

DRUG ANTAGONISM

HISTAMINE AND ITS ANTAGONISTS

Histamine

Histamine is a naturally occurring amine formed from the amino acid histidine and found in most body tissue in an inactive bound form, often in mast cells. The active free histamine is released from cells in response to stimuli such as physical trauma or antigen- antibody reactions. Various chemicals can also cause release of histamine like proteolytic enzyme, snake venom, insect bite, detergents and drugs like: tubocurarine, morphine, vancomycin.

- » Histamine acts as a local hormone (autocoid) i.e. it is a local chemical transmitter between the cells from which it is released and cells in the immediate vicinity.
- » The actions of histamine which are clinically important are those on smooth muscle, blood vessels, skin and secretory glands.
- » Histamine has no effects when taken by mouth because it is metabolized rapidly by histaminase in G.I.T.
- » Injection of histamine I.V. however as little as 0.1 mg cause systemic vasodilatation with rapid fall in blood pressure, acceleration in HR, elevation in C.S.F pressure, flushing of the face, headache and gastric acid secretion is stimulated. These effects last only a few minutes.
- » Injection of 10 mg of histamine intradermally produce the **triple response of Lewis** which include:
 - » **1- Flush**: which is a localized erythema; due to vasodilatation.
 - » **2- Wheal**: localized edema due to the increase in capillary permeability.
 - » **3- Flare**: is arteriolar dilatation causing erythema; due to an axon reflex.

There are 4 types of histamine receptors:

- » **1- H1- receptors**: mediate the oedema and vascular effect of histamine and antagonized by H1 blocker like diphenhydramine.
- » **2- H2-receptors**: mediate the effect on gastric secretion. Antagonized by H2 blocker like cimetidine.
- » **3- H3,H4 – receptors**: which are found in the brain and mediate the alertness.

Histamine antagonists

The effect of histamine can be opposed in three ways:

- » 1- By preventing histamine from reaching its sites of action (receptors), e.g. by competition (the H₁-and H₂- receptor antagonists).
- » 2- By using a drug with opposite effects, e.g. histamine constricts bronchi, causes vasodilatation and increases capillary permeability.
Adrenaline opposes these effects by a mechanism unrelated to histamine. This is a physiological antagonism.
- » 3- By preventing the release of histamine from cells in which it is stored; adrenal steroids and sodium cromoglycate can suppress the effects on cells of antigen-antibody reactions.

» **Adrenaline**

Adrenaline is a catecholamine formed from tyrosine. It is secreted by adrenal medulla. Adrenaline has alpha and beta - effects. When it is given s. c. there is intense vasoconstriction, which slows absorption and so prolongs and smoothes the effects. Therefore it is given I.m or I.v in anaphylactic shock for its mix action (cardiovascular & bronchial). Provide the best compromise for speed & simplicity of use in an emergency; it may also stabilize mast cell membrane & reduce release of vasoactive autotoxins. Adrenaline opposes the action of histamine on bronchi, blood vessels and capillary permeability, by physiological antagonism.

Procedure:

- » 1- Cleanse the forearm with a swab of cotton wool soaked in alcohol.
- » 2- Place one drop of histamine (1: 1000) on the skin and prick through it so that the drug is introduced intradermally. Record the response in the form of a colored diagram in your notebook.
- » 3- On another skin site, place two drops of a 1:1000 solution of diphenhydramine and then one drop of histamine. Prick intradermally through this mixture.
- » 4- Prick intradermally through one drop of 1:1000 adrenaline on another skin site.
- » 5- For control prick another area of the skin through one drop of 0.9 % NaCl. Record the response obtained and compare with those seen in (2, 3, 4).