

DRUGS RELATED TO BALANCE SYSTEM

The overall incidence of dizziness, vertigo & 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 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

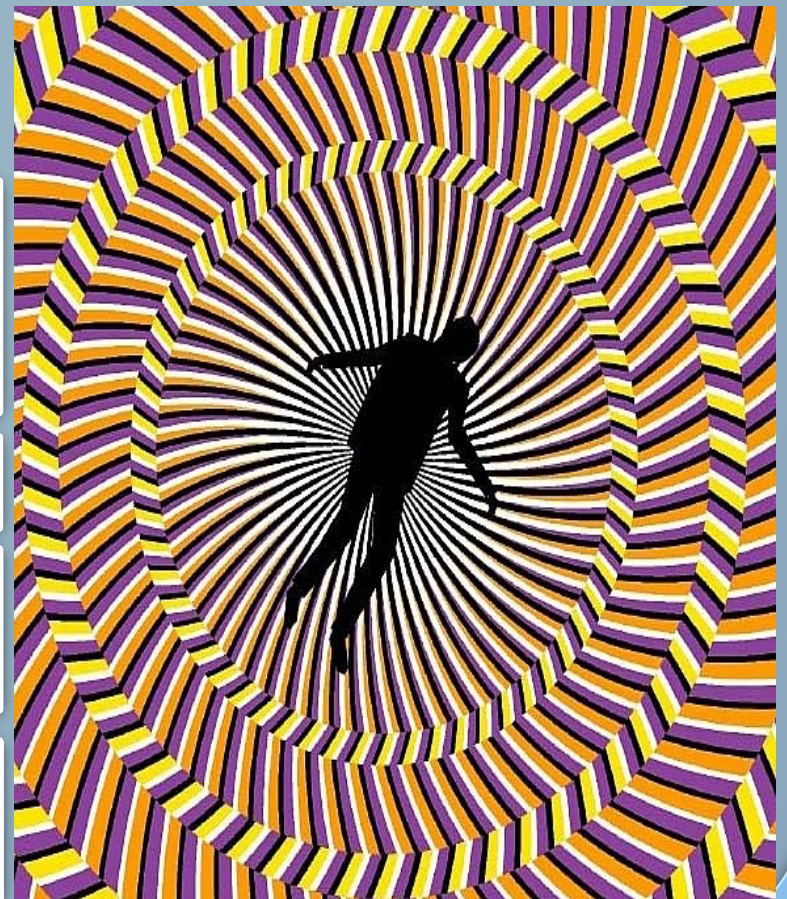
ILOS

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.



DRUGS RELATED TO BALANCE SYSTEM

Balance Disorders

Definition

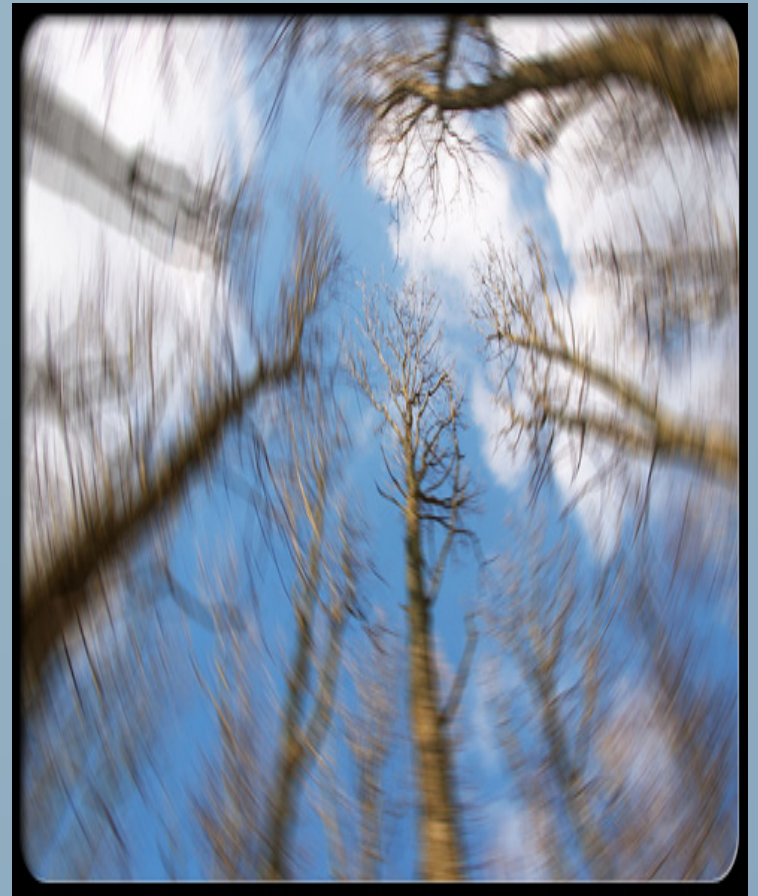
Terms

Dizziness

Light headedness

Ménière's disease

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).

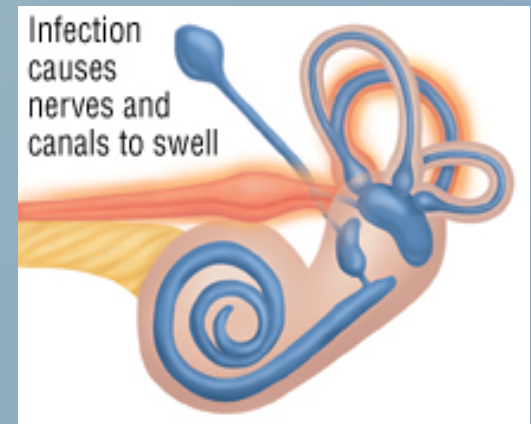
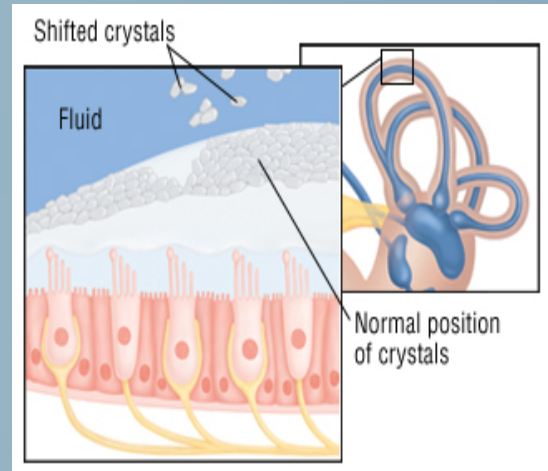


BALANCE DISORDERS

Benign paroxysmal positional vertigo:-A change in head position causes a sudden sensation of spinning

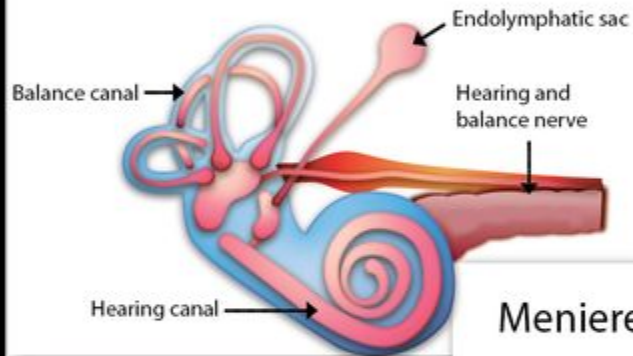
Acute labyrinthitis:-Inflammation of the balance apparatus of the inner ear, probably caused by a viral infection

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

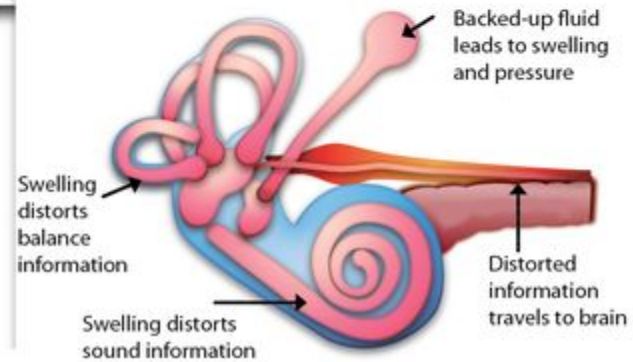


Meniere's disease

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 & autonomic complains (e.g., vertigo & vomiting)

Prophylactic treatment

Aims to reduce the recurrence of specific vertiginous conditions

- Diuretics (but not loop diuretics)

- Corticosteroids

- Ca & K Channel Blocker & antihistamine e.g. **Cinnarizine**.

SYMPTOMATIC CONTROL

Vestibular suppressants

Antiemetics

are drugs that reduce the intensity of vertigo & nystagmus evoked by a vestibular imbalance, e.g :

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

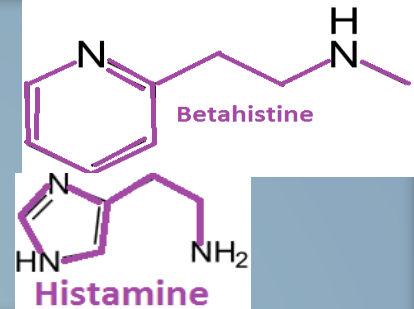
In small dosages useful for the management of acute vertigo

Minimize anxiety & panic associated with vertigo

e.g. **Lorazepam, Clonazepam, Diazepam**

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

3-Betahistine



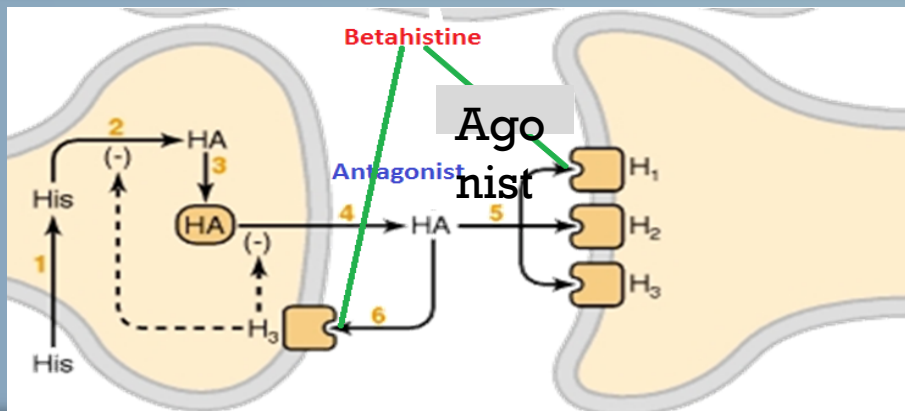
Mechanism of Action:-

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

By stimulating H₁ receptors located on blood vessels in the inner ear → local vasodilation & 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.



Pharmacokinetics of betahistine

Formulated as tablet or oral solution

Rapidly & completely absorbed

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

Low protein binding.

Contraindications

- Phaeochromocytoma
- Bronchial asthma
- History of peptic ulcer
- Hypersensitivity reactions.

ADRs:-

Headache

Nausea

GIT side effects.

Clinical indications

Betahistine is indicated for treatment of Ménière's syndrome.

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

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

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 & nausea such as:

Antihistamines e.g. Dimenhydrinate

Phenothiazines e.g. prochlorperazine

Dopamine antagonists e.g. metoclopramide & domperidone.



DIMINHYDRINATE

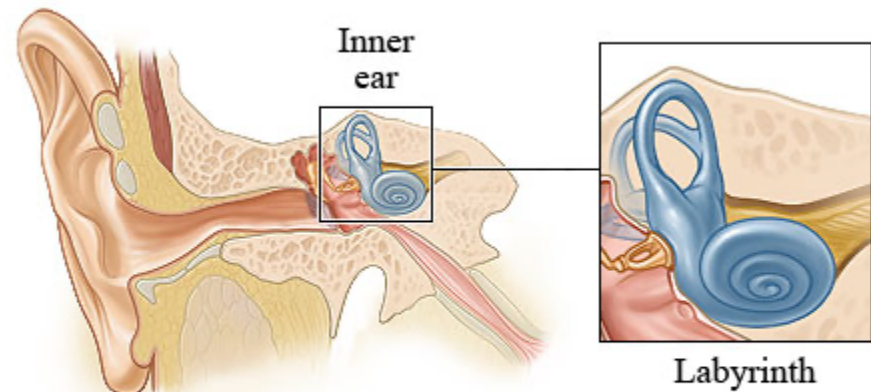
- Block H₁ receptors in CRTZ
- Sedative effects
- Weak anticholinergic effects

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

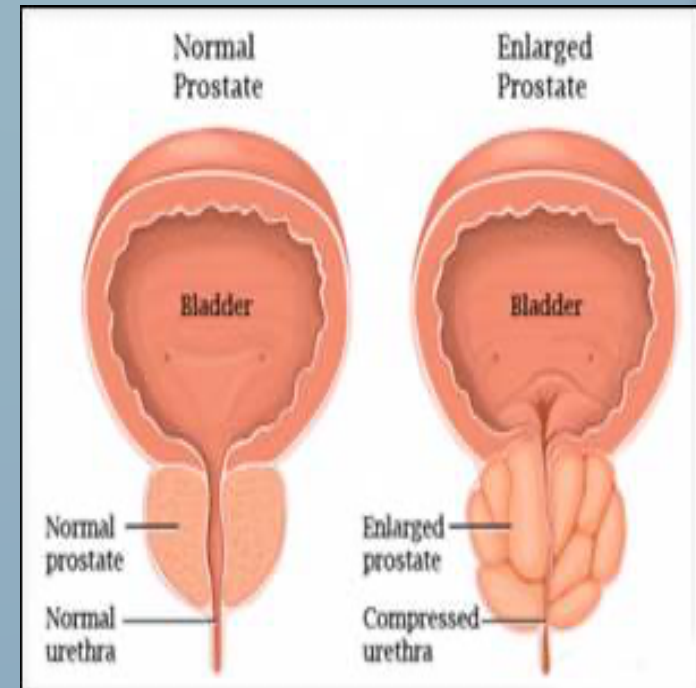
Indications

In vertigo

Prevent nausea & vomiting associated with motion sickness.



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DIMINHYDRINATE

ADRs:-

Sedation

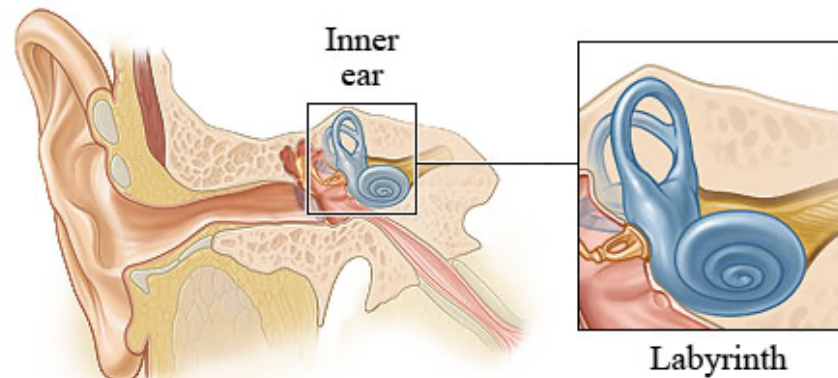
Dizziness

Anticholinergic side effects.

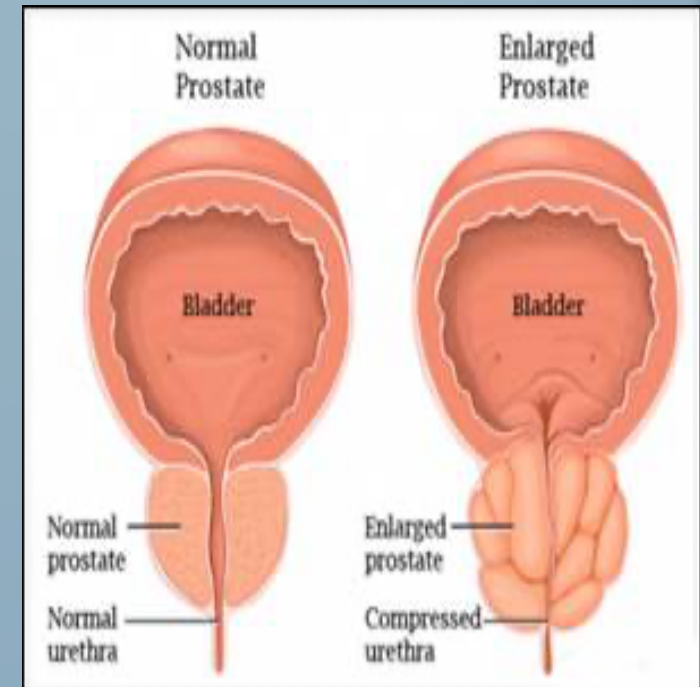
Contraindications:-

Glaucoma

Prostatic enlargement



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PROCHLORPERAZINE

Antipsychotic, some sedation + antiemetic

**Mechanism of action:
Blocks DOPAMINE receptors at CRTZ**

Indications:

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

Metoclopramide & DOMPERIDONE

block DOPAMINE D2 receptors in the CRTZ of the medulla, resulting in potent central antinausea & antiemetic action

Has some sedative action

Has potent **gastroprokinetic** effect

ADRS:-

Restlessness or drowsiness

Extrapyramidal manifestations on prolonged use.

CINNARIZINE

Mechanism of action

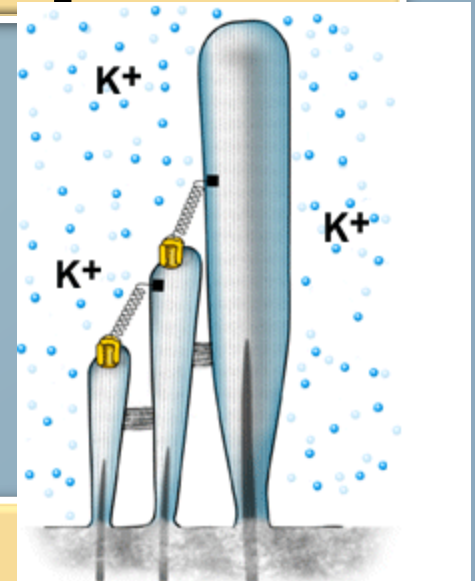
Selective Ca^{2+} channel blocker (vascular smooth muscle relaxation), antihistamine, antiserotonin, antidopamine

It promotes cerebral blood flow

Increased hydrostatic pressure on hair cells activates K^+ currents

Cinnarizine inhibits K^+ currents.

Inhibition of K^+ currents lessen the vertigo & 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.

Clinical uses:-

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

ADRS:-

Sweating
Drowsiness & Headache
Muscle rigidity & tremor

Contraindications

Parkinsonism
Car drivers.

DRUGS INDUCING VERTIGO

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

Vestibular toxins

Drugs altering fluid & electrolyte balance: **Diuretics**

Drugs altering vestibular firing (neuronal depressants):

Anticonvulsants

Antidepressants

Sedative hypnotics

Alcohol

Cocaine

Mixed ototoxins

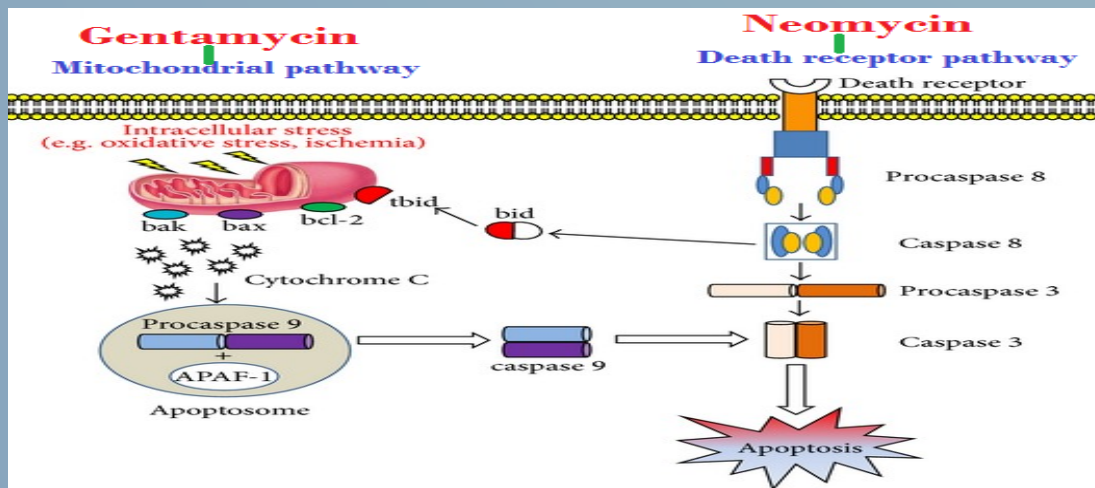
Alter function

MIXED OTOTOXINS

Aminoglycoside antibiotics;
e.g. *gentamycin*, *kanamycin*,
neomycin, *streptomycin*

Gentamycin → Induce apoptosis
by evoking free radicals →
Mitochondrial Pathway

Neomycin → Induce apoptosis
by activating caspases →
Death Receptor Pathway



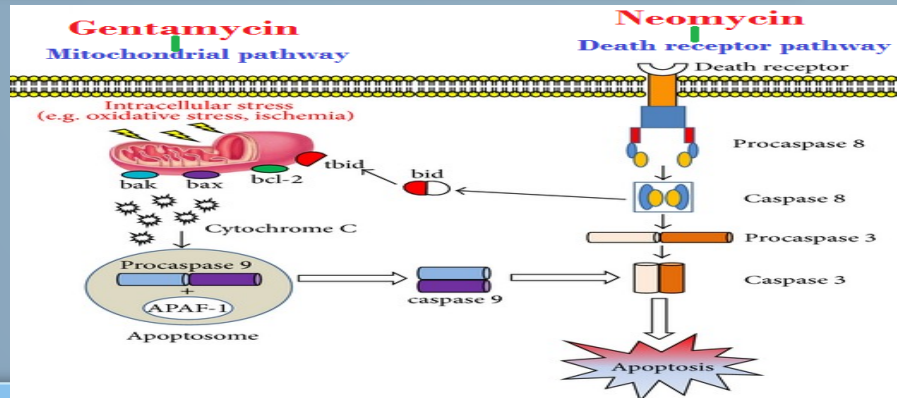
Alter structures

MIXED OTOTOXINS

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

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

Alter function



Alter structures

SYNOPSIS

