Hypertension

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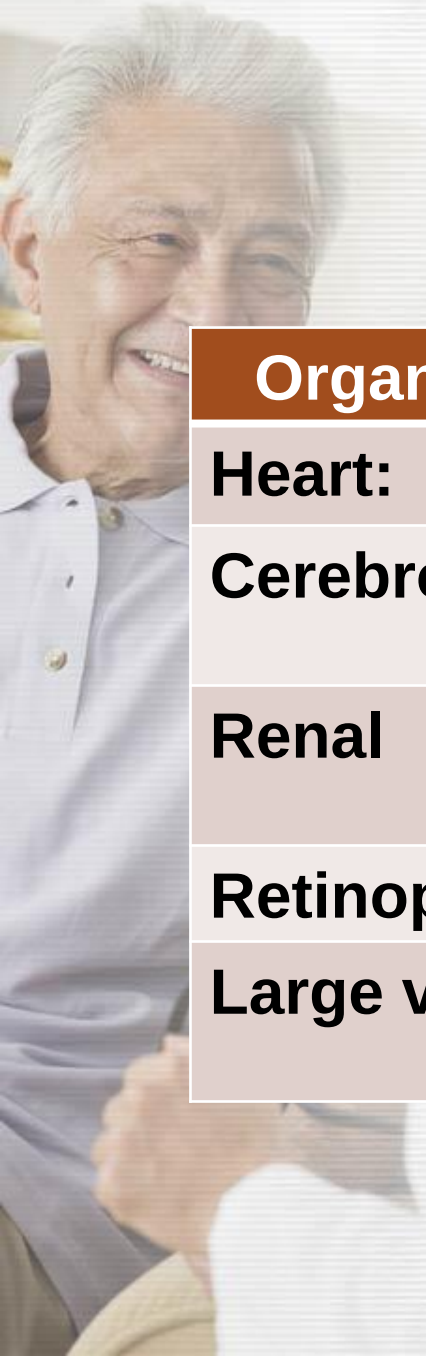
Hypertension

- It is a **sustained ↑** of arterial Bl.P ≥ 140/90 placing the patient at increased risk for TOD in vascular beds including: retina, brain, heart, kidneys, & large arteries

- HTN should not be diagnosed on the basis of one measurement alone, unless it is > 210/120 mm Hg or accompanied by TOD.

Manifestation of TOD



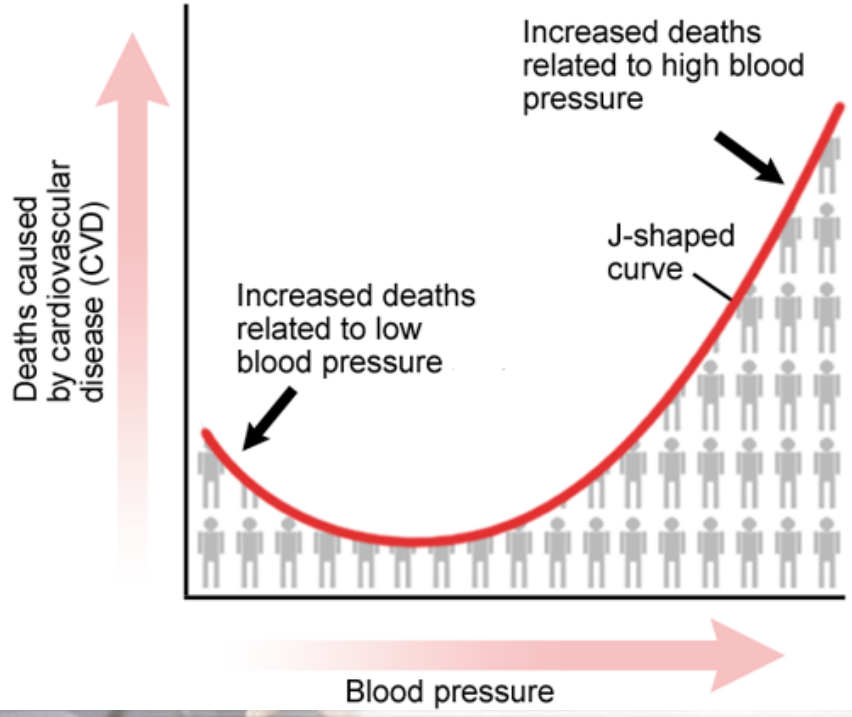
Organ system	Manifestation
Heart:	Pulmonary edema, MI, CAD, LVH
Cerebrovascular	Intracerebral bleeding, coma, seizures, mental status changes, TIA, stroke
Renal	Hematuria, azotemia Serum Cr >1.5 mg/dL, proteinuria
Retinopathy	Papilledema, hemorrhages
Large vessels	Aneurysmal dilation, Aortic dissection Accelerated atherosclerosis

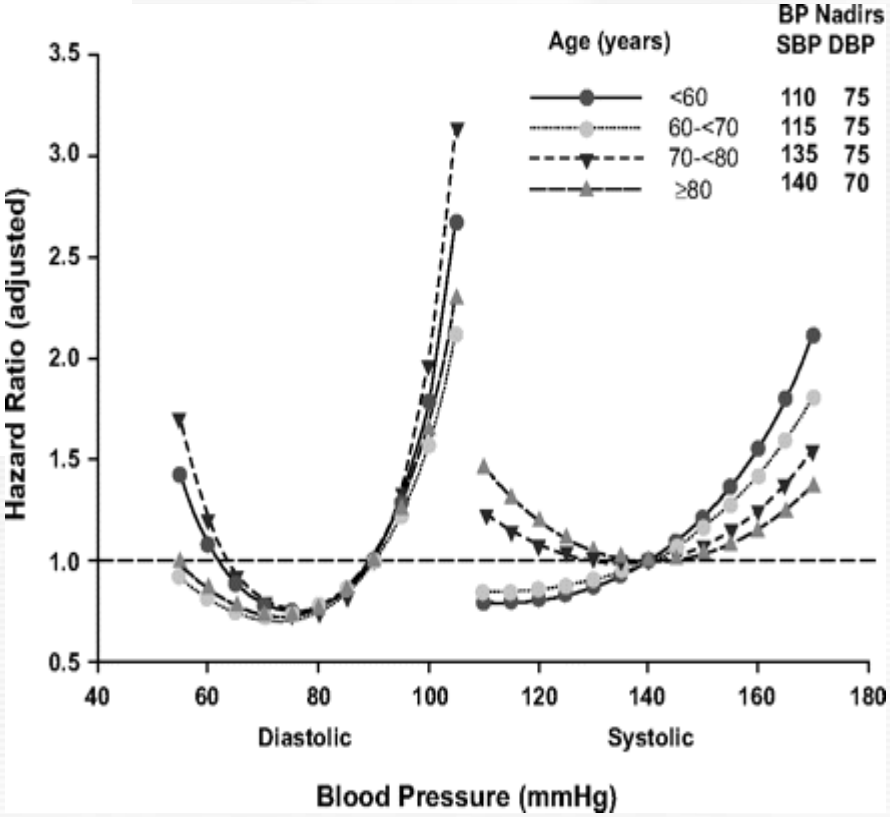
Facts

- **Systolic BP (SBP)** ↑ with age until the 8th decade.
- **Diastolic BP (DBP)** ↑ up to age 50, after which it plateaus or slightly ↓
- DBP is the best indicator of CV risk < 50 years. With ↑ age, there is a shift to SBP as the principal risk predictor.
- It is now clear that SBP has a continuous relationship with stroke & IHD risk.
- It can be difficult to get SBP to target, particularly in the elderly

- **PP** (SBP-DBP) is a marker of arterial stiffness.
- Wide PP more accurately predicts adverse CV outcome but the majority of outcome data from clinical trials is for SBP & DBP, so the major guidelines are based on these, rather than on PP.

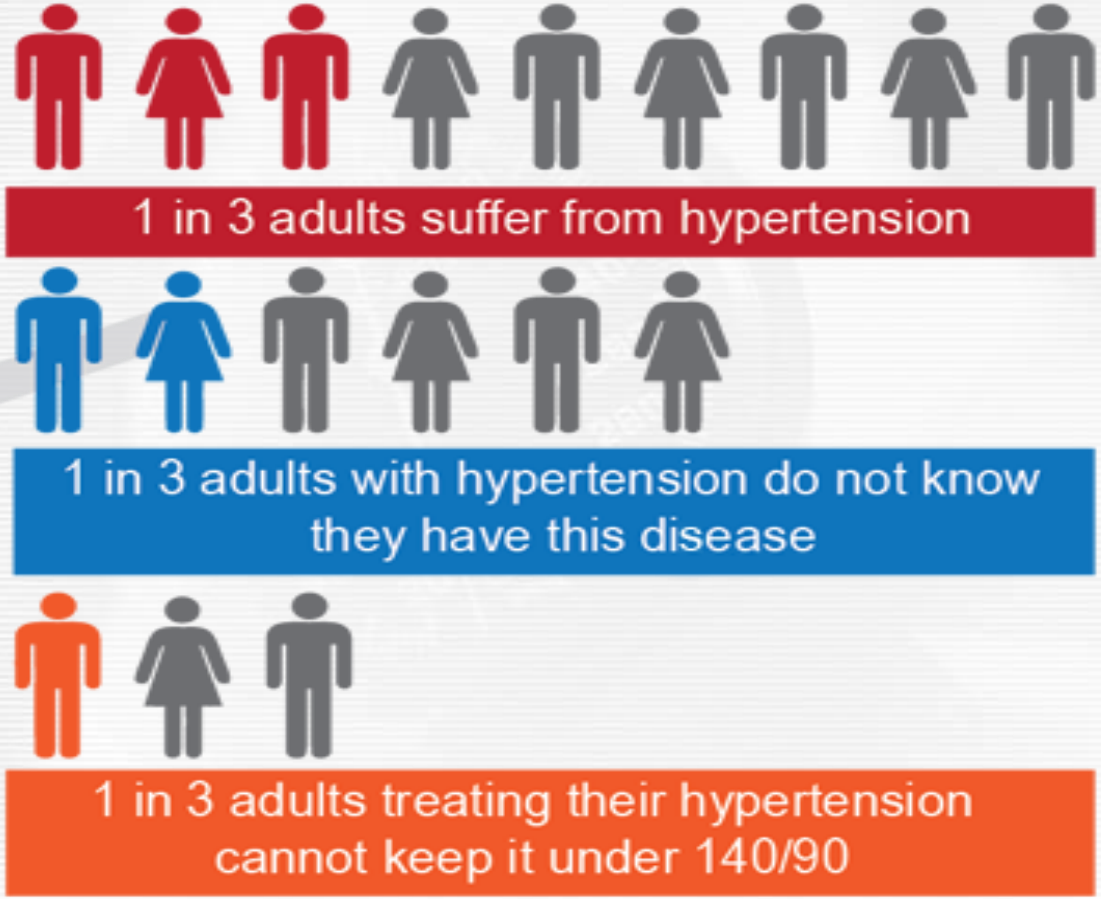
“J-curve” phenomenon





Epidemiology

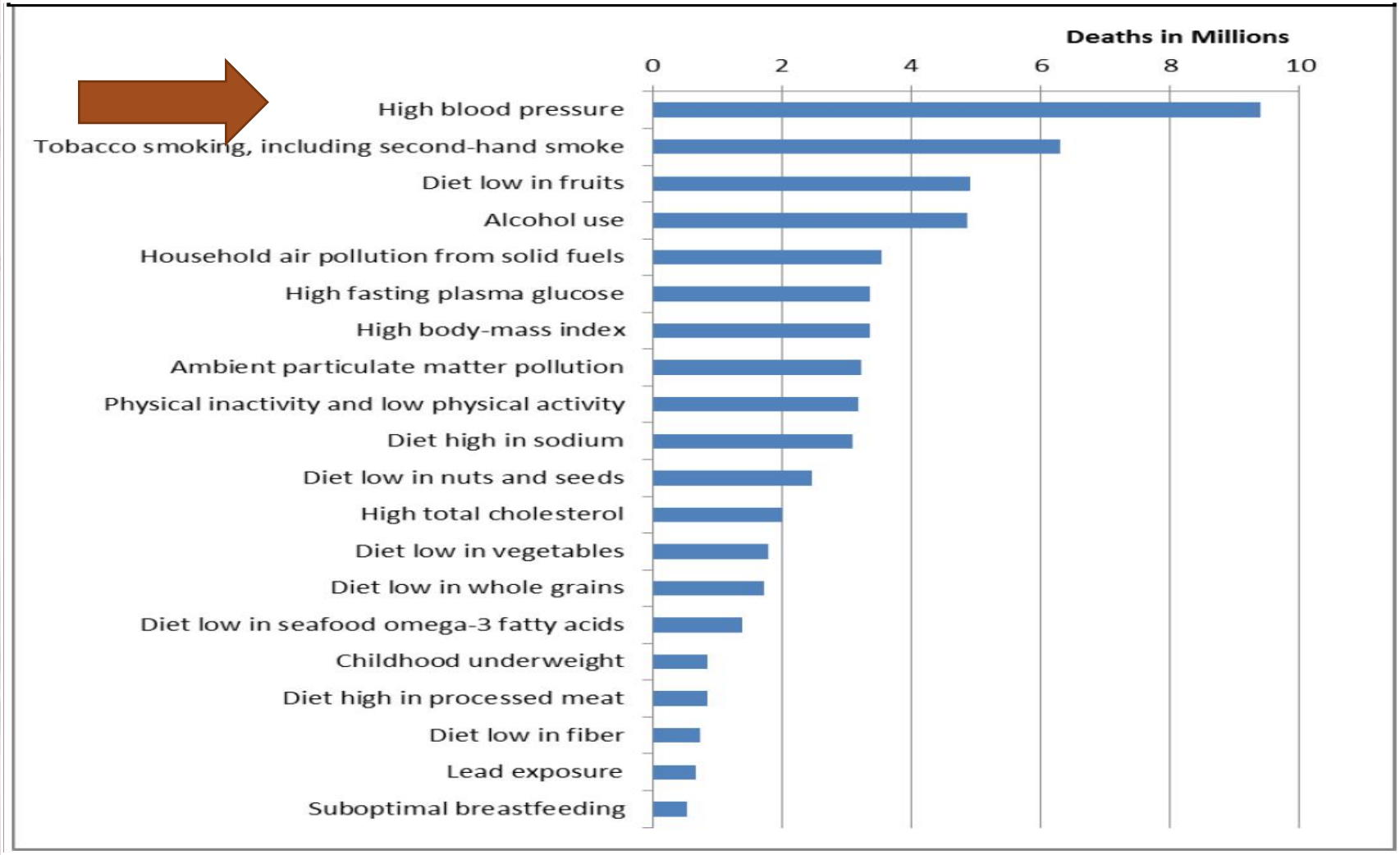
- The most common cause for an outpatient visit to a physician,



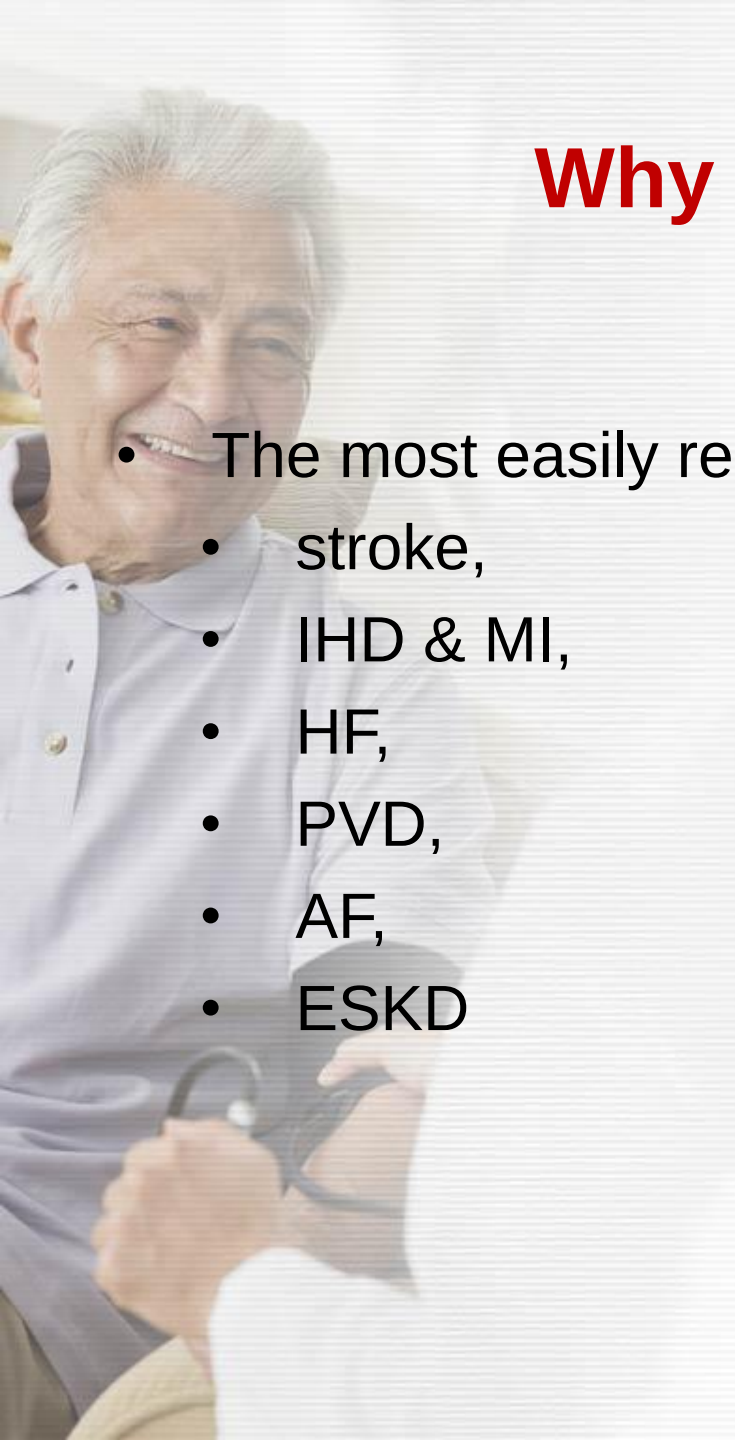
Hypertension in Egypt

- **Egyptian National hypertension Project (NHP),1991–1993:**
  - 26.3% of adult Egyptians had HTN
  - 50% of them > 60 years.
  - 60% of patients, were complicated
  - Only 38% of were aware of having HTN,
  - Only 24% were receiving treatment,
  - Only 8% were controlled

Why treat HTN?



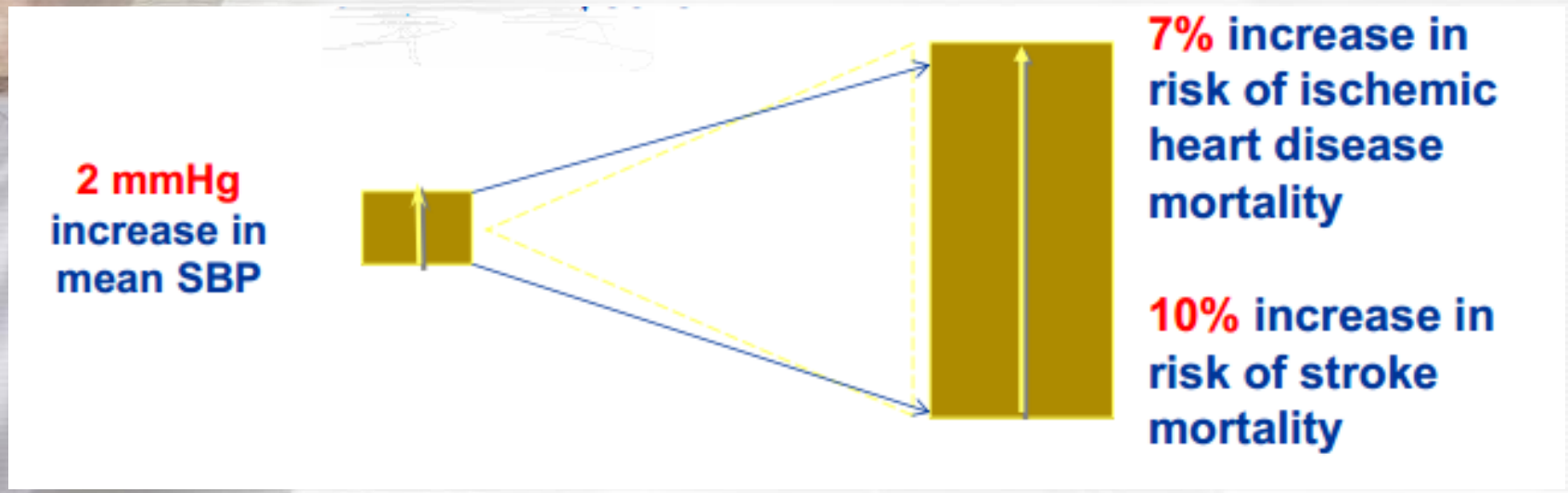
Global Burden of Disease Study 2010 , *Lancet* 2012; 380: 2224–60



Why treat HTN? (contin.)

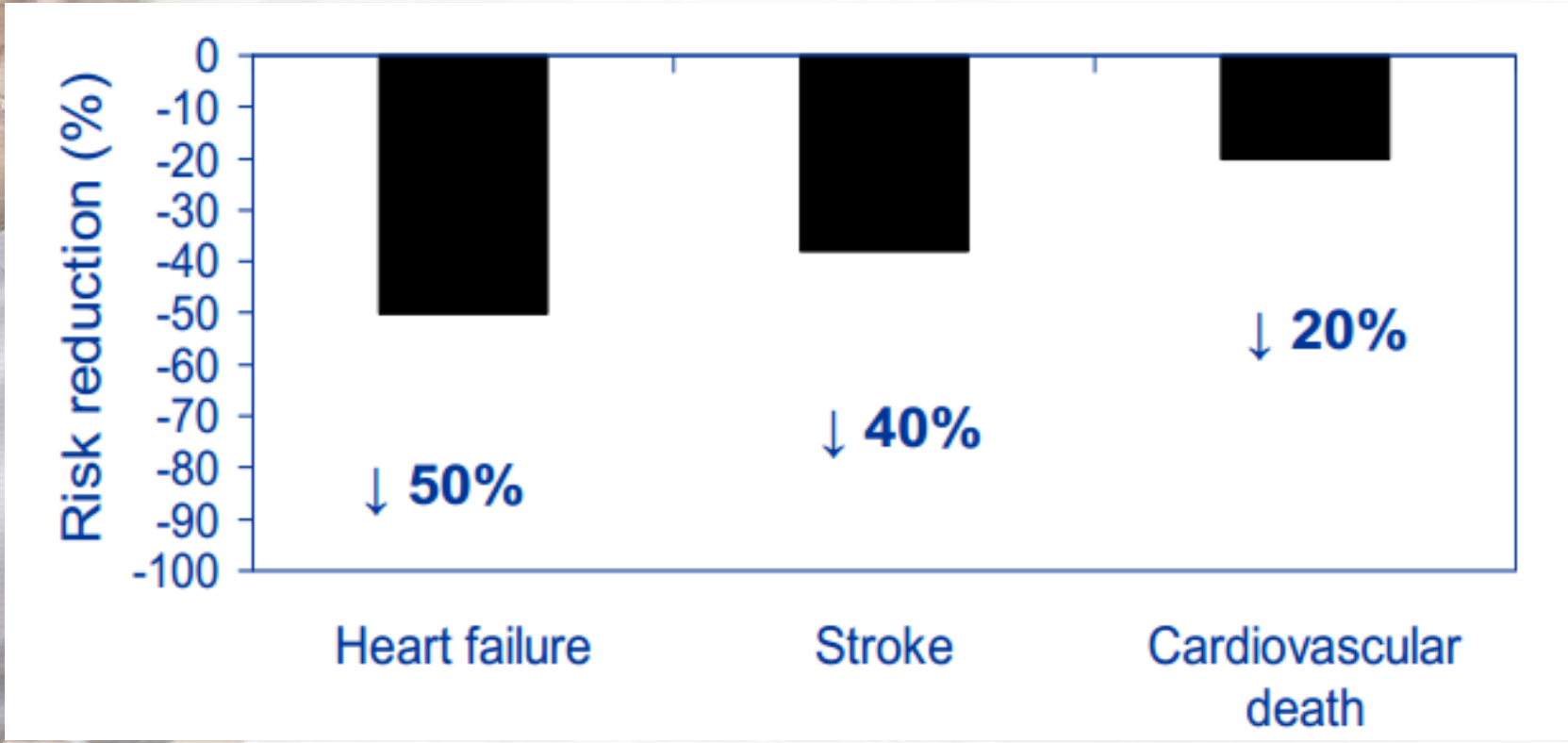
- The most easily recognized treatable risk factor for:
  - stroke,
  - IHD & MI,
  - HF,
  - PVD,
  - AF,
  - ESKD

Why treat HTN? (contin.)



- Prospective Studies Collaboration. *Lancet.* 2002;360:1903-1913

Why treat HTN? (contin.)



- Hebert, Archives Int Med 1993; Moser, Am Coll Cardiol 1996

Hypertension

- **Causes:**

1. **1ry:** "**Essential**" or "**Idiopathic**": 90-95% of cases

2. **2ry:** about 5% of cases
   - **Disease:**
     - Renal or renovascular disease
     - Coarctation of the aorta
     - Endocrine disease: eg:
       - Phaeochomocytoma
       - Cushing syndrome
       - Acromegaly
   - **Drugs** (Iatrogenic)

Drug-Induced HT:

1- Hormones:

- Steroids
- Estrogens & OC
- Erythropoietin

2- Autonomic:

- Phenylpropanolamines
- Clonidine withdrawal
- Ergotamine
- Sibutramine (Meridia)
- Methylphenidate

3- CNS:

- Amphetamines
- Anxiolytic: Buspirone
- Anesthetic:
  - Ketamine
  - Desflurane
- Antiepileptic: Carbamazepine
- Antiemetic: Metoclopramide
- Antidepressants: Venlafaxine

4- Antiinflammatory: NSAIDs

5- Immunosuppressive:

Cyclosporine/tacrolimus

Risk factors for 1ry HT

Controllable Risk Factors

1- ↑Salt intake
2- ↑Alcohol
3- ↑Stress
4- ↑Weight (Obesity)
5- ↓exercise

Uncontrollable Risk Factors

1- Heredity
2- Age
   - Men: 35 – 50
   - Women: after menopause
3- Race :More in African Americans

JNC 7 Classification of BP:

- The 7th report of the Joint National Committee on Detection, Evaluation & Treatment of High BP (JNC 7) classifies adult BP as shown

Classification	Systolic BP (mmHg)	Diastolic BP. (mmHg)
Normal	<120	<80
Prehypertension	120–139	80–89
Stage 1 hypertension	140–159	90–99
Stage 2 hypertension	≥160	≥100

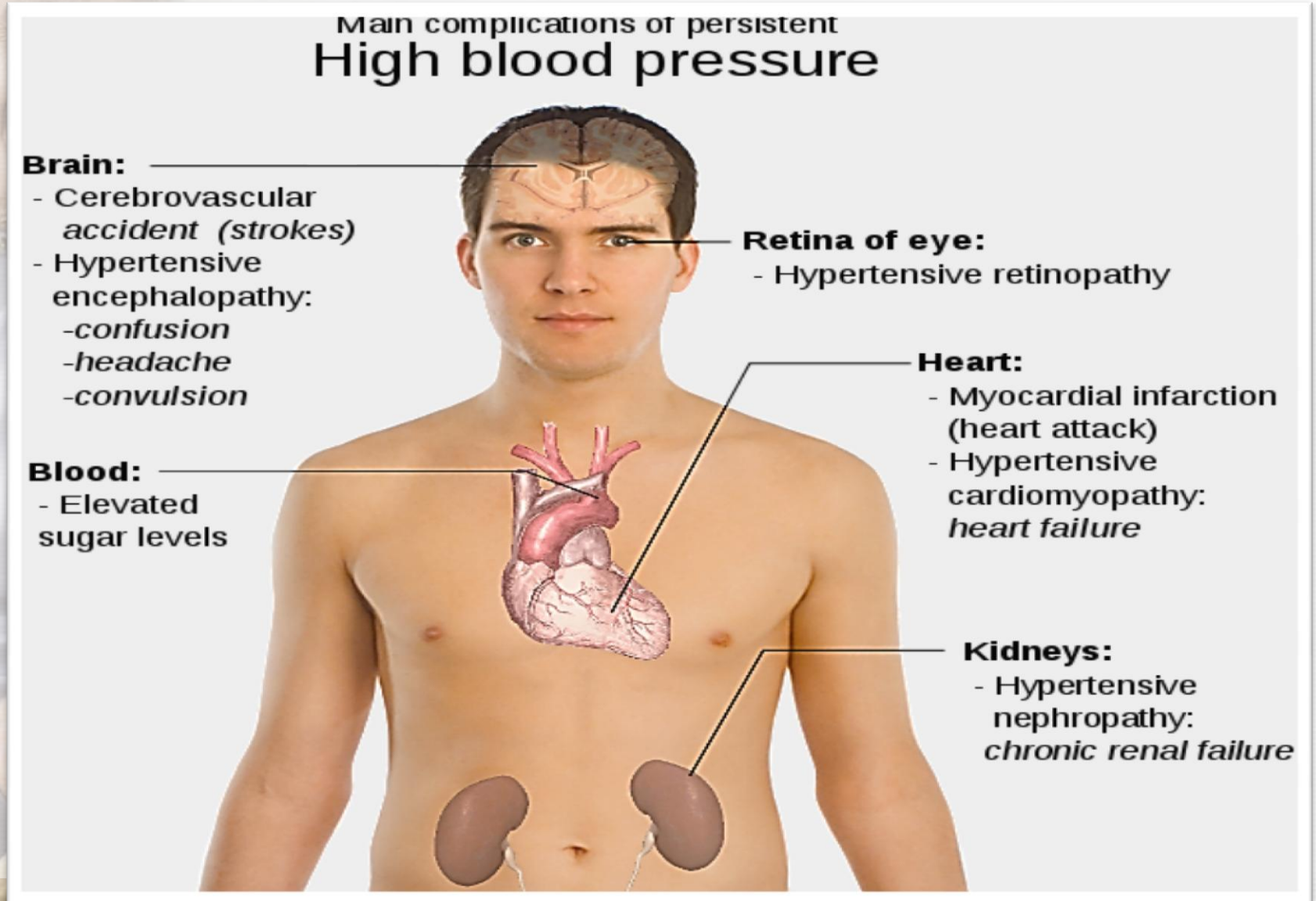
NB.:

- If systolic & diastolic lie in different stages, the highest is considered
- Diastolic bl.pr. is generally more reliable, while, systolic is more important in elderly

Manifestations

- **Usually NO SYMPTOMS! “The Silent Killer”**
- **May have:**
  - **Headache**
  - **Blurry vision**
  - **Chest Pain**
  - **Frequent urination at night**

Complications of HT

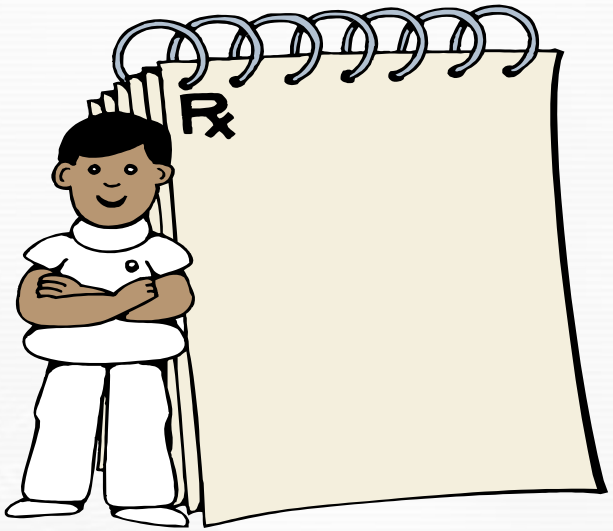


Ambulatory BP monitoring (ABPM)

- Now recommended in the UK by the NICE for the diagnosis of HTN.
- ABPM correlates better with TOD & provides a more accurate diagnosis of HTN.
- **Nocturnal dipping:** mean wake SBP falls by at least 10% during sleep.
  - ‘Super’ dipping (20–30%) is associated with neurological complications.
  - Non-dipping, or reverse dipping, is associated with increased CV mortality & TOD

Treatment of HT

- Nonpharmacological
- Pharmacological



Non pharmacological therapy

❑ Include:

	Approximate SBP Reduction
1- DASH eating plan	8-14 mmHg
2- ↓ Dietary sodium	2-8 mmHg
3- ↓ Alcohol consumption	2-4 mmHg
4- ↓ Weight	5-20 mmHg/ 10 kg weight loss
5- ↑ Physical activity	4-9 mmHg

❑ Indication:

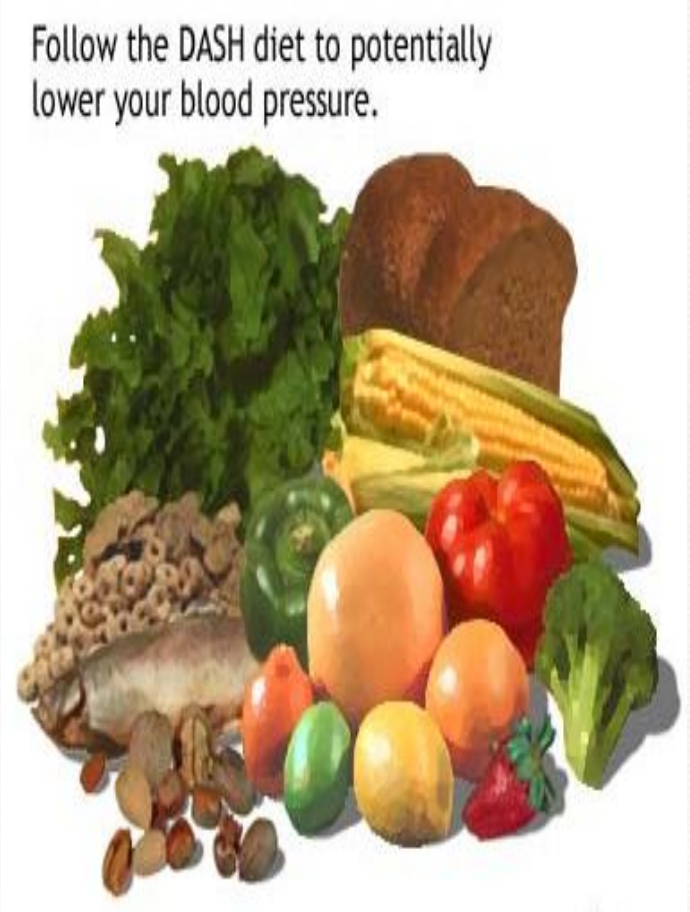
- patients with prehypertension.
- Patients diagnosed with stage 1 or 2 hypertension should be placed on lifestyle modifications & drug therapy concurrently.

DASH Eating Plan

1. ↓ saturated fat, cholesterol & total fat
2. ↓ red meat
3. ↓ sweets & sugar containing beverages

4. ↑fruits, vegetables & fiber
5. ↑ low fat diary products & plant protein
6. ↑ magnesium, potassium & calcium

- DASH Can reduce BP in 2 weeks (SBP, 8-14 mmHg)



Pharmacological treatment

- **1st line 1ry options: (ABCD)**
  - **Diuretics, ACE inhibitors (or ARBs)* , CCBs & β-Blockers****

- **Later line alternatives:**
  - **Sympatholytics**:
    - central α_2-agonists,
    - α_1-Blockers,
    - peripheral adrenergic neuron antagonists (guanithidine, reserpine, α-methyldopa)
    - direct renin inhibitors (Aliskiren)
  - **Direct arterial vasodilators:** (hydralazine, minoxidil, diazoxide)

***ACE inhibitors (or ARBs) are contraindicated in pregnancy**

****BBs are removed now from JNC 8**

Goal & ttt choice

Patient	Goal
• Age □ 60 y without DM or CKD	< 150/90 mmHg
• Age □ 60 y: HTN without major comorbidities • All ages: HTN + DM or CKD	< 140/90 mmHg

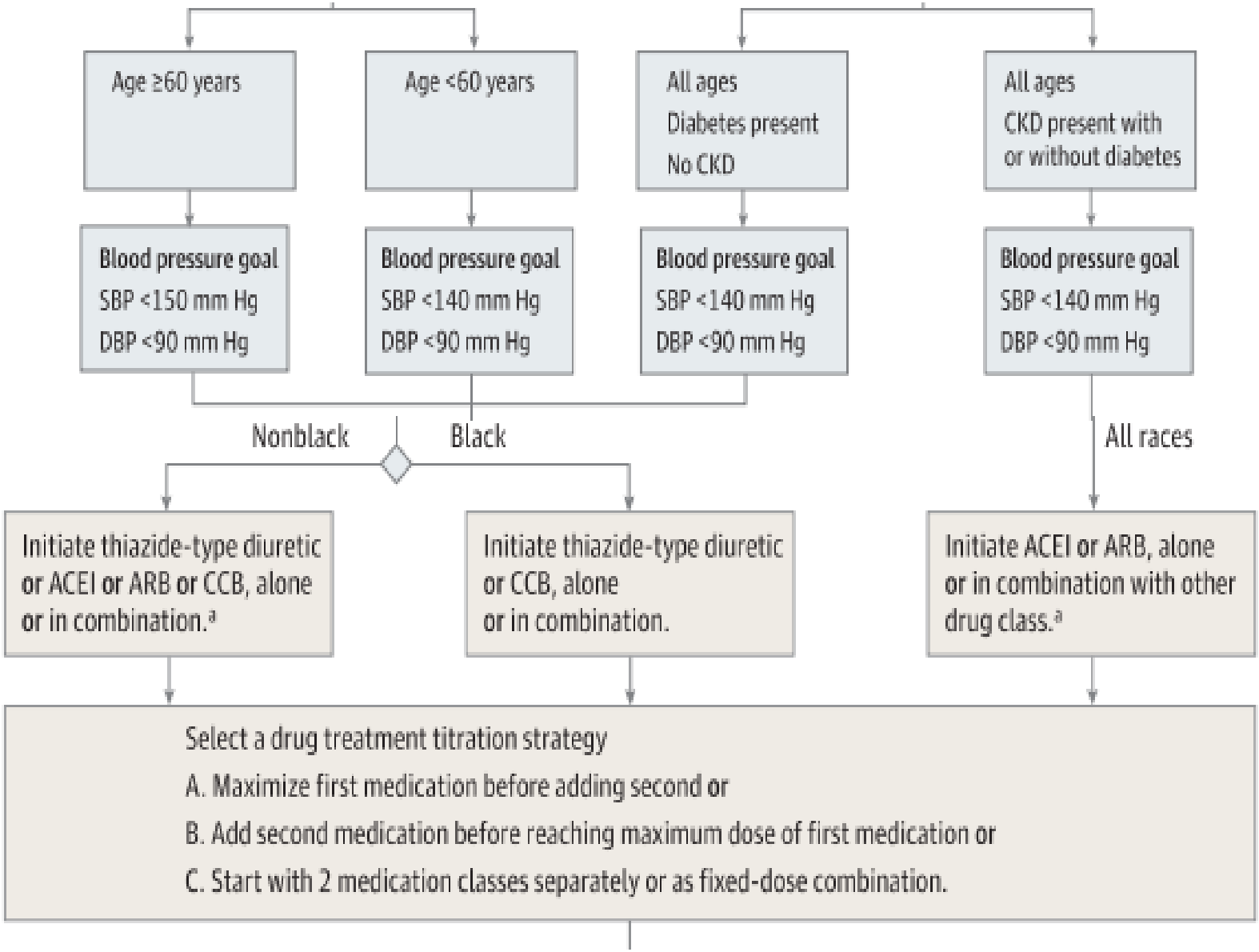
Patient	Treatment
Non-black	Initiate A,C, D alone or in combination
Black	Initiate C, D alone or in combination
All races with CKD	Initiate A alone or in combination with other drug classes

- Once antihypertensive medications have been started, they should be given for at **least 1 month** to achieve the treatment goal.

- If the BP goal is not reached within 1 month, the dose of the initial medication could be increased or a 2nd agent could be added

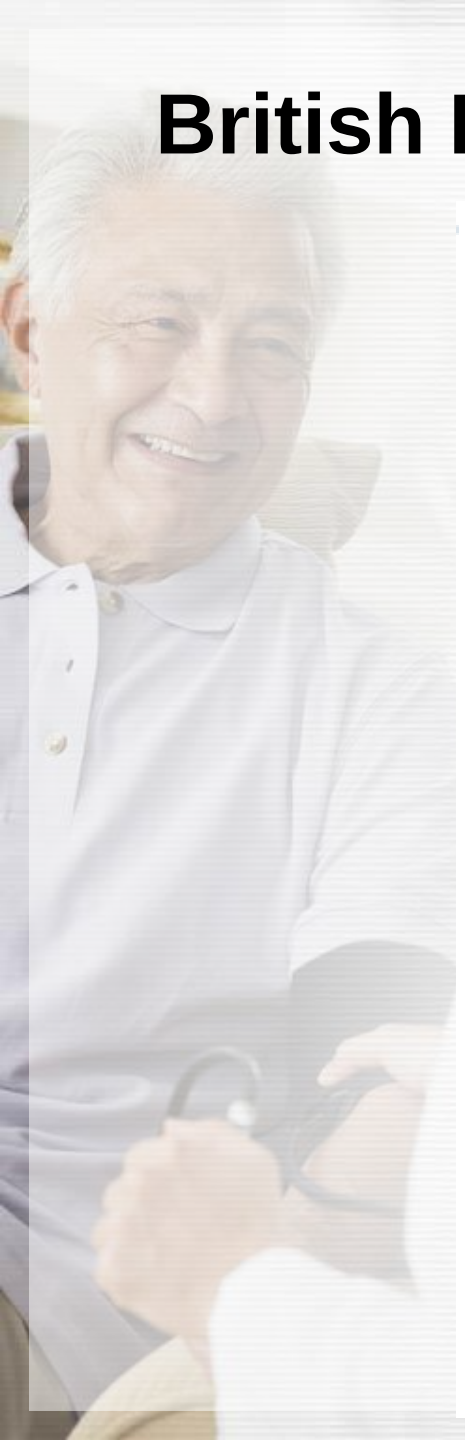
- If the BP goal cannot be reached with two medications, adding a 3rd medication is indicated.

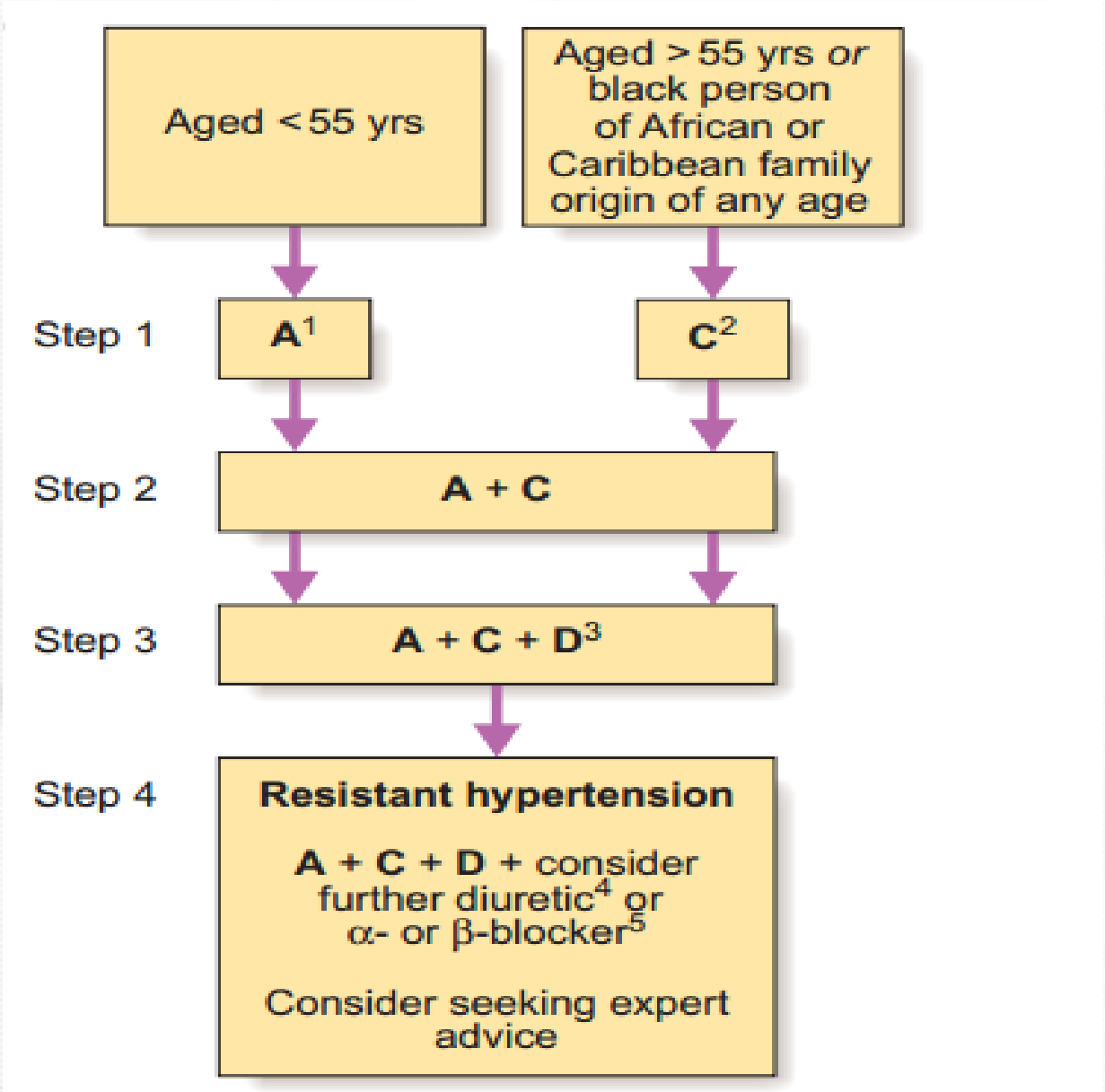
JNC-8 Hypertension Treatment Choices



James et al JAMA December 13 2014

British Hypertension Society guidelines.





Diuretics

1. **Thiazides:**
   - As Hydrochlorthiazide (HCTZ)
   - Chlorthalidone, Metolazone, indapamide

2. **Loop Diuretics:**
   - Furosemide (lasix) twice daily
   - Torsemide once daily

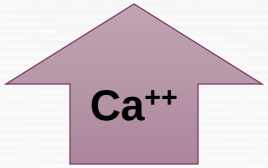
3. **Potassium-Sparing Diuretics:**
   1. **Non-aldosterone antagonists**: *Triamterene* & *Amiloride*.
   2. **Aldosterone antagonists (more potent)** : *Spironolactone & Eplerenone*

1- Thiazide Diuretics

- **Indication:**
  - **<u>of choice</u>** for treating HT *(it has both diuretic & direct VD effect)*
  - **NB.:** The action of thiazides is limited in patients with renal insufficiency (CrCl < 30 mL/min) due to reduced secretion into their site of action. An exception is **metolazone & indapamide**, which retain their potent action in patients with renal dysfunction

- **Dosage:**
  - Starting dose of HCTZ (Esidrex) or chlorthalidone of 12.5 mg once daily.
  - Maintenance dose of 25 mg once daily effectively lower BP with low incidence of SE.

- **SE:**
  - ***<u>Hpokalemia</u>*** , **Hypo**natremia , **Hypo**magnesemia, **Hypo**chloremic alkolosis
  - **Hyper** uricemia , **Hyper** glycemia , **Hyper** lipidemia , **Hyper** sensitivity
  - **<u>Hyper</u>**calcemia

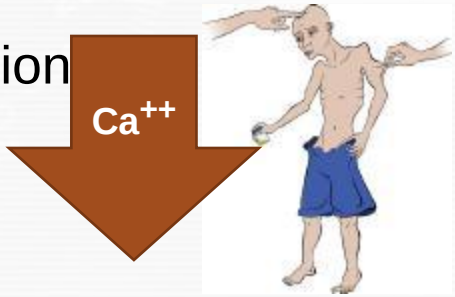


2- Loop diuretics

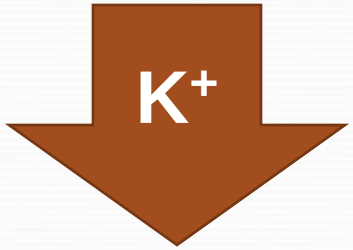
- **Indication:**
  - of choice for:
    - severe CKD (CrCl < 30 mL/min)
    - Lt ventricular dysfunction, or severe edema (because potent diuresis is often needed in these patients).

- **SE:**
  - ***Hpokalemia*** , **Hypo**natremia , **Hypo**magnesemia, **Hypo**chloremic alkolosis
  - **Hyper** uricemia , **Hyper** glycemia , **Hyper** lipidemia , **Hyper** sensitivity
  - **D**ecrease calcium, **D**eafness, **D**ehydration

    Drug-drug interaction



- ***NB.:*** *Loop diuretics have less effect on serum lipids & glucose*



Hypokalemia

- **Manifestation:**
  - Muscle fatigue or cramps.
  - Serious cardiac arrhythmias may occur, esp. in patients:
    - receiving digitalis,
    - with LV hypertrophy,
    - with IHD.

- **Monitoring:**
  - Serum K^+ should be measured at baseline & within 4 w of initiating therapy or after increasing diuretic doses.

- **Management:**
  1. Intermittent use of the least effective dose
  2. K^+ rich food (bananas, potatoes, avocados)
  3. KCl supplement (20 – 40 mEq/day)
  4. Add K^+ sparing diuretic

3- K^+-Sparing Diuretics

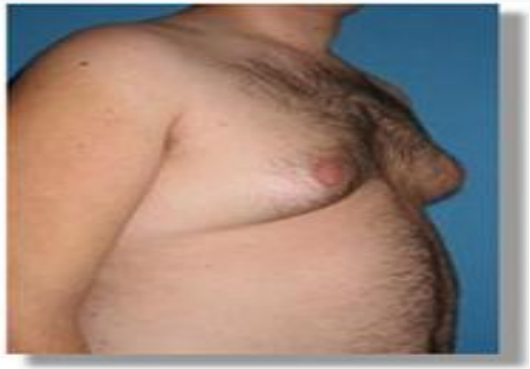
⌘ **Indication:**

- ⌘ Patients who develop hypokalemia while on a thiazide diuretic.
- ⌘ Spironolactone may be useful in resistant HTN

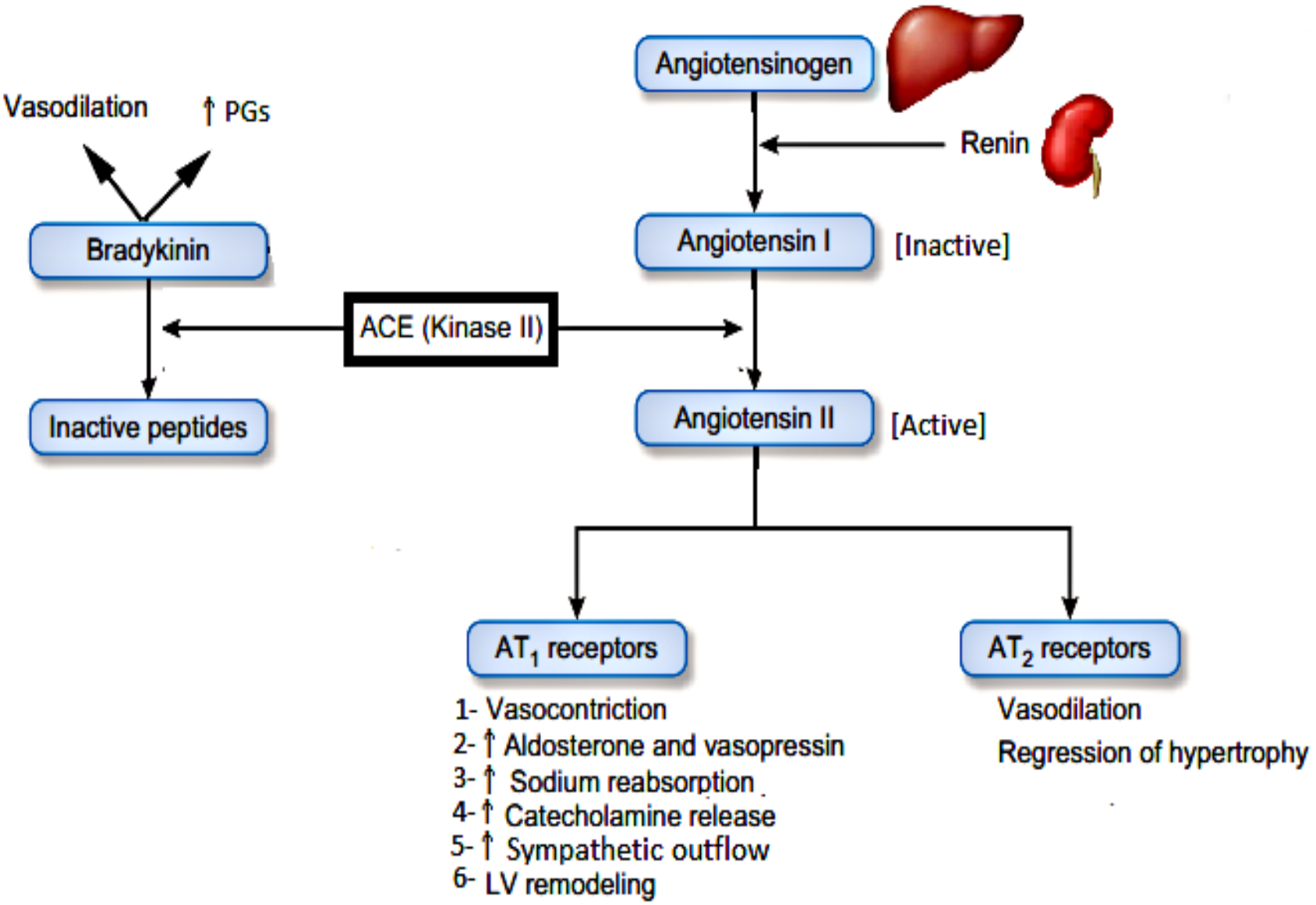
⌘ **SE:**

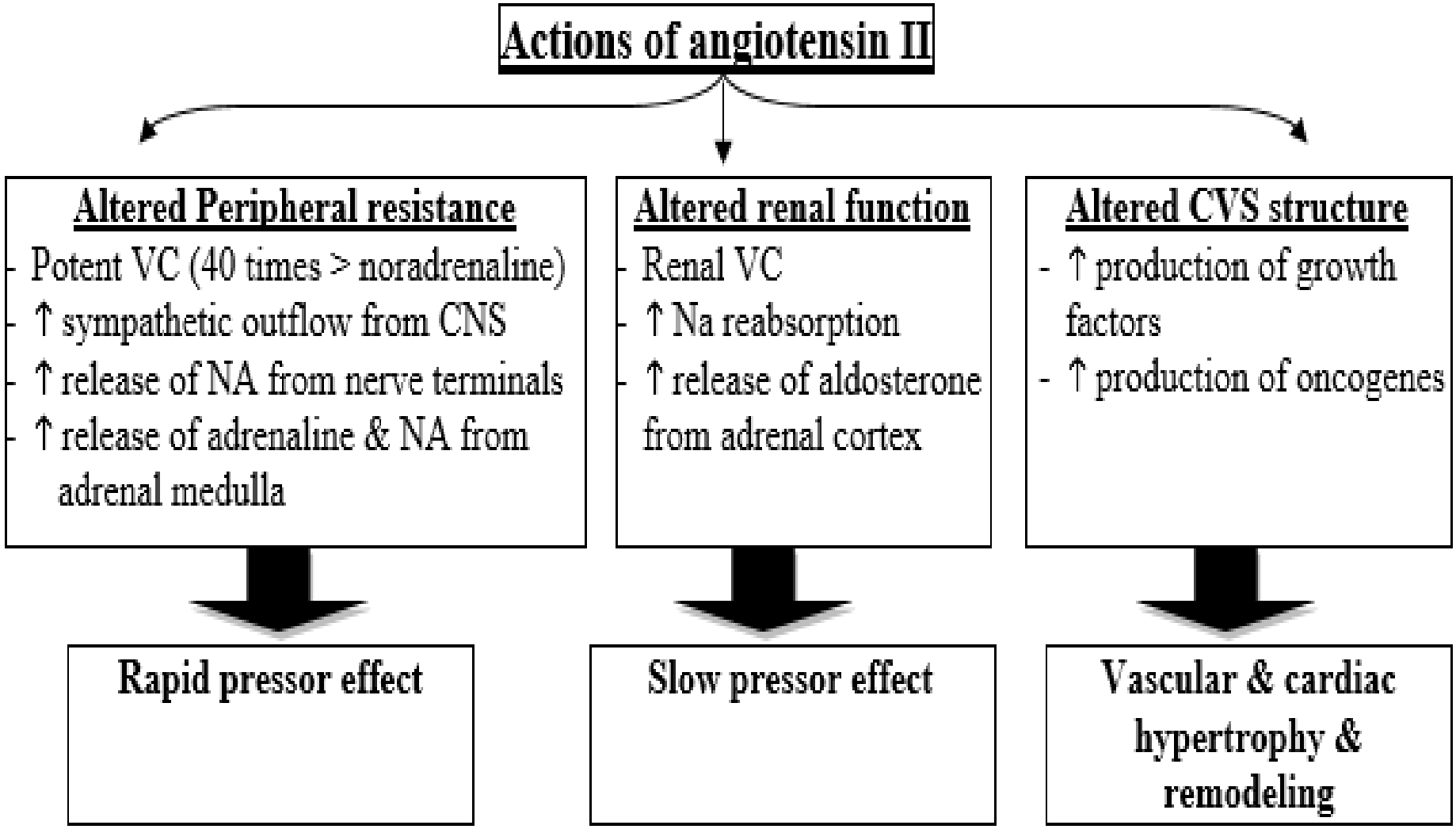
- **Hyperkalemia**, especially in:
  - chronic kidney disease
  - DM,
  - concurrent treatment with an ACE.I, ARB, NSAID, or K^+ supplement.

- **Gynecomastia** with **Spironolactone** (in up to 10% of patients), but this effect occurs rarely with eplerenone.



ACEIs


Angiotensinogen
Renin
Angiotensin I
[Inactive]
ACE (Kinase II)
Angiotensin II
[Active]
Vasodilation
↑ PGs
Bradykinin
Inactive peptides
AT1 receptors
1- Vasocontriction
2- ↑ Aldosterone and vasopressin
3- ↑ Sodium reabsorption
4- ↑ Catecholamine release
5- ↑ Sympathetic outflow
6- LV remodeling
AT2 receptors
Vasodilation
Regression of hypertrophy


Actions of angiotensin II
Altered Peripheral resistance
- Potent VC (40 times > noradrenaline)
- ↑ sympathetic outflow from CNS
- ↑ release of NA from nerve terminals
- ↑ release of adrenaline & NA from adrenal medulla
Altered renal function
- Renal VC
- ↑ Na reabsorption
- ↑ release of aldosterone from adrenal cortex
Altered CVS structure
- ↑ production of growth factors
- ↑ production of oncogenes
Rapid pressor effect
Slow pressor effect
Vascular & cardiac hypertrophy & remodeling

ACEIs

1. ***S.H containing:***
   - **Captopril (capoten): [**Active drug, given 2-3 times daily, absorption is affected by food]

2. ***Non-S.H containing:***
   - **Active drug**
     - Lisinopril (zestril) & *Enalaprilate* (given IV in emergency hypertension)
   - **Prodrugs**
     - Enalapril (renitec) - Perindopril - Benazepril - Ramipril – Trandolapril - Fosinopril

NB.:

- *Enalaprilate* (enalaprilic acid) is the active metabolite of *Enalapril*
- ACE.I is more effective in young white patients than in black or elderly
- All depend on renal excretion EXCEPT **fosinopril** (both renal & hepatic)

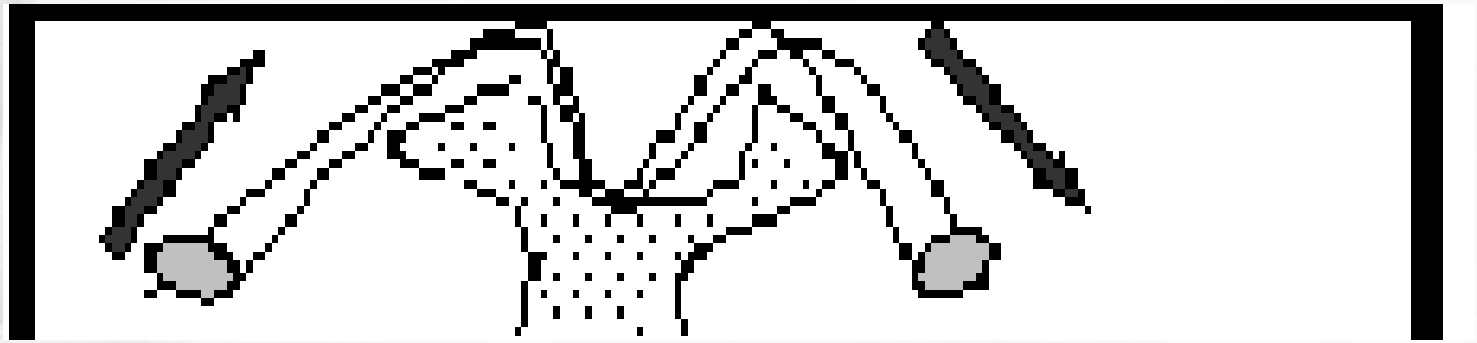
ACEIs dosing in HTN

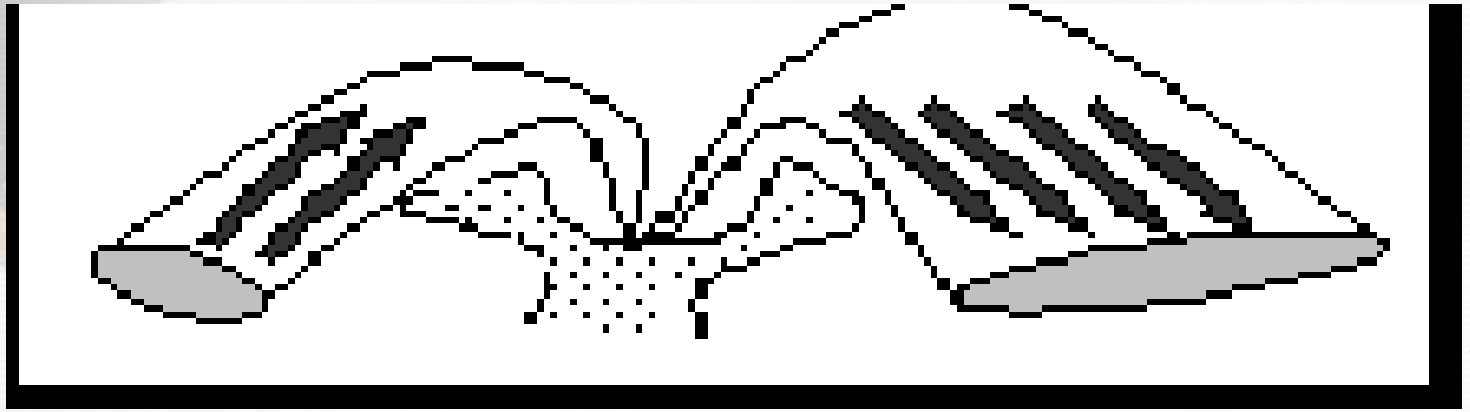
Drug	Usual Starting Dose (mg/d)[a]	Usual Dosage Range (mg/d)	Dosing Frequency
Benazepril	10	20–40	Daily to BID
Captopril	25	50–100	BID to TID
Enalapril	5	10–40	Daily to BID
Fosinopril	10	20–40	Daily
Lisinopril	10	20–40	Daily
Moexipril	7.5	7.5–30	Daily to BID
Perindopril	4	4–16	Daily
Quinapril	10	20–80	Daily to BID
Ramipril	2.5	2.5–20	Daily to BID
Trandolapril	1	2–4	Daily

ACEIs

Indications:

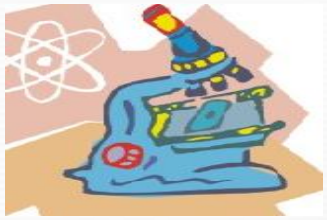
As 1st line treatment esp in DM , CKD ??? And HF ?????





ACEIs

Side effects:



1) *Related to S.H:*

1. Allergy
2. ↓ Taste (Dysgeusia)
3. Protinuria
4. Neutropenia

2) *Related to ↓ ACE*

1. Cough due to ↑ bradykinin
2. 1st dose Hypotension (esp. in elderly & heart failure). So tart with low dose with slow dose titration
3. Hyperkalemia
4. ARF esp. in bilateral renal art. stenosis

ACEIs

Contraindications:

1. Hypotension
2. Pregnancy (They are fetopathic➔ may cause oligohydramnios – pulmonary hypoplasia – growth retardation – fetal death)
3. Bilateral renal artery stenosis

Drug interactions:

1. Na^+ depleting **d**iuretics ➔ ↑ initial Hypotension
2. K^+ retaining **d**iuretics ➔ ↑ hyperkalemia
3. NS**A**ID ➔ ↓ Hypotensive Effect Through Inhibition of Bradykinin & PGs
4. **A**ntacids ➔ ↓ absorption

AT-II Blockers (ARBs)

- **<u>Candesartan - Losartan (Cozar) - Olmesartan – Valsartan – Eprosartan -Irbesartan – Telmisartan</u>**

- Actions & Uses ➔ As ACEI
- Side effects ➔ As ACEI but ***with less cough***

ARBs dosing in HTN

Drug	Starting Dose (mg/d)[a]	Usual Dosage Range (mg/d)	Dosing Frequency
Azilsartan medoxomil	80	80	Daily
Candesartan cilexetil	16	8–32	Daily to BID
Eprosartan mesylate	600	600–800	Daily to BID
Irbesartan	150	75–300	Daily
Losartan potassium	50	25–100	Daily to BID
Olmesartan medoxomil	20	20–40	Daily
Telmisartan	40	20–80	Daily
Valsartan	80–160	80–320	Daily

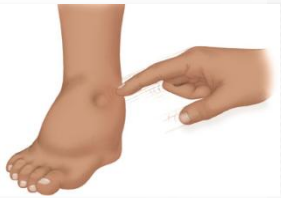
CCB

Classification:

- **Dihydropyridine:**
  - Short acting: Nifedipine (Adalat, Epilat)
  - Long acting: Amlodipine (Norvasc) – nisoldipine – felodipine – isradipine
- **Non-dihydropyridine:** Verapamil (isoptin) – Diltiazem (cardizem)

Side effects:

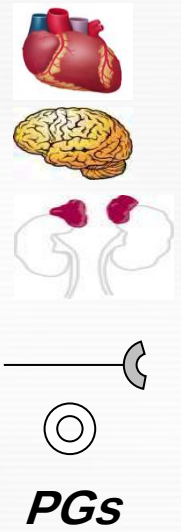
1. ***Bl.V.:*** Headache – flush – Hypotension – ankle oedema
2. ***Heart:***
   - **Brady**cardia with *Diltiazem* & marked with *verapamil*
   - Reflex **Tachy**cardia with *nifedipine*
3. ***G.I.T.:*** Constipation is marked with *verapamil*.



β-Blockers

- **indications:**
  1. HT with tachyarrhythmia
  2. HT with compelling indication (eg.: HF, CAD)

- **Mechanism of antihypertensive effect:**
  1. Block β-1 of Heart ➔↓ COP.
  2. Block β-1 of CNS ➔↓ Sympathetic outflow.
  3. Block β-1 of Kidney ➔↓Renin.
  4. Block Pre-synaptic β ➔↓Release of Nor-adr.
  5. Resetting the sensitivity of Baro-receptors.
  6. ↑ Prostacyclin (VD) synthesis



- **Classification:**
  1. **according to Selectivity**
  2. **according to Lipid solubility**

Classification according to Selectivity

	ISA	L.A	Notes
A. Non- selective:			
Pindolol	+	+	
Oxprenolol	+	+	
Propranolol (Inderal)	No	+	Extensive hepatic 1st pass metabolism
Sotalol	No	No	
Nadolol	No	No	
Timolol	No	No	Eye drop in glaucoma.
B. Cardio-selective (B_1)			
Acebutolol	+	+	
Atenolol (Tenormin)	No	No	
Bisoprolol (Concor)	No	No	
Betaxolol	No	No	
Metoprolol (Lopressor)	No	+	
Esmolol	No	No	Ultrashort. I.V. Infusion.

NB.: Vasodilator B- Blockers:

1. **β_2-Partial agonist:**
   - Celiprolol: (Selective β_1 Block – No ISA – No LA)

2. **Nitrogenic effect** (↑ production of NO)**:**
   - Nebivolol

3. **α_1-blocking effect:**
   - Labetalol – Bucindolol – Carvedilol (dilatrend) - Medraxalol

Classification of according to Lipid solubility

	Lipophilic	Hydrophilic
1. G.I.T. Absorption:	- Well Absorbed.	- Poorly absorbed.
2. Passage across B.B.B.:	- Pass BBB - has CNS. effects.	- Not pass BBB - has little CNS effect
3. Metabolism:	- Extensive hepatic.	- Mainly Renal.
4. Duration of Action:	- Short (4-6 Hours)	- Longer (12-24 Hs)
5. Examples:	- Propranolol. - Oxprenolol. - Metoprolol. - Timolol	- Nadolol. - Atenolol. - Sotalol. - Bisoprolol

SE & contraindications

	Side effects	Contraindications
I. CNS:	- Sedation - depression - sleep disturbances (only in lipophilic B.B. crossing BBB)	Severe depression (use hydrophilic B.B.)
II. CVS: **1.Heart:** **2.B.V.** **3.B.P.**	1.Heart failure - Heart block - Bradycardia ---- 2.Cold extremities, Raynaud's phenomenon, numbness, tingling 3.Hypotension----------	• H.F. - Hear block - severe bradycardia • With Verapamil: ➜ H.F. & H. Block • Variant angina . • Raynaud's phenomenon & P.V.D & alone in pheochromocytoma • Hypotension
III. Respiration	- Precipitate acute attack of B.A. in asthmatics	- BA (use cautiously selective B_1)*
IV. Metabolism	1. **Hypoglycemia** (severe in patient receiving insulin or oral hypoglycemic [coma can occur without warning (silent death)] 2. Hyperkalemia 3. Atherosclerosis (↓ HDL & ↑ Triglycerides)	• Hypoglycemia in insulin or oral hypoglycemic treatment.
V. Others	Sudden withdrawal➜ withdrawal syndrome ➜ sympathetic over activity and precipitation of anginal attack even myocardial infarction	• Never stop suddenly.

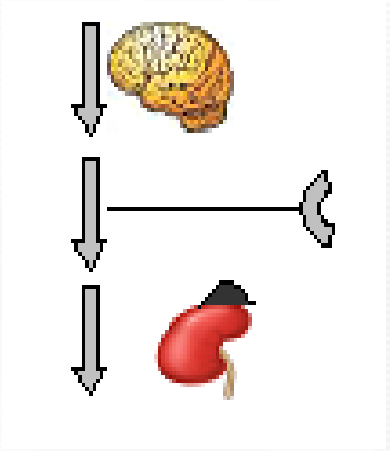
* cardioselectivity is dose dependent and is lost as dosages are increased. Therefore, **no β-blocker is totally safe in pts with BA**

α_1-Receptor Blockers

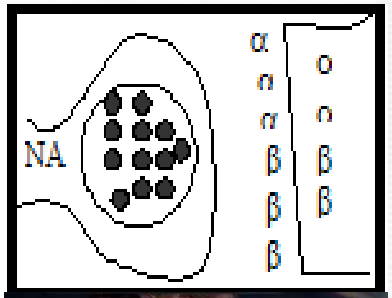
- **Prazosin (Minipress),**
- **Terazosin,**
- **Doxazosin (Cardura)**

- **Side Effects:**
  1. **Initial Syncopal Attack** (1st dose phenomenon). Attack of severe postural hypotension. Start by small dose while patient is recumbent (at bed time), then increase the dose gradually
  2. **Sexual dysfunction** & failure of ejaculation after long use in males
  3. **Salt & H_2O retention** as it ↓C.O. →↓ R.B.F. So, Diuretic is added.

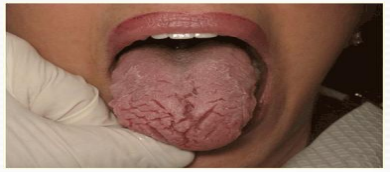
Central α_2-Agonists



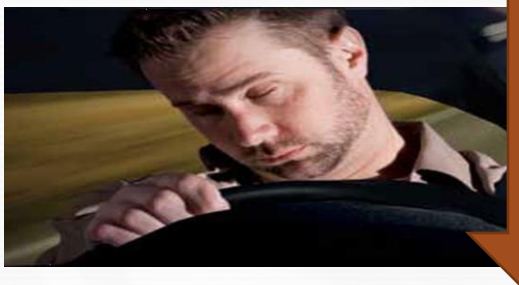
- **Include:**
  - **Clonidine,** guanabenz, guanfacine, & methyldopa
- **Mechanism:**
  - Selective α_2 & Imidazoline I_1 Agonist (15 : 1)
    ➔Hypotension by:
    1. ↓ Sympathetic outflow from C.N.S.
    2. Presynaptic ↓Release of N.A.
    3. Kidney: ↓ Release of Renin



- **Side effects of centrally acting drugs**
  1. ***Dropping dose suddenly (Sudden Withdrawal)***
     ➔ ***Rebound severe HT***
     ttt by reusing Clonidine or by α-Blocker + βB.
  2. ***Drowsiness & Sedation***
  3. **Dry mouth (xerostomia) & Dry nasal mucosa**



- ***Moxonidine (Physiotens) & Rilmenidine (Hyperium):***
  - They are selective I_1 agonist used in ttt of hypertension
  - *Less liable to cause sedation*



Peripheral adrenergic neurone depressants

- **Include**
  - Guanethidine
  - Reserpine
  - Methyldopa (act centrally also)

Guanethidine	Reserpine	α-Methyldopa
***Kinetic**	***Kinetic:**	***Kinetic**
- Incompletely absorbed - Not pass BBB - Slowly excreted in urine	- Well absorbed - Passes BBB - Slowly excreted in urine	- Well absorbed - Passes BBB - Transformed to α-methyl NA
Mechanism (↓Release)	**Mechanism: (Depletion)**	**Mechanism (↓ synthesis & Central)**

Side effects

1) Parasymp. Predominance:
   1. Nasal congestion
   2. Bradycardia
   3. Postural hypotension
   4. Diarrhea

2) Others:
   1. **Parotid pain**
   2. Failure of ejaculation

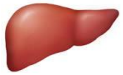
1) Parasymp. Predominance:
   1. Nasal congestion {Stuffiness}
   2. Bradycardia
   3. Hypotension
   4. Diarrhea

2) Others:
   1. Na & H_2O retention
   2. Weight gain
   3. **Peptic ulcer**
   4. Endocrinal disturbance
   5. Breast cancer.
   6. Impotence

3) C.N.S:
   1. Psychic depression
   2. Nightmares
   3. Parkinsonism

1) Parasymp. Predominance:
   1. Nasal congestion
   2. Bradycardia
   3. Hypotension
   4. Diarrhea

2) Other:
   1. Na & H_2O retention
   2. weight gain
   3. **Liver toxicity**
   4. **Bone marrow Depression**



3) C.N.S:
   1. Psychic depression
   2. Night mares
   3. Parkinsonism
   4. **Sedation**

Direct renin inhibitors (Aliskirin (Tecturna®))

- Inhibit directly the renin
- Similar to ACEIs & ARBs & contraindicated in pregnancy
- Used once orally as an alternative antihypertensive agent

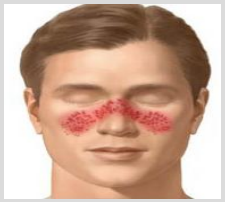
Direct Arterial Vasodilators

- **Include:**
  - Hydralazine - Minoxidil - Diazoxide

- **Actions & effects :**
  1. Direct Arterio-dilator ➔ ↓ Bl.Pr ➔ useful in Hypertension
  2. ↓ Bl.Pr ➔ ↑ symp & ↓ after load ➔↑ Co ➔ useful in H.F

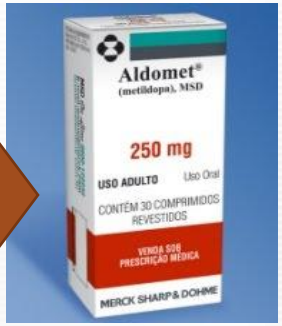
- **Disadvantages & general SE:**
  1. ↓ Bl.Pr ➔ ↑ sympathetic leading to:
     - Tachycardia & Angina ➔ **[Add β- blockers]**
     - ↑Rennin ➔ edema ➔ **[Add diuretic]**

     *(So, **not** used alone, but in combination with βB& diuretics)*
  2. V.D ➔ Headache – congestion – flush

(1) Hydralazine	(2) Minoxidil	(3) Diazoxide
Side effects		
1. Hypersensitivity in the form of: - Rash - Rheumatoid arthritis - **Systemic lupus erythematosus like syndrome**  2. GIT upset 3. Peripheral neuritis	. Hypertrichosis	1. Hyperglycemia 2. Hyperuricemia (as it is related to Thiazide diuretic)
Uses		
Orally& I.V 1. Hypertension & emergency 2. H.F	Orally 1. Hypertension 2. H.F 3. Locally in alopecia	I.V Emergency Hypertension

SPECIAL POPULATIONS

- **Pregnancy:**
  - **Methyldopa (Aldomet)** is the drug of choice
  - Alternatives: BB & CCBs.
  - ACEI & ARBs are contraindicated (teratogens)



- **African Americans:**
  - **Thiazides & CCBs** are 1ST Lines (if they have no CKD).

- **Older People:**
  - **Diuretics & ACEI** can be used safely, but in **smaller-than-usual** initial doses, and titrations should occur over a longer period to minimize the risk of hypotension.
  - **CCBs & thiazide-type diuretics should be used instead of ACEIs & ARBs in patients 75 with impaired kidney function due to the risk of hyperkalemia.**

HYPERTENSIVE CRISIS

- **Definition:** Severe elevation of BP ≥ 180/**120** & may be classified into:

Hypertensive urgency:	Hypertensive emergency:
• without or with **chronic** EOD (eg. Encephalopathy, unstable angina, AKI & papilledema) • Not life threatening • **ttt:** adjusting maintenance therapy by adding a new antihypertensive and/or increasing the dose of a present drug.	• Associated with **acute** EOD • Life threatening • **ttt:** require immediate BP reduction to limit new or progressing target-organ damage.

Goal in treatment of hypertensive crisis

- **The goal:** **not** to lower BP to normal; as rapid drops in BP may cause end-organ ischemia or infarction.

Hypertensive urgency:	Hypertensive emergency:
• Reductions of BP with oral drugs to **stage 1** values over a period of 24-48 hours. • Should be reevaluated within & no later than 7 days (preferably after 1-3 days).	• Reduction of BP with IV drugs. The initial target is ↓ **MAP 25%** within minutes to hours. • If BP is then stable, diastolic BP can be reduced to **100-110** mm Hg within the next 2-6 hours. • Additional gradual decrease toward the **goal** BP after 24 -48 hours.

Treatment of hypertensive crises

Hypertensive urgency:	Hypertensive emergency:
Short-acting oral drugs (**captopril or labetalol**) followed by careful observation for several hs to ensure gradual BP reduction. • **Captopril** 25-50 mg may be given at 1- 2 h intervals. Onset:15- 30 min • **Clonidine** (0.1–0.2 mg) followed by 0.1 mg/hour until the desired response • **Labetalol** 200-400 mg, followed by additional doses every 2- 3 h. • **NB.:** Immediate-release ***Nifedipine*** should never be used for urgencies due to risk of severe hypotension leading to MI & strokes	**Nitroprusside** is the drug of choice in most cases. • Given as a IV infusion (0.25 -10 mcg/kg/min.) • Onset: immediate & disappears within 1-2 min of discontinuation. • When infusion is continued □72 h., serum **thiocyanate levels** should be measured, & infusion should be stopped if the level □12 mg/dL. • **NB.:** Exception in emergency: patients with an acute ischemic stroke where maintaining an elevated BP is needed for a longer period of time.

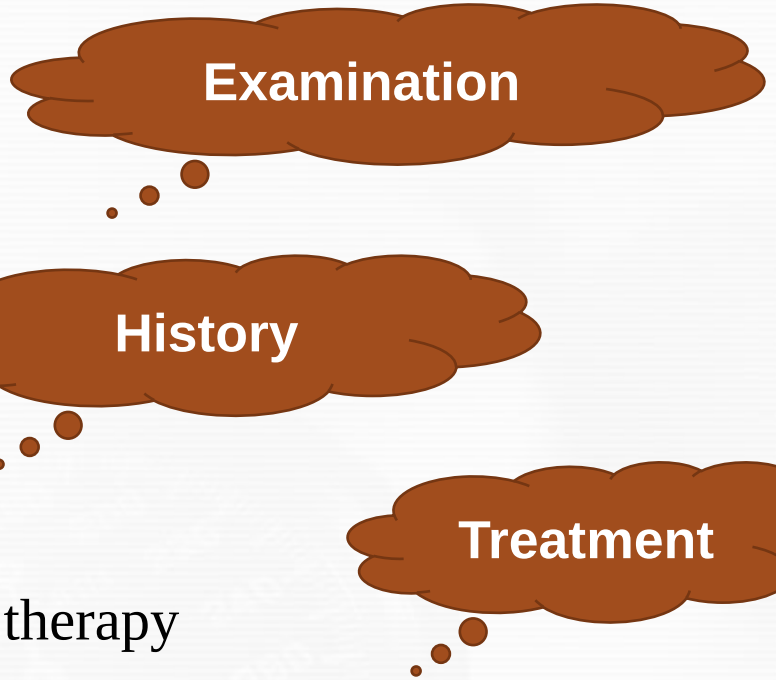
Other Parentral drugs used in emergency HT

- Nitroprusside
- Nitroglycerin
- Nicardipine - Clivadipine

- Diazoxide
- Esmolol
- Enalaprilate
- Fenoldopam

- Hydralazine
- Labetalol

Causes of Resistant HT



1. Improper BP measurement
2. Identifiable causes of HTN

3. Excess sodium intake
4. Excess alcohol intake

5. Inadequate diuretic or medication therapy
6. Drug actions & interactions:
    - NSAIDs, sympathomimetics, oral contraceptives, OTC drugs & herbal supplements

NB.: Resistant HT usually respond to aldosterone antagonist (spironolactone) (This effect is seen in those with or without elevated aldosterone)

GOOD LUCK

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