Sereen Draghmeh

Pain

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**.
    - It not like any sensation is **multidimentional**
- Pain is more than a direct response to a stimulus. It is a **personal** (two people exposed to the same stimuli may perceive it differently) ,**multidimensional experience**.
- It is **accompanied by motivated behavioral responses** (e.g withdraw from the pain, fight this painful stimuli) and **emotional reactions** (crying, stress, anger) .
- Also, the **subjective perception** of **pain** can be **influenced by other past** or **present experiences**.
    - like how many people are scared from the dentist , once they hear the word dentist they recall the memories of the smell of the dental clinic and the sound of the drill and the pain that happened and once theyre in the dental clinic they have an exaggerated pain experience due to the past experience

Pain Stimuli

- Pain can be **elicited** by **multiple types** of **stimuli**, classified as:
  - **Mechanical**
  - **Thermal**
  - **chemical**.
    - **Stimuli** for **pain** is **nociceptors** which are **free nerve endings** and the stimulation of them are excessive mechanical thermal and maybe chemical
    - The **chemical** is **very important** cause **even** if it **started** as **thermal** or **mechanical** It will **end** up as **chemical stimuli** since they will all release chemicals which stimulate the nociceptors
- Some of the **chemicals** that **excite** the **chemical type** of **pain** are:
  - **Bradykinin**
  - **potassium ions**
  - **proteolytic enzyme**
  - **Prostaglandins**
    - The **prostaglandins** are **important** since they **sensitize** the **pain receptors** (theyre **part** of the **inflammatory process**) **once they're** out they will **sensitize** the **pain receptors** in the **area** (normally when we mentioned sensory receptors we used to say adaptation occurs in which even

with the same stimuli there would be a decreased perception) in **pain** it's the **opposite** in which **even with** the **same stimuli** the **perception** of **pain** will **still occur** because the **nociceptors** are **sensitized** so **higher perception** of the **pain occurs**

- That's why **when** we **treat** the **pain** we may **give** the **patient nonsteroidal anti-inflammatory** drugs to **reduce** the **sensitization** on the sensory receptors that occurs due to PG

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**.
  - **Hyperalgesia** in simple terms is a **stimuli** that **usually** is **normal stimuli** but in **certain situation** it can be **painful when there** is **sensitization**
- **Possible causes** of **hyperalgesia** are the following:
  - (1) **excessive sensitivity** of the **pain receptors**, called **primary hyperalgesia** (e.g. sunburn).
    - Primary like at the sensory receptor level, **excessive sensitivity** of the **pain receptor** like **sun burn** (common example) – someone touching them lightly will cause it to hurt a lot since the receptors are excessively sensitive
  - (2) **facilitation** of **sensory transmission**, called **secondary hyperalgesia**.
    - Secondary hyperalgesia is **fasciation** of **sensory transmission** and **occurs** in the **area surrounding** the **injured** are not in the injured are, and **usually related** to the **spinal cord** and the **thalamus processing**

Fast (acute) Pain

- **Pain** in **general** can be **divided into fast and slow pain** since **pain** is **transmitted through anterolateral spinothalamic pathway** through the **alpha delta or C fibers**

- **fast pain** is **transmitted** though the **alpha delta fibers** while the **slow pain** through the **C fibers**

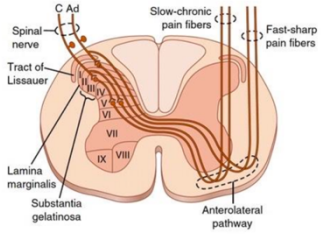
- The **fast-sharp pain signals** are elicited by either **mechanical** or **thermal pain stimuli**.
  - The stimuli for fast pain is mechanical or thermal, its very **acute** and **sharp pain**
    - e,g when you walk and step on a pin, the stimuli was mechanical here, or if u held a hot pan the stimuli here is thermal . these are the two types of stimuli in fast pain, thermal or mechanical
- 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 Aδ fibers** at velocities between 6 and 30 m/sec.
- a **fast-sharp pain** is **followed** a **second** or so later **by a slow pain**.
  - For fast pain when it occurs e,g stepping on a pin, in the beginning there is very sharp fast pain, then throbbing occurs (it differs with different intensity) this means that there is stimulation of two types of pain, fast and slow, it starts with fast, with the alpha delta fibers, then with the slow pain, with the C fibers , but its **difficult to discriminate between these two fibers, but the fast pain occurs first**
    - So fast pain is followed by the slow pain within a second or less
- The **sharp pain plays** an **important role** in **making** the **person react immediately** to **remove himself** or **herself** from the **stimulus**.
  - **Fast pain** is very **important** as it is a **protective mechanism**

Chronic (slow) Pain

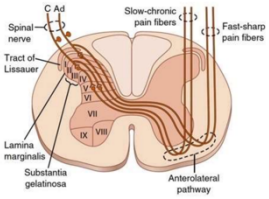
- There is a **difference between chronic** and **slow pain** since the **slow pain** can be **within** a **second** of the **fast pain** while the **chronic pain** is **within** a **long duration**, **clinically** usually **we say 6 weeks to call it chronic**
- **Slow pain** can occur in the **skin** and **in almost any deep tissue or organ.**
  - The fast pain is only felt in the skin and subcutaneous layers you can't feel it in the deep viscera while the **slow pain** can be **felt** in the **skin and most** of the **deep tissues** and **organs**
- this **type** of **pain** is **elicited mostly** by **chemical types** of **pain** stimuli.
  - The stimulus in the slow pain, is **chemical** and **can be mechanical** and **thermal** that stays for a long time but it **destroys tissue**, so it **turns** into **chemical stimulus**.
- 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**
  - **Slow pain** is **more** with the **suffering type** of **pain** ,

Pain Pathways:

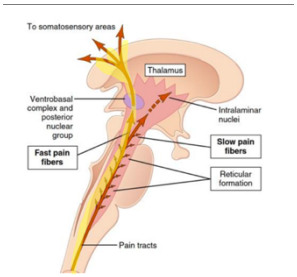
- Even though **all pain receptors** are **free nerve endings**, these endings use **two separate pathways** for **transmitting pain signals** into the **central nervous system**
- The **two pathways** mainly correspond to the two types of pain:
  - a **fast-sharp pain pathway**.: **Neospinothalmic pathway**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



Neospinothalamic tract



- Tract: **Fast pain tract**
- Pain fibers: **alpha delta fibers** for the fast pain
- Pathway:
  - **Alpha delta fibers enter** the **dorsal horn** and **synapse** with the **second order neuron** in **lamina 1**
  - It will then **decussate** once synapsing to **cross** the **other side passing** through the **anterior commissure** to the **anterior lateral spinothalamic** tract to **go up** to the **thalamus** to the **vasobasal complex**
    - The **posterior column pathway also synapsed here**, in the **same nucleus**
    - This is **important** because this **means** that the **localization of** the **fast pain** is **much better** than that of the **slow pain**
  - **Once** the **second order neuron ascends** it will **synapse** with the **third order neuron to go** to the **primary somatosensory area** in the **cerebral cortex**
  - 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**.
    - The **fast pain** fibers also **branch out** to **form reticular formations** which **switch on** the **button** for **consciousness** about the **pain**
      - This is **makes sense** because **people cant sleep when** they're in **pain**



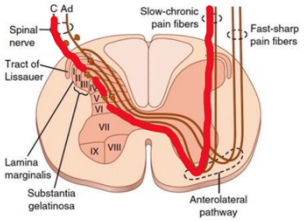
  - A **few fibers also terminate** in the **posterior nuclear group** of the **thalamus**. **From these thalamic** areas, the **signals** are **transmitted** to **other basal areas** of the **brain**, **as well as to** the **somatosensory cortex**

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 lemnisci 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 Aδ pain nerve fiber endings**.

Paleospinothalamic pathway

- Tract: **Slow pain tract**
- Pain fibers: **uses C fibers**
  - The **C fibers** are **unmyelinated** and **slow** so the **conduction velocity slower**
- Pathway:
  - The **C fibers** will **enter** the **dorsal horn** and **synapse** with **multiple interneurons**
  - **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**.
    - The **multiple synapses contributes** to the **fact** that is a **slow conduction** of **pain** since it **increases** the **delay**
  - Then it **crosses** the **midline** (**decussation**) to the **anterolateral spinothalamic pathway** up to the **spinal cord** to the **brain** stem
    - While they **ascend** they also **form reticular formations** which **activate reticulate nuclei activating** the **consciousness about pain**



  - But the **majority** of **them didn't go** to the **ventrobasal complex**, **instead** they **went** to **different areas**
  - **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**.
      - **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**
      - Reticular nuclei for the consciousness of pain
    - (2) the **tectal area** of the **mesencephalon deep** to the **superior** and **inferior colliculi**.

- **2 superior colliculi** for the **spinovisual reflex**, also called the **starter reflex**
- **2 inferior colliculi** for the **auditory**

- (3) the **periaqueductal gray region** **surrounding** the **aqueduct of Sylvius**.

- **Information** is also **sent** to the **hypothalamus**, **thalamus** and the **intraluminal nuclei** and **other subcortical brain regions**
- 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**.
- 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**
- **These lower regions** of the **brain appear** to be **important for feeling the suffering types of pain.**

Neurotransmitters

- The **neurotransmitter** in the **Paleospinothalamic pathway** is **mainly substance P** while in the **neospinothalamic pathway** its **glutamate**
- The **categories** for **neurotransmitters**:
  - **Small molecules rapidly** acting
    - The small molecules **act very rapidly** since they're **already ready** and **packed** in the **vesicles** so that they're released quickly
    - Example: **Glutamate**
  - **Peptides**
    - The **pepties** are **synthesized** in the **cell body** so it **needs time** to **go down** to the **terminal** to get **released** and its **not packed** and **ready** so it **contributing to the slow pain**
    - Example: **Substance P**

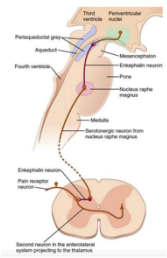
- **Type C pain fiber** terminals **entering** the **spinal cord release both glutamate transmitter** and **substance P transmitter**.
- The **glutamate transmitter acts instantaneously** and **lasts** for **only** a **few milliseconds**.
- **Substance P** is **released much more slowly**, **building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

Localization of Slow Pain

- **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

- **If we give** the **same stimuli** to **2 people they will perceive pain differently** this is **due to** the **presence** of the **endogenous analgesia system in our body**
- We don't know a lot about the mechanisms of the endogenous analgesic system or when it starts or why it starts but **we know when** we **activate this area specifically the periventricular nuclei** in the **hypothalamus** and the **periaqueductal grey area electrical stimulation** will **enduce suppression** of the **pain**



- The **periventricular nuclei** and the **periaqueductal grey areas** will **activate nucleus Ralph** which then will **activate** the **interneurons** in the **dorsal horn** these **interneurons interact** with the pain **signal coming** so they will **either cause post synaptic inhibition** of **presynaptic inhibition**
- The **main areas** are the **periaqueductal grey**, the **periventricular area** * the **hyperthalmaus the ralph magnus nuclei** and the **pain inhibitory complex** in the **dorsal column**
- 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**.

Neurotransmitters

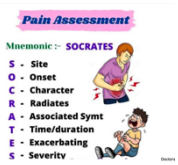
- **Several transmitter substances**, **especially enkephalin** and **serotonin**, are **involved** in the **analgesia system**.

- The **enkephalin** is **believed** to **cause both presynaptic and postsynaptic inhibition** of **incoming type C and type Aδ pain fibers** where they **synapse** in the **dorsal horns**.

Pain control

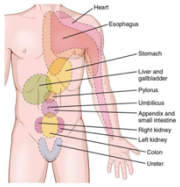
- A **mechanism** to **control pain**:
  - 1. **Medication**
    - giving drugs like **NSAID**
    - giving **opioids** when the **pain** is **higher**
      - **side effect** of it that we are afraid of mainly is **respiratory depression** so we got to be careful
      - for a **morphine overdose** we give **naloxone**
  - 2. **Electrical Stimulation**
    - we can also give **electrical stimulation to areas lie the periaqueductal gray matter** and the **periventricular areas since** they **induce the endogenous analgesic system** so **stimulating them** will **enhance this analgesic effect**
  - 3. **Surgery**
    - we can also do **surgery for extraction for the cortex**
    - its **not very effective** since **there are so many integrations** and **interconnections** with **different areas** in the **PNS** and **CNS** so its **not** the **ideal option**
  - 4. **Lateral inhibition**
    - We can **add heat or ice** to the **pain** to give **thermal stimulation** of the **cold/hot receptors** to that **lateral inhibition occurs**
  - **Acupuncture**
    - Can help to **trigger the release of endorphins**
  - **Exercise**
- **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**.
- **Stimulation** of **large-type Aβ 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**

- **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 relives pain** by **activating sensory neurons** that **ultimately trigger** the **release** of **neurotransmitters** that **function** as **analgesics** such as **endorphins**, **enkephalins, and dynorphins**.
- **Exercise**
- **Distraction**
- **Deep breathing**



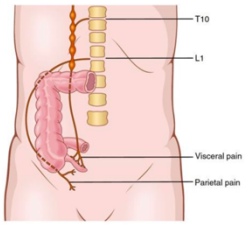
Visceral pain

- **Not all tissues in our bodies have pain receptors like the brain, cartilage, parenchyma of the liver**, **alveoli in the lung, bone**
  - but when someone breaks their bone or has liver damage the **reason** why **we feel pain** is **because of the layers** in which we **have periosteum** is **extensively supplied** by **pain receptors** as well as the **capsule of** the **liver**
- **Transmission** of the **visceral pain** from the **sensory receptors** to the **central nervous system** is **through** the **autonomic neurons** to the **spinal cord to get processed**
  - In **appendicitis** , the **pain** will be **transmitted through** the **autonomic nerve fibers** and **will go to T10** so that's **why we feel the pain in the periumbilical region** this **pain** is called **referred pain**, it **went to T10 due to its embryological origin**
- **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**.
  - The type of fibers are **C fibers** which means it's a **slow type of pain**, the **presentation** is **dull, aching, not specific**
- 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**.
- **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**.
  - The **stimuli** is **chemical mainly** e.g **ischemia** in **which it causes no O2 due** to **impairment** so it **releases certain chemicals due to death of certain cells**



- There could also be **chemical damage** to the **viscera like perforation** of the **gastric wall** which will **cause** the **released** of **acidic gastric secretions irritating** this **viscera** and **parietal peritoneum**

- 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.



- **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

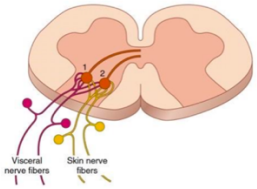
- When a **disease affects** a **viscus**, the **disease process often spreads** to the **parietal peritoneum**, **pleura**, or **pericardium**.
- These **parietal surfaces**, like the **skin**, are **supplied** with **extensive pain innervation** from the **peripheral spinal nerves**.
- **parietal sensations** 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**.

To **differentiate between local** and **referred pain** is by **looking** at the **associated symptoms and** by **putting pressure** on the **areas** of the **skin that is in pain**, if the **patient felt tenderness** that **means** its **more local than referred since** if it was **referred pain then that segment** on the **skin doesn't** have **an issue** so it **shouldn't be tender**, but this isnt in all cases. Plus **referred pain** is **localized** in **dermatomal segments**