Medicine Team Notes

Hypertension

429 Medicine Team

Special thanks to: Zeina AlHalees

Definition

- The 4th most common cause of death worldwide
- Directly and indirectly responsible for >20% of all deaths
- 29-30% incidence of hypertension in the 18 year and older population of the United States
- 9.1% and 8.7% the population of Saudi Arabia with hypertension 160/95 mmHg
- Onset stage 25-55 years mainly in 40-50y
- Occurs over 30% of persons older than 65 y
- Only 34% of persons with hypertension have their blood pressure under control
- In 90%-95% of cases no cause can be found: primary hypertension (essential)
- Secondary hypertension 5-10%

BP Classification	Systolic BP mmHg		Diastolic BP mmHg
Normal	<120	And	<80
Pre-hypertension	120-139	Or	80-89
Stage 1 Hypertension	140-159	Or	90-99
Stage 2 Hypertension	≥160	Or	≥100

Essential Hypertension

Unknown (multifactorial) etiology

Risk Factors

- Age & gender (more common in men)
- Obesity; metabolic syndrome
- Excessive salt intake; low potassium intake
- Excessive alcohol intake
- Polycythemia
- Lack of exercise
- Non-steroid anti-inflammatory drugs
- Family history of essential HTN
- Caffeine and smoking increase the BP acutely but are NOT risk factors for the development of chronic essential HTN

Secondary Hypertension

- Primary renal disease (most common); **renal artery stenosis**, CKD, polycystic kidneys
- Oral contraceptives (most common secondary cause in young females) /drugs
- Sleep apnea syndrome
- Pheochromocytoma (a catecholamine-secreting tumor)
- Primary hyperaldosteronism (aldosterone-secreting adenoma/adrenal hyperplasia)
- Renovascular disease (due to atherosclerosis; elderly or fibromuscular dysplasia; young ♀)
- Other endocrine disorders e.g. thyrotoxicosis, acromegaly, Cushing's
- Coarctation of the aorta (congenital; constriction at origin of Lt. subclavian)

Stages

National Institute for Health and Clinic Excellence Hypertension Guidelines 2011
•Stage 1
-Clinical Blood Pressure – 140/90 mmHg
-Ambulatory Blood Pressure Monitoring (ABPM) – 135/85 mmHg
-Home Blood Pressure Monitoring (HBPM) - 135/85 mmHg

•Stage 2
-Clinical Blood Pressure – 160/100 mmHg
-Ambulatory Blood Pressure Monitoring (ABPM) – 150/95 mmHg
-Home Blood Pressure Monitoring (HBPM) - 150/95 mmHg

•Severe hypertension (Stage 3)
-Clinical Blood Pressure – 180/110 mmHg

Measurement of Blood Pressure

•Apply to adults on no antihypertensive medications and who are not acutely ill
•If there is a great difference in category between SBP & DBP, the higher value determines the severity of the hypertension
•When measuring on both arms: take the HIGHER reading
•When measuring on one arm several times: take the LOWER reading

Types of Instruments

- Sphygmomanometer
- Home blood pressure monitoring
- Ambulatory pressure monitoring

Measurement

- Patient should be seated with the back straight and the arm supported at heart level. The patient should rest for 5 minutes before 2nd measurement
- The bladder of the pressure cuff should encircle at least 80% of the upper arm
- BP varies widely throughout a 24-hr period; a single elevated reading is not diagnostic.
- If BP is ≥140/90 mmHg, perform second reading. If second reading is still high, take third reading.
- The diagnosis of mild hypertension should not be made until the blood pressure has been measured on at least three to six visits
- Average of 10 to 15 mmHg decrease between visits 1 and three

White Coat Hypertension

A phenomenon in which patients exhibit elevated BP in a clinical setting but not in other settings. It is believed that this is due to the anxiety.

- Approximately 20 to 25% of patients with mild office hypertension
- More common in elderly
- Infrequent in patients with office diastolic pressures ≥105 mmHg

Complications

1. The major complications of HTN are cardiac complications (coronary artery disease [CAD], CHF w/left ventricular hypertrophy [LVH]), stroke, and renal failure. These account for the majority of deaths associated with untreated HTN.
2. HTN has effects on the following organs (target organ damage):
   a. **Cardiovascular system**
      i. HTN is a major risk factor for CAD, with resultant angina and MI.
      ii. CHF is a common end-result of untreated HTN as LVH occurs
      iii. Most deaths due to HTN are ultimately due to MI or CHF
      iv. HTN predisposes the patient to peripheral vascular disease (PVD).
      v. HTN is associated with increased incidence of aortic dissection
   b. **Eyes (retinal changes)**
   c. **CNS**
      i. Increased incidence of intra-cerebral **hemorrhage (stroke)**
      ii. Increased incidence of other stroke subtypes as well (transient ischemic attacks [TIAs], **ischemic** stroke, and **lacunar** stroke)
      iii. Hypertensive **encephalopathy** when BP is severely elevated (uncommon)
   d. **Kidney**
      i. **Arteriosclerosis** of afferent and efferent arterioles and glomerulus—**"nephrosclerosis"**
      ii. Decreased GFR and dysfunction of tubules—with eventual renal failure

- Begins as blood pressure arise above 110/75 mmHg
- More common in cigarette smoking, dyslipidemia, and diabetes. In older patients, systolic pressure
  - Risk of heart failure at all ages
- Life-threatening emergency

Hypertensive Emergency

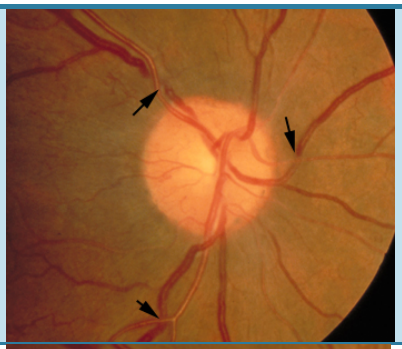
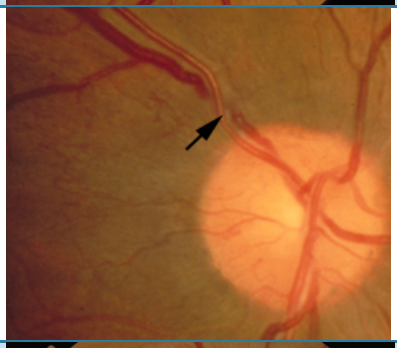
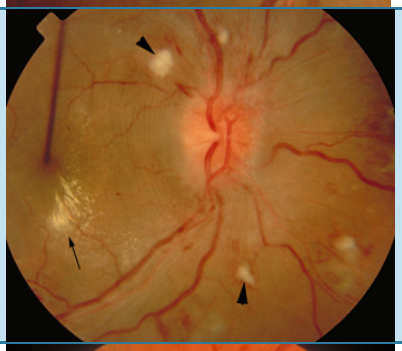
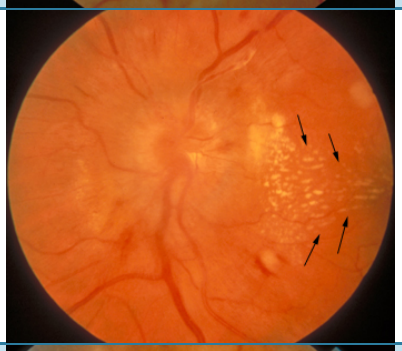
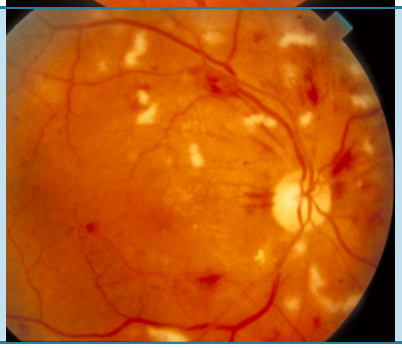
Severe hypertension (diastolic blood pressure >120 mmHg) in end organ damage (MI, STROKE, AKI, CHF) = severe headache, altered mentation, visual disturbances. Give IV agents e.g. nitroprusside, labetalol, or nitroglycerin

Hypertensive Urgency

- Severe hypertension (diastolic blood pressure above 120 mmHg) in asymptomatic patients with no evidence of acute end-organ
- There is **no proven benefit from rapid reduction of BP** in these patients
- BP should be lowered over a period of 24 hours with oral agents

Malignant Hypertension

- Marked hypertension with encephalopathy (confusion etc) & retinal hemorrhages, exudates, or papilledema
- Associated with a diastolic pressure >120 mmHg

Grade	Description	A:V Ratio	
I	• ***Normal A:V ratio is 2:3*** • **Minimal Narrowing of the retinal arteries** • **Generalized arteriolar constriction seen as "silver wiring"** • **Vascular tortuosities**	**50%**	
II	Narrowing of the retinal arteries in conjunction with regions of focal narrowing and arteriovenous nipping (the vessel wall thickens due to arteriolosclerosis, the vein is displaced. If, as the artery crosses over the vein, the vein is compressed, it will appear "nicked")	**33%**	
III	**Abnormalities seen in Grades I and II, as well as** • **Retinal hemorrhages (intra-retinal)** • **Hard exudation (exudation of fluid & lipids)** • **Cotton-wool spots (contain cell organelles; are due to damage to nerve fibers)**	**25%**	
IV	Abnormalities encountered in Grades I through III, as well as • Swelling of the optic nerve head • Macular star (**Blurring of the borders of the optic disk with hemorrhages**)	**<20%**	
	Flame-shaped hemorrhages (blood accumulates at the level of nerve fiber layer)		

Diagnosis

Clinical Presentation

- Asymptomatic
- Headache
- Chest discomfort
- Symptoms of complications

Screening

- Every two years for persons with systolic and diastolic pressures <120 mmHg and 80 mmHg
- Yearly for persons with a SBP of 120 to 139 mmHg OR DBP of 80-89 mmHg

History

- Presence of precipitating or aggravating factors
- Natural course of the blood pressure
- Extent of target organ damage
- Presence secondary HTN of other risk factors for cardiovascular disease

Duration of hypertension	**Presence of other risk factors**
Last known normal blood pressure	Smoking
Course of the blood pressure	Diabetes
Prior treatment of hypertension	Dyslipidemia
Drugs: types, doses, side effects	Physical inactivity
Intake of agents that may cause hypertension	**Dietary history**
Estrogens	Sodium
Adrenal steroids	Alcohol
Cocaine	Saturated fats
Sympathomimetics	**Psychosocial factors**
Excessive sodium	Family structure
Family history	Work status
Hypertension	Educational level
Premature cardiovascular disease or death	**Sexual function**
Familial diseases: pheochromocytoma, renal disease, diabetes, gout	**Features of sleep apnea**
Symptoms of secondary causes	Early morning headaches
Muscle weakness	Daytime somnolence
Spells of tachycardia, sweating, tremor	Loud snoring
Thinning of the skin	Erratic sleep
Flank pain	
Symptoms of target organ damage	
Headaches	
Transient weakness or blindness	
Loss of visual acuity	
Chest pain	
Dyspnea	
Claudication	

Physical Examination

- To evaluate for signs of end-organ damage
- For evidence of a cause of secondary hypertension

Accurate measurement of blood pressure
General appearance
Distribution of body fat
Skin lesions
Muscle strength
Alertness
Fundoscopy
Hemorrhage
Papilledema
Cotton-wool spots
Neck
Palpation and auscultation of carotids
Thyroid
Heart
Size
Rhythm
Sounds
Lungs
Rhonchi
Rales
Abdomen
Renal masses
Bruits over aorta or renal arteries
Femoral pulses
Extremities
Peripheral pulses
Edema
Neurologic assessment
Visual disturbance
Focal weakness
Confusion

Laboratory Tests

- Routine Tests
  - Electrocardiogram
  - Urinalysis
  - Blood glucose, and hematocrit
  - Serum potassium, creatinine, or the corresponding estimated GFR, and calcium
  - Lipid profile, after 9- to 12-hour fast, that includes high density and low-density lipoprotein cholesterol, and triglycerides
- Optional tests
  - Measurement of urinary albumin excretion or albumin/creatinine ratio
- More extensive testing for identifiable causes is not generally indicated unless BP control is not achieved

Treatment

Who Should Be Treated?

- Persistently elevated BP after 3-6 visits over a several month period
- If the SBP is persistently ≥140 and/or the DBP is persistently ≥90 mmHg
- SBP is persistently > 130 mmHg and/or the DBP is > 80 mmHg in patients w/CVS disease, post-myocardial infarction, heart failure, CKD & DM
- Patients with office hypertension, normal values at home, and no evidence of end-organ damage should undergo ambulatory blood pressure monitoring
- Blood Pressure Target:
  - Age > 80 yrs - 150/90 mmHg
  - Age < 80 yrs (high risk) – 130/80 mmHg
  - Age < 80 yrs (no risk) – 140/90 mmHg
- ABPM, HBPM
  - Age > 80 yrs - 145/85 mmHg
  - Age < 80 yrs (no risk) – 130/80 mmHg

Benefits: Average Percent Reduction	
Stroke incidence	35-40%
Myocardial infarction	20-25%
Heart failure	50%
Renal Failure	35-50%

Lifestyle Modifications

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

Diet

- Diet high in fruits and vegetables and low-fat dairy products
- Recommends 7-8 servings/day of grain products, 4-5 vegetable, 4-5 fruit, 2-3 low/non-fat dairy products, 2 or less meat, poultry, and fish

Follow Up & Monitoring

- Patients should return for follow-up after 4 weeks and adjustment of medications until the BP goal is reached
- More frequent visits for stage 2 HTN or with complicating co-morbid conditions.
- Serum potassium and creatinine monitored 1–2 times per year.

Risk of Hypertension for each 2-mmHg increase in systolic blood pressure:

- Increase risk of cardiovascular mortality by 7%
- Increase risk of stroke by 10%

Drug Therapy

- A low dose of initial drug should be used, slowly titrating upward.
- Optimal formulation should provide 24-hour efficacy with once-daily dose.
- Combination therapies may provide additional efficacy with fewer adverse effects

Thiazides & Diuretics

Thiazides	**Hydrochlorothiazide, Metolazone, Chlorthalidone, Indapamide**
Loop Diuretics	Furosemide, Ethacrynic acid, Bumetanide, Torsemide
Aldosterone Blockers	Spironolactone, Amiloride, Eplerenone
Combinations	Hydrochlorothiazide & triamterene, Hydrochlorothiazide & amiloride, Hydrochlorothiazide & spironolactone

- Commonly the first line treatment in mild-moderate hypertension.
- Often used in combination with other antihypertensive agents.
- Proven benefit in stoke and myocardial infarction reduction.
- **Mechanism**
  - Decrease plasma volume & reduce peripheral resistance
  - Full antihypertensive effect may take 10-12
  - At the doses used side effect low
- **Adverse effects:**
  - Idiosyncratic reactions (rashes - may be photosensitivity, purpura)
  - Metabolic and electrolyte changes
    - *Hyponatremia, hypomagnesia*
    - *Hypokalemia* (combine with potassium-sparing diuretics)
    - *Hyperuricemia* (most diuretics reduce urate clearance)
    - *Hyperglycemia*
    - *Hypercalcemia* (thiazides ↓ urinary Ca^{+2} clearance →precipitate clinically significant hypercalcemia in hypertensive patients with hyperparathyroidism)
    - *Hypercholesterolemia* (↑ in plasma cholesterol concentration)

ß - Blockers

- ***Cardio-selective*** **:**
  - **b_1 blocker :** *atenolol, metoprolol, Betxoioi, bisoprolol.*
  - **b_1 blockers with ISA** : *acebutol.*
  - **b_1 + a_1 blockers** : *labetalol, carvedilol.*
- ***Cardio non-selective*** **:**
  - **b_1 + b_2 blockers** : *nadolol, propranolol.*
  - **b_1 + b_2 blockers with ISA** : *pindolol.*
- ***Note : Partial agonist activity*** (intrinsic sympathomimetic activity – ISA) - may be an advantage in treating patients with asthma because these drugs will cause bronchodilation; they have moderate (lower) effect on lipid metabolism, cause lesser vasospasms and negative inotropic effect.

Atenolol, Bisoprolol, Betaxolol, Metoprolol:

- Cardio-selective beta-blockers are preferable.
- Mechanism of action may involve:
  - Reduction in peripheral resistance.
  - Inhibition of renin release.
  - Reduce heart rate.
- **NOT** recommended used as first line therapy.
- When used alone effective in 50-60% of patients.
- When used in conjunction with a diuretic increase response rate to 60-80%.
- **Contraindications**: Asthma Heart failure, Bradycardia, Reynaud's
- **Adverse Drug Reactions:** Tiredness, bradycardia, cold hands & feet, muscle fatigue

ACE (Angiotensin Converting Enzyme) Inhibitors

Enalapril, Lisinopril, Ramipril, Perindperil

- Competitively inhibit the actions of angiotensin converting enzyme (ACE).
- ACE converts angiotensin I to active angiotensin II.
- Angiotensin II is a potent vasoconstrictor, a hypertrophogenic agent & reduces aldosterone
- **Contraindications:**
  - Bilateral Renal artery stenosis.
  - Renal failure
  - Hyperkalaemia
- **Adverse Drug Reactions:**
  - Cough 10-15%
  - **Hyperkalemia.**
  - First dose hypertension
  - Taste disturbance
  - Renal impairment in renal artery stenosis.
  - Angioneurotic oedema

Renin-Angiotensin-Aldosterone System

Renin is produced by the juxta-glomerular cells of the kidneys and is released in response to:

- ↑ renal sympathetic activity
- ↓ intra-renal blood pressure at the juxta-glomerular cells
- ↓ delivery of Na^+ and Cl^- to the macula densa

Renin converts Angiotensinogen (produced by the liver) to Angiotensin I. Angiotensin I is then converted into Angiotensin II by the ACE found in the lungs. Angiotensin II acts as a powerful vasoconstrictor and dipsogen increasing:

- The sympathetic activity
- Tubular Na^+ and Cl^- reabsorption, water retention & ↓ K^+ excretion
- Aldosterone secretion from the adrenal gland cortex → salt and water retention
- ADH secretion from the posterior lobe of the pituitary gland → water absorption from the collecting duct
- Arteriolar vasoconstriction

ARBs (Angiotensin II Receptor Blockers)

Losartan, Valsartan, Candesartan, Irbesartan:

- Angiotensin II antagonists competitively block the actions of angiotensin II at the AT1 receptor.
- Advantage over ACE inhibitors:
  - Cough 2%-5%.
  - Less hyperkalemia

ARBs
Candesartan cilexitil
Candesartan cilexitil/HCTZ
Eprosartan, Eprosartan/HCTZ
Irbesartan ± hydrochlorothiazide
Losartan ± hydrochlorothiazide
Olmesartan ± hydrochlorothiazide
Telmisartan ± hydrochlorothiazide
Valsartan ± hydrochlorothiazide

Calcium-Channel Blockers

Amlodipine, Verapamil, Diltiazem & Nifedipine, Felodipine

- Short acting dihydropyridines should not be used as first line therapy
- **Mechanism:**
  - Relaxing large and small arteries and reducing peripheral resistance
  - Reducing cardiac output
- **Contraindications:**
  - Acute MI
  - Heart failure, bradycardia (Verapamil, Diltiazem)
- **Averse Drug Reactions:**
  - Flushing
  - Headache
  - Ankle oedema
  - Indigestion and reflux esophagitis
- Rate limiting (Verapamil, Diltiazem) cause:
  - Bradycardia
  - Constipation

NONDIHYDROPYRIDINES
Diltiazem
Verapamil
DIHYDROPYRIDINES
Amlodipine
Felodipine
Isradipine
Nicardipine
Nifedipine
Nisoldipine

α - Blockers

Prazosin, Terazosin, Doxazosin

- Selectively block post-synaptic a1-adrenoceptors
- Reduce vascular smooth muscle contraction in arteries
- **Adverse Drug Reactions:**
  - First dose hypotension
  - Dizziness
  - Dry mouth
  - Headache

Central Sympatholytics

- α_2-agonist actions
- ***Methyldopa***: false transmitter
- **Clonidine, Moxonidine**: direct a_2-agonist, imidazol receptor agonists
- Limited use in the treatment of hypertension
- Methyldopa → hypertension during pregnancy
- Causes symptoms of **drowsiness** and **fatigue** that are intolerable to many adult patients in long-term use
- They are seldom used to treat essential hypertension
- Clonidine is potent but poorly tolerated (rebound hypertension, if it is discontinued abruptly, is an uncommon but severe problem)

Peripheral Neuronal Antagonists

Reserpine

Direct Vasodilators

Hydralazine, minoxidil

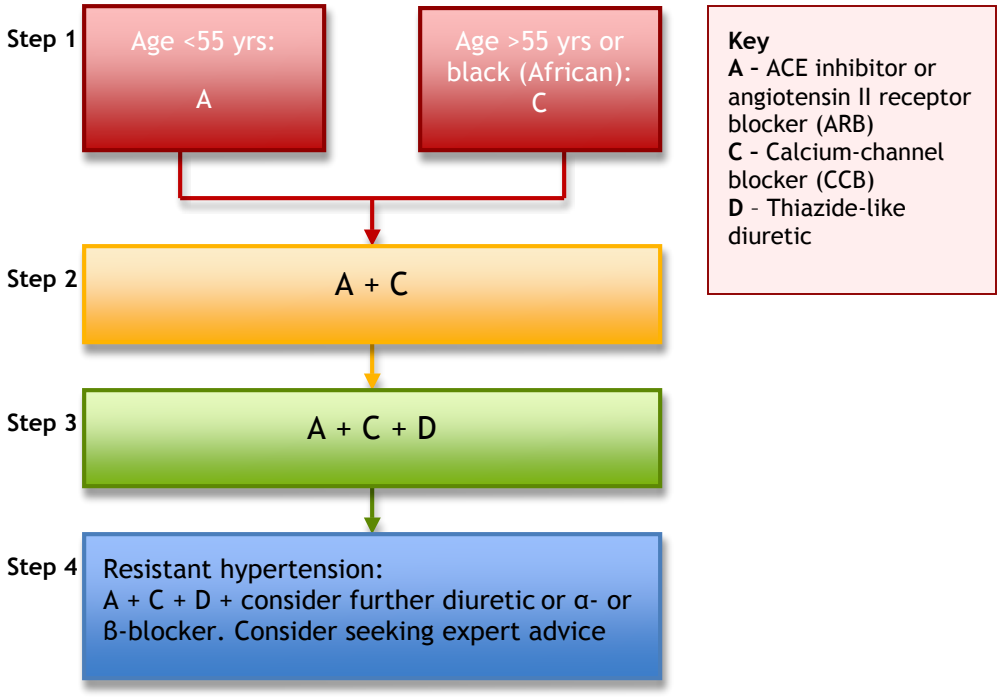
High-Risk Group Therapy

Heart Failure	**Thiazides, B-Blockers, ACEI, ARB, Aldosterone Antagonist**
Post-MI	B-Blockers, ACEI, Aldosterone Antagonist
High CAD Risk	Thiazides, B-Blockers, ACEI, CCB
Diabetes	Thiazides, B-Blockers, ACEI, ARB, CCB
Chronic Kidney Disease	ACEI, ARB, **Thiazide**
Recurrent Stroke Prevention	Thiazides, ACEI, CCB

Combination Therapies

- ACE inhibitors and diuretics
- Angiotensin II receptor antagonists and diuretics
- Calcium antagonists and ACE inhibitors
- Angiotensin II receptor antagonists & β-adrenergic blockers NOT RECOMMENDED
- Other combinations (β-adrenergic blockers and diuretics)

Summary



Additional Notes:

Classification	Systolic BP (mm Hg)		Diastolic BP (mm Hg)	Recommended Management
Normal	<120	and	<80	No Treatment
Prehypertension	120–139	and	80–89	Lifestyle modification
Stage I	140–159	or	90–99	Lifestyle modification, drug therapy
Stage II	≥160	or	≥100	Lifestyle modification and drug therapy (2-drug combination for most)

Medication	Side Effects
Thiazide diuretics	**Hypokalemia,** hyperuricemia, hyperglycemia, elevation of cholesterol and triglyceride levels, metabolic alkalosis, hyperuricemia, hypomagnesemia
β-blockers	Bradycardia, bronchospasm, sleep disturbances (insomnia), fatigue, may increase TGs and decrease HDL, depression, sedation, may mask hypoglycemic symptoms in diabetic patients on insulin
ACE inhibitors	Acute renal failure, hyperkalemia, dry cough angioedema, skin rash, altered sense of taste, contraindicated in pregnancy

- Exercise and diet improve multiple risk factors with virtually no side effects
- Exercise may reduce or eliminate the need for antihypertensive medications
- **Initiation of pharmacologic therapy depends on total cardiovascular risk and/or co-morbid conditions. CVS risks:**
  - Current cigarette smoking (dose-dependent risk)
  - Hypertension
  - Diabetes mellitus
  - Low HDL cholesterol (<35 mg/dL); high HDL (>60 mg/dL) is a negative risk factor (subtract 1 from total)
  - Age
    - Male: >45 years of age
    - Female: >55 years of age
  - Male gender—if you count as a risk factor, do not count age
  - Family history of **premature** CAD
    - MI/sudden death in male first-degree relative <55 years of age
    - MI/sudden death in female first-degree relative <65 years of age
- Thiazides, ACE inhibitors, calcium channel blockers, and ARBs are contraindicated in pregnancy. ß-Blockers and hydralazine are safe.
- If diabetic, ACEI/ARB is first-choice (because of protective effect on kidneys)
- If “white coat hypertension” is suspected, there are two options for determining whether the increased BP persists outside the office.
  - 24-hour ambulatory blood pressure monitoring is the most effective.
  - Home blood pressure monitoring is an alternative.