


AUTOCOIDS

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Intended Learning Outcomes

Understand the biological actions of Autocoids:
Histamine; Serotonin (5-HT); Prostanoids and
leukotrienes; Platelet-activating factor; Bradykinin;
Neuropeptides; Cytokines; Nitric oxide



Describe examples of drugs that affect the
autocoid activity with their clinical
applications

Histamine

Substance produced from the histidine stored within mast cell granules.

Functions

- Dilation of blood vessels
- Smooth muscle constriction (bronchi)
- Mucus production
- Tissue swelling
- Itching (during allergic reactions)
- Increased secretion of acid by the stomach (H₂)
- H₃ is Presynaptic neurotransmitter: arousal and sleep, cognition, attention, and other body functions.

Antihistamines/ Histamine (1) Antagonist

Only agents that block the action of histamines on H_1 receptors.

Treat allergies, hives, and other allergic reactions.

Second-generation agents (e.g loratadine) are less sedating and preferred antiallergy medicines.

Side Effects & Uses: First-generation Antihistamines



Sedation



Drying of mucous membranes



Confusion and urinary retention, esp. older adults



Can also be used to treat insomnia,
motion sickness, or vertigo

E.g. chlorpheniramine

Prostanoids

The end products of the cyclooxygenase pathway of the metabolism of arachidonic acid.

- Prostaglandin
 - Prostaglandins: **PGD₂**, **PGE₂**, **PGF_{2α}**, **PGI₂**
- Thromboxanes
- **Thromboxane A₂**

Eicosonoids include prostanoids and leukotriens

Leukotrienes

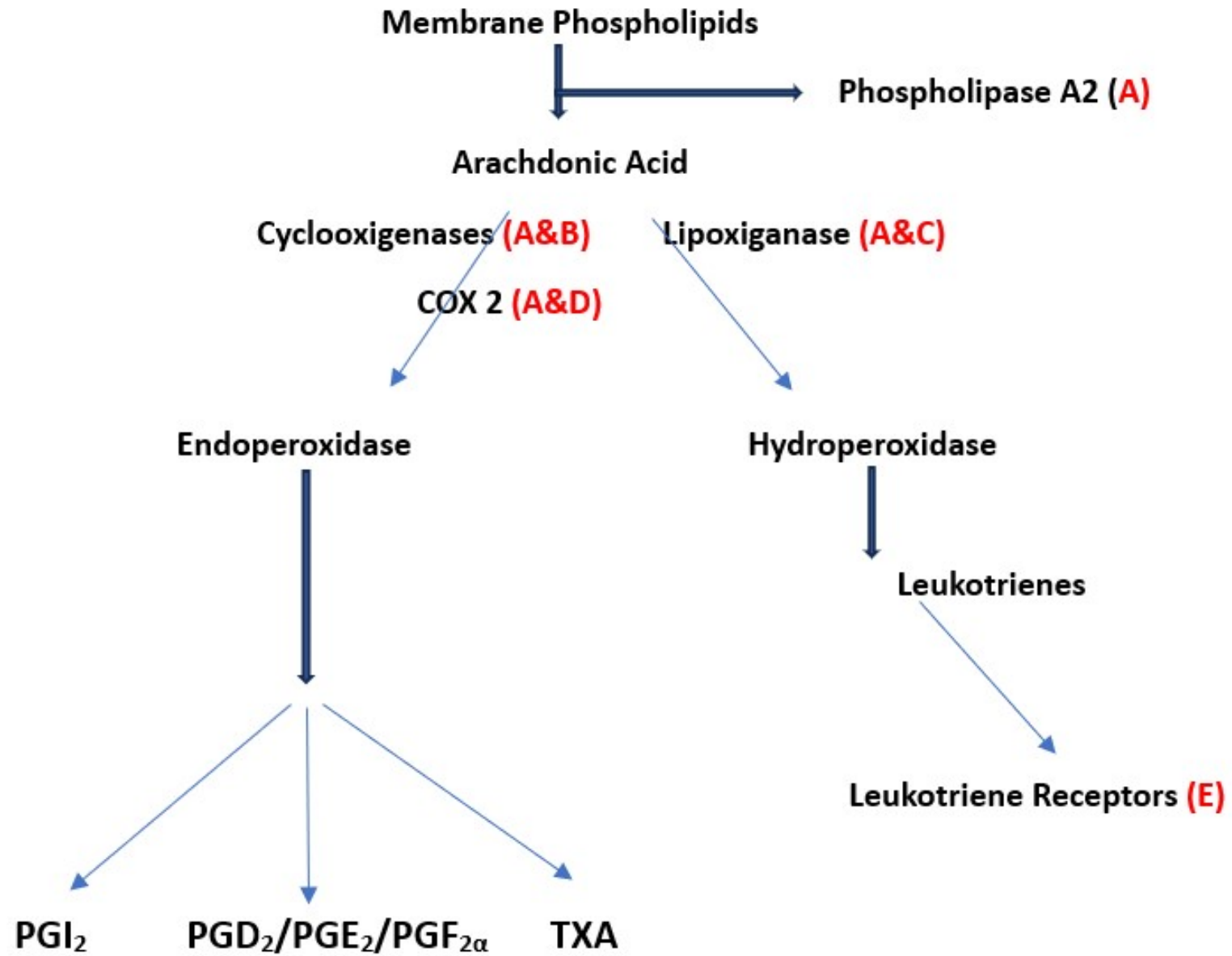
Group of arachidonic acid metabolites that are chemical mediator of allergic reactions and inflammation.

Leukotrienes C₄, D₄, and E₄ are derived from leukotriene A₄.

Response to inflammation or tissue injury.

- Asthma, psoriasis, rheumatoid arthritis, and inflammatory bowel disease.

powerful bronchoconstrictors and vasodilators seen in systemic anaphylaxis.



A= Glucocortocoids B= NSAIDS C= Zileuton D= Selective COX 2 inhibitors E= Lukasts

Platelet Activating Factor (ABBR: PAF)

A phospholipid that affects the signaling between cells in inflammation, sepsis, and thrombosis.

- Released by mast cells and basophils

Activated eosinophils

Platelet Activating Factor Inhibitors

Glucocorticoids -inhibits LTs, ILs and PAR

Rupatadine: **antihistamine** and PAF antagonist used to treat allergies

Etizolam: **benzodiazepine** analog and PAF antagonist used to treat anxiety and panic attacks

Lexipafant (Zacutex): treatment of pancreatitis

Bradykinin

Vasodilating plasma kinin consisting of nine linked amino acids.

Functions

- Bronchoconstrictor
- Increases capillary permeability
- stimulates release of antidiuretic hormone

Bradykinin B2 Receptor Antagonists

Hereditary angioedema agents (HAE)

- E.g., Icatibant (Firazyr)

Indication:

- Treatment of attacks of hereditary angioedema in >18 yr

MOA

- Antagonizes the effects of bradykinin which are responsible for symptoms of HAE.

Therapeutic Effects:

- Decreased Sx of HAE
 - Skin swelling
 - Skin pain
 - Abdominal pain
 - laryngeal edema

Neuropeptide



A neurotransmitter consisting of a short chain of chemically linked amino acids.



Most secreted as prohormones that are modified by proteolysis to be biochemically active in the body

Neuropeptide Clinical Applications

Calcitonin peptide: inhibit bone resorption in the treatment of hypercalcemia, osteoporosis, and Paget's disease.

Desmopressin: A synthetic analog of vasopressin used to reduce renal excretion of water in central diabetes insipidus and nocturia.

Vasopressin: A peptide hormone used to increase blood pressure in patients with vasodilatory shock who are resistant to fluid and catecholamine therapy.

Angiotensin II: is a peptide hormone of the RAAS system used to raise blood pressure in septic or other forms of shock.

Somatostatin: is a natural peptide hormone used to treat acute bleeding from esophageal varices, gastrointestinal ulcers, and gastritis; and restrict secretions of the upper intestine, pancreas, and biliary tract.

Cytokine

Proteins produced and released by cells to change the cells that produce them (autocrine effect) and altering other cells close to them (paracrine effect); a few affect cells systemically (endocrine effect).

- Includes any of the circulating substances in the blood that deplete lean body mass in **critical illness**.
- Interleukins (**IL-1, IL-6, and IL-8**) , interferons, **tumor necrosis factors (TNF)**, erythropoietin, and colony-stimulating factors.

Provide signals to regulate immunological aspects of cell growth

- Function during inflammation and specific immune response
- Each secreted by a specific cell in response to a specific stimulus
 - Monocytes or macrophages - > monokines
 - Lymphocytes -> lymphokines

Cytokine Antagonists (Immuno-suppressants)

Drug	MOA	Clinical indications
Reslizumab Mepolizumab	Bind and neutralize the biological activity of IL-5, suppressing production and survival of eosinophils	Severe eosinophilic asthma
Daclizumab and Basiliximab	Anti-IL-2 receptor monoclonal antibodies Bind to IL-2 receptor on surface of activated T cells → Block IL-2 mediated T-cell activation	Prevention of organ transplant rejection
Infliximab Etanercept Adalimumab	<ul style="list-style-type: none"> Infliximab, adalimumab - TNF monoclonal antibody Entanercept bind to TNF 	Rheumatoid arthritis Crohn's disease Psoriasis Psoriatic arthritis Ankylosing spondylosis
Glucocorticoids -inhibits LTs, ILs and PAR		

Serotonin

Vasoconstrictor found in platelets, gastrointestinal mucosa, mast cells, carcinoid tumors, and the central nervous system

Functions via cellular receptors:

- Intestinal motility
- Nausea and vomiting
- Sleep-wake cycles
- Obsessive-compulsive behaviors
- Depression
- Eating

Selective serotonin reuptake inhibitors (SSRIs)

Antidepressants

- E.g., Fluoxetine (Prozac)

MOA

- Selectively inhibits the reuptake of serotonin in the CNS.

Therapeutic Effects:

- Antidepressant action
- Decreased behaviors associated with:
 - panic disorder
 - bulimia

Serotonin 2C Receptor Agonists

Weight control agents

- E.g., Lorcaserin (Belviq)

Indication

- Chronic weight management
- Body mass index (BMI) of ≥ 30 kg/m²
- weight-related comorbidity (hypertension, type 2 diabetes, dyslipidemia)
- Addition to lifestyle modification

MOA

- Acts as a serotonin 2C receptor agonist; increases satiety by activating 5-HT_{2C} receptors located on anorexigenic neurons in the hypothalamus.

Therapeutic Effect:

- Decreased appetite with leading to weight loss

Serotonin Syndrome

Life-threatening drug-induced increase in synaptic serotonin concentrations

- Stimulation of peripheral and CNS serotonergic receptors

Drug combinations that synergistically increase synaptic 5-HT

Mainly drug interaction between serotonergic agents

- Selective serotonin reuptake inhibitors [SSRIs] and monoamine oxidase inhibitors [MAOIs])

Usually within 24 hours

Sx: Mental status change, neuromuscular hyperactivity, and autonomic instability

Nitric Oxide (Endothelium- derived Relaxing Factor)

Soluble gas produced in the body by endothelial cells, neurons in the brain, and macrophages during inflammation.

Functions

- Potent vasodilator
- Inhibits adhesion, activation, and aggregation of platelets
- Inhibits inflammatory process induced by mast cells
- Controls chemotaxis of lymphocytes
- Regulates smooth muscle cell proliferation
- Penile erection, and other sexual functions
- Participates in programmed cell death
- Interacts with oxygen radicals to form metabolites that destroy pathogens.

Nitric Oxide

- Administered as mixture of inhaled gas
 - Decreases recruitment of lymphocytes
 - Acute respiratory distress syndrome
 - Oxygenation but does not affect patient survival



The End

Thank you for participating

