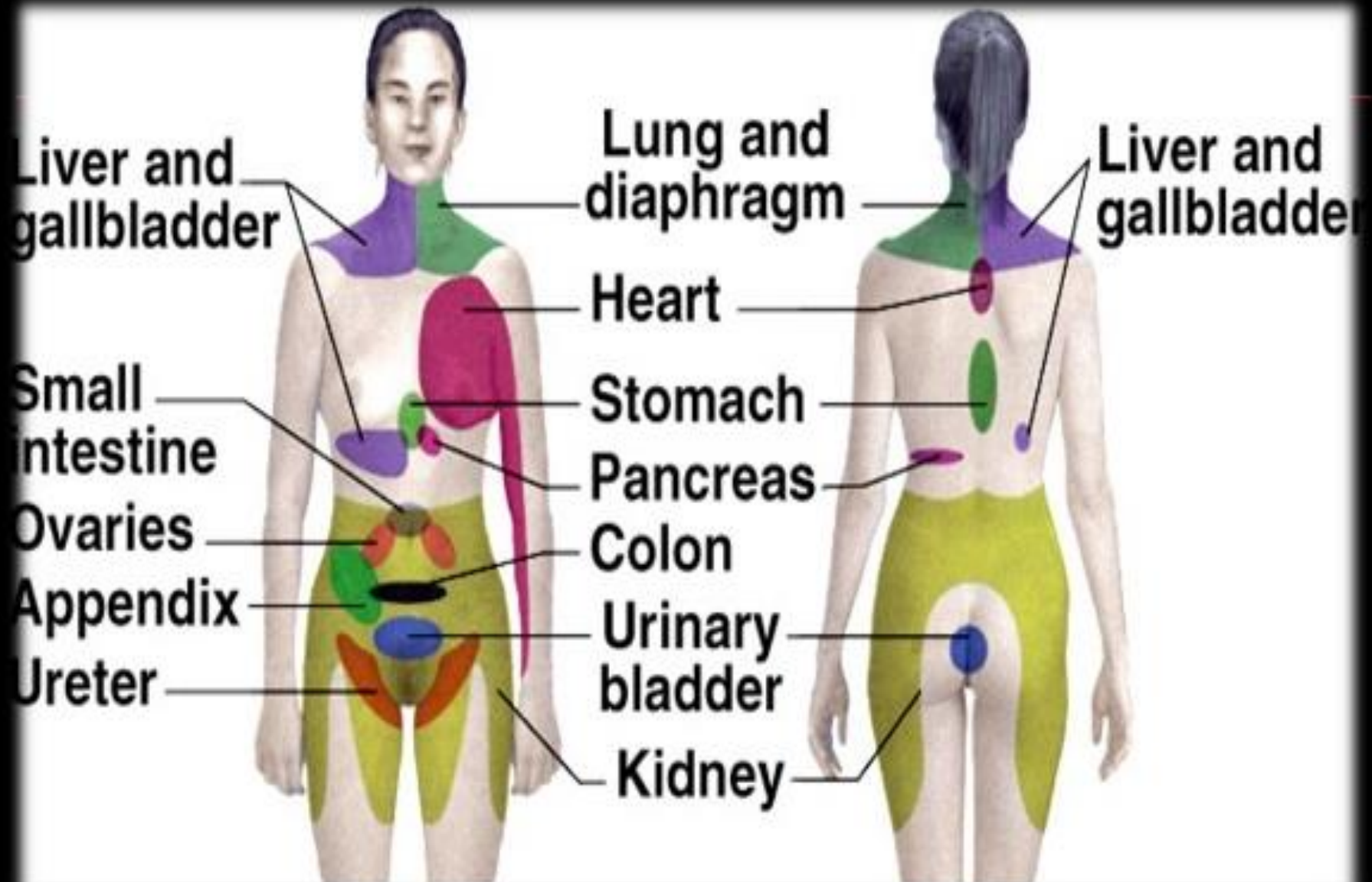
- **Cardiac pain** is referred to the jaw, left shoulder & inner side of left arm.
- Pain of **appendicitis** is referred to periumbilical region.
- Pain from the **ureter** is referred to testicular region.



Progression of Pain in Appendicitis



# Referred Pain

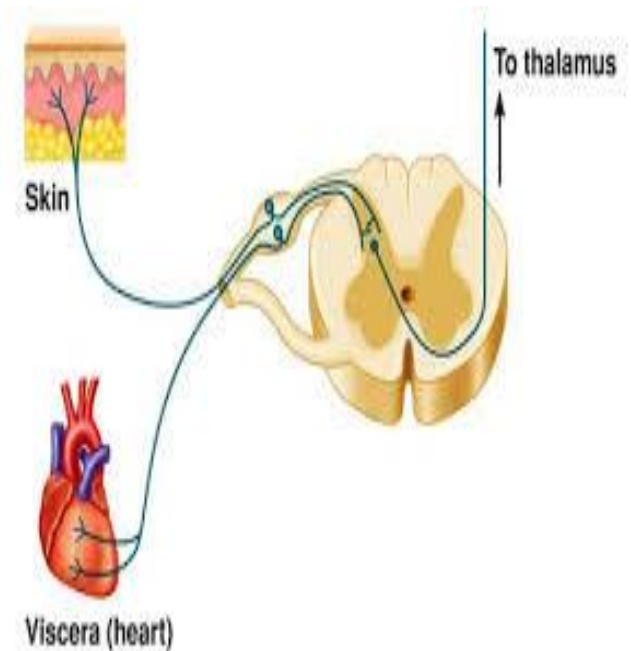


<i>Organ</i>	<i>Site of referred pain</i>
<i>Meninges</i>	<i>Back of head &amp; neck</i>
<i>Heart</i>	<i>Central chest, left arm</i>
<i>Diaphragm</i>	<i>Shoulder tip</i>
<i>Esophagus</i>	<i>Behind sternum</i>
<i>Stomach, duodenum</i>	<i>Epigastrium</i>
<i>Small bowel, pancreas</i>	<i>Around umbilicus</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*

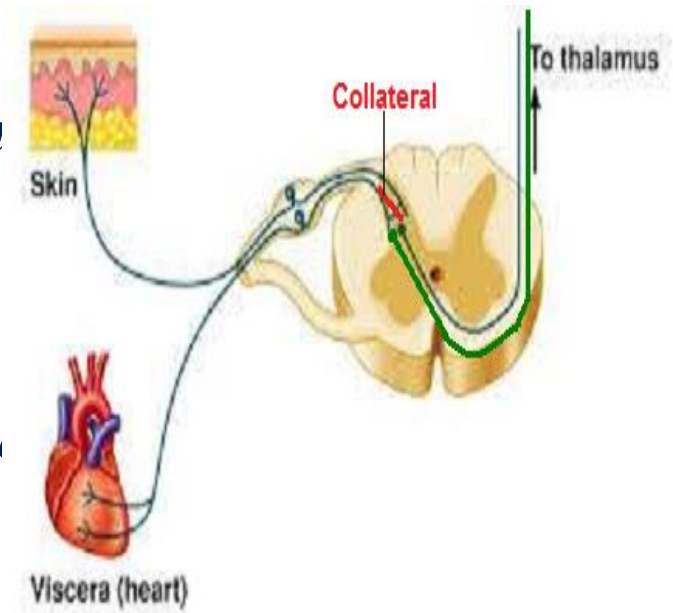
## *Convergence theory*

- 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.*
- Sensory cortex is accustomed to receive pain from skin as the frequency of somatic pain is much more frequent than visceral pain.*
- The cortex would misinterpret the origin of visceral pain impulse and project (feel) pain as it is coming from the skin.*



# 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*

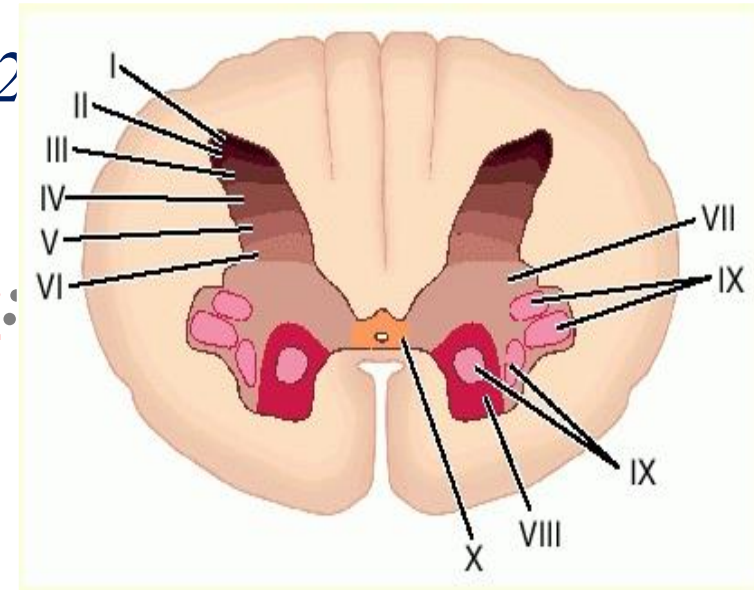
*Pain sensation is carried by **lateral spinothalamic tracts** which includes 2 pathways:-*

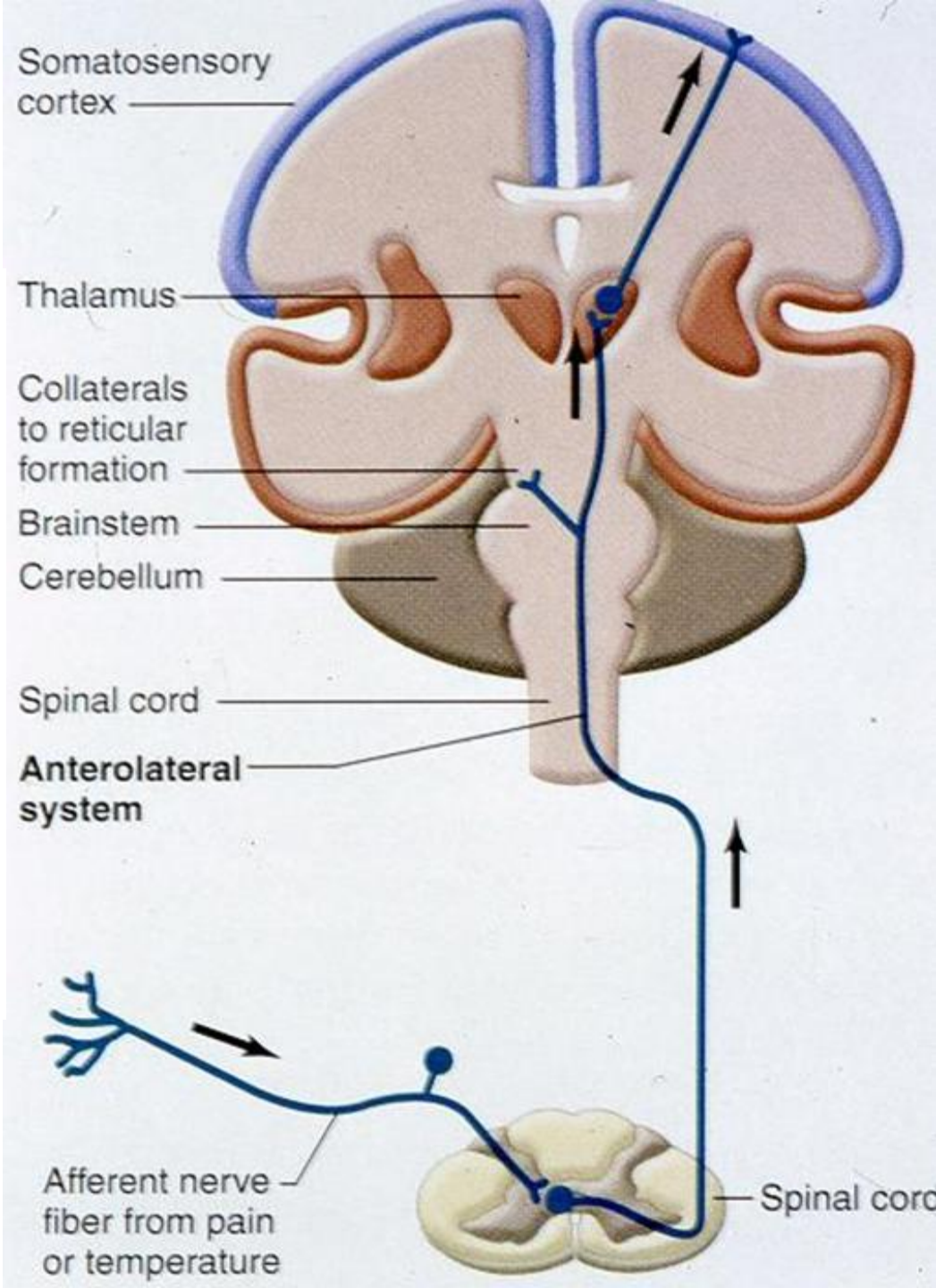
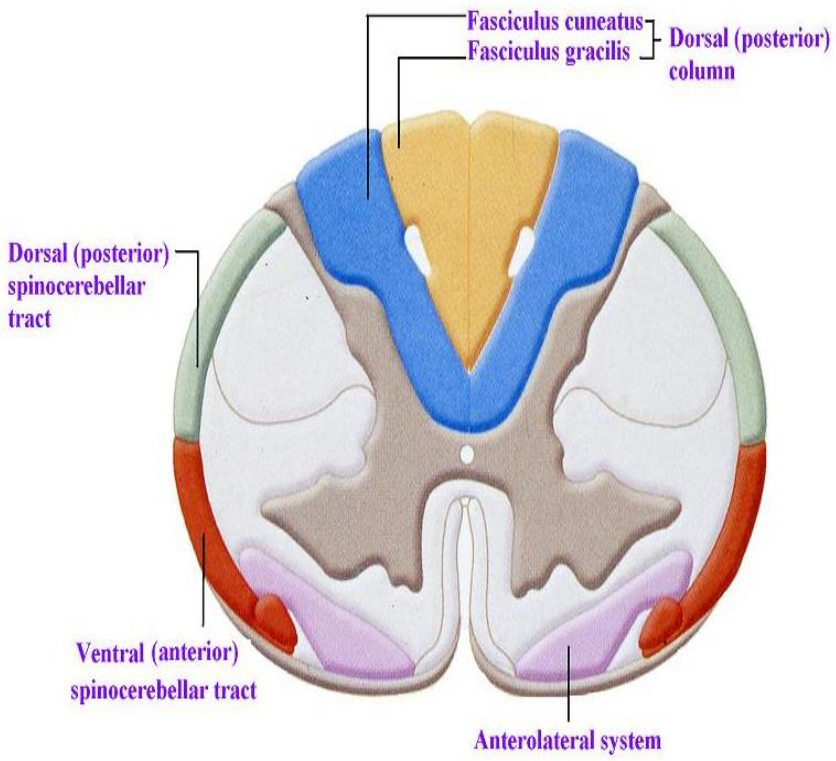
## *A) The neospinothalamic pathway:*

*This transmits fast pain & thermoceptive sensation.*

### *○ First order neurons*

*Are mainly **A $\delta$**  afferent nerves. They ascend few segments in Lissauer' tract & 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 & project to somatosensory cortex.*

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

*This transmit slow pain sensation & thermoceptive sensation.*

### **○ First order neurons**

*They are mainly **type C fibers**. They enter spinal cord via dorsal roots, ascend a few segments in Lissauer' tract & terminate at substantia gelatinosa in laminae II & III of dorsal horn.*

## ○ 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,*

\* *Project to all parts of cerebral cortex.*

# *Role of cerebral cortex in pain perception*

- \* 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

The text "Thank You" is rendered in a highly decorative, cursive script. The letters are filled with a deep red color and outlined with a thick, metallic gold border. The text is embellished with clusters of vibrant red roses and green foliage. Two white doves are depicted in flight, one positioned above the letter 'T' and the other above the letter 'Y'. The entire graphic is set against a plain white background.