



Pharmacology

Subject : Eicosanoids

Lec no : 18

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وقل رب زدني علما

تجدون في guidance مادة الفارما على موقع النادي :



للوصول الى guidance الفارما و تفاريغ
المادة كاملة :



كل اعمال الفريق العلمي تنشر على قناة
التليغرام



شرح دكتور شريف و دكتور طارق للمادة

شرح فودة لمادة الميند

شرح فودة لمادة الفايثيل

تفاريغ دفعة الاز جداااا قوية ، خاصة مادة
الفايثيل لانها بتحتاج تفاريغ كثير ، و برضه
تفاريغ جيبة بشفعة وريد قوية

جداول رح تساعدكم كتبيبيبي
بحفظ الادوية بمادة الفايثيل

كويبات الدكاترة

WHAT ARE EICOSANOIDS ?

- Eicosa: (Greek) = 20.

They are compounds which are derived from polyunsaturated fatty acids with 18, 20 & 22 carbon skeletons.

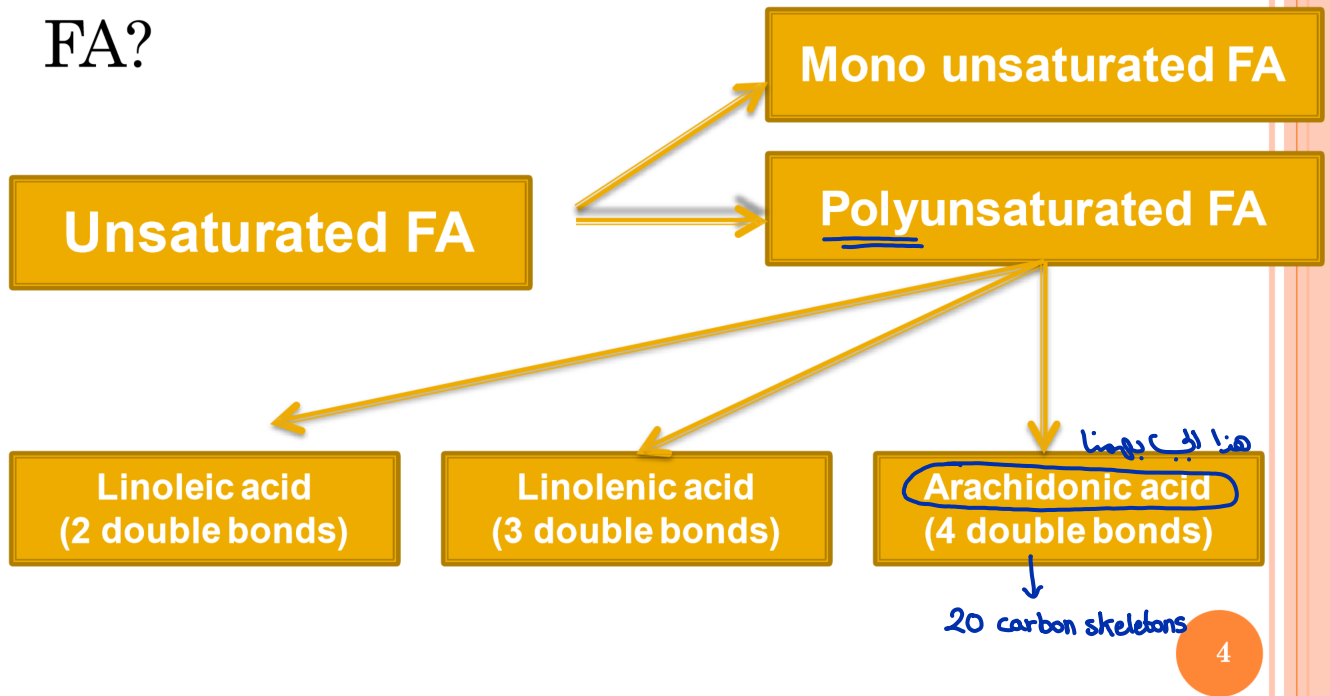
- **Needs receptors:** either plasma membrane or intracellular binding protein.

○ **Eicosanoids** is a Generic term for the 20 Carbon related compounds like:

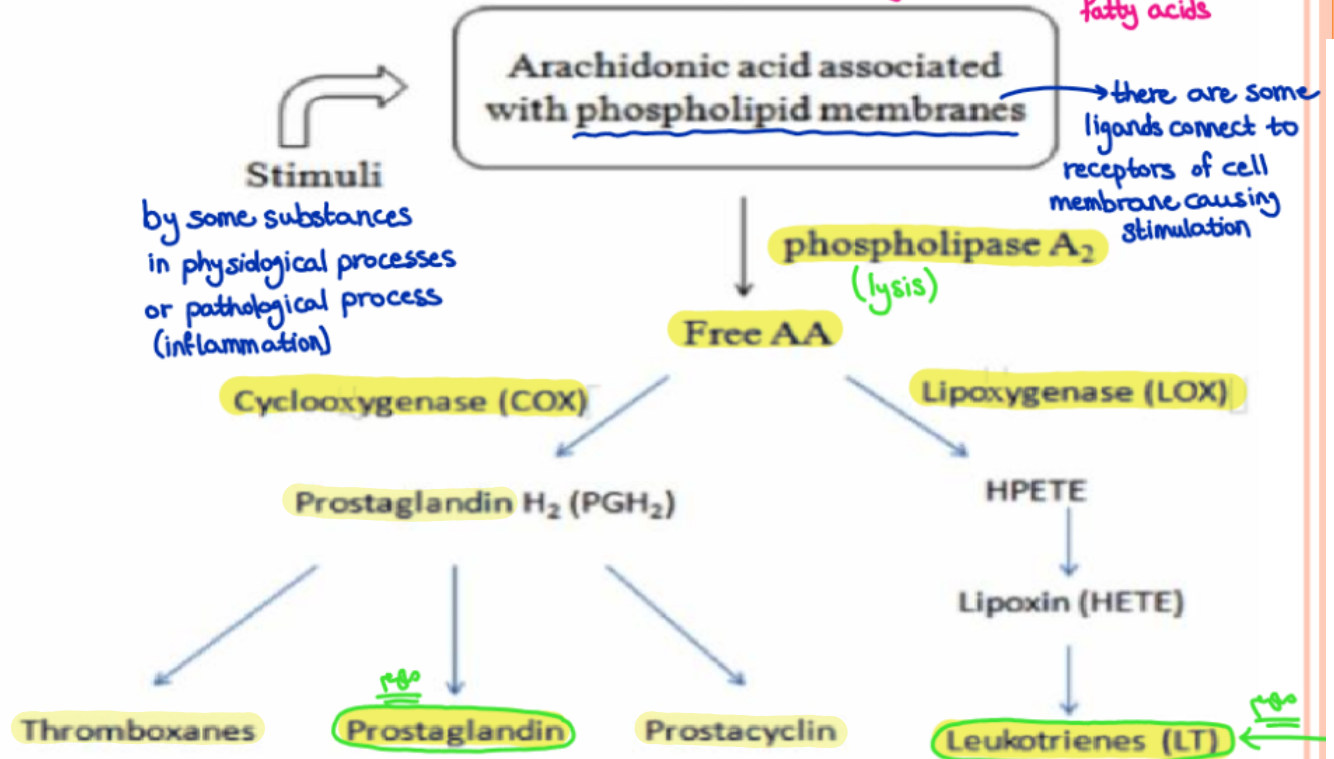
- I. Prostaglandins (PGs)
- II. Prostacyclins (PGI₂)
- III. Thromboxanes (TX)
- IV. Leukotrienes (LT)
- V. Lipoxins (LX)

FATTY ACIDS

- LOWER FA VS. HIGHER FA?



*if Arachidonic Acid exposed to certain enzymes → Liberation of free fatty acids



*ligands can be hormones or growth factors or drugs.

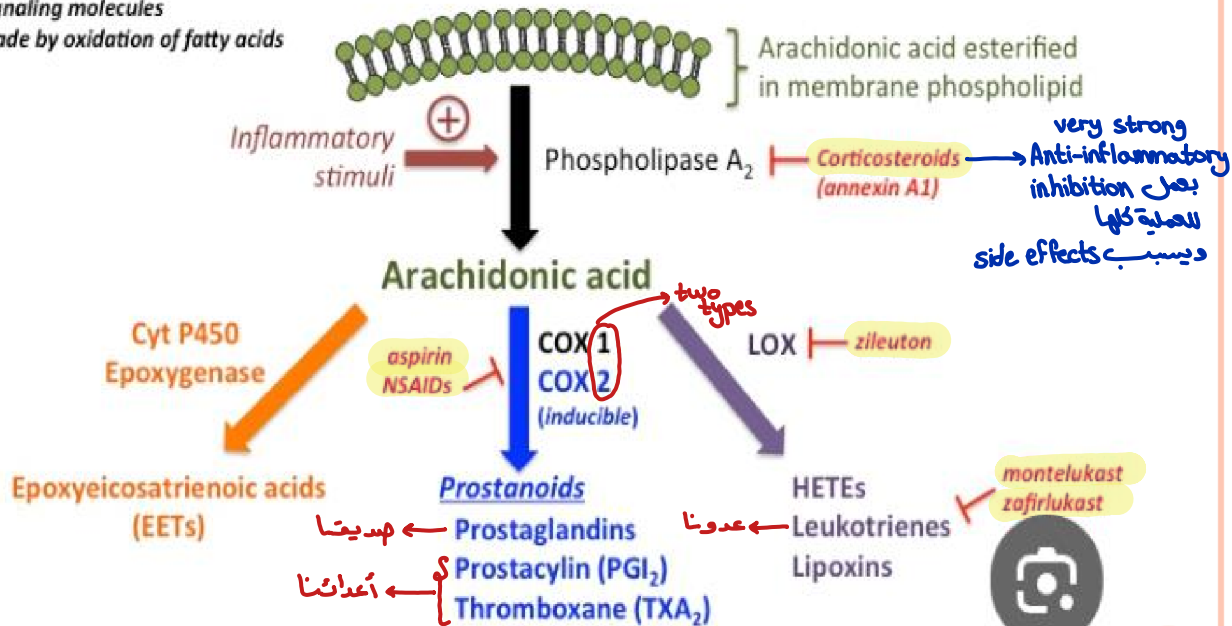
INHIBITION OF PG SYNTHESIS

الدوية الخمراد
حفظ + مهمة
بتعمل inhibition

Prostaglandin

Eicosanoids

signaling molecules
made by oxidation of fatty acids



very strong
Anti-inflammatory
inhibition
بعمل
للعملية كلها
side effects
ديسبب

two types

NSAIDs → Nonsteroidal anti-inflammatory drugs

INHIBITION OF PG SYNTHESIS

- Inhibited by structurally unrelated compounds
 - E.g. Corticosteroids (Cortisol) → works on Phospholipase A₂
- Non-steroidal anti-inflammatory drugs → works on COX 1, 2
- Aspirin inhibits PG synthesis → works on COX 1, 2
 - **Aspirin** – irreversibly blocks synthesis of cyclooxygenase
- **Indomethacin & Phenylbutazone** – reversibly blocks synthesis of cyclooxygenase.

← ما يمكن
منه

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↓ Pathological (COX 2)

Role Of PGs In Immunity And Inflammation

○ Prostaglandins are produced in more amounts at the time of:

- **Fever**
- **Pain**
- **Nausea and Vomiting** (there is nothing to reflex or protect from HCl by mucous membrane)
- **Inflammation** (Chemotaxis & release of mediators)

↓ Physiological (COX-1)

الجماعة دول
أيسقاتنا ↓

Biological effects

1- PGE₁, E₂, I₂ (Useful & supportive inside the body)

- -VD. → Vasodilation (cardiovascular) which causes edema
- Lung: Bronchodilation.
- GIT: ++ mucus production. → to protect stomach
- Ut: Cont. of pregnant uterus. during delivery
- Relax non pregnant uterus.
- Kid: ++ **RBF**. promotes urine formation and urine output.
↓ Renal Blood Flow
- Thus helps in removing waste out of the body.
- PGI₂: -- Platelet aggregation. (inhibition) → يحمي الجسم من صدمات الجلطات

الجماعة دول
أيسقاتنا ↓ no clinical use

2-PGF_{2a}, **TXA₂**, LTb₄:
↑ Thromboxane A₂ → Leukotriene B₄

- -VC. (LTs produce inflamm. VD). → involved in pathologic dilation "inflammation" so it's the major cause of edema
- Lung: Bronchospasm. (Bronchoconstriction)
- GIT: ++ mucus production.
- Ut: Cont. of pregnant uterus.
- Kid: --RBF. promotes urine formation and urine output. Causes Renal failure
- ↓ Aspirin inhibits TXA₂ so inhibits thrombosis (platelet aggregation)
- TXA₂: ++ Platelet aggregation. causes thrombosis
- LTs: chemotaxis. (attraction of inflammatory cells to the site of the inflammation).

Uses:

1. PGE₁

- i.v to produce controlled hypotension in some surgeries
- Intracavernous in cases of impotence in case of erectile dysfunction to cause vasodilation & increase blood flow in sex organs
- Tried as vasodilator in peripheral vascular diseases.
- TGV.** → Transposition of great vessels to maintain patent ductus arteriosus
- Misoprostol (cytotec) PGE₁ analogue used orally in peptic ulcers. (++ mucous membrane) to increase the thickness of mucous coat of the stomach

↓
الاسم الآخر التجاري

3-Epoprostenol (PGI₂) antiplatelet aggregation.

4PGE₂ tried in bronchial asthma but it is irritant.

5-PGE₂ & PGF_{2a} for induction of abortion and labor. (القطلة الصناعي)

6- PGs in Kidneys increases GFR and promotes urine formation and urine out put. Thus helps in removing waste out of the body.

اسم القطرة eyedrop

7-Latanoprost is PGF_{2a} used topically in treatment of glaucoma. in which increased pressure in the eye can lead to gradual loss of vision.

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8-PGE₂ is used in organ transplantation to reverse rejection

* TGV → in congenital anomaly التنصبات الخلقية
Pulmonary artery يكون Aorta مكان
وأماكن معكوسة & Aorta بجمل
nonoxygenated blood & arises from
right side

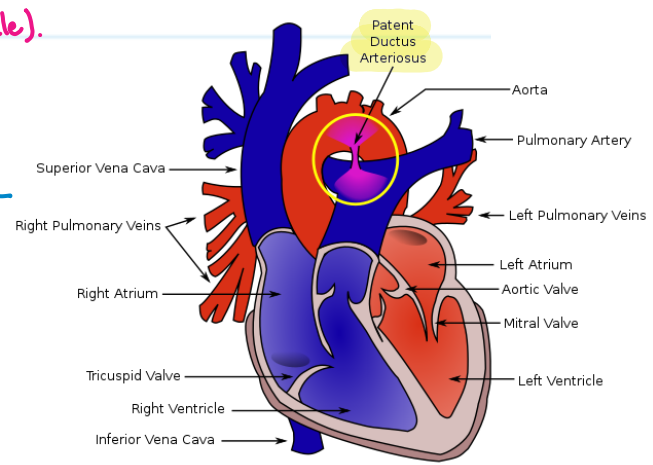
بينهم يكون من فتحة بتسك
بعد أسبوعين من الولادة فيجاءوا
مفوضين بطلبه دواء عنثان
oxygenated blood يتغذى إلى
Aorta

هذه الفتحة تسمى
patent ductus
arteriosus
ويكون عند الطفل
cyanosis

*GFR → Glomerular filtration rate

* Glucoma → we give the patient a drug to cause drainage to vitreous fluid (aqueous humor) السائل داخل العين
to decrease intraocular pressure by tissue directly (muscle).

← بعد أسبوعين من الولادة
بعمولة عملية
correction surgery
إذا تسكرت قبل بموت
الطفل



2. Prostacyclins (PGI₂)

Prostacyclins are type of **Eicosanoids/ Prostanoids**.

Principally **formed in vascular endothelium**

They are Platelet Aggregation Inhibition Factors

Biosynthesized by enzyme **Prostacyclin Synthetase**.

ROLES OF PROSTACYCLINS

- Prostacyclins are **Vasodilators**.
- Prostacyclins like Prostaglandins **inhibit platelet aggregation**.
- Prostacyclins **prevent Thrombus/clot formation**.
→ for patients of hemodialysis/open heart surgery

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THROMBOXANE

- Are produced by platelets (**called thrombocytes**)
- Act in formation of blood clot
- And reduction of blood flow to the site of clot

Increases

Vasoconstriction

Platelet aggregation

Lymphocyte proliferation

Bronchoconstriction

LEUKOTRINES

لماذا

Types of Leukotrienes:
LTB₄, LTC₄, LTD₄ and LTE₄

Drugs affecting:

-An **Antiasthmatic drug Prednisone** inhibits **Leukotriene biosynthesis**. → reduce the effect of Leukotrienes in tissue

-Montilucast and Zafirlucast: block receptors. → Antiallergic specially in Asthma for children (safe & effective with less side effects)

Ziluten : inhibit lipooxygenase enz.

→ reduce levels of Leukotrienes in tissue

Mechanism of action:

Kinins act by stimulation of 2 subtypes of **Gq** coupled receptors α_1
.That increases intracellular calcium through increasing I3P and DAG:

↓
increases vasoconstriction
causes Bronchospasm
(when muscles that line bronchi tighten)

Effect Of Leukotrienes

1-Leukotrienes are biologically active **components of Slow Reacting Substances (SRS-A)**. causes fluid leakage from blood vessels to an inflamed area

2-Leukotrienes are **100-1000 times more potent** than **Histamine** during allergic reactions

SRS-A are released during **Allergic reactions/Anaphylaxis**.

3-LTB₄ is a **potent chemotactic agent**.

(chemical substance which mediates movement of cells).

4-Leukotrienes by action are:

Bronchoconstrictors

Vasoconstrictors -

Levels Of Leukotrienes Increased In:
Allergies

Allergic rhinitis → التهاب الأنف التحسسي

Asthma

Overproduction: **Anaphylactic shocks**.

LIPOXINS

↓ not common
أحد

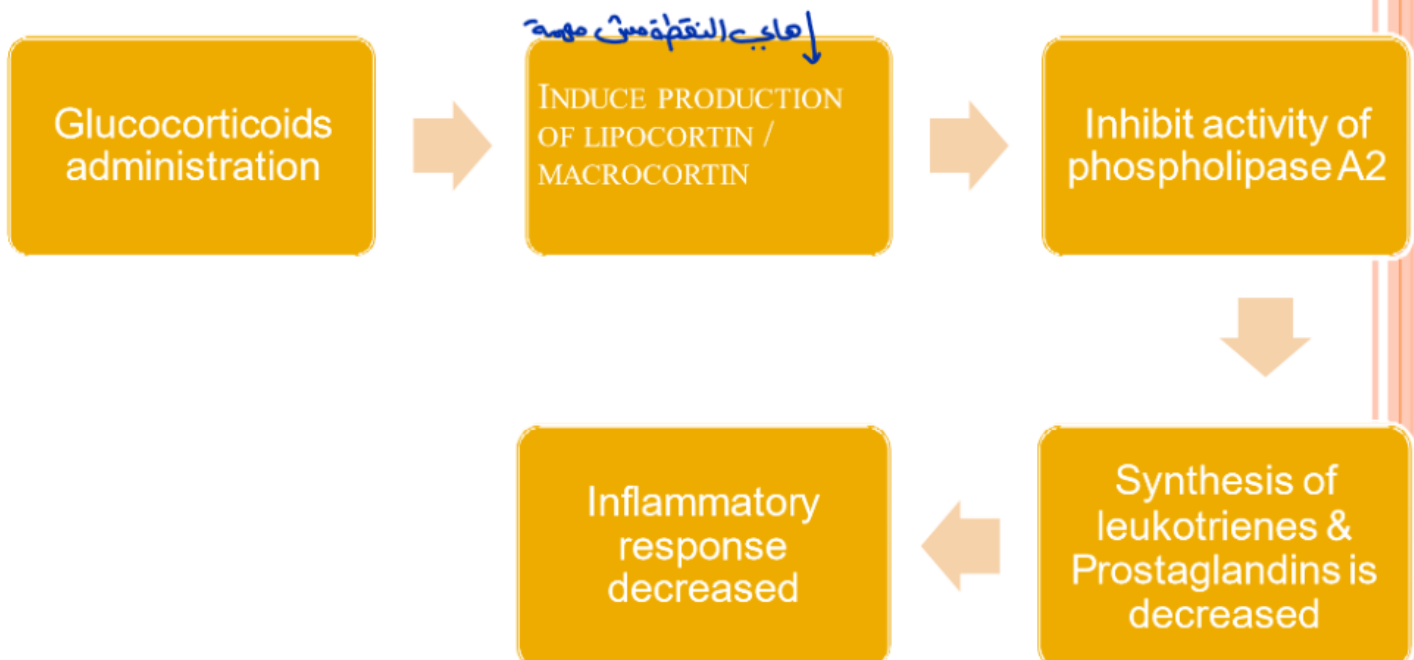
○ **Lipoxins** are Eicosanoids produced in Leukocytes of human body.

Lipoxins are essential in **maintaining tissue homeostasis and resolve inflammation.**

○ **Lipoxins are:**

- Vasoactive/Vasodilators
- Anti-inflammatory
- Anti-proliferative
- Pro-resolving
- Immunoregulatory
- Chemotactic substances

ROLE OF DRUGS



Pharmacological applications of Eicosanoids

1. Cardiovascular use- pulmonary arterial hypertension, peripheral vascular disease. for keeping the ductus arteriosus open until surgery in neonates carrying certain cardiac malformations and platelet anti-aggregating agents. (with patients have risk of thrombosis: Hemodialysis/ischemic heart)
2. Digestive Uses- indicated in the treatment of gastro duodenal ulcer and for the prevention of NSAID-induced ulcers. (or to protect stomach from excess secretion so give them prostaglandin)
المسكنات or Cortisone
3. Gynecological and obstetrical uses - They induce cervical dilatation and uterine contractions, particularly in late pregnancy. Used for medical termination of pregnancy and induction of labour.
أمرأهن النساء *توليد*
جاء موعد الولادة في الشهر التاسع ولما ما حصلت ولادة
Abortion
because of medical cause (mother with Heart disease.)
4. Ophthalmologic Use- lower intraocular pressure. in case of Glucoma
5. Anti-inflammatory use- Inhibitors of cyclo-oxygenases have anti-inflammatory properties and include nonsteroidal anti-inflammatory drugs or NSAID. The useful effects in therapeutics are-

5.
هون
موتوني
الحاينع
الحايب

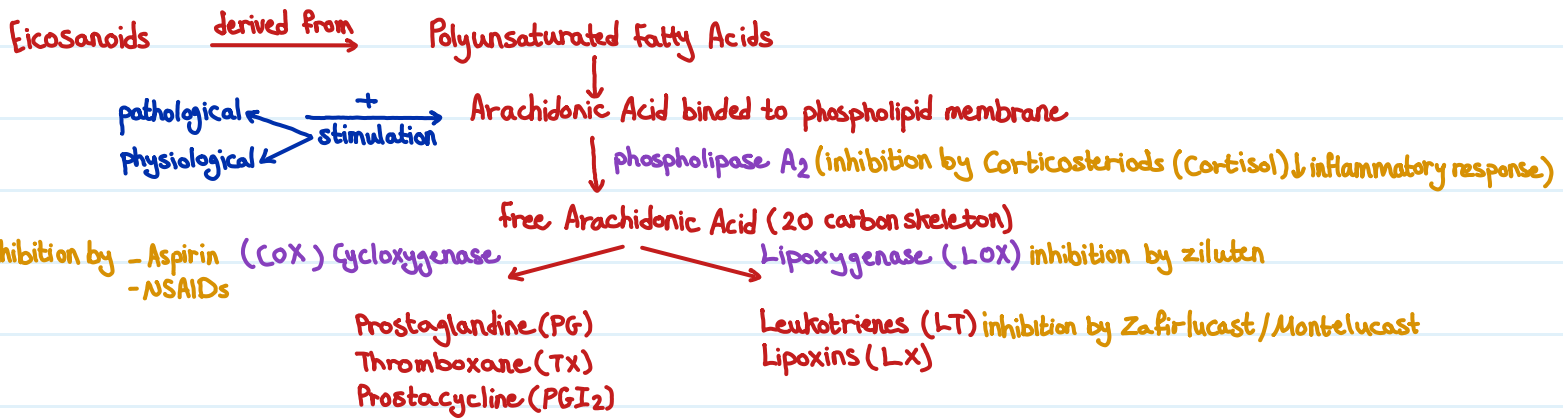
anti-inflammatory effect

analgesic effect

antipyretic effect (خافهن الحرارة)

inhibition of platelet aggregation and decrease of

thromboembolic risk (well-known with aspirin at low doses)



* Biological effects:

- PGE₁, PGE₂, PGI₂ : \rightsquigarrow Supportive
 \downarrow PGE₁

Vasodilation: Pulmonary arterial hypertension / peripheral vascular disease / Transposition of great vessels (to maintain patent ductus arteriosus) / Controlled hypotension / Impotence (erectile dysfunction) /

Bronchodilation: Bronchial Asthma (PGE₂)

Kidneys: ++ Renal Blood flow / ++ Glomerular filtration rate / promotes urine production & urine out put so helps in removing wastes from the body.

GIT: ++ mucous membrane in case of peptic ulcer to protect stomach (by Misoprostol or cytotec-PGE₁)

Uterus: Contraction of pregnant uterus & Cervical dilation in abortion or labour / Relax of nonpregnant uterus (PGE₂ / PGF₂ α)

Epoprostenol (PGI₂) \rightarrow inhibition of platelets aggregation (patients with open heart / Hemodialysis) so protection from clot or thrombosis

- PGF₂ / TXA₂ / LTB₄ : \rightsquigarrow clinically not use $\ddot{\text{A}}$

Vasoconstriction except LTB₄ \rightarrow Vasodilation

- \rightarrow active (SRS-A) during allergies / Anaphylaxis which cause leakage of fluid from blood vessels to the inflamed area (major cause of edema)
- \rightarrow Chemotaxis (attraction of inflammatory cells to the inflamed site)

Bronchospasm / GIT: ++ mucous membrane / Contraction of uterus / kidney: -- Renal Blood flow causes kidney failure

TXA₂ \rightarrow ++ Platelet aggregation which causes thrombosis

PGF₂ α \rightarrow \downarrow Intraocular pressure in cause of Glucoma (by Latanoprost)

PGF₂ \rightarrow in organ transplantation to reverse rejection

* LT is G γ (α) receptor which increases calcium intracellularly (100 - 1000 times more potent than Histamine)

* Role of PGs in immunity & inflammation (produce in more amounts): Fever / Pain / Inflammation / Nausea & Vomiting

* LT levels increased in: Allergies / Asthma / over production in Anaphylactic shock