# HYPERTENSION

- ✓ Hypertension is not a disease but an important risk factor for cardiovascular complications.
- ✓ Hypertension is important because elevated blood pressure (BP) confers a greater risk of stroke, heart failure, renal disease, peripheral vascular disease, and coronary artery disease including angina, myocardial infarction, and sudden death.
- ✓ There is a continuous, direct relationship between elevations in blood pressure and increases in these risks.
- ✓ Blood pressure measured using a mercury sphygmomanometer showing a reading of 120/80 mmHg is considered as an average for an adult.
- ✓ A person whose reading are consistently above 140/90 mmHg may be said of have hypertension, although factors such as age have to be considered.
- ✓ After 1990, it was realized that in the treatment of hypertension, just lowering the blood pressure is not enough but it is important to prevent hypertension cardiovascular and renal disorders.
- ✓ It was also found that many a times hypertension is associated with target end organ damage.
- ✓ Considering these, WHO defined various stages of hypertension as follows:

| Category | Systolic | Diastolic |
|---|---|---|
| **Normal** | < 130 | < 85 |
| **High normal** | 130-139 | 85-89 |
| **Hypertension** | | |
| **Stage 1 (mild)** | 140-159 | 90-99 |
| **Stage 2 (moderate)** | 160-179 | 100-109 |
| **Stage 3 (severe)** | 180-209 | 110-119 |
| **Stage 4 (very severe)** | ≥ 210 | ≥ 120 |

**RISK FACTORS**

- ✓ **Age:** The risk of high blood pressure increases as you age. Through early middle age, high blood pressure is more common in men. Women are more likely to develop high blood pressure after menopause.
- ✓ **Race:** High blood pressure is particularly common among blacks, often developing at an earlier age than it does in whites. Serious complications, such as stroke and heart attack, also are more common in blacks.
- ✓ **Family history:** High blood pressure tends to run in families.
- ✓ **Being overweight or obese:** The more weight, the more blood need to supply oxygen and nutrients to tissues. As the volume of blood circulated through blood vessels increases, so does the pressure on artery walls.
- ✓ **Not being physically active:** People who are inactive tend to have higher heart rates. The higher heart rate, the harder heart must work with each contraction and the stronger the force on arteries. Lack of physical activity also increases the risk of being overweight.
- ✓ **Using tobacco:** Not only does smoking or chewing tobacco immediately raise blood pressure temporarily, but the chemicals in tobacco can damage the lining of artery walls. This can cause arteries to narrow, increasing blood pressure. Secondhand smoke also can increase blood pressure.

- ✓ **Too much salt (sodium) in your diet:** Too much sodium in diet can cause body to retain fluid, which increases blood pressure.
- ✓ **Too little potassium in your diet:** Potassium helps balance the amount of sodium in cells. If don't get enough potassium in diet or retain enough potassium, may accumulate too much sodium in blood.
- ✓ **Too little vitamin D in your diet:** It's uncertain if having too little vitamin D in diet can lead to high blood pressure. Vitamin D may affect an enzyme produced by your kidneys that affects blood pressure.
- ✓ **Drinking too much alcohol:** Over time, heavy drinking can damage heart. Having more than two drinks a day can raise blood pressure.
- ✓ **Stress:** High levels of stress can lead to a temporary, but dramatic, increase in blood pressure. If try to relax by eating more, using tobacco or drinking alcohol, may only increase problems with high blood pressure.
- ✓ **Certain chronic conditions:** Certain chronic conditions also may increase your risk of high blood pressure, including high cholesterol, diabetes, kidney disease and sleep apnea.

**COMPLICATION**

| **COMPLICATIONS OF HYPERTENSION** |
|---|
| Myocardial infarction |
| Stroke :<br>Cerebral/brainstem infarction<br>Cerebral haemorrhage<br>Lacunar syndrome<br>Multi-infarct disease |
| Hypertensive encephalopathy/malignant hypertension |
| Dissecting aortic aneurysm |
| Hypertensive nephrosclerosis |
| Peripheral vascular disease |

**EPIDEMIOLOGY**

- ✓ It is estimated that approximately 30% of the population (50 million Americans) has high BP (≥140/90 mm Hg).
- ✓ Estimates from the National Health and Nutrition Examination Survey from 1999–2000 indicate that the prevalence is 30.1% and 27.1% among men and women, respectively.
- ✓ This represents a significant increase of 5.6% in women from 1988 to 2000, whereas the prevalence in men has remained unchanged.
- ✓ BP values increase with age, and hypertension is very common in the elderly.
- ✓ The lifetime risk of developing hypertension among those 55 years of age and older who are normotensive is 90%.
- ✓ Most patients have prehypertension BP values before they are diagnosed with hypertension, and 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).

- ✓ In the older population (age ≥ 60 years), the prevalence of hypertension is 65.4% (estimated in 2000), which is significantly higher than the 57.9% prevalence estimated in 1988.

**ETIOLOGY**

- ✓ Hypertension is a heterogeneous medical condition.
- ✓ In most patients it results from unknown pathophysiologic etiology (**Essential or Primary hypertension**).
- ✓ While this form of hypertension cannot be cured, it can be controlled.
- ✓ A small percentage of patients have a specific cause of their hypertension (**Secondary hypertension**).
- ✓ There are many potential secondary causes that are either concurrent medical conditions or are endogenously induced.
- ✓ If the cause of secondary hypertension can be identified, hypertension in these patients potentially can be cured.

**ESSENTIAL HYPERTENSION**

- ✓ Patients with arterial hypertension and no definable cause are said to have **Primary, Essential, or Idiopathic hypertension**.
- ✓ Undoubtedly, the primary difficulty in uncovering the responsible mechanisms in these patients.
- ✓ Patients are attributable to the variety of systems that are involved in the regulation of arterial pressure: peripheral and/or central adrenergic, renal, hormonal, and vascular.
- ✓ Several abnormalities have been described in patients with essential hypertension, often with a claim that one or more of them are primarily responsible for the hypertension.
- ✓ While it is still uncertain whether these individual abnormalities are primary or secondary, varying expressions of a single disease process, or reflective of separate disease entities, the accumulating data increasingly support the latter hypothesis.
- ✓ Therefore, just as pneumonia is caused by a variety of infectious agents, even though the clinical picture observed may be similar, so essential hypertension likely has a number of distinct causes.
- ✓ Thus, the distinction between primary and secondary hypertension has become blurred, and the approach to both the diagnosis and therapy of hypertensive patients has been modified.

➢ **ENVIRONMENT**

- ✓ A number of environmental factors have been implicated in the development of hypertension, including salt intake, obesity, occupation, alcohol intake, family size, and crowding.
- ✓ These factors have all been assumed to be important in the increase in blood pressure with age in more affluent societies, in contrast to the decline in blood pressure with age in less affluent groups.

➢ **SALT SENSITIVITY**

- ✓ The environmental factor that has received the greatest attention is salt intake.
- ✓ Even this factor illustrates the heterogeneous nature of the essential hypertensive population, in that the blood pressure is particularly responsive to the level of sodium intake in only ~60% of hypertensives.
- ✓ The cause of this special sensitivity to salt varies, with primary aldosteronism, bilateral renal artery stenosis, renal parenchymal disease, and low-renin essential hypertension accounting for about half the patients.

- **ROLE OF RENIN**
  - ✓ Renin is an enzyme secreted by the juxtaglomerular cells of the kidney and linked with aldosterone in a negative feedback loop.
  - ✓ While a variety of factors can modify its rate of secretion, the primary determinant is the volume status of the individual, particularly as related to changes in dietary sodium intake.
  - ✓ The end product of the action of renin on its substrate is the generation of the peptide angiotensin II.
  - ✓ In consequence, some hypertensive patients have been defined as having low-renin and others as with sodium restriction, adrenal responses are enhanced and the renal vascular responses reduced having high-renin essential hypertension.
  - **LOW-RENIN ESSENTIAL HYPERTENSION**
  - ✓ Approximately 20% of patients who by all other criteria have essential hypertension have suppressed plasma renin activity.
  - ✓ This situation is more common in diabetics and the elderly.
  - ✓ Though these patients are not hypokalemic, have expanded extracellular fluid volumes, and one unproven suggestion is that they have sodium retention and renin suppression due to excessive production of an unidentified mineralocorticoid.
  - ✓ There are data to suggest that the low-renin state confers a beneficial natural history compared to that in patients with normal or high-renin hypertension.
  - **NONMODULATING ESSENTIAL HYPERTENSION**
  - ✓ Another subset of hypertensive patients who are also salt-sensitive has a reduced adrenal response to sodium restriction.
  - ✓ In these individuals, sodium intake does not modulate either adrenal or renal vascular responses to angiotensin II.
  - ✓ Hypertensives in this subset have been termed **Nonmodulators** because of the absence of the sodium-mediated modulation of target tissue responses to angiotensin II.
  - ✓ These individuals make up 25 to 30% of the hypertensive population, have plasma renin activity levels that are normal to high if measured when the patient is on a low-salt diet, and have hypertension that is salt-sensitive because of a defect in the kidney's ability to excrete sodium appropriately.
  - ✓ They also are more insulin-resistant than other hypertensive patients, and the pathophysiologic characteristics can be corrected by the administration of an angiotensin-converting enzyme (ACE) inhibitor.
  - ✓ Nonmodulation is much more frequent among males and postmenopausal females.
  - **HIGH-RENIN ESSENTIAL HYPERTENSION**
  - ✓ Approximately 15% of patients with essential hypertension have plasma renin activity levels above the normal range.
  - ✓ It has been suggested that plasma renin plays an important role in the pathogenesis of the elevated arterial pressure in these patients
- **CELL MEMBRANE DEFECT**
  - ✓ Another postulated explanation for salt-sensitive hypertension is a generalized cell membrane defect.

- ✓ It has been assumed that an abnormality in sodium transport reflects an undefined alteration in the cell membrane and that this defect occurs in many, perhaps all, cells of the body, particularly the vascular smooth-muscle cells.
- ✓ The defect leads to an abnormal accumulation of calcium in vascular smooth muscle, resulting in a heightened vascular responsiveness to vasoconstrictor agents.
- ✓ This defect has been proposed to be present in 35 to 50% of essential hypertensive persons on the basis of studies using red cells.

➢ **INSULIN RESISTANCE**

- ✓ Insulin resistance and/or hyperinsulinemia have been suggested as being responsible for the increased arterial pressure in some patients with hypertension.
- ✓ While it is clear that a substantial fraction of the hypertensive population has insulin resistance and hyperinsulinemia, it is less certain that this is more than an association.
- ✓ Insulin resistance is common in patients with diabetes mellitus type 2 and in obesity; both of these conditions are more common in hypertensive than in normotensive subjects
- ✓ Hyperinsulinemia can increase arterial pressure by one or more of F**our mechanisms**.
  1) Hyperinsulinemia produces renal sodium retention (at least acutely) and increases sympathetic activity. Either or both of these effects could lead to an increase in arterial pressure.
  2) Another mechanism is vascular smooth-muscle hypertrophy secondary to the mitogenic action of insulin.
  3) Insulin also modifies ion transport across the cell membrane, thereby potentially increasing the cytosolic calcium levels of insulin-sensitive vascular or renal tissues.
  4) Insulin resistance may be a marker for another pathologic process, e.g., nonmodulation, which could be the primary mechanism increasing blood pressure.

➢ **GENETIC CONSIDERATIONS**

- ✓ Hypertension is one of the most common complex genetic disorders, with genetic heritability averaging ~30%.

➢ **FACTORS THAT MODIFY THE COURSE OF ESSENTIAL HYPERTENSION**

- ✓ Age, race, sex, smoking, alcohol intake, serum cholesterol, glucose intolerance, and weight all may alter the prognosis of this disease.
- ✓ The younger the patient when hypertension is first noted, the greater is the reduction in life expectancy if the hypertension is left untreated.
- ✓ There is also no question that a positive correlation exists between obesity and arterial pressure.
- ✓ A gain in weight is associated with an increased frequency of hypertension in persons with previously normal blood pressure, and weight loss in obese persons with hypertension lowers their arterial pressure and, if they are being treated for hypertension, the intensity of therapy required to keep them normotensive.

➢ **NATURAL HISTORY**

- ✓ Because essential hypertension is a heterogeneous disorder, variables other than the arterial pressure modify its course.
- ✓ Thus, the probability of developing a morbid cardiovascular event with a given arterial pressure may vary as much as 20-fold depending on whether associated risk factors are present.

| RISK FACTORS FOR AN ADVERSE PROGNOSIS IN HYPERTENSION |
|---|
| Black race |
| Youth |
| Male sex |
| Persistent diastolic pressure >115 mmHg |
| Smoking |
| Diabetes mellitus |
| Hypercholesterolemia |
| Obesity |
| Excess alcohol intake |
| Evidence of end organ damage<br>1. Cardiac<br>a. Cardiac enlargement<br>b. Electrocardiographic signs of ischemia or left ventricular strain<br>c. Myocardial infarction<br>d. Congestive heart failure<br>2. Eyes<br>a. Retinal exudates and hemorrhages<br>b. Papilledema<br>3. Renal: impaired renal function<br>4. Nervous system: cerebrovascular accident |

**SECONDARY HYPERTENSION**

- ✓ As noted earlier, in only a small minority of patients with elevated arterial pressure can a specific cause be identified.
- ✓ Yet these patients should not be ignored for at least two reasons:
  1. Correction of the cause may cure their hypertension, and
  2. These secondary forms of the disease may provide insight into the etiology of essential hypertension.

➢ **RENAL HYPERTENSION**

- ✓ Hypertension produced by renal disease is the result of either
  1. An alteration in renal secretion of vasoactive materials resulting in a systemic or local change in arteriolar tone, or
  2. A derangement in the renal handling of sodium and fluids leading to volume expansion.
- ✓ The main subdivisions of renal hypertension are **Renovascular hypertension**, including Preeclampsia and Eclampsia, and **Renal parenchymal hypertension**.
- ✓ A simple explanation for **renal vascular hypertension** is that decreased perfusion of renal tissue due to stenosis of a main or branch renal artery activates the renin-angiotensin system.
- ✓ Circulating angiotensin II elevates arterial pressure by directly causing vasoconstriction, by stimulating aldosterone secretion with resulting sodium retention, and/or by stimulating the adrenergic nervous system.
- ✓ Activation of the renin-angiotensin system has also been offered as an explanation for the hypertension in both acute and chronic **Renal parenchymal disease**.

- ✓ In this formulation, the only **difference between Renovascular and Renal parenchymal hypertension** is that the decreased perfusion of renal tissue in the renal parenchymal disease results from inflammatory and fibrotic changes involving multiple small intrarenal vessels.
- ✓ There are enough differences between the two conditions, however, to suggest that other mechanisms are active in renal parenchymal disease.
- ✓ Specifically,
    1. Peripheral plasma renin activity is elevated far less frequently in renal parenchymal than in renovascular hypertension;
    2. Cardiac output is said to be normal in renal parenchymal hypertension (unless uremia and anemia are present) but slightly elevated in renovascular hypertension
    3. Circulatory responses to tilting and to the Valsalva maneuver are exaggerated in the in renal parenchymal disease and
    4. Blood volume tends to be high in patients with severe renal parenchymal disease and low in patients with severe unilateral renovascular hypertension.
- ✓ Alternative explanations for the hypertension in renal parenchymal disease include the possibilities that the
    1. Damaged kidneys produce an unidentified vasopressor substance other than renin,
    2. Fail to produce a necessary humoral vasodilator substance (perhaps prostaglandin or bradykinin),
    3. Fail to inactivate circulating vasopressor substances, and/or
    4. Are ineffective in disposing of sodium.
- ✓ A rare form of renal hypertension results from the excess secretion of renin by juxtaglomerular cell tumors or nephroblastomas.
- ✓ The initial presentation is similar to that of hyperaldosteronism, with hypertension, hypokalemia, and overproduction of aldosterone.
- ✓ However, in contrast to primary aldosteronism, peripheral renin activity is elevated instead of subnormal.
- ✓ This disease can be distinguished from other forms of secondary aldosteronism by the presence of normal renal function and unilateral increases in renal vein renin concentration without a renal artery lesion.

**ENDOCRINE HYPERTENSION**

- ➢ **ADRENAL HYPERTENSION**
    - ✓ Hypertension is a feature of a variety of adrenal cortical abnormalities.
    - ✓ In primary aldosteronism, there is a clear relationship between the aldosterone-induced sodium retention and the hypertension.
    - ✓ Normal individuals given aldosterone develop hypertension only if they also ingest sodium.
    - ✓ Since aldosterone causes sodium retention by stimulating renal tubular exchange of sodium for potassium, hypokalemia is a prominent feature in most patients with primary aldosteronism, and, therefore, the measurement of serum potassium provides a simple screening test.
    - ✓ The effect of sodium retention and volume expansion in chronically suppressing plasma renin activity is critical for the definitive diagnosis.

- ✓ In most clinical situations, plasma renin activity and plasma or urinary aldosterone levels parallel each other, but in patients with primary aldosteronism, aldosterone levels are high and relatively fixed because of autonomous aldosterone secretion, whereas plasma renin activity levels are suppressed and respond sluggishly to sodium depletion.
- ✓ Primary aldosteronism may be secondary to either a tumor or bilateral adrenal hyperplasia.
- ✓ It is important to distinguish between these two conditions preoperatively, since the hypertension in the latter case is usually not modified by operation.
- ✓ The sodium-retaining effect of large amounts of glucocorticoids also offers an explanation for the hypertension in severe cases of Cushing's syndrome.
- ✓ Moreover, increased production of mineralocorticoids has also been documented in some Patients with Cushing's syndrome.
- ✓ However, the hypertension in many cases of Cushing's syndrome does not seem volume-dependent, leading investigators to speculate that it may be secondary to glucocorticoid-induced production of renin substrate (angiotensin-mediated hypertension). In the forms of the adrenogenital syndrome due to C- 11 or C-17 hydroxylase deficiency, deoxycorticosterone accounts for the sodium retention and the resulting hypertension, which is accompanied by suppression of plasma renin activity.
- ✓ In patients with pheochromocytoma, increased secretion of epinephrine and norepinephrine by a tumor (most often located in the adrenal medulla) causes excessive stimulation of adrenergic receptors, which results in peripheral vasoconstriction and cardiac stimulation.
- ✓ This diagnosis is confirmed by demonstrating increased urinary excretion of epinephrine and norepinephrine and/or their metabolites.

- ➢ **ACROMEGALY**
  - ✓ Hypertension, coronary atherosclerosis, and cardiac hypertrophy are frequent complications of this condition.
- ➢ **HYPERCALCEMIA**
  - ✓ The hypertension that occurs in up to one-third of patients with hyperparathyroidism ordinarily can be attributed to renal parenchymal damage due to nephrolithiasis and nephrocalcinosis.
  - ✓ However, increased calcium levels can also have a direct vasoconstrictive effect.
  - ✓ In some cases, the hypertension disappears when the hypercalcemia is corrected.
  - ✓ Thus, paradoxically, the increased serum calcium level in hyperparathyroidism raises blood pressure, while epidemiologic studies suggest that a high calcium intake lowers blood pressure.
- ➢ **COARCTATION OF THE AORTA**
  - ✓ The hypertension associated with coarctation may be caused by the constriction itself or perhaps by the changes in the renal circulation, which result in an unusual form of renal arterial hypertension.
  - ✓ The diagnosis of coarctation is usually evident from physical examination and routine x-ray findings.

**MALIGNANT HYPERTENSION**

- ✓ Malignant or accelerated hypertension is an uncommon condition characterized by greatly elevated BP associated with evidence of ongoing small vessel damage.

- ✓ This is evident in the optic fundus, where papilloedema, haemorrhages and/or exudates may be present.
- ✓ Renal damage, including haematuria, proteinuria and impaired renal function, is also characteristic.
- ✓ The condition may be associated with hypertensive encephalopathy, which is caused by small vessel changes in the cerebral circulation associated with cerebral oedema.
- ✓ The clinical features are confusion, headache, visual loss and coma.
- ✓ Malignant hypertension is a medical emergency that requires hospital admission and rapid control of BP over 12-24 hrs towards normal levels.
- ✓ In the absence of treatment, malignant hypertension is usually fatal, with a 1- year survival of less than 20%.

## THE VARIOUS FORMS OF HYPERTENSION

| SYSTOLIC HYPERTENSION WITH WIDE PULSE PRESSURE |
|---|
| I. Decreased compliance of aorta (arteriosclerosis) |
| II. Increased stroke volume |
| A. Aortic regurgitation |
| B. Thyrotoxicosis |
| C. Hyperkinetic heart syndrome |
| D. Fever |
| E. Arteriovenous fistula |
| F. Patent ductus arteriosus |
| **SYSTOLIC AND DIASTOLIC HYPERTENSION (INCREASED PERIPHERAL VASCULAR RESISTANCE)** |
| I. Renal |
| A. Chronic pyelonephritis |
| B. Acute and chronic glomerulonephritis |
| C. Polycystic renal disease |
| D. Renovascular stenosis or renal infarction |
| E. Most other severe renal diseases (arteriolar nephrosclerosis, diabetic nephropathy, etc.) |
| F. Renin-producing tumors |
| II. Endocrine |
| A. Oral contraceptives |
| B. Adrenocortical hyperfunction |
| 1. Cushing's disease and syndrome |
| 2. Primary hyperaldosteronism |
| 3. Congenital or hereditary adrenogenital syndromes ($17\alpha$-hydroxylase and $11\beta$-hydroxylase defects) |
| C. Pheochromocytoma |
| D. Myxedema |
| E. Acromegaly |
| III. Neurogenic |
| A. Psychogenic |
| B. Diencephalic syndrome |
| C. Familial dysautonomia (Riley-Day) |
| D. Polyneuritis (acute porphyria, lead poisoning) |
| E. Increased intracranial pressure (acute) |
| F. Spinal cord section (acute) |
| IV. Miscellaneous |
| A. Coarctation of aorta |
| B. Increased intravascular volume (excessive transfusion, polycythemia vera) |
| C. Polyarteritis nodosa |
| D. Hypercalcemia |
| E. Medications, e.g., glucocorticoids, cyclosporine |
| V. Unknown etiology |
| A. Essential hypertension (>90% of all cases of hypertension) |
| B. Toxemia of pregnancy |
| C. Acute intermittent porphyria |

**SYMPTOMS AND SIGNS**

- ✓ Most patients with hypertension have no specific symptoms referable to their blood pressure elevation and are identified only in the course of a physical examination.
- ✓ When symptoms do bring the patient to the physician, they fall into **three categories**.
- ✓ They are related to
    1. The elevated pressure itself,
    2. The hypertensive vascular disease, and
    3. The underlying disease, in the case of secondary hypertension.
- ✓ Though popularly considered a symptom of elevated arterial pressure, headache is characteristic of only severe hypertension; most commonly such headaches are localized to the occipital region and are present when the patient awakens in the morning but subside spontaneously after several hours.
- ✓ Other complaints that may be related to elevated blood pressure include dizziness, palpitations, easy fatigability, and impotence.
- ✓ Complaints referable to vascular disease include epistaxis, hematuria, blurring of vision owing to retinal changes, episodes of weakness or dizziness due to transient cerebral ischemia, angina pectoris, and dyspnea due to cardiac failure.
- ✓ Pain due to dissection of the aorta or to a leaking aneurysm is a rare presenting symptom.
- ✓ Examples of symptoms related to the underlying disease in secondary hypertension are polyuria, polydipsia, and muscle weakness secondary to hypokalemia in patients with primary aldosteronism or weight gain, and emotional lability in patients with Cushing's syndrome.
- ✓ The patient with a pheochromocytoma may present with episodic headaches, palpitations, diaphoresis, and postural dizziness.

**PATHOPHYSIOLOGY**

- ➢ **HUMORAL MECHANISMS**
    - ✓ Several humoral abnormalities may be involved in the development of essential hypertension.
    - ✓ These abnormalities may involve the **RAAS**, **Natriuretic hormone**, and **Hyperinsulinemia**.
    - **THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM (RAAS)**
        - ✓ The RAAS is a complex endogenous system that is involved with most regulatory components of arterial BP.
        - ✓ Activation and regulation are governed primarily by the kidney.
        - ✓ The RAAS regulates sodium, potassium, and fluid balance.
        - ✓ Therefore, this system significantly influences vascular tone and sympathetic nervous system activity and is the most influential contributor to the homeostatic regulation of BP.
        - ✓ Renin is an enzyme that is stored in the juxtaglomerular cells, which are located in the afferent arterioles of the kidney.
        - ✓ Juxtaglomerular cells function as a baroreceptor-sensing device.
        - ✓ Decreased renal artery pressure and kidney blood flow are sensed by these cells and stimulate secretion of renin.
        - ✓ A decrease in sodium and chloride delivered to the distal tubule stimulates renin release.

- ✓ Catecholamines increase renin release probably by directly stimulating sympathetic nerves on the afferent arterioles that, in turn, activate the juxtaglomerular cells.
- ✓ Decreased serum potassium and/or intracellular calcium is detected by the juxtaglomerular cells, resulting in renin secretion.
- ✓ Renin catalyzes the conversion of angiotensinogen to angiotensin I in the blood. Angiotensin I is then converted to angiotensin II by angiotensin-converting enzyme (ACE).
- ✓ After binding to specific receptors (classified as either AT1 or AT2 subtypes), angiotensin II exerts biologic effects in several tissues.
- ✓ The AT1 receptor is located in brain, kidney, myocardium, peripheral vasculature, and the adrenal glands.
- ✓ These receptors mediate most responses that are critical to cardiovascular and kidney function.
- ✓ The AT2 receptor is located in adrenal medullary tissue, uterus, and brain. Stimulation of the AT2 receptor does not influence BP regulation.
- ✓ Circulating angiotensin II can elevate BP through pressor and volume effects.
- ✓ The pressor effects include direct vasoconstriction, stimulation of catecholamine release from the adrenal medulla, and centrally mediated increases in sympathetic nervous system activity.
- ✓ Angiotensin II also stimulates aldosterone synthesis from the adrenal cortex.
- ✓ This leads to sodium and water reabsorption that increases plasma volume, total peripheral resistance, and ultimately, BP.
- ✓ Clearly, any disturbance in the body that leads to activation of the RAAS could explain chronic hypertension.
- ✓ The heart and brain contain a local RAAS.
- ✓ In the heart, angiotensin II is also generated by a second enzyme, angiotensin I convertase (human chymase).
- ✓ Activation of the myocardial RAAS increases cardiac contractility and stimulates cardiac hypertrophy.
- ✓ In the brain, angiotensin II modulates the production and release of hypothalamic and pituitary hormones and enhances sympathetic outflow from the medulla oblongata.
- ✓ Peripheral tissues can locally generate biologically active angiotensin peptides, which may explain the increased vascular resistance seen in hypertension

- **NATRIURETIC HORMONE**
  - ✓ Natriuretic hormone inhibits sodium and potassium ATPase and thus interferes with sodium transport across cell membranes.
  - ✓ Inherited defects in the kidney's ability to eliminate sodium can cause an increased blood volume.
  - ✓ A compensatory increase in the concentration of circulating natriuretic hormone theoretically could increase urinary excretion of sodium and water.
- **INSULIN RESISTANCE AND HYPERINSULINEMIA**
  - ✓ Evidence has linked insulin resistance and hyperinsulinemia with the development of hypertension, sometimes referred to as the metabolic syndrome.

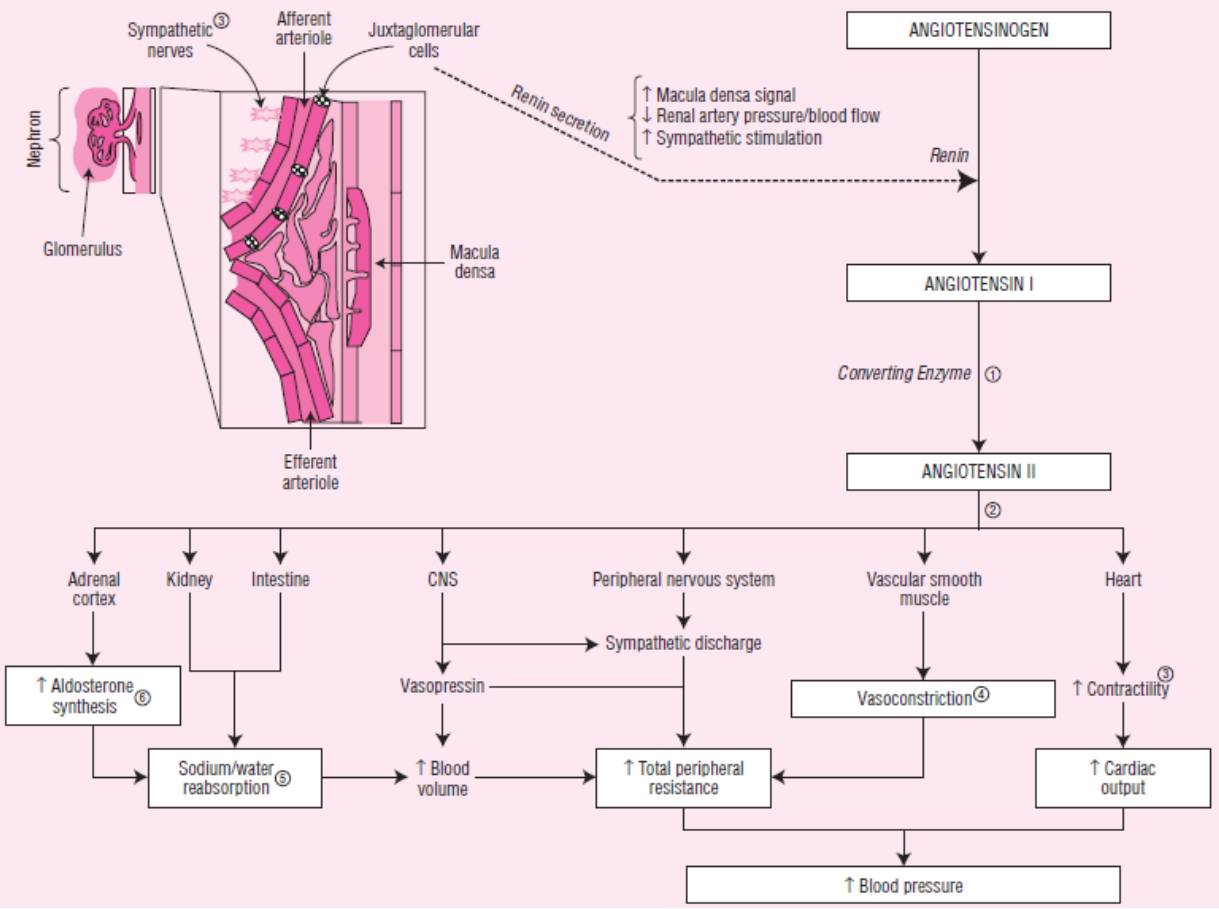
- ✓ Hypothetically, increased insulin concentrations may lead to hypertension because of increased renal sodium retention and enhanced sympathetic nervous system activity.
- ✓ Moreover, insulin has growth hormone–like actions that can induce hypertrophy of vascular smooth muscle cells.
- ✓ Insulin also may elevate BP by increasing intracellular calcium, which leads to increased vascular resistance.

➢ **NEURONAL REGULATION**

- ✓ The central and autonomic nervous systems are intricately involved in the regulation of arterial BP.
- ✓ A number of receptors that either enhance or inhibit norepinephrine release are located on the presynaptic surface of sympathetic terminals.
- ✓ The $\alpha$ and $\beta$ presynaptic receptors play a role in negative and positive feedback to the norepinephrine containing vesicles located near the neuronal ending.
- ✓ Stimulation of presynaptic $\alpha$-receptors ($\alpha_2$) exerts a negative inhibition on norepinephrine release.
- ✓ Stimulation of presynaptic $\beta$-receptors facilitates further release of norepinephrine.
- ✓ Sympathetic neuronal fibers located on the surface of effector cells innervate the $\alpha$- and $\beta$-receptors.
- ✓ Stimulation of postsynaptic $\alpha$-receptors ($\alpha_1$) on arterioles and venules results in vasoconstriction.
- ✓ There are two types of postsynaptic $\beta$-receptors, $\beta_1$ and $\beta_2$.
- ✓ Both are present in all tissue innervated by the sympathetic nervous system.
- ✓ However, in some tissues, $\beta_1$-receptors predominate, and in other tissues, $\beta_2$-receptors predominate.
- ✓ Stimulation of $\beta_1$-receptors in the heart results in an increase in heart rate and contractility, whereas stimulation of $\beta_2$-receptors in the arterioles and venules causes vasodilation.
- ✓ The baroreceptor reflex system is the major negative-feedback mechanism that controls sympathetic activity.
- ✓ Baroreceptors are nerve endings lying in the walls of large arteries, especially in the carotid arteries and aortic arch.
- ✓ Changes in arterial pressure rapidly activate baroreceptors, which then transmit impulses to the brain stem through the ninth cranial nerve and vagus nerves. In this reflex system, a decrease in arterial BP stimulates baroreceptors, causing reflex vasoconstriction and increased heart rate and force of cardiac contraction.
- ✓ These baroreceptor reflex mechanisms may be blunted in the elderly and in those with diabetes.
- ✓ Stimulation of certain areas within the central nervous system can either increase or decrease BP.
- ✓ The purpose of these neuronal mechanisms is to regulate BP and maintain homeostasis. Pathologic disturbances in any of the four major components (autonomic nerve fibers, adrenergic receptors, baroreceptors, or central nervous system) conceivably could lead to chronically elevated BP.
- ✓ These systems are physiologically interrelated.
- ✓ A defect in one component may alter normal function in another, and such cumulative abnormalities then may explain the development of essential hypertension.

- **PERIPHERAL AUTOREGULATORY COMPONENTS**
  - ✓ Abnormalities in renal or tissue autoregulatory systems could cause hypertension.
  - ✓ It is possible that a renal defect in sodium excretion may develop first, which can then cause resetting of tissue autoregulatory processes, resulting in a higher arterial BP.
  - ✓ The kidney usually maintains normal BP through a volume pressure adaptive mechanism.
  - ✓ When BP drops, the kidneys respond by increasing retention of sodium and water.
  - ✓ These changes lead to plasma volume expansion, which increases BP.
  - ✓ Conversely, when BP rises above normal, renal sodium and water excretion are increased to reduce plasma volume and cardiac output.
  - ✓ This ultimately will maintain homeostatic BP conditions.
  - ✓ Local autoregulatory processes maintain adequate tissue oxygenation.
  - ✓ When tissue oxygen demand is normal to low, the local arteriolar bed remains relatively vasoconstricted.
  - ✓ However, increases in metabolic demand trigger arteriolar vasodilation that lowers peripheral vascular resistance and increases blood flow and oxygen delivery through autoregulation.
  - ✓ Intrinsic defects in these renal adaptive mechanisms could lead to plasma volume expansion and increased blood flow to peripheral tissues, even when BP is normal.
  - ✓ Local tissue autoregulatory processes that vasoconstrict then would be activated to offset the increased blood flow.
  - ✓ This effect would result in increased peripheral vascular resistance and, if sustained, also would result in thickening of the arteriolar walls.
  - ✓ This pathophysiologic component is plausible because increased total peripheral vascular resistance is a common underlying finding in patients with essential hypertension.
- **VASCULAR ENDOTHELIAL MECHANISMS**
  - ✓ Vascular endothelium and smooth muscle play important roles in regulating blood vessel tone and BP.
  - ✓ These regulating functions are mediated through vasoactive substances that are synthesized by endothelial cells. It has been postulated that a deficiency in the local synthesis of vasodilating substances (e.g., prostacyclin and bradykinin) or excess vasoconstricting substances (e.g., angiotensin II and endothelin I) contribute to essential hypertension, atherosclerosis, and other diseases.
  - ✓ Nitric oxide is produced in the endothelium, relaxes the vascular epithelium, and is a very potent vasodilator.
  - ✓ The nitric oxide system is an important regulator of arterial BP. Hypertensive patients may have an intrinsic deficiency in nitric oxide release, resulting in inadequate vasodilation.
- **ELECTROLYTES AND OTHER CHEMICALS**
  - ✓ Epidemiologic and clinical data have associated excess sodium intake with hypertension.
  - ✓ Population-based studies indicate that high-salt diets are associated with a high prevalence of stroke and hypertension.
  - ✓ Conversely, low-salt diets are associated with a low prevalence of hypertension. Clinical studies have shown consistently that dietary sodium restriction lowers BP in many (but not all) patients with elevated BP.

- ✓ The exact mechanisms by which excess sodium leads to hypertension are not known. However, they may be linked to increased circulating natriuretic hormone, which would inhibit intracellular sodium transport, causing increased vascular reactivity and increased BP.
- ✓ Altered calcium homeostasis also may play an important role in the pathogenesis of hypertension.
- ✓ A lack of dietary calcium hypothetically can disturb the balance between intracellular and extracellular calcium, resulting in an increased intracellular calcium concentration. This imbalance can alter vascular smooth muscle function by increasing peripheral vascular resistance.




## CLINICAL EVAULATION/DIAGNOSIS

### ➢ HISTORY

- ✓ A strong family history of hypertension, along with the reported finding of intermittent pressure elevation in the past,
- ✓ Secondary hypertension often develops before the age of 35 years or after 55.
- ✓ A history of repeated urinary tract infections suggests chronic pyelonephritis, although this condition may occur in the absence of symptoms.
- ✓ A history of weight gain is compatible with Cushing's syndrome, and one of weight loss is compatible with pheochromocytoma.

- ✓ A number of aspects of the history aid in determining whether vascular disease has progressed to a dangerous stage.
- ✓ These include angina pectoris and symptoms of cerebrovascular insufficiency, congestive heart failure, and/or peripheral vascular insufficiency.
- ✓ Other risk factors that should be asked about include cigarette smoking, diabetes mellitus, lipid disorders, and a family history of early deaths due to cardiovascular disease.
- ✓ Finally, aspects of the patient's lifestyle that could contribute to the hypertension or affect its treatment should be assessed, including diet, physical activity, family status, work, and educational level.

➢ **PHYSICAL EXAMINATION**

- ✓ The physical examination starts with the patient's general appearance.
- ✓ For instance, are the round face and truncal obesity of Cushing's syndrome present?
- ✓ Is muscular development in the upper extremities out of proportion to that in the lower extremities, suggesting coarctation of the aorta?
- ✓ The next step is to compare the blood pressures and pulses in the two upper extremities and in the supine and standing positions (for at least 2 min).
- ✓ A rise in diastolic pressure when the patient goes from the supine to the standing position is most compatible with essential hypertension; a fall, in the absence of antihypertensive medications, suggests secondary forms of hypertension.
- ✓ Funduscopic findings provide one of the best indications of the duration of hypertension and of prognosis.
- ✓ A useful guide is the **Keith-Wagener-Barker classification** of funduscopic changes, in which classification from normal through grade IV retinopathy is based upon the presence of arteriolar light reflex, arteriovenous crossing defects, hemorrhages and exudates; the specific changes in each fundus should be recorded and a grade assigned.

**Classification of Hypertensive**

| | Hypertension | | | | |
|---|---|---|---|---|---|
| | Arterioles | | | | |
| | General Narrowing, | Focal | | | |
| Degree | AV ratio[a] | Spasm[b] | Hemorrhages | Exudates | Papilledema |
| Normal | 3:4 | 1:1 | 0 | 0 | 0 |
| Grade I | 1:2 | 1:1 | 0 | 0 | 0 |
| Grade II | 1:3 | 2:3 | 0 | 0 | 0 |
| Grade III | 1:4 | 1:3 | + | + | 0 |
| Grade IV | Fine, fibrous cords | Obliteration of distal flow | + | + | + |

- ✓ Palpation and auscultation of the carotid arteries for evidence of stenosis or occlusion should be carried out.

- ✓ In examination of the heart and lungs, evidence of left ventricular hypertrophy and cardiac decompensation should be sought.
  - Is there a left ventricular lift?
  - Are third and fourth heart sounds present?
  - Are there pulmonary rales?
  - A third heart sound and pulmonary rales are unusual in uncomplicated hypertension.
- ✓ Their presence suggests ventricular dysfunction.
- ✓ Chest examination also includes a search for extracardiac murmurs and palpable collateral vessels that may result from coarctation of the aorta.
- ✓ The most important part of the abdominal examination is auscultation for bruits originating in stenotic renal arteries.
- ✓ Bruits due to renal arterial narrowing nearly always have a diastolic component or may be continuous and are best heard just to the right or left of the midline above the umbilicus or in the flanks.
- ✓ The abdomen should also be palpated for an abdominal aneurysm and for the enlarged kidneys of polycystic renal disease.
- ✓ The femoral pulses should be felt, and, if they are decreased and/or delayed in comparison with the radial pulse, the blood pressure in the lower extremities must be measured.
- ✓ Even if the femoral pulse is normal to palpation, arterial pressure in the lower extremities should be recorded at least once in patients in whom hypertension is discovered before the age of 30 years.

➢ **LABORATORY INVESTIGATION**

- ✓ The basic laboratory studies that should be performed in all patients are described in Table.
- ✓ Renal status is evaluated by assessing the presence of protein, blood, and glucose in the urine and measuring serum creatinine and/or blood urea nitrogen.
- ✓ Microscopic examination of the urine is also helpful.
- ✓ The **Serum potassium level** should be measured both as a screen for **Mineralocorticoid-Induced Hypertension** and to provide a baseline before diuretic therapy is begun.
- ✓ A blood glucose determination is helpful both because diabetes mellitus may be associated with accelerated arteriosclerosis, renal vascular disease, and diabetic nephropathy in patients with hypertension and because primary aldosteronism, Cushing's syndrome, and pheochromocytoma may all be associated with hyperglycemia.
- ✓ The possibility of hypercalcemia may also be investigated.
- ✓ Serum cholesterol, high-density lipoprotein cholesterol, and triglyceride levels identify other factors that predispose to the development of arteriosclerosis.
- ✓ An electrocardiogram should be obtained in all cases.
- ✓ The echocardiogram is more sensitive than either the electrocardiogram or physical examination in determining whether cardiac hypertrophy is present and may be a useful addition to the baseline evaluation of a hypertensive patient, particularly as left ventricular hypertrophy is an independent cardiovascular risk factor and its presence indicates the need for vigorous antihypertensive therapy.

- ✓ Because of the cost of an echocardiogram and the uncertainty as to whether the resultant information would modify therapy, it is unclear that routine follow-up echocardiograms during therapy are justified.
- ✓ The chest roentgenogram may also be helpful by providing the opportunity to identify aortic dilation or elongation and the rib notching that occurs in coarctation of the aorta.
- ✓ Most patients do not require ABPM, but readings are useful in diagnosing white coat hypertension and also in evaluating refractory hypertension, circadian patterns of blood pressure, and relation of blood pressure to symptoms like dizziness and visual changes.
- ✓ ABPM readings are good predictors of future cardiovascular events. Mean 24-h systolic pressure >135 mmHg has been associated with a nearly double cardiovascular risk.
- ✓ When the normal nocturnal decline in blood pressure ("dipping") is absent, readings correlate well with the prevalence and extent of target organ damage in hypertensive individuals.

**TABLE 230-7 Laboratory Tests for Evalution of Hypertension**

**BASIC TESTS FOR INITIAL EVALUATION**

1. Always included
   a. Urine for protein, blood, and glucose
   b. Microscopic urinalysis
   c. Hematocrit
   d. Serum potassium
   e. Serum creatinine and/or blood urea nitrogen
   f. Fasting glucose
   g. Total cholesterol
   h. Electrocardiogram
2. Usually included, depending on cost and other factors
   a. Thyroid-stimulating hormone
   b. White blood cell count
   c. HDL and LDL cholesterol and triglycerides
   d. Serum calcium and phosphate
   e. Chest x-ray; limited echocardiogram

**SPECIAL STUDIES TO SCREEN FOR SECONDARY HYPERTENSION**

1. Renovascular disease: angiotensin-converting enzyme inhibitor radionuclide renal scan, renal duplex Doppler flow studies, and MRI angiography
2. Pheochromocytoma: 24-h urine assay for creatinine, metanephrines, and catecholamines
3. Cushing's syndrome: overnight dexamethasone suppression test or 24-h urine cortisol and creatinine
4. Primary aldosteronism: plasma aldosterone: renin activity ratio

## DIAGNOSIS OF SECONDARY HYPERTENSION

- ✓ The abrupt onset of severe hypertension and/or the onset of hypertension of any severity in a patient under the age of 35 or over the age of 55 should lead to laboratory tests to exclude renovascular hypertension and pheochromocytoma, and the finding on physical examination of bilateral upper abdominal masses consistent with polycystic renal disease should lead to the performance of an abdominal ultrasound.
- ✓ An elevated creatinine or blood urea nitrogen level, associated with proteinuria and hematuria, should prompt a detailed workup for renal insufficiency.
- ✓ A familial history of hypertension, particularly with early age of onset, should spark consideration of a genetic form. Special studies for secondary hypertension are also indicated if there is therapeutic failure with the initial drug program.

- ✓ The specific diagnostic measures depend on the most likely causes of secondary hypertension.

- **PHEOCHROMOCYTOMA**
  - ✓ A history of headaches, palpitations, anxiety attacks, unusual sweating, hyperglycemia, and weight loss should also lead to tests to exclude pheochromocytoma.
  - ✓ The easiest and best screening procedure for pheochromocytoma is the measurement of catecholamines and their metabolites in a 24-h urine sample collected while the patient is hypertensive.
  - ✓ Measurement of plasma catecholamine levels may also be useful, while the assay of plasma-free metanephrines holds promise for heightened sensitivity.
  - ✓ These tests may be indicated even in patients who do not have episodic hypertension, since over half the patients with pheochromocytoma have fixed hypertension.
  - ✓ Provocative tests are seldom, if ever, indicated, although occasionally a suppressive test may be useful.
- **CUSHING'S SYNDROME**
  - ✓ A 24-h urine test for cortisol and creatinine or the administration of 1 mg of dexamethasone at bedtime, followed by the measurement of plasma cortisol at 7 to 10 A.M., is the best test to screen for the presence of Cushing's syndrome.
  - ✓ A urine cortisol level of <2750 nmol (100 μg) or suppression of the plasma cortisol level to <140 nmol/L (5 μg/dL) effectively rules out Cushing's syndrome.
- **RENOVASCULAR HYPERTENSION**
  - ✓ The presence of an abdominal bruit should lead to a workup for renovascular hypertension.
  - ✓ Suspicion for this form of hypertension should also be especially high in patients with deterioration of renal function after institution of ACE inhibitor therapy or in older patients with atherosclerotic disease.
  - ✓ Over the past decades the standard approach to screen for renovascular hypertension has progressed from the rapid-sequence intravenous pyelogram to one of three noninvasive techniques:
    1. The captopril-enhanced radionuclide renal scan (the preferred choice),
    2. A duplex Doppler flow study or magnetic resonance (MR) angiography with gadolinium enhancements.
    3. Perhaps the most sensitive and specific screening test, **the spiral computed tomography (CT) scan**, which gives a three-dimensional view, also requires giving an intravenous contrast agent.
  - ✓ The definitive test for surgically correctable renal disease is the combination of a renal angiogram and renal vein renin determinations.
  - ✓ The renal arteriogram both establishes the presence of a renal arterial lesion and aids in the determination of whether the lesion is due to atherosclerosis or to one of the fibrous or fibromuscular dysplasias.
  - ✓ It does not, however, prove that the lesion is responsible for the hypertension, nor does it permit prediction of the chances of surgical cure.
  - ✓ It must be noted that
    1. Renal artery stenosis is a frequent finding by angiography and at postmortem in normotensive individuals, and

2. Essential hypertension is a common condition and may occur in combination with renal arterial stenosis that is not responsible for the hypertension.

- ✓ Bilateral renal vein catheterization for measurement of plasma renin activity is therefore used to assess the functional significance of any lesion noted on arteriography.
- ✓ When one kidney is ischemic and the other is normal, all the renin released comes from the involved kidney.
- ✓ In the most straightforward situation, the ischemic kidney has a significantly higher venous plasma renin activity than the normal kidney, by a factor of ≥1.5.
- ✓ Moreover, the renal venous blood draining the uninvolved kidney exhibits levels similar to those in the inferior vena cava below the entrance of the renal veins.
- ✓ Significant benefit from operative correction may be anticipated in at least 80% of patients with the findings described above if care is taken to prepare the patient properly beforerenal vein blood sampling, i.e., by discontinuing renin-suppressing drugs, such as beta blockers, for at least 10 days; restricting the patient to a low sodium intake for 4 days; and/or giving a converting-enzyme inhibitor for 24 h.
- ✓ When obstructing lesions in the branches of the renal arteries are demonstrated by arteriography, an attempt to obtain blood samples from the main branches of the renal vein should be made in an effort to identify a localized intrarenal arterial lesion responsible for the hypertension.

- ➢ **PRIMARY ALDOSTERONISM**
  - ✓ These patients usually exhibit hypokalemia.
  - ✓ Diuretic therapy often complicates the picture when the hypokalemia is first observed and needs to be assessed.
  - ✓ Given the presence of hypokalemia, the relation between plasma renin activity and the aldosterone level becomes the key to the diagnosis of primary aldosteronism.
  - ✓ The aldosterone concentration or excretion rate is high and plasma renin activity is low in primary aldosteronism, and these levels are relatively unaffected by changes in sodium balance.
  - ✓ Thus, the aldosterone:renin ratio is high.
  - ✓ A critical part of the evaluation after primary aldosteronism has been established is to determine whether disease is unilateral or bilateral, because surgical removal of the lesion usually reduces arterial pressure only in patients with unilateral disease.

**TREATMENT**

- ➢ **OVERALL GOAL OF THERAPY**
  - ✓ The overall goal of treating hypertension is to reduce hypertension-associated morbidity and mortality.This morbidity and mortality are related to target-organ damage (e.g., cardiovascular events, cerebrovascular events, heart failure, and kidney disease).
  - ✓ Reducing risk remains the primary purpose of hypertension therapy, and the choice of drug therapy is influenced significantly by evidence demonstrating such risk reduction.
  - ✓ Most patients have a goal BP of less than 140/90 mm Hg.
  - ✓ However, this goal is lowered to less than 130/80 mm Hg for patients with diabetes or chronic kidney disease.

**GOAL BP VALUES RECOMMENDED BY THE JNC7**

- Most patients < 140/90 mm Hg
- Patients with diabetes < 130/80 mm Hg
- Patients with chronic kidney disease < 130/80 mm Hg (estimated GFR < 60 mL/min, serum creatinine > 1.3 mg/dL in women or > 1.5 mg/dL in men, or albuminuria > 300 mg/day or ≥ 200 mg/g creatinine)

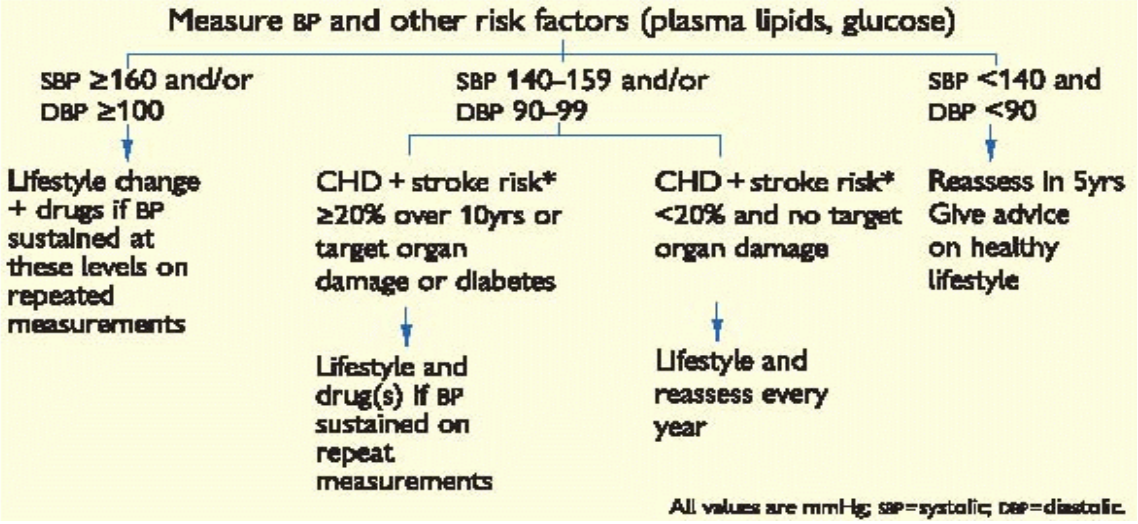
- **NON-PHARMACOLOGICAL TREATMENT**
  - ✓ It is possible to lower the BP in some individuals with non-pharmacological measures.
  - ✓ If non-pharma- cological treatment does not succeed during a 4-6 month period, drug treatment should be initiated.
  - ✓ Even for those on antihypertensive drug treatment, adherence to certain life-style modifications is strongly recommended.
- **LIFE-STYLE CHANGES**
  - Stop smoking/tobacco chewing*
  - Lose weight
  - Limit alcohol intake (<30 ml/d of ethanol)
  - Limit sodium intake (<2.3 g/d)
  - Maintain adequate intake of potassium, calcium and magnesium
  - Reduce intake of saturated fat and cholesterol
  - Exercise aerobically on a regular basis, meditation, shavasana
- **SODIUM RESTRICTION**
  - ✓ Modest salt restriction may help lower the BP; rigid restriction is not a practical solution.
  - ✓ Marked sodium restriction may be counter-productive due to stimulation of the renin-angiotensin-aldosterone axis.
  - ✓ A moderate diet, i.e., 2 g sodium per day is not only a useful therapeutic measure but is also feasible.
  - ✓ This target can be accomplished by eliminating table salt, by reducing the salt in cooking, and by consuming more natural food and less processed food.
- **POTASSIUM ENRICHMENT**
  - ✓ In certain patient groups (the elderly), potassium supplementation may yield measurable therapeutic benefits.
  - ✓ While large-scale, general recommendations cannot be made, hypertensive patients should be encouraged to consume a diet rich in potassium (vegetables, fruits).
- **CALCIUM SUPPLEMENTATION**
  - ✓ The effects of calcium supplementation in hypertension are highly variable and unpredictable.
  - ✓ The best advice is to ensure proper intake of calcium in the diet.

- **OTHER SUPPLEMENTS**
  - ✓ Despite the curiosity provoked by the role of magnesium supplemenation, high fibre diet, omega fatty acids, etc., these modalities cannot be recommended with confidence to treat hypertension.
- **REDUCING ALCOHOL INTAKE**
  - ✓ Excessive consumption of alcohol could elevate BP levels.
  - ✓ Therefore alcohol use should be curtailed (or prohibited) for patients with hypertension.
- **PHYSICAL EXERCISE, RELAXATION, AND STRESS REDUCTION**
  - ✓ A purely static physical exercise increases the systolic BP and therefore should be avoided. Regular dynamic exercise may lower the BP and protect against coronary events.
  - ✓ Bio-feedback, stress reduction, relaxation, and yoga training (particularly shavasana) yield benefits in the short-term and whenever possible should be encouraged.
- **WEIGHT CONTROL**

✓ For obese patients with hypertension, weight loss should be vigorously pursued.

✓ Weight control also decreases salt sensitivity and increases the effectiveness of anti-hypertensive drug therapy.

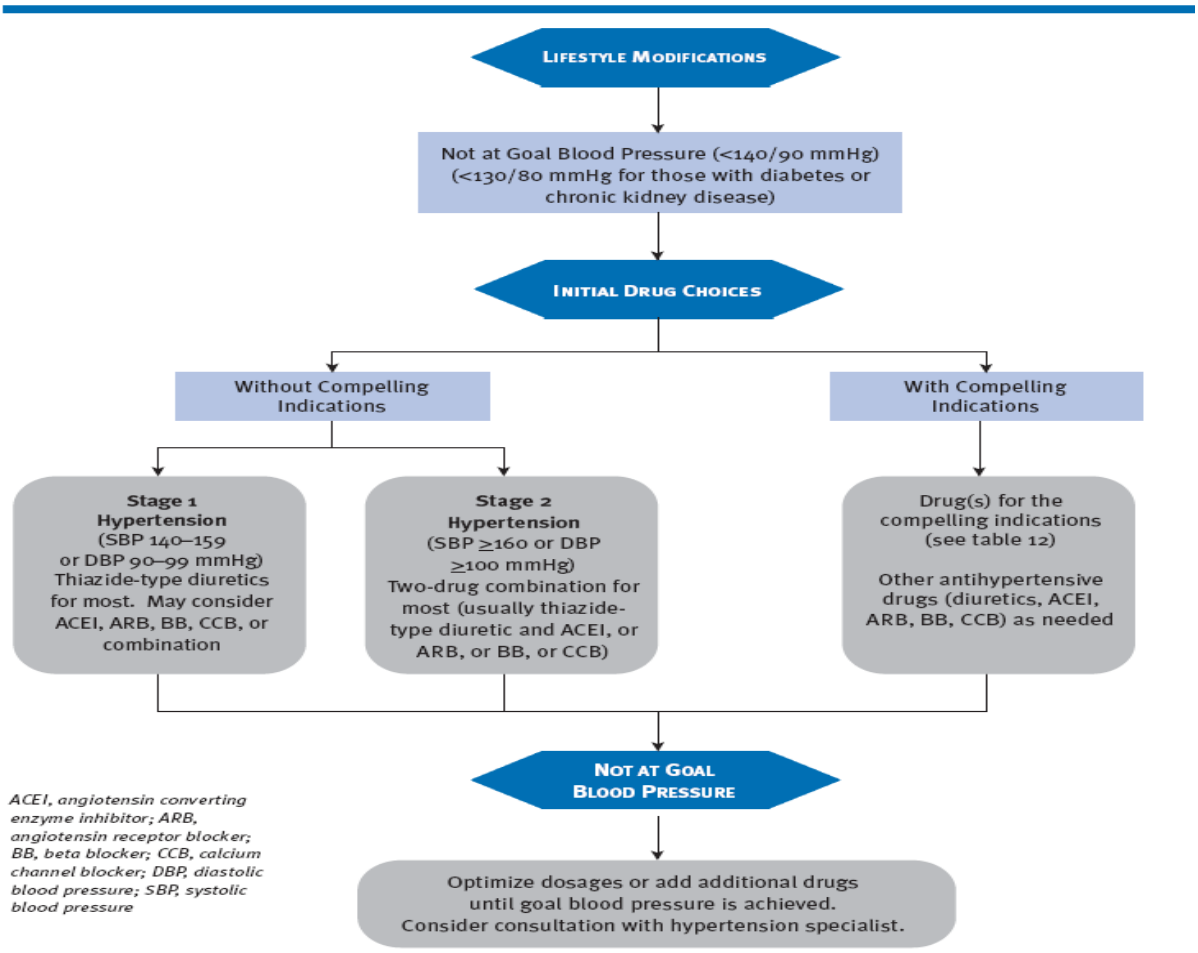
| **Initial Blood Pressure** | | **MANAGEMENT** |
|---|---|---|
| **Systolic** | **Diastolic** | |
| Malignant Hypertension | | Admit and treat immediately |
| >220 | >120 | Repeat several times at the same attendance and treat immediately if blood pressure persists in this range |
| 180-219 | 110-190 | Confirm over 1-2 weeks and treat if BP remain in this range |
| 160-179 | 100-109 | Repeat over 3-4 weeks (end organ damage present) or 2-12 weeks (no organ damage), institute non-pharmacological measures and treat if blood pressure persists in this range |
| 140-159 | 90-99 | Repeat over several weeks, institute non-pharmacological measures. Treat if remains in this range and patient has target organ damage, cardiovascular complications or an estimated 10 year cardiovascular risk > 20%. Otherwise reassess annually |
| 135-139 | 85-89 | Reassess annually |
| <135 | <85 | Reassess in 5 years |

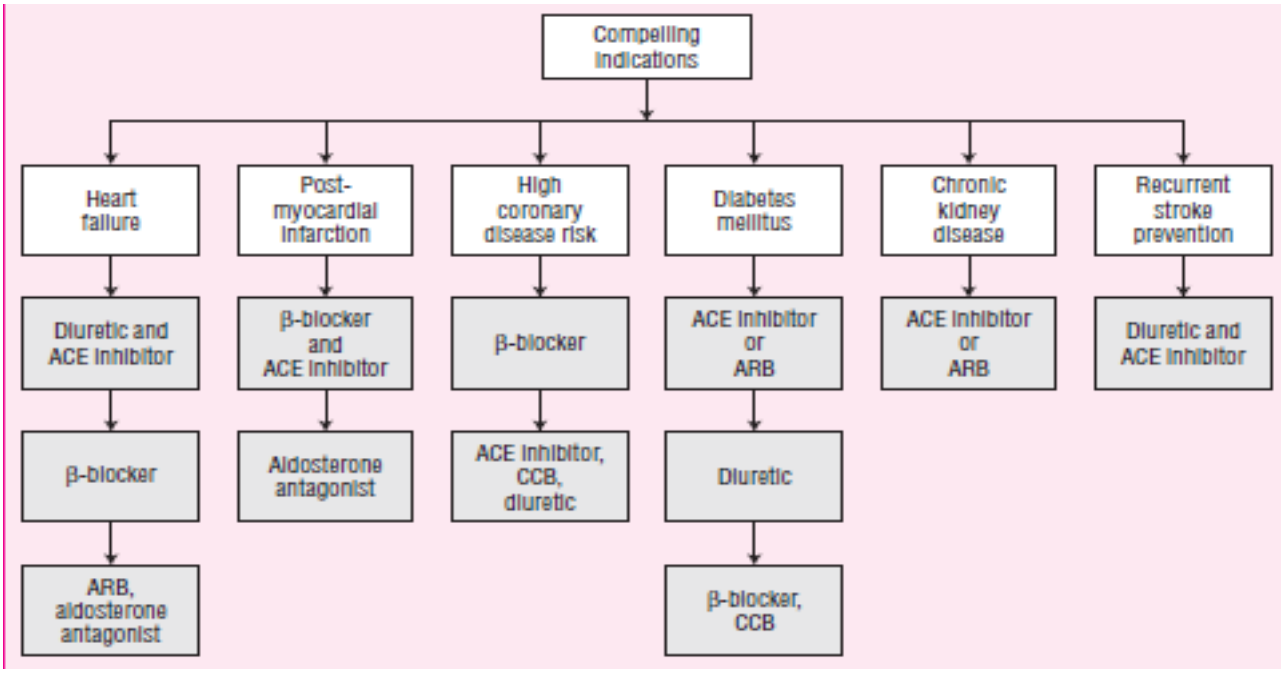



- **DRUGS**
  - ✓ Essential hypertension is not curable.
  - ✓ The ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial study suggests that adequate) BP reduction is more important than the specific drug used; but ALLHAT did not include $\beta_2$-blockers, and new data cast doubt on their value, particularly atenolol, and especially if combined with a thiazide. Conversely, ACE inhibitors may provide added renal benefit in diabetics or if GFR.
    - If >55yrs, and in Black patients of any age, 1st choice is a $Ca^{2+}$ channel blocker or thiazide. If <55, 1st choice is ACE-inhibitors (or ARB if ACE-inhibitors intolerant, eg from cough).
    - If initial [prescription take] was with a $Ca^{2+}$ channel blocker or a thiazide, and a 2nd drug is needed, add an ACE-inhibitors. If initial [prescription take] was with ACE-inhibitors, add a $Ca^{2+}$ channel blocker or a thiazide.
    - If treatment with 3 drugs is needed, try ACE-inhibitors, $Ca^{2+}$ channel blocker and thiazide.
    - If BP still uncontrolled on adequate doses of 3 drugs, add a 4th and get help.
    - If a 4th drug is needed, consider: higher dose thiazide (unlikely to help) or a new diuretic, eg spironolactone (monitor U&E), or $\beta_2$-blockers.
    - $\beta_2$-blockers are not 1st-line for hypertension, but consider in younger people, particularly: if intolerance or contra-indication to ACE-inhibitor/ARB (angiotensin receptor blockers) exists, or she is a women of child-bearing potential, or there is sympathetic drive. Here, if therapy is initiated with a $\beta_2$-blocker and a 2nd drug is needed, add a $Ca^{2+}$ blocker not a thiazide to reduce risk of developing diabetes.

## ➢ INITIATING PHARMACOLOGIC THERAPY

| Hypertension | Intervention |
|---|---|
| Stage 1 or 2 (BP 140-179/90-109 mmHg) | - Encourage lifestyle changes for 3-6 months |
| | - If BP remains high, |
| | *prescribe monotherapy for patients with CV risk factors or TOD; |
| | * monitor patients with BP 140-149/90-94 mmHg and absence of CV risk factors and TOD |
| Stage 3 (BP 180-209/110-119 mmHg) | - Encourage lifestyle changes |
| | - Prescribe monotherapy and monitor patient; consider therapy with second antihypertensive drug |
| Stage 4 (BP ≥ 210/≥120 mmHg) | - Encourage lifestyle changes |
| | - Prescribe therapy, possibly with multiple drugs |
| | - If evidence of TOD, consider hospitalising patient |






- **ANTIHYPERTENSIVE DRUG CLASSES**
  - **DIURETICS**
    - ✓ These drugs are both inexpensive and well tolerated by most patients.
    - ✓ Their diuretics action is achieved by blockade of renal tubular sodium reabsorption.
    - ✓ Initially, they reduce blood pressure by reducing circulating blood volume but in the longer term blood volume is restored towards normal and the fall in BP is associated with a reduction in total peripheral resistance, suggesting a direct vasodilatory action.
    - ✓ Thiazide and thiazide-like diuretics may cause hypokalaemia, small increase in LDL-cholesterol and triglyceride, and gout associated with impaired urate excertion, erectile dysfunction.
    - ✓ BP lowering occurs with very low doses of thiazide diuretics. Increasing the dose substantially increases the risk of metabolic disturbance without causing further BP reduction.
    - ✓ Loop diuretics are no more effective at lowering BP than thiazides unless renal function is significantly impaired or patient is receiving agents that inhibit the rennin-angiotensin system. They are also a suitable choice if heart failure is present.
    - ✓ Spironolactone, an aldosterone antagonist, is not suitable for first-line therapy but is an increasingly important option for patient with resistant hypertension. There is a risk of hyperkalaemia, especially if used in combination with ACE inhibitors or ARB.
  - **β – ADRENORECEPTOR ANATAGONIST**
    - ✓ Inexpensive
    - ✓ Their use is likely to decline because they seem less effective at preventing stroke and they are commonly associated with adverse effects, such as lethargy, impaired

concentration, aching muscles, vivid dreaming, erectile dysfunction, exacerbation of asthma, intermittent claudication.
- ✓ Also increase the risk of diabetes.
- ✓ Most suitable for younger hypertensive who have another indication for β-blocker, such as coronary heart disease.

- **RENIN-ANGIOTENSIN-ALDOSTERONE ANTAGONISTS**
  - ✓ ACE inhibitors more expensive, Cough very common effect, appropriate for use in younger patients and those with cardiac failure or diabetes.
  - ✓ Angiotensin receptor blockers more expensive, especially for patients in whom ACE inhibitor indicated but not tolerated due to cough
  - ✓ More effective in preventing vascular events than atenolol in patients with LVH
- **CALCIUM CHANNEL BLOCKERS**
  - ✓ Verapamil's effects are primarily on the heart, reducing heart rate and cardiac output.
  - ✓ Long-acting dihydropyridines (Nifedipine, Amlodipine) are preferred because they are convenient for patients and avoid large fluctuations in plasma drug concentrations that may be associated with adverse effects.
  - ✓ Adverse effects are common: Oedema and flushing
  - ✓ Gum hypertrophy may occur with dihydropyridines and constipation in verapamil.
- **α – BLOCKERS**
  - ✓ It prevent NA induced vasoconstriction, as a result, they reduce total peripheral resistance and BP.
  - ✓ Prazosin: short-acting and causing first-dose hypotension
  - ✓ Terazosin and Doxazosin: Longer acting.
  - ✓ Most expensive and adverse effect is common.
  - ✓ Less effective than thiazides at preventing heart failure.
- **DIRECT ACTING VASODILATORS**
  - ✓ Poorly tolerated
  - ✓ Only use in severe hypertension
  - ✓ Adverse effect: Oedema, Posture hypotension, Headache
- **CENTRALLY ACTING VASODILATORS**
  - ✓ Poorly tolerated
  - ✓ Only use in severe hypertension or hypertension of pregenancy, third-line drug
  - ✓ Adverse effects: Tiredness, Depression

**SPECIAL CONSIDERATIONS**

- ✓ Five groups of patients with hypertension require special consideration because of associated conditions: those with renal disease, coronary artery disease, or diabetes mellitus; women of reproductive age; and the elderly.
- ➢ **RENAL DISEASE**
  - ✓ Reduction of arterial pressure in hypertensive patients with impaired renal function is often accompanied initially by an increase in serum creatinine.
  - ✓ This change does not represent further structural renal damage and should not deter the physician from continuing the therapy, since achievement of blood pressure control may eventually reduce the value toward normal.
  - ✓ However, if serum creatinine increases in a patient treated with an ACE inhibitor, care needs to be exercised, because these patients may have bilateral renal artery disease.

- ✓ Their renal function will continue to deteriorate as long as the ACE inhibitor is given.
- ✓ Thus, ACE inhibitors should be used cautiously in patients with impaired renal function, and renal function should be assessed frequently (every 4 to 5 days) for the first 3 weeks.
- ✓ While these drugs are contraindicated in patients with bilateral renal artery stenosis, together with angiotensin receptor blockers they are the drugs of choice in patients with unilateral renal artery stenosis and a normally functioning contralateral kidney and probably also in patients with chronic renal failure with or without diabetes mellitus.

➢ **CORONARY ARTERY DISEASE**

- ✓ Beta blockers, important in reducing mortality after myocardial infarction and in the treatment of angina, are useful antihypertensive agents in patients with coronary artery disease.
- ✓ ACE inhibitors are useful in these patients as well, especially those with hypertension and left ventricular dysfunction.

➢ **DIABETES MELLITUS**

- ✓ The diabetic patient with hypertension is particularly challenging to treat because multiple agents are usually needed to achieve goal blood pressure and because many of the agents used to lower blood pressure can affect glucose metabolism adversely.
- ✓ ACE inhibitors or angiotensin receptor blockers should be first-line therapy in hypertensive individuals with type 2 diabetes.
- ✓ They have no known adverse effects on glucose or lipid metabolism and minimize the development of diabetic nephropathy by reducing renal vascular resistance and renal perfusion pressure—the primary factor underlying renal deterioration in these patients.
- ✓ Meta-analyses of clinical studies have demonstrated that setting a lower blood pressure goal in diabetic patients is ideal to prevent progression of end-organ disease, with current recommendations shifting from 130/85 mmHg downward to 130/80.
- ✓ The average hypertensive diabetic patient will require at least three medications to achieve appropriate control.

➢ **WOMEN OF REPRODUCTIVE AGE**

- **ORAL CONTRACEPTIVES**
  - ✓ In patients receiving these agents who do become hypertensive, the mechanism is likely to be activation of the renin-angiotensin-aldosterone system.
  - ✓ The estrogen component of oral contraceptive agents stimulates the hepatic synthesis of the renin substrate angiotensinogen, which in turn favors the increased production of angiotensin II and secondary aldosteronism.
  - ✓ However, only a small number of women taking oral contraceptives actually have an increase in arterial pressure to a level >140/90mmHg, and in about half of these, the hypertension will remit within 6 months of stopping the drug.
  - ✓ Why some women taking oral contraceptives develop hypertension and others do not is unclear but may be related to
    1. Increased vascular sensitivity to angiotensin II,
    2. The presence of mild renal disease,
    3. Familial factors (>50% have a positive family history for hypertension),
    4. Age (hypertension is significantly more prevalent in women over age 35),
    5. The estrogen content of the contraceptive, and/or

6. Obesity.
   - ✓ Indeed, some investigators have suggested that oral contraceptives simply unmask women with essential hypertension.

- **PREGNANCY**
  - ✓ The patient who is pregnant and hypertensive or who develops hypertension during pregnancy (pregnancy- induced hypertension, preeclampsia, eclampsia) is particularly difficult to treat. Because it is uncertain whether autoregulation of uterine blood flow occurs, lowering blood pressure in the pregnant hypertensive patient may result in reduced placental and fetal perfusion.
  - ✓ Thus, a conservative approach to lowering blood pressure is usually indicated.
  - ✓ In the second and third trimesters, antihypertensive agents are often not indicated unless the diastolic pressure exceeds 95mmHg.
  - ✓ In general, severe salt restriction and/or diuretics are not used because of the associated increase in fetal wastage.
  - ✓ Beta blockers need to be used cautiously for similar reasons.
  - ✓ Methyldopa and hydralazine, and to a lesser extent calcium channel antagonists, are the antihypertensive agents used most often, because they have no known adverse effects on the fetus.
  - ✓ Little is known about the safety of other antihypertensive agents in pregnancy, except that nitroprusside, ACE inhibitors, and angiotensin receptor blockers may cause adverse effects on the fetus and are contraindicated.

➢ **ELDERLY PATIENTS**
  - ✓ Hypertensive patients who are over age 65, and particularly those over age 75, offer substantial challenges to the physician.
  - ✓ Several studies have reported that healthy elderly patients, whether male or female, who are treated with relatively modest doses of antihypertensive agents show a substantial reduction in strokes and stroke-related deaths.
  - ✓ This is true whether the patient has systolic and diastolic hypertension or isolated systolic hypertension.

**HYPERTENSIVE URGENCIES AND EMERGENCIES**

- ✓ Hypertensive urgencies and emergencies both are characterized by the presence of very elevated BP, greater than 180/120 mm Hg.
- ✓ However, the need for urgent or emergent antihypertensive therapy should be determined based on the presence of acute or immediately progressing target-organ injury but not elevated BP alone.
- ✓ Urgencies are not associated with acute or immediately progressing target-organ injury, whereas emergencies are.
- ✓ A common error with hypertensive urgency is overly aggressively antihypertensive therapy.
- ✓ This treatment likely has been perpetrated by the classification terminology *urgency.*
- ✓ Hypertensive urgencies ideally are managed by adjusting maintenance therapy by adding a new antihypertensive and/or increasing the dose of a present medication.
- ✓ This is the preferred approach to these patients because it provides a more gradual reduction in BP.
- ✓ Very rapid reductions in BP to goal values should be discouraged because of potential risks.

- ✓ Since autoregulation of blood flow in chronically hypertensive patients occurs at a much higher range of pressures than in normotensive persons, the inherent risks of reducing BP too precipitously include cerebrovascular accidents, myocardial infarction, and acute kidney failure.
- ✓ All patients with hypertensive urgency should be reevaluated within no more than 7 days (preferably after 1 to 3 days).
- ✓ Acute administration of a short-acting oral antihypertensive agent (captopril, clonidine, or labetolol), followed by careful observation for several hours to ensure a gradual reduction in BP, is an option for hypertensive urgency.
- ✓ Oral captopril is one of the agents of choice and can be used in doses of 25–50 mg at 1- to 2-hour intervals.
- ✓ The onset of action of oral captopril is 15 to 30 minutes, and a marked fall in BP is unlikely to occur if no hypotensive response is observed within 30 to 60 minutes.
- ✓ For patients with hypertensive rebound following withdrawal of clonidine, 0.2 mg clonidine can be given initially, followed by 0.2 mg hourly until the DBP falls below 110 mmHg or a total of 0.7 mg clonidine has been administered.
- ✓ A single dose may be all that is necessary.
- ✓ Labetolol can be given in a dose of 200–400 mg, followed by additional doses every 2 to 3 hours.
- ✓ Oral or sublingual immediate-release nifedipine has been used in the office setting, nursing homes, and hospitals for acute BP lowering but is potentially dangerous.
- ✓ This approach produces a rapid reduction in BP. Immediate-release nifedipine should never be used for hypertensive urgencies because of reports of severe adverse events such as myocardial infarctions and strokes.
- ✓ Hypertensive emergencies are those rare situations that require immediate BP reduction to limit new or progressing target-organ damage.
- ✓ Hypertensive emergencies generally require parenteral therapy.
- ✓ The goal in hypertensive emergencies is not to lower BP to less than 140/90 mmHg; rather, a reduction in mean atrial pressure (MAP) of up to 25% within minutes to hours is the initial target.
- ✓ If the BP is then stable, BP can be reduced toward 160/100–110 mm Hg within the next 2 to 6 hours.
- ✓ Precipitous drops in BP may lead to end-organ ischemia or infarction. If patients tolerate this reduction well, additional gradual reductions toward goal BP values can be attempted after 24 to 48 hours.
- ✓ The exception to this guideline is for patients with an acute ischemic stroke, in whom maintaining an elevated BP is needed for a much longer period of time.
- ✓ The clinical situation should dictate which intravenous medication is used to treat hypertensive emergencies.
- ✓ Regardless, therapy should be provided in a hospital or emergency room setting with intraarticular BP monitoring.
- ✓ Nitroprusside is widely considered the agent of choice for most cases but can be problematic in patients with chronic kidney disease.
- ✓ It is a direct-acting vasodilator that decreases peripheral vascular resistance but does not increase cardiac output unless left ventricular failure is present.
- ✓ Nitroprusside can be given to treat most hypertensive emergencies, but in aortic dissection, propranolol should be given first to prevent reflex sympathetic activation.

- ✓ Since nitroprusside is metabolized to cyanide and then to thiocyanate, which is eliminated by the kidneys, serum thiocyanate levels should be monitored when infusions are continued longer than 72 hours.
- ✓ Nitroprusside should be discontinued if the concentration exceeds 12 mg/dL. The risk of thiocyanate accumulation and toxicity is increased in patients with impaired kidney function.
- ✓ Fenoldopam is a dopamine-1 agonist that is a popular alternative to nitroprusside. It is used often for perioperative hypertension.
- ✓ Similar to nitroprusside, it has a very quick onset of action and can be titrated easily by adjusting the continuous infusion rate.
- ✓ Conversely, it can improve renal blood flow and is especially useful in patients with kidney insufficiency.
- ✓ Intravenous nitroglycerin dilates both arterioles and venous capacitance vessels, thereby reducing both cardiac afterload and preload, which can decrease myocardial oxygen demand.
- ✓ It also dilates collateral coronary blood vessels and improves perfusion to ischemic myocardium.
- ✓ These properties make intravenous nitroglycerin ideal for the management of hypertensive emergency in the presence of myocardial ischemia.
- ✓ Intravenous nitroglycerin is associated with tolerance when used over 24 to 48 hours and can cause severe headache.
- ✓ The hypotensive response of hydralazine is less predictable than with other parenteral agents.
- ✓ Therefore, its major role is in the treatment of eclampsia or hypertensive encephalopathy associated with renal insufficiency.

**EFFECTS OF HYPERTENSION**

- ✓ Patients with hypertension die prematurely; the most common cause of death is heart disease, with stroke and renal failure also frequent, particularly in patients with significant retinopathy.

➢ **EFFECTS ON THE HEART**

- ✓ Cardiac compensation for the excessive workload imposed by increased systemic pressure is at first sustained by concentric left ventricular hypertrophy, characterized by an increase in wall thickness.
- ✓ Ultimately, the function of this chamber deteriorates, the cavity dilates, and the symptoms and signs of heart failure appear.
- ✓ Angina pectoris may also occur because of the combination of accelerated coronary arterial disease and increased myocardial oxygen requirements as a consequence of the increased myocardial mass.
- ✓ On physical examination, the heart is enlarged and has a prominent left ventricular impulse.
- ✓ The sound of aortic closure is accentuated, and there may be a faint murmur of aortic regurgitation.
- ✓ Presystolic (atrial, fourth) heart sounds appear frequently in hypertensive heart disease, and a protodiastolic (ventricular, third) heart sound or summation gallop rhythm may be present.

- ✓ Electrocardiographic changes of left ventricular hypertrophy may occur, but the electrocardiogram substantially underestimates the frequency of cardiac hypertrophy compared with that observed with the echocardiogram.
- ✓ Evidence of ischemia or infarction may be observed late in the disease.
- ✓ Most deaths due to hypertension result from myocardial infarction or congestive heart failure.
- ✓ Recent data suggest that some of the myocardial damage may be mediated by aldosterone in the presence of a normal/high salt intake rather than just the increased blood pressure or an increase in angiotensin II levels per se.

➢ **NEUROLOGIC EFFECTS**

- ✓ The neurologic effects of long-standing hypertension may be divided into retinal and central nervous system changes.
- ✓ Because the retina is the only tissue in which the arteries and arterioles can be examined directly, repeated ophthalmoscopic examination provides the opportunity to observe the progress of the vascular effects of hypertension.
- ✓ The Keith-Wagener-Barker classification of the retinal changes in hypertension has provided a simple and excellent means for serial evaluation of hypertensive patients.
- ✓ Central nervous system dysfunction also occurs frequently in patients with hypertension.
- ✓ Occipital headaches, most often occurring in the morning, are among the most prominent early symptoms of hypertension.
- ✓ Dizziness, light-headedness, vertigo, tinnitus, and dimmed vision or syncope may also be observed, but the more serious manifestations are due to vascular occlusion, hemorrhage, or encephalopathy.
- ✓ The pathogeneses of the former two disorders are quite different.
- ✓ Cerebral infarction is secondary to the increased atherosclerosis observed in hypertensive patients, whereas cerebral hemorrhage is the result of both the elevated arterial pressure and the development of cerebral vascular microaneurysms (Charcot-Bouchard aneurysms).
- ✓ Only age and arterial pressure are known to influence the development of the microaneurysms.
- ✓ Thus, it is not surprising that arterial pressure shows a better association with cerebral hemorrhage than with either cerebral or myocardial infarction.
- ✓ Hypertensive encephalopathy consists of the following symptom complex: severe hypertension, disordered consciousness, increased intracranial pressure, retinopathy with papilledema, and seizures.
- ✓ The pathogenesis is uncertain but is probably not related to arteriolar spasm or cerebral edema. Focal neurologic signs are infrequent and, if present, suggest that infarction, hemorrhage, or transient ischemic attacks are more likely diagnoses.
- ✓ Although some investigators have suggested that prompt lowering of arterial pressure in these patients may adversely affect cerebral blood flow, most studies indicate that this is not the case.

➢ **EFFECTS ON THE KIDNEY**

- ✓ Arteriosclerotic lesions of the afferent and efferent arterioles and the glomerular capillary tufts are the most common renal vascular lesions in hypertension and result in a decreased glomerular filtration rate and tubular dysfunction.

- ✓ Proteinuria and microscopic hematuria occur because of glomerular lesions, and ~10% of the deaths caused by hypertension result from renal failure.
- ✓ Blood loss in hypertension occurs not only from renal lesions; epistaxis, hemoptysis, and metrorrhagia also occur frequently in these patients.

**MALIGNANT HYPERTENSION**

- ✓ In addition to marked blood pressure elevation (usually diastolic blood pressure > 130 mmHg) in association with papilledema and retinal hemorrhages and exudates, the full-blown medical emergency of malignant hypertension may include manifestations of hypertensive encephalopathy, such as severe headache, vomiting, visual disturbances (including transient blindness), transient paralyses, convulsions, stupor, and coma.
- ✓ These manifestations have been attributed to spasm of cerebral vessels and to cerebral edema.
- ✓ In some patients who have died, multiple small thrombi have been found in the cerebral vessels.
- ✓ Cardiac decompensation and rapidly declining renal function are other critical features of malignant hypertension.
- ✓ Oliguria may, in fact, be the presenting feature.
- ✓ The vascular lesion characteristic of malignant hypertension is fibrinoid necrosis of the walls of small arteries and arterioles, and this development can be reversed by effective antihypertensive therapy.
- ✓ The pathogenesis of malignant hypertension is unknown.
- ✓ However, at least two independent processes—dilation of cerebral arteries and generalized arteriolar fibrinoid necrosis—contribute to the associated signs and symptoms.
- ✓ The cerebral arteries dilate because the normal autoregulation of cerebral blood flow decompensates as a result of the markedly elevated arterial pressure.
- ✓ Cerebral blood flow therefore is excessive, producing the encephalopathy associated with malignant hypertension.
- ✓ Many patients also show evidence of a microangiopathic hemolytic anemia; this secondary phenomenon could contribute to the deterioration of renal function.
- ✓ Most patients also have elevated levels of peripheral plasma renin activity and increased aldosterone production, and these effects may be involved in causing vascular damage.
- ✓ Perhaps <1% of hypertensive patients develop the malignant phase, which can occur in the course of both essential and secondary hypertension.
- ✓ Rarely, it is the first recognized manifestation of hypertension, and it is unusual for it to occur in patients under treatment.
- ✓ The average age at diagnosis is 40, and men are affected more often than women.
- ✓ Prior to the availability of effective therapy, the life expectancy after diagnosis of malignant hypertension was <2 years, with most deaths being due to renal failure, cerebral hemorrhage, or congestive heart failure.
- ✓ With the advent of effective antihypertensive therapy, at least half the patients survive for >5 years.

➢ **TREATMENT**

- ✓ Malignant hypertension is a medical emergency that requires immediate therapy.

- ✓ However, it needs to be distinguished from severe hypertension, in which overly aggressive therapy could result in a potentially hazardous reduction in myocardial and cerebral perfusion.
- ✓ The initial aims of therapy should be
  1. Correction of medical complications, and
  2. Reduction of diastolic pressure by one-third, but not to a level <95 mmHg.
- ✓ The drugs available for treatment of malignant hypertension can be divided into two groups on the basis of time of onset of action.
- ✓ If the patient has hypertensive encephalopathy or pulmonary edema, and if arterial pressure must be reduced rapidly, then one from the immediate-acting group should be used, but they are not satisfactory for long-term management.
- ✓ Furosemide is an important adjunct to the therapy just discussed.
- ✓ Given either orally or intravenously, it serves to maintain sodium dieresis in the face of a falling arterial pressure and thus will speed recovery from encephalopathy and congestive heart failure as well as maintain the sensitivity to the primary antihypertensive drug.
- ✓ Digitalis may also be indicated if there is evidence of cardiac decompensation.
- ✓ In patients with malignant hypertension in whom the existence of pheochromocytoma is suspected, urine should be collected for measurement of the products of catecholamine metabolism, and drugs that might release additional catecholamines, such as methyldopa, reserpine, and guanethidine, must be avoided.
- ✓ The parenteral drug of choice in these patients is phentolamine, administered with care to avoid a precipitous reduction in arterial pressure.