

NO → Smooth m. → cGMP → V.d

from endothelial

neostigmine, edrophonium ^{يرفعه الجعج}
بعد العملية (التضيق)

تحدث هذه المحاضرة عن الأدوية والمركبات المحفزة لل
.Ach receptors

سواء تلك التي تؤثر مباشرة على المستقبل أو تؤثر على
الإنزيم الذي يحطم ال Ach، هي تدعم غالباً ال
parasympathetic، تعالج بعض الأمراض.

GIT M₂ → relax
^{+ gastro urinary T} M₃ → contraction

Nicotine ^{يعزز} is
parasympathetic

Nicotine at low con. stimulant.
at high con. blocker.

cholinesterase inhibitors

revers. Neostigmine, physostigmine, ^{well absorbed} edrophonium, pyridostigmine, ambenonium,
irrevers. echothiophate, soman, Marathim, parathion, ^[organophosphates] sarin

pralidoxime → before aging → cholinesterase regenerator.

Ach ^{يقلح} \rightarrow Myasthenia, curare, glaucoma ^{يعمل على} [β -blockers + prostaglandin], ileus, Megacolon, Urinary retention

Fibrillation of muscle
⊗ Antidromic firing → entire unit

Sjogren syndrome → dry mouth $\xrightarrow{2^{nd}}$ cevimeline

Alzheimers \rightarrow Tacrine (toxic)
Donepezil

⊗ edrophonium → diagnostic test
- Myasthenic → crisis
- cholinergic

⊗ atropine \rightarrow Ach and his friends \rightarrow 2 دليج 2

anticonvulsions وهو diazepam \rightarrow central \rightarrow NTE

⊗ organophosphates \rightarrow delayed neuropathy \rightarrow NTE
 \rightarrow Intermediate syndrome \rightarrow Muscle weakness

⊗ Varinaciline → partial agonist
for nicotinic receptors.

⊗ M receptors constitutively active
Atropine M blockers

⊗ Atropine in the heart

blocking M₁ increases Ach → bradycardia
then blocking M₂ → Tachycardia.

⊗ atropine = anti muscarinic drugs

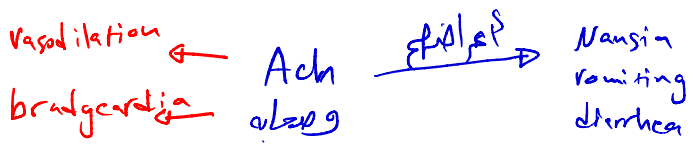
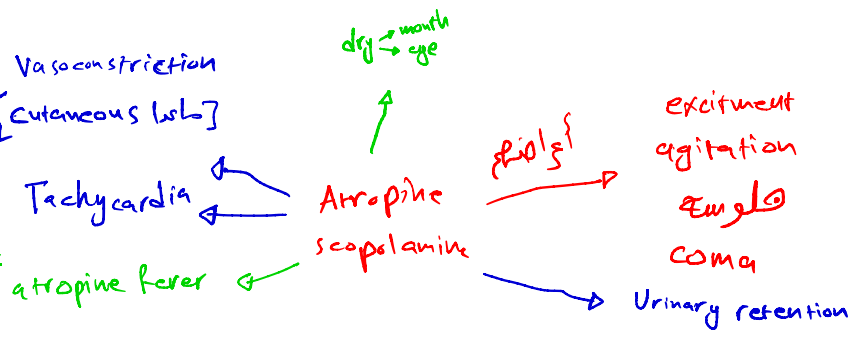
⊗ We don't use it to treat asma

لأنه M₁, M₃ يخرّبوا على بعض
M₂ → constriction
M₂ → secretion
بعض الأجزاء
طبياً blocking them

eye → Atropine causes cycloplegia, Mydriasis, Glucoma, synecchia +
phenylphrine → fundoscopic examination

⊗ scopolamine → bass أو راح أو
Motion أو يعالج أو (دوار البحر)
ينسبني/الم العملية والولادة

⊗ لو نسي hyperactive carotid sinus reflex vagal discharge
أكثر أو atropine يعالج
لأنه يثبته أو parasym.

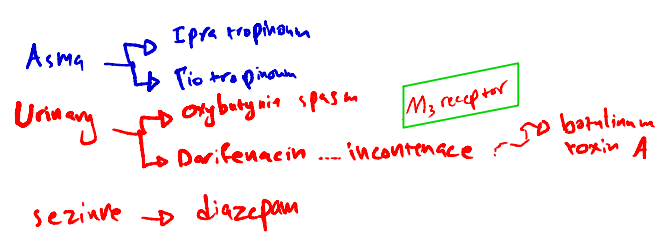
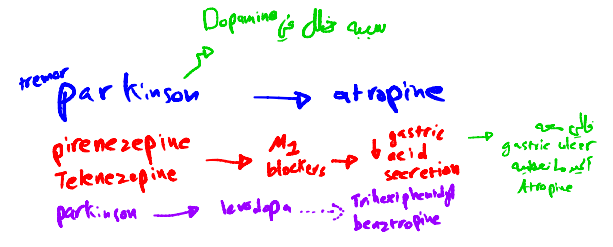


طبيعاً بالمنطق ما دام ال Ach يسوي (يعمل) diarrhea فال atropine يُعتبر علاج لها، هم دائماً أعداء عكس بعض وهكذا.....

⊗ Atropine and diphenoxylate (Lomotil) → anti diarrhoea.

⊗ The doctor said:
تعالج (remember that one of the Solanaceae plants is called Mandragora, who eat it become crazy) مصدر ال atropine البجاني

⊗ Atropine may cause ganglionic blockade which cause orthostatic hypotension → sympathomimetic + 2 شد phenylphrine
موتوفاة 24



α_1
 phoxyprine
 methoxamine

α_2
 clonidine
 methylnorepinephrine

$\alpha + \beta \rightarrow$ epinephrine, norepinephrine ($\beta_2 \times$)

β_1 Dobutamine
 $\beta_1 + \beta_2$ Isoproterenol
 β_2 Albuterol (salbutamol), terbutaline, Ritodrine

α_{1+2} vasoconstriction. β_2 vaso dilation

• types of β_1 negative feedback all α_2
 2. β_1 is present in vasodilation in genes central hypertension

• Trimethaphan \rightarrow blocker for ganglionic receptors in para.

$\beta_1 \rightarrow$ \uparrow cardiac output
 $\beta_2 \rightarrow$ dilation \rightarrow \downarrow perf. resistance

systolic \rightarrow maintain, if slightly decrease
 diastolic \rightarrow \uparrow total pressure \downarrow

• Dopamine

1. low doses \rightarrow vasodilation \rightarrow renal, sphincters, coronary, cerebral β_1 receptor
 (IV infusion) \rightarrow \downarrow pref. resistance
 \rightarrow Natriuresis
 \rightarrow oliguria \rightarrow \downarrow β_1

2. Moderate doses \rightarrow β_1 agonist \rightarrow cardiac output \uparrow

3. high doses \rightarrow α agonist \rightarrow vaso constriction

$\beta_2 \rightarrow$ bronchodilation

eye \rightarrow α agonist \rightarrow \downarrow ocular pressure
 \rightarrow β antagonist \rightarrow \downarrow production of aqueous humor.

bladder \rightarrow control urine
 \rightarrow ejaculation

insulin \rightarrow $\beta \uparrow$
 \rightarrow $\alpha_2 \downarrow$

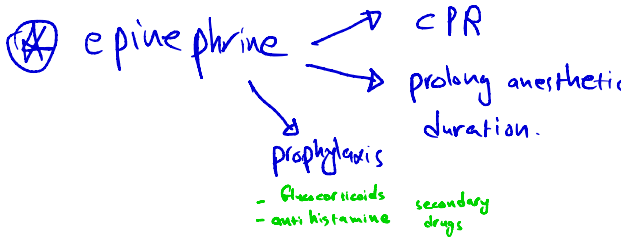
renin \rightarrow $\beta_1 \uparrow$
 \rightarrow $\alpha_2 \downarrow$

• CNS \rightarrow catecholamines can't reach (BBB).
 amphetamine \rightarrow β_2
 elevation of mood
 euphoria
 insomnia
 anorexia

\leftarrow morphine \rightarrow $\beta_1 \uparrow$ \rightarrow $\beta_2 \downarrow$
 focus on boring tasks
 Psychotic (Jho)

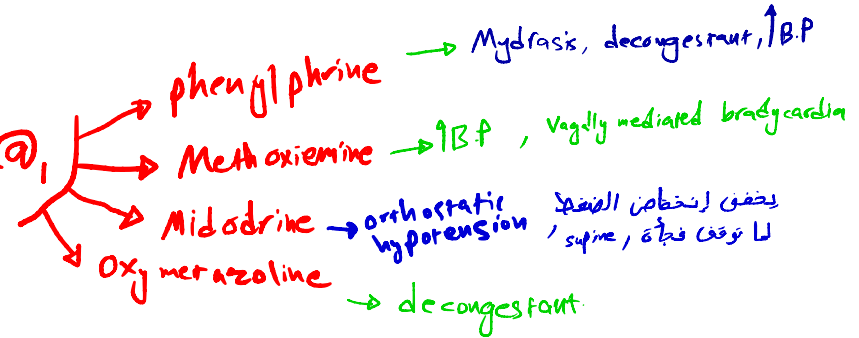
$\beta_3 \rightarrow$ lipolysis \uparrow
 $\beta_2 \rightarrow$ glycogenolysis \uparrow
 \rightarrow K^+ uptake

lipolysis into Jh

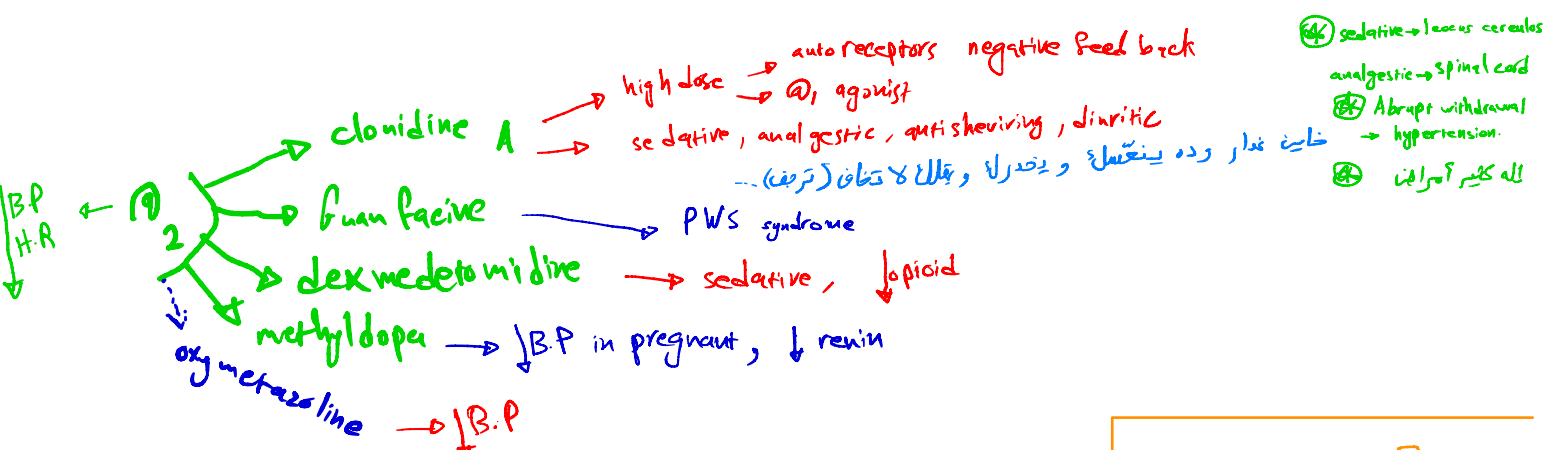


⊛ NE → baroreflex → bradycardia.

⊛ relief heart failure → Dopamine
Dobutamine



فينا كلون فدا
Fina clon phedate Gu



+ Inotropic ← β₁ ⊛
+ chronotropic ←
↓ diastolic P.

⊛ Isoproterenol → β₁₊₂ → heart block

⊛ Dobutamine → (+) β₁ agonist and α₁ antagonist
→ (-) α₁ agonist
* inotropic > chronotropic
Isoproterenol = قارة

⊛ Salbutamol, terbutaline → Asma
ritaline → uterine rest in premature labor.

⊛ Mixed acting → ephedrine → الستيرويد
→ stress incontinence
→ pseudoephedrine → decongestant.
↑ NE + β₂ active

⊛ Indirect acting → Amphetamine like displacers → ↑NE + dopamine, mood alterer, depressant of appetite
→ NETX → Atomoxetine, cocaine
↳ nasopharyngeal surgery, نزف + ألم

⊛ Tyramine → oral inactive because MAO
→ ↑B.P, release stored catecholamines

⊛ Dopamine agonists → levodopa
→ Fenoldopam → ↓B.P

non-selective → phenoxybenzamine
 → phentolamine

Treat, Raynaud's syndrome → Prazosin
 ↓
 pheochromocytoma, reflex tachycardia, ↓ B.P., orthostatic hypotension
 ↓
 diagnose, side effects → Tachycardia, arrhythmias, Miosis, nasal stuffiness
 Myocardial ischemia.

α₁-inhibi → Prazosin
 → Terazosin
 → Doxazosin
 → Tamsulosin

↓ Urinary retention, ↓ B.P., treat prostatic hypertrophy, side effect: first dose phenomenon - posture by prazosin.
 improves urine flow
 ↑ bioavailability
 ↑ half-life
 pressure ↓, ↓ bladder pressure, ↓ edema

α₁ α₂ negative feedback → reflex tachycardia ⊕
 ↓ ejaculation ⊕

α₂ → Yohimbine ↓ B.P., ↑ erectile, ↑ ADH
 → phosphodiesterase-5 (sildenafil) Viagra

Aphrodisiac: القوت

local anesthetic (membrane stabilizing) → lipid solubility ← β-blockers (in approx differences) in ⊕
 Liver → lipophilic: 1. propranolol, 2. metoprolol, 3. oxprenolol, 4. carvedilol
 Kidney → hydrophilic: 1. acebutalol, 2. Atenolol, 3. bisoprolol, 4. Nadolol, 5. Sotalol.

⊕ β-blockers → يعالج hypertension, angina, heart failure, MI.

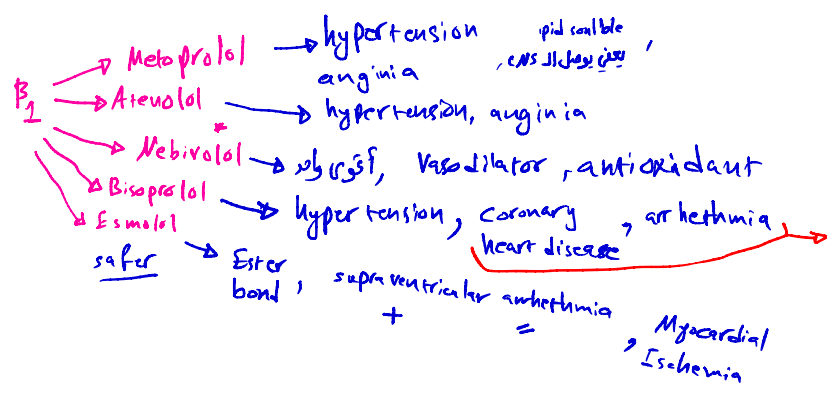
β₂ → positive feedback ⊕

⊕ β₂-blocker يضر لال ولبت Asma وحواس
 ⊕ β-blockers, α agonists, prostaglandin cholinomimetics, diuretics → intraocular pressure

block cardiomyopathy → ↑ insulin, Glycogenolysis ← β₂ α! ⊕
 ↓ HDL, ↑ LDL lipolysis ← β₃

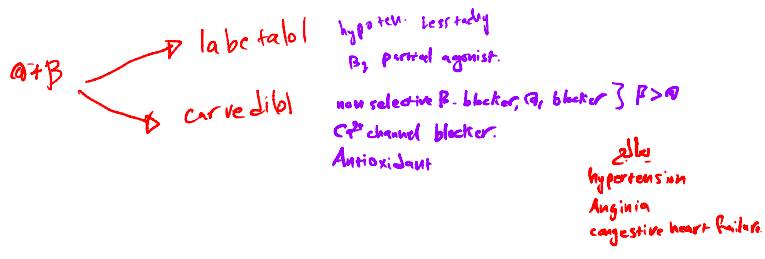
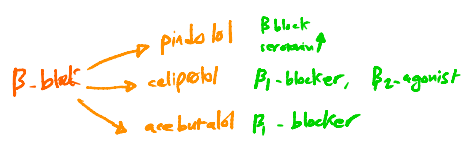
non-selective β → Propranolol
 → Nadolol longer
 → Timolol eye
 → Sotalol class III antiarrhythmics K⁺ channel, non-receptor blockade, supra →
 Thyroid storm, severe fright, alcohol withdrawal, Migraine
 Metoprolol, Atenolol, Timolol, Nadolol
 يسون (معا) الجهد

safer for Asme patients



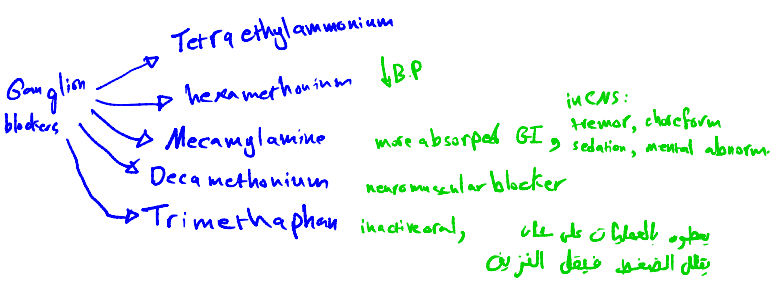
لا يوجد في Myocardial remodeling فهو يظل العمر والأعلى ربيد الله

⊕ Metoprolol, bisoprolol, carvedilol → ↓ mortality in C. heart diseases.



⊕ Toxicity of B-blockers

- brady cardia. reflex ↓ سبب
- coolness of hand and feet. B₂ ↓ سبب
- vivid dreams, mild sedation, depression.
- non-selective → Asma
- Heart failure ↓ فشل قلوب في علاجهم
- B-blocker + Verapamil → bradycardia, heart failure, cardiac conduction abnormal.
- B₂-blocker → diabetic patient, خطر



depolarizing blockade ↔ nicotine, Ach ⊕

nondepolarizing competitive blockade
 nicotine or Ach ليزيد التنافس في المستقبلات

⊕ Ganglion blockers

- in eye:** symp ↓ سبب, cycloplegia, dilation pupil
- in CVS:** para ↓ سبب ↓ BP, ↓ contractility, posture hypotension, tachycardia. moderate
- GI:** inhibition ↓ secretion ↓ motility
- sexual:** ↓ erection, ↓ ejaculation
- sweating:** ↓
- GU:** Urinary retention, Prostatic hyperplasia

إن تلمني عجائز بنزار فأراني بما فعلت مجيدا