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*

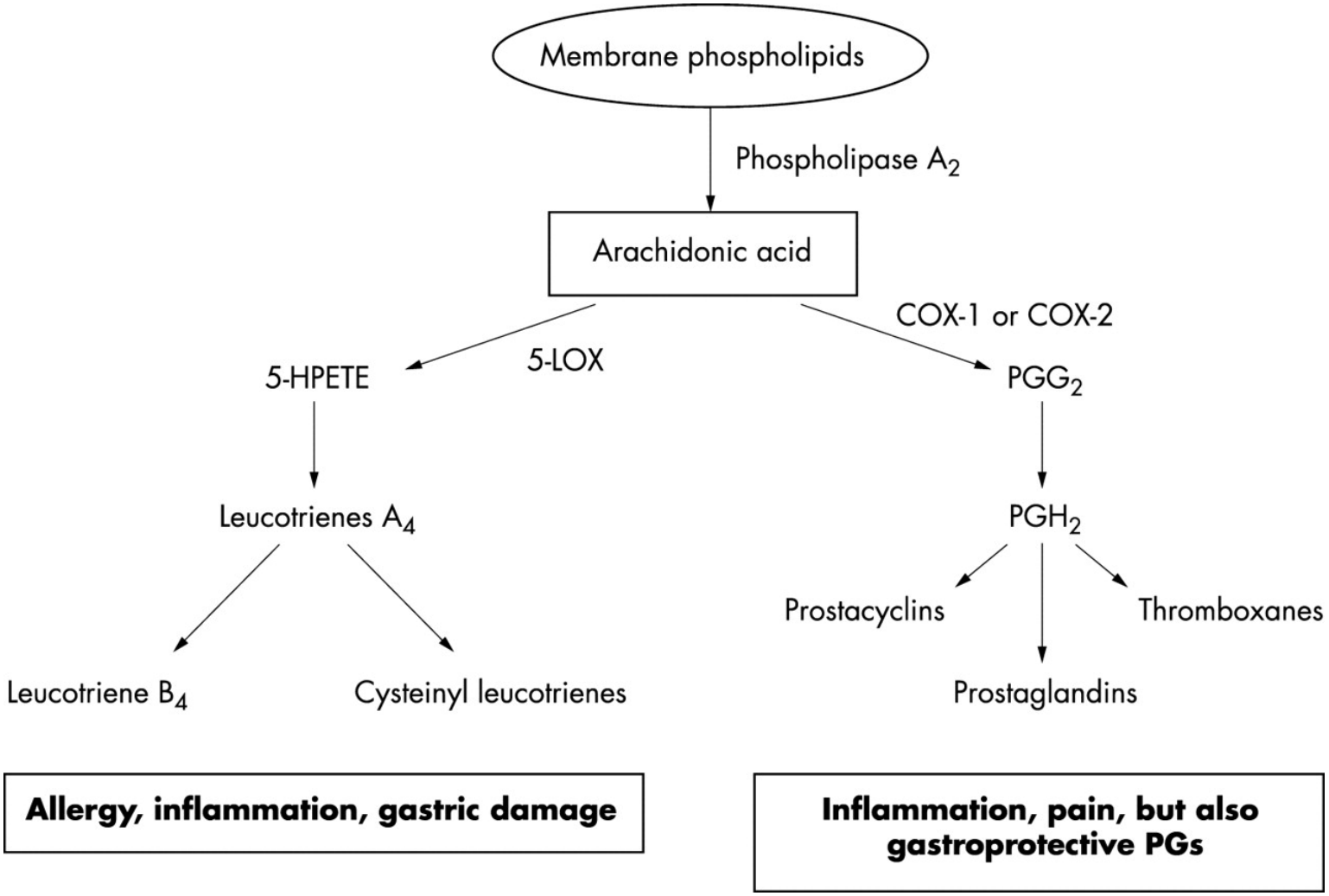
Cyclooxygenase

- 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.



ARD

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

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

NSAIDS

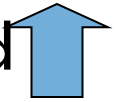
- Use NSAIDs cautiously in elderly clients
  - Potential for increased bleeding

Pharmacological Effects of NSAIDs

- Anti-inflammatory effects - modifications of inflammatory reactions including a decrease in inflammatory protaglandins PGI2 and PGE2
- Analgesic effect - reduction of certain sorts of pain
- Antipyretic effect - lowering of raised temperature, partly due to decreased release of protaglandins 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)