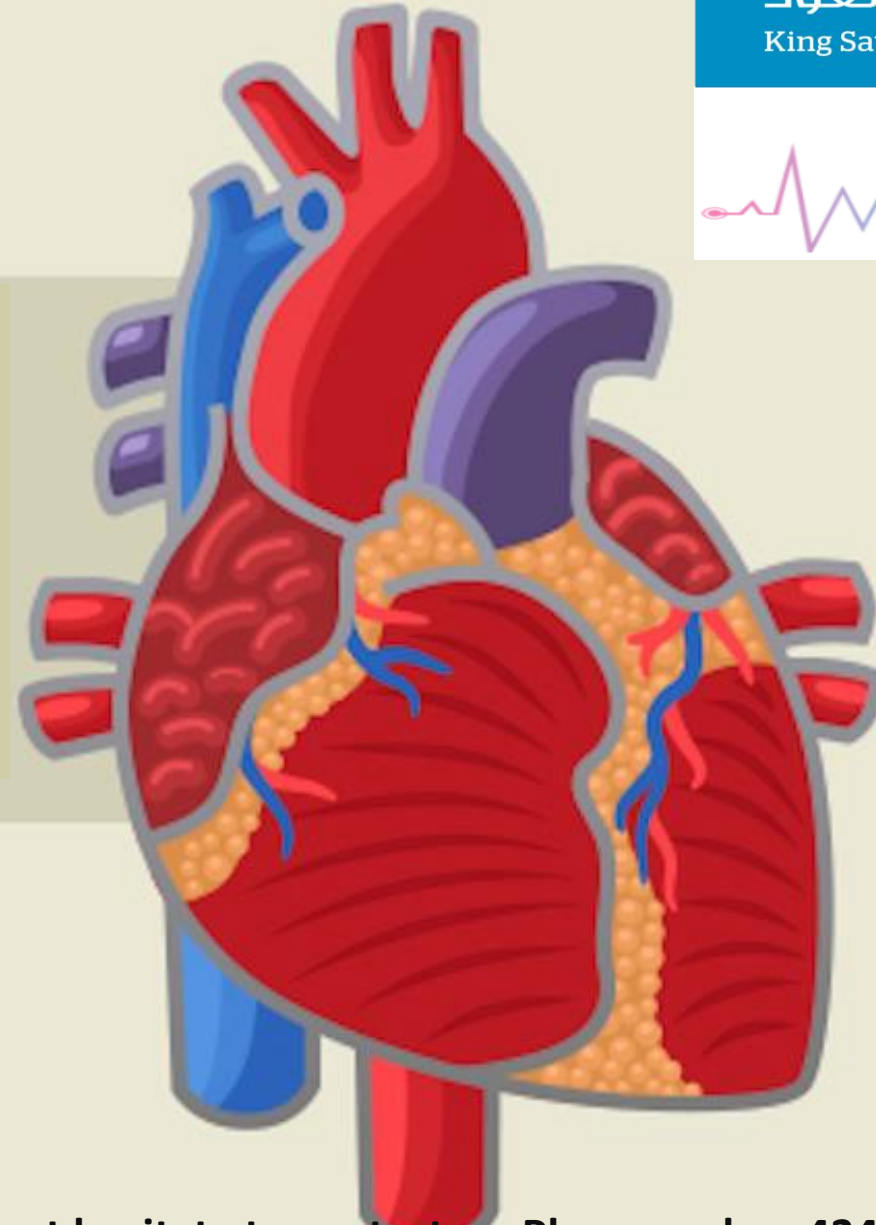




1&2

Alpha & Beta Adrenergic Blockers.



Cardiovascular Block.

Additional note: Gray color

For any correction, suggestions or any useful information do not hesitate to contact as: Pharmacology434@gmail.com

- Adrenergic drugs :
 1--in diabetic patient will decrease glycogen
 2-- blood pressure will decrease
 3--heart rate will decrease
 - MAO "monoaminoxidate" will depress the epinephrine and norepinephrine and it's adrenergic drug

Adrenergic drugs

- Adrenergic depressants
 - Adrenolytic
 - Adrenergic antagonists
 - Adrenergic receptor blockers
- } Same meaning

Adrenergic stimulants
(Sympathomimetic)

Adrenergic depressants

Adrenoceptor Blockers
(Adrenolytic)

Alpha-adrenergic receptor blockers

Beta-adrenergic receptor blockers

Alpha & beta-adrenergic receptor blockers

Adrenergic Neuron Blockers
(Sympatholytic)

- False transmitters (alpha-2 agonist):
 -Methyldopa (a-methyl tyrosine): used as antihypertensive in pregnancy.
- Deplete storage:
 -Reserpine (not used anymore)
- Inhibit release & enhance uptake:
 -Ganethidine (not used anymore)

- 1-Methyldopa act as agonist at α_2 -adrenoceptor (presynaptic, auto-receptor) thus inhibit the release of norepinephrine leading to decrease blood pressure.
- 2-Methyldopa will act in direct but ganethidine will act direct for this we need more doses of methyldopa than ganethidine.
- 3-Clonidine: similar to Methyldopa.

ALPHA-BLOCKER



a ADRENOCEPTOR BLOCKERS

Non- selective (blocks a1 & a2)

Irreversible (long acting)	Phenoxybenzamine	Used in irreversible shock, and before removal of Pheochromocytoma to prevent Hypertensive crisis.
Reversible (short acting)	Phentolamine	Before removal of Pheochromocytoma to prevent hypertensive crisis.

ADRs: **tachycardia**

Pheochromocytoma: will increase blood pressure + norepinephrine +tachycardia for this we combine it with b-blocker to decrease the side effect especially the tachycardia side effect.

Selective

Blocks a1	Prazosin: (short acting) Doxazosin: (long acting)	-Used in *Raynaud's disease : induce peripheral vasodilatation. -Benign prostatic hypertrophy (BPH). -Can be used in hypertension & heart failure. Adverse effects: Postural hypotension , syncope, fluid retention, headache, nasal stuffiness, decreased ejaculation & impotence.
	Tamsulosin (uroselective):	Used in Benign prostatic hypertrophy to cause contraction of the bladder wall, relaxes bladder neck & sphincters.
Blocks a2	Yohimbine	Release NE & ADH / Aphrodisiac**

*Raynaud's phenomenon: is excessively reduced blood flow in response to cold or emotional stress, causing discoloration of the fingers, toes, and occasionally other areas.

** Aphrodisiac: increase in sexual desire.

**phenocromocytoma: (small vascular tumor of the adrenal medulla)

1- Tamsulosin is better for (BPH) because it has less side effect especially in hypertension and heart failure.

2- Uroselective means no function in blood vessels



β-Adrenoceptor Blockers

Pharmacodynamics Classification

Pharmacokinetic Classification

1. According to extent of blocked of each type

2- According to presence of agonistic/antagonistic action (ISA)* = PARTIAL AGONISTS or only antagonistic action
*Intrinsic sympathetic activity

Non-selective	Selective	Without (ISA)	With (ISA)
<p>Block b1 & b2: Propranolol Timolol Pindolol</p> <p>Block b & a1: Labetalol Carvidolol</p>	<p>Block b1 >> b2 (blocks b1 more than b2 or excessive blocking of b1 leads to blocking of b2?)</p> <p>Atenolol Bisoprolol metaprolol</p>	<p>Propranolol Timolol Atenolol Bisoprolol Carbidolol</p>	<p>labetolol</p>

Pharmacokinetic Classification (According to their lipid solubility)

	Lipophilic	Hydrophilic
Oral absorption	Complete	Irregular
Liver metabolism	Yes	No
t_{1/2}	Short	Long
CNS side effects	High	Low
Examples	Propranolol Timolol Labetalol >Carvedilol	Atenolol Bisoprolol

Propranolol:

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

Dynamics:

- Has membrane stabilizing action

-Has sedation action

Kinetics: Completely absorbed, 70% destroyed during 1st pass metabolism, 90-95% protein bound, **cross BBB**

Characteristics

On Heart



By blocking β_1 :

- 1- Inhibit heart properties: \downarrow cardiac output.
- 2- Has anti-ischemic effects: \downarrow cardiac work + \downarrow O₂ consumption.
- 3- Has anti-arrhythmic effects: \downarrow excitability, automaticity & conductivity + by membrane stabilizing activity.

On Blood Vessels (BV)



By blocking β_2 :

Vasoconstriction: \downarrow blood flow to muscles specially and other organs except brain
 \rightarrow Cold extremities + intermittent claudication.

On Blood Pressure (BP)



By blocking β_1 & β_2 :

- 1-Antihypertensive action by inhibiting heart properties: \downarrow cardiac output.
- 2- Vasoconstriction to kidney BV: \downarrow renin & aldosterone secretion.
- 3-pre-synaptic inhibition of NE release from adrenergic nerves
- 4- inhibiting sympathetic outflow in CNS

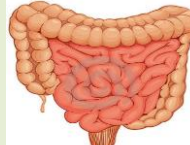
On Bronchi



By blocking β_2 :

Bronchospasm especially in susceptible patients.

On Intestine + Metabolism



In Intestine: by blocking β_2 : \uparrow Intestinal motility. it can cause some diarrhea and cramps

In Metabolism: by blocking mainly β_2 :

In liver: \downarrow Glycogenolysis \rightarrow Hypoglycemia

In pancreas: \downarrow Glucagon secretion In adipocytes: \downarrow Lipolysis

In skeletal muscles: \downarrow Glycolysis

On Peripheral & Central Nervous System



-Decrease tremors and anxiety.

- \downarrow myocardial O₂ demand.
- \uparrow Redistribution of blood flow in the myocardium.
- \downarrow free fatty acids.
- Anti-arrhythmic action.
- \downarrow incidence of sudden death

Indications (Uses)

- 1-Hypertension
- 3-Angina
- 5-Migraine (As a prophylactic drug)
- 7-Chronic glaucoma: \downarrow IOP \rightarrow by \downarrow secretion of aqueous humor
- 9-Anxiety (specially social and performance type)

- 2-Arrhythmias " used in ventricular arrhythmias more than atrial
- 4-Myocardial infarction \rightarrow \downarrow infarct size \rightarrow **Cardio protective** \rightarrow \downarrow death
- 6-Pheochromocytoma (used with α blockers never alone)
- 8-Tremors
- 10-Hyperthyroidism: Controls tachycardia, tremors, sweating, Protects heart against sympathetic over-stimulation, Lowers conversion rate of T₄ into T₃

PROPRANOLOL SIDE EFFECTS

Due to Block of Cardiac β_1 Receptors:

1. **Heart Failure**
2. **Bradycardia**
3. **Hypotension**

Due to Blockage of β_2 Receptors (only with non-selective β blockers):

Asthma – Emphysema – Chronic Bronchitis – Erectile dysfunction – Impotence – Hypoglycemia - \uparrow triglycerides – Cold extremities & intermittent claudication

Important:

All β –blockers

mask hypo-glycemic manifestations (headache, tremor & tachycardia) \rightarrow develop COMA

Explanation: If the patient is diabetic and the doctor gave him B-blocker drugs, it may lead to COMA. Because B-blocker drugs cause suppression of the sympathetic action, so the patient won't know that he is having hypoglycemia (no tremors or tachycardia).

Common side effects:

1. Depression and nightmares (Because they cross BBB)
2. Gastrointestinal Disturbances
3. Sodium Retention
4. Hypersensitivity reactions

Selective β_1 Blockers:

They are SAFER in: Asthma – Diabetes – Dyslipidemias – Raynaud's phenomenon – Vascular diseases

Side Note: Understanding the actions of the drugs very good will make it easy to know the side effects without memorizing them because basically they are the extreme effects of the actions themselves

Propranolol

Contraindications

- Depressed myocardial functions [**Uncompensated HF, Heart Block, Massive Myocardial Infarction.**]
- Hypotension
- Bronchial Asthma (**safer with cardio-selective β -blockers**).
- Peripheral vascular disease (**safer with cardio-selective β -blockers**).
- Diabetic patients > (Type I) (specially on Insulin) **for fear of hypoglycaemia**

For non compliant patients we give ISA partial agonist so some receptors will be stimulated and the body won't increase the number of beta receptors.

***Propranolol with ISA**
Better in patients that exhibit excessive bradycardia Also in non compliant for fear of sudden stoppage.

***Sudden stoppage will give rise to a withdrawal manifestations** So the drug must be withdrawn gradually to prevent Rebound angina, arrhythmia, myocardial infarction & hypertension.

pharmacological Interactions

- 1-with **verapamil (block Ca Channel)** \Rightarrow severe bradycardia \ heart block.
- 2- with **anti-diabetic drugs** \Rightarrow (insulin > sulfonylureas) > Non selective β -blockers may lead to hypo-glycaemia.
- 3-with **NSAIDs** \Rightarrow hypertensive effect , because theyformation of vasodilating prostaglandins.
- 4-with **quinidine** \Rightarrow HF **If a patient takes NSAIDs we have to increase the dose of the b-blocker (or any other anti-hypertension drug).
- 5-with **cocaine, amphetamine or a-blocker overdose** \Rightarrow Rebound hypertension & impaired tissue perfusion.
- 6- with **Tubocurarine** \Rightarrow Enhanced neuromuscular blockade.
- 7- with **ergot alkaloids** \Rightarrow in migraine Claudications, parasthesia.

Labetalol

Blocks β & α ,

Rapid acting, non-selective with little ISA & local anesthetic effect

Do not alter serum lipids or blood glucose

Used in Severe hypertension in pheochromocytoma

May be used pregnancy-induced hypertension

ADR: Orthostatic hypotension, sedation & dizziness

Carvedilol

Blocks $\beta > \alpha$, (so more vasodialating)

Non-selective with no ISA & no local anesthetic effect.

Has antioxidant action

Favorable metabolic profile.

Used effective in congestive heart failure reverses its pathophysiological changes

ADR: Edema

Summary

Agents specifically indicated for **hypertension**

Atenolol, Bisoprolol > Metoprolol, Propranolol

Agents specifically indicated for **cardiac arrhythmia**

Propranolol > Atenolol

Agents specifically indicated for **congestive heart failure**

Carvedilol, Bisoprolol, Metoprolol

Agents specifically indicated for **myocardial infarction**

Atenolol, Metoprolol, Propranolol

Agents specifically indicated for **glaucoma**

Timolol

Agents specifically indicated for **migraine prophylaxis**

Timolol, Propranolol

SIDE EFFECTS OF ADRENERGIC ANTAGONISTS

B-BLOCKERS



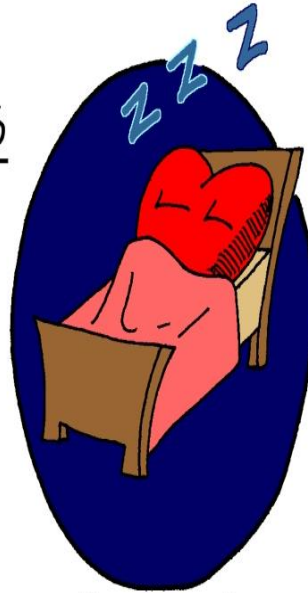
Hypotension



Symptoms of CHF

Examples:

- Propranolol (Inderal)
- Atenolol (Tenormin)
- Metoprolol (Lopressor)



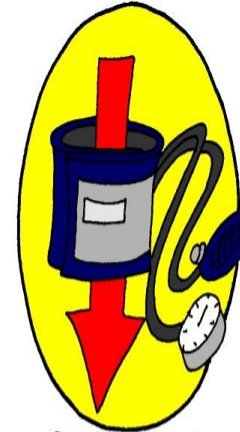
Bradycardia (AV-Block)



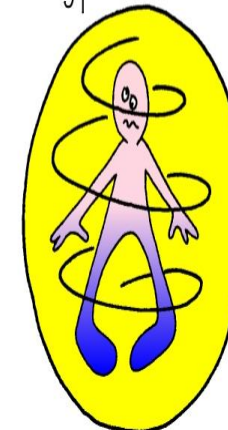
Drowsiness, Depression

SIDE EFFECTS OF ADRENERGIC ANTAGONISTS

α-BLOCKERS



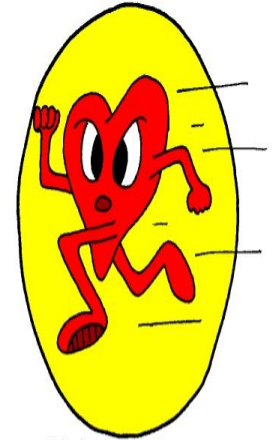
Orthostatic Hypotension



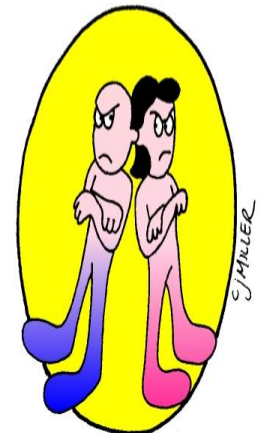
Vertigo

Examples:

- Doxazosin (Cardura)
- Clonidine (Catapres)
- Methyldopa (Aldomet)



Palpitations

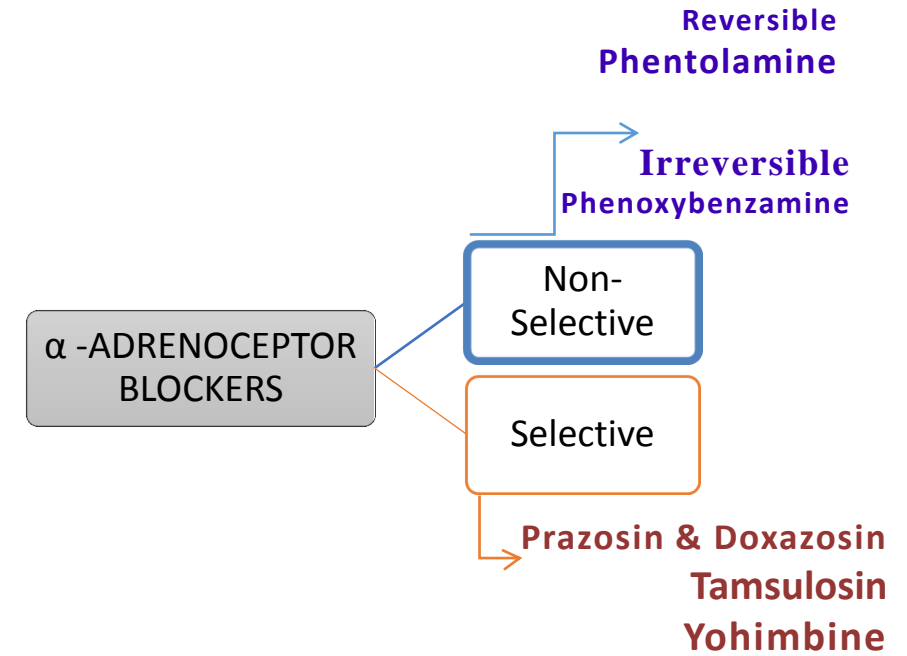


Sexual Dysfunction

SUMMARY

Drug	Type	Uses	Note
Methyldopa	Sympatholytic	Anti-hypertension in pregnancy	-False Transmitters of a-methyl tyrosine
Phenoxybenzamine	N.S, Irreversible, α_1 & α_2	In Irreversible shock *Before removal of Pheochromocytoma	-
Prazosin	S, Short acting, α_1	Raynaud's disease	nasal stuffiness, ↓ ejaculation & impotence
Tamsulosin	S, uroselective	Benign prostatic hypertrophy	-
Propranolol	N.S. B_1 & B_2	Arrhythmias Migraine Hyperthyroidism Anxiety Tremors	Has membrane stabilizing action Has sedative action
Timolol	N.S.	Chronic glaucoma migraine prophylaxis	-
Labetalol	N.S. b & α_1	Severe hypertension in pheochromocytoma hypertensive crisis	local anesthetic effect
Carvedilol	N.S. b & α_1	congestive heart failure	Has antioxidant
Atenolol	S. B_1	Hypertension Angina Pheochromocytoma myocardial infarction	Block $B_1 \gg B_2$ Hydrophilic Long T 1/2

S= Selective, S.N= Non selective :* to prevent hypertensive crisis



Propranolol Contraindications

Depressed myocardial functions [Uncompensated HF, Heart Block, Massive Myocardial Infarction.
 •Hypotension
 •Peripheral vascular disease (safer with cardio-selective β -blockers).

Hypotension
 Bronchial Asthma (safer with cardio-selective β -blockers).

Diabetic patients > (Type I) (specially on Insulin) for fear of hypoglycaemia

MCQs

1- Which of the following is a sympatholytic drug that depletes storage of the neurotransmitter :

- A) Methyldopa B) Gaunthidine
- c) Reserpine D) Non or above

2- A 50 year old woman has been taking a drug for her congestive heart failure condition. Few weeks later she notice some Edema in her foot. what most likely the drug is :

- A) Carvedilol B) Labetalol
- C) Propranolol D) Metoprolol

3- A 60 year old asthmatic man comes in for a checkup and complains that he is having some difficulty in "starting to urinate" physical examination indicates that the man has a blood pressure of 160\100 mm Hg , and slightly enlarged prostate . which of the following medications would be useful in treating both of these conditions :

- A) Tamsulosin B) Doxazosin
- C) Propranolol D) Phentolamine

4- A 29 pregnant woman has a mild hypertension condition started few weeks after pregnancy . what is the best drug for her case :

- A) Reserpin B) Phentolamine
- C) Methyldopa D) Parazosin

5- Ahmad is A 40 year old man has been diagnosed with Pheochromocytoma and his doctor prescribed hem a drug with only one does a day as Ahmad wants. Ahmad will continue using that drug until the day of his surgical procedure. what most likely the drug is:

- A) Phentolamine B) Phenoxybenzamine
- C) Parazosin D) Reserpine

6- Which of the following beta blockers has a ISA effect

- A) Propranolol B) Bisoprolol
- C) Timolol D) Labetalol

Answers : 1) C 2) A

- 3) B , we have two problems in this case 1- he has prostatic hypertrophy 2- he has high blood pressure if you chose a) Tamsulosin which is uroselective we only solve the first one so the best answer is b . We may also think of Propranolol but the patient is asthmatic .
- 4) C 5) B , you may think of Phentolamine but it is short acting because it is reversibly bindibg . and his does was once a day .
- 6) D

MCQs

7- Which one of the following is NOT a character of Propranolol :

- A) Lipophilic
- B) Non selective drug
- C) Has ISA effect
- D) Has local anesthetic effect

8- A 30 year old male has come to the ER with a sever asthmatic attack after taking antihypertensive drug . what is the drug he used :

- A) Prazosin
- B) Propranolol
- C) Doxazosin
- D) Reserpine

• 9- Which one of the following is uroselective ?

- A) Tamsulosin.
- B) Doxazosin.
- C) Prazosin.
- D) Phenoxybenzamine.

• 10- Which one of the following is used to treat Reynaud's disease

- A) Prazosin .
- B)Doxazosin.
- C) Timolol.
- D) A & B.

11- Patient with cardiac problems came to the clinic and he has asthma, which drug should the doctor give him ?

- A) Selective B1 Blockers.
- B) Non-Selective b Blockers.
- C) selective B2 Blockers.
- D) Non of above.

12- The interaction between Verapamil and Propranolol will lead to ?

- A) Bradycardia.
- B) heart block.
- c) tachycardia.
- d) A & B.

13- Patient has irreversible shock, what drug should we give him?

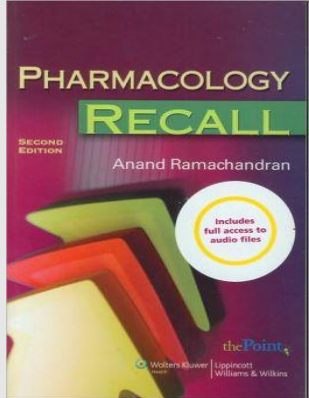
- A) Phenoxybenzamine
- B) Atenolol
- C) Labetalol
- D) Timolol

Answer:

- 7) C
- 8) B
- 9) A
- 10) D
- 11) A
- 12) D
- 13) A

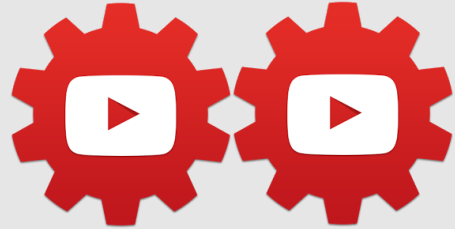
To make the Pharmacology easier:

- The Recall Pharmacology book:



- Helpful Youtube Chanel:
"hasan dahshan"

- For this lecture:



GOOD LUCK!

This Lecture was done by:

Fetoon Alnemari

Haneen Alkhanbashi

Rana aljunidel

Mada albatli

Lulu aldaej

Dania Raslan

Mashael Hussain

Sarah Aljasser

Ghadah aloudah

