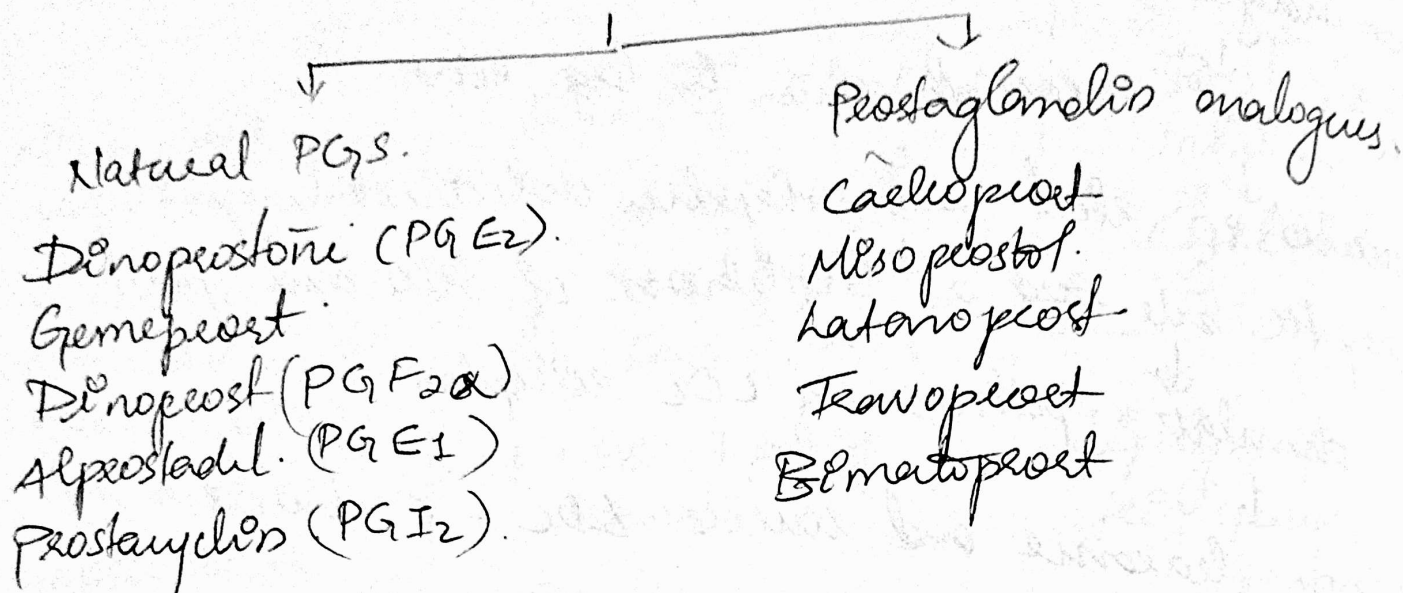
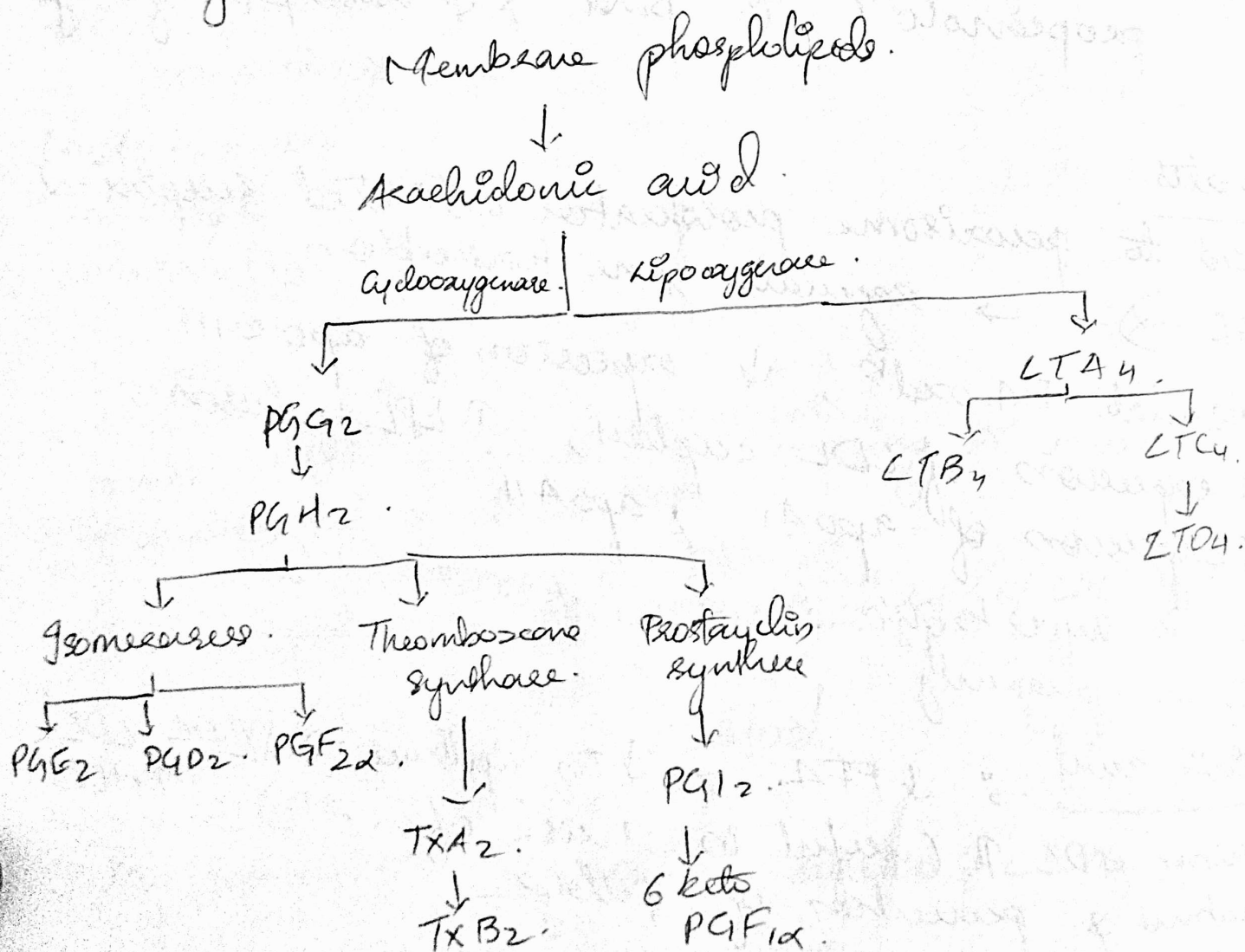


PROSTAGLANDINS.



Synthesis.



COX-1 → constitutively - functions.
 COX-2 → constitutively in brain & kidney,
 inducible INFLAMMATION
 COX-3 → genes of fever, site of action of paracetamol.
 Lipooxygenase pathway → lung, WBC, platelets.
 LTB₄ - potent chemotactic.
 LTM → anaphylaxis.

Degradation : occurs in most tissues, fastest in lungs.
 usually survives to few minutes. Excreted in urine.
 PGI₂ → catabolized mainly in kidney.

Inhibition of synthesis.
 NSAIDs → inhibits COX product synthesis.
 • Aspirin acetylates COX.
 others are competitive & reversible inhibitors.
 Glucocorticoids inhibit release of arachidonic acid
 from membrane lipids.

Prostanoid receptors
 G protein coupled receptors.
 5 families → DP (PGD₂),
 EP (PGE₂),
 FP (PGF_{2α}),
 IP (PGI₂),
 TP (Tx A₂).

3 groups : (i) constitutive gp (EP, FP, TP)
 couples with Gq protein, IP₃-DAG
 cause smooth muscle work, platelet aggregation.

(ii) Relaxant group.
couple with G_s protein -
activate adenylyl cyclase $\rightarrow$ cAMP $\rightarrow$ PKA
smooth muscle relaxation, inhibition of platelet
aggregation.

(iii) Inhibitory receptor (EP_3)
 $\rightarrow$ couples with G_i protein.
inhibits adenylyl cyclase.
inhibits lipolysis.

Actions:

① PGE_2 .

- $\rightarrow$ Blood vessels $\rightarrow$ VD, $\downarrow$ BP.
- $\rightarrow$ heart - weak inotropic, reflex cardiac stimulation.
- $\rightarrow$ platelets $\rightarrow$ variable effect.
- $\rightarrow$ uterus $\rightarrow$ contraction, softening of cervix.
- $\rightarrow$ bronchi - dilatation, inhibits histamine release.
- $\rightarrow$ stomach $\rightarrow$ $\downarrow$ acid secretion, $\uparrow$ mucus production.
- $\rightarrow$ intestine - contracts longitudinal muscles.
relaxes circular muscles.
 $\uparrow$ peristalsis.
 $\uparrow$ Cl^- & H_2O secretion.
- $\rightarrow$ Kidney - Natriuretic.
 $\downarrow$ Cl^- reabsorption.
inhibit ADH action, VD, renin release.
- $\rightarrow$ CNS $\rightarrow$ Pyrogenic
Aff. nerves $\rightarrow$ sensitizes to noxious stimuli $\rightarrow$ pain.
- $\rightarrow$ Endocrine system - Release of ant. pit. H, steroids, etc.
TSH like action.
- $\rightarrow$ Metabolism - Antilipolytic, insulin-like action, mobilizes
from fat.

② PGF₂

- Blood vessels → constricts larger vessels & some arterioles
- uterus → contraction, Potent uterine
- Bronchi → constriction
- Intestine → spasmogenic, ↑ fluid & electrolyte secretion

③ PGI₂

- Blood vessels → VD, ↓↓ BP.
- Platelets → Anti aggregation.
- Bronchi - dilatation, inhibits histamine release.
- Stomach → ↓ acid secretion, mucosal VD.
- Intestine → weak spasmogenic, inhibits toxin-induced fluid secretion
- Kidney - stimulates, VD, renin release.
- Aff. nerve → tenderness.

TXA₂

- Blood vessels - VC.
- Platelets → ↑ aggregation & release reaction
- uterus → contraction
- Bronchi - constriction
- Intestine → weak spasmogenic
- Kidney → vasoconstriction.
- PGF₂ & → ↑ mucosal outflow, ↓ IOT.

USES.

I. OBSTETRIC USES.

① Abortion.

- Intravaginal PG_{E2} pessary
Mifepristone 600mg orally + misoprostol } 1st Trimester.
Methotrexate + Misoprostol.
- Extra amniotic Puffalon PG_{E2} + IV inf. oxytocin
or intra amniotic carboprost + hypertonic saline
for mid-trim & aborion.

② Induction of labour

- PG_{E2} or PGF_{2} instead of oxytocin in
toxaemic and renal failure patients.
- PG_{E2} → augment labour in primiparae.

③ Cervical priming.

- low doses of PG_{E2} .
Dinoprostone Intravaginal.

④ Post Partum Hemorrhage

- Carboprost inf. IM. in patients unresponsive
to ergometrine and oxytocin.

II. Non - OBSTETRIC USES.

⑤ Glaucoma.

- Topical $PGF_{2\alpha}$ analogues → Latanoprost, Travoprost
bimatoprost → First choice drugs in wide
angle glaucoma.

⑥ Peptic ulcer :
prevention & Rx of NSAID associated GI injury
and blood loss.
Misoprostol.

⑦ Maintains patency of ductus arteriosus :
in congenital heart disease until corrective
surgery
PGI₂ - Alprostadil given.

⑧ To avoid platelet damage :
during hemodialysis or cardiopulmonary bypass.
To increase haemat of platelets for transfusion.
~~PGI₂~~ PGI₂ → Epoprostenol.

⑨ Pulmonary hypertension
PGI₂ - Epoprostenol IV infusion
Iloprost or Treprostinil
lowers pul. artery resistance.

⑩ Peripheral vascular diseases
PGI₂ or PGE₁, infused IV → relieve pain,
promote healing of ischemic ulcers in severe cases
of intermittent claudication and in Raynaud's disease.

⑪ Erectile Dysfunction . Alprostadil sup & i.t. pens.
oral sildenafil / tadalafil → now preferred.

S/E : N, V, D, uterine cramps, conjunctivitis, vaginal
bleeding, flushing, shivering, fever, malaise, fall
in BP, tachycardia, chest pain.