



NOTES ON CYCLO-OXYGENASE, ARACHIDONIC ACID, AND PROSTAGLANDINS

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The accompanying figure provides in succinct form a synopsis of the most useful details concerning arachidonic acid metabolism. The purpose of the figure is summarise where COX occurs, what it does to what, and what the actions of prostaglandins are.

The figure is coded. Enzymes are drawn in ellipses, with their name in italics. Substrates and products are printed in Times Roman font. Clinical features of physiological effects are printed in italics. Parenthetic information is printed in dotted boxes. Block arrows indicate the action of an enzyme on a substrate. Conventional arrows indicate the fate of a product or the action of a product on a physiological system.

Area 1 of the figure encapsulates the two isoforms of COX, and the tissues in which each is respectively mainly found. [Note how COX2 is located in musculoskeletal tissues]

Area 2 indicates the preliminary chemical pathway. PLA2 acts on membrane phospholipids to produce arachidonic acid. Lipoxygenase can act on arachidonic acid to produce leukotrienes. [The significance of this step is that if arachidonic acid is NOT used by the COX pathway, the arachidonic acid builds up; more is available for Lipoxygenase; and more leukotrienes are produced. This is the basis for the bronchospasm side effect of NSAIDS.]

COX can act on arachidonic acid to produce PGG2. COX also acts on PGG2 to produce PGH2. Either COX1 or COX2 can do this. IT is just that when COX2 is induced, it produces a lot of PGG2 and PGH2.

{ Parenthetically, in Area 3, there is a note that COX can also act on polycyclic hydrocarbons to produce oxygenated hydrocarbons that are carcinogenic. }

PGH2 can have its own actions, or it is converted to other PGs.

Area 4 is designed to summarise the actions of the various PGs.

The greatest number and big effects belong to PGE2. It has direct effects, and indirect effects because of its ability to produce vasodilation. The "flavour" of PGE2 is "hot and wet".

- It produces fever.
- Since it vasodilates it lowers blood pressure.
- Because it vasodilates it promotes blood flow to the GIT and Kidney, which enhances its direct effects.

- In the GIT, it makes for anti-acid, (reduces acid secretion, promotes bicarbonate, and promotes mucus which protects against acid).
- In the Kidney, it makes for diuresis (hence "wet").
- In the uterus it causes contraction of smooth muscle.

The other PGs have a mixture of effects. These are not necessarily like those of PGE2. Some are opposite. Consequently, at times there is tension between the various PGs.

PGH2 increases blood pressure. [competes against PGE2]

PGI2 has on the GIT the same effects as PGE2. [Memory tip: all PGs have same effect on GIT]

PGI2 inhibits the uterus. [competes against PGE2]

PGI2 inhibits platelet aggregation which is what thromboxane is trying to promote.

Observation: PGI2 is a real bastard for not keeping this simple and uniform. That will help you remember the specifics.