Management of Hypertension

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Definition

- Hypertension is defined as the presence of a BP elevation to a level that places patients at increased risk for target organ damage in several vascular beds, including the retina, brain, heart, kidney, and large conduit arteries.
- The public health burden of hypertension, characterized by a BP of greater than 140/90 mm Hg, is enormous, affecting an estimated 50 million Americans.

Manifestations of Target Organ Diseases

- Large vessels
  - Aneurysm dilatation.
  - Accelerated atherosclerosis
  - Aortic dissection.
- Cardiac
  - Acute : pulmonary edema, myocardial infarction
  - Chronic : clinical or ECG evidence of CAD; LVH by ECG or echocardiography
- Cerebrovascular
  - Acute : intracerebral bleeding, coma, seizures, mental status change, TIA, stroke
  - Chronic : TIA, stroke
- Renal
  - Acute : hematuria, azotemia
  - Chronic : serum creatinie > 1.5 mg/dl, proteinuria >1+ on dipstick
- Retinopathy
  - Acute : papilledema, hemorrhage
  - Chronic : hemorrhage, exudates, arterial nicking

Classification of Blood Pressure for Adults

BP Classification	SBP mm Hg	DBP mm Hg
Normal	<120	and <80
Prehypertension	120–139	or 80–89
Stage 1 hypertension	140–159	or 90–99
Stage 2 hypertension	>/ 160	or >/ 100

TABLE 2. ***Changes in Blood Pressure Classification***

JNC 6 Category	SBP/DBP	JNC 7 Category
Optimal	< 120/80	**Normal**
Normal	120–129/80–84	**Prehypertension**
Borderline	130–139/85–89	
Hypertension	≥ 140/90	**Hypertension**
Stage 1	140–159/90–99	Stage 1
Stage 2	160–179/100–109	Stage 2
Stage 3	≥ 180/110	

Sources: The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med* 1997;157:2413–46.

The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *JAMA* 2003;289:2560–2571.

Identifiable Causes of Hypertension

- Chronic kidney disease
- Coarctation of aorta
- Cushing syndrome & other glucocorticoid excess states including chronic steroid therapy
- Drug-induced or related
- Obstructive uropathy
- Pheochromocytoma
- Primary aldosteronism or other mineralcorticoid excess states
- Renovascular hypertension
- Sleep apnea
- Thyroid or parathyroid disease

Causes of Resistant Hypertension

- Improper BP measurement
- Volume overload
  - Excess sodium intake
  - Volume retention from kidney disease
  - Inadequate diuretic therapy
- Drug-induced or other causes
  - Nonadherence
  - Inadequate doses
  - Inappropriate combinations
  - Nonsteroidal anti-inflammatory drugs; cyclooxygenase 2 inhibitors
  - Cocaine, amphetamines, other illicit drugs
  - Sympathomimetics (decongestants, anorectics)
  - Oral contraceptive hormones
  - Adrenal steroid hormones
  - Cyclosporine and tacrolimus
  - Erythropoietin
  - Licorice (including some chewing tobacco)
  - Selected over-the-counter dietary supplements and medicines (eg, ephedra, ma haung, bitter orange)
- Associated conditions
  - Obesity
  - Excess alcohol intake
- Identifiable causes of hypertension

Common Substances Associated With Hypertension in Humans

- **Prescription Drugs**
  - ***Cortisone and other steroids*** (both cortico- and mineralo-), ACTH
  - ***Estrogens*** (usually just oral contraceptive agents with high estrogenic activity)
  - ***Nonsteroidal anti-inflammatory drugs***
  - ***Phenylpropanolamines and analogues***
  - ***Cyclosporine and tacrolimus***
  - ***Erythropoietin***
  - ***Sibutramine***
  - **Ketamine**
  - **Desflurane**
  - **Carbamazepine**
  - **Bromocryptine**
  - **Metoclopramide**
  - **Antidepressants (especially venlafaxine)**
  - **Buspirone**
  - **Clonidine, BB combination**
  - **Pheochromocytoma: BB without -blocker first; glucagon**
  - **Clozapine**
- **Street drugs and other "natural products"**
  - ***Cocaine and cocaine withdrawal, Ma huang, "herbal ecstasy," and other phenylpropanolamine analogs***
  - **Nicotine and withdrawal, Anabolic steroids, Narcotic withdrawal, Methylphenidate, Phencyclidine**
  - **Ketamine, Ergotamine and other ergot-containing herbal preparations, St. John's wort**
- **Food substances**
  - ***Sodium chloride, Ethanol,*** **Licorice, Tyramine-containing foods (with MAO-I)**
- **Chemical elements and other industrial chemicals**
  - **Lead, Mercury, Thallium and other heavy metals, Lithium salts, especially the chloride**

Cardiovascular Risk Factors

- Major risk factors
  - Hypertension
  - Age (older than 55 for men, 65 for women)
  - Diabetes mellitus*
  - Elevated LDL (or total) cholesterol or low HDL cholesterol*
  - Estimated GFR <60 mL/min
  - Family history of premature cardiovascular disease (men aged <55 or women aged <65)
  - Microalbuminuria
  - Obesity* (body mass index 30 kg/m^2)
  - Physical inactivity
  - Tobacco usage, particularly cigarettes
- Target organ damage
  - Heart
    - Left ventricular hypertrophy
    - Angina/prior myocardial infarction
    - Prior coronary revascularization
    - Heart failure
  - Brain
    - Stroke or transient ischemic attack
    - Dementia
  - Chronic kidney disease
  - Peripheral arterial disease
  - Retinopathy

Recommendations for Follow-Up Based on Initial Blood Pressure Measurements for Adults Without Acute End Organ Damage

Initial Blood Pressure, mm Hg*	Follow-Up Recommended **
Normal	Recheck in 2 years
Prehypertension	Recheck in 1 year ***
Stage 1 hypertension	Confirm within 2 months ***
Stage 2 hypertension	Evaluate or refer to source of care within 1 month. For those with higher pressures (eg, >180/110 mm Hg), evaluate and treat immediately or within 1 week depending on clinical situation and complications.

Lifestyle Modifications to Manage Hypertension*^

Modification	Recommendation	Approximate Systolic BP Reduction, Range
Weight reduction	Maintain normal body weight (BMI 18.5–24.9)	5–20 mm Hg/10-kg weight loss
Adopt DASH diet eating plan	Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat	8–14 mm Hg
Dietary sodium reduction	Reduce dietary sodium intake to no more than 100 mEq/L (2.4 g sodium or 6 g sodium chloride)	2–8 mm Hg
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week)	4–9 mm Hg
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks per day (1 oz or 30 mL ethanol [eg, 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey]) in most men and no more than 1 drink per day in women and lighter-weight persons	2–4 mm Hg

DASH, Dietary Approaches to Stop Hypertension.

Combination Drugs for Hypertension

- ACEIs and CCBs
  - Amlodipine-benazepril hydrochloride
  - Enalapril-felodipine
  - Trandolapril-verapamil
- ACEIs and diuretics
  - Benazepril-hydrochlorothiazide
  - Captopril-hydrochlorothiazide
  - Enalapril-hydrochlorothiazide
  - Fosinopril-hydrochlorothiazide
  - Lisinopril-hydrochlorothiazide
  - Moexipril-hydrochlorothiazide
  - Quinapril-hydrochlorothiazide

Combination Drugs for Hypertension

- ARBs and diuretics
  - Candesartan-hydrochlorothiazide
  - Eprosartan-hydrochlorothiazide
  - Irbesartan-hydrochlorothiazide
  - Losartan-hydrochlorothiazide
  - Olmesartan medoxomil-hydrochlorothiazide
  - Telmisartan-hydrochlorothiazide
  - Valsartan-hydrochlorothiazide
- BBs and diuretics
  - Atenolol-chlorthalidone
  - Bisoprolol-hydrochlorothiazide
  - Metoprolol-hydrochlorothiazide
  - Nadolol-bendroflumethiazide
  - Propranolol LA-hydrochlorothiazide
  - Timolol-hydrochlorothiazide

Combination Drugs for Hypertension

- Centrally acting drug and diuretic
  - Methyldopa-hydrochlorothiazide
  - Reserpine-chlorthalidone
  - Reserpine-chlorothiazide
  - Reserpine-hydrochlorothiazide
- Diuretic and diuretic
  - Amiloride-hydrochlorothiazide
  - Spironolactone-hydrochlorothiazide
  - Triamterene-hydrochlorothiazide

Guidelines for Treatment of Hypertension Based on Compelling Indications for Individual Drug Classes

	Diuretic	ß-Blocker	ACE Inhibitor	ARB	Calcium Antagonist	Aldosterone Antagonist
Heart failure	+	+	+	+		+
Post-myocardial infarction		+	+			+
High coronary disease risk	+	+	+		+	
Diabetes	+	+	+	+	+	
Chronic kidney disease			+	+		
Recurrent stroke prevention	+		+			

Parenteral Drugs for Treatment of Hypertensive Emergencies

- Vasodilators
  - Sodium nitroprusside : 0.25 – 10 μg/kg/min as IV infusion.
  - Nicardipine hydrochloride : 5–15 mg/h IV
  - Fenoldopam mesylate : 0.1–0.3 μg/kg per min IV infusion
  - Nitroglycerin : 5–100 μg/min as IV infusion
  - Enalaprilat : 1.25–5 mg every 6 h IV
  - Hydralazine hydrochloride : 10–20 mg IV, 10–40 mg IM
- Adrenergic inhibitors
  - Labetalol hydrochloride : 20–80 mg IV bolus every 10 min, 0.5–2.0 mg/min IV infusion
  - Esmolol hydrochloride : 250–500 μg/kg/min IV bolus, then 50–100 μg/kg/min by infusion; may repeat bolus after 5 min or increase infusion to 300 μg/min
  - Phentolamine : 5–15 mg IV bolus

Classification of Hypertension in Pregnancy

- **Chronic hypertension**
  - BP 140 mm Hg systolic or 90 mm Hg diastolic prior to pregnancy or before 20 weeks gestation
  - Persists >12 weeks postpartum
- **Preeclampsia**
  - BP 140 mm Hg systolic or 90 mm Hg diastolic with proteinuria (>300 mg/24 h) after 20 weeks gestation
  - Can progress to eclampsia (seizures)
  - More common in nulliparous women, multiple gestation, women with hypertension for 4 years, family history of preeclampsia, hypertension in previous pregnancy, renal disease
- **Chronic hypertension with superimposed preeclampsia**
  - New onset proteinuria after 20 weeks in a woman with hypertension
  - In a woman with hypertension and proteinuria prior to 20 weeks gestation:
    - Sudden 2- to 3-fold increase in proteinuria
    - Sudden increase in BP
    - Thrombocytopenia
    - Elevated AST or ALT
- **Gestational hypertension**
  - Hypertension without proteinuria occurring after 20 weeks gestation
  - Temporary diagnosis
  - May represent preproteinuric phase of preeclampsia or recurrence of chronic hypertension abated in midpregnancy
  - May evolve to preeclampsia
  - If severe, may result in higher rates of premature delivery and growth retardation than mild preeclampsia
- **Transient hypertension**
  - Retrospective diagnosis
  - BP normal by 12 weeks postpartum
  - May recur in subsequent pregnancies
  - Predictive of future primary hypertension

Treatment of Chronic Hypertension in Pregnancy

- **Methyldopa**
  - Preferred on the basis of long-term follow-up studies supporting safety
- **BBs**
  - Reports of intrauterine growth retardation (atenolol)
  - Generally safe
- **Labetalol**
  - Increasingly preferred to methyldopa because of reduced side effects
- **Clonidine**
  - Limited data
- **Calcium antagonists**
  - Limited data
  - No increase in major teratogenicity with exposure
- **Diuretics**
  - Not first-line agents
  - Probably safe
- **ACEIs, angiotensin II receptor antagonists**
  - Contraindicated
  - Reported fetal toxicity and death

Treatment of Acute Severe Hypertension in Preeclampsia

- Hydralazine
  - 5 mg IV bolus, then 10 mg every 20 to 30 minutes to a maximum of 25 mg, repeat in several hours as necessary
- Labetalol (second-line)
  - 20 mg IV bolus, then 40 mg 10 minutes later, 80 mg every 10 minutes for 2 additional doses to a maximum of 220 mg
- Nifedipine (controversial)
  - 10 mg PO, repeat every 20 minutes to a maximum of 30 mg
  - Caution when using nifedipine with magnesium sulfate, can see precipitous BP drop
  - Short-acting nifedipine is not approved by US Food and Drug Administration for managing hypertension
- Sodium nitroprusside (rarely when others fail)
  - 0.25 μg/kg/min to a maximum of 5 μg/kg/min
  - Fetal cyanide poisoning may occur if used for more than 4 hours

Clinical Criteria Defining the Metabolic Syndrome in ATP III

- Waist circumference
  - >102 cm (>40 inches) for men
  - >88 cm (>35 inches) for women
- Blood pressure
  - 130 mm Hg systolic and/or
  - 85 mm Hg diastolic
- Fasting glucose
  - 110 mg/dL or 6.1 mmol/L
- Triglycerides
  - 150 mg/dL or 1.69 mmol/L
- HDL cholesterol
  - <40 mg/dL (1.04 mmol/L) in men
  - <50 mg/dL (1.29 mmol/L) in women

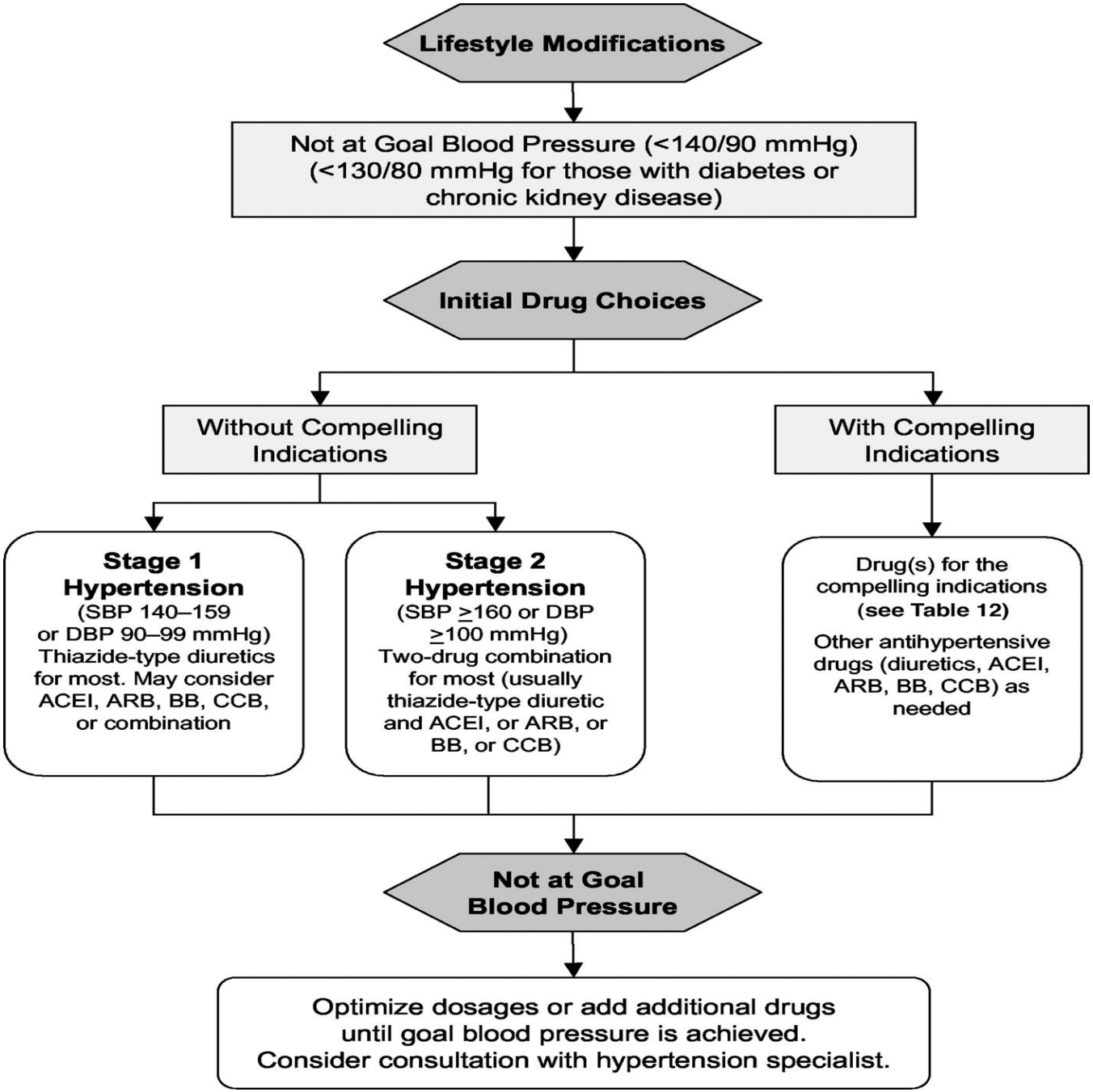
JAMA 2001;285:2486–2497.

Medical Therapy of Peripheral Arterial Disease

- Stop smoking
- Achieve ideal body weight
- Structure exercise program
- Achieve goal blood pressure
- Control lipids (goal LDL <100 mg/dL)
- Prevent or control diabetes
- Administer antiplatelet therapy (aspirin, clopidogrel, or both)
- Consider use of Cilostazol for symptoms of claudication if exercise alone is ineffective

Screening Tests for Identifiable Hypertension

Diagnosis	Diagnostic Test
Chronic kidney disease	Estimated GFR
Coarctation of the aorta	CT angiography
Cushing syndrome and other glucocorticoid excess states including chronic steroid therapy	History/dexamethasone suppression test
Drug-induced/related	History; drug screening
Pheochromocytoma	24-hour urinary metanephrine and normetanephrine
Primary aldosteronism and other mineralocorticoid excess states	24-hour urinary aldosterone level or specific measurements of other mineralocorticoids
Renovascular hypertension	Doppler flow study; magnetic resonance angiography
Sleep apnea	Sleep study with O_2 saturation
Thyroid/parathyroid disease	TSH; serum PTH


Lifestyle Modifications
Not at Goal Blood Pressure (<140/90 mmHg) (<130/80 mmHg for those with diabetes or chronic kidney disease)
Initial Drug Choices
Without Compelling Indications
With Compelling Indications
Stage 1 Hypertension (SBP 140–159 or DBP 90–99 mmHg) Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination
Stage 2 Hypertension (SBP ≥160 or DBP ≥100 mmHg) Two-drug combination for most (usually thiazide-type diuretic and ACEI, or ARB, or BB, or CCB)
Drug(s) for the compelling indications (see Table 12)
Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed
Not at Goal Blood Pressure
Optimize dosages or add additional drugs until goal blood pressure is achieved. Consider consultation with hypertension specialist.

Key Messages From JNC 7

- In individuals older than age 50 years, SBP is a more important CVD risk factor than DBP
- Beginning at 115/75 mm Hg, CVD risk doubles for each increment of 20/10 mm Hg throughout the BP range.
- Those who are normotensive at 55 years of age will have a 90% lifetime risk of developing hypertension.
- Those with SBP 120 to 139 mm Hg or DBP 80 to 89 mm Hg should be considered prehypertensive and require health-promoting lifestyle modifications to prevent a progressive rise in blood pressure and CVD.
- Thiazide-type diuretics should be initial drug therapy for most, either alone or combined with drugs from other classes.
- Certain specific high-risk conditions are compelling indications for the use of other antihypertensive drug classes (angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, ß-blockers, calcium channel blockers).
- Two or more antihypertensive medications will be required to achieve goal BP in most hypertensive patients.
- For patients with BP >20/10 mm Hg above the BP goal, initiation of therapy using two agents, one of which will usually be a thiazide diuretic, should be considered
- Hypertension will be controlled only if patients are motivated to stay on their treatment plan. Positive experiences, trust in the clinician, and empathy improve patient motivation and satisfaction.