



جامعة ٦ أكتوبر
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AUTACOIDS



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LOs

- Define & classify autacoids
- Revise the physiology of histamine
- Enumerate the actions & indications of antihistaminics related to H-receptors blockade
- Classify anti-histaminics explaining the differences between different classes as related to actions, indications & adverse effects

Definition

Diverse group of substances

- Produced by **various tissues**
- Induce **slow contraction** of smooth muscle

They include

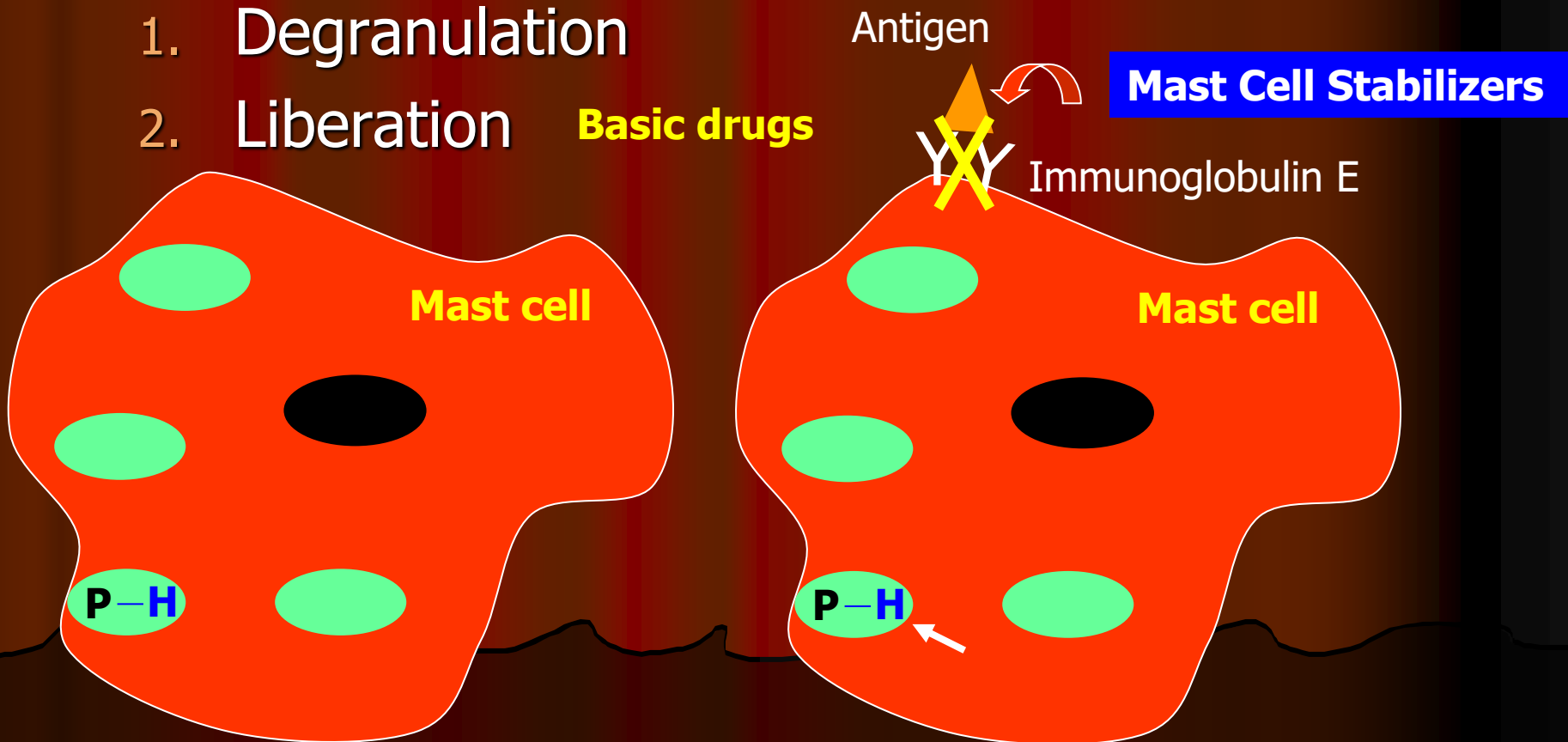
- Amines e.g. **Histamine** & Serotonin
- Eicosanoids e.g. **Prostaglandins** & Leukotrienes
- Polypeptides e.g. Angiotensin & Kinins

Histamine

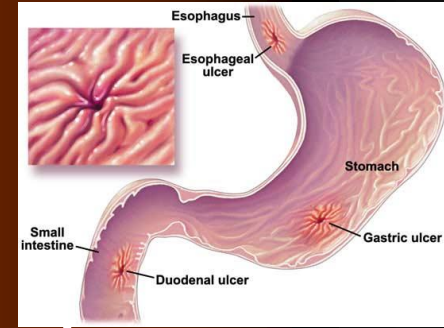
1. **Synthesis:** decarboxylation of histidine
2. **Storage:** in **storage granules** in mast cells
3. **Release:**

1. Degranulation

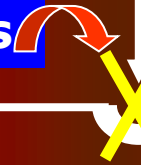
2. Liberation **Basic drugs**



4. Actions



Antihistaminics



H₁-Receptors

Bronchospasm



Bronchial Asthma



Triple Response



Local Allergy



H₂-receptor Ant



H₂-Receptors

Vasodilatation



Anaphylactic shock



Vomiting



Motion sickness



Peptic ulcer



H₁-receptors blockers (Antihistaminics)

First Generation

e.g. chlorpheniramine

1. *H₁-receptor blockade*
 - **Allergic reactions** e.g. allergic rhinitis, urticaria, anaphylactic shock
2. *CNS depression:*
 1. *Sedation*
OTC hypnotic
DROWSINESS is the most common adverse effect
In *children* they may cause CNS *stimulation*
 2. *Cough suppression=Antitussive:*
Dry cough

3. *Autonomic Receptor Blockade*

*** Muscarinic receptor blockade (atropine-like actions)**

1. *Antiemetic effect*

Vomiting e.g.

motion sickness (Dimenhydrinate)

vomiting of pregnancy (Doxylamine)

2. *Antiparkinsonian effect*

Parkinsonism

Atropine-like effects e.g. dry mouth, constipation, urine retention ...etc

*** Alpha-adrenoceptor blockade**

Postural Hypotension

New generations

HYDROPHILIC

1) They do not cross the blood brain barrier → free from sedation

2) Slow elimination → long duration of action

- **Terfenadine, Astemizole:**

They induce serious arrhythmia with enzyme inhibitors

- **Fexofenadine, Cetirizine, Loratadine, Desloratadine, Azelastine :**

They are not liable to cause serious arrhythmia

Summary

- Autacoids may be amines, eicosanoids, polypeptides
- Histamine is synthesized by decarboxylation of histidine, stored in granules in mast cells & released to act on H1 receptors (mediate allergic reactions) and H2 receptors (mediates HCl secretion)
- First generation antihistaminics is sedating & is used mainly as: anti-allergic, antitussive, OTC hypnotic, antiparkinsonian & antiemetic
- Second generation antihistaminics is non-sedating & is used only as antiallergic
- The most common adverse effects are drowsiness, dry mouth and hypotension.

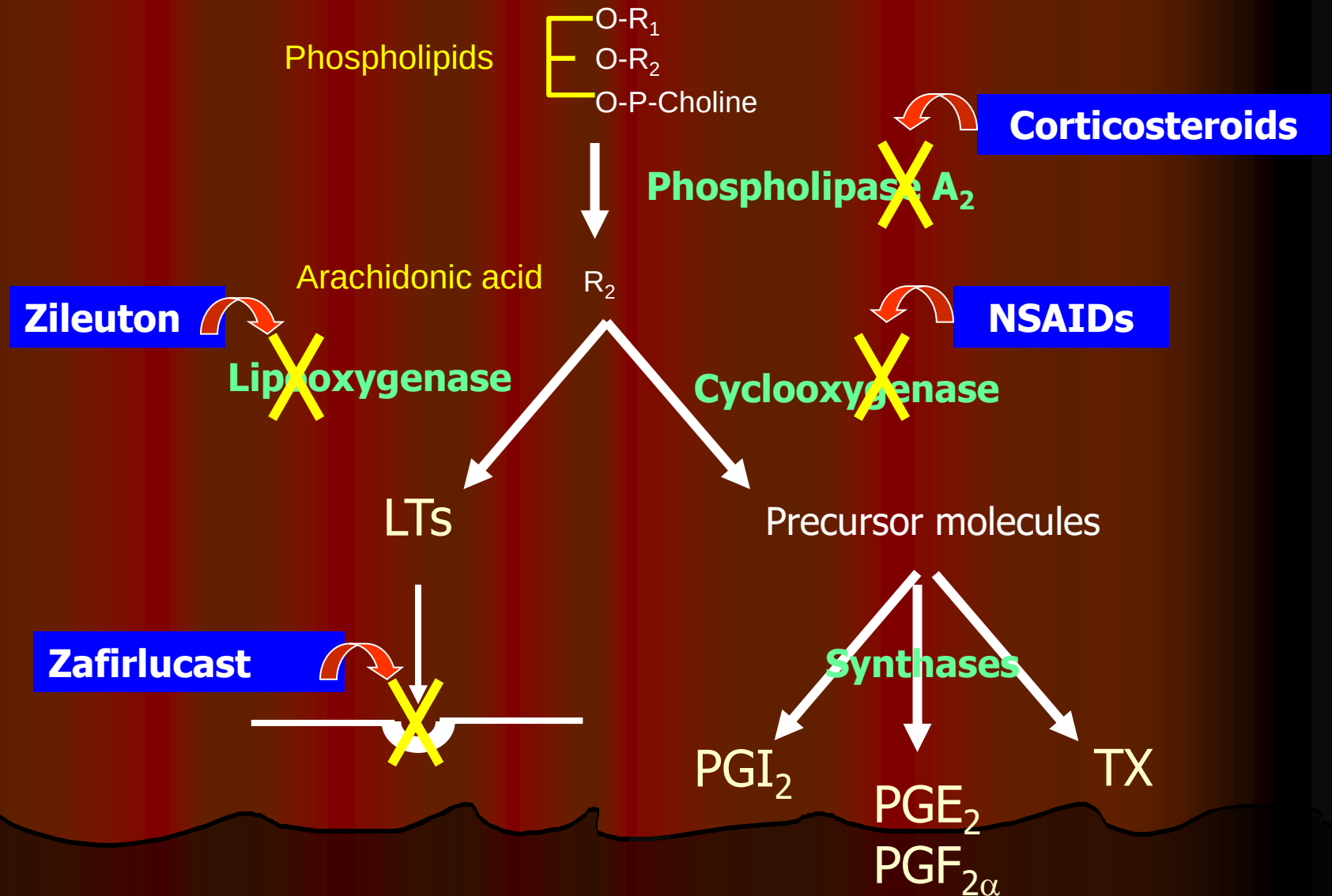
Eicosanoids

Prostaglandins; PG
Leukotrienes; LT &
Thromboxanes; TX

LOs

- Revise the physiology of eicosanoids
- Classify prostaglandins
- Enumerate differences between various PGs as related to the actions & indications.
- Enumerate the adverse effects of PGs

Synthesis



PGE is similar to PGF

1. Uterine contraction *best with PGE₂*

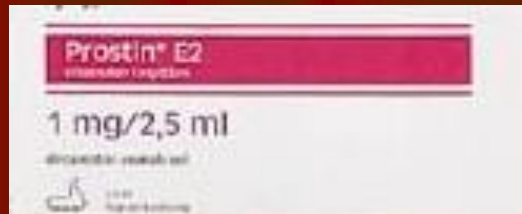
Dinoprostone for induction of labor or abortion

- Intravaginal

- Vaginal gel

- Vaginal tablets

- Vaginal insert to be removed upon onset of labor.



- Intracervical:

- Cervical gel

- Cervical suppositories



2. Intestinal contraction *best with PGE₁*

Lubiprostone for Idiopathic constipation

It is a Cl⁻ channel opener → ↑ Intestinal secretion

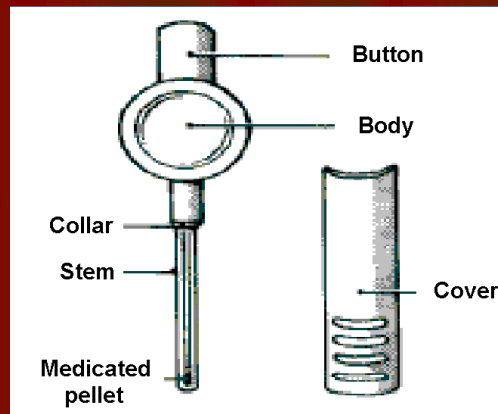
PGE is opposite to PGF

3. Vasodilatation (*best with PGE₁*) *Alprostadil is used for*

Delay closure of PDA (patent of ductus arteriosus)

Erectile dysfunction → blood entrapment in the penis.

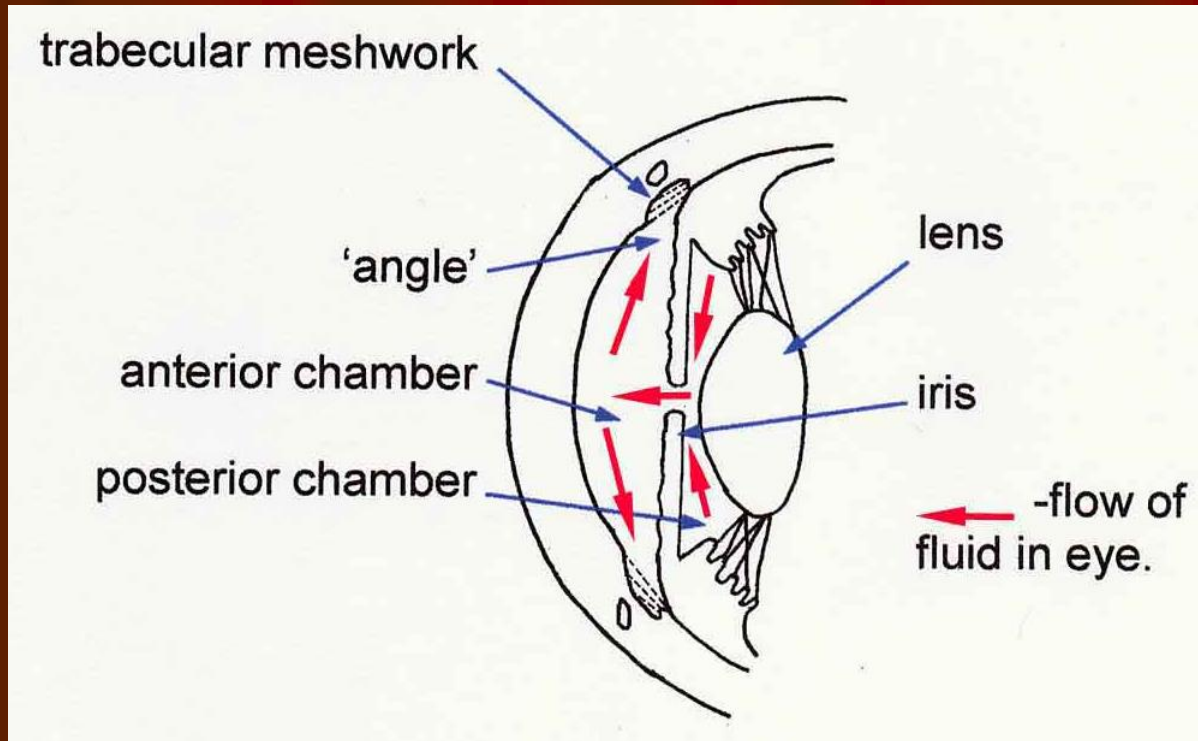
Urethral pellet
Urethral cream
Local injections



- However, it induces local symptoms:
 - penile pain & urethral burning
 - may vaginal itching in the female partner.

4. Bronchodilatation

PGF2 α



- Increases aqueous flow

Latanoprost

may be of choice in simple glaucoma

It may gradually change eye color



PGI₂ (Epoprostenol) is opposite to TXA₂

VD & Inhibition of platelet aggregation

- It is used in treatment of pulmonary hypertension by infusion pump through a central venous catheter.



- Newer analogues

Iloprost: Inhalation



Beraprost: Orally



Adverse effects of PGs

Colic & diarrhea are the worst adverse effects

May increase menstrual bleeding

$\text{PGF}_{2\alpha}$ precipitates asthmatic attacks in asthmatics

PGE_1 may $\rightarrow$ headache, dizziness & tachycardia

Summary

- Eicosanoids include PGs, LTs & TXs
- PGs are synthesized from phospholipids by the enzyme PLA2 followed by COX enzyme
- PGs available for clinical use are:
 - PGE2 for induction of labour & abortion (Dinoprostone)
 - PGF2 α for induction of abortion (carboprost) and glaucoma (latanoprost)
 - PGE1 for PDA & erectile dysfunction (Alprostadiol) and constipation (Lubiprostone)
- The most common A/E are colic, diarrhea, bronchospasm local vaginal reaction & menstrual bleeding