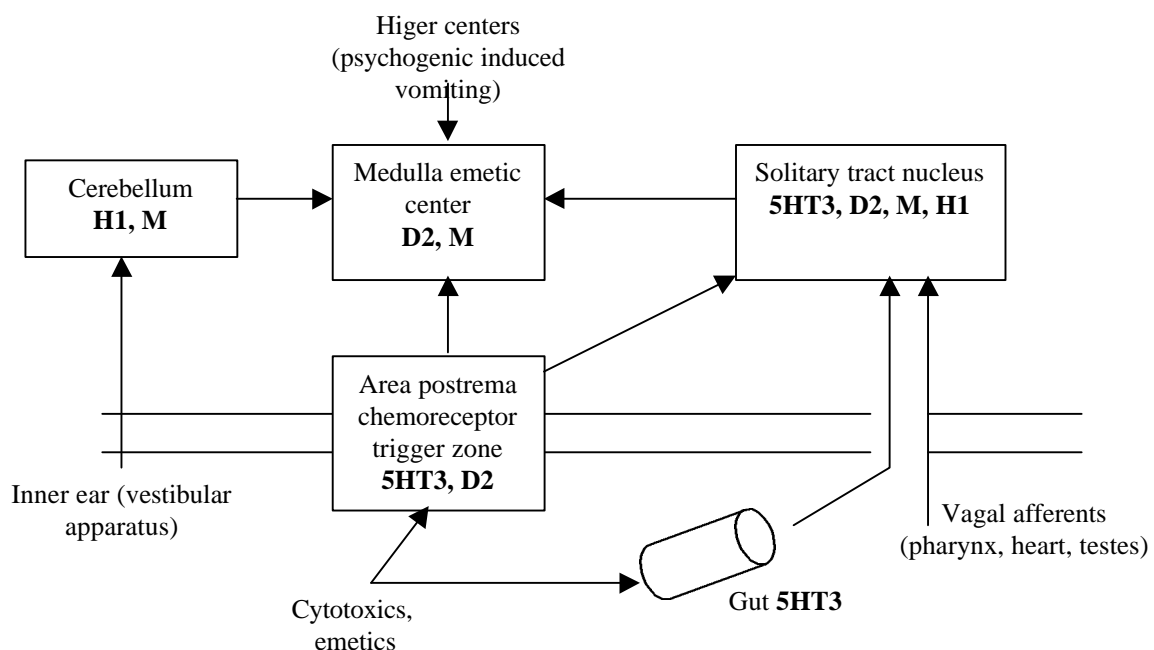


ANTI EMETICS

Theories of nausea and vomiting

- The main area in the brain responsible for vomiting is the vomiting center
 - This area is located in the lateral reticular formation of the medulla
 - It receives input from many areas:
 - Chemoreceptor trigger zone
 - Located in the floor of the 4th ventricle in the area postrema
 - It picks up circulating chemical in the blood
 - It is important because it lies outside the BBB, therefore, circulating toxins (e.g. bacterial food poisoning toxins, chemotherapy) can cause vomiting, even though they do not pass through the BBB
 - Vestibular apparatus
 - Tractus solitarius
 - vagal afferents from the gut, heart and testes
 - Direct input from gut (reflex)



- It is important to know the receptors involved in the emetic response
 - On the CTZ:
 - 5HT3
 - D2
 - On the vagal afferents:
 - 5HT3
 - In the vomiting center
 - Muscarinic
 - H1 receptors

Drugs which causes nausea and vomiting

- **Apomorphine (and Bromocriptide)**
 - A D2 agonist used in the treatment of parkinsons
 - It acts on the D2 receptor in the CTZ to cause vomiting
- **Morphine**
 - In excess amounts, also acts on D2 receptors
- **Syrup of Ibericat**
 - Irritates the gut, causing activation of 5HT3 receptors
- **Cisplatin**
 - Anti cancer drug which causes release of serotonin in the gut, which then acts on 5HT3 receptors

Anti emetic drugs

- For motion sickness
 - **Promethazine**
 - H1 antagonist (classical)
 - Used as a sedative in children (it is a very safe sedative)
 - Also has antimuscarinic actions
 - It is very effective at preventing motion sickness (since the vestibular afferents input in the vomiting center which has H1 and Muscarinic receptors)
 - Not used for the driver because it makes them drowsy
 - **Hyocine (scopolamine)**
 - Muscarinic antagonist (M2)
 - Used as a patch behind the ear

- For CTZ mediated vomiting
 - **Prochlorperazine**
 - A phenothiazine
 - A D2 antagonist
 - Has no antipsychotic effects
 - It is useful as an antiemetic as well as for dizziness
 - Has minor anticholinergic effects (it may work in motion sickness, however, the above drugs are preferred)
 - Since it blocks D2 receptors elsewhere (e.g. substantia nigra), it will cause extrapyramidal effects
 - Chlorpromazine, another phenothiazine, can also be used as an antiemetic, although it tends to be very sedative. It also has antipsychotic effects
 - **Metaclopramide**
 - A D2 antagonist
 - Also a weak 5HT3 antagonist
 - Increases the motility of the gut in the upper regions (hence it does not cause diarrhoea - only facilitates gastric emptying)
 - This is useful because when someone is nauseous, there is often gastric stasis, which means that drugs given by the oral route will not be absorbed effectively. Also, the drugs should not be given when the person is about to vomit, otherwise they will just vomit up the drug.
 - Metaclopramide will help the absorption of drugs because it stimulates gastric emptying

- For vomiting associated with vagal afferents (gut disorders, heart, testes, gut irritants - all stimulate the 5HT3 receptor on the vagal afferents)
 - **Ondansetron**
 - A 5HT3 antagonist
 - Excellent antiemetic
 - It is very effective in patients receiving cancer chemotherapy (radiation or cisplatin - both of which stimulate the release of serotonin in the gut)
 - Can also be used for CTZ nausea (though its main use is in conjunction with anti cancer drugs)