

التغريخ من ريكوردات د. انعام
+ أغلب ملاحظات د. نجانين

* احفظوا الـ جنتهارات
لانه الدكتور بـتجيب منكم
بالأ سئلة

Pharmacotherapy 1

Hypertension

HTN

لـ أنا لحنـت الـتبه HPT منوها 😊

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رب اسر في صري
ويسري امرى واحلل
عفة من لسانى يفقه قولى

الجامعة الهاشمية

The Hashemite University



Topic outline:

- ✓ Definition
- ✓ Epidemiology
- ✓ Etiology
- ✓ Pathophysiology
- ✓ Clinical Presentation ⇒ Selection بتعدنا نضل
- ✓ Diagnostic Considerations
- ✓ Treatment - Goals of Therapy
- ✓ Non-pharmacologic Therapy
- ✓ Pharmacotherapy
- ✓ Individual Antihypertensive Agents
- ✓ Compelling Indications *other condition مع HTN لما يكون في*
- ✓ Special Populations (*face, pregnant, older,*)
- ✓ Team-Based Collaborative Care (*الدكتورة شالغنا*)
- ✓ Monitoring the Pharmacotherapy Plan
- ✓ Resistant Hypertension
- ✓ Hypertensive Urgencies and Emergencies

إذا مره كان طبيبي ومره كان عالي
هي مره ما قبل ال HTN

بشكلها *elevated BP* ولا ترمى يوصل يوصل
عزادات

دائماً ، مش لزوج طبيعي ، على طول مرتفع

الضغط مرتفع بال Artery مش بال Vine

Hypertension (HTN): sustained elevation of arterial blood pressure (BP)

عالي واه أرقام

✓ One of the most significant risk factors for cardiovascular (CV) disease. ← من الأهم
→ (MI, dyslipidemia, Stroke)

Healthy شخصين
بوجود القراءة بعد عمر ال 18

✓ Screening, early detection, and control of hypertension → decreased risk of stroke الجلالة على الدماغ
myocardial infarction (MI), and heart failure (HF)

Acute Coronary Syndrome (ACS) → Unstable Angina
يشتمل على القلب minor Stroke

✓ But in Jordan, preventive and interventional programs are limited and not well structured and organized with shortage of recent data on HTN prevalence, awareness, control, and its risk factors

الدراسات عن الأردن محدودة
Role تبصنا

Problem → systolic
→ Diastolic

Risk Factors بتختلف من مكان لكان
ال guideline عالمية
لوعملت دراسات محلية بتساعدني اعظم
ال population التي عندي

➤ Epidemiology

الانتشار

Prevalence:

من كل ٣ افراد في واحد عنده #HTN

- ✓ Almost one-third of Jordanian adults have hypertension (33.8% among men and 29.4% among women-2017 study)
- ✓ An overall estimated prevalence of hypertension in adults in Arab countries is 29.5%.
- ✓ An overall worldwide hypertension prevalence of 26% in the adult population

Awareness rate: كم وعي الناس عن #HTN

- ✓ 57.7% of men and 62.5% of women are aware of hypertension in Jordan (2017 study, was 39.8% and 51.8%, respectively, in 2009)
- ✓ varied from 18% to 79.8% with an overall rate of 46% in Arab countries
- ✓ 25 to 75% worldwide (almost half to two-thirds of patients in developed countries)

النسب واحة

➤ Epidemiology

الناس عندها HTN

ليس Controlled

Controlled HTN:

ارتفعت

الضغط

تقريبًا

- ✓ Almost one-third (30.7% of men and 35.1% of women) of Jordanian adults on antihypertensive medications (% were 17.4% and 18.6%, respectively, in 2009) - possible reasons for the poor HTN control in Jordan:

- ✓ inadequate management of hypertension,
- ✓ not using evidence-based practices, and
- ✓ poor adherence to medication.

- ✓ Patients in Jordan aged ≥ 50 years were more likely to have hypertension, to be aware of the disease and to have better control compared to younger patients.

بكونوا حايضين على

- ✓ In Arab countries: 8% to 44%.

حالههم وعندهم مشاكل أخرى كمان + اقل انشغال بحياتهم

- ✓ The low control rate was also seen in USA and European countries.

➤ Epidemiology

Complications:

- ✓ The complications of hypertension account for 9.4 million deaths worldwide/yr
- ✓ It is estimated that up to 1.58 billion adults will suffer from complications of hypertension by 2025, worldwide.
- ✓ Approximately one in three adult (age 20 years or older) Americans have elevated BP.
- ✓ Among hypertensive patients, 54.1% are at their goal BP, 76.5% are treated, and 82.7% are aware they have hypertension.
- ✓ The overall incidence is similar between men and women.

↳ American Statistics

Table 1: Number of deaths from selected causes by age groups: Jordan MoH, 2009

Cause of death	اسباب الوفاة	الجنس	Under 1 year	1-4 years	5-14 years	15-24 years	25-44 years	45-64 years	65 years and over	Not stated	Total
Diseases of the circulatory system (I00-I99)		هذا ارقام الوفايات	5	12	8	25	231	1343	3675	19	5318
Acute rheumatic fever and chronic rheumatic heart diseases (I00-I09)			0	0	0						
Hypertensive diseases (I10-I15)			0	1	1						
Ischaemic heart diseases (I20-I25)			2	0	1						
Acute myocardial infarction (I21-I22)			1	0	1						
Other ischaemic heart diseases (I20,I23-I25)			1	0	0						
Pulmonary heart disease and disease of pulmonary circulation (I26-I28)			0	0	0						
Heart failure (I50)			2	7	2						
Other forms of heart disease (I30-I49,I51)			1	3	0						
Cerebrovascular diseases (I60-I69)			0	1	3						
Atherosclerosis (I70)			0	0	0						
Aortic aneurysm and dissection and other aneurysms (I71-I72)			0	0	0						31
Other diseases of the circulatory system (I73-I99)			0	0	1				15	0	28

Controlled HTN ⇒ العرین معده
 HTN لكن قراءات منخفضة
 بتكون على Target
 وامترب لا Normal

ان Target Range هو جودين
 بعدين وواج نحللهم

نسبة عالية
 ↓
 هورا بسبب
 HTN

لما نعرف المسبب يمكننا نعرف Target العلاج

Therapeutic Expectation

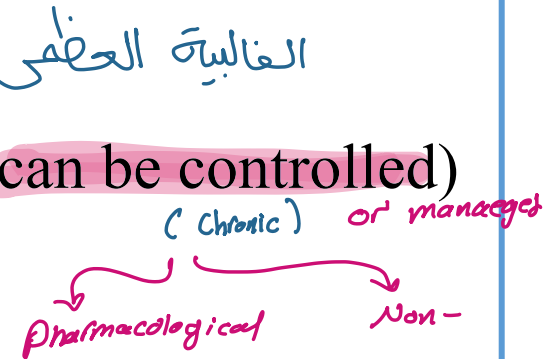
Etiology

السبب غير معروف
Genetic & environmental

Essential (or primary) HTN

- Over 90% of individuals with high BP have essential HTN Primary الغالبية العظمى عندهم
- HTN results from unknown pathophysiologic etiology (cannot be cured, can be controlled)
- Genetic factors may play a role in the development of essential HTN

RAAS → أي خلل فيه يعني خلل BP يرتفع
 Sympathetic → Catechol amine (NE, epinephrine)
 Para-sympathetic



Secondary HTN

كان في سبب HTN

- Less than 10% of patients - either a comorbid disease or a drug (or other product) is responsible for elevating BP (Table 2)
- Patients have a specific cause of their HTN → can be cured
- Removing the offending agent (when feasible) or treating/correcting the underlying comorbid condition should be the first step in management

Hyperthyroidism NSAIDs

لو السبب صعب نشيلها ما بتعالج

لو مثلنا المسبب بنزل الفعول

ليس مش بكل الحالات

ازالة المسبب

Table 33-1: Secondary causes of hypertension

1 Diseases

Chronic kidney disease, Cushing's syndrome, Coarctation of the aorta, Obstructive sleep apnea, Parathyroid disease, Pheochromocytoma, Primary aldosteronism, Renovascular disease, Thyroid disease

Handwritten notes: \uparrow Cortisol \uparrow (pointing to Cushing's syndrome), Surgical in infant (pointing to Coarctation of the aorta), Hypertension (بأدوا البعوض) (pointing to Chronic kidney disease), hormonal problem (pointing to Thyroid disease)

2 Drugs associated with hypertension

(For some patients, the addition of these agents can be the cause of elevated BP or can exacerbate underlying hypertension. Identifying a temporal relationship between starting the suspected agent and developing elevated BP is most suggestive of drug-induced BP elevation).

Handwritten notes: علاقة زمنية (temporal relationship), قبل الدواء كان الضغط الطبيعي (before the drug, the pressure was normal), بعده ارتفع (after it, it increased), لوقتنا الدواء يرجع الضغط طبيعي (at our time, the drug returns the pressure to normal), مش Confirmative (not confirmative), ما قطعنا الضغط بالتحسين (we didn't cut the pressure with improvement)

Amphetamines, Corticosteroids (cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone, triamcinolone), Calcineurin inhibitors (cyclosporine, tacrolimus), Decongestants (pseudoephedrine, phenylephrine), Ergot alkaloids (bromocriptine, dihydroergotamine, methysergide), Erythropoiesis-stimulating agents (erythropoietin, darbepoetin), Estrogen-containing oral contraceptives, Nonsteroidal anti-inflammatory drugs-cyclooxygenase-2 selective (celecoxib) and nonselective, Others: desvenlafaxine, venlafaxine, bupropion

Handwritten notes: systemic (pointing to Amphetamines), organ transplantation Drug (pointing to Calcineurin inhibitors), Use for 5 Days (pointing to Decongestants), Systemic (pointing to Ergot alkaloids), Chronic kidney disease (pointing to Erythropoiesis-stimulating agents), لعلاج الأنيميا (for anemia) (pointing to Erythropoiesis-stimulating agents)

Table 2: Secondary causes of hypertension

Situations related to drug use

β-blocker or centrally acting α-agonists (when abruptly discontinued), β-blocker without α-blocker first when treating pheochromocytoma) use of a monoamine oxidase inhibitor (isocarboxazid, phenelzine, tranylcypromine) with tyramine-containing foods or certain drugs

Clonidine → Up Regulation → Rebound HTN

→ Anti-depressant

* لمتخلنا بـ لمتخلنا بـ
 الامور تمام هيك
 B-Blocker ← α₁-Blocker
 لو عكسنا
 ترتيب الادوية مع حسب طبية
 Receptors
 بدخل بـ
 Hypertension Crises
 ا؟ فكونا منها

Street drugs and other products

Cocaine and cocaine withdrawal, Ephedra alkaloids, Nicotine and withdrawal, anabolic steroids, narcotic withdrawal, ergot-containing herbal products, St. John's wort

"illegal"

Food substances

Sodium, Ethanol, Licorice

➤ Pathophysiology

Arterial BP

- ✓ Arterial BP is the pressure in the arterial wall measured in mm Hg.
- ✓ Two arterial BP values: systolic BP (SBP) and diastolic BP (DBP)
- ✓ SBP represents the peak value, which is achieved during cardiac contraction. *left Ventricular Contraction*
- ✓ DBP is achieved after contraction when the cardiac chambers are filling, and represents the minimum value. *↳ When Ventricular are filling (Relax)*
- ✓ Mean arterial pressure (MAP) is the average pressure throughout the cardiac cycle of contraction. It is sometimes used clinically to represent overall arterial BP, especially in hypertensive emergency. *2/3 ⇒ Diastole 1/3 ⇒ Systole وقت cycle or one systole contraction one Diastole Relaxation*
- ✓ During a cardiac cycle, two-thirds of the time is spent in diastole and one third in systole.

Therefore, the MAP is calculated by using the following equation:

$$\text{MAP} = (\text{SBP} \times 1/3) + (\text{DBP} \times 2/3)$$

*Monitoring Parameter in HTN crises
بمعلوما ICU ولازم التدخل يكون سريع*

*emergency بحالات ال
بمعتني Systolic اكثر من Diastolic*

- ✓ Arterial BP is mathematically defined as the product of cardiac output (CO) and total peripheral resistance (TPR) according to the following equation:

$$BP = CO \times TPR$$

- ✓ CO is the major determinant of SBP, whereas TPR largely determines DBP.
- ✓ **CO** is a function of stroke volume, heart rate (HR), and venous capacitance.
- ✓ An increase in CO normally results in a **compensatory decrease** in TPR; likewise, an increase in TPR results in a decrease in CO.

SV: Volume of Blood ejected from left ventricle in one contraction

Venous Return تصيلها

أي درجة Vine يكون مطوية وتوصل الدم إلى درجة Vine يكون مطوية وتوصل الدم إلى درجة Vine يكون مطوية وتوصل الدم

SV ↑ → CO ↑
HR ↑ → CO ↑

بحالة السيام

$$CO = \text{Stroke Volume} \times \text{HR}$$

$$\frac{V}{\text{Beat}} * \frac{\text{Beat}}{\text{min}} = V/\text{min}$$

Venous Capacitance ↑ → CO ↓

SV ↓
CO ↓
TPR ↑

Normal BP

Systolic ← CO ↑
Diastolic ← TPR ↑ → BP ↑

كل ما القلب عمل Filling أكثر
يكون SV أكبر ← CO ↑
أو Veines هي التي يرجع الدم على
القلب صح؟! فهي لازم تعمل
Contraction

Vain Relaxation يعني كانه في
Venous return ↓ يعني
CO ↓
↑ Capacitance بحالة ال

Activation of CVS

↓

Brain Stem → ↑ catechol amines → B-Receptor
 "Stimulation the heart"

↳ B₁-Receptors

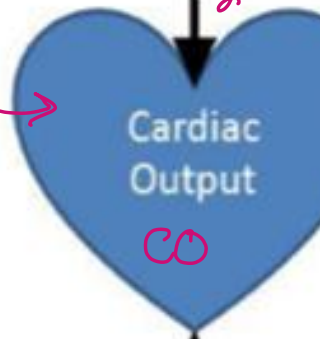
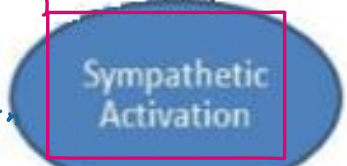
↳ ↑ HR, ↑ Contractility

⇒ B₁-Blockers

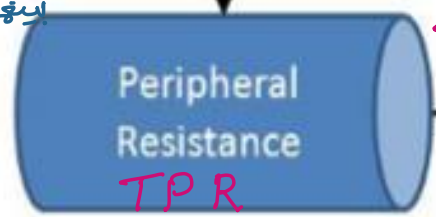
↳ ↓ HR, ↓ Contract
 (-ve) inotropic
 (-ve) Chronotropic



(Stroke + Plasma) Volume
 HR, Contractility



في حالة Compensacion
 اي نوع اذا بلع واحد بخل
 الثاني
 عشان BP يظل
 Normal



Construction
 Aging (↑ stiffness)

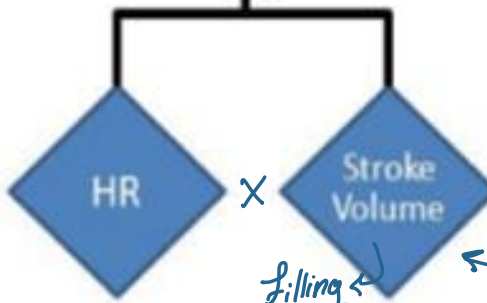
TPR
 جاي من Vessels نضيق
 عندهم ابي اسه
 Vascular tone

↳ α₁-Receptors "peripheral"

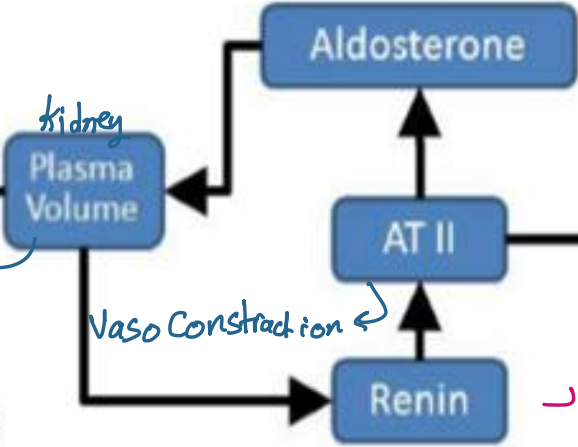
↳ Vaso construction

⇒ α₁-Blockers

↳ Vaso dilation



Relaxation ← بعلية ال
 Volume ← Filling



↑ Vaso construction
 ↑ Pressure

← من Angiotensin 2
 لما يزيد لانه RAA فيه
 مشكلة بتراكم

← elasticity ?!

← عن Vaso dilater's بقولوا ال
 TPR

يعني BP يتحكم فيه شغلين

① Hormonal Regulation

② Neuronal Regulation

Adapted from APhA's Completed Review for Pharmacy. Gourley, DR. 2004

HTN ↓, Heart protective, Nephro protective
 1st Line

← ACEIs / CCBs / α₁ Inhibitors / Nitrates
 High Risk of Hypotension ← Artery

Long term Chronic & Sustained

Hormonal Regulation

Renin-angiotensin system

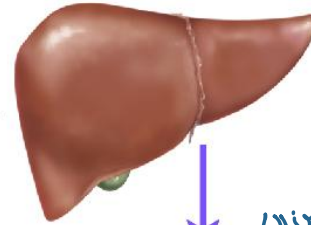
Trigger for the Kidney

Drop in blood pressure
Drop in fluid volume

RAAS

Renal Perfusion ↓
Volume Depletion

liver

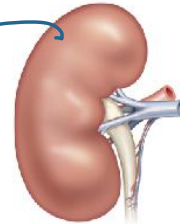


Juxtaglomerular Cell

Renin release from kidney

angiotensinogen

Renin



↳ Sensor NaCl for GFR

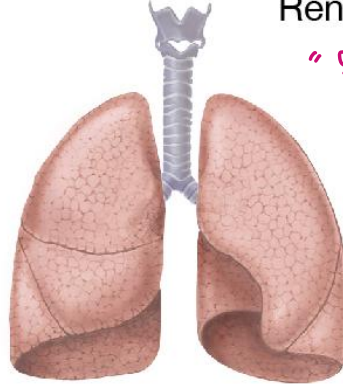
Renin acts on angiotensinogen to form **angiotensin I.**

يكون بالدم بينه الكبد ما يعمل اشي

No effect

ACE (angiotensin-converting enzyme) release from lungs

ACEI



ACEI في انجيوتنسين 1 بيبي من Tissues ما يثروا عليه

ACE acts on angiotensin I to form **angiotensin II.**

"Vasopressor"

ARBs

ARBs

Angiotensin II acts on the adrenal gland to stimulate release of **aldosterone.**

Cortex



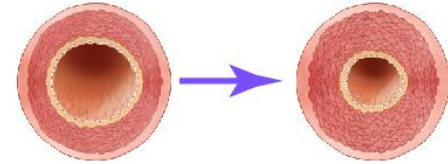
Aldosterone Antagonist

Aldosterone acts on the kidneys to stimulate reabsorption of salt (NaCl) and water (H₂O).

Na & H₂O Retention

لوارتفع كثرى بعمل Cardiac Fibrosis

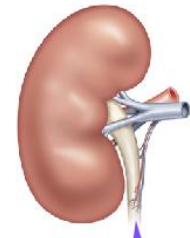
الأوعية مكان عملها



Angiotensin II also acts directly on blood vessels, stimulating vasoconstriction (narrowing).

TPR ↑

Centrally Rapid Response



NaCl H₂O

Renial B₁ Receptors يزيد افراز ال Renial
B₁ Receptors في
First line agent
B-Blocker
بكون على

لو ال RAAS مش
تعال مزيج ؟
↳ Volume depletion
↳ Vasoconstriction
↳ ↑ Aldosterone
↳ Heart Remodeling

Neuronal Regulation

في 2 Baro Receptors

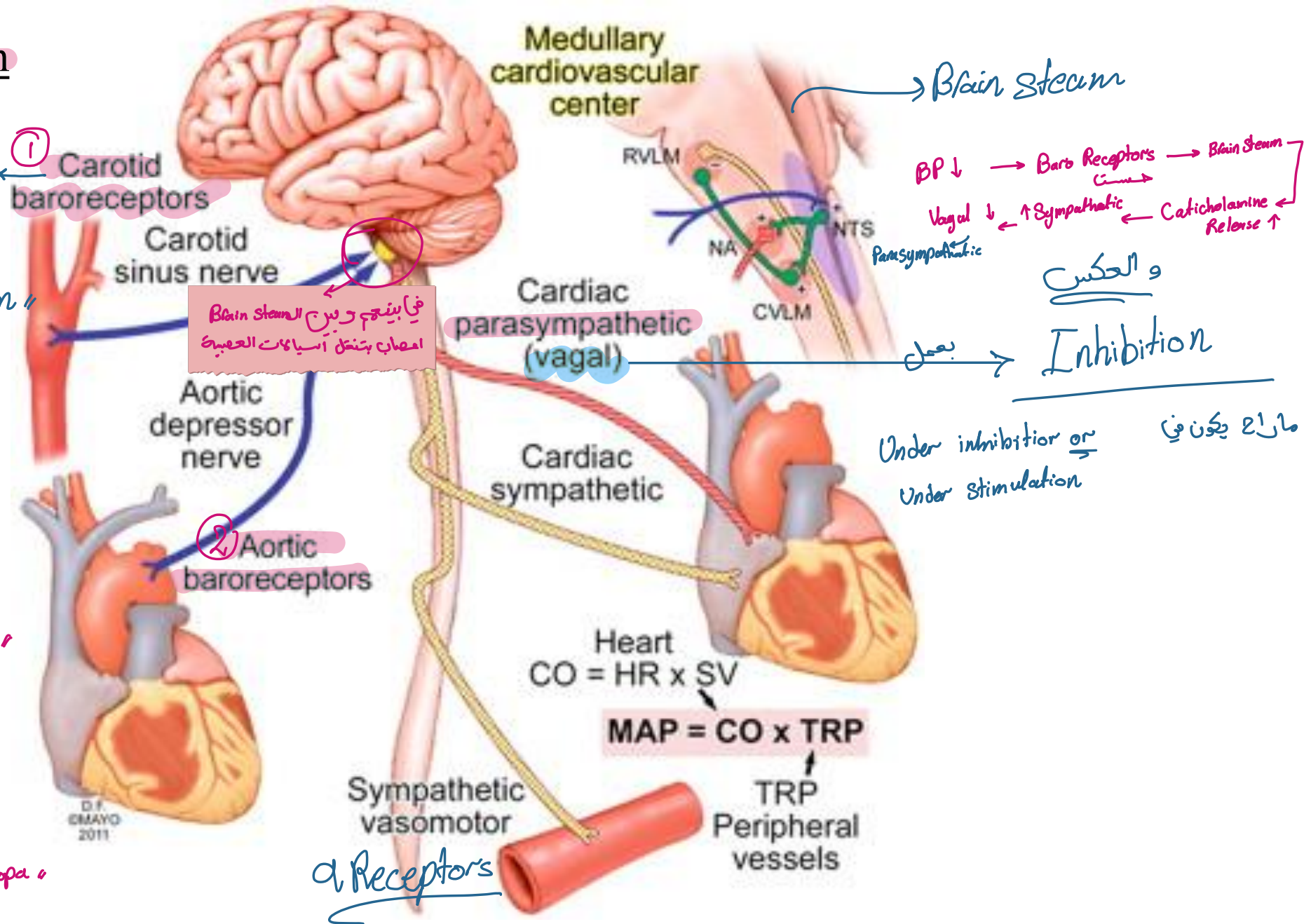
وجود Carotid Arteris التي بالقرب من اتجاه الدماغ

Baro Receptors Reflex

- Compensatory "Short Term"
- +ve feedback

α_1 - Receptors Post synaptic
 Blocking بعلو "Doxazosin"
 antagonist
 Centrally acting agent → Rapid
 Acute بعلو بحالات ال

α_2 - Receptors Presynaptic
 Activation بعلو "Clonidine, Methyl dopa"
 agonist



BP ↓ → Baro Receptors → Brain stem
 Vagal ↓ ↑ Sympathetic ← Catecholamine Release ↑

العكس و Inhibition
 Under inhibition or Under stimulation
 ما زال يكون في

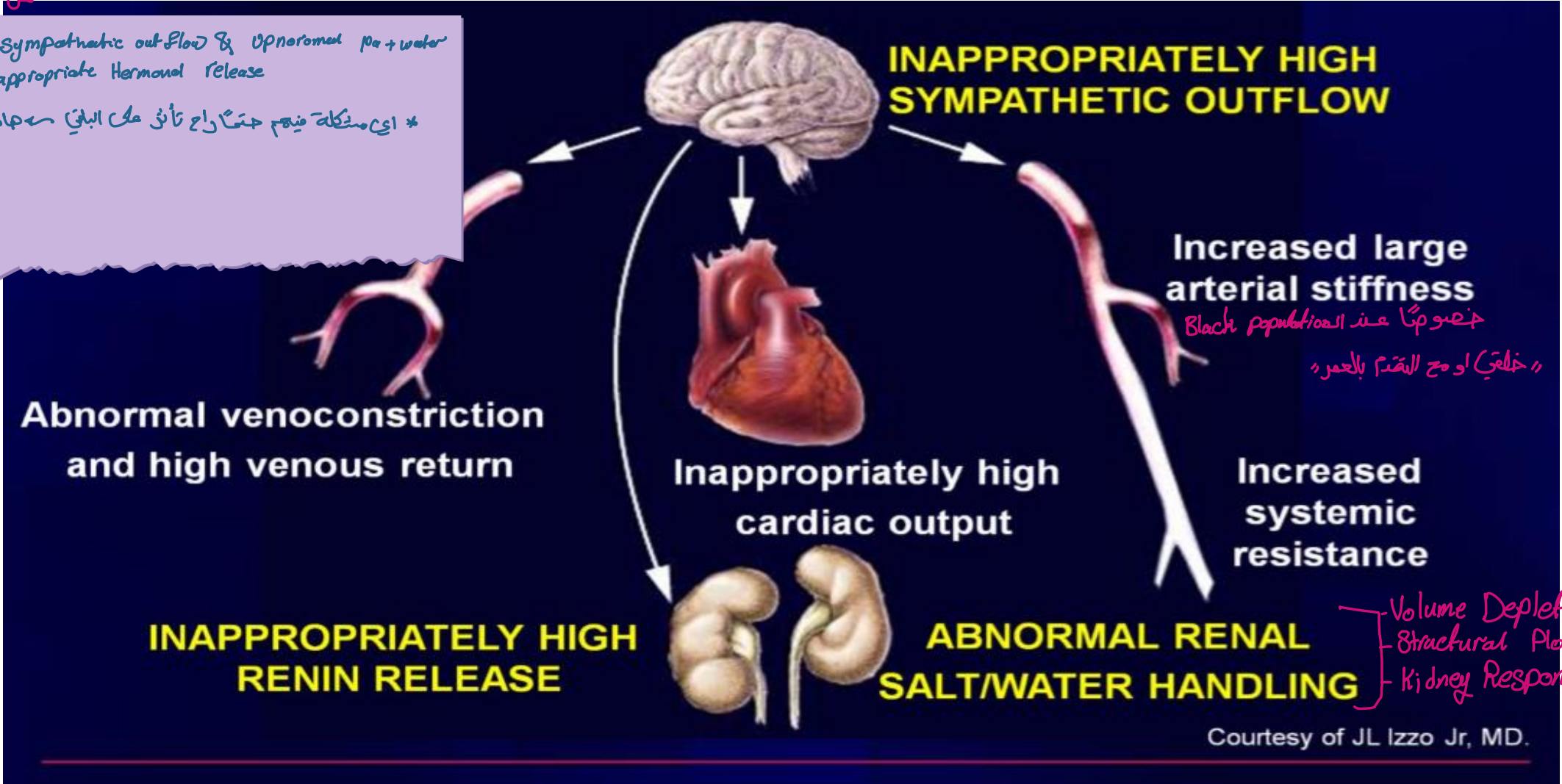
α Receptors

كل مرلينا
حالته
تختلف
من الأخرى

Different systems are physiologically interrelated. A defect in one component (pathologic disturbances) may alter normal function in another. Therefore, cumulative abnormalities may explain the development of essential hypertension.

عشان هيلبس في أكثر من Subclassه لاجابه

inappropriate sympathetic outflow & upnormal Na+ water Retention + inappropriate hormonal release
* اي مشكلة فيهم جتا راج تأني على البني سجاد ابي يبي في
Primary HTP



➤ Clinical Presentation

General: may appear healthy or may have additional CV risk factors:

- Age (greater than or equal to 55 years for men, greater than or equal to 65 years for women)
- Diabetes (type 1 or type 2)
- Dyslipidemia
- Albuminuria
- Family history of premature CV disease
- Overweight (BMI 25-29.9 kg/m²) or Obesity (BMI ≥30 kg/m²)
- Physical inactivity
- Tobacco use

Symptoms: usually none related to elevated BP.

Signs: previously elevated BP values.

- يتساءل عن أهله إذا جدا منهم باربعه CVD events
 على عمر شخصي (قبل 55 → H, 65 → F)

First degree → (الأم الأب الأولاد والأخوة)

Relative

Silent Killer → Screening
 مشان هيك

TIA, Unstable Angina, Events → الجلطات
 إذا حيا عمل قسطرة Revascularization ركب شبكية قلب شرايين Atherosclerotic

الوزن
 الطول²

Modifiable

أعراض مثل :- (Nausea, Headache) ما ينربطها عادة مع HTN

Why kidney function test is important

- HTN → Silent Disease
 HTN associated complications
- Already Have kidney problem → Cause the HTN 2^o Cause
 exclusion any Secondary Causes
- The baseline (مشان اعرف إذا اللها بأقوى الكلى إيجابياً أو سلبياً)
 Monitoring of therapy

→ Kidney function test → other CV Risk factor → DM

Routine laboratory tests: BUN, serum creatinine, fasting lipid panel, fasting blood glucose, serum electrolytes (sodium, potassium), hemoglobin and hematocrit, and spot urine albumin-to-creatinine ratio.

+ CBC :- لو كان عنده انيميا بعد Load على القلب
 BVC/3 = Hemoglobin → لو ما عالجت ممكن HF تعمل
 Risk factor عندك كمن Risk factor ← به ياخذ Aspirin
 Anti-Platelet
 Albuminuria 8- 1° line (ACE or ARBs)

May have normal values and still have hypertension.

Abnormal values consistent with either additional CV risk factors or hypertension-related damage.

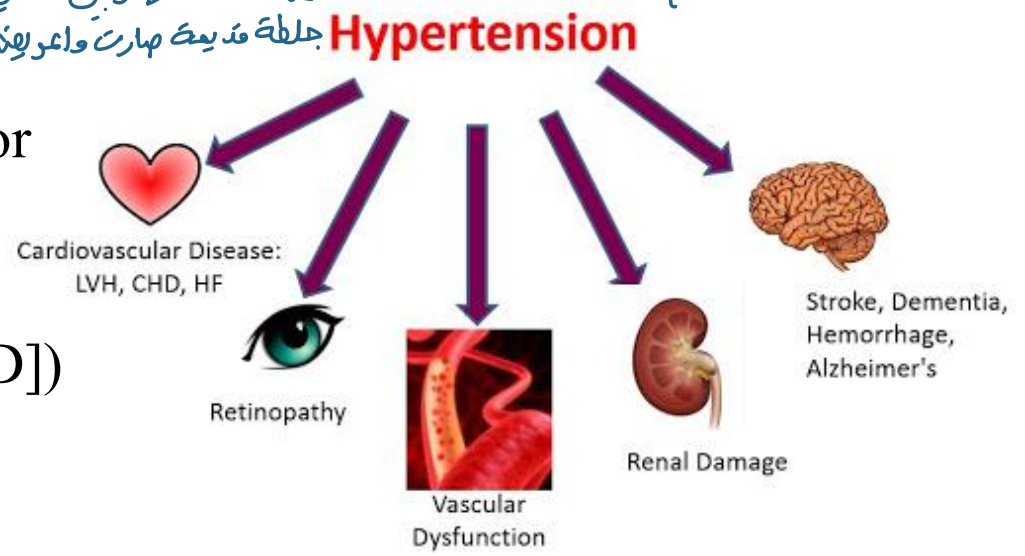
"Complication"

→ المريض هو بحكيه

Hypertension-related complications: (PMH or diagnostic findings)

Irreversible Control على الـ ضغط
 الدكتور المستشفى
 عمل ECG وبين انه في جلطة قديمه هارت واعرفه ما حسن فيني

- Brain (stroke, transient ischemic attack, dementia) "TIA"
- Eyes (retinopathy) ممكن المريض بوحد دوا ما يمشي بس ضغطه مش Controlled
- Heart [left ventricular hypertrophy [LVH], angina, prior MI, prior coronary revascularization, HF) → Stent مركب
- Kidney (chronic kidney disease [CKD])
- Peripheral vasculature (peripheral arterial disease [PAD])



➤ Diagnostic considerations

- ✓ Hypertension is called the silent killer because most patients do not have symptoms.
- ✓ The primary physical finding is elevated BP.
- ✓ The diagnosis of hypertension cannot be made based on only one elevated BP measurement.
- ✓ The average of two or more measurements taken during two or more clinical encounters is required to diagnose hypertension.
 (Handwritten: عيادة أو مركز صحي ← مش من البيت)
- ✓ Outside of clinical setting measurements (ambulatory and self-BP monitoring) are recommended for diagnostic confirmation before starting antihypertensive therapy.
 (Handwritten: من البيت ← Confirmation → من الدكتور 24 hr)
- ✓ For patients without a history of CAD, noncoronary [atherosclerotic vascular disease] (ASCVD), LV dysfunction, or DM, it is also important to estimate future risk of CV disease and clinical ASCVD.
 (Handwritten: 1, 2, 3, Systolic HF, العر وال Gender العمر دور, Peri pheral بالمجان مثلاً أو Coronary Artery عندهم اياه بكان في ال)
- ✓ The 10-year risk of clinical ASCVD (defined as coronary death or nonfatal MI, or fatal or nonfatal stroke) can be found at: <http://tools.acc.org/ASCVD-Risk-Estimator/>
 (Handwritten: لو هارت عندهم Secondary prevention Aspirin يكون لازم يوجد بحسب من هاي الحاسبة Primary prevention → Aspirin)

بحسبها للناس الصريحة انه ليس عندهم ASCVD من الناس

الى اصلا لها عندهم لانه هم هيك هيك عندهم risks على
tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/



ASCVD Risk Estimator Plus

10 year

Estimate Risk

Therapy Impact

Advice

فاكثي factors ناقصين ممكن اننا نتحسين

App should be used for primary prevention patients (those without ASCVD) only.

Current Age * **Sex *** Male Female **Race *** White African American Other

Age must be between 20-79

Systolic Blood Pressure (mm Hg) * **Diastolic Blood Pressure (mm Hg) °**

Value must be between 90-200 Value must be between 60-130

Total Cholesterol (mg/dL) * **HDL Cholesterol (mg/dL) *** **LDL Cholesterol (mg/dL) °**

Value must be between 130 - 320 Value must be between 20 - 100 Value must be between 30-300

History of Diabetes? * Yes No **Smoker? ° *** Current Former Never

On Hypertension Treatment? * Yes No **On a Statin? °** Yes No **On Aspirin Therapy? °** Yes No

modifiable

=

+

ممكن اني اقلها ولو المرين ماعم يتعالج مزبوا راج ترفع

الدكتورة بالمحاضرة جربت تغير factors جربوا وسوفوا الفرق