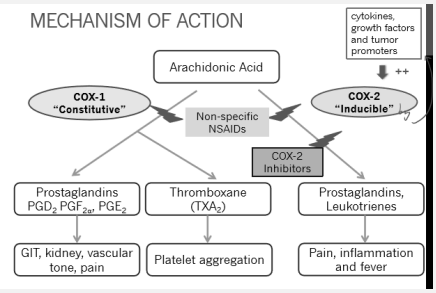
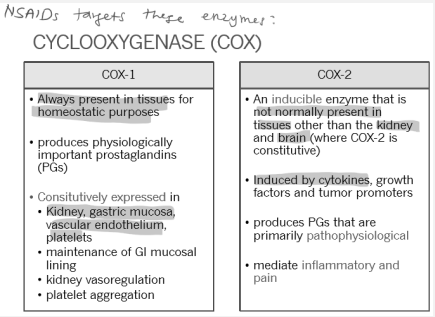
MOA



Enzyme targets by NSAIDs

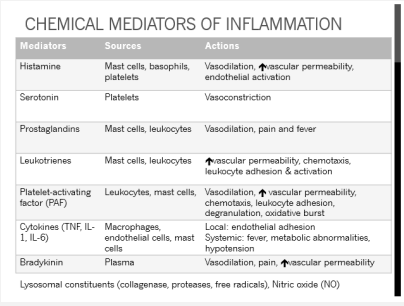


REMEMBER

COX-2
= C = K = Kidney
= 2 = B = Brain

COX-1 = 1 = Number 1 so good at affecting everything else

Chemical mediators of inflammation



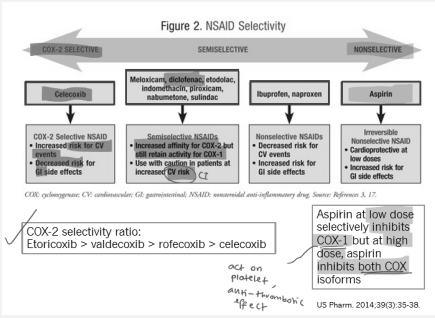
CHEMICAL MEDIATORS OF INFLAMMATION

Mediators	Sources	Actions
Histamine	Mast cells, basophils, platelets	Vasodilation, ↑vascular permeability, endothelial activation
Serotonin	Platelets	Vasoconstriction
Prostaglandins	Mast cells, leukocytes	Vasodilation, pain and fever
Leukotrienes	Mast cells, leukocytes	↑vascular permeability, chemotaxis, leukocyte adhesion & activation
Platelet-activating factor (PAF)	Leukocytes, mast cells,	Vasodilation, ↑ vascular permeability, chemotaxis, leukocyte adhesion, degranulation, oxidative burst
Cytokines (TNF, IL-1, IL-6)	Macrophages, endothelial cells, mast cells	Local: endothelial adhesion Systemic: fever, metabolic abnormalities, hypotension
Bradykinin	Plasma	Vasodilation, pain, ↑vascular permeability

Lysosomal constituents (collagenase, proteases, free radicals), Nitric oxide (NO)

extra information

Common NSAIDs



NOTES:
* Cannot take other NSAIDs before taking aspirin because they may prevent aspirin action
* COX-2 selective has less AE of GI
* Naproxane less CVS effect dt antithrom-boxane

REMEMBER:

"ABCDiN"
- Aspirin
- iBuprofen, Naproxen
- COX-2 selective
- Diclofenac

COX-2 Selective, remember **"-coxib"**
main: Celecoxib

Beneficial effects of inhibition PG synthesis

Analgesia

> ↓Bradykinin, 5-HT (serotonin)

Antipyretic

> ↓ IL-1, reset thermostat

Anti-inflammatory

> ↓ PGE2, PGI1

Antithrombotic

> by aspirin at low dose (permanent acetylation, inhibit platelet activation)

Arteriosus (NSAIDs for closure of patent ductus arteriosus)

Adverse effect

nSAIDS

> Allergy
> Impaired
> Renal function
> Damage stomach wall (ulcer)

Contraindication

Bleeding

> Avoid in patient:
> -Anticoagulants
> -Pregnancy 3rd trimester (premature close DA, risk bleeding)
> Inhibit platelet cycloxygenase (COX), thereby **blocking the formation of thromboxane A2 (TXA2)** and impairing TXA2 dependent platelet aggregation

Asthma

> Inhibition of COX pathway shifts the arachidonic acid metabolism to **Lipoxy-genase (LOX) pathway** leading to **increased leukotriene synthesis**

Allergy

Stomach (Peptic ulcer, gastritis)

> Mucosal damage by –
> COX-1 inhibition: Reduced blood flow
> Topical irritation: Epithelial damage
> COX-2 inhibition: Leukocyte adherence
> *Can prescribe PPI for gastro-protection

CVS event

> angina, recent cardiac bypass usrgery, MI, any CV events

REMEMBER
CBARS