



# ***Pharmacology***

***Subject :***

***Lec no : 16***

***Done By : Raneem Azzam***

*وَقُلْ رَبِّ زِدْنِي عِلْمًا*



# **Sympatholytic Drugs**

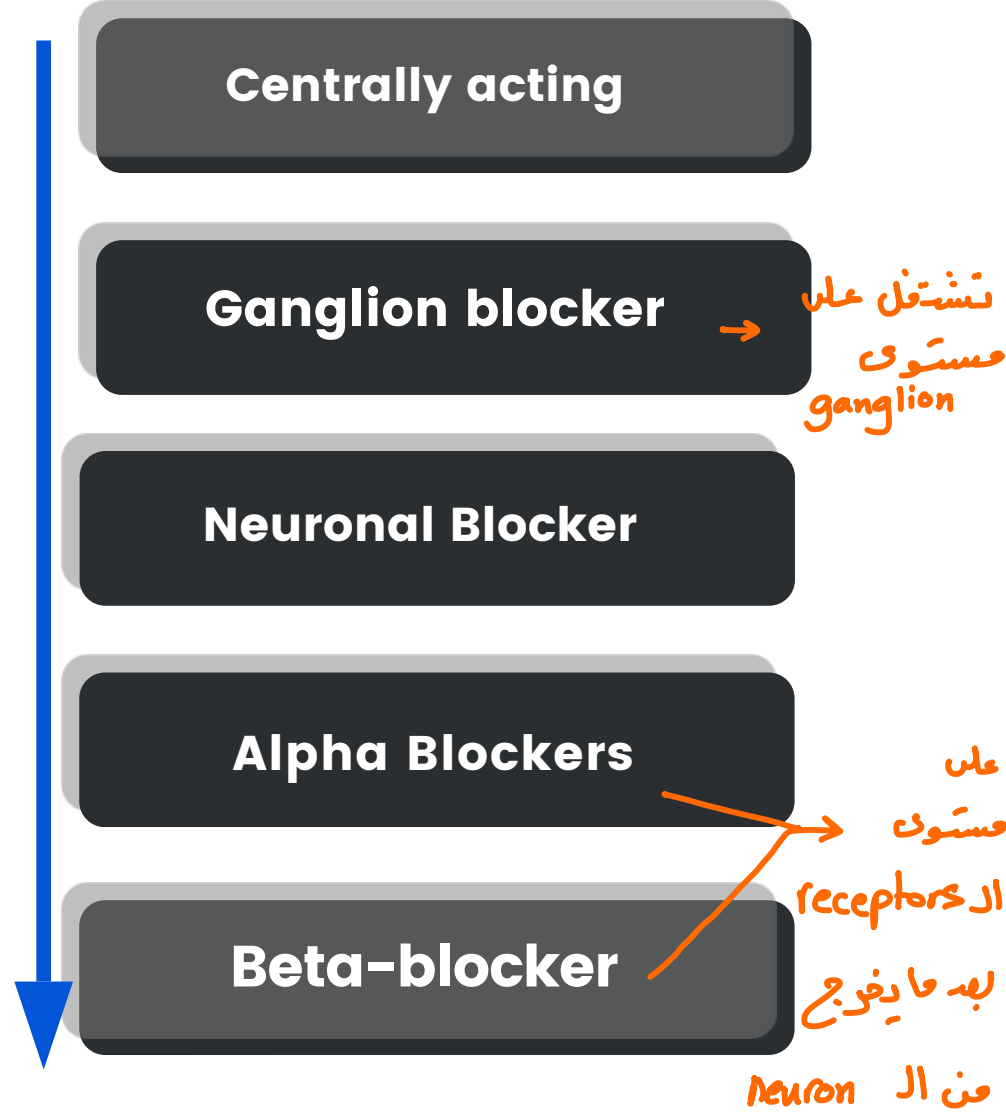
\* الدكتوراة من المحاضرة إلى  
قبل وهي تحكي " أنا  
فختبر اللم كثير من المحاضرة !

كيف ببلش  
يشغل

## ANTIADRENERGIC DRUGS

The drugs which block the  
action of sympathet NS

الادوية التي بتمنع ال action تاع الادرينالين  
عن طريق انها بتشغل على ال receptors



# 1-Centrally acting $O_2$ - Agonists

- Clonidine - →

Methyldopa

-Guanafacin

-guanabenz

هذا  
الاصم



# Mechanism of action of central $\alpha_2$ agonists

Stimulates central alpha-2 adrenoceptors

reduce sympathetic outflow from the CNS

1-decreased heart rate →  
reduction of cardiac output

2-reduce vasoconstriction →  
reduction of peripheral vascular  
resistance

↓ blood pressure

حاجة انا بحتجها لما يكون  
فيه hypertension

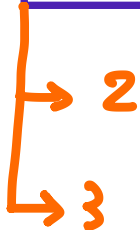
بتقلل كد حاجة

# 2-Ganglion Blockers



- Trimethaphan (I.V. infusion).

احفظوهم ك اسماء بس مش رح ناخذ mechanism



# **3-Adrenergic Neuron Blockers**



**Guanethidine.**

**Reserpine.**

# 4-Adrenergic Receptor Blockers

## 1- Alpha-Adrenergic Blockers

## 2- Beta-Adrenergic Blockers

انا بدي اقفلها عشان مش عاوز ال  
sympathetic يشتغل هسا او  
بدي اياها في treatment بس  
اقفلها



# **1-Alpha-Adrenergic Blockers**

# Classification

## - Selective $\alpha_1$ -blockers:

- Doxazocin
- Prazocin
- Terazosin
- Tamsulosin
- Trimazosin

هدول بيس

$\alpha_1$	Effector tissues: smooth muscle, glands	$G_q$	$\uparrow IP_3, DAG$	$\uparrow Ca^{2+}$ , causes contraction, secretion	أي حاجة متجيب فيها سيرة ال $Ca^{2+}$ بتزيد يعني contraction
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ما تقسي

+ المعافرة إالي قبل

## - Non Selective $\alpha$ -blockers -

بتقفل الاثنين

- Phenoxybenzamine
- Phentolamine
- Tolazoline
- Selective  $\alpha_2$ -blockers
- Yohambine

حاج يقابلنا  
غير هون هالاسم

# PRAZOCIN

## Selective $\alpha_1$ -blocker

### Actions:

بمس يلتغي شغل الأدرينالين على ال receptors شو رح يصير؟

- 1-VD of veins ( decrease venous return)
- 2- VD of arteries ( decrease TPR and congestion)
- 3-Relax sphincter of UB
- 4- No reflex tachycardia

كل إي كان يعمل  $\alpha$   
ال يلتغي ويصير العكس \*  
ال نكس وناقشه يعني

# PRAZOCIN

## Therapeutic Uses:

- Hypertension
- Benign Prostatic Hypertrophy (BPH)
- Peripheral vascular disease (PVD)
- Heart failure

بدي اتجنب ال VC في هاي  
الحالات مشان هيك بعمل block

# PRAZOCIN

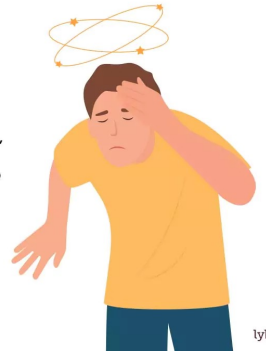
## Side Effects:

- Orthostatic hypotension (1st dose)
- Dry mouth and GIT upset
- Headache and drowsiness
- Oedma
- Rash and pruritis



### What is Orthostatic Hypotension?

A person with orthostatic hypotension, sometimes referred to as postural hypotension, experiences a sharp drop in blood pressure while rising from a seated or reclining position.



[www.lybrate.com](http://www.lybrate.com)

lybrate



Oedma

# Tamsulosin

→ **Selective  $\alpha 1$ -blocker**

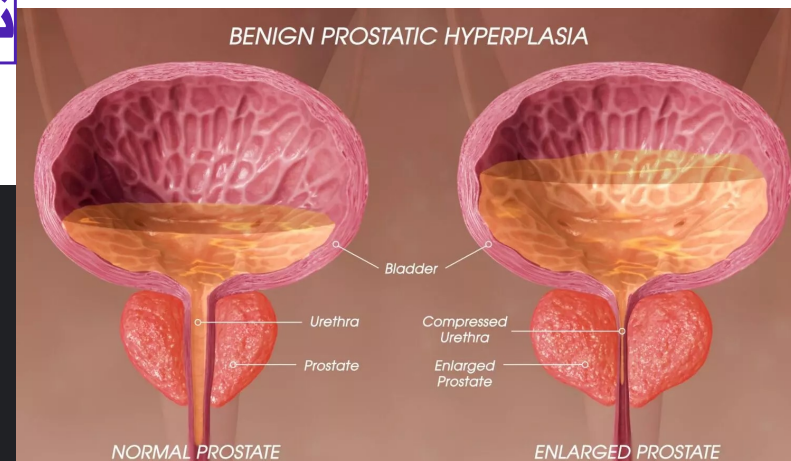
ال  $\alpha 1$  receptors تاعت ال  
urinary bladder

→ **Uses:**

→ **-In Treatment of : BPH**

تضخم البروستات

Tamsulosin is used to treat men who have symptoms of an enlarged prostate gland, which is also known as benign enlargement of the prostate (benign prostatic hyperplasia or BPH). Benign enlargement of the prostate is a problem that can occur in men as they get older. The prostate gland is located below the bladder.



# **Beta-Adrenergic Blockers**

# Classification

**Beta 1**

- 1-CVS: Heart: Increase all cardiac properties (Contractility-Conductivity-Excitability-Heart rate) and C.O.P-O2 consumption
- 2-SME: - Eye: Ciliary epithelium → ↑ aqueous secretion (IOP)
- 3-Other actions:
  - Kidney: Renin secretion
  - CNS: ↑ sympathetic outflow

**Beta 2**

- 1-CVS: VD of skeletal and coronary blood vessels
- 2-SME: - Eye: Ciliary epithelium → ↑ aqueous secretion (IOP)
- Bronchi: relaxation

## Classification

### 1. According to selectivity:

- Non-selective :block beta1 and beta2 →
- Cardio-selective: block beta1

هاي بتقفل الاثنين ودي مش حلوة ، بحيث انا لما بركز على target واحد كل ما كانت ال side effects عندي اقل (كل ما يكون دقيقة بال selective receptor)

β / α بتقفل

- Block alpha and beta receptors : e.g Labetalol

زيادة  
التيالول هو من حاصرات بيتا (Beta blockers) تستخدم لعلاج ارتفاع ضغط الدم وبعض بمروره او مدموجا مع مميزات البول. تتنزل اليه عمل الاليتالول في توسيع الاوعية الدموية واطلاء ضربات القلب بهدف خفض ضغط الدم

### 2. According to generation: → chemical classification

1st generation: non selective beta-blockers.

2nd generation: cardioselective beta1-blockers.

3rd generation: vasodilator beta-blockers. They either have:

- Beta2-agonistic activity: celiprolol & dilevalol.
- Direct V.D & alpha-blocking effect: carvedilol &

### 3-According to (ISA): intrinsic sympathomimetic activity (ISA)

Antagonist (no ISA): propranolol, timolol, atenolol & metoprolol.

Partial agonists (have ISA): oxprenolol, pindolol, acebutolol, practolol

بزيادة انو ال effect السها حالي

It's act antagonist but when increased the dose act as agonist

بفيدني بشو ؟ انو انا الدوا بستخدمو بعمل ال action بتاعو ، ويرجع بعد هيك بتقلب ال agonists ف بتجنب شوي من ال side effect تاعه



11/11

## ➤ **Non-selective beta blockers**

**- Propranolol**

**- Propranolol** pindolol

**- Nadolol**

**- Timolol**

# PROPRANOLOL

- Non selective (blocks  $\beta_1 + \beta_2$ )

- No ISA

## Kinetics:

- Well absorbed orally (highly lipophilic)

- Extensively metabolized in the liver

- 90-95% bound to PP

\*  $\uparrow\uparrow$   $\downarrow$  <sup>1st</sup> Metabolism

- Metabolites excreted in urine

# PROPRANOLOL

## Actions: علاج عُنشِي من قوت لعتت

1- CNS: ↓ sympathetic flow (Antianxiety) ← س تستخدمو

2- Respiratory: bronchoconstriction

3- C.V.S: كل ال Cardiac properties بتقل ف بالتالي بقل ال cardiac output

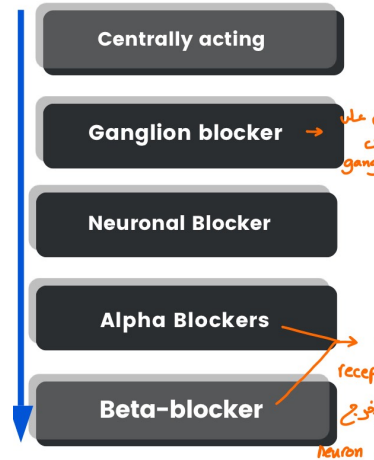
### \*Heart:

-ve inotropic

- ve dromotropic

-ve chronotropic (↓ C.O.P, ↓ cardiac work, ↓ O2 consumption)

**\*BL.v:** decrease blood flow to the tissues



الادريينالين احيانا بس يزيد  
يعمل anxiety ف احد الحلول  
انو نقل الاكشن تاع الادريينالين

\* blood pressure:  $\beta$ -blockers decrease the blood pressure through:

1. Decrease C.O.P

قللت ال cardiac properties ف ال bump صار ضعيف مش قوي

2. Inhibition of renin release.

ال renin بعمل VC بالتالي بزيد ال bp

3. Resetting of baroreceptors.

البيتا بلوكر بتعمل لها اعادة اعداد (يصير استشعارها لارتفاع ضغط الدم more sensitive) كيف؟ تبدأ تتصرف لما يبقى الارتفاع دوت اقل من 30 يعني مارج استنى لازيد 30 حتى اتصرف

4. Presynaptic  $\beta_2$ -blockade decreases NE release.

5. Central inhibition of sympathetic outflow.

6. Modulation of prostaglandin synthesis in favor of

the vasodilator ones as prostacycline

لما بتخلج بتعمل

Resetting allows the baroreceptor reflex to operate over a wide range of arterial pressures rather than being confined to a single range defined by one buffer curve. Resetting is not complete. That is, if the receptors are exposed to a change in pressure of 30 mm Hg the buffer curves shift by less than 30 mm Hg.

# PROPRANOLOL

## Therapeutic Uses:

### - Hypertension

### -IHD:angina, MI, B blockers acts by:

➤ decrease oxygen demand by decreasing cardiac work.

➤ Increase oxygen supply by:

➤ Increasing diastolic coronary perfusion time. → decreasing cardiac work لا يغير عملته

➤ Shifting of subepicardial blood flow to subendocardial flow. ↴

➤ Inhibition of platelet aggregation. رح يصير فيه shifting للblooms من اماكن لاماكن اكثر اهمية

Platelet aggregation inhibitors work in different places of the clotting cascade and prevent platelet adhesion, therefore no clot formation.

Aspirin, the most commonly used antiplatelet drug changes the balance between prostacyclin (which inhibits platelet aggregation) and thromboxane (that promotes aggregation)

# PROPRANOLOL

## Therapeutic Uses:

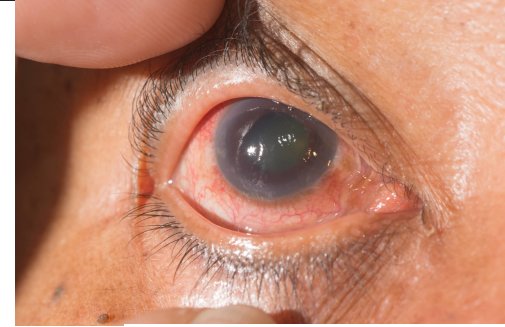
- Glucoma
- Hyprerthyroidism
- Ventricular and supra ventricular arrhythmias
- Pheochromocytoma with alpha-blockers.
- Prophylaxis in migraine headache.
- Anxiety and essential tremors.
- Portal hypertension.

في اشياء بتزود ال sensitivity ، وانا ما بدى الادرينالين  
يشغل كثير ف بروج قافلها  
receptors of adrenaline

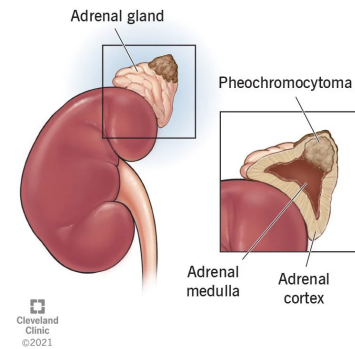
لازم بس نذكر  
المرض نحكى with...

فهون احنا منعطي بيتا بلوكر حتى  
يصير ، relaxation of portal vein  
فبقلل حدوث ال hypertension فيه

What is glaucoma? Glaucoma is a group of eye diseases that can cause vision loss and blindness by damaging a nerve in the back of your eye called the optic nerve. The symptoms can start so slowly that you may not notice them. The only way to find out if you have glaucoma is to get a comprehensive dilated eye



Pheochromocytoma



Cleveland Clinic  
©2021

Portal hypertension is elevated pressure in your portal venous system. The portal vein is a major vein that leads to the liver. The most common cause of portal hypertension is cirrhosis (scarring) of the liver

في ال Pheochromocytoma  
بنقلل ال الفا و البيتا

# PROPRANOLOL

## Side Effects:

كل هاد بسبب اني قلت الادريينالين

- Bronchoconstriction
- Arrhythmia
- Sexual impairment لانوال blood flow الهاقل
- Fatigue, dizziness, vivid dreams, nightmares
- Cold hands and allergic reactions
- Prolong insulin hypoglycemia and mask the hypoglycemic symptoms
- Increase VLDL, triglycerides, and lower HDL
- Oculo-muco-cutaneous syndrome with practolol

هسا انت قافل البيتا receptors و صار للمريض hypoglycaemia شو رحويصير؟  
هل ال sympathetic رح يحس بحاجة؟ رح ياخذ رد فعل حتى و ال receptor مقفو؟  
لاا، فرح يصير mask والمريض بدون اى مقدمات يفقد وعيو

مشان هيك خلي بالك من حد معو سكري وبيأخذ

لما بيحصل عندنا hyperglycaemia في جهاز إنذار  
بشغل جوا الجسم بتوضح عليه أعراض انه عنده  
hyperglycaemia، ايه هو جهاز الإنذار دوت ال  
sympathetic stimulation  
function of  $\beta_2$  ↓

- -Liver: Glycogenesis → ↑ glucose

اخذ بالي جدا جدا وانا بستخدمو فين

# PROPRANOLOL

## Precautions & Contraindications:

- Bronchial asthma **هو اصلا عندو risk انها تقفل اروح انا اقلها اكثر**
- Partial heart block and A.V block
- Variant angina **ال angina ٣ انواع من ضمنهم ال variant وهاد النوع بالذات ما بصير ينعموا بلوك ليه؟ هاد النوع عندو super sensitive adrenergic receptors in coronary بتعرض لاي ستريس ولو بسيط تلاقي صار خلل في coronary ،، طب بني ادم زي هاد بنفع اقل عندو البيتتا الي بتعمل VD وبتحميه واسيبه لالفا؟ طبعا لا**
- Peripheral vascular diseases
- Used with caution in DM **يرجعلو ال disease بشكل شديد**
- Can not be stopped suddenly as **Abrupt**
  - discontinuation increases the risk of IHD due to
  - upregulation of beta-receptors.

TYPE E – END OF USE

توكينو على هادي

\* الأعراض ال إنسحابية \*

Drug withdrawal syndromes and rebound



# Cardio selective beta blockers selective beta1 blockers

- **-ATENOLOL** ✓
- **-METOPROLOL** ✓
- **-BISOPROLOL** ✗
- **-ESMOLOL** ✓
- **-ACEBUTOLOL** ✓

# Revision

## Summary

### Sites functions, Agonists and antagonists of Adrenoceptors

Receptor	Site	Action	Agonists	Antagonists
Alpha 1	Effective organs	VC, mydriasis, spasm of GIT&bladder sphincters, ejaculation.	Phenylephrine Dopamine Noradrenaline Adrenaline	Prazosin Phentolamine Phenoxybenzamine
Alpha 2	Pre & post-synaptic & CNS	Inhibit sympathetic outflow from CNS, decrease release of renin & insulin and inhibit lipolysis	Noradrenaline Adrenaline Clonidine guanfacine guanabenz	Phentolamine Phenoxybenzamine Yohimbine
Beta 1	Heart, presynaptic & kidney	Increase H.R & contr., increase release of NA, renin & lipolysis.	Dopamine Dobutamine Noradrenaline Adrenaline Isoprenaline	<u>Selective <math>\beta_1</math> blocker</u> Atenolol Acebutolol Metoprolol Practolol Esmolol
Beta 2	Bronchi, BV, GIT, uterus, bladder & pancreas	Bronchodilation, VD, reax GIT, uterus & bladder, increase release of insulin & glycogenolysis	Salbutamol Isoprenaline Adrenaline noradrenaline	<u>Non Selective <math>\beta</math> blocker</u> Propranolol Pindolol Nadolol Oxprenolol

## Classification of beta blockers, uses and side effects

Drug	Uses	Side effects
<b><u>Cardioselective <math>\beta_1</math> blockers :</u></b> Atenolol Acebutolol .Metoprolol. Practolol Bisoprolol Esmolol.	MI, Angina, Arrhythmia, Hypertension, Hyperthyroidism, Pheochromocytoma with alpha-blockers, Glaucoma, Migraine, Anxiety, tremors& Portal hypertension.	AV block, heart failure, hypotension. Bronchospasm, Cold extremities, Fatigue, night mare, depression & hallucination . Prolong insulin hypoglycemia and mask the hypoglycemic symptoms.
<b><u>Non selective <math>\beta</math>-blockers (<math>B_{1&amp;2}</math>)</u></b> Propranolol. Pindolol Oxprenolol. Nadololol. Sotalol.		

بهمني بشتغل على اي receptors  
(بيقتل اي واحد)

پالي قلناهم واحنا  
حاشين

## Alpha blockers and their uses

$\alpha$ - blockers	Action	Uses
Phentolamine	<ul style="list-style-type: none"><li>• <math>\alpha_1</math>, <math>\alpha_2</math> blocker</li><li>• Ach &amp; Histamine like - action</li><li>• Antiserotonin</li><li>• Short duration.</li></ul>	<ul style="list-style-type: none"><li>• Diagnosis of pheochromocytoma</li></ul>
Phenoxybenzamine	<ul style="list-style-type: none"><li>• <math>\alpha_1</math>, <math>\alpha_2</math> blocker</li><li>• Atropine-like action</li><li>• Antihistamine &amp; antiserotonin</li><li>• Long duration</li></ul>	<ul style="list-style-type: none"><li>• Treatment of pheochromocytoma</li><li>• PVD</li><li>• Shock</li></ul>
Prazosin	Selective $\alpha_1$ blocker	<ul style="list-style-type: none"><li>• Hypertension</li><li>• CHF</li><li>• PVD</li><li>• Bladder neck</li></ul>