ANALGESICS

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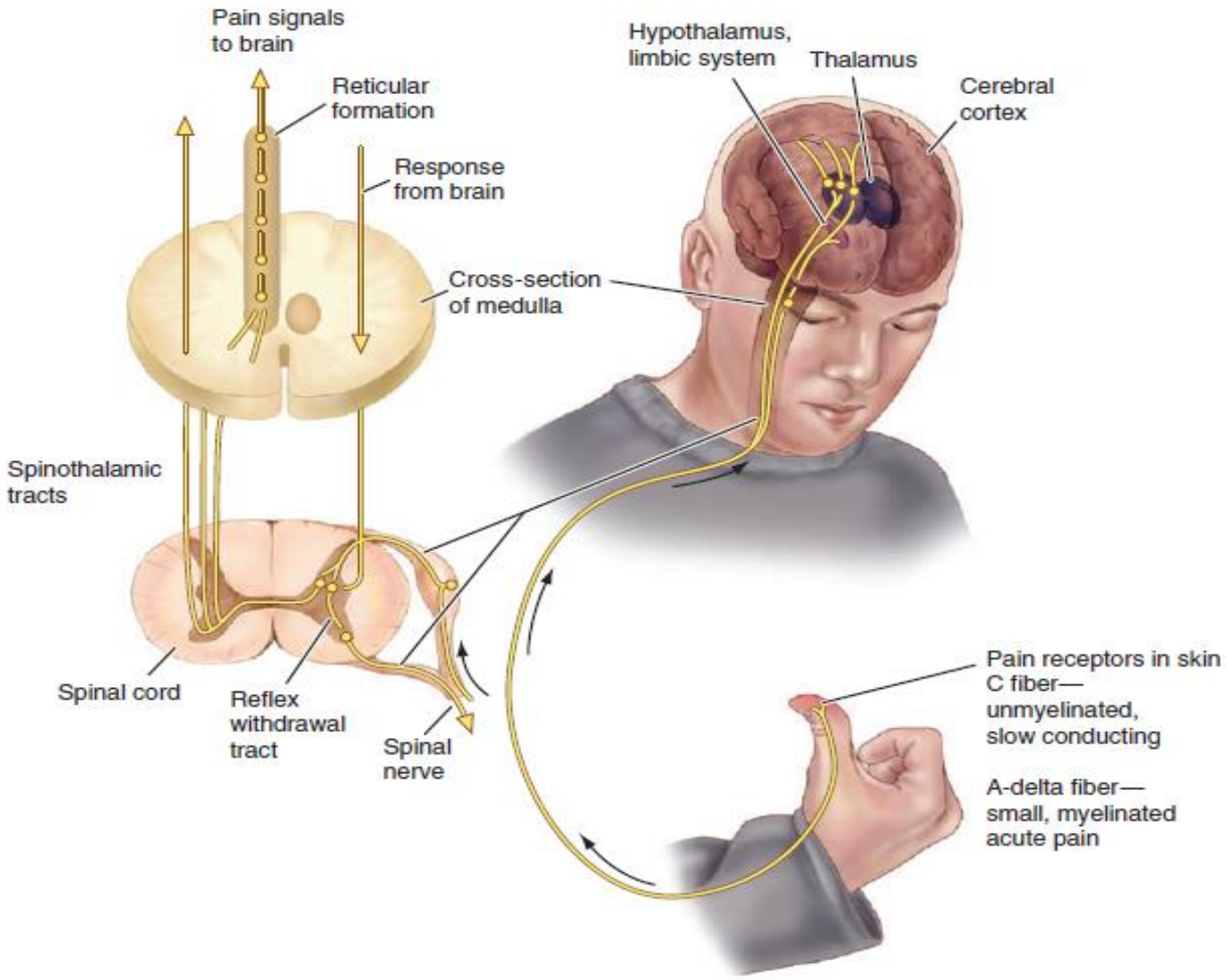
Pain

- Universal, complex, subjective experience
- Number one reason people take medication
- Generally is related to some type of tissue damage and serves as a warning signal

Key Terms

- **Narcotics:** drugs, originally derived from opium, that react with specific opioid receptors throughout the body
- An **analgesic** or **painkiller** is any member of the group of drugs used to achieve analgesia, relief from pain.

NEURONAL PATHWAYS OF PAIN



Pharmacologic Pain management

The overall goal of pain management is to maintain a patient pain level that allows self-care and activities of daily living

- The selection of a specific medication depends on many factors:
  - Severity of the pain
  - Potential adverse events
  - Drug interactions
  - Contraindications

ANALGESICS

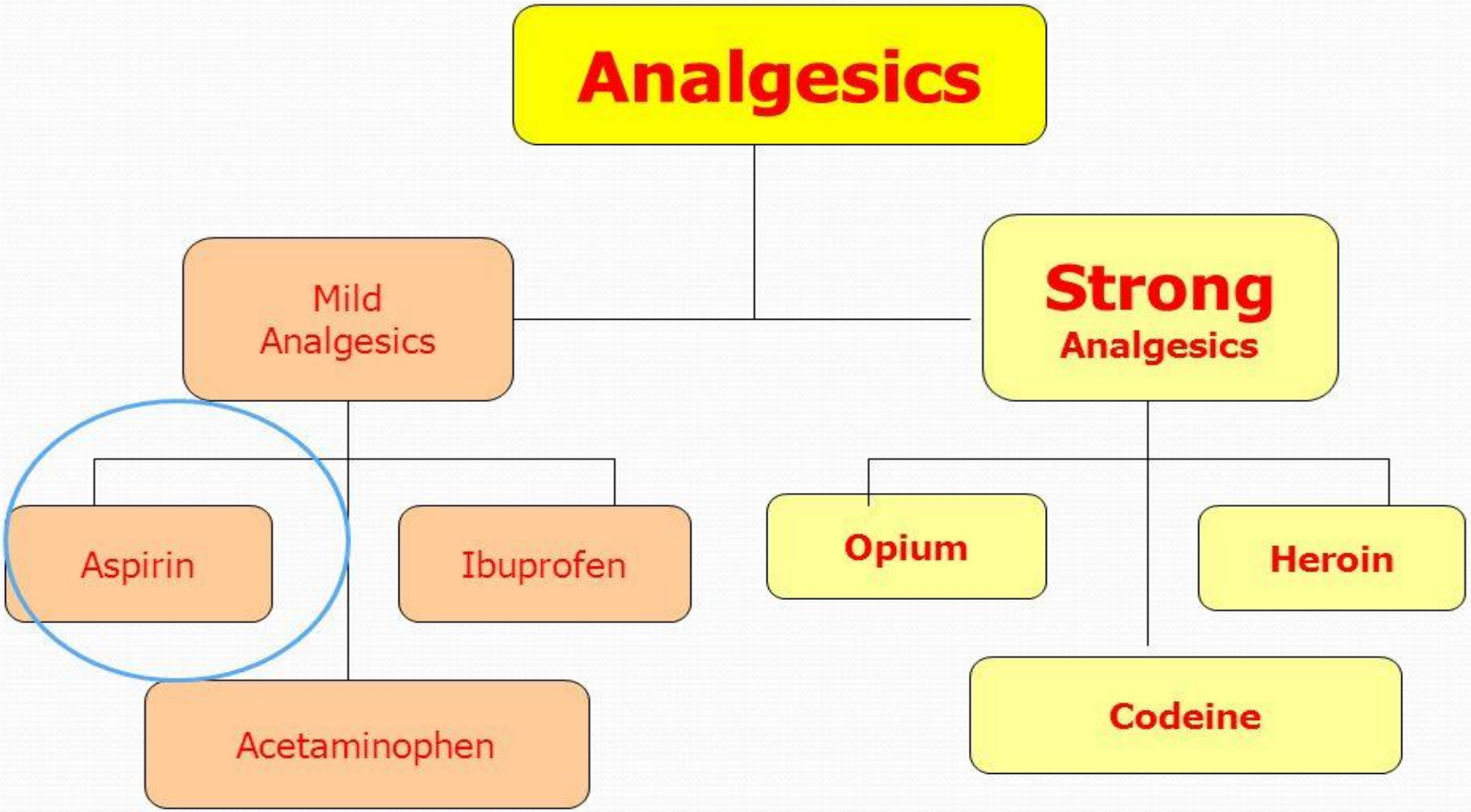
- 2 types of analgesics

1.opioid analgesics (**narcotic analgesics**)

2.nonopioid analgesis (**non-narcotic analgesics)**

- The adjuvant analgesics.
  - The adjuvant analgesics have no pain relief activity when used alone
  - They are able to enhance the analgesic action of opioids and nonopioids

Classification of Analgesics

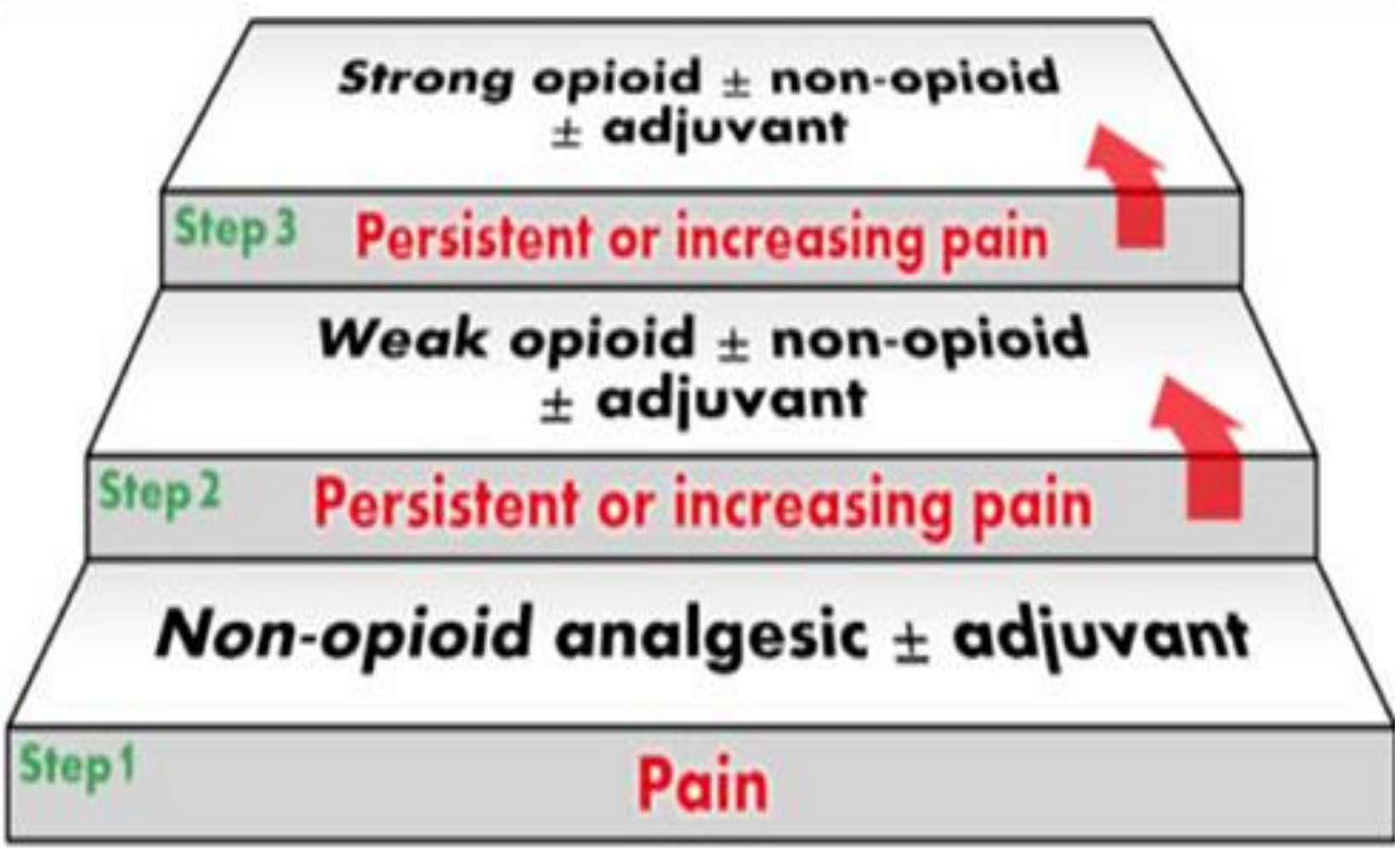


Pharmacological management of pain

The management of acute and chronic pain is based on WHO analgesic ladder.

- **Mild Pain** (ratings of less than 4): treated with **non opioid analgesics**.
- **Moderate pain** (4 to 6): **PO opioids** are added to the baseline treatment.
- **Severe pain** (7 to 10): **parenteral opioids** are used. If chronic pain has neuropathic qualities, adjuvant analgesics are added

WHO Pain Management ladder



OPIOID ANALGESICS(NARCOTIC ANALGESICS)

- Originated from the opium poppy plant
- They achieve their beneficial effects by their actions in the CNS.
- Opioid analgesics are drugs that relieve moderate to severe pain by

➢ Reducing perception of pain sensation

➢ Producing sedation

➢ Decreasing the emotional upsets often associated with pain

Mechanism of Action

Opioids exert their actions by interacting with three types of receptors in the CNS

Major receptor types

- Mu
- Kappa
- delta

MOA Cont..

The **mu** and **kappa receptors** are the most important for pain management

- Activation of the mu receptor is responsible for:
  - The analgesic properties of the opioids
  - The opioid adverse effects such as respiratory depression and physical dependence
- Mu receptor activation results in **analgesia**, **respiratory depression**, **,euphoria** and **sedation**
- Activation of Kappa receptor leads to **analgesia** and **sedation** but has no effect on respiratory depression and euphoria

CATEGORIES OF OPIOID DRUGS

- **Pure opioid agonists:** activate both mu and kappa receptor
  - e.g. morphine and codeine
- **Mixed opioid agonist-antagonist:** occupy one receptor and block (or have no effect) on the other
  - E.g. pentazocine, butorphanol, and buprenorphine
- **Opioid antagonists:** block both mu and kappa receptors;
  - eg. naloxone

Narcotic agonists

- Morphine
- Morphine-like drugs
- Acts on mu, kappa, and delta receptors to produce prototypical narcotic effects

Examples

- Morphine
- Fentanyl
- Hydrocodone
- meperidine
- Pethidine
- tramadol,…….

INDICATIONS FOR USE

- ***The main indication for use of opioids is to***:

- Prevent or relieve acute and chronic pain
- Before and during surgery to promote sedation, decrease anxiety, facilitate induction of anesthesia and decrease the amount of anesthesia required
- Before and during invasive diagnostic procedures e.g.: endoscopic examination

INDICATIONS FOR USE

- During labor and delivery(obstetric analgesic)
- Treat GI disorders, such as abdominal cramping and diarrhea
- Treating severe, unproductive cough(codeine is generally used)

CONTRAINDICATIONS

- ***These drugs are contraindicated or must be used with cautiously in people with***:

- Respiratory depression
- Chronic lung diseases
- Liver or kidney diseases
- Prostatic hypertrophy
- Increased intracranial pressure
- Hypersensitivity reactions to opiates and related drugs

Morphine

- Indication
- Relieve acute or chronic severe pain
- IV: maximal analgesia and respiratory depression usually occur within 10 to 20min
- IM action occur in 30 min
- SC:60 to 90 min
- Oral :chronic pain

SIDE EFFECTS

- Sedation and anxiolytic
  - Drowsiness and lethargy
  - Apathy
  - Cognitive impairment
  - Sense of tranquility
- Depression of respiration
  - Main cause of death from opioid overdose
  - Combination of opioids and alcohol is especially dangerous

SIDE EFFECTS

- Cough suppression
  - Opioids suppress the “cough center” in the brain
- Pupillary constriction
  - pupillary constriction in the presence of analgesics is characteristic of opioid use

SIDE EFFECTS

- Nausea and vomiting
  - Stimulation of receptors in an area of the medulla called the chemoreceptor trigger zone causes nausea and vomiting
  - Unpleasant side effect, but not life threatening
- Gastrointestinal symptoms
  - Opioids relieve diarrhea as a result of their direct actions on the intestines

SIDE EFFECTS

- Other effects
  - Opioids can release histamines causing itching or more severe allergic reactions including bronchoconstriction
  - Opioids can affect white blood cell function and immune function

Agonists-antagonists

- These agents have agonist activity at some receptors and antagonist activity at others.
- Because of agonists activity ,they are potent analgesics with a lower abuse potential than pure agonist; because of antagonist activity

Eg:buprenorphine,dezocine,pentazocine

Narcotic antagonists

- Narcotic antagonists reverse the analgesic and depressant effects of narcotic agonists by displacing the agonists from their receptor sites
- This group includes Naloxone and naltrexone

Naloxone

- Indication:relieve severe CNS and respiratory depression that occurs with narcotic overdose
- Route and dosages:
- Adults:IV,IM,SC 0.1-0.4mg q2-3 min PRN
- Children:IV,IM,SC 0.01/kg q2-3 min PRN

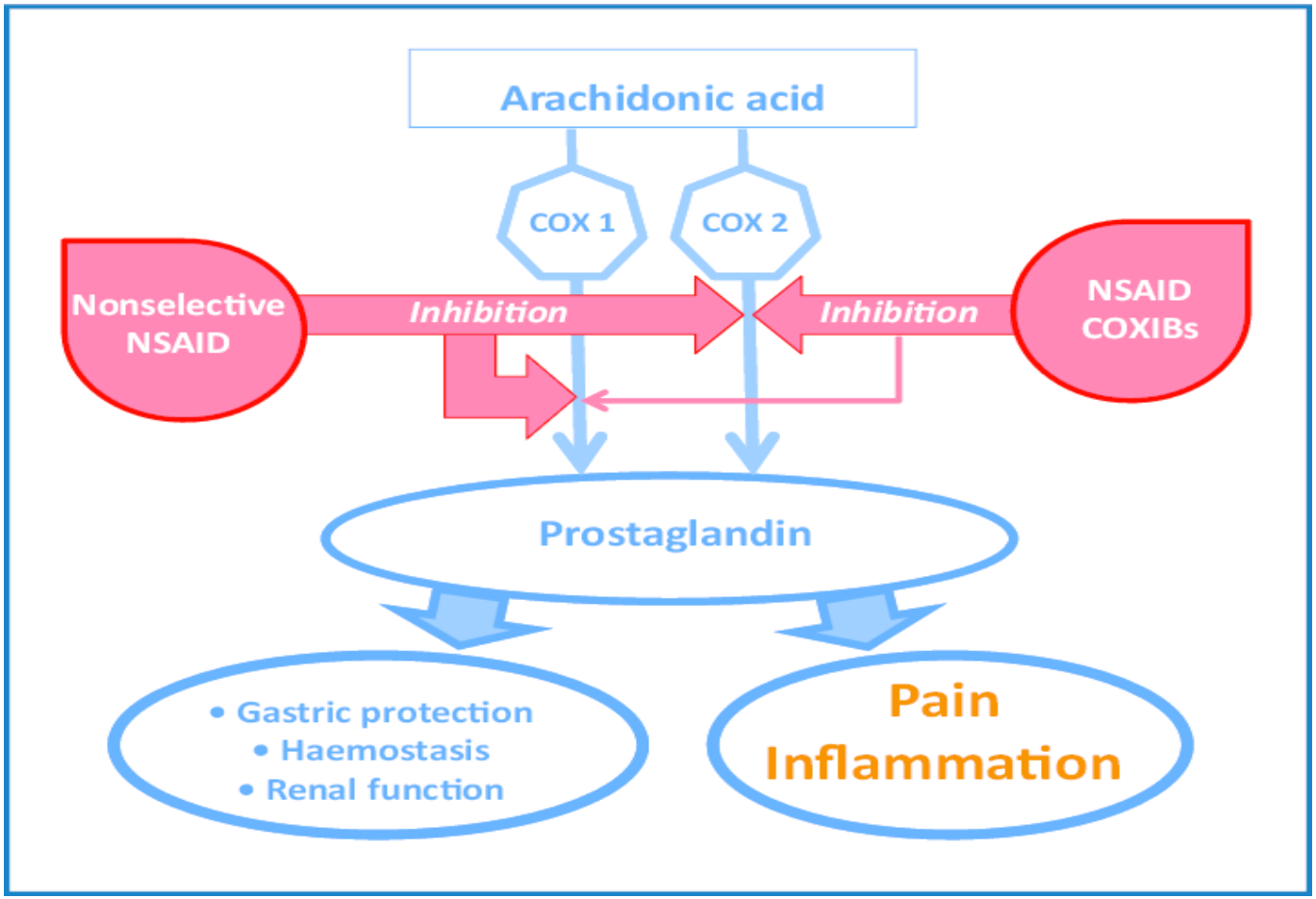
Nonopioid analgesics

ANALGESIC-ANTIPYRETIC-ANTI-INFLAMMATORY DRUGS AND RELATED DRUGS

NSAIDs

- The analgesic-antipyretic-anti-inflammatory drugs relieve pain ,fever and inflammation
- NSAIDs except acetaminophen
- Most of these drugs inhibits prostaglandins

NSAID


Arachidonic acid
COX 1
COX 2
Nonselective NSAID
Inhibition
Inhibition
NSAID COXIBs
Prostaglandin
• Gastric protection
• Haemostasis
• Renal function
Pain
Inflammation

PROSTAGLANDINS

Prostaglandins are substances synthesized in the body from arachidonic acid in response to:

- Physical stimuli
- Chemical stimuli
- Hormonal stimuli
- Bacterial stimuli
- Other stimuli

PROSTAGLANDIN FUNCTIONS

- In inflammatory process, prostaglandins potentiate the pain and edema caused by ***bradikinin, histamin, and other substances*** released in area of tissue damage
- Regulate smooth muscle in blood vessels, GIT, Resp System and reproductive system

PROSTAGLANDIN FUNCTIONS

- Protection of GI mucosa from effects HCl
- Regulate renal blood flow and distribution
- Control platelet function
- Maintain a PDA(patent ductus arteriosus) in the fetus

PROSTAGLANDIN FUNCTIONS

- Prostaglandin is fever-producing agents
- Manifestation of inflammation: ***redness, heat, edema and pain***

MECHANISM OF ACTION

- NSAIDs inactivate cyclooxygenase (prostagladin synthetase),the enzyme that initiates the formation of prostaglandins from arachidonic acid.

➢ To relieve pain NSAIDs act peripherally to prevent sensitization of pain receptors

➢ ***Fever***: on hypothalamus to reset thermostat at lower level

➢ **Inflammation**: prevent prostaglandin action

INDICATIONS

- Pain
- Fever
- Osteoarthritis
- Rhematoid arthritis
- Juvenule rheumatoid arthritis
- Dysmenorrhea
- Acute painful shoulder
- Spondylitis, bursitis
- Gout, Tendinitis

CONTRAINDICATIONS

- PUD
- GIT or other bleeding disorders
- Impaired renal function
- hypersensitivity

EXAMPLES OF NSAIDS

- Acetylsalicylic acid(aspirin),diclofenac,
- fenoprofen,
- ibuprofen,
- indometacin(indocid),
- naproxen,….
- acetaminophen

ASPIRIN

Indications:

- ✓ Pain of low to moderate intensity
- ✓ Rheumatoid arthritis
- ✓ Headache
- ✓ Muscular ache
- ✓ Fever
- ✓ Cold, influenza and other respiratory infections

INDICATIONS

- ✓ Dysmenorrhea
- ✓ Acute rheumatic fever
- ✓ Rheumatoid arthritis and other musculoskeletal disorders
- ✓ Risk for myocardial infarction or stroke from thrombosis due to its antiplatelet activity

COMMON ADVERSE EFFECTS

- Platelet Dysfunction
- Gastritis and peptic ulceration with bleeding (inhibition of PG + other effects)
- Acute Renal Failure in susceptible
- Sodium+ water retention and edema
- Analgesic nephropathy

COMMON ADVERSE EFFECTS

- Prolongation of gestation and inhibition of labor.
- Hypersensitivity (not immunologic but due to PG inhibition)
- GIT bleeding and perforation

Acetaminophen

- Equal in effectiveness to ASA in analgesic and antipyretic effects
- Lacks anti-inflammatory actions
- Ethanol induces drug-metabolizing enzymes in liver. Resulting rapid metabolism of acetaminophen produces enough toxic metabolite to exceed glutathione.
- Need glutathione to inactivate toxic metabolites.

Acetaminophen Poisoning

- Toxicity occurs with 20g or more.
- Creates toxic metabolite that is inactivated by glutathione.
- OD supply of glutathione is depleted and toxic metabolite damages liver cells
- Not to exceed 4g/day
- Treatment—gastric lavage, charcoal, antidote is Mucomyst (acetylcysteine). Provides cysteine, a precursor to glutethione.

Drugs used in Gout and Hyperuricemia

- Zyloprim (allopurinol)—prevents or treats hyperuricemia
- Uric acid is formed by purine metabolism and an enzyme xanthine oxidase.
- Allopurinol prevents formation by inhibiting xanthine oxidase.

Antigout Medications

- **Colchicine**: used to treat or prevent acute attacks of gout. Drug of choice for acute attacks. Decreases inflammation by affecting leukocytes.
- **Benemid** (probenecid) increases urinary excretion of uric acid. Not effective in acute attacks.
- **Anturane** (sulfinpyrazone) uricosuric similar to Benemid. Not for acute attacks.

Guidelines for Treating Gout

- Maintenance drugs are Zyloprim, Benemid and Anturane
- Colchicine needed for several weeks to prevent acute attacks while serum levels are being lowered
- Need high fluid intake, alkaline urine to prevent renal calculi

Drugs Used for Migraines

- **Selective serotonin 5-HT1 receptor agonists**
- Increase serotonin in the brain
- Constrict blood vessels
- Contraindicated in patient's with history of MI, angina, uncontrolled HTN.

Drugs used for migraines

- Drugs vary in onset with sub q **sumatriptan** acting the most rapidly and starting within 10 minutes; most clients get relief within 1-2 hours
- Drugs are metabolized in the liver by monoamine oxidase or by cytochrome p450 enzymes; sub q administrations causes more adverse effects than the oral drugs.

Migraine Meds

- **Ergotamine tartrate** - ergot alkaloid used only in treatment of migraine
- Work by constricting blood vessels
- Most effective when given **sublingual** or by inhalation
- Contraindicated in pregnancy, HTN, CAD, renal or hepatic disease and even in severe infections

Guidelines for Treating Migraine

- **Start out with acetaminophen, aspirin,** or other **NSAIDs**
- **Moderate to severe migraines**, **sumatriptan** or other related drugs.
- For severe and frequent migraines, prophylaxis is indicated. Use **ASA and NSAIDs**.

Rheumatoid Arthritis

- NSAIDs
- Corticosteroids
- Immunosuppressants—methotrexate
- Enbrel, Remicade and Arava. Affect tumor necrosis factor and other cytokines.

GENERAL PRINCIPLES OF PAIN MANAGEMENT

1. Mild to moderate pain: begin with the use of nonnarcotic drugs
2. Moderate to severe pain: narcotic drugs
3. Non pharmacologic measures: should always be used. Massage

1. Non pharmacologic measures include:

- ✓ Relaxation therapy
- ✓ Guided imagery
- ✓ Music distraction
- ✓ Exercise

Nursing considerations
Nonopioids analgesics

- Paracetamol should be given as ordered or as indicated for fever or pain.
- Pt teaching should emphasize taking the medication as indicated to avoid liver damage and acute toxicity
- Pt should also be taught the signs of acetaminophen overdose include: bleeding, malaise, fever, sore throat and easy bruising (due to hepatotoxicity)

Nursing consideration: Non narcotics

- Adult pts who take more than 2.6 gr/24 hrs are at risk for liver damage
- **Acetylcysteine** may be given through NGT or Orogastric tube
- Taking tramadol with food or a snack may help to decrease G.I upset.

Nonopioids analgesics

- Those taking 10 gr or more are at high risk for severe liver damage and death if possible after ingestion of more than 15 gr.
- Liver damage from acetaminophen may be minimized by timely dosing with **acetylcysteine**.
- Use of a straw will help minimize contact with mucous membranes of the mouth and is recommended

Narcotics

- Administer medications as ordered after checking for the 5 rights of drug administration
- Documentation should be stricter
- Double check against the original physician's order
- Return at the appropriate time to assess for the effects of the drug on the pain and presence of any adverse effects.

Narcotics

- Antiemetic therapy may be needed if nausea and vomiting from the narcotic occurs or is present prior to dosing
- Minimize the risk of falls from the adverse effects of the drugs including confusion, hypotension and decreased sensorium.
- Withhold the dose and contact the physician if there is any decline in the pt's condition or if the vital signs are abnormal **(RR< 12 breaths per/min)**

Narcotics

- Oral forms of narcotics should be used first, if ordered and if no nausea or vomiting
- Taking the dose with food may help minimize GI upset
- For cancer pts, IM may not be the option
- Monitor the pt's pupils along with the vital signs: Pinpoint pupils may indicate overdose
- Antidote Naloxone reverses an opioid overdose or opioid-induced respiratory depression

Narcotics

- Intravenous administration of narcotic agonists: the nurse should always follow the manufacturer's guidelines and institutional policies regarding specific dilatational amounts and solution as well as the time period for infusion
- Watching for adverse effects
- Monitor urinary output and bowel status

Narcotics

- IV naloxone :0.4 to 2mg in undiluted form over 15 seconds or as ordered
- If reconstitution is needed: 0.9%NaCl
- Emergency resuscitation equipments should be nearby in the event of respiratory or cardiac arrest

- THANKS