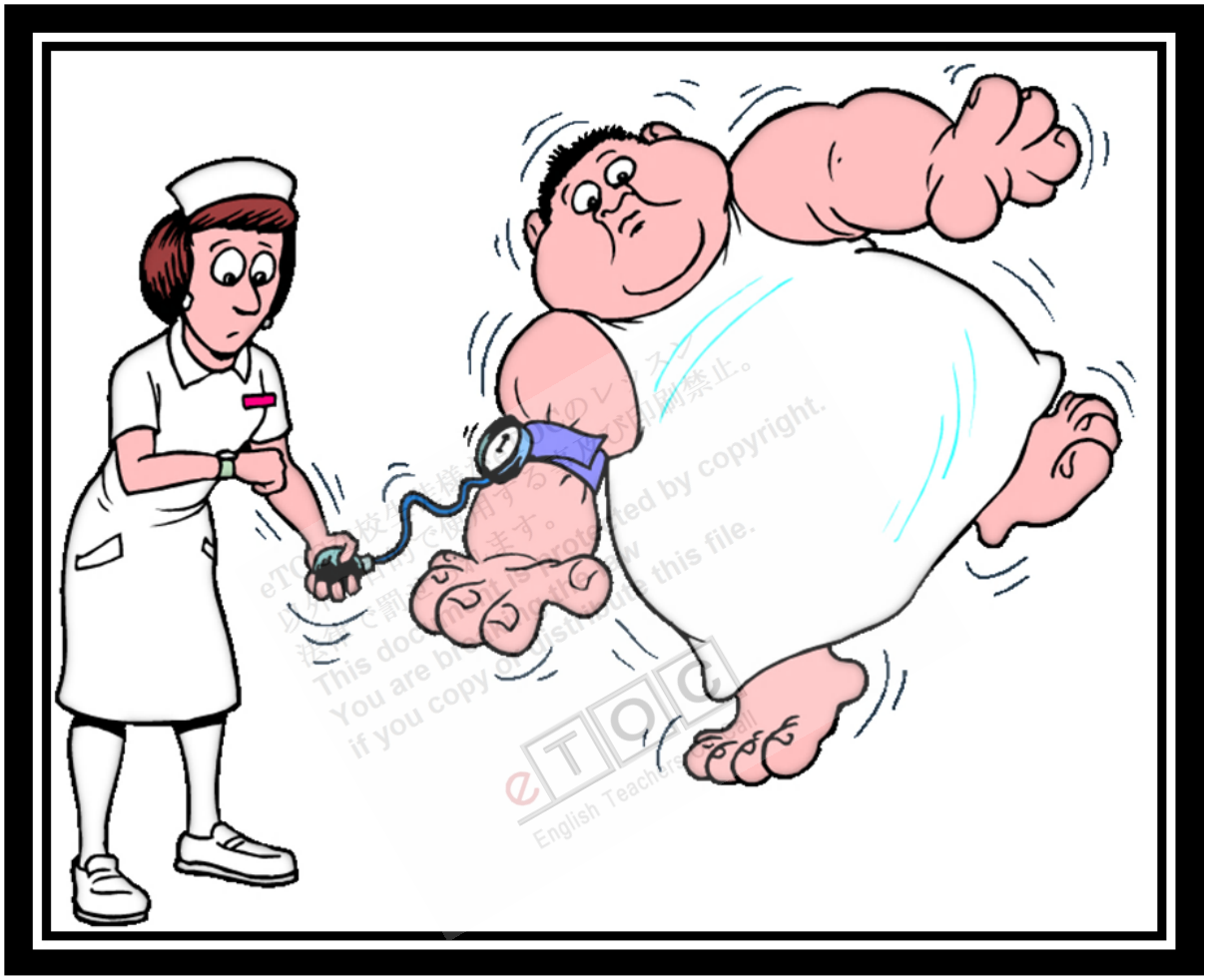
Hypertension Part 1

Overview of Hypertension



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Hypertension *is sustained* ***elevation*** *of resting systolic BP (≥ 140 mm Hg), diastolic BP (≥ 90 mm Hg), or both. Hypertension with no known cause (primary; formerly, essential hypertension) is most common. Hypertension with an identified cause (secondary hypertension) is usually due to a renal disorder. Usually, no symptoms develop unless hypertension is severe or long-standing. Diagnosis is by* ***sphygmomanometry****. Tests may be done to determine cause, assess damage, and identify other cardiovascular risk factors. Treatment involves lifestyle changes and drugs, including diuretics, β - blockers, ACE inhibitors, angiotensin II receptor blockers, and Ca channel blockers.*

In the US, about 65 million people have hypertension. Only about 70% of these people are aware that they have hypertension, only 59% are being treated, and only 34% have adequately controlled BP. In adults, hypertension occurs more often in blacks (32%) than in whites (23%) or Mexican Americans (23%), and morbidity and mortality are greater in blacks.

BP increases with age. About two thirds of people > 65 have hypertension, and people with a normal BP at age 55 have a 90% lifetime risk of developing hypertension. Because hypertension becomes so common with age, the age-related increase in BP may seem innocuous, but higher BP increases **morbidity** and **mortality** risk. Hypertension may develop during pregnancy.

Etiology

Hypertension may be primary (85 to 95% of cases) or secondary.

Primary hypertension: Hemodynamics and physiologic components (eg, plasma volume, activity of the renin-angiotensin system) vary, indicating that primary hypertension is unlikely to have a single cause. Even if one factor is initially responsible, multiple factors are probably involved in sustaining elevated BP (the mosaic theory). In afferent systemic arterioles, malfunction of ion pumps on **sarcolemmal membranes** of smooth muscle cells may lead to chronically increased vascular tone. Heredity is a **predisposing factor**, but the exact mechanism is unclear. Environmental factors (eg, dietary Na, obesity, stress) seem to affect only **genetically susceptible** people.

Secondary hypertension: Causes include renal parenchymal disease (eg, chronic glomerulonephritis or pyelonephritis, polycystic renal disease, connective tissue disorders, **obstructive uropathy**), **renovascular disease**, **pheochromocytoma**, **Cushing's syndrome**, **primary aldosteronism**, **congenital adrenal hyperplasia**, **hyperthyroidism**, **myxedema**, and **coarctation of the aorta**. Excessive alcohol intake and use of oral contraceptives are common causes of curable hypertension. Use of sympathomimetics, NSAIDs, corticosteroids, cocaine, or licorice commonly contributes to hypertension.

Pathophysiology

Because BP equals cardiac output (CO) × total peripheral vascular resistance (TPR), pathogenic mechanisms must involve increased CO, increased TPR, or both.

In most patients, CO is normal or slightly increased, and TPR is increased. This pattern is typical of primary hypertension and hypertension due to pheochromocytoma, primary aldosteronism, renovascular disease, and renal parenchymal disease.

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In other patients, CO is increased (possibly because of venoconstriction in large veins), and TPR is inappropriately normal for the level of CO. Later in the disorder, TPR increases and CO returns to normal, probably because of autoregulation. Some disorders that increase CO (**thyrotoxicosis**, **arteriovenous fistula**, **aortic regurgitation**), particularly when stroke volume is increased, cause isolated systolic hypertension. Some elderly patients have isolated systolic hypertension with normal or low CO, probably due to **inelasticity** of the aorta and its major branches. Patients with high, fixed diastolic pressures often have decreased CO.

Plasma volume tends to decrease as BP increases; rarely, plasma volume remains normal or increases. Plasma volume tends to be high in hypertension

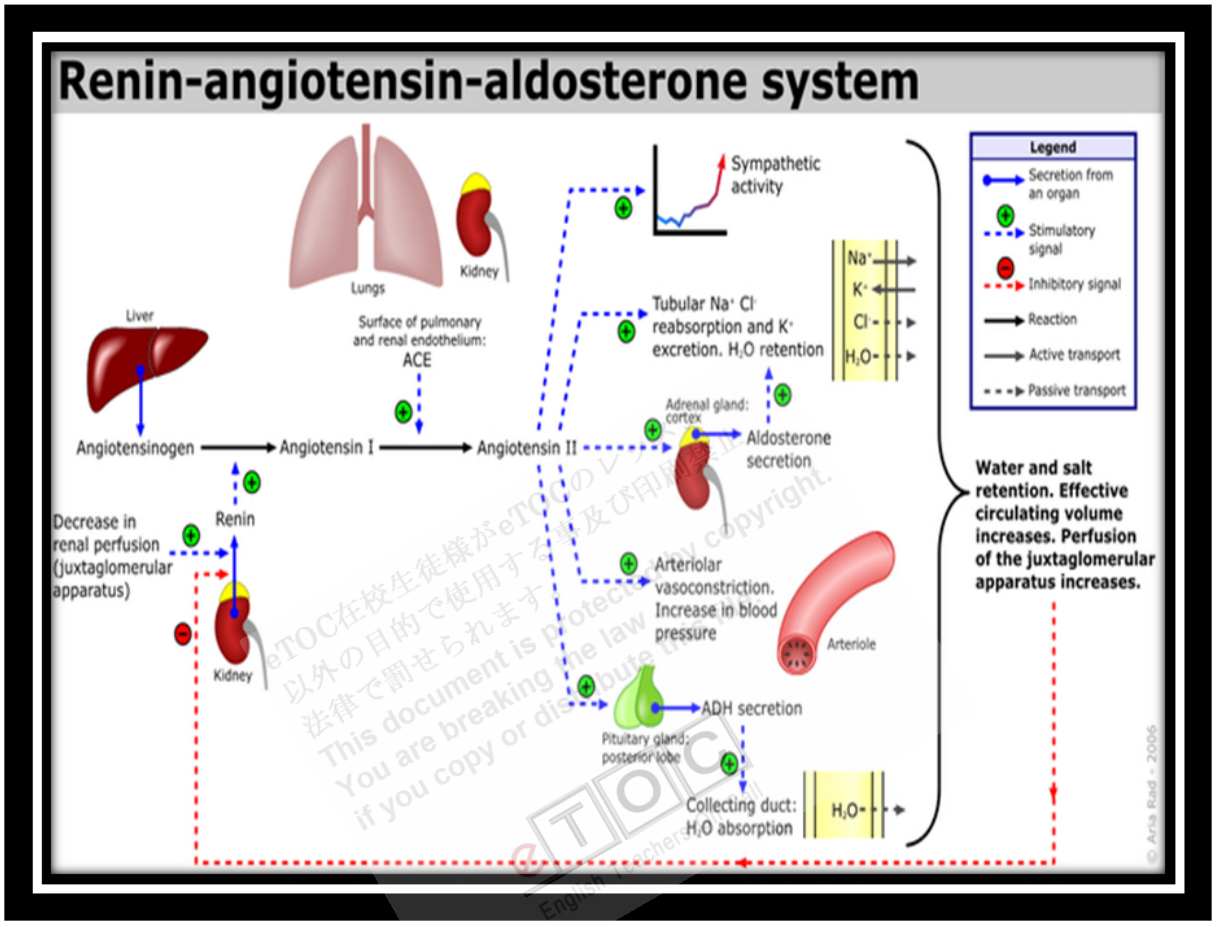
due to primary **aldosteronism** or **renal parenchymal disease** and may be quite low in hypertension due to **pheochromocytoma**. Renal blood flow gradually decreases as diastolic BP increases and arteriolar sclerosis begins. GFR remains normal until late in the disorder; as a result, the filtration fraction is increased. Coronary, cerebral, and muscle blood flow is maintained unless severe atherosclerosis coexists in these vascular beds.

Abnormal Na transport: In many cases of hypertension, Na transport across the cell wall is abnormal, because the Na-K pump (Na^+, K^+-ATPase) is defective or inhibited or because permeability to Na^+ is increased. The result is increased intracellular Na, which makes the cell more sensitive to sympathetic stimulation. Ca follows Na, so accumulation of intracellular Ca may be responsible for the increased sensitivity. Because Na^+, K^+-ATPase may pump norepinephrine back into sympathetic neurons (thus inactivating this neurotransmitter), inhibition of this mechanism could also enhance the effect of norepinephrine, increasing BP. Defects in Na transport may occur in normotensive children of hypertensive parents.

Sympathetic nervous system: Sympathetic stimulation increases BP, usually more in patients with prehypertension (systolic BP 120 to 139 mm Hg, diastolic BP 80 to 89 mm Hg) or hypertension (systolic BP ≥ 140 mm Hg, diastolic BP ≥ 90 mm Hg, or both) than in **normotensive patients**. Whether this **hyperresponsiveness** resides in the sympathetic nervous system or in the **myocardium** and vascular smooth muscle is unknown. A high resting pulse rate, which may result from increased sympathetic nervous activity, is a well-known predictor of hypertension. In some hypertensive patients, circulating plasma **catecholamine** levels during rest are higher than normal.

Renin-angiotensin-aldosterone system: This system helps regulate blood volume and therefore BP. Renin, an enzyme formed in the juxtaglomerular apparatus, catalyzes conversion of angiotensinogen to angiotensin I. This inactive product is cleaved by ACE, mainly in the lungs but also in the kidneys and brain, to angiotensin II, a potent vasoconstrictor that also stimulates autonomic centers in the brain to increase sympathetic discharge and stimulates release of aldosterone and ADH. **Aldosterone** and ADH cause Na and water retention, elevating BP. Aldosterone also enhances K excretion; low plasma K (<3.5 mEq/L) increases vasoconstriction through closure of K channels. Angiotensin III, present in the circulation, stimulates aldosterone

release as actively as angiotensin II but has much less pressor activity. Because **chymase enzymes** also convert angiotensin I to angiotensin II, drugs that inhibit ACE do not fully suppress angiotensin II production.



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Renin secretion is controlled by at least 4 mechanisms, which are not mutually exclusive: (1) A renal vascular receptor responds to changes in tension in the afferent arteriolar wall; (2) a **macula densa receptor** detects changes in the delivery rate or concentration of NaCl in the distal tubule; (3) circulating **angiotensin** has a negative feedback effect on renin secretion; and (4) via the renal nerve, the sympathetic nervous system stimulates renin secretion mediated by β-receptors.

Angiotensin is generally acknowledged to be responsible for renovascular hypertension, at least in the early phase, but the role of the renin-angiotensin-aldosterone system in primary hypertension is not established. However, in

black and elderly patients with hypertension, renin levels tend to be low. The elderly also tend to have low angiotensin II levels.

Hypertension due to chronic renal parenchymal disease (**renoprival hypertension**) results from the combination of a renin-dependent mechanism and a volume-dependent mechanism. In most cases, increased renin activity is not evident in peripheral blood. Hypertension is typically moderate and sensitive to Na and water balance.

Vasodilator deficiency: Deficiency of a vasodilator (eg, bradykinin, nitric oxide) rather than excess of a vasoconstrictor (eg, angiotensin, norepinephrine) may cause hypertension. If the kidneys do not produce adequate amounts of vasodilators (because of renal parenchymal disease or bilateral nephrectomy), BP can increase. Vasodilators and vasoconstrictors (mainly endothelin) are also produced in endothelial cells. Therefore, endothelial dysfunction greatly affects BP.

Pathology and complications: No pathologic changes occur early in hypertension. Severe or prolonged hypertension damages target organs (primarily the cardiovascular system, brain, and kidneys), increasing risk of coronary artery disease (CAD), MI, stroke (particularly hemorrhagic), and renal failure. The mechanism involves development of generalized arteriolosclerosis and acceleration of **atherogenesis** . Arteriolosclerosis is characterized by medial hypertrophy, hyperplasia, and **hyalinization**; it is particularly apparent in small arterioles, notably in the eyes and the kidneys. In the kidneys, the changes narrow the arteriolar lumen, increasing TPR; thus, hypertension leads to more hypertension. Furthermore, once arteries are narrowed, any slight additional shortening of already hypertrophied smooth muscle reduces the lumen to a greater extent than in normal-diameter arteries. These effects may explain why the longer hypertension has existed, the less likely specific treatment (eg, renovascular surgery) for secondary causes is to restore BP to normal.

Because of increased **afterload**, the left ventricle gradually hypertrophies, causing diastolic dysfunction. The ventricle eventually **dilates**, causing dilated cardiomyopathy and heart failure (HF) due to systolic dysfunction. Thoracic aortic dissection is typically a consequence of hypertension; almost all patients with abdominal aortic aneurysms have hypertension.

Symptoms and Signs

Hypertension is usually asymptomatic until complications develop in target organs. Dizziness, flushed facies, headache, fatigue, **epistaxis**, and nervousness are not caused by uncomplicated hypertension. Severe hypertension (hypertensive emergencies) can cause severe cardiovascular, neurologic, renal, and retinal symptoms (eg, symptomatic coronary atherosclerosis, HF, hypertensive encephalopathy, renal failure).

A 4th heart sound is one of the earliest signs of hypertensive heart disease.

Retinal changes may include arteriolar narrowing, hemorrhages, exudates, and, in patients with encephalopathy, papilledema. Changes are classified (according to the Keith, Wagener, and Barker classification) into 4 groups with increasingly worse prognosis: constriction of arterioles only (grade 1), constriction and sclerosis of arterioles (grade 2), hemorrhages and exudates in addition to vascular changes (grade 3), and papilledema (grade 4).

Diagnosis

- Multiple measurements of BP to confirm
- Urinalysis and urinary albumin: creatinine ratio; if abnormal, consider renal ultrasonography
- Blood tests: Fasting lipids, creatinine, K
- Renal ultrasonography if creatinine increased
- Evaluate for aldosteronism if K decreased
- ECG: If left ventricular hypertrophy, consider echocardiography
- Sometimes thyroid-stimulating hormone measurement
- Evaluate for **pheochromocytoma** if BP elevation sudden and labile or severe

Hypertension is diagnosed and classified by sphygmomanometry. History, physical examination, and other tests help identify etiology and determine whether target organs are damaged.

BP must be measured twice—first with the patient supine or seated, then after the patient has been standing for ≥ 2 min—on 3 separate days. The average of these measurements is used for diagnosis. BP is classified as normal, prehypertension, or stage 1 (mild) or stage 2 hypertension. Normal BP is much lower for infants and children.

Ideally, BP is measured after the patient rests > 5 min and at different times of day. A BP cuff is applied to the upper arm. An appropriately sized cuff covers two thirds of the biceps; the bladder is long enough to encircle > 80% of the arm, and bladder width equals at least 40% of the arm's circumference. Thus, obese patients require large cuffs. The health care practitioner inflates the cuff above the expected systolic pressure and gradually releases the air while listening over the brachial artery. The pressure at which the first heartbeat is heard as the pressure falls is systolic BP. Disappearance of the sound marks diastolic BP. The same principles are followed to measure BP in a forearm (radial artery) and thigh (popliteal artery). **Sphygmomanometers** that contain mercury are most accurate. Mechanical devices should be calibrated periodically; automated readers are often inaccurate.

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BP is measured in both arms; if BP in one arm is much higher, the higher value is used. BP is also measured in a thigh (with a much larger cuff) to rule out **coarctation of the aorta**, particularly in patients with diminished or delayed femoral pulses; with coarctation, BP is significantly lower in the legs. If BP is in

the low-hypertensive range or is markedly labile, more BP measurements are desirable. BP measurements may be sporadically high before hypertension becomes sustained; this phenomenon probably accounts for **"white coat hypertension,"** in which BP is elevated when measured in the physician's office but normal when measured at home or by ambulatory BP monitoring. However, extreme BP elevation alternating with normal readings is unusual and possibly suggests pheochromocytoma or unacknowledged drug use.

History: The history includes the known duration of hypertension and previously recorded levels; any history or symptoms of CAD, HF, or other relevant coexisting disorders (eg, stroke, renal dysfunction, peripheral arterial disease, **dyslipidemia**, diabetes, **gout**); and a family history of any of these disorders. Social history includes exercise levels and use of tobacco, alcohol, and stimulant drugs (prescribed and illicit). A dietary history focuses on intake of salt and stimulants (eg, tea, coffee, caffeine-containing sodas, energy drinks).

Physical examination: The physical examination includes measurement of height, weight, and waist circumference; **funduscopic examination** for retinopathy; auscultation for bruits in the neck and abdomen; and a full cardiac, respiratory, and neurologic examination. The abdomen is palpated for kidney enlargement and abdominal masses. Peripheral arterial pulses are evaluated; diminished or delayed femoral pulses suggest aortic coarctation, particularly in patients < 30.

Testing: The more severe the hypertension and the younger the patient, the more extensive is the evaluation. Generally, when hypertension is newly diagnosed, routine testing to detect target-organ damage and cardiovascular risk factors is done. Tests include urinalysis, spot urine albumin: creatinine ratio, blood tests (creatinine, K, Na, fasting plasma glucose, lipid profile), and ECG. Thyroid-stimulating hormone is often measured. Ambulatory BP monitoring, renal radionuclide imaging, chest x-ray, screening tests for pheochromocytoma, and renin-Na profiling are not routinely necessary. Peripheral plasma renin activity is not helpful in diagnosis or drug selection.

Depending on results of initial tests and examination, other tests may be needed. If urinalysis detects albuminuria (proteinuria), cylindruria, or microhematuria or if serum creatinine is elevated (≥ 1.4 mg/dL in men; ≥ 1.2

mg/dL in women), renal ultrasonography to evaluate kidney size may provide useful information. Patients with hypokalemia unrelated to diuretic use are evaluated for **primary aldosteronism** and high salt intake.

On ECG, a broad, notched P-wave indicates atrial hypertrophy and, although nonspecific, may be one of the earliest signs of hypertensive heart disease. Left ventricular hypertrophy, indicated by a sustained **apical thrust** and abnormal QRS voltage with or without evidence of ischemia, may occur later. If either of these findings is present, echocardiography is often done. In patients with an abnormal **lipid** profile or symptoms of CAD, tests for other cardiovascular risk factors (eg, C-reactive protein) may be useful.

If coarctation of the aorta is suspected, chest x-ray, echocardiography, CT, or MRI helps confirm the diagnosis.

Patients with **labile**, significantly elevated BP and symptoms such as headache, palpitations, tachycardia, excessive perspiration, tremor, and pallor are screened for pheochromocytoma (eg, by measuring plasma free **metanephrines**).

Patients with symptoms suggesting Cushing's syndrome, a connective tissue disorder, eclampsia, acute **porphyria**, hyperthyroidism, **myxedema**, **acromegaly**, or CNS disorders are evaluated.

Table 1

JNC 7 Classification of Blood Pressure in Adults

Classification	BP (mm Hg)
Normal	< 120/80
Prehypertension	120–139/80–89
Stage 1	140–159 (systolic) or 90–99 (diastolic)
Stage 2	≥ 160 (systolic) or

	≥ 100 (diastolic)
□ JNC = Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.	

Reference: http://www.merckmanuals.com