HYPERTENSION

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- ***Diagnosis of hypertension:***
- 1. multiple readings (under various conditions and times) for at least 4-6 weeks
  2. 24-hour ambulatory blood pressure recordings (especially if variable readings)

Types of hypertension:

1. Primary, essential, or idiopathic hypertension (>90%)
2. Secondary, identifiable, hypertension (<10%)

JNC7 Classification of hypertension

Blood pressure 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**

- Prehypertension is not disease category and not for drug therapy (lifestyle modification needed to reduce risk of developing hypertension)
- All people with stage 1 or 2 hypertension need drug therapy. Treatment goal is < 140/90 mmHg. If there are diabetes or kidney disease, treatment goal is < 130/80 mmHg.

Mechanisms of primary hypertension

- Idiopathic (mostly)
- genetic and environmental factors
- renal retension of excess sodium → fluid overload →increase cardiac output
- pressor hormones and locally acting substances acting as vascular growth promotors leading to hypertension, as below:

obesity (hyperinsulinemia)
stress (catecholamines)
sodium excess (natriuretic hormone)
renal ischemia (angiotensin)
acromegaly (growth hormone)
endothelial cell dysfunction
(decrease nitric oxide release and endothelial-derived constricting factors) etc.

pressor growth promoters

turnover of cell membrane phospholipids

heart: increase preload
increase contractility

vessels: functional constriction
structural hypertrophy

increase cardiac output

increased peripheral resistance

hypertension (= cardiac output X peripheral resistance)

Mechanisms of secondary hypertension

1. ***Renal parenchymal disease (most common)***
   - hypertensive nephrosclerosis
   - diabetic nephropathy
   - ureteral obstruction
   - vasculitis
   - polycystic kidney disease
   - analgesic nephropathy (due to prolonged use of analgesics) etc.
2. ***Renovascular hypertension***
   - due to atherosclerotic or fibroplastic diseases → obstruction of renal artery

   Diagnosis = isotopic renography
   plasma renin measurement after oral catopril challenge
   renal arteriography
   renal vein renin assay
   magnetic resonance arteriography

- ***Adrenal disease:*** **due to excess of aldosterone, cortisol, catecholamines**
  - **primary aldosteronism: considered when hypertension and hypokalemia coexist, and high plasma aldosterone/renin ratio. Diagnosed by adrenal CT or MRI (for adrenal adenoma)**
  - **congenital adrenal hyperplasia**
  - **pheochromocytoma: diagnosed by urine or plasma assays of catecholamines, followed by adrenal CT or MRI to localize the tumor**

4. ***Coarctation of aorta*** **= congenital narrowing of aorta at any level of thoracic or abdominal aorta → hypertension in arms but weak or absent femoral pulses. Diagnosed by echocardiogram, aortography.**
5. ***Hormonal disturbances*** **eg. acromegaly, hypo- and hyperthyroidism, hyperparathyroidism, Cushing syndrome, etc.**
6. **Oral contraceptive, drugs, pregnancy-induced hypertension, neurological disorders (brain tumor, encephalitis, sleep apnea etc)**

Complications of hypertension

Hypertension → pulsatile flow, endothelial cell dysfunction, smooth muscle cell hypertrophy → vascular complications

Vascular complications:

1. **Hypertensive: accelerated-malignant hypertension, hemorrhagic stroke, heart failure, nephrosclerosis, aortic dissection**
2. **Atherosclerotic: coronary artery disease, sudden death, arrhythmias, atherothrombotic stroke, peripheral vascular disease**

Target organ damage:

1. **Eye : hypertensive and arteriosclerotic retinopathy**
2. **Heart: left ventricular hypertrophy, sudden death, myocardial ischemia and infarction**
3. **Kidney: microalbuminuria, proteinuria, nephrosclerosis, renal insufficiency, uremia, end-stage renal disease**
4. **Brain: stroke**

Metabolic abnormalities **eg. dyslipidemia, hyperinsulinemia**

Association of hypertension with other conditions:

obesity, sleep apnea, physical inactivity, excess alcohol intake, smoking, hematologic disease (eg polycythemia), hyperuricemia, diabetes etc.

Screening for secondary hypertension

If there are features of "inappropriate hypertension", such as:

- **onset before age 20 or after 50**
- **organ damage eg. serum creatinine > 1.5 mg/dl, cardiomegaly etc.**
- **hypokalemia, abdominal bruit, variable pressures with tachycardia, sweating, tremor, family history of renal disease etc.**
- **poor response to antihypertensive treatment**

Hypertensive crisis

- **Mostly appear in the setting of preexisting primary hypertension (< 1%)**

Characteristics:

- **diastolic pressure > 140 mmHg**
- **funduscopic findings: hemorrhage, exudate, papilledema**
- **neurologic findings: headache, confusion, somnolence, stupor, visual loss, focal deficits, seizure, coma**
- **cardiac findings: prominent apical impulse, cardiac enlargement, heart failure**
- **renal findings: oliguria, azotemia**
- **gastrointestinal : nausea vomiting**

Therapy of hypertension

life style modification

Blood pressure (BP) > 140/90 mmHg

(for those with diabetes or renal disease,BP>130/80)

without compelling indications

stage 1 hypertension: drugs”

thiazide for most

stage 2 hypertension:

two-drug combination for most

with compelling indications

“compelling

- **Goal is to prevent complications**
- **Life style modifications (nondrug therapy):**

  stop smoking and alcohol abuse, weight reduction, dietary sodium restriction, diet control, physical exercise

COMMON ORAL ANTIHYPERTENSIVE DRUGS

1. ***Diuretics:***

   mechanism of action – increase urinary sodium excretion and decrease plasma volume, cardiac output and peripheral resistance

   side effects (if high dose) - hypokalemia, hypomagnesemia, hyperuricemia, hyperlipidemia, hyperglycemia and insulin resistance, hypercalcemia, poor sexual performance (also common in hypertension per se)

2. *Alpha blockers (eg. doxazosin)*

- excellent for old men with hypertension and prostate hypertrophy because decreasing smooth muscle tone of bladder neck and prostate

mechanism of action: decrease peripheral resistance

side effects: postural hypotension, dizziness, weakness, headache

3. *Beta blockers*

mechanism of action: decrease cardiac output and renin release

side effects: bronchospasm, peripheral vascular disease, fatigue, insomnia, nightmares, hallucinations

- ***Calcium antagonists***

  mechanism of action: vasodilator

  side effects: flushing, ankle edema, constipation

5. ***Renin-angiotensin inhibitors (ACEI and ARB)***

   mechanism of action: decrease peripheral resistance with little effect on heart rate, cardiac output and plasma volume

   side effects: cough, hypersensitivity reaction

ANTIHYPERTENSIVE DRUG THERAPY

- **diuretics unsurpassed in preventing complications, therefore used as “preferred initial agent”**
- **if there are compelling indications (or contraindications), use the appropriate “compelling durgs”, as below:**

Class of drug	*compelling indications*	*compelling contraindications*
Diuretics	**heart failure, elderly, coronary disease, systolic hypertension, diabetes, stroke prevention**	**gout, dyslipidemia, sexually active men**
Beta blockers	**coronary disease, post-infarction, tachyarrhythmia, heart failure, diabetes**	**asthma, chronic lung disease, heart block, dyslipidemia, peripheral vascular disease**

ACE inhibitors	heart failure,coronary disease, post-infarction, diabetes, chronic renal disease, stroke prevention	pregnancy, hyperkalemia, renal artery stenosis
Angiotensin II antagonists	ACEI cough, heart failure	pregnancy, renal artery stenosis, hyperkalemia
Calcium antagonists	coronary disease, diabetes, elderly, systolic hypertension, peripheral vascular disease	heart block, heart failure