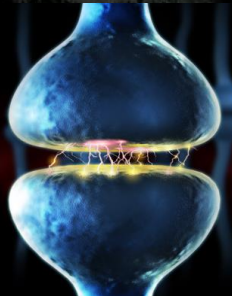


King Saud University
College of Medicine
2nd Year, 1st Block



LECTURE 2:

DRUGS RELATED TO BALANCE

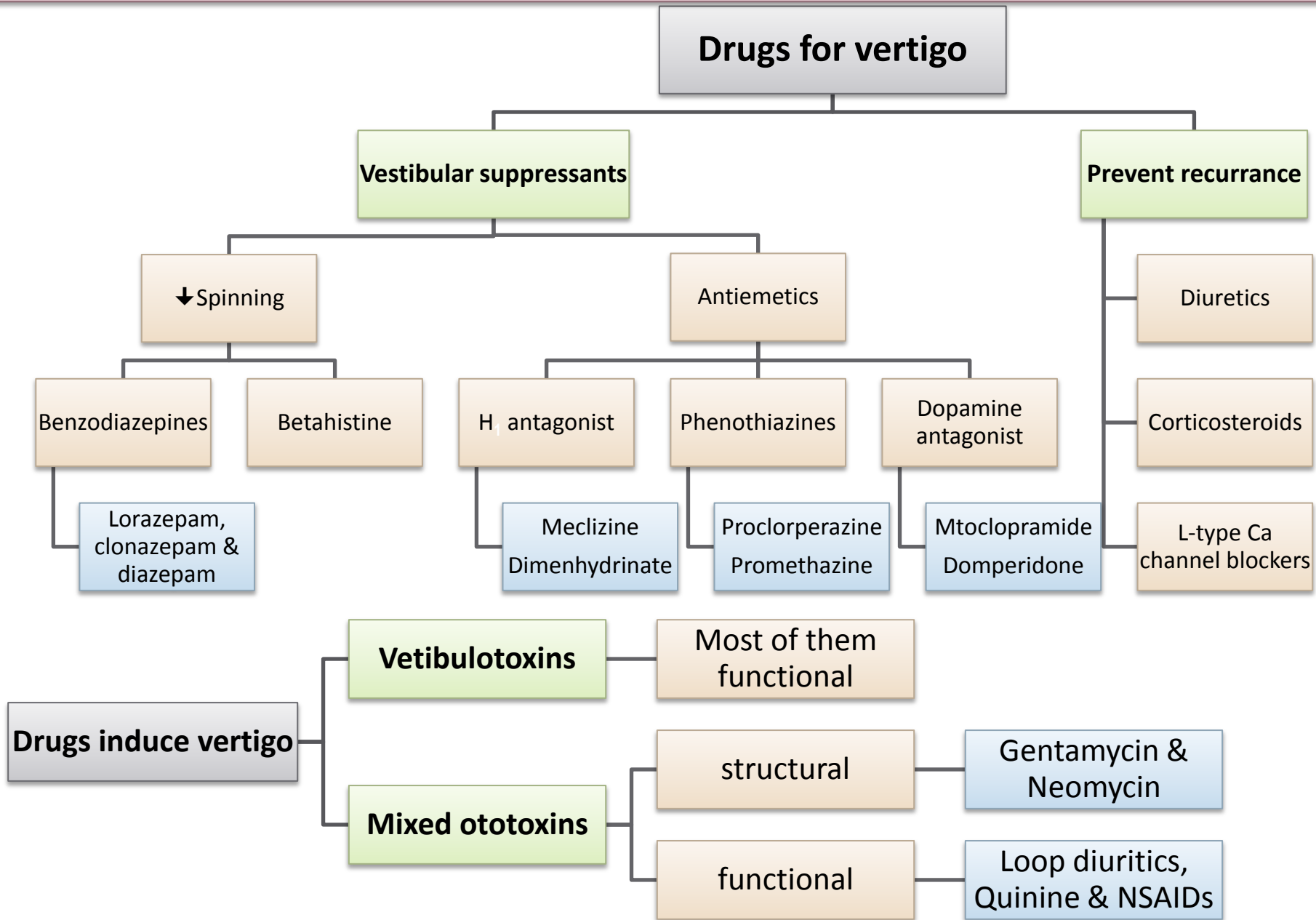


CNS Block

Objectives

- ✓ Recognize causes and symptoms of balance disorders.
- ✓ Identify the transmitters involved in vestibular transmission
- ✓ Segregate classes of drugs used in the management protocols to control or prevent vertigo
- ✓ Identify drugs that can precipitate

Mind Map



Introduction

(to understand)

*How does vertigo happen ?

Movement of the fluid in the semi-circular canal [in plane of the movement] lags

Impulses from eyes

touch and position sensors in the neck, spine and limbs

All of these → stimulating nerve endings → firing impulses along the **vestibular nerve** → To vestibular nuclei → relay stations → The processed output goes → **Conscious brain interpreted as a sense of position in space** →

+Eye muscles to stabilize

+Neck spine & limbs to control posture and movement

Introduction

(to understand)

*Transmitters Involved In Vestibular Firing :

Main Transmitters

Glutamates (excitatory +)

Acetylcholine (excitatory +)

GABA (inhibitory -)

Glycine (inhibitory -)

Modulatory Transmitters

(change neurotransmitter effects)

Histamine

Noradrenaline

Introduction

(to understand)

*The difference between vertigo and dizziness :

VERTIGO	DIZZINESS
<ul style="list-style-type: none">- a type of dizziness that creates the sense That you or your environment is <u>SPINNING</u> (بِدور)- <u>BALANCE DISORDER</u> (the individual will feel unsteady when standing or walking)- Associated with spinning you might feel :<ul style="list-style-type: none">• Nausea or vomiting• Sweating• Nystagmus (abnormal eye movements)	<p>Lighted headedness</p>

* Causes of vertigo

1- CNS : Impact on

- vestibular nuclei
- afferent inputs
- efferent outputs

2- Inner ear (**MENIERE'S***): Vestibular hair cell stimulation unrelated to head and body motions. (next slide)

3- Others : (MOTION SICKNESS,, electrolyte disturbances : e.x. ↑ BP, ↑ cholesterol, diabetes etc... Or ↓ equalization of air pressure in middle ear).

Introduction

(to understand)

Ménière's disease* is a disorder of the (effect inner ear fluid homeostasis)

✓ that can affect hearing and balance.

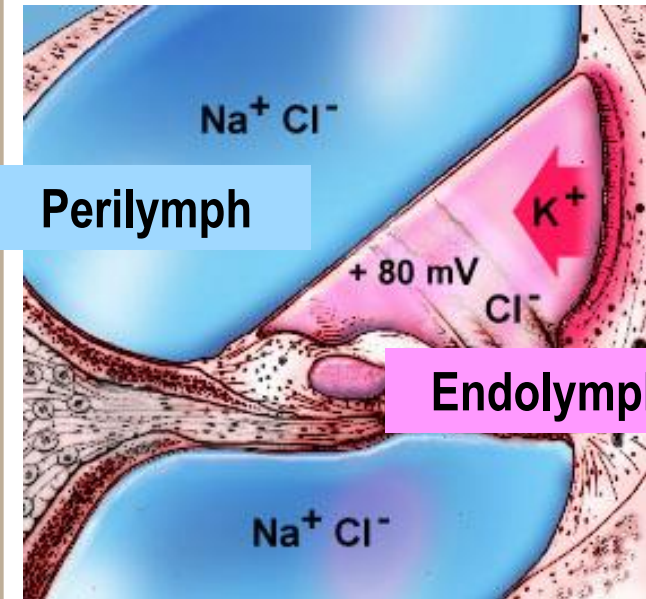
✓ It is characterized by episodes of

- vertigo
- tinnitus
- progressive hearing loss .

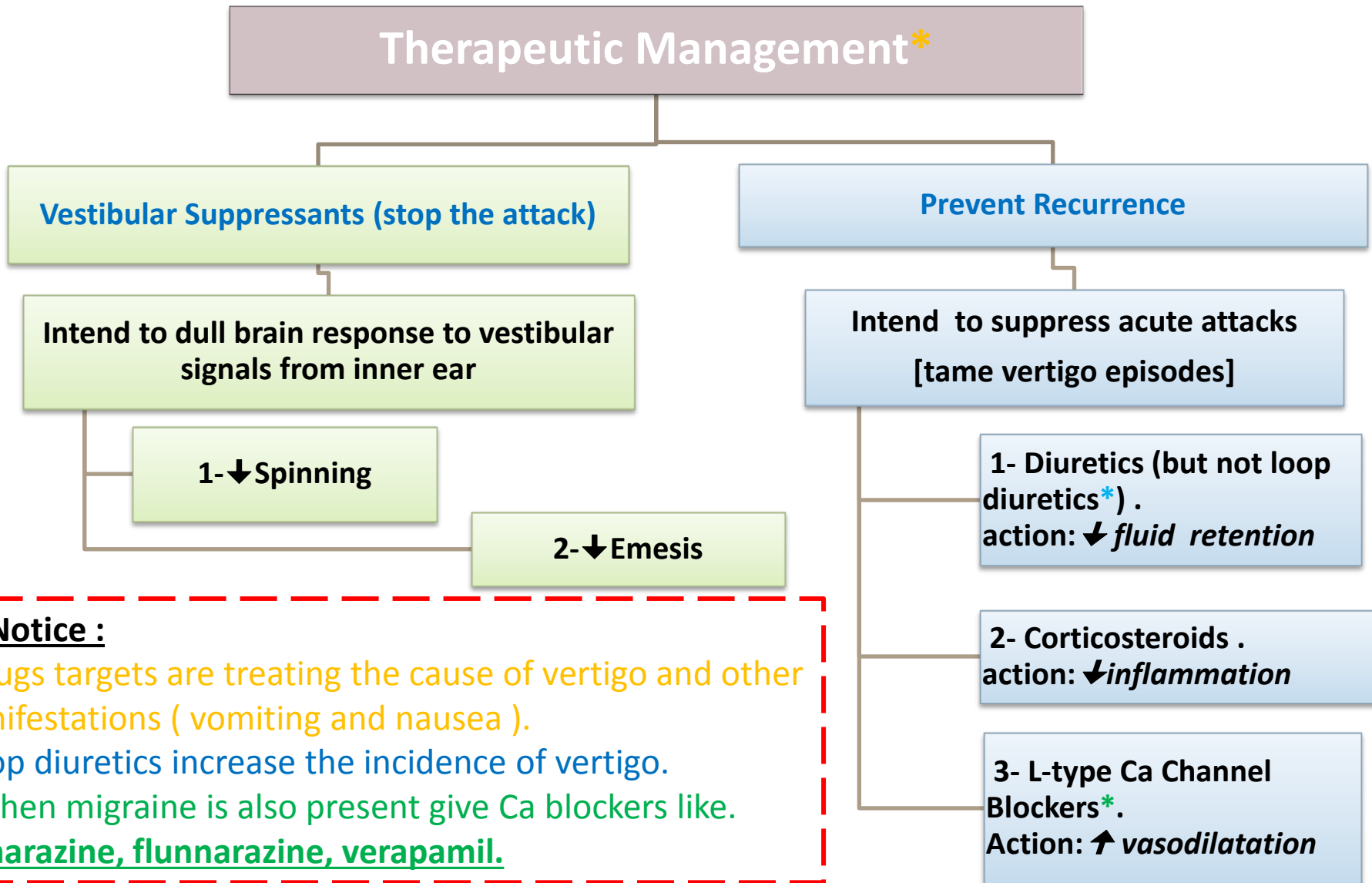
✓ Pathophysiology

(Inner ear chamber is filled with perilymph & endolymph)

1. ↑endolymphatic pressure (hydrolymphatic hydrops)→
2. microscopic breaks of separating membrane often with
3. vestibular hair loss → depolarization and functional loss



Drugs used to control or prevent vertigo episodes



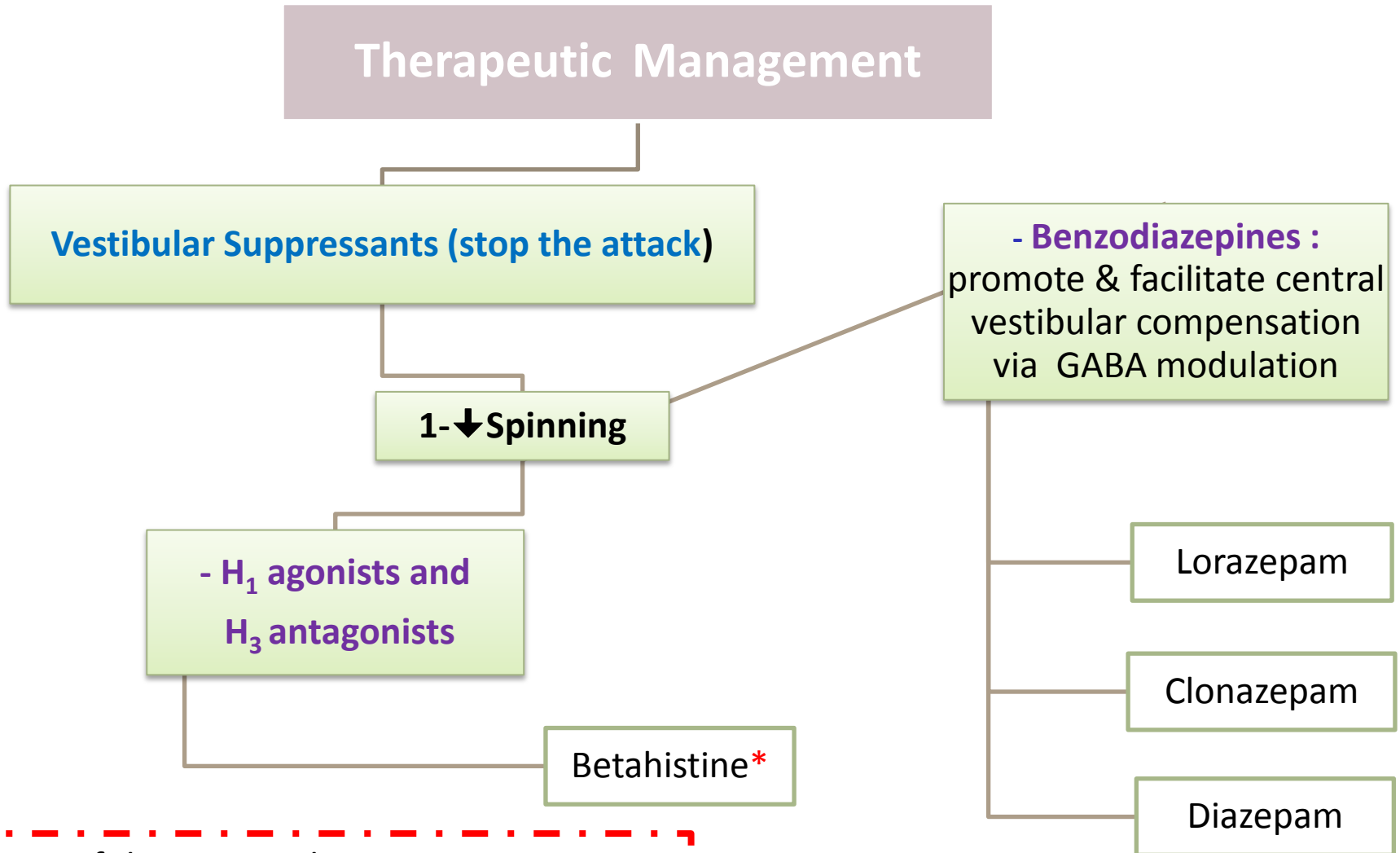
- **Notice :**

*Drugs targets are treating the cause of vertigo and other manifestations (vomiting and nausea).

*loop diuretics increase the incidence of vertigo.

* When migraine is also present give Ca blockers like. **cinnarazine, flunarazine, verapamil.**

Drugs used to control or prevent vertigo episodes

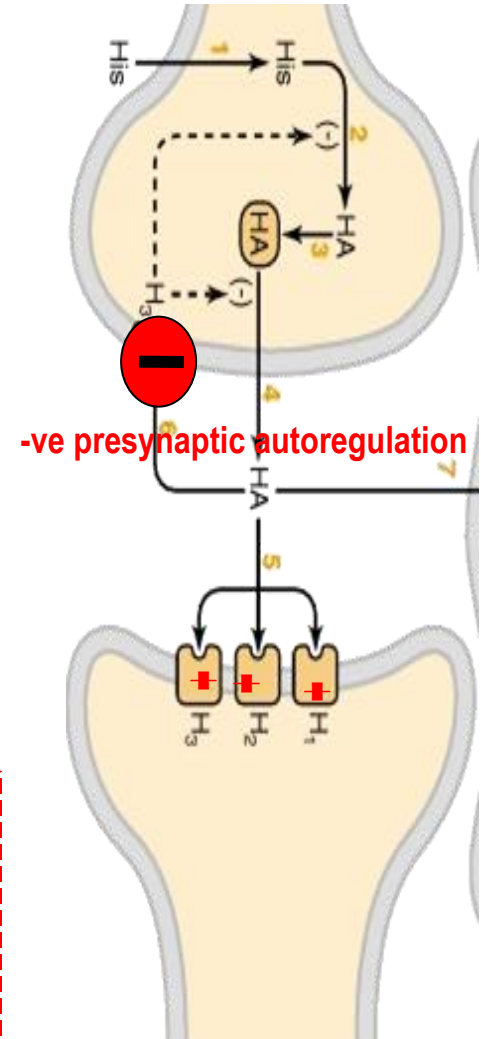


- **Note** : if the patient does not response to the betahistine then try Benzodiazepines

Betahistine (VESTIBULAR SUPPRESSANTS)

• Pharmacological action :

- Weak agonist at H₁ receptors → regulates inner ear fluid homeostasis (labyrinthine circulation) → inducing vaso-dilatation in middle ear → relieves pressure in inner ear
(هنا يقوم بتوسيع الأوعية الدموية البعيدة عن الأذن الداخلية مما يؤدي إلى نزوح الدم بعيدًا عن الأذن الداخلية مما يساعد في تخفيض الضغط عليها)
- Strong antagonism of H₃ autoreceptors → ↑ augmenting effects on H₁ receptors in the brain →
 - ↑ Histamine synthesis in tuberomammillary nuclei of the posterior hypothalamus to promote & facilitate central vestibular compensation
 - ↑ Histamine release in vestibular nuclei
- ↑ levels of neurotransmitters such as 5HT (serotonin) in the brainstem, which inhibits the activity of vestibular nuclei.



يشغل على H1 RECEPTOR as agonist بدال الهستامين ويسوي نفس الاكشن حقه اللي هو تنشيطها.
يشغل على H3 RECEPTOR as antagonist ، الهستامين كان يثبط شغل ال presynaptic receptor فيمنع ان الهستامين يفرز ، هنا راح يصير العكس ويفرز الهستامين عن طريق تثبيط نفس ال presynaptic receptor .
يتم افراز الهستامين على ال BVS محددة والموجودة باماكن معينة بالدماغ .

Betahistine (VESTIBULAR SUPPRESSANTS)

• Pharmacokinetics

- (short duration so it is taken many times per day and the dose usually two tablets)
- **Tablet form , rapidly & completely absorbed**
- **$t_{1/2}=2-3h$**
- **Partially metabolized (active) & excreted in urine**

• ADRs

- **Headache**
- **Nausea**
- **Gastric effects**
- **↓ appetite and weight loss** (with chronic use)

• Contraindications

- **Peptic ulcer**
- **Pheochromocytoma** (adrenal medulla tumors release more adrenaline while this drug release more adrenaline)
- **Bronchial asthma** (because bad histamine effect)

Drugs used to control or prevent vertigo episodes

Therapeutic Management

Vestibular Suppressants (stop the attack)

2-↓Emesis

H1 antagonist

(Antihistamine, Anticholinergic).

Dimenhydrinate

Meclizine,

Dopamine Antagonists

Dopamine antagonist, gastroprokinetic.

Drug of choice No.2 if the sedation is important.

Metoclopramide,

Domperidone
(doesn't cross BBB)

-Phenothiazines

Dopamine antagonists, sedation.

used more commonly in severe cases of vertigo (drug of choice No.1)

Prochlorperazine,

Promethazine

Antiemetics

Dimenhydrinate (Dramamine)

Antiemetics, H₁ Antagonist, Antihistamines

- Block H1 receptors in CRTZ (chemoreceptor target zone).
- Sedative effects.
- Weak anticholinergic effects.
- > antiemetic < sedating than Meclizine.

Indications

- In vertigo.
- In control of **MOTION SICKNESS** by ↓ excitability in the labyrinth & blocking conduction in vestibular-cerebellar pathways.

ADRs

- Sedation.
- Dizziness.
- Anticholinergic side effects.

Contraindications

- Glaucoma.
 - Prostatic enlargement.
-

Antiemetics

Prochlorperazine

Antiemetics, A Piperazine Phenothiazines

- Block dopamine receptors at CRTZ. (dopamine antagonist)
- Antipsychotic.
- Some sedation.

Indications

- One of the best antiemetics in vertigo.(sedating & has some vestibular suppressant action).

Metoclopramide

Antiemetics, Dopamine Antagonists

- A potent central antiemetic acting on CRTZ.
- Some sedating action.
- Potent gastroprokinetic effect.

Indications

- In vertigo.
- Can be effective in preventing motion sickness.

ADRs

- Restlessness or drowsiness.
- Extrapyrarnidal manifestations on prolonged use.

Drugs Inducing Vertigo

Drugs Inducing Vertigo

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

Vestibulotoxins

(cause functional damage only)

Drugs altering fluid & electrolyte

Diuretics:

- Antihypertensives.

Drugs altering vestibular firing:

- Anticonvulsants.

- Antidepressants.

- Sedative hypnotics.

- Alcohol.

- Cocaine.

Mixed Ototoxins

(cause functional & structural damage)

Aminoglycoside antibiotics:

gentamycin, kanamycin, neomycin, streptomycin, tobramycin, netilmicin.

Fluoroquinolones, Vancomycin, Polymixin

Quinine, chloroquine, quinidine

Nitrogen mustard

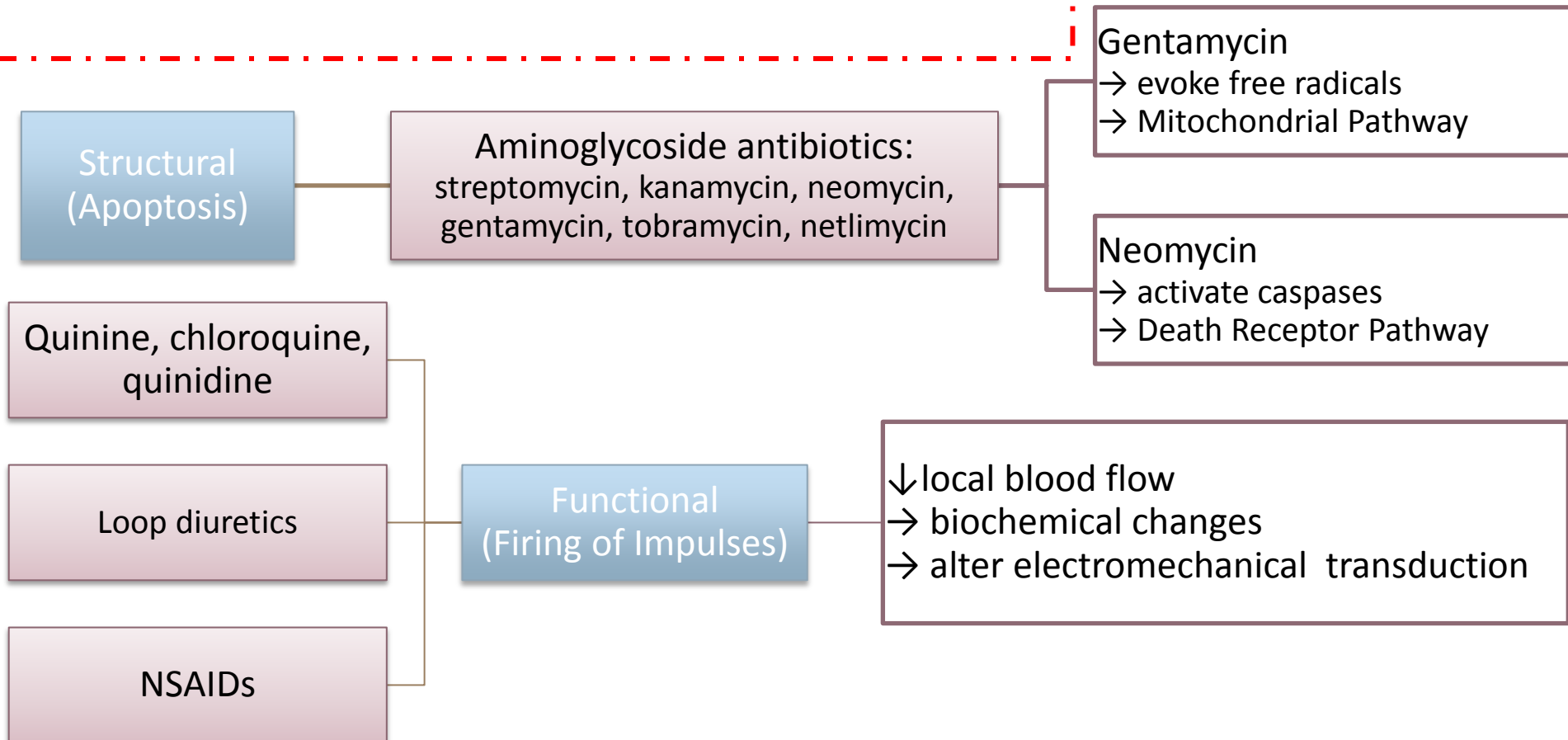
Loop diuretics

NSAIDs

Tobacco

Drugs Inducing Vertigo

Caspase : the enzyme that activate the final stage to produce apoptosis.
Neomycine and Gentamycine **both** will leads to apoptosis → permanent structural damage.



summary

Drug		action	Adverse effect	
Drugs for Prevent Recurrence	Diuretics	(↓ fluid retention)	-----	
	Corticosteroids	(↓inflammation)	Gain weight.	
	L-type Ca Channel Blockers	(↑vasodilatation)	May cause hypotension.	
Vestibular Suppressants : ↓ Spinning	Betahistine	Act on H1 as an agonist and cause → vasodilatation. Act on H3 as an antagonist and cause → inhibition in the pre-synaptic receptor H3 → ↑ Histamine release.	1/ headache, Nausea and Gastric effects. 2/ Contraindication in Pheochromocytoma And bronchial asthma patient.	
	Benzodiazepines	Act as GABA “suppressant affect”	-----	
Vestibular Suppressants : ↓ Emesis	H ₁ antagonist:	Meclizine	1/ Strong sedating affect 2/vertigo	-----
		DIMENHYDRINATE	1/ Control of motion sickness 2/ Sedative affect 3/ Less use In vertigo	1/ Sedation and Dizziness 2/ contraindication in Glaucoma and Prostatic enlargement
	Phenothiazines:	Prochlorperazine	1/antipsychotic , some sedation and antiemetic 2/ the best antiemetic in vertigo	-----
	Dopamine Antagonists	METOCLOPRAMIDE	1/Vertigo 2/ in preventing motion sickness	Gastroprokinetic parkinsonism-like-action

M C Q S

Q1: which one of the antiemetics drugs that do not cross BBB ?

- A- promethazine
- B- domperidone
- C- metoclopramide

Q2: the best drug for sickness motion is :

- A- betahistine
- B- prochlorperazine
- C- dimenhydrinate

Q3: neomycin induces apoptosis through :

- A- death receptor pathway
- B- biochemical changes
- C- mitochondrial pathway

Q4: which type of these diuretics is functional ototoxin ?

- A- thiazide diuretics
- B- K-sparing diuretics
- C- loop diuretics

Q5: gentamycin promote apoptosis by:

- A- activate caspase
- B- evoke free radicals
- C- A & B

Q6: Sami, 30 years old male, is going in cruise trip then suddenly he feel dizzy & nauseous. Which drug of these can treat his symptoms ?

- A- promethazine
- B- dimenhydrinate
- C- metoclopramide

Q7: which of these is the best antiemetics drug in vertigo ?

- A- betahistine
- B- prochlorperazine
- C- dimenhydrinate

Q8: which one of these can't be prescribed in case of bronchial asthma?

- A- betahistine
- B- metoclopramide
- C- dimenhydrinate

Q9: what is the antiemetic drug that has gastrokinetic effect ?

- A- betahistine
- B- prochlorperazine
- C- metoclopramide

Q10: betahistine is :

- A- weak H₁ agonist
- B- strong H₃ antagonist
- C- A & B

Answers : 1.B , 2.C , 3. A , 4.C , 5.B , 6.B , 7.B , 8.A , 9.C , 10.C

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**We hope that we made this lecture easier for you
Good Luck !**



CNS Block