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HYPERTENSION: PREVALENCE, HEALTH RISKS, AND MANAGEMENT STRATEGIES

[1]Ahmed Ahmed, [2]Eiman Shams Elddin Elgailani, [3]*Heyam Saad Ali

[1]General Surgery-Colorectal Department, Nottingham Hospital, United Kingdom.
[2]Department of Clinical Pharmacy & Pharmacy Practice, Dubai Pharmacy College, UAE.
[3]Department of Pharmaceutics Dubai Pharmacy College Dubai, UAE.

***Correspondence for Author: Heyam Saad Ali**

Department of Pharmaceutics Dubai Pharmacy College Dubai, UAE.

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ABSTRACT

Hypertension is the most common cause of cardiovascular disease which is abnormally due to sustained elevated blood pressure (Systolic blood pressure of 140 mm Hg or greater and/or diastolic blood pressure of 90 mm Hg or greater) in any blood vessel (usually arterial), such as pulmonary or portal. It has been called "the silent killer" because it usually does not cause symptoms for many years until a vital organ is damaged. The risk of mortality or morbidity rises progressively with increasing systolic and diastolic pressures, with each measure having independent prognosis value; for example, isolated systolic hypertension is associated with a 2-3 fold increase in cardiac mortality. The level at which blood pressure is associated with a significant increase in risk also depend on age, sex, race and other environmental factors. Abnormally high blood pressure in the arteries also increases the risk of problems such as stroke, aneurysm, heart failure, heart attack, and kidney damage. Blood pressure levels are strongly familial but no clear genetic pattern has been discerned. The strong familial risk for cardiovascular diseases should also be considered. This review familiarizes the silent killer, hypertension with a focus on recent research on etiology, prevalence, pathophysiology and treatment of hypertension.

KEYWORDS: Stroke, aneurysm, heart failure, heart attack, and kidney damage.

INTRODUCTION

Hypertension is the most common cause of cardiovascular disease which is abnormally due to sustained elevated blood pressure (Systolic blood pressure of 140 mm Hg or greater and/or diastolic blood pressure of 90 mm Hg or greater) in any blood vessel (usually arterial), such as pulmonary or portal. It has been called " the silent killer" because it usually does not cause symptoms for many years until a vital organ is damaged.[1] The risk of mortality or morbidity rises progressively with increasing systolic and diastolic pressures, with each measure having independent prognosis value; for example, isolated systolic hypertension is associated with a 2-3 fold increase in cardiac mortality.[2] The level at which blood pressure is associated with a significant increase in risk also depend on age, sex, race and other environmental factors. Abnormally high blood pressure in the arteries also increases the risk of problems such as stroke, aneurysm, heart failure, heart attack, and kidney damage. Blood pressure levels are strongly familial but no clear genetic pattern has been discerned. The strong familial risk for cardiovascular diseases should also be considered.[3]

1.1 Prevalence

The Prevalence of hypertension depends on both the racial composition of the population studied and the criteria used to define the condition. The number of Americans who have hypertension is estimated to be more than 50 million (20% of U.S.A population).[4] It occurs more often in blacks – 38% of black adults have high blood pressure, compared with 29% of whites. The prevalence of various forms of secondary hypertension depends on the nature of the population studied and how extensive the evaluation is. There are no available data to define the frequency of secondary hypertension in the general population, although in middle aged males it has been reported to be 6%. On the other hand, in referral centers, it has been reported to be as high as 35%. The various forms of hypertension and their frequencies are given in the following table.[5]

Table 1. Prevalence of various forms of hypertension in the general population and in specialized referral clinics.

Diagnosis	General Population, %	Specially Clinic, %
Essential hypertension	92-94	65-85
Renal hypertension Parenchymal	2-3	4-5
Renovascular	1-2	4-16
Endocrine hypertension: Primary aldosteronism	0.3	0.5-12
Cushing's syndrome	<0.1	0.2
Pheochromocytoma	<0.1	0.2
Oral contraceptive-induced	2-4	1-2
Miscellaneous	0.2	1

Predominant age: Essential hypertension usually has its onset in the 20's to 30's.

Predominant sex: Males > Females (males tend to run higher pressure than females but more importantly have a significantly higher risk of cardiovascular disease at any given blood pressure).

1.2 Physiology

Blood pressure is determined by cardiac output and peripheral vascular resistance (BP = CO x PVR). Cardiac output is determined by stroke volume and heart rate (CO=SV x HR).

Peripheral resistance is inversely proportional to the fourth power of the internal radius of the blood vessels. Therefore, variations in the internal lumen of blood vessels profoundly affect the blood pressure. Blood pressure varies naturally over a person's life. Infants and children normally have much lower blood pressure than adults. Activity also affects blood pressure, which is higher when a person is active and lower when a person rests.

Blood pressure varies with the time of day too; it's highest in the morning and lowest at night during sleep. Also blood pressure is affected by emotional upset and other factors.[6]

1.3 Control of Blood Pressure

The pressure in the arteries can be increased in various ways. For one, the heart can pump with more force, putting out more fluid each second.[7] Another possibility is that the large arteries can lose their normal flexibility and become stiff, so that they can't expand when the heart pumps blood through them. Thus, the blood from each heartbeat is forced through less space than normal and the pressure increases.[8] That's what happens in elderly people whose arterial walls become thickened and stiff because of arteriosclerosis. Blood pressure is similarly increased in vasoconstriction-when the tiny arteries (arterioles) are temporarily constricted as a result of stimulation by nerves or by hormones in the blood. A third way in, which the pressure in the arteries can be increased, is for more fluid to be added to the system. This happens when the kidneys malfunction and aren't able to remove enough salt and water form the body. The volume of blood in the body increases, so the blood pressure increases.[9]

Conversely, if the heart's pumping activity diminishes, it the arteries are dilated, or if fluid is removed form the system, the pressure falls. Adjustments of these factors are governed by changes in kidney function and in the autonomic nervous system.[10]

The sympathetic nervous system temporarily increases blood pressure during the fight-or-flight response (the body's physical reaction to a threat). The sympathetic nervous system increases both the speed and force of the heartbeats. It also narrows most arterioles, but expands those in certain areas, such as in skeletal muscle where an increased blood supply is needed. In addition, the sympathetic nervous system decreases the kidneys excretion of salt and water, thereby increasing the body's blood volume. The sympathetic nervous system also releases the hormones epinephrine (adrenaline) and norepinephrine (noradrenaline), which stimulate the heart and blood vessels.[11]

The kidneys control blood pressure in several ways. If blood pressure rises, they increase their excretion of salt and water, which lowers blood volume and brings the blood pressure back down to normal. Conversely, if blood pressure falls, the kidneys decrease their excretion of salt and water, so that blood volume increases and blood pressure returns to normal. The kidneys also can increase blood pressure by secreting an enzyme called rennin, which triggers the production of a hormone called angiotensin, which in turn triggers the release of a hormone called aldosterone.

Because the kidneys are important in controlling blood pressure, many kidney diseases and abnormalities can cause high blood pressure. For example, a narrowing of the artery supplying one of the kidneys (renal artery stenosis) can cause hypertension. Kidney inflammation

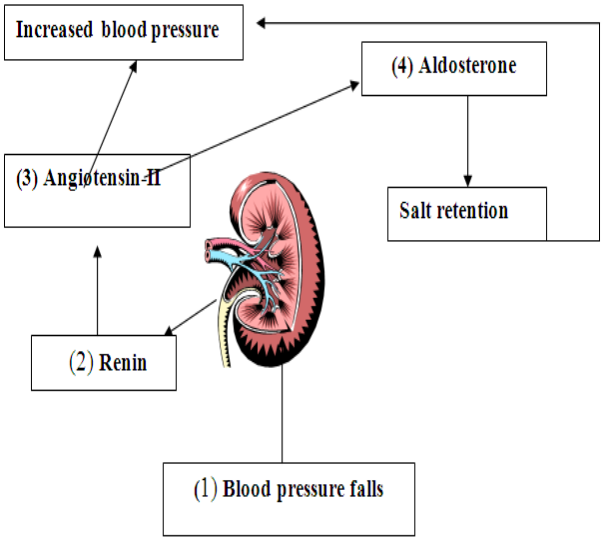
of various types and injury to one or both kidneys can also cause blood pressure to rise.

Whenever a change causes an increase in blood pressure, a compensatory mechanism is triggered to counteract it and keep the pressure at normal levels. So an increase in the volume of blood pumped out by the heart, which tends to increases blood pressure, causes the blood vessels to dilate and the kidneys to increase their excretion of salt and water, which tends to reduce blood pressure. However, the presence of arteriosclerosis makes arteries stiff and prevents the dilation that would otherwise lower blood pressure back to normal. Arteriosclerotic changes in the kidneys can impair the kidney's ability to excrete salt and water, which tends to increase blood pressure.[12]

1.4 Regulating Blood Pressure

The Renin-Angiotensin-Aldosterone System

A fall in blood pressure (1) causes the release of rennin-a kidney enzyme. Renin (2) in turn activates angiotensin-II (3), a hormone that causes the muscular walls of the small arteries (arterioles) to constrict, increasing blood pressure. Angiotensin-II also triggers the release of the hormone aldosterone from the adrenal gland (4), which causes the kidneys to retain salt (sodium) and excrete potassium. The sodium retains water, thus expanding the blood volume and increasing blood pressure.[13]



1.5 Types of hypertension

Hypertension is categorized according to etiology of the disease into[13]:

A) *Essential Hypertension*, and

B) Secondary hypertension.

1.5.1 Essential Hypertension

The type of arterial hypertension with no definable cause is said to be primary, essential, or idiopathic hypertension. It constitutes 90% of hypertension cases. The primary difficulty in uncovering the mechanism (s) responsible for the hypertension in these patients is attributable to the variety of systems that are involved in regulation of arterial pressure-peripheral and/or central adrenergic, renal, hormonal, and vascular and to complexity of the relationships of these systems to one another. In most cases, elevated blood pressure is associated with an overall increase in resistance to flow of blood through arterioles, while cardiac output is usually normal.[14]

Generally, essential hypertension has a multi factorial, etiology in which some factors are recognized such as:
Genetic factors, environment, humoral mechanisms insulin resistance, fetal factors, salt sensitivity and sodium ion vs. chloride or calcium.[15]

1. Genetic factors

Blood pressure levels tend to correlate within a family and adoption studies have confirmed that this must be partly due to genetic factors but the genes that contribute to essential hypertension have not yet been identified.[16]

2. Fetal factors

Studies have shown a relationship between lower birth weight and subsequent higher blood pressure due to fetal adaptation to intrauterine under nutrition with long-term changes in blood vessel structure or in the function of hormonal system.

3. Environmental factors

A number of environmental factors have been specifically implicated in the development of hypertension, including salt intake, obesity, occupation, alcohol intake, family size, stress, and crowding.[17]

4. Insulin resistance

An association between diabetes and hypertension has been recognized, but more recently hyperinsulinaemia, glucose intolerance, reduced levels of HDL cholesterol, hypertriglyceridemia and central obesity (all are related to insulin resistance) have been described to be associated with hypertension. This association is called the "metabolic syndrome" or "syndrome X". However, it is difficult to define the mechanism linking insulin resistance with hypertension.[18]

5. Humoral mechanisms

The autonomic nervous system, as well as the renin angiotensin, natriuretic peptide and kallikrein-kinin system, plays a role in the blood pressure regulation and has been implicated in the pathogenesis of essential hypertension. However, there is no evidence that any of these systems is directly involved.[19]

Classes of Primary Hypertension

Primary Hypertension is classified into 2 subclasses, which are:

a. Benign essential hypertension, which occurs above the age 40 yrs. It is characterized by a slowly progressive rise in the blood pressure and a long course for 30 years or more.

b. Malignant essential hypertension which affects mainly young adults and it is characterized by a rapid progressive rise in the blood pressure and a short fatal course without effective treatment, there is one yr.; survival of less than 20%. In this type, the diastolic pressure is > 130 mm Hg or >140 mm Hg. Hypertensive encephalopathy is the clinical condition of fluctuating neurological signs in association with very high blood pressure and usually, advanced retinal changes.[20]

1.5.2 Secondary Hypertension

This type is present in a small minority of patients with an elevated arterial pressure caused by a specific identified cause. These patients should be cured for the reason that with correction of the cause, their hypertension can be cured. Nearly, all the secondary forms are related to an alteration in hormone secretion (such as adrenocortical dysfunction (Cohn's syndrome, adrenal hyperplasia, Cushing's syndrome, pheochromocytoma, hyperparathyroidism, acromegaly, diabetes mellitus and thyrotoxicosis) and /or renal function (may be nephrogenic which is characterized by increase in volume of circulating blood or peripheral vascular resistance, or renovascular which results from a narrowing of the renal artery in atherosclerosis). Also secondary hypertension can be caused by cardiovascular causes such as coarctation of the aorta and drugs e.g. oral contraceptives, other steroids, carbenoxolone, vasopressin, and monoamine oxidase inhibitors taken concomitantly with tyramine-containing foods. Hypertension may develop during pregnancy, which usually resolves after delivery. Pre-eclampsia is a syndrome consisting of pregnancy included hypertension which is associated with hepatic, neurologic, hematologic, or renal involvement.[21],[22],[23]

1.6 Signs & Symptoms

In most people, high blood pressure causes no specific symptoms referable to their blood pressure except in extremes or after related cardiovascular complications develop. Headache can be seen especially with higher blood pressure, which is often present on awaking and occipital in nature. Other symptoms are widely, but erroneously, believed to be associated with high blood pressure: nosebleeds, dizziness, flushed face, palpitations, impotence and tiredness. Although people with high blood pressure may have these symptoms, they occur just as frequently in those with normal blood pressure. If a person has high blood pressure that is severe or long standing and untreated, symptoms such as headache, fatigue, nausea, vomiting, shortness of breath, restlessness and blurred vision occur because of damage to the brain, eyes, heart and kidneys. Occasionally, people with severe high blood pressure develop drowsiness and even coma caused by brain swelling. This condition, called hypertensive encephalopathy, requires emergency treatment.

Examples of symptoms related to underlying disease in secondary hypertension are polyuria, polydipsia and muscle weakness secondary to hypokalemia in patients with primary aldosteronism or weight gain and emotional liability in patients with Cushing's syndrome. The patient with a pheochromocytoma may present with episodic headaches, palpitations, diaphoresis and postural dizziness.[24]

1.7 Causes of Hypertension

1) Over 90% of hypertension has no identified cause. These can be labeled essential or primary hypertension.[25]

2) Secondary causes of hypertension include six areas; Renal parenchymal, Endocrine, Vascular, Chemical, Neurogenic and others discussed next.[26]

a) Renal parenchymal

- Glomerulonephritis.
- Pyelonephritis.
- Polycystic kidneys (usually inherited).
- Kidney tumor.
- Injury to the kidney.
- Radiation therapy affecting the kidney.

b) Endocrine

- Primary hyperaldosteronism.
- Pheochromocytoma.
- Hyperthyroidism.
- Cushing's syndrome.
- Acromegaly.
- Diabetes mellitus.
- Hyperparathyroidism.

c) Vascular

- Coarctation.
- Renal artery stenosis.
- Polyarteritis nodosa.
- Aortic insufficiency.

d) Chemical

- Oral contraceptives.
- NSAIDs.
- Decongestants.
- Antidepressants.
- Sympathomimetics.
- Many industrial chemicals.
- Corticosteroids.
- Ergotamine alkaloids.
- Lithium.
- Cyclosporine.
- Erythropoietin.
- Cocaine.
- Alcohol abuse.
- Licorice (excessive amounts).

e) Neurogenic

- Brain tumor.
- Cerebral hemorrhage.
- Encephalitis.
- Meningitis.
- After cerebral accidents.

f) Other Causes
- Pregnancy complicated by pre-eclampsia.
- Acute intermittent porphyria.
- Acute lead poisoning.

1.8 Risk factors
- Family history.
- Obesity.
- Alcohol.
- Excess dietary sodium.
- Stress.
- Physical inactivity.
- Psycho emotional stress.
- Personality character.
- Type of occupation.
- Excessive intake of stimulants (e.g., coffee).
- Fatty foods.[27]

1.9 Pathology of hypertension

Hypertension is a disease largely of vasculature. The pathogenesis of hypertension is likely due, in part, to functional and perhaps structural changes in blood vessels. Moreover, the primary consequences of hypertension consist of pathological vascular changes, including accelerated atherosclerosis and hyaline and hyperpalstic arteriolosclerosis as well as arteriolitis in some cases of severe hypertension.[28]

1.9.1 Vascular Pathology in Hypertension

Hypertension accelerates atherogenesis and causes changes in the structure of the walls of blood vessels that potentiate both aortic dissection and cerebrovascular hemorrhage. In addition, hypertension is associated with two forms of small blood vessel disease: hyaline arteriolosclerosis and hyperplastic arteriolosclerosis. Both lesions are clearly related to elevations of blood pressure, but other causes may also be involved.[29],[30]

a) In Benign hypertension

Hyaline arteriolosclerosis: This condition is encountered frequently in elderly patients, whether normotensive or hypertensive, but it is more generalized and more severe in patients with hypertension. The condition is also seen commonly in diabetes and forms part of the microangiography characteristic of diabetic disease, the vascular lesion consists of a homogeneous, pink, hyaline thickening of the walls of arterioles with loss of underlying structural detail and with narrowing of the lumen and loss of elasticity.

It is believed that the lesions reflect leakage of plasma components across vascular endothelium and increasing extracellular matrix production by smooth muscle cell. Presumably, the chronic hemodynamic stress of hypertension or a metabolic stress in diabetes accentuates endothelial injury, thus resulting in leakage and hyaline deposition. The narrowing of the arteriolar lumina causes impairment of the blood supply to affected organs, particularly well exemplified in the kidneys. Thus *hyaline arteriolosclerosis is major morphologic characteristic of benign nephrosclerosis*, in which the arteriolar narrowing causes diffuse renal ischemia and symmetric contraction of the kidney.[31]

b) In malignant hypertension

Hyaline arteriolosclerosis and arteriolar elastosis, which are more, marked than in benign hypertension.

Hyperplastic arteriolosclerosis

The hyperplastic type of arteriolosclerosis is generally related to more acute of severe elevations of blood pressure and is therefore characteristic of malignant hypertension (diastolic pressures usually over 110-120 mm Hg). This form of arteriolar disease can be identified with the light microscope by virtue of its onionskin, concentric, laminated thickening of the walls of arterioles with progressive narrowing of the lumina. With the electron microscope, these reduplicated cells have the appearance of smooth muscle cells. The basement membrane is likewise thickened and reduplicated. Frequently, but not invariably, these hyperplastic changes are accompanied by deposits of fibrinoid and acute necrosis of the vessel walls, referred to as *necrotizing arteriolitis*. The arterioles in all tissues throughout the body may be affected, favored sites being the kidney, periadrenal fat, gallbladder and peripancreatic and intestinal arterioles.[32]

1.9.2 Kidney pathology in hypertension

a) Kidney lesion (benign nephroscelrosis) in benign hypertension

Benign nephrosclerosis occurs as a result of sclerosis of renal arterioles and small arteries. The resultant effect is focal ischemia of parenchyma supplied by the thickened narrowed vessels.

In morphological gross appearance, the kidneys are either normal in size or moderately reduced. The cortical surface has a fine granular and shows small retention cysts. Arterioles are thick walled and have narrow lumen.

On histological examination, arterioles and small arteries are thickened and hyalinized (hyaline arteriolosclerosis). Consequent to the hyaline vascular narrowing, there is patchy ischemic atrophy, which consists of (1) foci of tubular atrophy and interstitial fibrosis and (2) a variety of glomerular alterations. The later include collapse of glomerular basement membranes, deposition of collagen within Bowman's space, periglomerular fibrosis and total sclerosis of glomeruli.

In addition to arteriolar hyalinization, the larger interlobular and arcuate arteries exhibit a characteristic lesion that consist of reduplication of the elastic lamina and increased fibrous tissue in the media, with consequent narrowing of the lumen. This change, called *fibroelastic hyperplasia*, often accompanies hyaline arteriolosclerosis and increases in severity with age and in the presence of hypertension.[33]

b) Kidney lesion (malignant nephrosclerosis) in malignant hypertension

Malignant nephrosclerosis is the form of renal disease associated with the malignant or accelerated phase of hypertension. Grossly, the kidney size is dependent on the duration and severity of the hypertensive disease. Small, pinpoint petechial hemorrhages may appear on the cortical surface from rupture of arterioles or glomerular capillaries.

Blood vessels are prominent, thick and narrow. Microscopically, two histologic alterations characterize blood vessels in malignant hypertension:

1. *Fibrinoid necrosis of arterioles*: This appears as an eosinophilic granular change in the blood vessels wall. In addition, there is often an inflammatory infiltrate within the wall, giving rise to *necrotizing arteriolitis***.**
2. In the interlobular arteries and arterioles there is intimal thickening caused by a proliferation of elongated, concentrically arranged cells, smooth muscle cells, together with fine concentric layering of collagen. This alteration is known as *hyperplastic arteriolitis*, also referred to as *"onion-skinning***"**. The lesion correlates well with renal failure in malignant hypertension. Sometimes the glomeruli become necrotic and infiltrated with neutrophils and the glomerular capillaries may thrombose (*necrotizing glomerulitis*). The arteriolar and arterial lesions result in considerable narrowing of all vascular lumina, with ischemic atrophy and infarction distal to the abnormal vessels.[33]

1.9.3 Cardiac lesions in hypertension

a) Cardiac lesions (hypertensive cardiomyopathy) in benign hypertension

Hypertensive heart disease is the response of the heart to the increased demands induced by systemic hypertension. One of the criteria for the diagnosis of systemic (left-sided) hypertensive disease is the presence of left ventricular hypertensive hypertrophy (usually concentric) in the absence of other cardiovascular pathology that might have induced it. It was established that even mild hypertension (levels only slightly above 140/90 mm Hg), if sufficiently prolonged, induces left ventricular hypertrophy, which can lead to myocardial dysfunction, cardiac dilation, congestive heart failure and sudden death. In gross picture, the heart in compensated stage of the disease is characterized by left ventricular hypertrophy without dilation of the left ventricle because systemic hypertension induces left ventricular pressure overload. The thickening of left ventricular wall is present and may exceed 2.0 cm and the heart is enlarged. The increased thickness of the left ventricular wall imparts stiffness that impairs diastolic filling. This often induces left atrial enlargement.

Microscopically the earliest change is an increase in transverse myocyte diameters. At more advanced stage, the cellular and nuclear enlargement becomes somewhat more prominent and irregular, with variation in cell size among adjacent cells and interstitial fibrosis. The biochemical, molecular and morphological changes that occur in hypertensive hypertrophy are similar to those noted in other conditions of myocardial overload.[34]

b) Cardiac lesion in malignant hypertension

Slight hypertrophy of the left ventricle is seen with malignant hypertension.[35]

1.9.4 Retinal changes in primary hypertension

Hypertensive and hypertension induced arteriolosclerotic changes in the retinal vessels provide useful prognostic clues to the physician. Retinal changes in hypertension are characterized by arteriolosclerosis of retinal arterioles resulting in narrowing and decrease in diameter of retinal vessels. In acute severe hypertension, at the onset of malignant hypertension, these initially appear as focal spasm. In chronic hypertension, the narrowing is more diffuse. Histologically, they manifest a hyaline or onion-skin thickening of the arteriolar walls. The hypertensive retinopathy is categorized as follows: -[36]

1. **Grade I**: Generalized narrowing of the arterioles.
2. **Grade II**: grade I changes and focal arteriolar spasms.
3. **Grade III**: grade II changes, flame shaped hemorrhages, dot-and blot hemorrhage, cotton-wool spots, and hard waxy exudates.
4. **Grade IV**: all grade III changes plus optic disc edema.

Histologically, flame-shaped hemorrhages seen with hypertension are extravasated erythrocytes within the retinal nerve fiber layer. Their typical shape results from the confinement of the red blood cells within spaces between the nerve fibers, which run in parallel fashion.

Dot-and blot hemorrhages are seen in inner nuclear layer with spreading to the outer plexiform layer. Cotton-wool spots are microinfarctions of the nerve fiber layer. Hard and waxy exudates are composed of extravasated lipophilic material located in the outer plexiform layer.[37]

1.9.5 Cerebral lesions in hypertension

Hypertension gives rise to rupture of the small cerebral hemorrhages, which resorb, leaving a slit-like cavity surrounded by brownish discoloration (slit hemorrhages). On microscopic examination, slit hemorrhages show focal tissue destruction, pigment-laden macrophages and gliosis.[38]

In addition, petechiae and fibrinoid necrosis of arterioles in gray and white matter may be seen microscopically in patients with hypertensive encephalopathy.

Vascular (multi-infarct) dementia, a syndrome characterized by dementia, gait abnormalities and focal neurological defect, is caused by multifocal vascular disease, consisting largely of cerebral atherosclerosis,

vessel thrombosis or emobilization from carotid vessels or from the heart, or cerebral arteriolar sclerosis resulting in multiple, bilateral, gray matter (cortex, thalamus, basal ganglia) and white matter infarcts.[39]

1.10 Management of hypertensive patients

Management of patients should be considered in 3 stages[40]:

1. **Assessment**
2. **Non-pharmacological treatment**
3. **Drug treatment**

1.10.1 Assessment of patients

Diagnosis is conducted by measuring blood pressure after the person sits or lies for 5 minutes. A reading of 140/90 mm Hg or more is considered high, but a diagnosis of hypertension is based on repeated reproducible measurements of elevated blood pressure. If a person has an initial high reading, the blood pressure is measured again and then measured twice on at least 2 other days to make sure that the high pressure persists. The readings not only determine the presence of high pressure but also are used to classify its severity. Following table shows categories of hypertension according to blood pressure readings.

Table 2: Categories of Hypertension according to blood pressure readings.

Category	Systolic Blood Pressure	Diastolic Blood Pressure
Normal blood pressure	Below 130 mm Hg	Below 85 mm Hg
High normal blood pressure	130-139	85-89
Stage 1 (mild) hypertension	140-159	90-99
Stage 2 (moderate) hypertension	160-179	100-109
Stage 3 (severe) hypertension	180-209	110-119
Stage 4 (very severe) hypertension	210 or higher	120 or higher

When arterial pressure fluctuates which occurs in most persons, whether they are normotensive or hypertensive. Those who are classified as having labile hypertension are patients who sometimes, but not always, have arterial pressures within the hypertensive range. These patients are often considered to have borderline hypertension. During the assessment period, secondary causes of hypertension should be excluded. Special tests should be considered only if the history, physical, or basic laboratory evaluation indicates the possibility of reversible secondary hypertension.[41]

1. History

Patients with mild hypertension are usually asymptomatic. Certain features in the history might suggest secondary hypertension such as repeated urinary tract infections suggest chronic pyelonephritis, although this condition may occur in the absence of symptoms.[42] A history of nocturia and polydipsia suggests renal or endocrine diseases, while trauma to either flank or an episode of acute flank pain may be due to the presence of renal injury. A history of weight gain is compatible with Cushing's syndrome, and weight loss and attacks of sweating and palpitations with pheochromocytoma. A number of aspects of history aid in determining whether vascular disease has progressed to dangerous stages, which include angina pectoris, cerebrovascular insufficiency, congestive heart failure and /or peripheral vascular insufficiency.

Breathlessness may be present owing to left ventricular hypertrophy or cardiac failure, whilst angina or peripheral claudication may represent atheromatous disease. Higher levels of blood pressure may be associated with headaches, epitaxis or nocturia.

Sustained hypertension can become accelerated or enter a malignant phase, although this is unusual in treated complying patients. Though a patient with a malignant hypertension often has a blood pressure above 200/140, it is papilledema, usually accompanied by retinal hemorrhages and exudates and not the absolute pressure level that defines this condition. Malignant hypertension may also present with severe headaches, visual disturbances, fits and transient loss of consciousness or symptoms of heart failure.[43]

The history of use of adrenal steroids, estrogen or other medications is of obvious significance. A Strong family history of hypertension, along with reported findings in the past, favors the diagnosis of essential hypertension. Other risk factors that should be elicited include cigarette smoking, diabetes mellitus, lipid disorders and family history of early deaths due to cardiovascular disease. Finally, aspects of patient's lifestyle, which could contribute to the hypertension or affect its treatment, should be assessed, including diet, physical activity, family status, work and educational level.[44]

2. Examination

The elevated blood pressure is usually the only abnormal sign. Signs of an underlying cause should be sought, such as renal artery bruit in renovascular hypertension, or radio-femoral delay in coarctation of the aorta. The cardiac examination detected by ECG and chest X-rays

may also reveal features of left ventricular hypertrophy and a loud aortic second sound. If cardiac failure develops, there may be a sinus tachycardia and a third heart sound.

An abnormal heart, called the fourth heart sound is one of the earliest heart changes caused by high blood pressure. In early stages, heart changes are best detected by echocardiography (a test that uses ultrasound waves to create an image of the heart).[45]

Fundoscopy is an essential part of the examination for any hypertensive patient, because the changes in retina are similar to changes in blood vessels else where in the body and fundoscopic findings provide one of the best indications of the duration of hypertension and of prognosis, hence a doctor can classify the seriousness of the high blood pressure. The abnormalities are graded according to the Keith-Wagener classification:

- **Grade 1** – tortuosity of the retinal arteries with increased reflectiveness (silver wiring).
- **Grade 2** – grade 1 plus the appearance of arterovenous nipping produced when thickened retinal arteries pass over the retinal veins.
- **Grade 3** – grade 2 plus flame-shaped haemorrhages and soft ('cotton wool') exudates actually due to small infarcts.
- **Grade 4** – grade 3 plus papilloedema (blurring of the margins of the optic disc).

Grade 3 and 4 are diagnostic for malignant hypertension.

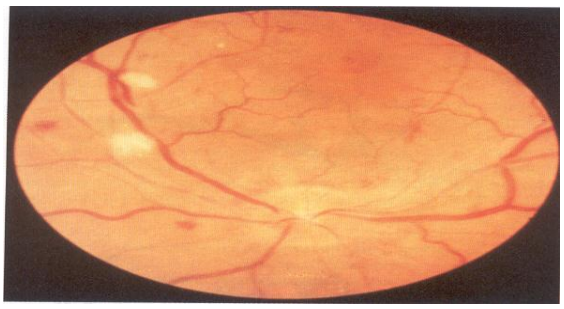


Figure 1: - Fundus showing hypertensive changes (Grade 4 retinopathy with papilloedema, haemorrhage and exudates).

One of the most important parts of abdominal examination is auscultation for bruits originating in stenotic renal arteries. Bruits are present in many patients with renal artery stenosis fibrous dysplasia and arteriosclerosis.[46]

The abdomen also should be palpated for abdominal aneurysm and for the enlarged kidneys of polycystic renal disease. The femoral pulses must be carefully 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. Examination of the extremities for edema and a search for evidence of a previous cerebrovascular accident and/or other intracranial pathology should be performed.

Finally, the patient's height and weight should be recorded.[47]

3. Ambulatory blood pressure monitoring

Indirect automatic blood pressure measurements can be made usually over a 24-hour period using a measuring device worn by the patient. They are used to confirm the diagnosis in those patients with white coat hypertension, those who have a blood pressure increase that is due solely to the presence of a doctor or nurse. These patients do not have any evidence of target organ damage and unnecessary treatment can be avoided.

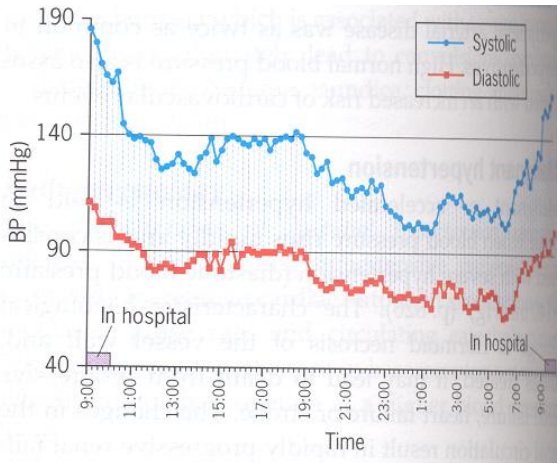


Figure 2: 24 hour ambulatory blood pressure monitoring showing white coat hypertension.

These devices may also be used to monitor the response of patients to drug treatment and, in particular, can be used to determine the adequacy of 24-hour control with once-daily medication.

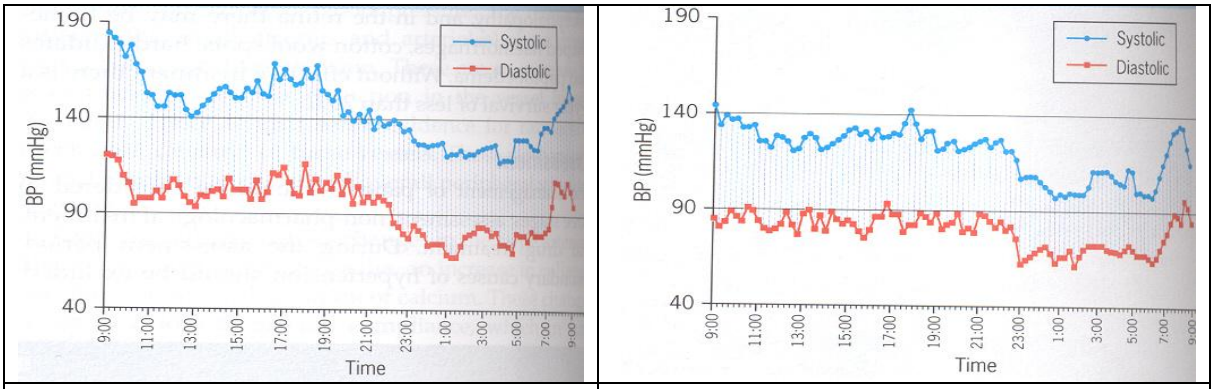


Figure 3: 24-hour ambulatory blood pressure monitoring showing: -
a) Pretreatment.
b) After three months treatment.

Ambulatory blood pressure recordings seem to be better predictors of cardiovascular risk than measurements in a clinic. It is possible to analyse the diurnal variation in blood pressure, and some evidence suggests that those hypertensive with a loss of the usual nocturnal fall in blood pressure ('non-dippers') have a worse prognosis than those who retain this pattern.[48]

4. Investigations

Laboratory studies should be performed extensively in patients presenting with hypertension to evaluate the patients for secondary forms of hypertension or subsets of essential hypertension. Laboratory studies are divided into those that should be performed in all patients with sustained hypertension (basic studies) and those that should be added if (1) form the initial evaluation a secondary form of hypertension is suggested and/or (2) arterial pressure is not controlled after initial therapy (secondary studies).[49]

5. Basic studies

Routine investigation of the hypertensive patient should include:

- Chest X-ray.
- ECG.
- Echocardiogram.

The ECG may show evidence of coronary artery disease of left ventricular hypertrophy, although echocardiography is a far more sensitive method for detection of left ventricular hypertrophy.[45]

The chest X–ray may show cardiomegaly or pulmonary congestion if heart failure is developing. Rib notching on the X-ray may be a sign of coarctation of the aorta and should be investigated further with an MRI (Magnetic Resonance Imaging) scan.

- Urinalysis.
- Serum urea, creatinine and BUN.

Early indications of kidney damage are detected primarily by examining the person's urine. 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 (BUN). If the urea or creatinine is elevated, more specific renal investigations are indicated, creatinine clearance, renal ultrasound and renal isotope scan. Microscopic examination of the urine is also helpful.[50]

Other blood chemistries, which include

- Fasting blood glucose.
- Serum calcium level.
- Serum uric acid level.
- Serum cholesterol (total & HDL) and triacylglycerides.
- Serum potassium level.
- Hemoglobin and hematocrit or CBC.
- WBC count.

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 all may be associated with hyperglycemia. Furthermore, since antihypertensive therapy with diuretics, can raise the blood glucose level, it is important to establish a baseline. The possibility of hypercalcemia also may be investigated. Serum uric acid determination is useful because of the increased incidence of hyperuricemia in patients with renal and essential hypertension and because, the level subsequently may be raised by treatment with diuretics. Serum cholesterol, HDL cholesterol and triglycerides may be measured to identify other factors that predispose to the development of arteriosclerosis.

A serum potassium level is needed both as a screen for mineralocorticoid induced hypertension and as a baseline prior to initiating diuretic therapy.[51]

6. Secondary studies

Certain clues from the history, physical examination, and basic laboratory studies may suggest an unusual cause for the hypertension and dictate the need for special

studies specially in case of abrupt onset of severe hypertension and/or of onset of hypertension of any severity under the age of 25 or after the age of 50 years to exclude renovascular hypertension, pheochromocytoma and other secondary hypertension. Special studies to screen for secondary hypertension are:

a) **Renovascular:** digital subtraction angiogram or rapid sequence IVP (Intravenous Pyelogram).
b) **Pheochromocytoma:** 24-h urine for creatinine, metanephrine/vanillyl mandelic acid and catecholamines or plasma catecholamines.
c) **Cushing's syndrome:** overnight dexamethasone suppression test or 24-h urine cortisol.
d) **Primary aldosteronism:** hypokalemia (diuretics may complicate the picture when K level is to be assessed) and identification of the relation between plasma renin activity and aldosterone level (key to diagnose primary aldosteronism-aldesterone concentration or excretion is high and plasma renin activity is low in primary aldosteronism).[52]

1.10.2 Non-pharmacological Treatment

Unless the patient has severe or malignant hypertension, there should be a period of assessment with repeated blood pressure measurements, combined with advice and non-pharmacological measures prior to the initiation of drug therapy.

All patients should be given advice on non-pharmacological measures that may lead to some reduction in blood pressure levels.

- ***Weight reduction*****: -** A number of trials have confirmed that weight reduction in overweight patients leads to a true fall in blood pressure.

- ***Reduction of heavy alcohol intake:*** - This can lead to a fall in blood pressure of 5-10 mm Hg.

- ***Salt restriction*****: -** Moderate salt restriction has been shown to be of benefit in some patients and seems to enhance the blood pressure lowering effects of some medication, particularly the ACE inhibitors, β-blockers and diuretics. The patient should be advised not to add salt to their food at the table or eat high salt containing foods.

- **Reduction of saturated fat and increase in monounsaturated fat intake**.
- **Potassium and calcium intake**, although absolute effect uncertain.
- ***Regular exercise*****: -** Moderate exercise in the form of jogging or brisk walking produces a beneficial effect on blood pressure that is independent of any reduction in weight.
- ***Biofeedback and behavioral therapy*****: -** There is some evidence for a positive short-term effect of these techniques in hypertensive patients.

The individual's overall cardiovascular risk should be addressed. Patients should be advised to avoid smoking, and hyperlipidaemia treated appropriately.

- **Patient's education**

Asymptomatic nature of hypertension and importance of lifetime treatment should be emphasized. Patient should be aware of drug complications and risk factors for cardiovascular diseases. Patient also should be informed about the importance of restriction to comprehensive preventive programs and he/she can have printed aids for high blood pressure education from some specialized medical centers in some western countries.[53]

1.10.2 Drug Treatment

The decision to commence specific drug therapy should usually be made only after a careful period of assessment, of up to six months, with repeated measurements of blood pressure. The aim of drug treatment to reduce the risk of complication of hypertension should be carefully explained to the patient. All of the drugs used to treat hypertension can be associated with side effects and since the benefits of drug treatment are not immediately apparent to the patient, compliance is a major problem.

Drug treatment should be tailored to the individual and treatment is most effective when patients and doctors communicate well and collaborate on the treatment program.

Different types of drugs reduce blood pressure by different mechanisms. Some doctors use a stepped approach to drug therapy: They start with one type of drug and add others as necessary. Other doctors prefer a sequential approach: They prescribe one drug; if it's ineffective, they discontinue it and prescribe another type of drug. In choosing a drug, a doctor considers such factors as the person's age, sex and race; the severity of the other conditions, such as diabetes or high blood cholesterol levels; the potential side effects, which vary from drug to drug; and the costs of the drugs and of tests needed to monitor their safety.

Most people tolerate their prescribed antihypertensive drugs without problems. But any antihypertensive drug can cause side effects. So if side effects do develop, a person should tell the doctor, who can adjust the dose or switch to another drug.[54]

Different classes of antihypertensive drugs are

a) Thiazide diuretics

- Hydrochlorothiazide
- Cyclopenthiazine
- Bendroflumethiazide
- Polythiazide
- Thiazide analogues: -

- Indapamide
- Chlorthalidone
- Metolazone

b) High ceiling diuretics
- Furosemide
- Bumetanide
- Pirentanide

c) K-sparing diuretics
- Aldosterone antagonist:

Sprironolactone
- Sodium channel blockers:

- Amiloride
- Triamterine

d) β-adrenergic blockers
- Propranolol
- Metoprolol
- Atenolol
- Esmolol
- Labetolol
- Carvidolol

e) α-adrenergic blockers
- Prazocin
- Terazocin
- Dexazocin
- Phenoxybenzylamine (in treatment of pheochomocytoma)

f) ACE inhibitors
- Captopril
- Enalapril
- Lisinopril
- Perindopril
- Ramipril
- Quinapril

g) Angiotensin-II receptor antagonists
- Losartan
- Valsartan
- Irbesartan
- Candesartan
- Telmisartan

h) Calcium channel blockers

1) Phenyl alkylamine:

Verapamil

2) Benzothiazepine:

Diltiazem

3) Dihydropyridine:

- Nifedipine
- Amlodipine
- Felodipine
- Nicardipine
- Nisoldipine
- Isradipine
- Nimodipine

i) Central sympatholytics
- Clonidine
- Methyldopa

j) Vasodilators

1) Arteriolar:

- Hydralazine
- Minoxidil
- Diazoxide

2) Arteriolar and venous:

- Sodium nitroprusside.

Thiazide diuretic is commonly the first drug given to treat high blood pressure. Diuretics help the kidneys eliminate salt and water, which decreases fluid volume throughout the body, thus lowering blood vessels to dilate. Because diuretics cause a loss of potassium in the urine, potassium supplements or potassium-retaining drugs sometimes must be taken along with the diuretics. Diuretics are particularly useful in blacks, the elderly, obese people and people with heart failure or chronic kidney failure.[55]

Adrenergic blockers block the effects of the sympathetic nervous system, the system that may rapidly respond to stress by raising blood pressure. The most commonly used adrenergic blockers, the beta-blockers are particularly useful in whites, young people and people who have had a heart attack or who have rapid heart rates, angina pectoris, or migraine headaches.

Angiotensin converting enzyme inhibitors lower blood pressure by dilating arteries. They are particularly useful in whites, young people, people with heart failure, and people with protein in their urine because of chronic kidney disease or diabetic kidney disease and men who are impotent as a side effect of taking another drug.[55]

Angiotensin-II blockers lower blood pressure by a mechanism similar to but more direct than the one used by angiotensin converting enzyme inhibitors. Because of the way they work, angiotensin II blockers appear to cause fewer side effects.

Calcium antagonists cause blood vessels to dilate by a completely different mechanism. They are particularly useful in blacks, the elderly, and people with angina pectoris, certain types of rapid heart rates, or migraine headaches. Recent reports suggest that people using short acting calcium antagonists may have an increased risk of death from heart attacks, but there are no reports suggesting such effects for long acting calcium antagonists.

Direct vasodilators dilate blood vessels by yet another mechanism. A drug of this class is almost never used alone; rather, it's added a second drug when another drug alone doesn't lower blood pressure sufficiently.[56]

Table 3: Advantages and disadvantages of drugs used in hypertension with respect to associated conditions.[57]

	Diuretic	B-Blocker	ACE inhibotor/Angiotensin II receptor antagonist	Ca-Channel blockers	α-Blocker
Diabetes	Care[a]	Care[a]	Yes	Yes	Yes
Gout	No	Yes	Yes	Yes	Yes
Dyslipidaemia	Care[b]	Care[b]	Yes	Yes	Yes
Ischaemic heart disease	Yes	Yes	Yes	Yes	Yes
Heart failure	Yes	Care[c]	Yes	Care[d]	Yes
Asthma	Yes	No	Yes	Yes	Yes
Peripheral vascular disease	Yes	Care	Care[e]	Yes	Yes
Renal artery stenosis	Yes	Care	No	Yes	Yes
Pregnancy	Caution	Not in late pregnancy	No	No	Caution

[a]Diuretics may aggravate diabetes: β-blockers worsen glucose intolerance and mask symptoms of hypoglycaemia.
[b]Both diuretics and β-blockers disturb the lipid profile.
[c]There is some evidence for beneficial effects of some β-blockers when used cautiously in heart failure.
[d]Verapamil and diltiazem may exacerbate heart failure, although amlodipine appears to be safe.
[e]Patients with peripheral vascular disease may also have renal artery stenosis, therefore ACE inhibitors should be used cautiously.

1.11 Management of hypertension in pregnancy

Many antihypertensive agents are contraindicated in pregnancy. Mild hypertension can be treated with methyldopa or labetolol. Pre-eclamptic hypertension can be treated with the same agents, or nifedipine, although the only method for reversal of overt pre-eclampsia is delivery. More severe hypertension or elcampsia requires treatment with intravenous hydralazine and may require termination of the pregnancy.[58]

1.12 Treatment of Secondary Hypertension

Treatment of secondary hypertension depends on the underlying cause of the high blood pressure. Treating kidney disease can sometimes normalize the blood pressure or at least lower it, so that drug therapy is more effective. A narrowed artery to the kidney may be dilated by inserting a balloon-tipped catheter and inflating the balloon. Or the narrowed part of the artery supplying the kidney can be bypassed; often such surgery cures the high blood pressure. Tumours that cause high blood pressure, such pheochromocytoma, usually can be removed surgically.[59]

1.13 Hypertensive Crisis

Hypertension affects move than 50-60 million Americans. With adequate control, fewer than 1% of patients experience a hypertensive crisis. Hypertensive crisis is a condition characterized by severe progressive functional impairment of the kidneys, eyes, heart and brain of patients with a sustained or sudden rise in systolic blood pressure, usually to levels greater than 220 mm Hg and diastolic blood pressure to level greater than 120 mm Hg. Crisis is seen most often in the 40-60 year age group in the setting of known hypertension of 2-10 years' duration. The most common associated diseases are essential hypertension, chronic pyelonephritis and glomerulonephritis. Other associated diseases include polyarteritis nodosa, systemic lupus erythematosis, toxemia of pregnancy, postirradiation of the renal area, congenitally small kidneys, hydronephrosis, nephrocalcinosis (the presence of calcium deposits in the kidneys), tuberculosis of the kidney, hyperadrenalcorticism, pheochromocytoma, primary aldosteronism, renin secreting tumor of the kidney and ingestion of ephedrine, amphetamines, or foods rich in tyramine by patients being treated with MAO inhibitors.[60]

1.13.1 Classification of Hypertensive Crisis

Hypertensive crisis is classified as hypertensive emergency or hypertensive urgency. Acute or ongoing vital organ damage, such as damage to the drain (encephalopathy), kidney (renal failure, hematuria), eye (retinal hemorrhage), or heart (congestive heart failure), in the setting of severe hypertension is considered a hypertensive emergency. It requires a prompt reduction in blood pressure within minutes or hours. The absence of target organ damage in the presence of severe elevation of blood pressure with systolic blood pressure greater than 220 mm Hg and diastolic blood pressure frequently more than 120 mm Hg is considered hypertensive urgency, and it requires reduction in blood pressure within 24-48 hours or over several days to weeks. It is usually not based on the absolute level of BP because individual with chronic hypertension may tolerate BP exceeding 200/120. Such patients tolerate the increased BP without immediate adverse effects. This is because of an upward shift in autoregulation of cerebral, renal and vascular bed. Severe hypertension should be distinguished from hypertensive crisis in the sense that it is elevated BP (diastolic BP $\geq$ 115 mm Hg) not yet leading to significant organ damage and does not necessarily require treatment during Emergency Department visit but does require close follow up with a primary care physician for long term BP control. In this case, beginning antihypertensive therapy in the emergency department may be appropriate and should be done in consultation with the patient's primary care physician, who is caring for the patient after the emergency department visit.[61]

1.13.2 Causes of Hypertensive Crisis

The most common hypertensive emergency is a rapid unexplained rise in BP in a patient with chronic essential hypertension and in patient whose hypertension is severe and poorly controlled.[61] *Other causes are*: -

- Renovascular hypertension.
- Eclampsia, pre-eclampsia.
- Acute glomerulonephritis.
- Pheochromocytoma.
- Abrupt Antihypertensive withdrawal syndromes like β-blockers and especially with clonidine.
- Head injuries and CNS trauma.
- Renin secreting tumors.
- Drug induced hypertension: including SSRIs, decongestants, appetite suppressants, steroids (including oral contraceptives), MAO inhibitors in combination with certain foods or drugs of abuse such as cocaine or amphetamine.
- Severe Burns.
- Vasculitis.
- Thrombotic thrombocytopenic purpura: a condition of skin rash resulting from bleeding into skin from small blood vessels. This may be due to a deficiency of blood platelets.
- Idiopathic hypertension.
- Postoperative hypertension: in 70% patients undergoing neurological, vascular and cardiac surgery.
- Coarctation of aorta.
- Withdrawal of CNS depressants.
- Diabetic nephropathy.

1.13.3 Risk factors

- History of hypertension.
- Drug abuse.
- Non-compliance with medications.
- Age: Hypertension emergencies occur most commonly in middle-aged patients. The peak incidence occurs in those aged 40-50 years.
- Increasing creatinine levels.
- If serum urea is 10 mmol/L or more.
- If there is presence of grade II-IV hypertensive retiopathy.
- Race: African Americans have a higher incidence of hypertensive emergencies than caucasians.
- Sex: Males are at great risk of hypertensive emergency than females.[62]

1.13.4 Prognosis

- The 1-year mortality rate is higher than 90% for patients with untreated hypertensive emergencies.
- Aggressive therapy is essential to save 60-75 % of such cases.
- Median survival duration is 144 months for all patients presenting to the Emergency Department (ED) with a hypertensive emergency.
- Five-year survival rate among all patients presenting with hypertensive crisis is 74%.[62]

1.13.5 Complications

- Congestive heart failure (C.H.F.).
- Myocardial infarction (M.I.).
- Renal failure.
- Retinopathy.
- Carebrovascular accident.
- Abrupt lowering of the BP may result in inadequate cerebral or cardiac blood flow, leading to stoke or myocardial ischemia.[63]

1.13.6 Causes of death

- Uremia.
- C.H.F.
- C.H.F. and uremia.
- Cerebrovascular accident.
- M.I.
- Aortic dissection.[64]

1.13.7 Pathophysiology

Hypertensive emergencies include hypertension associated with vascular damage (termed malignant hypertension) and hypertension associated with hemodynamic complications such as cardiac failure, stroke, or dissecting aneurysm. The major organ systems affected by high BP are the CNS, cardiovascular system, and renal system. Also eye changes occur in hypertensive emergencies.[65]

1. Central nervous system

The CNS is affected as the elevated BP overwhelms the normal cerebral autoregulation. Under normal circumstances, with an increase in BP, cerebral arterioles vasoconstriction and cerebral blood flow remains constant. During a hypertensive emergency, the elevated BP overwhelms arteriolar control over vasoconstriction and autoregulation of cerebral blood flow. This results in transudate leak across capillaries causing focal or generalized cerebral edema, multiple small thrombi in the brain and continued arteriolar damage. Subsequent fibrinoid necrosis causes normal autoregulatory mechanisms to fail, leading to clinically apparent papilloedema, the *sine qua non* of malignant hypertension. The end result of loss of autoregulations is hypertensive encephalopathy.[66]

2. Cardiovascular system

The cardiovascular system is affected as increased cardiac workload leads to cardiac failure; this is accompanied by pulmonary edema, myocardial ischemia, or myocardial infraction. There is a progressive arteriopathy with inflammation and necrosis of arterioles.[67]

3. Renal system

Some degree of renal failure is invariably present and may dominate the clinical picture in hypertensive crisis. The renal system is impaired when high BP leads to arteriosclerosis, fibrinoid necrosis, endarteritis of preglomerular arterioles and interlobular arteries of the kidney and an overall impairment of renal protective

autoregulation mechanisms. These result in ischemia and necrosis of glomeruli and renal failure which may be manifested as worsening renal function, hematuria, red blood cell (RBC) cast formation, and/or proteinuria. Vascular lesions occur in the kidney, which release renin, which in turn stimulates production of angiotensin and aldosterone, which further increases BP.

It is clear that these patients benefit from having their diastolic blood pressure lowered to the 90 to 100 mm Hg range. The reduction in blood pressure benefits the ischemic kidney and often results in a significant return of function, although a general worsening of renal function is often seen with the initial lowering of the blood pressure. Renal function, however, will in most patients improve in subsequent weeks and months.[68]

4. Ocular system

Early ocular changes may include soft exudates, hemorrhage and/or papilledema (present if disease process has progressed slowly). Papilledema is usually accompanied by a neuroretinitis, but can be seen alone. It should be noted, however, that the eye changes may continue to progress for a week or more after adequate BP control has been achieved. The underlying pathology is that fibroid necrosis of the arterioles with plasma leakage into surrounding areas, resulting in "cotton wool" exudates and flame shaped hemorrhages from capillary rupture. The papilledema arises from focal or generalized cerebral edema.[66]

1.13.8 Clinical presentation

Renal, eye, or central nervous system changes may dominate the clinical picture, but changes in all three are usually seen during the course of the illness.[69]

a) CNS manifestations

- Severe headaches (85%): Mild headache alone in association with elevated BP does not indicate a hypertensive crisis.
- Confusion and mental status changes.

Hypertensive encephalopathy may be sudden or gradual in onset and its clinical presentation consists of severe headache, mental confusion, and apprehension. If untreated, the syndrome may progress over a period of 12-48 hrs. to convulsions (seizures), stupor, coma and even death.

Hypertensive encephalopathy can be seen in some patients with toxemia of pregnancy and in children and adolescents with acute nephritis when blood pressures are around 140/90 mm Hg, since for these age groups such a reading may represent a 30 to 50 mm Hg rise diastolic pressure.[70]

- New-onset blurred vision (60%).
- Weight loss (75%).
- Nausea and vomiting.
- Weakness and fatigue (30%).
- Focal neurology deficits.

b) Cardiovascular manifestations

- Symptoms of congestive heart failure (C.H.F.).
- Angina (chest pain).
- Hypertension: Blood pressure levels are usually sustained but may show wide fluctuations. As isolated diastolic blood pressure reading of less or greater than 120 mm Hg neither excludes nor confirms the diagnosis and must always be interpreted in the light of the presenting history and physical findings.[71]

c) Renal manifestations

- History of hematuria (50% have haemorrhage).
- Oliguria.
- Elevated serum creatinine.
- Proteinuria.
- Progressive uremia: accounts for 30-60% of deaths in malignant hypertension.

All indicate high renal pressure or acute renal failure, which can represent hypertensive crisis as acute oliguric renal failure with or without associated encephalopathy.[72]

d) Ocular manifestations

- Visual disturbances that indicate retinopathy.
- Blurred vision.
- Loss of eye sight.

Varying degrees of blindness are present and usually resolve with appropriate therapy. Blindness is the result of neuroretinitis and/or severe obliterative arterial spasm.[73]

e) Other manifestations

- Abdominal pain.
- Shortness of breath, dyspnea and orthopnea.
- Pulmonary edema.
- Hemorrhage.
- Thrombosis.
- Embolus.
- Microangiopathic hemolytic anemia.[74]

1.13.9 Clinical evaluation

Hypertensive crisis should be determined through the following:

1. **History**: Focus history on the presence of end-organ damage, the circumstances surrounding the hypertension, and any identifiable etiology.[62]

▪ **Medications**

a) Use of hypertensive medications and compliance.
b) Use of illicit drugs (specifically alpha-adrenergic agents).
c) Other medication history.

▪ **Duration of hypertension.**
▪ **Duration of current symptoms.**

- **Other medical problems (e.g., prior hypertension, thyroid disease, Cushing's disease, Systemic Lupus, renal disease).**
- **Date of last menstrual period.**
- **History of current crisis.**

2. Clinical manifestations.

3. Physical examination

Use an approach based on organ systems to identify sings of end-organ damage.

a) CNS

- Focal neurologic findings.
- Seizures, stupor, coma.
- Papilloedema, hemorrhages, exudates, or evidence of closed angle glaucoma.

b) Cardiovascular

- Lung auscultation for evidence of pulmonary edema.
- Signs of CHF, including extra heart sounds.
- Jugular venous distension.
- Peripheral edema.
- Check for equal and symmetric BP and pulses bilaterally.

c) Check for abdominal masses and bruits.

Differential Diagnosis

- Acute Coronary Syndrome.
- Aneurysms, Abdominal.
- Anxiety.
- Congestive Heart Failure and Pulmonary Edema.
- Cushing Syndrome.
- Delirium Tremens.
- Encephalitis.
- Glomerulonephritis, Acute.
- Headache, Cluster.
- Headache, Migraine.
- Headache, Tension.
- Hyperthyroidism, Thyroid Storm and Graves Disease.
- Myocardial Infarction.
- Pregnancy, Eclampsia.
- Pregnancy, Preeclampsia.
- Stroke, Hemorrhagic.
- Stroke, Ischemic.
- Subarachnoid Hemorrhage.
- Systemic Lupus Erythematosus.

Other Problem to be considered

- Steroid use.
- Use of over the counter or recreational sympathomimetic drug.
- Pheochromocytoma.
- Acute vasculitis.
- Serotonin syndrome.
- Other CNS pathology.
- Coarctation of the aorta.

Lab Studies

- Serum electrolytes (may indicate hypokalemic alkalosis), BUN and creatinine for evidence of renal impairment.
- CBC and smear may indicate miroangiopathic hemolytic anemia, thrombocytopenia.
- Dipstick urinalysis to detect presence of hematuria or proteinuria as evidence of renal impairment.
- Microscopic urinalysis, evaluating for RBC or RBC casts as evidence of renal impairment.
- Urine drug screen in selected patients.
- Calcium, glucose, uric acid and lipid profiles.
- Subsequent work-up for renal artery stenosis or pheochromocytoma in selected patients.

Optional studies

- Toxicology screen.
- Endocrine testing.
- Pregnancy test.

Imaging studies

- Chest x-ray: is carried out to assess if hypertensive crisis is of cardiac origin. It may show pulmonary edema and cardiomegaly due to congestive heart failure. Also it may show mediastinal widening and blunting of the aortic knob consistent with a dissecting aneurysm.
- Head CT scan: indicated with abnormal neurologic exam to look for intracranial bleeding, edema, or infarction.
- Chest CT scan, transesophageal echo, or aortic angiogram: may be indicated for clinical suspicion of aortic dissection.

Pathological findings

Extreme blood pressure elevations can overwhelm the autoregulatory mechanisms for organ blood flow resulting in damage to the arteriolar and capillary beds. This process produces organ hemorrhages and edema from the leakage of blood and fluid.

Special tests

- Electrocardiogram (ECG) to assess for evidence of ischemia, infarction, or left ventricular hypertrophy.
- Fundoscopic examination may reveal papilloedema, exudates or hemorrhage.

Diagnostic procedures

- Blood pressure-measured with an appropriately sized cuff and two or more readings from both arms should be averaged before the blood pressure is accepted as elevated.
- Sphygmomanometer is recommended.

1.13.10 Treatment of Hypertension crisis

Goal of treatment

Optimal control of hypertensive situations balances the benefits of immediate decreases in BP against the risk of significant decreases in end-organ perfusion, especially

regional or global perfusion and blood flow to vital organs.[75]

The emergency physician must be capable of the following:

- Appropriately evaluating patients with an elevated BP.
- Correctly classifying the hypertension
- Determining the aggressiveness and timing of therapeutic interventions.
- Making disposition decisions.

An important point to remember in the management of the patient with any degree of BP elevation is to "treat the patient and not the number" because the goal of treatment in the first few hours or days is not normalization of blood pressure because chronic hypertension is associated with autoregulatory changes in blood flow to the vital organs such as brain, heart and kidney (autoregulation is the process that keeps the perfusion and blood flow to these organs fairly constant despite of fluctuation in BP). For example, cerebral blood flow is autoregulated within specific limits in both normal and hypertensive patients. Thus rapid normalization of BP may lead to cerebral hypoperfusion and brain injury because too rapidly decreased BP causes autoregulation to be too overridden and hence results in hypoperfusion and ischemia. Rather, the autoregulation should be lowered to normal range within days or week after the initial phase of treatment, so the BP should be lowered by about 20-25% within 2-6 hours in order to maintain diastolic BP at no les than 100-110 mm Hg. Subsequently the BP can be reduced to normal levels using oral medications over days to weeks.[76]

Pre-hospital Care

- Address the manifestations of a hypertensive emergency, such as chest pain or heart failure. Reduction of BP may not be indicated in the prehospital setting.
- Oxygen, furosemide and nitrates all may be appropriate.
- Under most circumstances, attempting to treat hypertension directly in the prehospital setting is unwise. In particular, rapid lowering of BP can critically decrease end-organ perfusion.

Emergency Department Care

The fundamental principle in determining the necessary ED care of the hypertensive patient is the presence or absence of end-organ damage.

- **Initial considerations**

1) Place patient who is not in distress in a quiet room and reevaluate after an initial interview.
This may lower BP (In one study, 27% of patients with an initial DBP>130 mm Hg hade their DBP fall below critical levels after relaxation without specific treatment).
2) If ongoing end-organ damage is thought to be secondary to the hypertensive state, prompt treatment IV medication is indicated. Monitor patient closely so that a rapid fall in BP can be avoided.
3) An arterial catheter is used to monitor BP.
4) Patient should be placed on cardiac monitor.
5) Screen for end-organ damage.
6) Do not wait for laboratory data to return before initiation of initial therapy.
7) Bed rest is needed.
8) Fluid intake and output must be monitored carefully and body weight measured daily as an indicator of total body fluid volume during the course of therapy.[77]

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