MedNotable.com

NSAIDs

Block both COX-1 and COX-2 by interacting with Arg120 (reversible)

Non-steroidal anti-inflammatory drug

- Carboxylic Acid
  - Salicylic Acids and Esters
    - **Acetylsalicylic Acid/ ASA (Aspirin®)**
      > Acetylates a serine (COX-1 S530 and COX-2 S516) blocking access to arachidonic acid
  - Acetic Acids
    - i) Phenylacetic Acids
    - ii) Carbo- and Hetero-Cyclic Acetic Acids
      Indomethacin (Indocin®)
  - Propionic Acids
    - **Ibuprofen (generic/ Motrin®)**
      > For RA and dysmenorrhea, accumulates in synovial fluid
    - **Naproxen (Alleve®)**
      > RA and gout, 20X more potent than ASA
- Enolic Acid
  - Pyrazolones
  - Oxicams
    - **Piroxicam (Feldene®)**
      > Prolonged half-life (30-85h) due to entero-hepatic circulation

COXibs

Celecoxib
Refecoxib/Vioxx (Off the market)

Blocks COX-2 (irreversible) Binds Val523, has a big bulky group

↑Risk Heart Attack, Strokes (reduces anti-thrombotic PGI_2)

Acetaminophen

Tylenol/Para-aminophenol

More central effects
NOT an anti-inflammatory drug

Mechanism by --| COX-3? (unknown)

High dose liver toxicity (if liver ENZ sat. form reactive intermediates)

Legend
- Side Effects
- Benefits

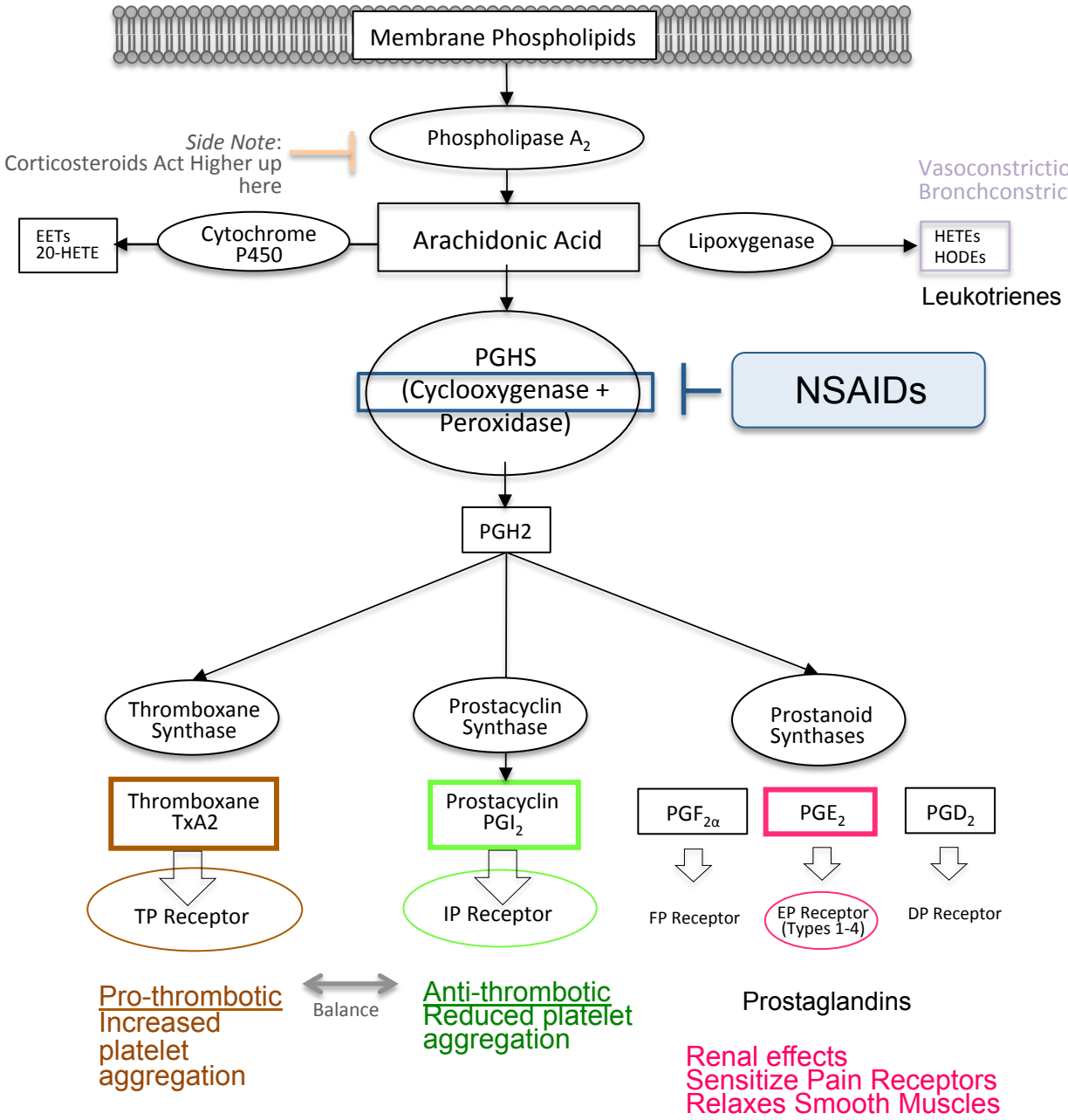
NSAIDs:
Intestinal (Block COX-1 in stomach, PGE2 receptor stops H^+ pumps, So NASIDs increase acid secretion, to prevent give synthetic prosentoid (mesoprostol), or have pill with enteric coating, or eat food to buffer)
Aspirin-induced asthma + skin rxn (leukotriene made more)

Aspirin:
ASA Reye's Syndrome in children, brain and liver problems, can be deadly (ASA never given to children)
Urate accumulation (Low dose ASA blocks urate secretion in glomerulus)
Bleeding
Not for pregnancy (PGE_2 causes smooth muscle contraction)

Both NSAIDs and COXibs → Renal Failure: Vasoconstriction (shunts to leukotriene arm) , ↑BP (Na^{2+} retention/perf edema, and ↓GFR)

NSAIDs and COXibs Stop Inflammation by stopping PGs ⊣ PGs involved in late stage of inflammation and increase vasopermeability, platelet aggregation at site of injury

All Stop **Fever** and **Pain** by preventing the formation of prostaglandins responsible for causing this ⊣
Fever (PGE_2 increases body temperature set point = heat)
Pain (PGs reduce stimulus threshold for Nociceptor Pain receptors = more sensitive)



If PG arm is blocked by NSAIDs/COXibs, Arachidonic Acid can be shunted to form more Leukotrienes