

The Cardio-

VASCULAR

System

- Anatomy
- Histology
- Pathology
- Pharmacology
- Physiology
- Microbiology

Lec #: 1

Dr. Name: **Malik Zihlif**

Done By: **Rakan Radi**

- Handout
- Sheet
- Slide

Drawn by Tarig Bushnaq





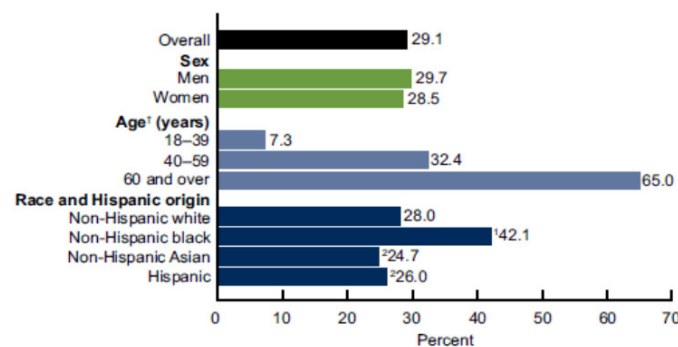
ANTIHYPERTENSIVE THERAPY

Al Salam Aleikom,

This subject is the core of the cardiovascular system as it's one of the most common issues nowadays; keeping in mind the CVDs are the main cause of death in Jordan. Hypertension in particular is common in the Jordanian population and also worldwide. The main aim of the drugs we are going to learn in today's lecture is to control hypertension (blood pressure) in one mechanism or another. Note that the drugs mainly control hypertension rather than stop its high incidence. Hypertension is known as the silent killer as it is asymptomatic which makes it hard to diagnose and due to facing an issue with compliance which means to convince the patient to stick to the drug and take it regularly. In houses you will find many extra boxes of antihypertensive drugs because patients don't take it unless they feel like taking it. Hypertension if not treated would lead to many more serious diseases such as congestive heart failure, myocardial infarction, renal damage and cerebrovascular accidents. So hypertension would not actually kill you as it is asymptomatic but its morbidity and mortality are due to end organ damage.

P.S. Slides 1-15 are fully covered in this sheet, no need to refer to them.

Prevalence:



Three things to be learnt from the figure above:

- Hypertension is *not a gender-related* disease, as its incidence in men is equal to that in women.
- Hypertension is *highly age-related*; as elderly (geriatrics) who are of **age 60** or older are more likely to develop it and also they are more prone to develop the aforementioned complications.
- Hypertension is *race-related*, as non Hispanic black has a higher incidence due to genetics, so they are going to need other special type of drugs.



Joint National Committee (JNC)

Joint National Committee, JNC, is a national committee which put the guidelines to treat hypertension which are renewed every 2-3 years; you need to keep updated with their latest recommendations. JNC 8 recommendations:

- In patients ≥ 60 years of age, start medications at blood pressure of $\geq 150/90$ mm Hg and treat to goal of $< 150/90$ mm Hg
- In patients < 60 years of age, start medications at blood pressure of $\geq 140/90$ mm Hg and treat to goal of $\leq 140/90$ mm Hg
- In all adult patients (despite the age) with diabetes or chronic kidney disease, start medications at blood pressure of $\geq 140/90$ mm Hg and treat to goal of $< 140/90$ mm Hg

The Case	When to start the treatment (BP)
Patients ≥ 60 years of age (NO diabetes or chronic kidney disease)	$\geq 150/90$ mm Hg
Patients < 60 years	$\geq 140/90$ mm Hg
Patients with diabetes or chronic kidney disease (regardless the age)	$\geq 140/90$ mm

Lifestyle Modifications

Remember the golden rule: Don't consider pill for every ill? So before starting the medication, we can modify the patient's lifestyle first, summarized in the next table are the modifications one can do and to which extent it could reduce the pressure:

Lifestyle Modification

Modification	Approximate SBP Reduction (range)
Weight reduction	5-20 mmHg/ 10 kg weight loss
Adopt DASH eating plan	8-14 mmHg
Dietary sodium reduction	2-8 mmHg
Physical activity	4-9 mmHg
Moderation of alcohol consumption.	2-4 mmHg



- DASH is a carbohydrates-low, protein-low diet which mainly focuses on eating fibers.
- Stiffness of the blood vessels is mainly due to calcium and sodium, so reducing sodium intake will reduce stiffness, and increased blood pressure is a stiffness problem thus reducing sodium intake will affect the blood pressure and reduce it by 2-8 mmHg.
- The doctor believes that there is no such thing as a moderate consumption of alcohol, as everyone has their own perception in deciding what's mild, moderate and heavy drinking. So, you either drink or don't.

Mechanisms controlling CO and TPR

1. Neural control: through the ANS by sympathetic and parasympathetic regulation. By affecting *baroreceptors* which affect the moment to moment control of blood pressure. When baroreceptors get activated they stimulate the release of adrenaline and noradrenalin, which in return would bind to β_1 receptors increasing the cardiac output, or α_1 receptors leading to vasoconstriction.
2. Hormonal control: for long term control. Mainly by the kidneys through controlling the blood volume by rennin-angiotensin-aldosterone system. Keep in mind that this system gets activated when you suffer from blood pressure issues for a long term rather than moment to moment alteration.
3. Local mediators: work locally on the blood vessels, like nitric oxide, bradykinin. So drugs are going to mimic one of these mechanisms to help in controlling the blood pressure.

Drugs Targets and General Effects

- I. **Vasomotor center:** α_2 receptors would inhibit the release of noradrenalin, works on feedback inhibition which would reduce the sympathetic outflow. So we give α_2 agonists as antihypertensive drugs. Example on this type: Methyldopa (best choice in case of pregnancy) and Clonidine (best choice in case of renal failure).
- II. **Sympathetic nerve terminals:** these drugs would deplete the adrenaline and noradrenalin. E.g.: Guanethidine and Reserpine (not used any more)
- III. **β receptors of the heart:** we give β blockers (end with suffix -lol)
- IV. **α receptors of vessels:** we give α_1 antagonists, so vasodilation would occur. E.g. Prazosin.
- V. **Kidneys:** for the long term control
 1. Kidney tubules: increase the excretion of water by giving a drug inducing diuresis (i.e. giving a diuretic) thus reducing the blood volume. E.g. Thiazide (a very popular drug used in hypertension).

2. Angiotensin Converting Enzyme inhibitors (ACE I); inhibits the synthesis of Angiotensin II which is the strongest vasoconstrictor in the body.
3. Angiotensin II receptor blockers on the vessels.
4. Renin inhibitors: Aliskiren.

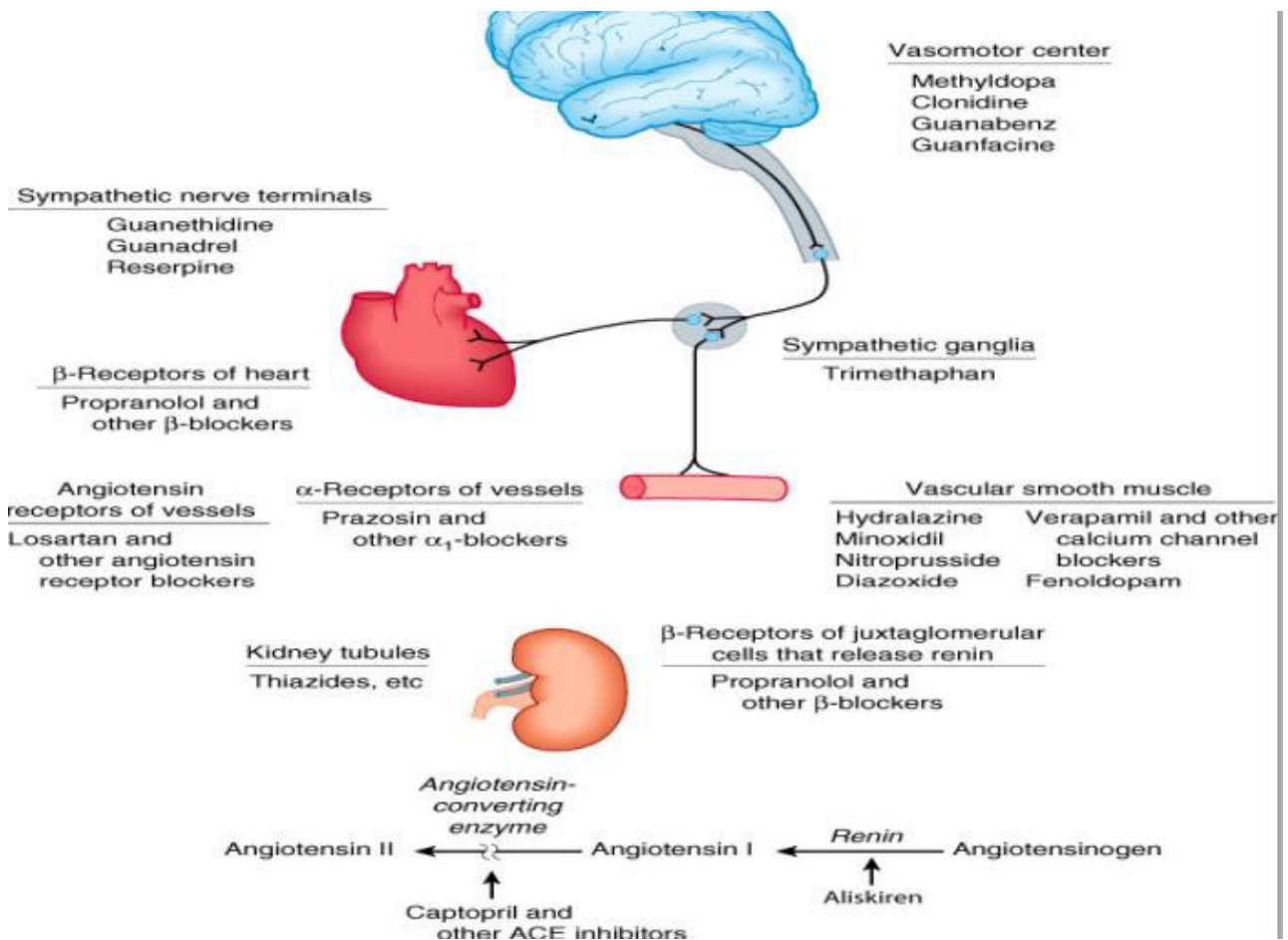
VI. Local mediators:

- # Ca channel blockers: reduce the action potential thus causing vasodilation
- # Increase NO: causing vasodilation
- # Potassium channel modulators: by manipulating the concentration of potassium around the membrane. (The doctor said that he would clarify this in the upcoming lectures.)

So in total we have 11 groups: 4 sympathetic, 4 kidney related and 3 local mediators

The doctor said that these points are really important and he explained them regarding this slide, I am not sure whether we need to know the names of the drugs which are mentioned in the slide and not mentioned before. But here is the slide just in case

اللهم صل على محمد وآل محمد

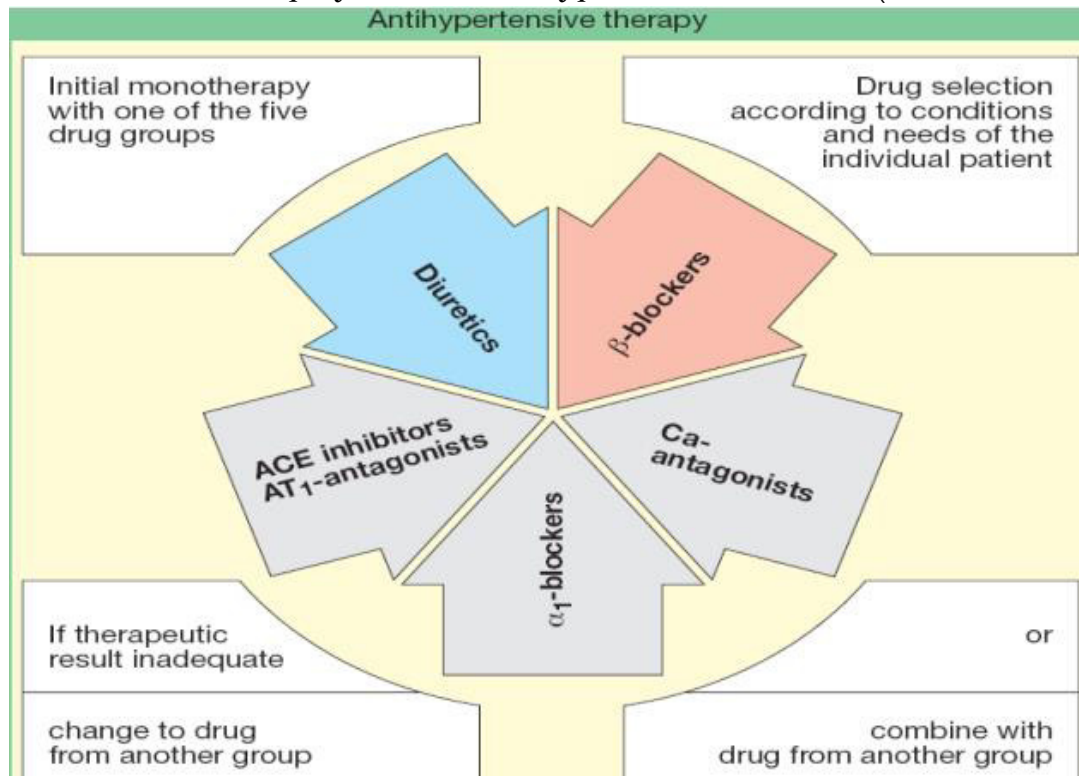




Which drug to whom?

JNC 6 settled on starting with B Blockers or Diuretics as a first line treatment but in JNC 8 they decided that B Blockers is not that great of a drug to be used as a first line treatment.

We have five main players used for hypertension control: (in the arrows)



Note that with ACEIs we use angiotensin receptor blocking agents (known as ARBs)

Keep in mind the Thiazide is a very good diuretic.

These drugs have different *efficacies* (i.e. different maximal effect), so based on the case we choose a specific one.

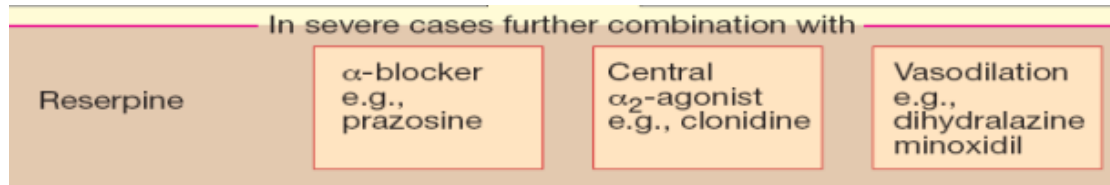
- **Diuretics** have **low efficacy**, they reduce the blood pressure by only 10-15 mmHg
- **ACEIs** have **moderate efficacy**; 25-30 mmHg
- **Ca channel blockers** have a **high efficacy** of 40 mmHg, regarding that the highest reduction in blood pressure an orally taken anti-hypertensive drug can cause is 40 mmHg.

So in case my patient's BP is 180/110, you should not use a diuretic alone, as we need to reduce it to 140/90 or 150/90 (remember the standards we clarified at the beginning of the lecture based on the age). ACEIs would be good if your patient is above 60, while if your patient is younger than 60, you should use Ca channel blockers due to having the highest efficacy. (exam question pattern)



If your patient's BP is 210/140, you should use combination therapy in order to have an additive (synergism) effect.

If your patient has a severe hypertension or not responding to any of the previous drugs, we use:



- Monotherapy of hypertension (treatment with a single drug) is desirable because compliance is likely to be better and cost is lower, and because in some cases adverse effects are fewer.
 - However, most patients with hypertension require two or more drugs, preferably acting by different mechanisms (polypharmacy).
- ⇒ Statistics show that:
- 82% of the patients in the U.S. are aware of hypertension and they know that it has end organ damage and thus must be controlled.
 - Treatment reaches 76% (so 95% of the patients who are aware will be treated)
 - Only 50% of the people in the U.S. suffering from hypertension are under actual control. The doctor believes that in Jordan, it would barely reach 35% due to the lack of compliance, as patients tend to stop taking the drug once they feel better without counseling the doctor.

What to choose first?

Initial antihypertensive therapy without compelling indications

- JNC 6: Diuretic or a beta-blocker
- JNC 7: Thiazide-type diuretics
- Most outcome trials base antihypertensive therapy on Thiazides
- JNC 8:
 - For the non-black population (including diabetes), initial antihypertensive treatment may include a Thiazide, ACEI, ARB, or CCB. (But also don't forget to take the efficacy in consideration).
 - For the black population (including diabetes), initial antihypertensive treatment should include a Thiazide or CCB. (So we conclude that "the black population" do not respond to ACEI and ARBs).



- For all patients with Chronic Kidney Disease (CKD); initial (or add-on) therapy for hypertension should include an ACEI or ARB (even for “the black population”).

So we conclude that ACEIs are a must for every patient with kidney problems regardless of their ethnicity.

The Patient	Initial Treatment
Non-black population	Thiazide, ACEI, ARB, or CCB
Black population	Thiazide or CCB
Chronic Kidney Disease (CKD)	Thiazide, ACEI, ARB, or CCB

Thiazide diuretic is the only diuretics used in hypertension treatment, as it reduces sodium absorption and increase water excretion. It will be further discussed in the next lecture.

*A random piece of info which I didn't know where to put:

Pharmacotherapy is to know when to use a drug and to which patient it should be given “it's something related to personalized medicine”.

Dedicated to Anasweh.

"ابدأ رحلة يقينك بثورة على النفس"