

DRUGS RELATED TO BALANCE SYSTEM

The overall incidence of dizziness, vertigo, and imbalance is 5-10%

It reaches 40% in patients older than 40 years.

Accounts for 3% of total visits to emergency department

The incidence of falling due to imbalance is 25% in subjects older than 65 years.

1% of falls results in hip fracture

Roughly 50% of fractured hips will not function normally.



The key to life is balance

DRUGS RELATED TO BALANCE SYSTEM

ILOS

To differentiate between classes of drugs used **to control** or to **prevent** vertigo

To hint on some disorders of balance

To detail on some drugs used **to control** or to **prevent** vertigo

To identify drugs that can precipitate vertigo



SYMPTOMS

Spinning (vertigo)

Confusion or disorientation

Falling or feeling as if one is going to fall

Nausea or vomiting

Sweating

Abnormal eye movement (nystagmus)

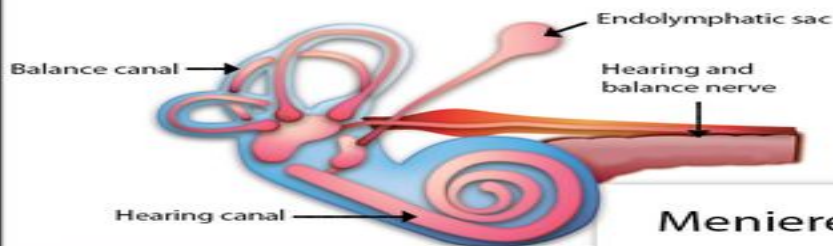


BALANCE DISORDERS

Ménière's disease:-This causes repeated episodes of dizziness, usually with ringing in the ear and progressive low-frequency hearing loss.

Meniere's disease

Healthy inner ear



Meniere's disease



PHARMACOLOGIC APPROACH

Specific treatment

Involves targeting the underlying cause of the vertigo (e.g., ear infection).



Symptomatic treatment

Involves controlling the acute symptoms and autonomic complaints (e.g., vertigo and vomiting)

Prophylactic treatment

Aims to reduce the recurrence of specific vertiginous conditions.

■ Diuretics (but not loop diuretics)

■ Ca /K Channel Blockers
■ Cinnarizine, Verapamil

Corticosteroids

SYMPTOMATIC CONTROL

Vestibular suppressants

Antiemetics

Vestibular suppressants are drugs that reduce the intensity of vertigo and nystagmus evoked by a vestibular imbalance.

1-Anticholinergics

2-Benzodiazepines

3-Betahistine



1-Anticholinergics

Anticholinergics inhibit firing in vestibular nucleus neurons

Reduce the velocity of vestibular nystagmus

e.g. **hyoscine**, also useful in motion sickness, sedation

ADRs:- dry mouth, blurred vision, sedation

2-Benzodiazepines

In small dosages useful for the management of acute vertigo

Minimize anxiety and panic associated with vertigo

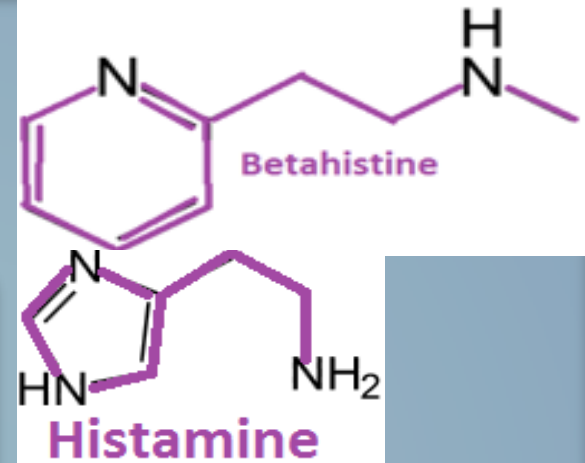
Lorazepam, Clonazepam, Diazepam

ADRs:- Dependence, impaired memory, increased risk of falling.

3-Betahistine

Mechanism of Action:-

It is a structural analog of histamine with weak histamine H₁ receptor agonist and more potent histamine H₃ receptor antagonist properties



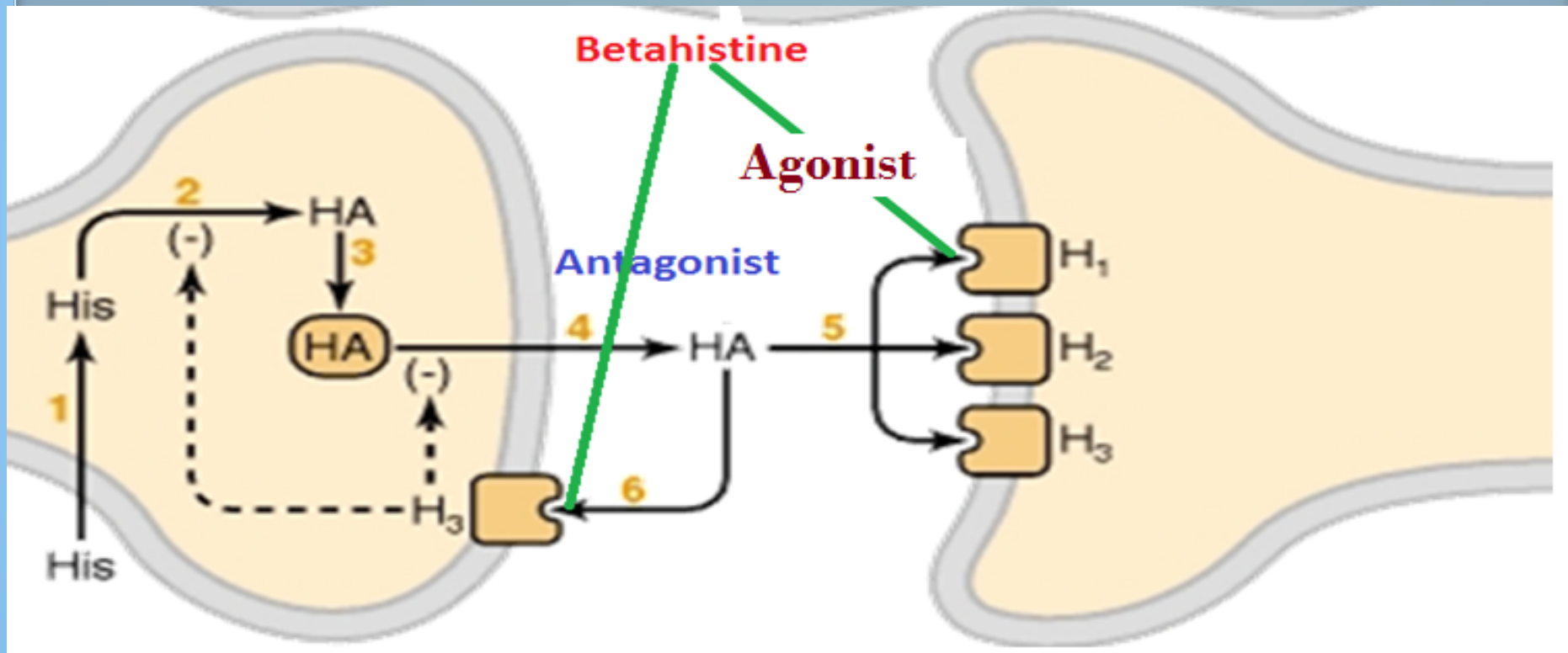
By stimulating H₁ receptors located on blood vessels in the inner ear → local vasodilation and increased permeability, which helps to reverse the underlying problem of endolymphatic hydrops.

By blocking H₃ receptors, Betahistine increases the local concentration of histamine in the inner ear.

Betahistine increases the level of serotonin in the brainstem → ↓ the activity of vestibular nuclei.

3-Betahistine

Mechanism of Action:-



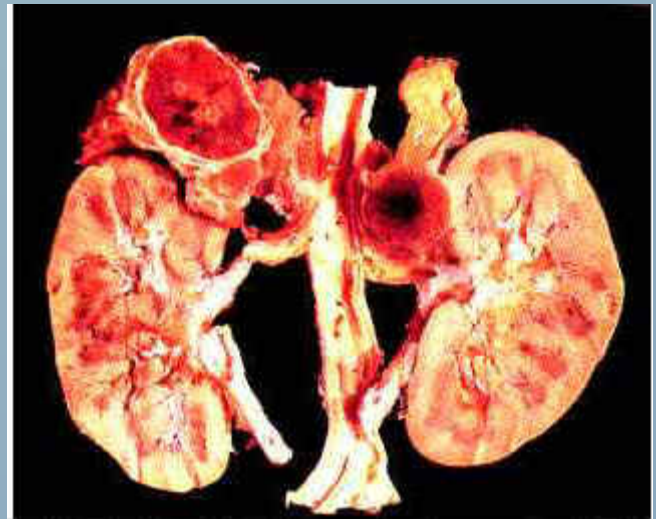
Pharmacokinetics

Formulated as tablet or oral solution

Rapidly and completely absorbed.

$t^{1/2}$ = 3-4 hours excreted in urine within 24 hours

Low protein binding



ADRs:-

Headache

Nausea

GIT side effects

Hypersensitivity reactions

Contraindications :-

Phaeochromocytoma

Bronchial asthma

History of peptic ulcer



Betahistine

Clinical indication

Betahistine is indicated for treatment of Ménière's syndrome.



94% of ENT surgeons in Britain prescribe betahistine for Ménière's disease, while in USA they think it is no better than a placebo .

Efficacy and safety of betahistine treatment in patients with Meniere's disease: primary results of a long term, multicentre, double blind, randomised, placebo controlled, dose defining trial (BEMED trial) BMJ 2016; 352

Betahistine

Clinical indication

Current evidence is limited as to whether betahistine prevents vertigo attacks caused by Meniere's disease, compared with placebo reactions



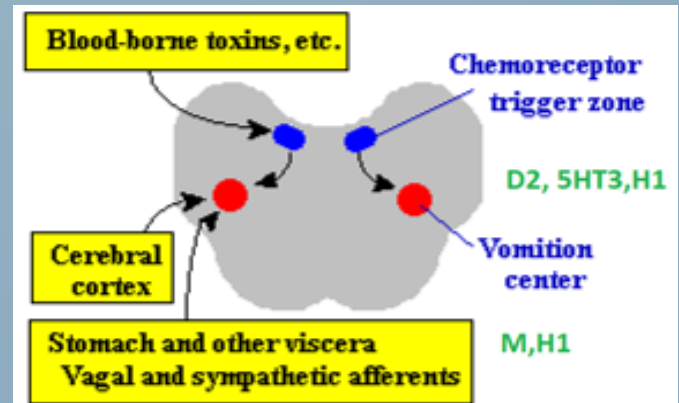
ANTIEMETICS

Antiemetics are drugs used to control vomiting and nausea

Antihistamines e.g. dimenhydrinate

Phenothiazines e.g. prochlorperazine

Dopamine antagonists e.g. **metoclopramide**



DIMINHYDRINATE

Block H₁ receptors in the vomiting center & CTZ

Sedative effects

Weak anticholinergic effects

↓ Excitability in the labyrinth & blocking conduction in vestibular-cerebellar pathways

Indications

In vertigo

Motion sickness



DIMINHYDRINATE

ADRs:-

Sedation

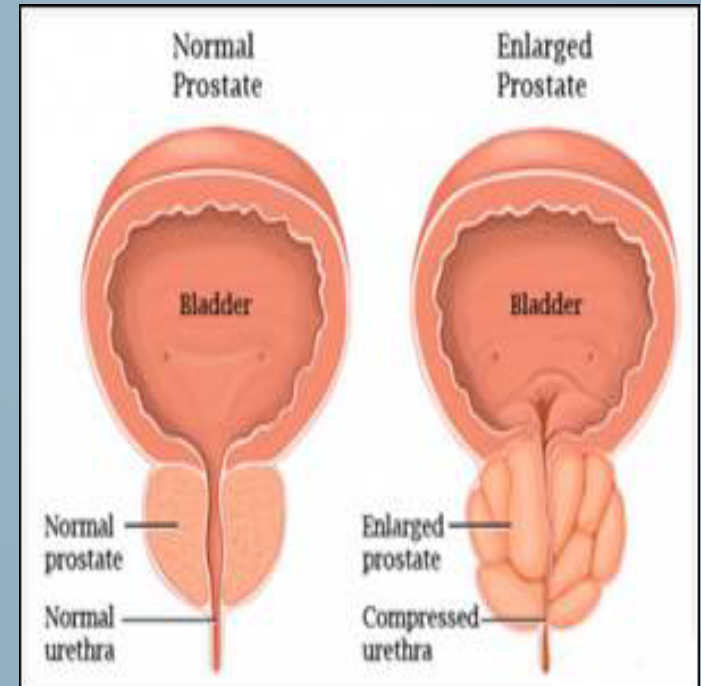
Dizziness

Anticholinergic side effects

Contraindications:-

Glaucoma

Prostatic enlargement



PROCHLORPERAZINE

Blocks dopamine receptors at CRTZ

Antipsychotic , some sedation + antiemetic

Indications

**One of the best antiemetics in vertigo,
has some vestibular suppressant action**



METOCLOPRAMIDE

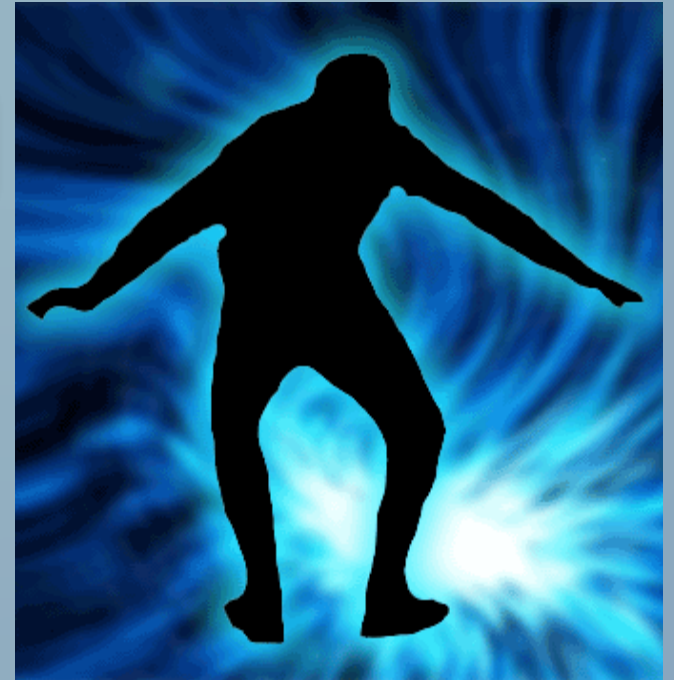
A potent central antiemetic acting on CRTZ

Has some sedative action

Has potent **gastroprokinetic** effect

ADRS:-

Restlessness or drowsiness
Extrapyramidal manifestations
on prolonged use



CINNARIZINE

Selective calcium & potassium channels blocker, antihistamine, antiserotonin, antidopamine

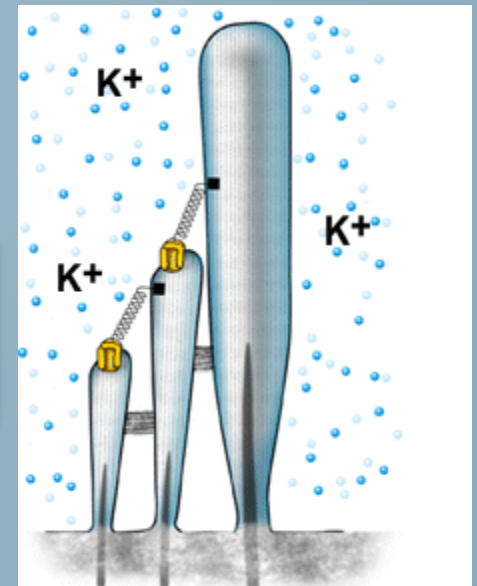
It promotes cerebral blood flow

Mechanism of action

Increased hydrostatic pressure on hair cells activates K^+ currents

Cinnarizine inhibits K^+ currents

Inhibition of K^+ currents lessen the vertigo and motion-induced nausea by dampening the over-reactivity of the vestibular hair cells.



PHARMACOKINETICS

Taken orally in tablet form

Rapidly absorbed

Low oral bioavailability due to hepatic first pass metabolism

If administered IV in lipid emulsion, it has better bioavailability



ADRS:-

Sweating

Drowsiness

Headache

Muscle rigidity and tremor

Contraindications

Parkinsonism

Car drivers

Clinical uses:-

Used to treat nausea and vomiting associated with motion sickness, vertigo, Meniere's disease.

DRUGS INDUCING VERTIGO

Drugs producing damaging effects on structure or function of labyrinthine hair cells &/ or their neuronal connections

Vesibular toxins

Drugs altering fluid & electrolyte balance

Diuretics

Drugs altering vestibular firing

Anticonvulsants

Antidepressants

Sedative hypnotics

Alcohol

Cocaine

Mixed ototoxins

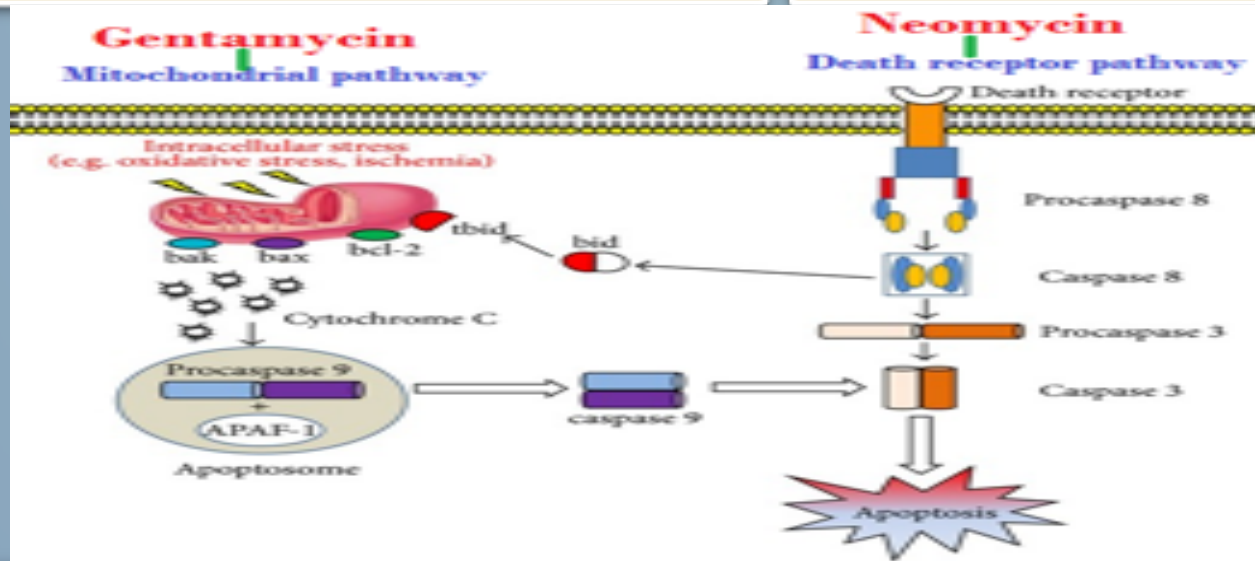
Alter function

MIXED OTOTOXINS

Aminoglycoside antibiotics;
gentamycin, kanamycin,
neomycin, streptomycin

Gentamycin → Induce apoptosis
by evoking free radicals →
Mitochondrial Pathway

Neomycin → Induce apoptosis
by activating caspases →
Death Receptor Pathway



Alter structures

MIXED OTOTOXINS

- ✚ Quinine, chloroquine, quinidine
- ✚ Nitrogen mustard
- ✚ Loop diuretics
- ✚ NSAIDs
- ✚ Tobacco

↓ Local blood flow →
biochemical changes → ↓
electromechanical
transduction → ↓ firing of
impulse

A lter function

SYNOPSIS

