Pharmacotherapy 1

ياسمين خليل

Hypertension – Part 2

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HTN Urgency = Severe HTN
↳ out patient with oral medications

PREVENT calculator: for 1° prevention too as 10 year ASCVD risk هاي الحقدة وأحدر

كل حرف هو كلمة

New slide

- Developed by the AHA in 2023, the Predicting Risk of Cardiovascular Disease EVENTs (PREVENT) equations estimate 10-year and 30-year risk for total CVD, including ASCVD and HF. It is the first risk tool to combine CV, kidney, and metabolic health measures to guide primary prevention-focused treatment decisions.

يتبعي risk الـ CVD وليس ASCVD للعشرة سنوات

صنع موجود في الحماية الأولى

(acute events) (10 years and life time) كانت ASCVD

as stroke, ...

- Validated for adults ages 30–79 years without known CVD

الأدنى كانت 40 – 79

- Three optional predictors, urine albumin-creatinine ratio (UACR), hemoglobin A1c (HbA1c), and social deprivation index (SDI), can personalize risk estimates.

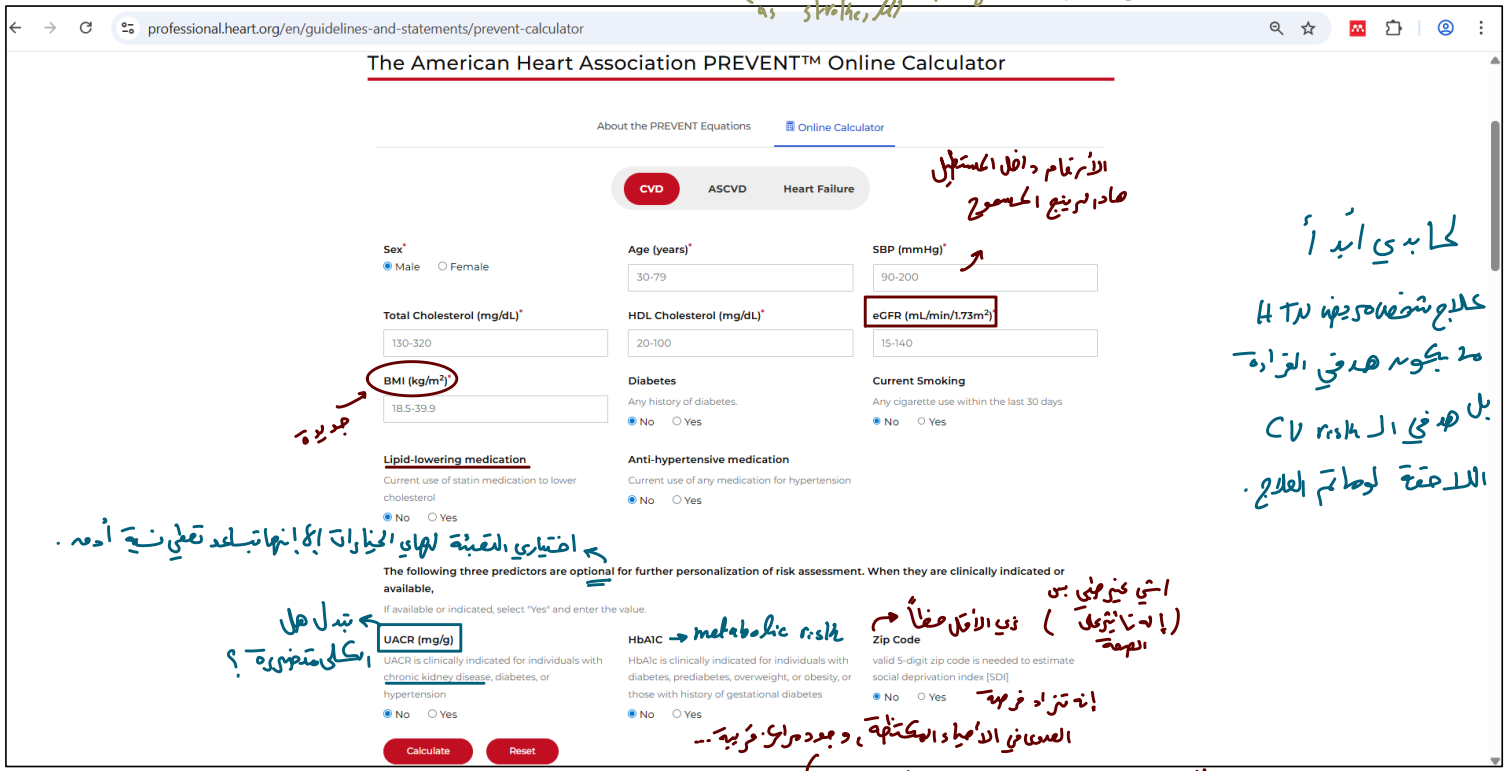
Physical activity & Family history ما موجود بشكل صريح

بس موجود أشياء مهم indication

body mass index , lipid profile

DBP & LDL هاي.

Overestimating for the risk هاي الحاسبة تميل



الأرقام داخل المستطيل عادي لا تضيع المعنى

جديدة

اختياري التقنية لهاي الخيارات إلا إنها تساعد تعطي نتيجة أدق.

تبدل هل بالكلى متضررة؟

اللي فيني بس ذي الأقل حظاً مهم (إنه نا نتوعى الفئة)

إنه تزاد فرصة العصاني الأمراض المكتشفة، وجود مراكز قريبة..

Social determinants of health

لحالات مثل أنا

علاج شخص عنده HTN مو بيكون هدفي الوزن

بل هدفي الـ CV risk اللي عندي لوضع العلاج.

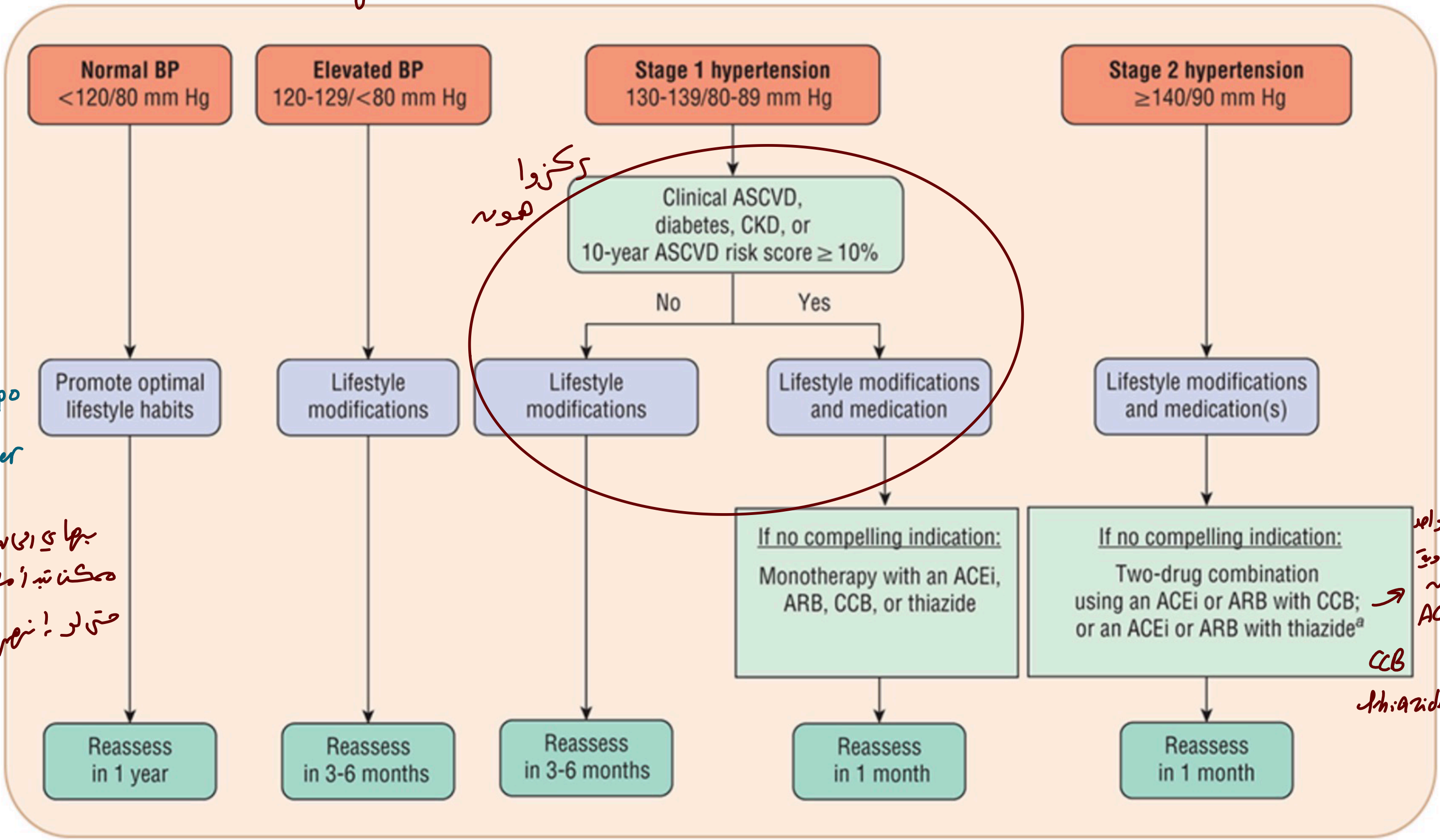
https://professional.heart.org/en/guidelines-and-statements/prevent-calculator

Updated slide

FIGURE 33-2 Algorithm for treatment of elevated BP and hypertension based on BP category at initial diagnosis.

a: Monotherapy with an ACEi, ARB, CCB, or thiazide is appropriate in patients presenting in Stage 2 hypertension if they are at high risk for orthostatic hypertension or are very elderly.

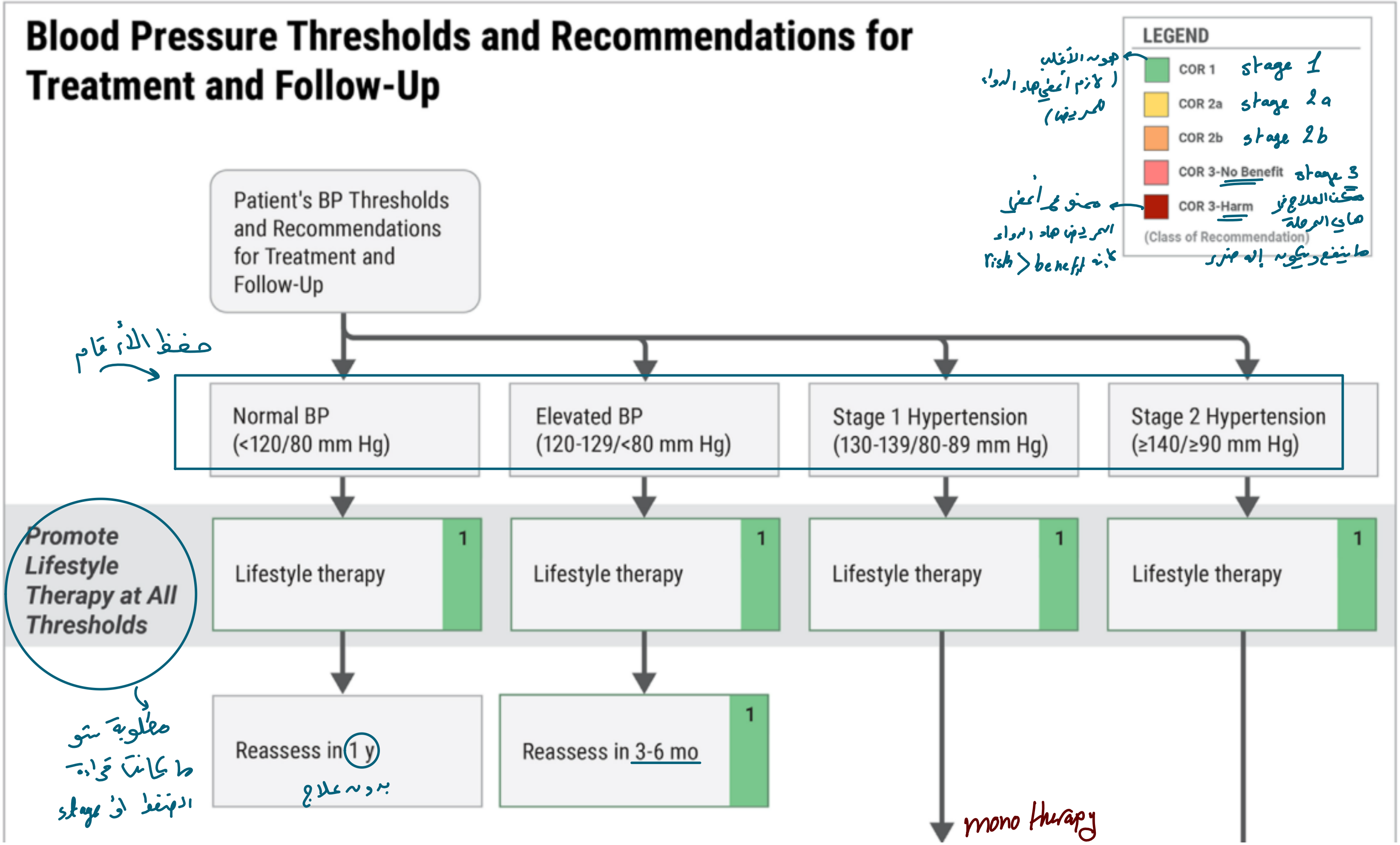
(ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CCB, calcium channel blocker.)



Source: Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, Lisa M. Holle, Jennifer Cocohoba, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*

New slide

2025 ACC/AHA hypertension guidelines



New slide

medical therapy = pharmacological therapy

لو مريض عنده HF و هو مريض stage 1 BP

1. ARBs / ACEIs ، رح نمشي على

2. β-blocker

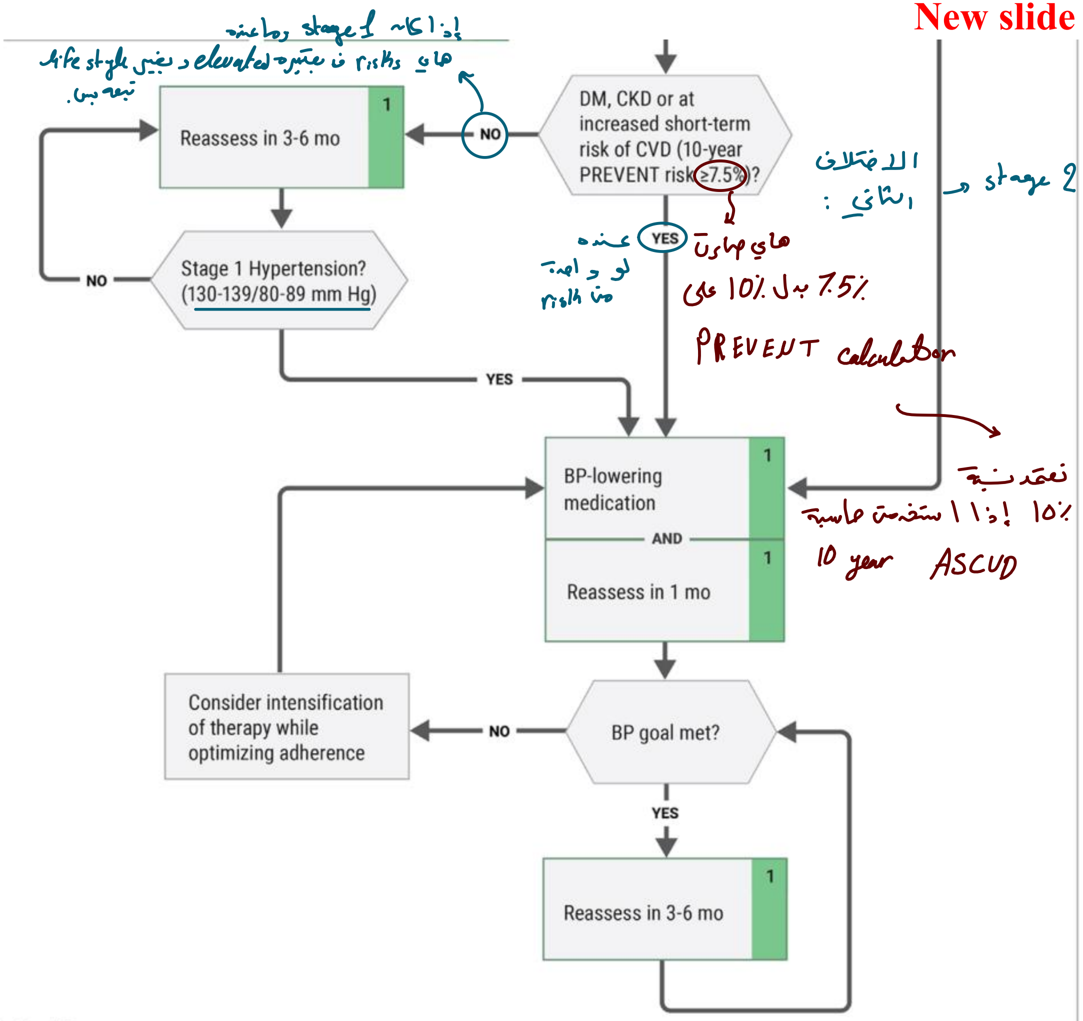
3. Mineralocorticoid receptor antagonist

4. Na^+ glucose cotransporter inhibitor

هادول كلهم في الضغط

← منشان كل مرضى stage 1 يحتاجوا علاج

أما stage 2 كلهم مباشرة بدهم علاج



➢ Patients with Compelling Indications:

هيهم تحت

كم لا يعني استخدام class واحد

خطوتي العلاج

Compelling indications represent specific comorbid conditions where evidence from clinical trials (reduction in CV morbidity and/or mortality) supports using specific antihypertensive classes to treat both the compelling indication and hypertension.

- اختيار الدواء لا يعتمد فقط على زيادة الضغط

لما اختار بختار واحد يخفض زيادة الضغط و يعالج أو يحاول يتوقف من المرض المزمن الثاني المصاب فيه المريض

ممكن 2 Drugs ينزلوا الضغط بنفس الفعالية بس واحد منهم يحمي النفرونات الكلى

← لازم ما نفكر أي دواء رح يعمل lowering للضغط

بل أي دواء يعمل improvement on the patient's outcomes

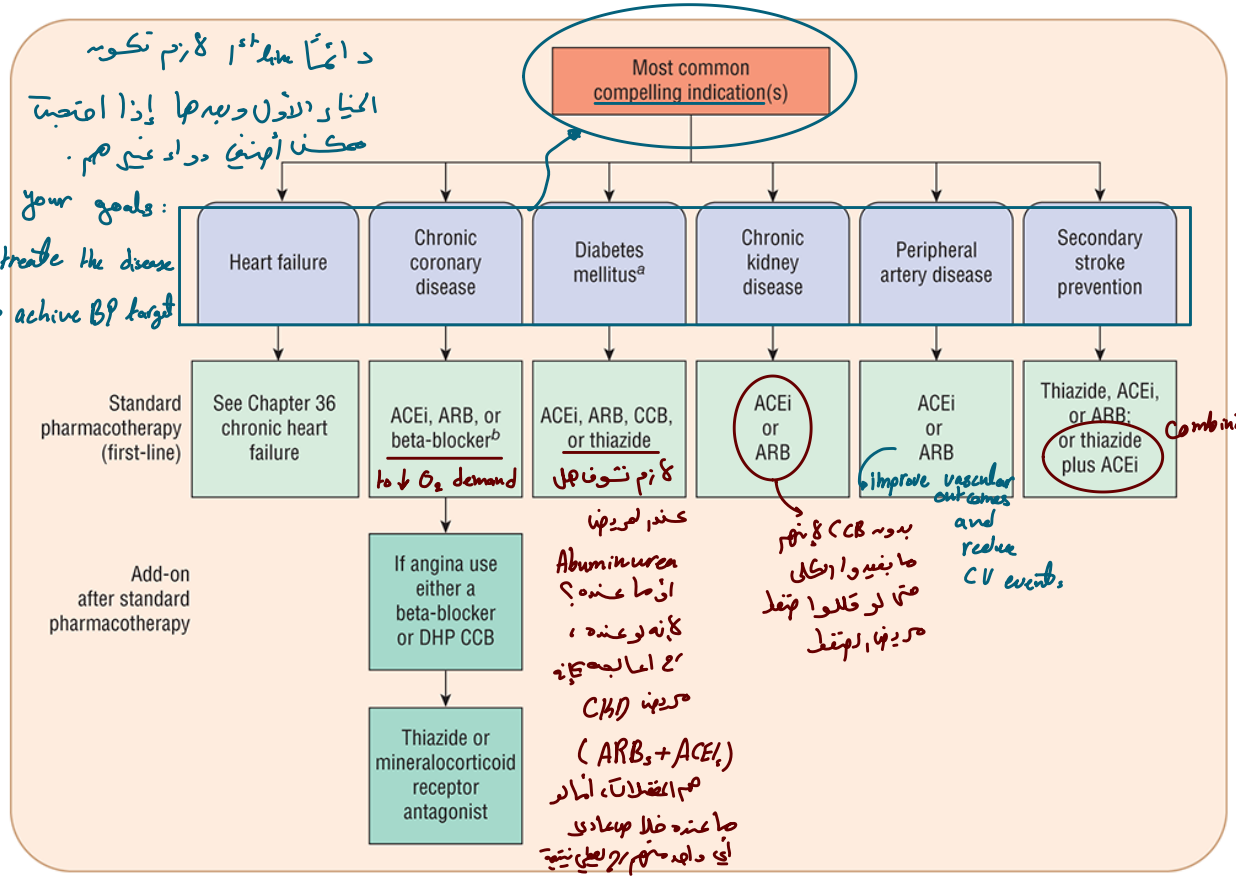
Updated slide

FIGURE 33-3 The most common compelling indications for individual drug classes.
Compelling indications for specific drugs are evidenced-based recommendations from outcome studies or existing clinical guidelines. The order of drug therapies serves as a general guidance that should be balanced with clinical judgment and patient response. Add-on pharmacotherapy recommendations are when additional medications are needed to lower blood pressure (BP) to achieve the goal. BP control should be managed concurrently with the compelling indication.

a: If albuminuria is present in diabetes, treat like chronic kidney disease and use an ACEi or ARB titrated to the maximum tolerated dose.

b: GDMT beta-blockers include carvedilol, metoprolol tartrate, metoprolol succinate, nadolol, bisoprolol, propranolol, and timolol. Avoid atenolol. Beta-blockers should not be used as first line without another indication (eg, recent MI with LVEF ≤50% [0.5], angina, arrhythmias).

(ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; DHP CCB, dihydropyridine calcium channel blocker.)



Updated slide

➢ Patients with Compelling Indications

✓ Heart Failure

- Antihypertensive agents are part of the mainstay of providing GDMT for patients with HF (HFrEF, mildly reduced, or preserved).

- Combination therapy with an ARB/neprilysin inhibitor (ACEi or ARB as an alternative), an evidence-based beta-blocker (ie, bisoprolol, carvedilol, or metoprolol succinate), and a MRA are antihypertensives that are part of the pillars of therapy for patients with HF, along with a SGLT-2i.

- Diuretics, usually a loop, are used if needed for edema, and additional non-antihypertensive agents are used as add-on therapy, depending on the type of HF being treated.

- Ensuring BP control is critical for preventing HF and slowing its progression in those with the disease.

✓ Chronic Coronary Disease (CCD) with HTN

Updated slide

include

- Chronic stable angina and a history of ACS (eg, unstable angina, coronary revascularization procedure, or acute MI) are forms of CCD or coronary artery disease/coronary heart disease.

- These are the most common forms of HTN-associated complications. Patients with CCD are at high risk for a CV event.

- RCTs support using an ACEi, ARB, or GDMT beta-blocker (ie, carvedilol, metoprolol tartrate, metoprolol succinate, nadolol, bisoprolol, propranolol, and timolol) for patients with CCD.

- An ACEi (or ARB as an alternative) improves cardiac remodeling and function and reduces CV events in patients with CCD.

- Beta-blocker therapy seems to be most effective in reducing the risk of CV events in patients with recent MI, ischemic symptoms (eg, angina), or left ventricular dysfunction (eg, LVEF ≤50%).

Updated slide

- Beta-blocker therapy has traditionally been a standard of care for treating patients with CCD and HTN for decades because it can reduce BP and improve angina symptoms by decreasing myocardial oxygen consumption and demand. They also decrease cardiac adrenergic stimulation and, in clinical trials, reduce the risk of a subsequent MI and sudden cardiac death.

- A long-acting nondihydropyridine CCB is an **alternative** to a GDMT beta-blocker (diltiazem and verapamil) in CCD in patients who do not tolerate or when a beta-blocker is contraindicated when used for angina. However, they should not be used in patients with CCD and significantly diminished LV dysfunction.

- The combined use of a nondihydropyridine CCB with a beta-blocker should be avoided in general due to the increased risk of bradycardia.

- A dihydropyridine CCB (eg, amlodipine, felodipine) is recommended as **add-on** therapy in CCD patients who have ongoing ischemic symptoms (angina or chest pain).

هون رح نحكي كيف نعمل safe combination بين الأدوية بعدما عرفنا قبل متى أولوية كل واحد منهم

Updated slide

- CCBs (especially nondihydropyridine CCBs) and beta-blockers provide anti-ischemic effects; they lower BP and reduce myocardial oxygen demand in patients with HTN and stable (and unstable) CCD.

= angina
والأولى هو B-blocker
ولما ما يكون في سيطرة منهم نستخدم dihydro CCB كإضافة Add-on

vasodilators (indirect anti-ischemic eff) — reduce HR

- A dihydropyridine CCB can be combined with a beta-blocker because there is no increased risk of bradycardia. Cardiac stimulation may occur with short-acting immediate-release dihydropyridine CCBs (eg, nifedipine) or beta-blockers with ISA, and these agents should be avoided in patients with CCD.

→ may cause reflux sympathetic activation (↑ HR, O_2 demand) بزيد الألم

B-blocker + intrinsic sympathomimetic activity = partial stimulation of B receptors, so less eff on reducing HR + less anti-ischemic eff so should be avoided

- In patients with CCD, angina, and ongoing uncontrolled high BP on an ACEi or ARB, once ischemic symptoms are controlled with beta-blocker and/or CCB therapy, the addition of other antihypertensive drugs can be added to provide additional CV risk reduction.

الترتيب في حالة CCD: نبدأ ب ACEI, أو ARBs وإذا كان عنده ischemia, LVD, 50% or less, MI مع نضيف B-blocker أو (nondi) CCB وإذا صار في سيطرة على ischemia وكان ضغط عالي لسا رح نضيف antihypertensive كمان، والـ symptoms والمدرات MRA
لأنهم رح تقلل BP بس ما إلها تأثير على ischemia

- Thiazides or an MRA can be added to provide additional BP lowering and further reduce CV risk. However, it should be noted that neither a thiazide nor an MRA provides anti-ischemic effects.

لا هاد ولا هاد رح يساعدني بالـ angina

✓ Diabetes

اللهم ارحم أبيهم واغفر له وعافه
وأعف عنه واجمعه وأهله والمسلمين
في الجنة

لهذا السبب هدفنا تقليل CV risk غير عن هدفنا في تقليل BP.

- CV disease is the primary cause of mortality in diabetes.

في السيطرة على BP أهم من الـ class إلي رح نختاره من 1st line للعلاج الضغط (CCB, ARBs, ACEIs, thiazid)

- HTN management is a very important risk reduction strategy.
- All four first-line antihypertensive agents have been shown to reduce CV events in diabetics.
- The evidence-based review performed for the 2017 ACC/AHA guideline found no difference in all-cause mortality, CV mortality, HF, or stroke between ACEI-, ARB-, CCB-, and thiazide-based regimens in patients with diabetes. This means that the benefit comes from lowering BP not from the class itself.

إلا إذا مريض DM + HTN أو HTN و albuminuria فالأفضل ACEIs + ARBs لأنهم رح يقللوا الـ damage في الكلى [kidneys protective]

- Traditionally, an ACEI or ARB was considered as a preferred antihypertensive agent for diabetics.
- The risk of kidney disease progression is low in absence of albuminuria.

أما DM + HTN بدون Albuminurea هون أي دواء من 1st line رح يزبط عادي

- Based on the weight of all evidence, any first-line agent can be used for controlling HTN for patients with diabetes in the absence of albuminuria.

أهم إشي اعرف هل في بالبول بروتين ألبيومين أو لا وعليه بصير يختار الـ class الأنسب، لو صار في خلاف أي واحد منهم تركوا الـ Combination

- Regardless of what agent is initially chosen, most patient will require combination therapy, which typically will include an ACEI or ARB with a CCB or thiazide.

ACEIs / ARBs with thiazid
or
ACEIs / ARBs with CCBs

- A β-Blocker is useful add-on therapy for BP control for patients with diabetes and should also be used to treat another compelling indication (eg, stable IHD).
- A β-Blocker (especially a nonselective agent) can possibly mask the signs and symptoms of hypoglycemia (eg, tremor, tachycardia, and palpitations **but not** sweating) in patients with tightly controlled diabetes.
- Patients may also have a delay in hypoglycemia recovery time.
- Unopposed α-receptor stimulation during the acute hypoglycemic recovery phase (due to endogenous epinephrine release intended to reverse hypoglycemia) may result in acutely elevated BP due to vasoconstriction.
- Despite these potential problems, β-blockers can be safely used for patients with diabetes.

✓ Chronic Kidney Disease

- The rate of kidney function deterioration is accelerated when both HTN and diabetes are present.

- Once patients have an estimated GFR < 60 mL/min/1.73 m^2 or albuminuria, they have significant CKD and risk of CV disease and progression to severe CKD increases.

High BP will increase intraglomerular presser → cause glomerular dam → protein leakage → progression on nephrone loss

- BP control can slow the decline in kidney function.

to slow the progression of CKD

- An ACEI or ARB has been shown to slow progression of CKD in diabetes & those without diabetes.

By lowering BP and RAAS blockage so extra renal protection

- The potential to produce acute kidney failure is particularly problematic in patients with bilateral renal artery stenosis or a solitary functioning kidney with stenosis (more common in patients with diabetes or those who smoke). Starting with low dosages and evaluating serum creatinine soon after starting the drug can minimize this risk.

bilateral renal artery stenosis or single

Updated slide

✓ Peripheral Arterial Disease (PAD)

اللهم صل وسلم وبارك على محمد

- PAD is a noncoronary form of ASCVD. out side the heart
  ليس رح تؤثر على القلب والدماغ

  الهدف تقلل ← في الأنسب ACEi + ARBs

- Patients with PAD are at an increased risk of major adverse cardiovascular events (MACE) as stroke, MI, HF, and CV death.

- An ACEi or ARB is recommended in patients with PAD to reduce the risk of MACE.

  رح يصير كخفيف الأوعية لما استخدم

- β-Blockers can theoretically be problematic for patients with PAD due to possible decreased peripheral blood flow secondary to unopposed stimulation of α1-receptors that results in vasoconstriction.

  but evidence finds that

- Available data indicate that β-blockers do not worsen (safe) claudication symptoms or cause functional impairment.

  muscle pain usually on calf

Updated slide

✓ Recurrent Stroke Prevention

- Achieving goal BP values in patients who have experienced an ischemic stroke (not hemorrhagic stroke) or TIAs is a primary modality to reduce risk of a second stroke or TIA.
- A thiazide, ACEi, or ARB is recommended as initial therapy when monotherapy is started.
- When combination therapy is needed, a thiazide in combination with an ACEi is an evidence-based antihypertensive regimen for patients with a history of stroke or TIA.
- Antihypertensive drug therapy should only be implemented **after** patients have stabilized following an acute cerebrovascular event, typically a few days after the event.
- The threshold for starting antihypertensive drug therapy in patients with a history of stroke is when BP is above 140/90 mm Hg.
- Once antihypertensive therapy is initiated, these patients should be treated to a goal of <130/80 mm Hg.

Updated slide

➢ Special Populations

- Selection of drug therapy should follow the recommendations provided by evidence-based guidelines, summarized in Figs. 33-2 and 33-3. .

with adjustments for tolerance + risk of falls

- There are some patient populations where the approach to drug therapy may be slightly altered (other agents have unique properties that benefit a coexisting condition but may not be based on evidence from outcome studies in hypertension).

✓ **Hypertension in Older People**

- Elderly patients are more sensitive to volume depletion & sympathetic inhibition than younger patients.
- This may lead to orthostatic hypotension which can increase the risk of falls due to the associated dizziness.
- Centrally acting agents (as clonidine) and α1-blockers should generally be avoided or used with caution in the elderly
- First-line antihypertensives provide significant benefits and can safely be used in older patients, especially those aged 80 years and older, but smaller-than-usual initial doses should be used for initial therapy, and dosage titrations over a more extended period are usually needed to minimize the risk of hypotension.

عند الشباب بعدّل الجرعة على حسب كل أسبوع ، لما حد يكبر كل أسبوعين تقريبًا
والأصح عند الكبار من 1st line هم thiazide و dihydro CCB
و Target BP هو systolic= أقل من 130 هاد إذا كانوا healthy أما إذا كانوا عندهم comorbidities بروح أوسع بين أقل من 150 أو أقل من 140

✓ Patients at Risk for Orthostatic Hypotension →

الكبار هم الأكثر عرضة أكبر من 80 سنة

- Orthostatic hypotension is a significant drop in BP when standing and can be associated with dizziness and/or fainting.
- Defined as a SBP decrease > 20 mm Hg or DBP decrease > 10 mm Hg when changing from supine to standing.
- The risk of orthostatic hypotension is increased in older patients and those with long-standing diabetes, severe volume depletion, and on concomitant venodilators (α-blockers, mixed α-/β-blockers, nitrates, and phosphodiesterase inhibitors).
- For patients with these risk factors, antihypertensive agents should be started in low doses, especially a thiazide, ACEI or ARB.

الكل

لا تتبع من إعفاد أو أكمال الخطة العلاجية.

Orthostatic hypotension

Updated slide

✓ Pregnancy

- HTN during pregnancy, defined as a BP ≥140/90 mm Hg, is a major cause of maternal and neonatal morbidity and mortality.
- It can be categorized as preeclampsia, eclampsia, **chronic HTN**, preeclampsia superimposed on chronic HTN, and gestational HTN.
- Many agents can be used to treat **chronic HTN** in pregnancy (Table 3).
- Unfortunately, there are few data regarding the most appropriate therapy in pregnancy.
- Labetalol, long-acting nifedipine, or methyldopa is recommended as first-line agents due to favorable safety profile.
- Other β-Blockers (other than atenolol) and CCBs are also reasonable alternatives.
- An ACEI, ARB, and direct renin inhibitor are known teratogens and are absolutely contraindicated.

Table 3: Treatment of Chronic Hypertension in Pregnancy

Updated slide

Drug/Class	Comments
Methyldopa:	Long-term follow-up data supports safety; considered a preferred agent
β-Blocker:	Generally safe, but intrauterine growth retardation reported (mostly with atenolol)
Labetalol:	Increasingly used over methyldopa because of fewer side effects; considered a first-line agent
Clonidine:	Limited data available; used mainly in third trimester
CCB:	Limited data available; no increase in major teratogenicity with exposure (except immediate release oral nifedipine should not be used); long-acting nifedipine considered a preferred agent
Thiazide:	Not preferred agents but probably safe in low doses if started prior to conception for essential hypertension. May consider in patients with salt-sensitive hypertension & reduced GFR in low doses
ACEI, ARB, direct renin inhibitor:	Contraindicated; major teratogenicity reported with exposure (fetal toxicity and death)

Updated slide

✓ Pulmonary Disease

- Cardioselective β-blockers can safely be used in patients with asthma or COPD (to treat a compelling indication eg, post-MI, coronary disease, or heart failure)
- The influence of comorbid conditions should only be complementary to, and never in replacement of, drug therapy choices recommended to treat a compelling indication.

✓ Metabolic Syndrome

- It has been defined as the presence of three of the following five criteria: abdominal obesity, elevated triglycerides, low HDL cholesterol, elevated BP (or receiving drug treatment for high BP), and elevated fasting blood glucose.
- Patients with metabolic syndrome are at increased risk of developing CV disease and/or type 2 diabetes.
- The cornerstone of treatment involves lifestyle modification (eg, weight loss if overweight or obese, exercise, dietary modifications).
- Any first-line antihypertensive can be used for patients with metabolic syndrome.

Updated slide

✓ Erectile Dysfunction

is multifactorial, vascular disease not drug side effect

- Most antihypertensive agents, particularly thiazides, beta-blockers, centrally acting alpha agonists, and MRAs, have been associated with erectile dysfunction in men.
- Hypertensive men frequently have ASCVD, which frequently results in erectile dysfunction.
- It is not clear if erectile dysfunction associated with antihypertensive treatment is solely a result of drug therapy or rather a symptom of underlying vascular disease (chronic arterial changes resulting from elevated BP, and lack of control) →These changes are even more pronounced in hypertensive men with diabetes.

Nebivolol: increase nitric oxide then vasodilation

- If a patient with high BP develops new-onset erectile dysfunction after the addition or titration of an antihypertensive associated with erectile dysfunction, it may be reasonable to:

• try a medication from a different drug class (eg, ACEi, ARB, or CCB instead of a thiazide)

• withdraw the medication and attempt a rechallenge, or

عند المرضى الي بصير عندهم Erectile dysfunction بعدما بيبدأوا أدوية، دمتقوا

منعمل switch للـ class مثلاً من thiazide لـ ARBs/ACEIs أو نتوقف عن الدواء وبعدين نرجع نبدأ فيه أو نستخدم class بديل صديق

• utilize a different medication from the same drug class if there is a compelling indication (eg, utilize the cardioselective nitric-oxide mediated vasodilating beta-blocker nebivolol if a beta-blocker is indicated).

Table 4: Fixed-Dose Combination Products →

Combination Drugs (Brand Name)	Strengths (mg/mg)	Daily Frequency
ACEI with CCB		
Amlodipine/benazepril (Lotrel)	2.5/10, 5/10, 10/20	1
Enalapril/felodipine (Lexxel)	5/5	1
Trandolapril/verapamil (Tarka)	2/180, 1/240, 2/240, 4/240	1 or 2
ARB with CCB		
Amlodipine/olmesartan (Azor)	5/20, 10/20, 5/40, 10/40	1
Telmisartan/amlodipine (Twynsta)	40/5, 40/10, 80/5, 80/10	1
Valsartan/amlodipine (Exforge)	5/160, 10/160, 5/320, 10/320	1
ACEI with a thiazide		
Benazepril/HCT (Lotensin HCT)	5/6.25, 10/12.5, 20/12.5, 20/25	1
Captopril/HCT (Capozide)	25/15, 25/25, 50/15, 50/25	1 to 3
Enalapril/HCT (Vaseretic)	5/12.5, 10/25	1
Fosinopril/HCT (Monopril HCT)	10/12.5, 20/25	1
Lisinopril/HCT (Prinizide, Zestoretic)	10/12.5, 20/12.5, 20/25	1
Moexipril/HCT (Uniretic)	7.5/12.5, 15/25	1 or 2
Quinapril/HCT (Accuretic)	10/12.5, 20/12.5, 20/25	1

Table 4: Fixed-Dose Combination Products

Combination Drugs (Brand Name)	Strengths (mg/mg)	Daily Frequency
ARB with a thiazide		
Azilsartan/chlorthalidone (Edarbyclor)	40/12.5, 40/25	1
Candesartan/HCT (Atacand HCT)	16/12.5, 32/12.5	1
Eprosartan/HCT (Teveten HCT)	600/12.5, 600/25	1
Irbesartan/HCT (Avalide)	75/12.5, 150/12.5, 300/12.5	1
Losartan/HCT (Hyzaar)	50/12.5, 100/25	1
Olmesartan/HCT (Benicar HCT)	20/12.5, 40/12.5, 40/25	1
Telmisartan/HCT (Micardis HCT)	40/12.5, 80/12.5	1
Valsartan/HCT (Diovan HCT)	80/12.5, 160/12.5	1
β-Blocker with a thiazide		
Atenolol/chlorthalidone (Tenoretic)	50/25, 100/25	1
Bisoprolol/HCT (Ziac)	2.5/6.25, 5/6.25, 10/6.25	1
Metoprolol succinate/HCT (Dutoprol)	25/12.5, 50/12.5, 100/12.5	1
Propranolol/HCT (Inderide)	40/25, 80/25	2
Propranolol LA/HCT (Inderide LA)	80/50, 120/50, 160/50	1
Metoprolol/HCT (Lopressor HCT)	50/25, 100/25	1 or 2
Nadolol/bendroflumethiazide (Corzide)	40/5, 80/5	1

يفضل نوزع أدوية الضغط على مرتين في اليوم كما أول ما وصلها لل max dose، ممكن مرة وحدة بس عشان أضمن 24h BP control، بنقرر إذا كان مفعوله ماشي ولا خلص بعد 12h من الجرعة الأولى

Table 4: Fixed-Dose Combination Products

Combination Drugs (Brand Name)	Strengths (mg/mg)	Daily Frequency
Direct renin inhibitor with thiazide		
Aliskiren/HCT (Tekturna HCT)	150/12.5, 150/25, 300/12.5, 300/25	1
Direct renin inhibitor with CCB		
Aliskiren/amlodipine (Tekamlo)	100/5, 150/10, 300/5, 300/10	1
ARB with CCB with a thiazide		
Amlodipine/valsartan/HCT (Exforge HCT)	5/160/12.5, 5/160/25, 10/160 /12.5, 10/160/25, 10/320/25	1
Olmesartan/amlodipine /HCT (Tribenzor)	20/5/12.5, 40/5/12.5, 40/5/25, 40/10/12.5, 40/10/25	1
Direct renin inhibitor with CCB with a thiazide		
Aliskiren/amlodipine/HCT(Amturnide)	150/5/12.5, 300/5/12.5, 300/5/25, 300/10/12.5, 300/10/25	1

HCT: hydrochlorothiazide

هاد الـ combination عشان نزيد الـ adherance والالتزام الدوائي، ونقلل عدد الحبات إلي بياخدها المريض عشان لو نسي وحدة... و نوصل للهدف بشكل أسرع (ما بندمج أدوية من نفس الـ class أو نفس MOA) وأكثر حدا مستفيد هم مرضى HTN stage 2

ما بنعمل combination بين ARBs و ACEIs لأنه بيزيد خطر Hypokalemia و Renal failure وما رح يضيف ها الفائدة للقلب

Updated slide

Resistant Hypertension

uncontrolled HTN → even when the patient takes 3 or more drugs (include: ACEIs, ARBs, CCBs, thiazide) on the max doses

- ✓ Resistant HTN is defined as failure to achieve goal BP using at least three antihypertensive drugs, commonly including a long-acting CCB, an ACEi or ARB, and a diuretic administered at maximum or maximally tolerated daily doses.
- ✓ This includes patients who are *adhering* to *full doses* of an appropriate *three-drug* regimen that *includes a diuretic*, but also includes patients who are controlled but require the use of four or more medications.
- ✓ Treatment of patients with resistant hypertension should ultimately follow the principle of drug therapy selection from the 2017 ACC/AHA guidelines.
- ✓ However, there are treatment philosophies that are related to the management of resistant hypertension: (a) assuring adequate diuretic therapy, (b) appropriate use of combination therapies, and (c) using alternative antihypertensive agents when needed.

Causes of Resistant Hypertension

Improper BP Measurement

Secondary hypertension

Volume overload:

- Excess sodium intake
- Volume retention from kidney disease
- Inadequate diuretic therapy

Drug-induced or other causes:

- Nonadherence
- Inadequate doses
- Agents listed in Table 33-1

Associated conditions:

- Obesity
- Excess alcohol intake
- Obstructive sleep apnea

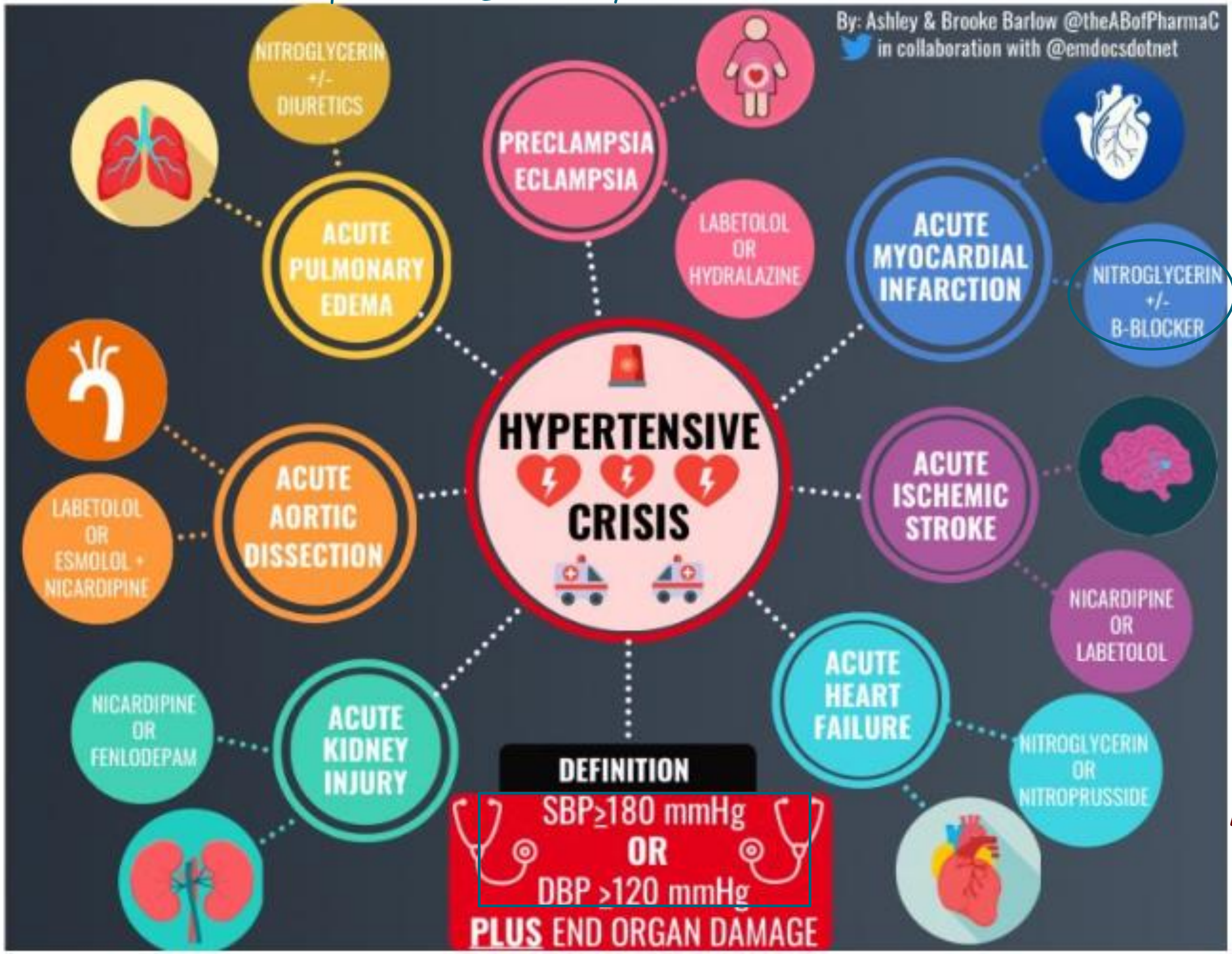
➢ Hypertensive Urgencies (2025 ACC/AHA update severe HTN) and Emergencies (Hypertensive crises)

- ✓ Both hypertensive urgencies and emergencies are characterized by the presence of very elevated (extreme) BP, typically greater than 180/120 mm Hg.
- ✓ The need for urgent or emergent antihypertensive therapy must be determined based on the presence of acute or immediately progressing end-organ injury, not elevated BP alone.
- ✓ Urgencies are not associated with acute or immediately progress emergencies are.
- ✓ Examples of acute end-organ injury include encephalopathy, intracranial hemorrhage, acute left ventricular failure with pulmonary edema, dissecting aortic aneurysm, unstable angina, and eclampsia or severe hypertension during pregnancy.

هاد المخطط مهم . احفظوه الله يعينكم

Eclampsia ماطو ←

Hydralazine + Labetalol =



في ICU ←

Emergency: 180/120 with end organ damage

Nicardipine

Labetalol

Nitroprusside (less used

Nitroglycerin (ischemia)

IV not oral مهم

Urgency (oral): 180/120 without end organ damage

Captopril

Amlodipine

Labetalol

اللهم ارحم والدينا
كما ربيانا صغارا

استثناءات بدها fast reduction

زي لما تكون الـ symptoms هو

لـ Aortic dissection

يعني الـ target sys = أقل من 120

بسرعة. وبهاي الحالة رح نستخدم

B-blocker to reduce shear stress.

✓ Hypertensive Urgency (Severe HTN)

- Hypertensive urgencies are ideally managed by *adjusting* maintenance therapy, by *adding* a new antihypertensive, and/or by *increasing the dose* of a present medication.
- This is the preferred approach to these patients as it provides a more **gradual** reduction in BP.
- Very rapid reductions in BP to goal values should be discouraged due to potential risks (CVA, MI, and acute kidney failure).
- Hypertensive urgency requires BP reductions with **oral** antihypertensive agents **to stage 1** over a period of **several hours to days**.
- All patients with hypertensive urgency should be reevaluated within and no later than 7 days (preferably after 1 to 3 days).
- Acute administration of a short-acting oral antihypertensive (eg, captopril, clonidine, labetalol) followed by careful observation for several hours to assure a gradual reduction in BP is an option for hypertensive urgency.

✓ Hypertensive Emergency → your goal is to lowering patient's BP + to avoid other on going organ damage.

Controlled but not rapid drop. (Acute kidney injury او stroke او ischemia على القلب او الدماغ)

- Hypertensive emergencies are those rare situations that require **immediate** BP reduction to limit new or progressing end-organ damage.
- Hypertensive emergencies require **parenteral** therapy, at least initially.
- The goal is a reduction in **MAP** of up to 25% within **minutes to hours**.
- If the patient is then stable, DBP can be reduced to 100 to 110 mm Hg within the next 2 to 6 hours.
- Abrupt drops in BP may lead to end-organ ischemia or infarction.
- If patients tolerate this reduction well, additional gradual reductions toward goal BP values can be attempted after 24 to 48 hours.
- The exception to this guideline is for patients with an acute ischemic stroke where maintaining an elevated BP is needed for a longer period of time.

tolerance يمكن ينزل مع الوريد

بعد استخدام Nitroglycerin لـ ischemia 48h

(التوسع) Vasodilator: أول اختيار وبعدها نبدأ بإعطاء B-blocker

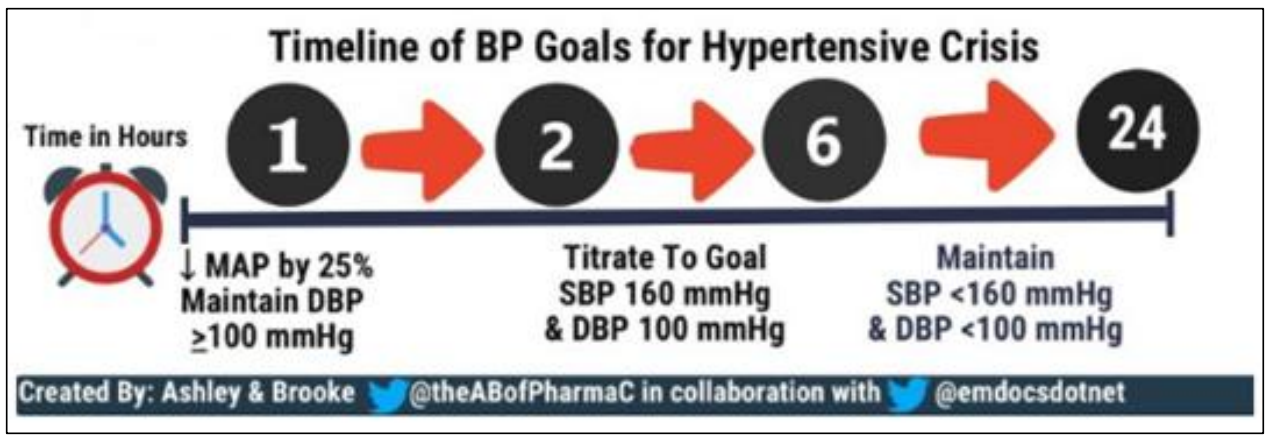


Table 5: Parenteral Antihypertensive Agents for Hypertensive Emergency

Drug	Dose	Onset (min)	Duration (min)	Adverse effects	Special indications
Clevidipine	1-2 mg/h (32 mg/h maximum)	2-4	5-15	Headache, nausea, tachycardia, hypertriglyceridemia	Most hypertensive emergencies except acute heart failure; caution with coronary ischemia; contraindicated in soy or egg allergy, defective lipid metabolism, and severe aortic stenosis
Enalaprilat	1.25-5 mg IV every 6 hours	15-30	360-720	Precipitous fall in pressure in high-renin states; variable response	Acute left ventricular failure; avoid in acute myocardial infarction, eclampsia

Table 5: Parenteral Antihypertensive Agents for Hypertensive Emergency

Drug	Dose	Onset (min)	Duration (min)	Adverse effects	Special indications
Esmolol hydrochloride	250-500 mcg/kg/min IV bolus, and then 50-100 mcg/kg/min IV infusion; may repeat bolus after 5 minutes or increase infusion to 300 mcg/min	1-2	10-20	Hypotension, nausea, asthma, first-degree heart block, heart failure	Aortic dissection; perioperative; avoid in patients already on β-blocker, bradycardic, or decompensated heart failure
Fenoldopam mesylate	0.1-0.3 mcg/kg/min IV infusion	<5	30	Tachycardia, headache, flushing	Most hypertensive emergencies; caution with glaucoma

Table 5: Parenteral Antihypertensive Agents for Hypertensive Emergency

Drug	Dose	Onset (min)	Duration (min)	Adverse effects	Special indications
Hydralazine hydrochloride	12-20 mg IV	10-20	60-240	Tachycardia, flushing, headache vomiting, aggravation of angina	Eclampsia
	10-50 mg intramuscular	20-30	240-360		
* **Labetalol hydrochloride**	20-80 mg IV bolus every 10 minutes; 0.5-2 mg/min IV infusion	5-10	180-360	Vomiting, scalp tingling, bronchoconstriction, dizziness, nausea, heart block, orthostatic hypotension	Most hypertensive emergencies except acute heart failure or heart block

صطلوب
الجدول كامل

Table 5: Parenteral Antihypertensive Agents for Hypertensive Emergency

Drug	Dose	Onset (min)	Duration (min)	Adverse effects	Special indications
Nicardipine hydrochloride	5-15 mg/h IV	5-10	15-30, may exceed 240	Tachycardia, headache, flushing, local phlebitis	Most hypertensive emergencies except acute heart failure; caution with coronary ischemia
* **Nitroglycerin**	5-100 mcg/min IV infusion (24 h)	2-5 (rapid within minutes)	5-10 (very short duration)	Headache, vomiting, methemoglobinemia, tolerance with prolonged use	Coronary ischemia (وهاد)

ببدأ سريعًا وبينتهي مفعوله سريعًا.

زي كبسة الضوء on/off مباشرة يشتغل ويطفي

هاي الأدوية إي صح اسمها Titratable drugs

نقدر نوقف المشكلة بسرعة لو صار اشي، مش زي All or non SubC injection

هاي النوعية من الأدوية نعطيها في الطوارئ، زي شخص مريض ضغطه 200/100 و بدأ نزل معه acute kidney failure (انتاجه ماء قليل) المريض يكون Progressive أو صار عنده mental changes ← هاي حالات طارئة بدها IV infusion = (on/off) Titratable drugs

السرعة في onset and duration الهدف منها إنه ما بدي ينزل ضغطه لل Target بل بدي أنزله بالتدريج عشان أوصل لل initial target بالأول بعدين target الحقيقي، ما المحكي بدنا نوصل بدقائق

لساعات وخلال الأيام بروح نوصله لل target، المريض 25 يكون في وحدات العناية الحثيثة ICU في المريض أو الطبيب [illegible] عليه [illegible] يراقب الوضع الضغط، يعني لو بدي أعطيه بـ 5 mg من دواء % للضغط، [illegible]

يدخل عليه بعد شوي ، روح يلاقي ضغط الوريد نزل 2-3 mmHg ، روح يرفع الجرعة بعد دقائقه إلى 10mg وينزل ضغطه صنيع بس لسا أعلى من initial target فيرفع الجرعة لـ 20mg (كل هاد تحت المراقبة طبعًا) .

Table 5: Parenteral Antihypertensive Agents for Hypertensive Emergency

نفرض لما رفع الجرعة نزل الضغط كثير فوراً مباشرة برجع ينزل .. ، فبروح ١ التأثير

Drug	Dose	Onset (min)	Duration (min)	Adverse effects	Special indications
* **Sodium nitroprusside**	0.25-10 mcg/kg/min IV infusion (requires special delivery system)	Immediate	1-2	Nausea, vomiting, muscle twitching, sweating, thiocyanate and cyanide intoxication	Most hypertensive emergencies; caution with high intracranial pressure, azotemia, or in chronic kidney disease

أستغفر الله العظيم وأتوب إليه

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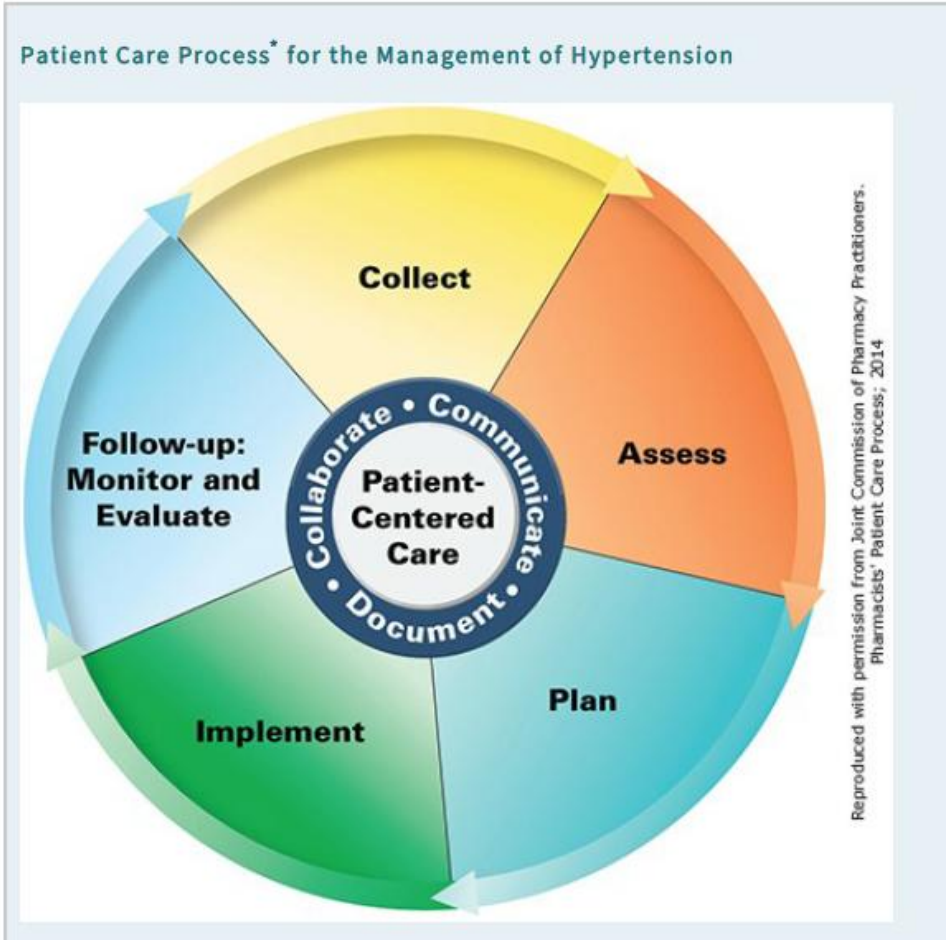
1935-1949 Charles Sidney Burwell (cardiologist, Dean of Harvard Medical School 1944):

"Half of what we are going to teach you is …….
wrong,
and half of it is …….
right.
Our problem is that we …….
don't know
which half is which."

الدكتورة علقت على مقولته
وحكت كيف إنه الـ
guidelines
تتغير مع الأيام وهادكا يلي السابه هو
الخطأ، بل إنه كان متاح بناءً على الموجود
والدين ممكن ما يكونه
High quality
up to date فخليكم
(ممكن تسأل مختصاني الاستشاري)

PATIENT CARE PROCESS



اللهم اختم لنا أعمالنا بالصالحات

هاي الخطوات
عشان لما عَرّدوا
على الـ Case
ما تفوتوا اي أو معلومة

Collect

- Patient characteristics (eg, age, race, sex, pregnant)
- Patient history (past medical, family, social—dietary habits, tobacco use)
- Home blood pressure (BP) readings
- Current medications and prior antihypertensive medication use
- Objective data (see Box A)
  - BP, heart rate (HR), height, weight, and body mass index (BMI)
  - Labs (eg, serum electrolytes, SCr, BUN)
  - Other diagnostic tests when indicated (eg, electrocardiogram [ECG])

Assess

- Presence of compelling indications (eg, chronic coronary disease, chronic kidney disease; see Fig. 33-3)
- Hypertension-related complications (eg, albuminuria, retinopathy; see Box A)
- Ten-year atherosclerotic cardiovascular disease (ASCVD) risk when indicated
- Current medications that may contribute to or worsen hypertension

- BP goal and whether the goal has been achieved (see Box A)
- Appropriateness and effectiveness of the current antihypertensive regimen
- For resistant hypertension if taking three or more antihypertensive medications (see Table 33-8)

Plan*

- Tailored lifestyle modifications (eg, diet, exercise, weight management; see Table 33-4)
- Drug therapy regimen including specific antihypertensive(s), dose, route, frequency, and duration; specify the continuation and discontinuation of existing therapies (see Tables 33-5, 33-6, 33-7, and 33-9)
- Monitoring parameters including efficacy (eg, BP, CV events, kidney function), safety (medication-specific adverse effects), and timeframe (see Table 33-10)
- Patient education (eg, purpose of treatment, dietary and lifestyle modification, drug therapy)
- Self-monitoring of BP, HR, and weight—where and how to record results
- Referrals to other providers when appropriate (eg, physician, dietician)

Implement*

- Provide patient education regarding all elements of the treatment plan
- Use motivational interviewing and coaching strategies to maximize adherence
- Schedule follow-up

Follow-up: Monitor and Evaluate

- Determine BP goal attainment
- Presence of adverse effects
- Occurrence of CV events and development/progression of kidney impairment
- Patient adherence to treatment plan using multiple sources of information

Collaborate with patients, caregivers, and other healthcare professionals.

اللهم اغفر لي ذنبي كله دقه وجله أوله
وآخره ما علمت منه وما لم أعلم

نهاية محاضرة وصلنا للـ Assignments إلي أعطيتهم من أول الفصل (محاضرة 18th Mar. 26) :

ليه بنعطي أول اشي α-blocker قبل الـ β-blocker للـ Pheochromocytoma ؟

و إذا غيرنا الترتيب بيدخل المريض بـ rebound hypertension أو Hypertensive crisis ؟

← هاد المريض في بدمه نسبة عالية من Circulating Catecholamine لأنه عنده Cancer في Adrenal gland فالـ Epinephrine+Norepin عاليين في الدم يعني عنده activation عالي جداً على الـ α_1-receptor

يعني Severe vasoconstriction و ضغط عالي و high heart rate = Tachycardia (دايمًا لحالها بدعم تحددوا العلاج، لأنسب حدوده تبعًا للسبب تبع المشكلة)

Severe vasoconstriction: Peripheral constriction أحسن اشي نعمل بلوك لـ α_1 زي Doxazosin

high heart rate = Tachycardia: control by β-blocker

← إلي حيصير : بلوك على α_1 و vasodilation و ممكن يؤدي إلى ارتفاع Heart rate أكثر وأكثر زي reflux tachycardia و ضغطه رح ينزل، فـ لا تتفاجأ HR

ممكن أعطي β-blocker ← المهم لا تفكروا إنه هيك الأمور تمام.

طيب العكس !

بدأنا معه بـ β-blocker فـ رح يصير Control على HR، عنا β_2 لا! إنه non-selective و α_1 المستقبلين Peripherally والاثنين adrenergic و بيجي norepin يرتبط معهم على نفس blood vessels، ويعمل vasoconstriction على α_1 ويعمل vasodilation لما يرتبط مع β_2 وبالعادة شغل NE إنه يزيد الضغط

يعني شغل α_1 يغلب β_2 ← إلي رح يصير vasoconstriction، فـ لما أعطي β-blocker رح يعمل بلوك على HR وكمان بلوك على peripherally β_2-receptor و β_2 في الأوعية الدموية

عاملة زي break لحاليجي catecholamines يرتبط على α و β_2 فـ β_2 لأنه بعمل توسيع الأوعية فـ رح يخفف الـ constriction إلي بعمله الارتباط على α_1 (لحاله هي حي زي المقصود break

إنها مخففة تأثير التهنية الناتج عن α مع إنه مش Severe vasoconstriction) فلما أخرب أن علاجي بـ β_2 وتخلية الأوعية موسعة وبدي أعطي بعده α_1 antago فـ ما في عندي. بس لهون الحالة

break إنه يخفف الـ constriction إلي صار منا بلوك α_1 وننتهي بـ Hypertensive crisis عشان هيك الترتيب (α_1 then β_2) مهم جداً. ← unopposed يعني ما في بريك

← يزداد تأثير البلوك على β_2 في الرئتين أصلاً عند الناس إلي عندها مشاكل في الجهاز التنفسي (بس مش مستحيل يصير تهنيه القصبات عند الناس إلي ما عندهم أمراض في الرئة).

عملنا Assignement كامل في أول محاضرة منا

12. Mrs. Nawal, is a 32-year-old woman with a history of type I diabetes mellitus and hypertension. She takes lisinopril 10 mg/day and uses insulin. During her clinic visit, a pregnancy test is performed to follow up on a positive home pregnancy test the patient performed. The results confirm a pregnancy. Her BP today is 162/105 mm Hg, and HR is 80 beats/ minute. Which one of the following is the best therapy for her BP at this time? Justify your answer for each choice.

a. Increase lisinopril to 20 mg/day and add hydrochlorothiazide.
(b.) Discontinue lisinopril and begin methyldopa.
c. Discontinue lisinopril and add candesartan.
(d.) // // // // Labetalol

لوما عندها DM بجوز الخيار the best هو D لأنه ألطف من ناحية SE و safe ، أما مع
مرضها السكري رح يصير مشكلة بين non-selective B- blocker ← Drug - Disease interaction عن طريق Delay the covery of hypoglycemia
وبرضو masking hypoglycemia symptoms + impaired glycemic control يعني بما إنها مريضة سكري رح اختار B ، ممكن تمشي الدكتورة في السؤال إنه المريض مش بس
سكري و tightly controlled فبهاي الحالة التحذير أعم ، Label وعلى فرض إنها معها history of recurrent hypoglycemia نفس الاشي label من الخيار الأول.
لو كانت صيغة السؤال هيك which of the following can be used to manage BP? يعني من آمن للحامل فالخيار B+D
← السؤال إلي صيغته منها which one is the best بحكم تفرض إنه في أكثر من خيار صح ، وأنتم عليكم تختاروا الأصح.

آخر اشي عن clonidine (α_2- agonist)، لازم نوقفه بالتدريج عشان ما يعمل rebound HyperTension عشان over expression إلي صار على المستقبلات شوفتا على صورة ما بعرف وينها 🫠

الفهم ليش لما نوقفه فجأة ؟ بصير down regulation of α_2 receptors

← الخلية إلي فيها مستقبلات α_2 وطلعتهم على السطح لما نكون إعطينا بشكل دائمي activation باستمرار و Clonidine ينافس على Norepin على الارتباط على α_2 وبعدهم يعملوا activation في الخلية ملاحظة إنه المستقبلات ما بتوقف شغل في تبدأ تعمل down regulation في يقل عدد مستقبلات α_2، يعني بدل 5 مستقبلات رح يصير 2، فلما أوقف clonidine ويصير بس NE لحاله يتنافس على المستقبل في بصير tone sympathetic أكثر وأكثر ويرتفع الضغط أكثر من قبل

→ β is ~~antagonist~~ : up regulation (بتخلي المستقبل يهد أو ما يشتغل)

→ α is ~~agonist~~ : down regulation (العكس)

الحمدلله رب العالمين