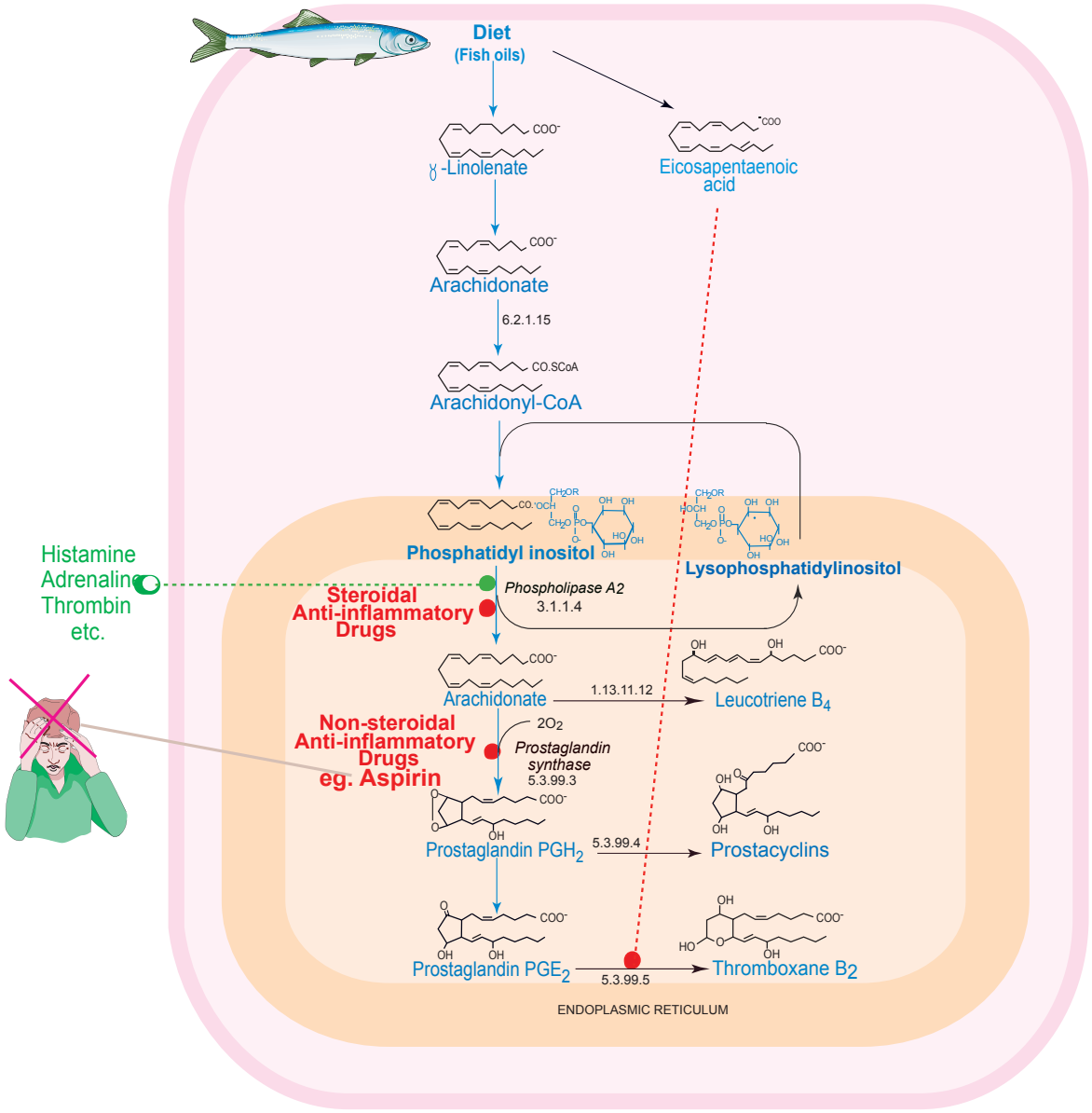
PROSTAGLANDINS,THROMBOXANES & LEUCOTRIENES



Prostaglandins and the other related eicosanoids are localised, almost ubiquitous, and transient "hormones" involved in a variety of physiological effects which can have very differing and even converse activities in differing tissues. These include involvement in inflammatory reactions such as rheumatoid arthritis, in the control of blood pressure, in blood clotting, in the induction of labour or in the aggravation of pain and fever.

Arachidonic acid arises from γlinolenic acid ñ an ìessentialî lipid which must be obtained from the diet. It is then metabolised to become an acyl group in phospholipids (especially phosphatidylinositol) which are part of the membrane of the endoplasmic reticulum, from whence it is released as the free arachidonic acid by phospholipase A2. This enzyme is activated by a variety of external stimuli such as adrenaline, histamine, or thrombin, and is inhibited by corticosteroids and other so-called Steroidal Anti-inflammatory Drugs which thus prevent the re-formation of arachidonic acid - the precursor of prostaglandin.

The oxidative cyclisation of arachidonate into prostaglandins takes place in the lumen of the endoplasmic reticulum by the prostaglandin synthase complex which has cyclooxygenase and peroxidase components, the former of which can be inhibited by aspirin and other non-steroidal anti- inflammatory drugs

The reaction by which Prostaglandin is formed from arachidonic acid is one of the great "hidden treasures " of metabolism which gives a very satisfying explanation of one of the most universal of drug therapies - why does aspirin relieve headaches - and worse?

ENZYMES

1.13.11.12	Lipoxygenase	5.3.99.4	Prostacyclin synthase
3.1.1.4	Phospholipase A2	5.3.99.5	Thromboxane A synthase
5.3.99.3	Prostaglandin E synthase	6.2.1.15	Arachidonate-CoA ligase