Cyclooxygenase (COX) Inhibition

Definition

Cyclooxygenase inhibition refers to the **blocking of COX enzymes**—key enzymes involved in the conversion of arachidonic acid into **prostaglandins** and **thromboxanes**, which mediate pain, inflammation, fever, and platelet aggregation.

This mechanism is the **primary action of NSAIDs (Nonsteroidal Anti-Inflammatory Drugs)**.

COX Isoenzymes

Isoform	Location	Function
COX-1	Constitutive (expressed in most tissues)	Protects gastric mucosa, supports renal perfusion, enables platelet aggregation (via TXA_2)
COX-2	Inducible (upregulated in inflammation)	Produces prostaglandins involved in pain, fever, inflammation
COX-3 *(hypothetical)*	Variant of COX-1 (not well understood)	May be inhibited by paracetamol/acetaminophen

NSAIDs and COX Inhibition

NSAIDs reduce pain and inflammation by inhibiting one or both COX isoforms:

Drug Type	COX Selectivity	Examples
Non-selective NSAIDs	Inhibit COX-1 and COX-2	Ibuprofen, Ketorolac, Diclofenac
COX-2 selective inhibitors	Preferentially inhibit COX-2	Celecoxib, Etoricoxib

Clinical Relevance in Surgery

Inhibition of COX-1 leads to:

- ↓ Thromboxane A_2 → ↓ Platelet aggregation → ↑ Bleeding risk
- ↑ Risk of gastrointestinal ulceration

Inhibition of COX-2 leads to:

- ↓ Inflammation and pain (therapeutic effect)
- Minimal effect on platelets → **safer in surgical patients**

⚠ Implications in Neurosurgery

- Concern: NSAIDs (especially COX-1 inhibitors) might increase **postoperative bleeding**
- Evidence: Recent meta-analyses suggest **no significant increase in bleeding** with NSAID use

after craniotomy when used judiciously (Cardoso et al., *Neurosurgery* 2025)

Summary

Cyclooxygenase inhibition is central to the action of NSAIDs. While effective for **analgesia and anti-inflammation**, COX-1 inhibition may impair **platelet function**, potentially increasing bleeding risk. **COX-2 selective inhibitors** offer a safer alternative in high-risk surgical contexts.