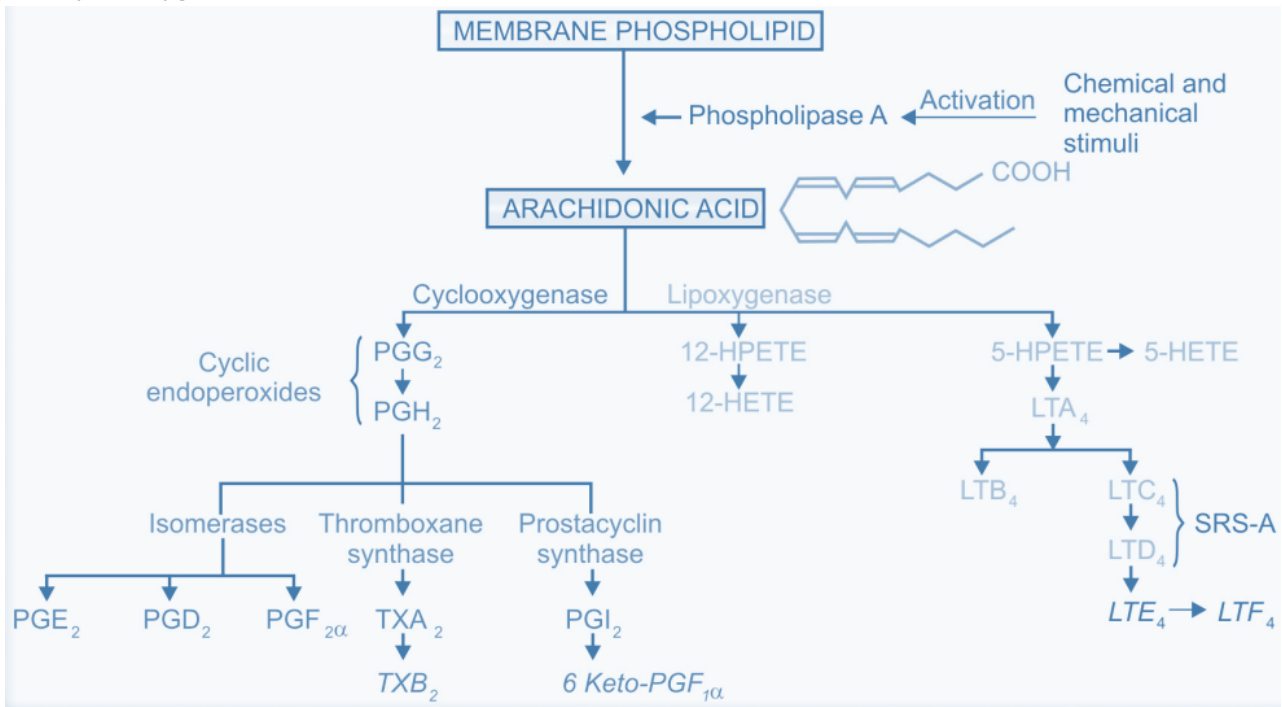


EICOSANOIDS/Prostaglandins

Interest in eicosanoids first arose in the 1930s after reports that semen contained a lipid substance, apparently originating from the prostate gland, which contracted uterine smooth muscle. Later, the factor was named as prostaglandin, and it was not a single substance but a whole family of compounds generated by virtually all cells from 20-carbon unsaturated fatty acid precursors

BIOSYNTHESIS: Prostaglandins and thromboxanes are synthesized from arachidonic acid (obtained from membrane phospholipids due to the action of phospholipase A₂; rate limiting enzyme) with the help of enzyme cyclooxygenase (COX)



PROSTANOID RECEPTORS There are five main classes of prostanoid receptor, all of which are G protein-coupled receptors. They are termed **DP, FP, IP, EP and TP receptors**, respectively, depending on whether their ligands are PGD, PGF, PGI, PGE or TXA species. *Some have further subtypes*; for example, there are four EP receptors.

Receptor	Physiological ligands	Distribution	General physiological effect
IP	PGI ₂ >> PGD ₂	Abundant in cardiovascular system, platelets, neurons and elsewhere	
DP ₁	PGD ₂ >> PGE ₂	Low abundance; vascular smooth muscle, platelets, CNS, airways, the eye	Generally inhibitory: e.g. smooth muscle relaxation, anti-inflammatory and anti-aggregatory effects
EP ₂	PGE ₂ > PGF _{2α}	Widespread distribution	
EP ₄	PGE ₂ > PGF _{2α}	Widespread distribution	
TP	TxA ₂ = H ₂ > D ₂	Abundant in cardiovascular system, platelets and immune cells. Two subtypes known with opposing actions	Generally excitatory: e.g. smooth muscle contraction pro-inflammatory and platelet aggregatory actions
FP	PGF _{2α} > PGD ₂	Very high expression in female reproductive organs	
EP ₁	PGE ₂ > PGF _{2α}	Myometrium, intestine and lung	
EP ₃	PGE ₂ > PGF _{2α}	Widespread distribution throughout body; many isoforms with different G protein coupling	Generally inhibitory: e.g. smooth muscle relaxation, anti-inflammatory and anti-aggregatory effects
DP ₂	PGD ₂ > PGF _{2α}	Different structure to other prostanoid receptors. Widely distributed especially in immune cells	

Major clinical uses of prostanoids:

- Gynaecological and obstetric:

- termination of pregnancy: gemeprost or misoprostol (a metabolically stable prostaglandin [PG]E analogue)

- induction of labour: dinoprostone or misoprostol

- postpartum haemorrhage: carboprost.

- Gastrointestinal:

- to prevent ulcers associated with non-steroidal anti-inflammatory drug use: misoprostol

- Cardiovascular:

- to maintain the patency of the ductus arteriosus until surgical correction of the defect in babies with certain congenital heart malformations: alprostadil (PGE₁);

- to inhibit platelet aggregation (e.g. during haemodialysis): epoprostenol (PGI₂), especially if heparin is contraindicated;

- primary pulmonary hypertension: epoprostenol

- Ophthalmic: – open-angle glaucoma: latanoprost eye drops