Autacoids

-Only things mentioned in the lecture that weren’t in the Doctor’s slides are written in this sheet.

*Slide #1:

• The word “autacoids” comes from “Auta” (self), and “Coid” (remedy). Autacoids → self-remedy drugs.
• Autacoids are substances that are produced normally in the body. They regulate many physiological and biological processes occurring in the body.
• They act in balance, examples:
  - Some autacoids act as vasoconstrictors (e.g. angiotensin II), others act as vasodilators (e.g. bradykinin).
  - Some autacoids affect the sympathetic system, others affect the parasympathetic system.
  - Some activate certain clotting factors, others have antithrombotic effects (e.g. antithrombin, protein C).

*Slide #2:

• Some of these types of autacoids don’t belong to a specific system; they have multifactorial effects.

*Slide #3:

• Apart from being used in some tests to assist the production of certain acids, histamine isn’t used clinically. The most widely used drugs are the specific antagonists of histamine, known as antihistamines. In order to understand the role of such drugs, we have to study histamine.
• The structures of histidine and histamine aren’t required.
**Endocrine System**

**Pharmacology (1)**

*Slide #4:*

- Histamine is present in many tissues everywhere in the body, particularly mast cells and basophiles.
- Histamine is also synthesized in the CNS, where it functions as a neurotransmitter. Recall that neurotransmission in the CNS is involved in many diseases such as depression and schizophrenia.
- Compound 48/80 is a synthetic histamine-like drug. It has similar actions as histamine and used to understand the specific actions of histamine that are mediated through interactions with different receptors.

*Slide #5:*

- Recall that allergy is a universal side effect of all drugs. Histamine particularly mediates allergy.
- When exposed to antigens, humans produce immunoglobulins (IgE) that are directed against that antigen (allergen). Mast cells have receptors that can bind to IgE. Upon second exposure to the allergen, mast cells become sensitized to it; the IgE molecules bound to the mast cell surface can bind to the allergen. Following this, histamine will be released. It interacts with specific receptors (H1 & H2), producing symptoms of an allergic reaction.
- What to do to reduce allergy:
  - Avoidance of allergic triggers is the first priority. It might be very difficult sometimes to identify the allergy triggers. Several different types of allergy tests are used to do this.
  - Inhibiting the release of histamine from mast cells using specific drugs. These drugs could be used as prophylactic agents to inhibit further release of histamine from mast cells, because once histamine has been released into the blood stream, it will trigger the allergic response, and there’s no other way to block this response except the use of antihistamines.
*Slide #6:

- H2 receptors are mainly used in the management of peptic ulcers.

*Slides #7, 8:

- H1 receptor blockers \( \rightarrow \) classical antihistamines, they’re the major drugs used in the management of allergy. These are highly specific drugs and can’t be used to treat peptic ulcers. In contrast, H2 receptor blockers are NEVER used as antihistamines. They’re devoid of any anti-allergic action and mainly used in the treatment of peptic ulcers. Make sure you fully understand this concept.

*Slide #9:

- Meniere’s disease: a disease of the inner ear that can affect the hearing and balance.

*Slide #10:

- Lewis triple response: produced by stroking the skin with an object. It represents the basis of allergenicity, and is used to identify weather an individual is allergic to a specific allergen or a drug by exposing the skin to small amounts of various substances and observing the reactions over time.
- First a red spot appears; then a red flare develops; eventually the red spot turns into an itchy wheal.
- This response is produced due to the release of histamine. It’s mediated by the interaction of histamine with both H1 & H2 receptors. Theoretically, both H1 & H2 blockers should be used to reduce allergy, but in practice, most patients respond to classical antihistamines (H1 blockers) without the need to use H2 blockers.
*Slide #11:

- There’s a negative feedback of histamine on its own release; when histamine binds to H2 receptors, it increases cAMP, and anything that increases cAMP is inhibited by mast cells.
- Metabolites of histamine are detected in urine in cases of excess production of histamine. They’re used to diagnose systemic mastocytosis which is characterized by increased histamine levels.

*Slide #12:

- Cromolyn sodium & nedocromil sodium are given as ophthalmic drugs (in cases of eye allergy), or by inhalation (in cases of bronchial asthma).

*Slide #13:

- Bronchial asthma is exacerbated during specific seasons, so these drugs are given as prophylactic agents 2 or 3 months before the allergy season approaches. They have a wide margin of safety so they can be given easily.
- Hay fever= allergic rhinitis. Recall that it doesn’t exhibit the symptoms of fever.
- Drugs that increase cAMP are effective in the management of anaphylactic shock, not only by reducing the release of histamine, but also by reducing the hypotension that is related to anaphylactic shock.

*Slide #14:

- Parenteral form is used mainly in cases of emergency.

*Slide #15:

- Antihistamines are widely used in cold remedies; not to treat cold because it’s a self-limiting viral infection that has no treatment, but
to reduce vasodilatation. The Dr emphasized that these drugs shouldn’t be used unless indicated by your physician.

*Slide #16:

- Motion sickness, previously called sea sickness. Antihistamines are effective against nausea and vomiting that come with motion sickness (antiemetic effect).
- OTC: over-the-counter drugs, given without prescription in cases of sleep disorder.

*Slide #17:

- There is marked individual variation in response and side effects of antihistamines.
- Although antihistamines have the ability to reduce nausea and vomiting, they’re contraindicated during pregnancy as they’re related to teratogenicity during the whole period of pregnancy (all trimesters).

*Slides #18, 19:

- You have to know the names of classical antihistamines. They’re widely used.
- There are two different types of antihistamine – the older group, sedating antihistamines, can enter the brain and cause drowsiness, while the newer non-sedating antihistamines do not.

*Slide #20:

- This table isn’t for memorizing. Just notice that non-sedating antihistamines have no anti-cholinergic or anti-motion sickness activity.
Eicosanoids: Prostaglandins and Leucotrienes.

*Slide #2:*
- The effects of prostaglandins are mediated through interactions with different receptors.

*Slides #3, 4:*
- This table isn’t required at this point.

*Slide #5:*
- Prostaglandins are inflammatory mediators generated by the release of arachidonic acid (AA) from the membrane phospholipids by phospholipase A2. Subsequently, cyclooxygenase (COX) and Prostaglandin synthase enzymes metabolize AA to prostaglandins including PGE$_2$, PGF$_{2\alpha}$, PGD$_2$, PGI$_2$ (prostacyclin), and TXA$_2$ (thromboxane).

*Slide #6:*
- PGE$_2$, PGF$_{2\alpha}$ are strong contractors of the uterus.
- Recently, they discovered a specific antagonist for PGD$_2$. It has a role in the management of certain allergic reactions.
- High concentrations of various prostaglandins are present in the joint fluid of people with rheumatoid arthritis and other inflammatory joint diseases. Pain killers are given to these patients in order to inhibit prostaglandins and reduce pain.

*Slides #10, 11:*
- Anti-inflammatory agents are classified into two major classes: steroidal and non-steroidal anti-inflammatory drugs (NSAIDs). Steroidal drugs include phospholipase A2 inhibitors. NSAIDs are nonselective inhibitors of cyclooxygenases, they decrease the formation of prostaglandins and thromboxanes.
**Pharmacology (1)**

- NSAIDs are contraindicated in bronchial asthma, because if you inhibit cyclooxygenases, there will be a shift toward the production of slow reacting substances of anaphylaxis, which are responsible for the severe bronchoconstriction in patients with anaphylaxis or bronchial asthma.

- Steroids are effective in certain types of asthma especially steroid-dependant bronchial asthma.

- The analgesic anti-inflammatory actions of all NSAIDs are mainly due to the inhibition of prostaglandin synthesis.

- A lot of people consider inhibitors of synthesis of prostaglandins as specific antagonists.

- Aspirin's ability to suppress the production of prostaglandins and thromboxanes is due to its irreversible inactivation of the cyclooxygenase (COX) enzyme, resulting in reduced platelet production of TXA₂. This makes aspirin different from other NSAIDs, which are reversible inhibitors. Aspirin inhibits the production of thromboxane for at least 14 days. The dose ranges from (50-325) mg. it’s an anti-platelet medicine, which means it reduces the risk of clots forming in your blood. This reduces your risk of having a stroke or heart attack.

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**Best wishes from me to you.**

**Your colleague: Aseel Nsairat.**