HYPERTENSION

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Cardiovascular Disease (CVD)

- Leading cause of death in most parts of world
- ~ 32% in OPT die of CVD
- Risk factors: HTN, DM, HLD, obesity, smoking
- Atherosclerosis is main cause of CVD events
- 1 billion worldwide with HTN, 7 mil deaths/yr
- ~ 1/4th of pop in OPT have HTN (age 35-60)
- Direct correlation between elevated BP and: stroke, MI, CKD, angina, CHF, death

Hypertension: Definition

- Elevation in blood pressure
- Systolic Vs. Diastolic pressure
- Effect of age on BP
- JNC 7 Definition (≥18 yr)

Classification	Systolic (mmHg)		Diastolic BP (mmHg)
Normal	< 120	and	< 80
Pre-hypertension	120-139	or	80-89
Stage I HTN	140-159	or	90-99
Stage II HTN	≥ 160	or	≥ 100

Hypertension: Types

- Primary (Essential)
  - 90% of cases
  - Unknown cause- genetics?
  - Incurable, goal is control
- Secondary- has an identifiable cause
  - < 10%
  - Conditions: CKD, Cushing syndrome, aortic coarctation, OSA, pheochromocytoma, aldosteronism, thyroid/parathyroid disorder, renal artery stenosis

Hypertension: Types

  - Substances: cocaine, methamphetamines, corticosteroids, calcineurin inhibitors, decongestants, ergot alkaloids, oral contraception, etc.
- White Coat Hypertension

Pathophysiology

- Cardiac output (CO) and Total Peripheral Resistance (TPR)
  - MAP = CO x TPR
  - CO = HR x SV
  - MAP = DBP + 1/3 (SBP-DBP)
- What increases CO?
  - Increased cardiac pre-load (fluid up, Na, etc.)
    - Frank Starling Law
  - SNS, RAAS via increasing HR, aldosterone and angiotensin II production

Pathophysiology

- What increases TPR?
  - RAAS activation
  - Sympathetic activation
  - Endothelial factors
  - Hyperinsulinemia (metabolic syndrome)

Clinical Presentation & Diagnosis

- *Silent Killer*
- Average of ≥ 2 BP readings per visit over ≥ 2 separate visits
- 24-h BP monitoring
- Rule out secondary causes, evaluate for target organ damage, test for co-morbidities
- Co-morbidities: DM, obesity (BMI > 30 kg/m^2), HLD, tobacco use, physical inactivity
- Other risk factors: family history of CVD, Age (≥55 for men, ≥65 for women)

Clinical Presentation & Diagnosis

- Target organ damage:
  - Eyes: retinopathy
  - Heart: angina, MI, LVH, CHF
  - Brain: stroke
  - Kidneys: CKD
  - Vascular: PAD
- Labs: lipid panel, HbA1C, Cr, UA or ACR, other labs for secondary causes

Treatment of Hypertension

- Reduces risk for MI, stroke, CKD, CHF, death
- For every 20 mmHg increase in SBP, or 10 mmHg increase in DPP, mortality doubles from ischemic heart disease and stroke
- Pharmacotherapy and lifestyle modifications are utilized

Treatment of Hypertension
Lifestyle Modification

- Weight loss
- Physical activity: 3-4x/wk, 40 min
- Sodium reduction: <2400 mg/d
- DASH diet (Dietary Approaches to Stop HTN)
  - high in fruits, vegetables, low-fat dairy, whole grains, fish, poultry, nuts
  - Low in sweets, saturated and unsaturated fats, red meat
- Moderate alcohol intake

Treatment of Hypertension
Pharmacotherapy (JNC 7)

BP Classification	SBP* mmHg	DBP* mmHg	Lifestyle Modification	Initial drug therapy	
				Without Compelling Indication	With Compelling Indications (See Table 8)
Normal	<120	and <80	Encourage		
Prehypertension	120–139	or 80–89	Yes	No antihypertensive drug indicated.	Drug(s) for compelling indications.‡
Stage 1 Hypertension	140–159	or 90–99	Yes	Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination.	Drug(s) for the compelling indications.‡ Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed.
Stage 2 Hypertension	≥160	or ≥100	Yes	Two-drug combination for most† (usually thiazide-type diuretic and ACEI or ARB or BB or CCB).	

Treatment of Hypertension
Pharmacotherapy (JNC 7): Compelling Indications

- Heart failure
  - Asymptomatic with ventricular dysfunction: BBs, ACEIs or ARBs
  - Symptomatic or end-stage: ACEIs, BBs, ARBs, aldosterone blockers, loop diuretic
- Ischemic heart disease
  - BBs and CCBs beneficial in stable angina
  - BBs and ACEIs beneficial in ACS (unstable angina/MI) and post-MI

Treatment of Hypertension
Pharmacotherapy (JNC 7): Compelling Indications

- Diabetes: BP goal < 130/80 mmHg
  - Thiazide diuretics, BBs, ACEIs, ARBs, CCBs reduce CVD and stroke
  - ACEIs and ARBs slow nephropathy
- CKD: goal BP < 130/80 mmHg
  - ACEIs, ARBs, slows progression of diabetic and non-diabetic CKD
- Pregnant or likely to become pregnant
  - Methyldopa, BBs, vasodilators are preferred
  - C/I: ACEIs/ARBs due to teratogenicity

Pharmacotherapy
Diuretics

- Thiazides: HCTZ, chlorthalidone, metolazone
  - 1st line if no compelling indications according to JNC7
  - Multiple mechanisms proposed
  - Very effective in controlling BP as part of 2-agent Rx
  - CV morbidity and mortality benefit
  - AHA considers ACEIs, ARBs, and CCBs prefered over thiazides
  - Most studies with chlorthalidone, likely class effect

Pharmacotherapy
Diuretics

- Not considered effective if GFR < 30 mL/min, switch to loop diuretic
- Common AEs: Hypo-Mg, Hypo-K, dyslipidemia, hyperglycemia, hyperuricemia, sexual dysfunction
- Associated with higher rates of DMII than other BP Rx
- Limit doses to minimize AE (HCTZ 50 mg, chlorthal 25 mg)
- Usual doses: HCTZ 12.5-25 mg/d, Chlorthalidone 6.25-25 mg/d
- QD dosing

Pharmacotherapy
Diuretics

- Loop Diuretics- furosemide, ethacrynic acid, torsemide, bumetanide
  - Potent diuretics
  - Same AE as Thiazides except:
    - No metabolic effects
    - Universal depletion of electrolytes (Na, Ca, K, Mg)
  - Usual dose: furosemide 20-80 mg PO in two divided doses for HTN
  - Loop diuretics have no ceiling effect- very large doses or continuous IV infusion may be required

Pharmacotherapy
Diuretics

- Loops & Thiazides: monitor closely populations with gout, arrhythmias, electrolyte imbalance, digoxin level, DM & HLD with thiazides
- K-Sparing Diuretics- triamterene, amiloride
  - Little effect on BP; weak diuretics
  - Primarily used to balance K loss 2/2 thiazide
  - Often in combination with thiazide or loop diuretics
  - Hyperkalemia (esp. if with ACEI/ARB, CKD, K supplements)
    - Needs close follow-up on K after initiation or dose change
  - Usual dose: amiloride 5-10 mg/d in 1 or 2 doses

Pharmacotherapy
Diuretics

- Aldosterone Antatonists- spironolactone, eplerenone
  - Not true diuretics- modulate vascular tone
  - K-sparing effect- ideal with thiazide and loop diuretics
  - AEs: same as with K-sparing diuretics, gynecomastia
  - Usual dose: spironolactone 25-50 mg/d in 1-2 doses
- All diuretics are best given in AM

Pharmacotherapy
ACE Inhibitors (ACEIs)

- Lisinopril, enalapril, captopril, benazepril..
- Per JNC 7, first line in compelling indications: CKD, DM, LVH/CHF, post-MI
- Target RAAS activation post-MI and in HF pts.
- Very effective in reducing BP; all equally effective at equipotent doses
- CV/renal benefits thought to be class effect
- Usual dose: lisinopril 10-40 mg/d, enalapril 5-40 mg/d
- QD dosing for most

Pharmacotherapy
ACE Inhibitors (ACEIs)

- AEs:
  - Hyper-K: rarely a reason to D/C, monitor periodically
  - Orthostatic HoTN
  - Dry cough: switch to ARBs
  - Decreased GFR: monitor periodically, titrate slowly especially in vulnerable pts, hold if GFR rises >30%, challenge at lower dose or slower titration
  - Rare angioedema
    - Do not rechallenge
    - Consider ARBs; cross-reactivity <10%
  - Teratogeneic, C/I in pregnancy

Pharmacotherapy
Angiotensin-Receptor Blockers (ARBs)

- Losartan, telmisartan, valsartan, candesartan, irbesartan..
- Equivalent in efficacy and outcomes to ACEIs, but with fewer AEs (less cough, angioedema)
- Same precautions/AEs apply as ACEIs
- Usual dose: losartan 50-100 mg/d, valsartan 80-320 mg/d
- QD dosing for most

Pharmacotherapy
Renin Inhibitors

- Aliskiren is first and only agent
- Direct Renin blocker
- No outcome data, unclear role
- Same precautions as ACEIs/ARBs

Pharmacotherapy
Calcium Channel Blockers (CCBs)

- DHP Vs. NDHP
- Ex: diltiazem, verapamil, amlodipine, felodipine, nifedipine (LA)
- IR nifedipine may precipitate reflex tachycardia
- Reduction in CVD events in pts with non-compelling indications
- Compelling indications: second line in CAD, DM
- NDHP ideal if pt suffers from SVTs

Pharmacotherapy
Calcium Channel Blockers (CCBs)

- Usual dosing: amlodipine 2.5-10 mg QD, diltiazem CD/XR/XT 120-420 QD (also available BID as SR)
- AEs (DHPs): dizziness, flushing, HA, peripheral edema, GI, gingival hyperplasia
- AEs (NDHP): bradycardia, AV block, acute HF, anorexia, nausea, peripheral edema, constipation
- CYP450 inhibition (verap>dilt)
- Caution with βBs, avoid giving both IV

Pharmacotherapy
Beta-Blockers

- Metoprolol, atenolol, carvedilol, propranolol, labetalol, acebutolol
- JNC7 lists as acceptable option for non-compelling indications but JNC8 opposes
  - Less reduction in CV events than ACEI, ARB, CCB, diuretics
  - Meta-analysis published in 2005 showing increased risk of stroke from βBs
- Compelling indications: first line in CAD, post-MI, CHF/LVH (bisoprolol, carvedilol, metoprolol succinate)

Pharmacotherapy
Beta-Blockers

- Generally, cardioselective agents preferred
  - Cardioselectivity is lost at higher doses
- Avoid βBs with +ISA, esp. post-MI, i.e. acebutolol
- Avoid non-selective βBs with asthma, COPD, PVD, or DM, i.e. propranolol, timolol, pindolol
- Avoid abrupt D/C; taper over 1-2 wks
  - Reflex tachycardia, cardiac ischemia

Pharmacotherapy
Beta-Blockers

- Usual doses: atenolol 25-100 mg QD, metoprolol tartrate 50-200 mg BID, metoprolol succinate 50-200 mg QD, carvedilol 6.25-25 mg BID
- AEs: bradycardia, heart block, AHF, possible erectile dysfunction
- Atenolol renally excreted and needs adjustment

Pharmacotherapy
Other Agents

- α1-Blockers
  - Prazosin, terazosin, doxazosin
  - Inferior to thiazide-type diuretics in preventiong CV events in HTN patients
  - Higher incidence of CHF Vs. chlorthalidone
  - Reserved for use in addition to first line, i.e. BPH
  - Syncope, dizziness, orthostatsis
- Central α2-Agonists
  - Clonidine, methyldopa, guanfacine, etc.
  - Orthostasis, sedation, dry mouth
  - Clonidine- resistant HTN, caution with rebound HTN, D/C βB days before clonidine

Pharmacotherapy
Other Agents

- Direct vasodilators
  - Hydralazine, minoxidil
  - Can cause reflex tachycardia and peripheral edema, use with βBs and diuretics
- Reserpine
  - Rarely used, numerous AEs
  - Depletes NE from sympathetic nerve endings

Pharmacotherapy
Misc.

- IV options for scheduled dosing
  - Enalaprilat- Q6h
  - Metoprolol- Q6h
- Hypertensive emergencies (≥180/120 WITH organ damage/impending damage)
  - Reduce BP slowly, 25% within minutes to first hour, then to 160/100 within the next 2-6h, then goal within 24-48h
  - Nitroprusside continuous infusion is DOC

Pharmacotherapy
Misc.

- Hypertensive Urgency (≥180/120 WITHOUT organ damage/impending damage)
  - Can treat with fast acting oral agents, i.e. captopril, clonidine
  - Goal BP is 120-140 within hours to a day
  - Rebound HTN often fits in this category

Monitoring

- F/U every 2-4 wks until stable and depending on regimen, severity, co-morbidities
- When stable, F/U can be annual or semi-annual
- Monitor for effectiveness, safety, compliance/convenience
- Minimize pill #
- Labs: depends on agent, may include electrolytes, BUN, Cr, uric acid, others to assess target-organ damage progression and co-morbidities

JNC 8

Criteria/JNC	JNC 7	JNC 8*
Evidence	RCT, observational, expert opinion	RCT and expert opinion
Focus	Comprehensive	Drug treatment only
Definition of HTN	>140/90	>140/90
Staging	Pre, Stage 1, Stage 2	None
Treatment Threshold	140/90 non-DM 130/80 DM & CKD	140/90 < 60 y/o 150/90 ≥ 60 y/o

*Non-black patients

JNC 8

Criteria/JNC	JNC 7	JNC 8
Thiazide Diuretics	Initial Rx unless compelling indication	Equal to ACEIs, ARBs, CCBs as initial Rx
β-Blockers	Included in initial options for gen. pop.	Not recommended anymore 2/2 stroke risk
CKD	Initial: ACEI/ARB	Initial OR add-on Rx should include ACEI/ARB
DM	Initial: ACEI/ARB	Does not differentiate Treat as general pop.
CHF, Post-MI, CAD	Addressed	Not addressed, defer to JNC 7 or other guidelines

Remember..

- Guidelines should not replace clinical judgment
- Guidelines change constantly- what you practice today may be proven wrong tomorrow
- JNC is only one of several other guidelines on HTN, but JNC 8 is closer to most than JNC 7