Hypertension
References

• Ch. 3 (Hypertension) in Pharmacotherapy; a pathophysiologic approach. 9th edition 2014.


• 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens. 2013 Jul;31(7):1281-357


**Terminology**

- **Arterial BP** is the **pressure** in the **arterial wall** measured in millimeters of mercury (**mm Hg**).

- **Systolic pressure**: the **peak** pressure exerted in the **arteries** when blood is **pumped** into them during ventricular **systole**.

- **Diastolic pressure**: the **lowest pressure** exerted in the **arteries** when blood is **draining off into** the vessels downstream during **ventricular diastole**.

- **Pulse pressure**: the **difference** between the systolic and diastolic pressure (normally= **40 mm Hg**).

- **Mean arterial blood pressure (MAP)**: the **average** pressure responsible for the **driving blood** forward through the **arteries into the tissues throughout the cardiac cycle**

  
  \[
  \text{MAP} = \left(\frac{1}{3} \text{SBP}\right) + \left(\frac{2}{3} \text{DBP}\right)
  \]

  
  **MAP= diastolic pressure + 1/3 pulse pressure**

**Note:**
- Historically more emphasis was placed on diastolic than on systolic blood pressure as a predictor of cardiovascular morbid and fatal events.
- However, a large number of observational studies has demonstrated that cardiovascular morbidity and mortality bear a **continuous relationship** with both **systolic and diastolic blood pressures**.
Hypertension: **Persistent** elevation in **arterial** blood pressure.
Epidemiology

• **Worldwide prevalence** of hypertension is estimated to include 1 billion individuals. There are an estimated 7 million deaths per year that may be related to the diagnosis of hypertension.

• The prevalence of hypertension differs based on age, sex, and ethnicity.

• BP values increase with age.

• Most patient have prehypertension BP values before they are diagnosed with hypertension.

• Most hypertension diagnoses occur between the third and fifth decades of life.

• Up to the age of 55 years, more men than women have hypertension.

• From the ages of 55 to 74 years, slightly more women have hypertension than men, with this sex difference becoming greater in the very elderly (≥75 years).
Figure 1. Prevalence of High Blood Pressure in Adults by Age and Sex (NHANES: 2005–2006)

NHANES indicates The National Health and Nutrition Examination Survey. Modified from Lloyd-Jones et al. (34).
Etiology

• The cause of hypertension is unknown in the majority of cases (primary hypertension), but for those with secondary hypertension, specific causes are indicated.

• Essential or primary hypertension: ~90% patients, hypertension results from an unknown pathophysiologic etiology. This form of hypertension cannot be cured, but it can be controlled.

• Secondary hypertension: A small percentage of patients have a specific cause of their hypertension; either concurrent medical conditions or are endogenously induced. If the cause can be identified, hypertension in these patients has the potential to be cured.

• Pseudohypertension

• White-Coat Hypertension and Masked Hypertension

• Resistant hypertension
# Secondary Causes of Hypertension

## TABLE 19-1 Secondary Causes of Hypertension

### Disease
- Chronic kidney disease
- Cushing syndrome
- Coarctation of the aorta
- Obstructive sleep apnea
- Parathyroid disease
- Pheochromocytoma
- Primary aldosteronism
- Renovascular disease
- Thyroid disease

### Drugs and Other Products Associated with Hypertension

#### Prescription drugs
- **Amphetamines** (amphetamine, dexamphetamine, dextroamphetamine, lisdexamfetamine, methylphenidate, phendimetrazine, phentermine) and anorexiant (sibutramine)
- **Anti-vascular endothelin growth factor agents** (bevacizumab, sorafenib, sunitinib)
- **Corticosteroids** (cortisone, dexamethasone, fludrocortisone, hydrocortisone, methylprednisolone, prednisolone, prednisone, triamcinolone)
- **Calcineurin inhibitors** (cyclosporine and tacrolimus)
- **Decongestants** (pseudoephedrine, phenylpropanolamine and analogues)
- **Ergot alkaloids** (ergonovine, methysergide)
- **Erythropoiesis stimulating agents** (erythropoetin and darbropoetin)
- **Estrogen-containing oral contraceptives**

#### SNRI
- Nonsteroidal antinflammatory drugs—Cyclooxygenase-2 selective (celecoxib) and nonselective (aspirin, choline magnesium trisalicylate, diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, medroxyprogesterone, mfenamic acid, meloxicam, nabumetone, naproxen, nafoxen sodium, oxaprozin, piroxicam, salicylate, sulindac, tolmetin)
- Others: Desvenlafaxine, venlafaxine, bupropion

#### Situations:
- **$\beta$-blocker** or centrally acting $\alpha$-agonists (when abruptly discontinued): **$\beta$-blocker** without $\alpha$-blocker first when treating pheochromocytoma; use of a monoamine oxidase inhibitor (isocarboxazid, phenelzine, tranylcypromine sulfate) with tryamine containing foods or certain drugs

#### Street drugs and other products
- Cocaine and cocaine withdrawal
- Ephedra alkaloids (e.g., Ma huang), “herbal ecstasy,” other pseudoephedrine or phenylpropanolamine analogues
- Nicotine and withdrawal, anabolic steroids, narcotic withdrawal, ergot-containing herbal products, St. John’s wort

#### Food substances
- Sodium
- Ethanol
- Licorice

---

*Agents of most clinical importance.*
Blood pressure can be affected by using, or stopping the use of, certain drugs or medications.
Coarctation of the aorta is a birth defect in which the aorta, the major artery from the heart, is narrowed. The narrowing results in high blood pressure before the point of coarctation and low blood pressure beyond the point of coarctation. Most commonly, coarctation is located so that there is high blood pressure in the upper body and arms and low blood pressure in the lower body and legs. Symptoms can include localized hypertension, cold feet or legs, decreased exercise performance, and heart failure.
Pheochromocytoma is a rare tumor in part of the adrenal gland. In most cases, the tumors are not cancerous and do not spread to other parts of the body. But, in about 30 percent of cases, the tumors are cancerous. Most people with pheochromocytoma have hypertension because the tumor causes the adrenal gland to produce too much adrenaline or noradrenaline. Patients can have attacks of high blood pressure that occur in sudden, short bursts, or the high blood pressure can be more continuous and long lasting.
Renovascular disease

Renovascular disease is a progressive condition that causes **narrowing or blockage** of the renal arteries or veins. It's the general term used for three disorders:

- renal artery occlusion,
- renal vein thrombosis,
- renal atheroembolism
Pathophysiology

• The **pathophysiology of primary hypertension** is heterogeneous, but ultimately exerts its effects through the two primary determinants of blood pressure: **cardiac output and peripheral resistance**.

• **Multiple factors** that control **BP** are potential contributing components in the **development of essential hypertension**.
  – humoral (i.e., the renin–angiotensin–aldosterone system [RAAS])
  – vasodepressor mechanisms (Vascular Endothelial Mechanisms),
  – abnormal neuronal mechanisms,
  – defects in peripheral autoregulation,
  – and disturbances in sodium, calcium, and natriuretic hormones.

most antihypertensives specifically target these mechanisms and components of the RAAS.
Factors involved in the pathogenesis of hypertension

Excess sodium intake → Renal sodium retention → ↑ Fluid volume → ↑ Preload

Reduced nephron number → Decreased filtration surface → ↑ Contractility

Stress → Sympathetic nervous over-activity

Genetic alteration → Renin-angiotensin excess

Obesity → Cell membrane alteration

Endothelium derived factors → Hyper-insulinemia

↑ Fluid volume → Venous constriction

Preload → Contractility

Blood pressure = Cardiac output X Peripheral resistance increased PR

Hypertension = Increased CO

Autoregulation
## Potential Mechanisms of Pathogenesis

Blood pressure (BP) is the mathematical product of cardiac output and peripheral resistance. Elevated BP can result from increased cardiac output and/or increased total peripheral resistance.

<table>
<thead>
<tr>
<th>Increased cardiac output</th>
<th>Increased cardiac preload:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Increased fluid volume from excess sodium intake or renal sodium retention (from reduced number of nephrons or decreased glomerular filtration)</td>
</tr>
<tr>
<td></td>
<td>Venous constriction:</td>
</tr>
<tr>
<td></td>
<td>• Excess stimulation of the renin–angiotensin–aldosterone system (RAAS)</td>
</tr>
<tr>
<td></td>
<td>• Sympathetic nervous system overactivity</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Increased peripheral resistance</th>
<th>Functional vascular constriction:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Excess stimulation of the RAAS</td>
</tr>
<tr>
<td></td>
<td>• Sympathetic nervous system overactivity</td>
</tr>
<tr>
<td></td>
<td>• Genetic alterations of cell membranes</td>
</tr>
<tr>
<td></td>
<td>• Endothelial-derived factors</td>
</tr>
<tr>
<td>Structural vascular hypertrophy:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Excess stimulation of the RAAS</td>
</tr>
<tr>
<td></td>
<td>• Sympathetic nervous system overactivity</td>
</tr>
<tr>
<td></td>
<td>• Genetic alterations of cell membranes</td>
</tr>
<tr>
<td></td>
<td>• Endothelial-derived factors</td>
</tr>
<tr>
<td></td>
<td>• Hyperinsulinemia resulting from the metabolic syndrome</td>
</tr>
</tbody>
</table>
1- Humoral (role of the RAAS, most influential contributor to the homeostatic regulation of BP)

- ACE inhibitors;
- angiotensin II receptor blockers;
- β-blockers;
- calcium channel blockers;
- diuretics;
- aldosterone antagonists;
- direct renin inhibitor. (aliskiren)
2. Neuronal Regulation

- Pathologic disturbances in any of the four major components of the neuroregulation system could conceivably lead to chronically elevated BP. These systems are physiologically interrelated:
  - **autonomic** nerve fibers (sympathetic and parasympathetic)
  - **adrenergic receptors** $\alpha_1, \alpha_2, \beta_1, \beta_2$ (presynaptic and postsynaptic)
  - **baroreceptors**, through the **ninth cranial nerve** and **vagus nerves to the brain stem** (is the major negative feedback mechanism that controls sympathetic activity)
  - **central nervous system**: stimulation of certain areas within the central nervous system (nucleus tractus solitarius, vagal nuclei, **vasomotor center**, and the area postrema) can either increase or decrease BP
3. Peripheral Autoregulatory Components:
   1. Renal (increase in BP...increase renal sodium and water excretion, decrease in BP.)
   2. Local oxygen tension

4. Vascular Endothelial Mechanisms:
   a deficiency in the local synthesis of vasodilating substances (prostacyclin and bradykinin, nitric oxide) or excess vasoconstricting substances (angiotensin II and endothelin I)

5. Electrolytes and Other Chemicals:
   - Population-based studies indicate that high salt diets are associated with a high prevalence of stroke and hypertension. (The exact mechanisms by which excess sodium leads to hypertension are not known.)
   
   - Some studies show that dietary calcium supplementation results in a modest BP reduction in patients with HTN.
   
   - Potassium (Potassium depletion may increase peripheral vascular resistance?)
# TABLE 3-3  Classification of Blood Pressure in Adults (Age ≥18 Years)\(^a\)

<table>
<thead>
<tr>
<th>Classification</th>
<th>Systolic Blood Pressure (mm Hg)</th>
<th>Diastolic Blood Pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td>and &lt;80</td>
</tr>
<tr>
<td>Prehypertension(^b)</td>
<td>120–139</td>
<td>or 80–89</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>140–159</td>
<td>or 90–99</td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>(\geq160)</td>
<td>or (\geq100)</td>
</tr>
</tbody>
</table>

\(^a\)Classification determined based on the average of two or more properly measured seated BP values from two or more clinical encounters. If systolic and diastolic BP values yield different classifications, the highest category is used for the purpose of determining a classification.

\(^b\)For certain patients, BP values within the prehypertension range are considered above goal (see Box 3-2).
Classification of BP – JNC7+8

- The following definitions were suggested in 2003 by the seventh report of the Joint National Committee (JNC 7) and reaffirmed in 2013 by JNC 8, and are based upon the average of two or more properly measured readings at each of two or more visits after an initial screen.
- It includes four categories: normal, prehypertension, stage 1 hypertension, and stage 2 hypertension.

**TABLE 19-3** Classification of Blood Pressure in Adults (Age ≥18 Years)\(^a\)

<table>
<thead>
<tr>
<th>Classification</th>
<th>Systolic Blood Pressure (mm Hg)</th>
<th>Diastolic Blood Pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Less than 120</td>
<td>and</td>
</tr>
<tr>
<td>Prehypertension(^b)</td>
<td>120–139</td>
<td>or</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>140–159</td>
<td>or</td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>≥160</td>
<td>or</td>
</tr>
</tbody>
</table>

These definitions apply to adults on no antihypertensive medications and who are not acutely ill.
- If there is a disparity in category between the systolic and diastolic pressures, the higher value determines the severity of the hypertension.
- The systolic pressure is the greater predictor of risk in patients over the age of 50 to 60 years.
- Prehypertension is not considered a disease category, but identifies patients whose BP is likely to increase into the classification of hypertension in the future.
- For certain patients, BP values within the prehypertension range are considered above goal.
Hypertensive crises

- **Hypertensive crises** are clinical situations where BP values are *very elevated*, typically greater than 180/120 mm Hg.

- Hypertensive crisis can be divided into:
  1. **Hypertensive emergencies** are extreme elevations in BP that are *accompanied* by *acute* or *progressing target-organ damage*.
  2. **Hypertensive urgencies** are *high elevations in BP without* acute or progressing *target-organ injury*. 
Cardiovascular Risk and Blood Pressure

• Epidemiologic data demonstrate a strong correlation between BP and CV morbidity and mortality.

• Risk of stroke, myocardial infarction, angina, heart failure, kidney failure, or early death from a CV cause are directly correlated with BP.

• Starting at a BP of 115/75 mm Hg, risk of CV disease doubles with every 20/10 mm Hg increase.

• Even patients with prehypertension have an increased risk of CV disease.

• Treating patients with hypertension with antihypertensive drug therapy provides significant benefits.
Cardiovascular Risk and Blood Pressure

• SBP is a **stronger predictor** of CV disease **than DBP** in **adults older than 50 years** of age and is the most important clinical BP parameter for most patients.

• **Patients with Isolated systolic hypertension** (**DBP values less than 90 mm Hg** and **SBP values >140 mm Hg**) have **higher pulse pressure values**. (a measure of arterial stiffness)
  – In these patients **pathophysiologic changes in their arterial vasculature** are **consistent with aging**. These changes decrease the compliance of the arterial wall and ↑ risk of CV morbidity and mortality.
  – **Higher pulse pressure values seen in those with isolated systolic hypertension** are **directly correlated** with risk of CV mortality.
  – By age 70, over 90% of hypertensive patients have isolated systolic hypertension
Clinical Presentation of Hypertension

General

• The patient may appear very healthy, or may have the presence of additional CV risk factors:
  1. Age (55 years for men and 65 years for women)
  2. Diabetes mellitus
  3. Dyslipidemia (elevated low-density lipoprotein-cholesterol, total cholesterol, and/or triglycerides; low high-density lipoprotein-cholesterol)
  4. Microalbuminuria
  5. Family history of premature CV disease
  6. Obesity (body mass index 30 kg/m²)
  7. Physical inactivity
  8. Tobacco use

Symptoms

• Most patients are asymptomatic. "silent killer"

Signs

• Previous BP values in the prehypertension or hypertension category.
Diagnostic Evaluation of BP

• **Diagnostic procedures aim at:**

1. establishing **blood pressure** levels;
2. identifying **secondary causes** of hypertension;
3. **evaluating** the **overall cardiovascular risk** by searching for other risk factors, target organ damage and concomitant diseases or accompanying clinical conditions.

• **The diagnostic procedures comprise:**
  – repeated **blood pressure measurements**
  – **medical history** (family and clinical)
  – **physical examination**
  – **laboratory and instrumental** investigations.
1- Measuring blood pressure

• In general the diagnosis of hypertension should be based on multiple blood pressure measurements (2), taken on separate occasions (2-3) over a period of time, although in particularly severe cases the diagnosis can be based on measurements taken at a single visit.

• Blood pressure can be measured by a mercury sphygmomanometer or other non-invasive devices (auscultatory or oscillometric semiautomatic devices).

• **office-based BP measurements** are considered the gold standard values that guide antihypertensive drug therapy.

• Correct BP measurements require that the clinician listen through a stethoscope that is placed over the brachial artery for the appearance of the five phases of the Korotkoff sounds.
Recommendations for measuring BP

- Patients should refrain from nicotine or caffeine ingestion for 30 minutes and be seated with the lower back supported in a chair and with their bare arm supported and resting near heart level.
- Feet should be flat on the floor (with legs not crossed).
- Measuring BP in the supine or standing position may be required under special circumstances (suspected orthostatic hypotension, volume depletion, or dehydration).
- The measurement environment should be relatively quiet and provide privacy.
- Measurement should begin only after a 5-minute period of rest.
- A properly sized cuff (pediatric, small, regular, large, or extra large,) should be used.
Phases of the Korotkoff sounds heard when indirectly measuring blood pressure.

**Phase 1:** The pressure at which the first faint clear tapping sounds are heard. These sounds gradually increase in intensity as the cuff deflates.

**Phase 2:** That time during cuff deflation when a murmur or swishing sounds are heard. They are softer and longer than in Phase 1.

**Phase 3:** The period during which sounds are crisp, loud with increased intensity.

**Phase 4:** That time when sounds are less distinct, and change to a muffled and soft (or blowing) quality.

**Phase 5:** The pressure when the last sound is heard and after which all sounds disappear.
Ambulatory and self blood pressure monitoring

• Either of these may be warranted in patients with suspected white coat hypertension (without hypertension-related target-organ damage) to differentiate white coat from essential hypertension.

• They may be helpful in patients with:
  1. apparent drug resistance,
  2. hypotensive symptoms while on antihypertensive therapy,
  3. episodic hypertension,
  4. autonomic dysfunction, /and
  5. to identify "nondippers" whose BP does not decrease by >10% during sleep and which may portend increased risk of BP-related complications

• As a comparison, the normal upper limit for BP in most patients is:
  – 140/90 mm Hg for office-based measurement,
  – ABPM
    • Twenty-four-hour average BP – Normotension is defined as a BP less than 130/80 mmHg, and hypertension is defined as a BP greater than or equal to 130/80 mmHg
    • Daytime (awake) BP – Normotension is defined as a BP less than 135/85 mmHg, and hypertension is defined as a BP greater than or equal to 135/85 mmHg
    • Nighttime (asleep) BP – Normotension is defined as a BP less than 120/70 mmHg, and hypertension is defined as a BP greater than or equal to 120/75 mmHg
    – Average of 135/85 mm Hg for self-BP measurements.

• Note:
  – the threshold for acceptable values is lower than that obtained during office-based measurements
Indications for ambulatory BP monitoring

- Main indications for ambulatory BP monitoring are for patients in whom the diagnosis of hypertension or response to therapy is unclear from office visits. Further indications include suspected syncope or hypotensive disorders, evaluation of vertigo, and dizziness.

- Ambulatory BP monitoring is also important for avoiding overtreatment in the elderly with white-coat hypertension and also to ensure diagnosis and treatment of those with masked hypertension (avoid under treatment).

- Ambulatory BP is a better predictor of risk than clinic or office BP measurement in older patients with isolated systolic hypertension.
The Concept of White Coat and Masked Hypertension

**Masked HTN:**
people who are truly hypertensive but in whom the diagnosis is missed by office BP measurements.

**White-coat HTN:**
BP may be elevated in the office but not on ambulatory BP

### Table

<table>
<thead>
<tr>
<th></th>
<th>Office SBP mmHg</th>
<th>Home/Ambulatory SBP mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>True Hypertensive</td>
<td>120-200</td>
<td>120-200</td>
</tr>
<tr>
<td>Masked HTN</td>
<td>120-200</td>
<td>120-200</td>
</tr>
<tr>
<td>True Normotensive</td>
<td>120-200</td>
<td>120-200</td>
</tr>
<tr>
<td>White Coat HTN</td>
<td>120-200</td>
<td>120-200</td>
</tr>
</tbody>
</table>
Pseudohypertension

• Pseudohypertension is when blood pressure measurements are elevated but the blood pressure is actually normal.

• Pseudohypertension is not very common, and it is almost always found in older patients (WHY?)

• Pseudohypertension is usually suspected in cases where:
  – The blood pressure reading is very high over time, but the patient has no signs of organ damage or other complications
  – Attempting to treat the measured high blood pressure causes symptoms of low blood pressure (dizziness, confusion, decreased urine output)

• While a finger blood pressure meter or other similar devices may provide some useful data in cases of suspected pseudohypertension, the only way to confirm the diagnosis is by directly measuring the intraarterial blood pressure. This is done inserting a needle directly into a small artery.
Resistant HTN

- Resistant hypertension is defined as that in which patients fail to attain their BP goal while treated with a three-drug regimen that utilizes full (maximum) antihypertensive doses, one of which is a diuretic.

<table>
<thead>
<tr>
<th>Table 4. Identifiable causes of hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep apnea</td>
</tr>
<tr>
<td>Drug-induced or related causes (see table 9)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>Primary aldosteronism</td>
</tr>
<tr>
<td>Renovascular disease</td>
</tr>
<tr>
<td>Chronic steroid therapy and Cushing's syndrome</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
</tr>
<tr>
<td>Coarctation of the aorta</td>
</tr>
<tr>
<td>Thyroid or parathyroid disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 9. Causes of resistant hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improper BP Measurement</td>
</tr>
<tr>
<td>Volume Overload and Pseudotolerance</td>
</tr>
<tr>
<td>Excess sodium intake</td>
</tr>
<tr>
<td>Volume retention from kidney disease</td>
</tr>
<tr>
<td>Inadequate diuretic therapy</td>
</tr>
<tr>
<td>Drug-Induced or Other Causes</td>
</tr>
<tr>
<td>Nonadherence</td>
</tr>
<tr>
<td>Inadequate doses</td>
</tr>
<tr>
<td>Inappropriate combinations</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs; cyclooxegenase 2 inhibitors</td>
</tr>
<tr>
<td>Cocaine, amphetamines, other illicit drugs</td>
</tr>
<tr>
<td>Sympathomimetics (decongestants, anorectics)</td>
</tr>
<tr>
<td>Oral contraceptives</td>
</tr>
<tr>
<td>Adrenal steroids</td>
</tr>
<tr>
<td>Cyclosporine and tacrolimus</td>
</tr>
<tr>
<td>Erythropoietin</td>
</tr>
<tr>
<td>Licorice (including some chewing tobacco)</td>
</tr>
<tr>
<td>Selected over-the-counter dietary supplements and medicines (e.g., ephedra, ma haung, bitter orange)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Associated Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>Excess alcohol intake</td>
</tr>
</tbody>
</table>
In the absence of end-organ damage, the diagnosis of mild hypertension should not be made until the blood pressure has been measured on at least three to six visits, spaced over a period of weeks to months.
Diagnostic algorithm for high Blood Pressure including Office, ABPM and Home Blood Pressure Measurement

BP: 140-179 / 90-109

ABPM (If available)

Clinic BP

Hypertension visit 3

≥ 160 SBP or
≥ 100 DBP → Diagnosis of HTN
< 160 / 100 → ABPM or HBPM

Hypertension visit 4-5

≥ 140 SBP or
≥ 90 DBP → Diagnosis of HTN
< 140 / 90 → Continue to follow-up

HBPM

≥ 135 SBP or ≥ DBP 85

< 135/85

Awake BP

< 135/85 and 24-hour < 130/80

Awake BP

≥ 135 SBP or
≥ 85 DBP
Or 24-hour
≥ 130 SBP or
≥ 80 DBP

Continue to follow-up

Diagnosis of HTN

Continue to follow-up

Diagnosis of HTN

In the absence of end-organ damage, a patient should not be labeled as having hypertension unless: the blood pressure is persistently elevated after three to six visits over a several month period; hypertension is revealed by 24-hour ambulatory monitoring; or the average of home blood pressure readings taken in the morning and evening daily for seven days is elevated.
2014 Canadian Hypertension Education Program Recommendations
Clinical Evaluation (Cont’d)

• Once it has been determined that the patient has persistent hypertension, an evaluation should be performed to ascertain the following information:
  – To determine the extent of target organ damage.
  – To assess the patient's overall cardiovascular risk status.
  – To rule out identifiable and often curable causes of hypertension.
### Table 3. Cardiovascular risk factors

<table>
<thead>
<tr>
<th>Major Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension*</td>
</tr>
<tr>
<td>Cigarette smoking</td>
</tr>
<tr>
<td>Obesity* (body mass index ≥30 kg/m²)</td>
</tr>
<tr>
<td>Physical inactivity</td>
</tr>
<tr>
<td>Dyslipidemia*</td>
</tr>
<tr>
<td>Diabetes mellitus*</td>
</tr>
<tr>
<td>Microalbuminuria or estimated GFR &lt;60 mL/min</td>
</tr>
<tr>
<td>Age (older than 55 for men, 65 for women)</td>
</tr>
<tr>
<td>Family history of premature cardiovascular disease</td>
</tr>
<tr>
<td>(men under age 55 or women under age 65)</td>
</tr>
</tbody>
</table>

### Target Organ Damage

- Left ventricular hypertrophy
- Angina or prior myocardial infarction
- Prior coronary revascularization
- Heart failure

### Table 4. Identifiable causes of hypertension

- Sleep apnea
- Drug-induced or related causes (see table 9)
- Chronic kidney disease
- Primary aldosteronism
- Renovascular disease
- Chronic steroid therapy and Cushing's syndrome
- Pheochromocytoma
- Coarctation of the aorta
- Thyroid or parathyroid disease

GFR, glomerular filtration rate.
* Components of the metabolic syndrome.
2- Guidelines for family and clinical history (ESC)

A comprehensive family history should be obtained with particular attention to hypertension, diabetes, dyslipidaemia, premature coronary heart disease, stroke, peripheral artery or renal disease.

**Box 4  Guidelines for family and clinical history**

1. Duration and previous level of high BP
2. Indications of secondary hypertension:
   a) family history of renal disease (polycystic kidney)
   b) renal disease, urinary tract infection, haematuria, analgesic abuse (parenchymal renal disease)
   c) drug/substance intake: oral contraceptives, liquorice, carbenoxolone, nasal drops, cocaine, amphetamines, steroids, non-steroidal anti-inflammatory drugs, erythropoietin, cyclosporin
   d) episodes of sweating, headache, anxiety, palpitation (phaeochromocytoma)
   e) episodes of muscle weakness and tetany (aldosteronism)
3. Risk factors:
   a) family and personal history of hypertension and cardiovascular disease
   b) family and personal history of dyslipidaemia
   c) family and personal history of diabetes mellitus
   d) smoking habits
   e) dietary habits
   f) obesity; amount of physical exercise
   g) snoring; sleep apnoea (information also from partner)
   h) personality

4. Symptoms of organ damage
   a) brain and eyes: headache, vertigo, impaired vision, transient ischaemic attacks, sensory or motor deficit
   b) heart: palpitation, chest pain, shortness of breath, swollen ankles
   c) kidney: thirst, polyuria, nocturia, haematuria
   d) peripheral arteries: cold extremities, intermittent claudication

5. Previous antihypertensive therapy:
   a) Drug(s) used, efficacy and adverse effects

6. Personal, family and environmental factors
3- Guidelines for physical examination (ESC)

**Box 5  Physical examination for secondary hypertension, organ damage and visceral obesity**

**Signs suggesting secondary hypertension and organ damage**

- Features of Cushing syndrome
- Skin stigmata of neurofibromatosis (phaeochromocytoma)
- Palpation of enlarged kidneys (polycystic kidney)
- Auscultation of abdominal murmurs (renovascular hypertension)
- Auscultation of precordial or chest murmurs (aortic coarctation or aortic disease)
- Diminished and delayed femoral pulses and reduced femoral BP (aortic coarctation, aortic disease)
Signs of organ damage
• Brain: murmurs over neck arteries, motor or sensory defects
• Retina: fundoscopic abnormalities
• Heart: location and characteristics of apical impulse, abnormal cardiac rhythms, ventricular gallop, pulmonary rales, peripheral oedema
• Peripheral arteries: absence, reduction, or asymmetry of pulses, cold extremities, ischaemic skin lesions
• Carotid arteries: systolic murmurs

Evidence of visceral obesity
• Body weight
• Increased waist circumference (standing position)
  M: > 102 cm; F: > 88 cm
• Increased body mass index \[ \text{[body weight (kg)/height (m)}^2] \]
• Overweight \( \geq 25 \text{ kg/m}^2 \); Obesity \( \geq 30 \text{ kg/m}^2 \)
Waist Circumference Measurement

- Last rib margin
- Mid distance
- Iliac crest

Courtesy J.P. Després 2006
The patient may have normal values and still have hypertension. However, some may have abnormal values consistent with either additional CV risk factors or HTN-related damage.
Recommended tests
- Echocardiogram
- Carotid ultrasound
- Quantitative proteinuria (if dipstick test positive)
- Ankle-brachial BP Index
- Fundoscopy
- Glucose tolerance test (if fasting plasma glucose >5.6 mmol/L (100 mg/dL)
- Home and 24 h ambulatory BP monitoring
- Pulse wave velocity measurement (where available)

Extended evaluation (domain of the specialist)
- Further search for cerebral, cardiac, renal and vascular damage. Mandatory in complicated hypertension
- Search for secondary hypertension when suggested by history, physical examination or routine tests: measurement of renin, aldosterone, corticosteroids, catecholamines in plasma and/or urine; arteriographies; renal and adrenal ultrasound; computer-assisted tomography; magnetic resonance imaging
<table>
<thead>
<tr>
<th>Causes</th>
<th>Historical Findings</th>
<th>Physical Examination Findings</th>
<th>Laboratory Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep apnea</td>
<td>Daytime fatigue and somnolence</td>
<td>Large neck circumference; overweight or obese</td>
<td>Abnormal sleep studies with frequent awakenings and anoxic episodes</td>
</tr>
<tr>
<td>Renovascular disease</td>
<td>Moderate or severe high BP before age 30 or after 55; rapidly progressive hypertension</td>
<td>Abdominal bruits; funduscopic hemorrhages</td>
<td>Suppressed or stimulated plasma renin activity; IVP (rapid sequence); digital subtraction angiography</td>
</tr>
<tr>
<td>Renoparenchymal disease</td>
<td>Dysuria, polyuria, nocturia; urinary tract infections; kidney stones; family history of polycystic or other types of kidney disease</td>
<td>Edema</td>
<td>Proteinuria; hematuria; bacteriuria</td>
</tr>
<tr>
<td>Coarctation of the aorta</td>
<td>Intermittent claudication</td>
<td>Diminished or absent femoral pulses compared with carotids; lower SBP in leg compared with arm</td>
<td>—</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>Paroxysmal headaches, palpitations, sweating, dizziness, and pallor</td>
<td>Nervousness, tremor, tachycardia, orthostatic hypotension</td>
<td>Clonidine suppression tests(^d); high urinary metanephrine or vanillylmandelic acid Hypokalemia</td>
</tr>
<tr>
<td>Primary aldosteronism</td>
<td>Weakness, polyuria, polydipsia, intermittent paralysis</td>
<td>Orthostatic hypotension</td>
<td></td>
</tr>
<tr>
<td>Cushing syndrome</td>
<td>Menstrual irregularity</td>
<td>Moon face; truncal obesity; buffalo hump; hirsutism; violet striae</td>
<td>(\uparrow) serum glucose; (\uparrow) plasma cortisol after suppression with dexamethasone</td>
</tr>
</tbody>
</table>

\(^d\) Failure of plasma catecholamines to \(\downarrow\) by 50% within 3 hours of administration of 0.3 mg clonidine highly suggests pheochromocytoma.
BP, blood pressure; IVP, intravenous pyelogram; SBP, systolic blood pressure.
Comments on Clinical Evaluation

- Many guidelines advocate “routine laboratory testing” in evaluation of patients with high BP. Despite such recommendations, there is little evidence to support routine laboratory testing, and clinicians should take a more deliberative and reasoned approach to ordering tests. Routine testing increases costs and may have adverse effects such as anxiety, pain/discomfort, additional testing, complications from such testing, and time and travel burden.

- The most important role for testing in an elderly patient with hypertension is to assess for organ damage and modifiable CVD risk factors, including tobacco smoking, hypercholesterolemia, diabetes mellitus, and excessive alcohol intake.
Hypertension Management (Goals)

• Hypertension is treated with both **lifestyle modifications** and **pharmacotherapy**.

• The presence of specific complications of hypertension or comorbidities (sometime referred to as “**compelling indications**”) in any given patient should be considered when selecting specific pharmacotherapy to treat hypertension.

• The **overall goal of treating hypertension** is to reduce associated morbidity and mortality. These manifest as **hypertension-associated complications** which are the primary causes of death in patients with hypertension.

• the specific choice of drug therapy is significantly influenced by evidence demonstrating such risk reduction.

• **Surrogate goal of therapy** is to achieve a desired target BP value
Hypertension-Associated Complications

• Atherosclerotic Vascular Disease:
  – **Coronary artery/heart** disease
    • Myocardial infarction [MI]
    • Acute coronary syndromes
    • Chronic stable angina
  – **Carotid artery** disease:
    • Ischemic stroke
    • Transient ischemic attack
  – **Peripheral arterial** disease
  – **Abdominal aortic aneurysm**

• Other forms of CV disease
  – Left ventricular dysfunction (heart failure)

• **Chronic kidney disease**
Risk factors for hypertension-associated complications

• Hypertension
• Cigarette smoking
• Obesity (BMI $\geq 30$ kg/m$^2$)
• Physical inactivity
• Dyslipidemia
• Diabetes mellitus
• Kidney disease
  • Microalbuminuria or estimated GFR $< 60$ ml/min

• Advanced age
  – Males $> 55$ yrs
  – Females $> 65$ yrs
• Family history of premature atherosclerotic vascular disease
  – Males $< 55$ yrs
  – Females $< 65$ yrs

• These are considered major CV risk factors that increase the likelihood of developing hypertension-associated complications, not hypertension.

BMI, body mass index; CV, cardiovascular; GFR, glomerular filtration rate.
Benefits of Lowering BP

- Why treat HTN?
  - 35-40% ↓ in stroke morbidity and mortality
  - 20-25% ↓ CAD events
  - 21% ↓ vascular mortality
  - 52% ↓ in CHF
  - 35% ↓ in LVH
Goal blood pressure

- Goal blood pressure depends upon age and the presence of comorbid conditions.
- Goal blood pressure is **less than 140/90 mmHg** in patients **younger than 60 years**.
- In the **general hypertensive** population of older adults (ie, **60 years and older, nondiabetic, no chronic kidney disease**), goal blood pressure is **<150/<90 mmHg** and, in patients aged 60 to 79 years, the systolic pressure should be further reduced to **<140 mmHg** if it can be achieved without producing significant side effects.
- In **older patients** with **diabetes or chronic kidney** disease, the blood pressure goal is **<140/<90 mmHg**.
- These **systolic blood pressure targets** also **apply to older adults** with **isolated systolic hypertension**. However, the **diastolic blood pressure** should be **reduced** to a minimum posttreatment diastolic pressure of **>60 mmHg** overall or **perhaps >65 mmHg** in patients with known **coronary artery disease** unless symptoms that could be attributable to **hypoperfusion** occur at higher pressures.
- Lower goals are **suggested** for patients with **certain comorbid conditions**, such as those with **atherosclerotic cardiovascular** disease or in patients with **proteinuric chronic kidney disease**. In addition, antihypertensive drugs are given to improve survival in a number of conditions (eg, heart failure, post-myocardial infarction), independent of the blood pressure. In these cases, lower blood pressure levels may be accepted to permit sufficient drug doses.

**Note:**
- **members of the eighth Joint National Committee (JNC 8) did not suggest** pharmacotherapy to lower the systolic **pressure below 140 mmHg** in older adults.
- In addition, **the 2013 ESH/ESC guidelines** recommended a goal blood pressure of **<150/<90 mmHg**, rather than **<140/90 mmHg**, in **those 80 years of age or older**.
<table>
<thead>
<tr>
<th>Guideline</th>
<th>Population</th>
<th>Goal BP, mm Hg</th>
<th>Initial Drug Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014 Hypertension guideline</td>
<td>General ≥60 y</td>
<td>&lt;150/90</td>
<td>Nonblack: thiazide-type diuretic, ACEI, ARB, or CCB; black: thiazide-type diuretic or CCB</td>
</tr>
<tr>
<td></td>
<td>General &lt;60 y</td>
<td>&lt;140/90</td>
<td>Diuretic, β-blocker, CCB, ACEI, or ARB</td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>&lt;140/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>CKD</td>
<td>&lt;140/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>CKD no proteinuria</td>
<td>&lt;140/90</td>
<td>Adamantidine, β-blocker, CCB, ACEI, or ARB</td>
</tr>
<tr>
<td></td>
<td>CKD + proteinuria</td>
<td>&lt;130/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td>ESH/ESC 2013^{37}</td>
<td>General nonelderly</td>
<td>&lt;140/90</td>
<td>Diuretic, β-blocker, CCB, ACEI, or ARB</td>
</tr>
<tr>
<td></td>
<td>General elderly &lt;80 y</td>
<td>&lt;150/90</td>
<td>ACEI, β-blocker (age &lt;60y), ACEI (nonblack), or ARB</td>
</tr>
<tr>
<td></td>
<td>General ≥80 y</td>
<td>&lt;150/90</td>
<td>ACEI, ARB</td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>&lt;130/80</td>
<td>ACEI or ARB with additional CVD risk</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ACEI, ARB, thiazide, or DHPCCB without additional CVD risk</td>
</tr>
<tr>
<td>CHEP 2013^{38}</td>
<td>General &lt;80 y</td>
<td>&lt;140/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>General ≥80 y</td>
<td>&lt;150/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>&lt;130/80</td>
<td>ACEI or ARB with additional CVD risk</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ACEI, ARB, thiazide, or DHPCCB without additional CVD risk</td>
</tr>
<tr>
<td>ADA 2013^{39}</td>
<td>CKD</td>
<td>&lt;140/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>&lt;140/80</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td>KDIGO 2012^{40}</td>
<td>CKD no proteinuria</td>
<td>&lt;140/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>CKD + proteinuria</td>
<td>&lt;130/80</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td>NICE 2011^{41}</td>
<td>General &lt;80 y</td>
<td>&lt;140/90</td>
<td>&lt;55 y: ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>General ≥80 y</td>
<td>&lt;150/90</td>
<td>≥55 y or black: CCB</td>
</tr>
<tr>
<td>ISHIB 2010^{42}</td>
<td>Black, lower risk</td>
<td>&lt;135/85</td>
<td>Diuretic or CCB</td>
</tr>
<tr>
<td></td>
<td>Target organ damage or CVD</td>
<td>&lt;130/80</td>
<td>Diuretic or CCB</td>
</tr>
</tbody>
</table>

Abbreviations: ADA, American Diabetes Association; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; CHEP, Canadian Hypertension Education Program; CKD, chronic kidney disease; CVD, cardiovascular disease; DHPCCB, dihydropyridine calcium channel blocker; ESC, European Society of Cardiology; ESH, European Society of Hypertension; ISHIB, International Society for Hypertension in Blacks; JNC, Joint National Committee; KDIGO, Kidney Disease: Improving Global Outcome; NICE, National Institute for Health and Clinical Excellence.