Lecture title: PHOSPHOLIPID-DERIVED MEDIATORS

Lecturer Affiliation: College of Veterinary Medicine

Summary:

PHOSPHOLIPID-DERIVED MEDIATORS

Eicosanoids

I- prostaglandins (PGs). I+II called = prostaniods

II- thromboxane (TXs).

III-leukotrienes (LT).

They are derived from polyunsaturated acids and arachidonic acid. The eicosanoids play key role in **inflammatory, cardiovascular, and reproductive** functions.

- Arachidonic acid is released from membrane phospholipids by **phospholipaseA2** in response to physical, chemical, hormonal, and neurotransmitter stimuli.

Arachidonic acid can be metabolized by three pathways.

1.The cyclooxygenase pathway:

Leads to prostaglandin, thromboxane, and prostacyclin production.

2. The 5-lipoxygenase pathway:

Leads to the synthesis of leukotrienes.

3. The CYP pathway:

A-Epooxygenase

B- ω-Hydroxylase

Prostaglandins and Thromboxane

Pharmacologic effects

	PGE_1	PGE_2	PGI_2	$PGF_2\alpha$	TXA_2	LTB_4
Blood vessels	**Vasodilation**			**Vasoconstriction**		**Vasodilation (inflammatory)**
Bronchial muscle	**Bronchodilation**			**Bronchoconstriction**		**Sever bronchoconstriction**
Edema	**+**			**-**		**+++++++**
Uterus	**1. NON pregnant relaxation** **2. Pregnant contraction**			**contraction**		
RBF	**Increase**			**Decrease**		**??????**

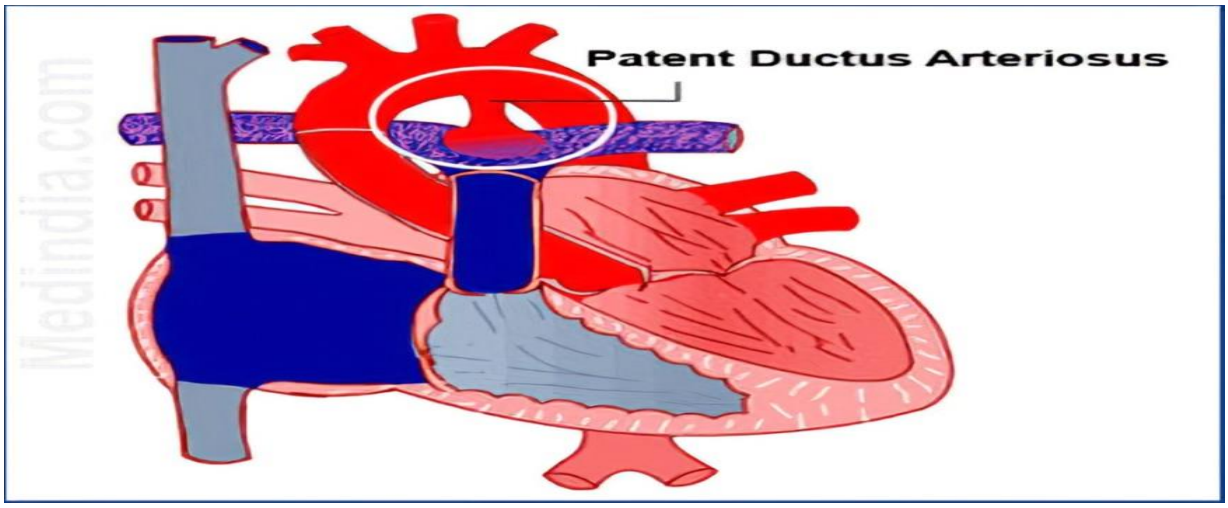
Platelet			**Decrease platelet aggregation**		**increase platelet aggregation**	
Other effect	**1. Increase mucous production in the stomach** **2. Fever**					**Chemotaxis**

Uses of Prostaglandins

I. Misoprostol: It is a PGE1 analog that has two functions which make it a useful protective agent for the GI tract. It directly inhibits gastric acid secretion by parietal cells and it facilitates PGE-mediated mucosal defenses.

II.PGE_1 (alprostadil):

1. Vasodilation in patient with erectile dysfunction.
2. Transposition of great vessels.
3. Induce labor



4.

III.PGE_2

1. Induce labor
2. Bronchodilation

IV.PGI_2

1. Inhibit platelet aggregation in hemodialysis and open-heart surgery.

2. Pulmonary arterial hypertension.

V.$PGF_2\alpha$

1. Induction of luteolysis and synchronization of estrus.
2. Treatment of pyometra or chronic estrus.
3. Expulsion of mummified fetus.
4. Induction of abortion.

Leukotriene inhibiters

1. Leukotriene receptors antagonism

Zafirlukast

Montelukast

2. LOX inhibitor

Zileuton

Mechanism of action: It blocks leukotriene synthesis by inhibiting 5-lipoxygenase.

Therapeutic uses: anti-asthmatic agents.

Cytokines

Cytokines have been classified on the basis of their biological responses into pro or anti-inflammatory cytokines

Major Cytokines include:

1. Lymphokins
2. Interleukins (IL)
3. Monokines
4. Chemokines
5. Interferons (IFN)
6. Tumor necrosis factors- alpha and beta
7. Colony stimulating factors