

# **NON-STEROIDAL ANTI- INFLAMMATORY DRUGS NSAIDS**

# Inflammation

- Natural, nonspecific defense mechanism
- Occurs in response to an injury or antigen
- Inflammation limits spread of injury or antigen
  - ▣ Contains injury
  - ▣ Destroys microorganism
- Acute—8 to 10 days
- Chronic—months or years

# Signs of Inflammation

- ☐ Swelling
- ☐ Pain
- ☐ Warmth
- ☐ Redness

# Chemical Mediators

- Alert surrounding tissue of injury
  - Histamine
  - Leukotrienes
  - Bradykinin
  - Complement
  - Prostaglandins

# Acute Inflammation

- Occurs after cellular injury causes release of chemical mediators
- Five basic steps
  - ▣ Vasodilation
  - ▣ Vascular permeability (edema)
  - ▣ Cellular infiltration (pus)
  - ▣ Thrombosis (clots)
  - ▣ Stimulation of nerve endings (pain)

# Nonsteroidal anti-inflammatory drugs (NSAIDs)

- Primary drugs for treatment of mild to moderate inflammation
- Include aspirin, ibuprofen, and COX-2 inhibitors
- All are analgesics and antipyretics
- Side effects vary
- Acetaminophen (=paracetamol) has no anti-inflammatory action and *is **not** an NSAID*

# Cyclooxygenase

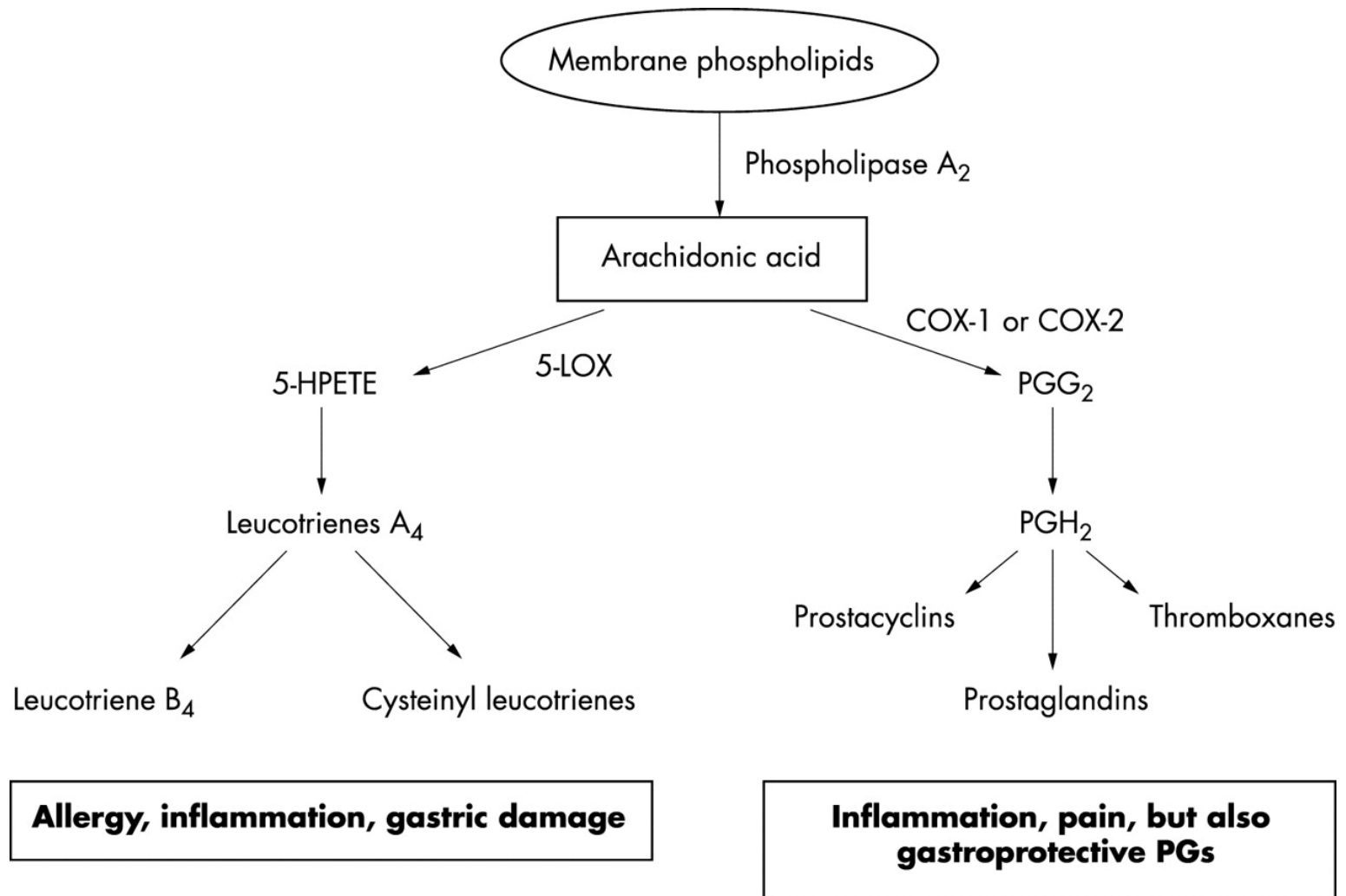
- Two forms of cyclooxygenase (COX)
- **Cyclooxygenase-1 (COX-1)**
  - ▣ Present in all tissues
  - ▣ Reduces gastric-acid secretion, promotes renal blood flow, promotes platelet aggregation
  - ▣ Inhibition of COX-1 results in bleeding, gastric upset, reduced renal function

# Cyclooxygenase

- **Cyclooxygenase-2 (COX-2)**
  - ▣ Present at sites of injury
  - ▣ Promotes inflammation, sensitizes pain receptors, mediates fever in brain
  - ▣ Inhibition of COX-2 results in suppression of inflammation



## Products and enzymes of arachidonic acid metabolism involved in the inflammatory process.



# Aspirin

- Treats inflammation by inhibiting both COX-1 and COX-2
- Readily available, inexpensive, effective
- Large doses needed to relieve severe inflammation

# Aspirin

## □ **Adverse effects:**

- ▣ Irritate digestive system
- ▣ May cause bleeding
- ▣ Salicylism may occur
  - Tinnitus, dizziness, headache, excessive perspiration

## □ Aspirin is contraindicated in pediatric clients

- ▣ Possibility of Reye's syndrome

( Associated with aspirin consumption by children with viral illness, a fatal condition, rash, vomiting, and liver damage)

# Ibuprofen

- Alternative to aspirin
- Inhibits COX-1 and COX-2
- Common side effect—nausea and vomiting
- Causes less gastric irritation and bleeding than aspirin

# COX-2 Inhibitors

- Newest and most controversial class
- No inhibition of COX-1
  - ▣ Do not affect blood coagulation
  - ▣ Do not irritate digestive system
- Were treatment of choice for moderate to severe inflammation

# COX-2 Inhibitors

- Rofecoxib found to double risk of heart attack and stroke—removed from market in 2004
- Valdecoxib also removed in 2005
- Celecoxib only remaining COX-2 inhibitor

# Non-steroidal Anti-inflammatory Drugs (NSAIDs)

- Prototype drug: ibuprofen
- Mechanism of action: to inhibit prostaglandin synthesis
- Primary use: for musculoskeletal disorders such as rheumatoid arthritis and osteoarthritis, mild to moderate pain, reduction of fever, primary dysmenorrheal pain
- Adverse effects: nausea, heartburn, epigastric pain, dizziness, bleeding

# NSAIDs

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- ☐ Aspirin
- ☐ Celecoxib
- ☐ Diclofenac
- ☐ Ibuprofen
- ☐ Indomethacin
- ☐ Ketoprofen
- ☐ Naproxen





# NSAIDS

- Use NSAIDs cautiously in elderly clients
  - Potential for increased bleeding

# Pharmacological Effects of NSAIDs

- Anti-inflammatory effects - modifications of inflammatory reactions including a decrease in inflammatory prostaglandins PGI<sub>2</sub> and PGE<sub>2</sub>
- Analgesic effect - reduction of certain sorts of pain
- Antipyretic effect - lowering of raised temperature, partly due to decreased release of prostaglandins in response to interleukin-1

# Ibuprofen

- Maximum daily dosage: **3200 mg**
- Renal impairment:  urine output, weight gain, rapid  Cr/BUN

# NSAIDs Side Effects

- G.I. disturbances (inhibition of PGE2 and PGI2)
- Common G.I. effects -- dyspepsia, diarrhea, nausea and vomiting.
- Antithrombotic effect (inhibition of TXA2 synthesis )
- Renal effects - acute renal insufficiency, allergic nephritis, chronic analgesic nephropathy
- Hepatotoxicity
- NSAIDs may also promote bleeding in combination with warfarin

# Antipyretic Drugs

- Acetaminophen = paracetamol
  - ▣ Not an NSAID
  - ▣ Contraindicated in clients with significant liver disease
  - ▣ Inhibits warfarin metabolism; may result in bleeding
  - ▣ Primary use: to relieve pain and reduce fever; no anti inflammatory actions
  - ▣ Adverse effects: possible liver damage; causes less gastric irritation than aspirin; does not affect blood coagulation

# Antipyretic Drugs

- Aspirin is contraindicated for pediatric clients because Reye's syndrome
- Acetaminophen is the antipyretic of choice for fevers

# Acetaminophen

- Maximum daily dosage: 4,000 mg/day
- Antidote: acetylcysteine (to prevent liver failure)