METHODOLOGICAL INSTRUCTIONS
FOR INDEPENDENT WORK OF STUDENTS
DURING PREPARATION FOR THE PRACTICAL LESSON

<table>
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<tr>
<th>Academic discipline</th>
<th>Internal medicine, including clinical pharmacology, clinical immunology and allergology, occupational diseases</th>
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<tr>
<td>Module 4</td>
<td>Fundamentals of internal medicine (cardiology, rheumatology, nephrology)</td>
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<td>Content module 1</td>
<td>Basics of diagnosis, treatment and prevention of diseases of the cardiovascular system</td>
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<tr>
<td>Topic of the lesson</td>
<td>Essential hypertension. Cardiopsychoneurosis</td>
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<td>Year of study</td>
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1. **Relevance of the topic.** According to the World Health Organization, elevated AT rates occur in 30 - 35% of the adult population, of which - in 75-90% of cases, hypertension is caused by essential hypertension (hypertension (GC)). In GC, the etiological factor remains unknown. Meanwhile, the risk factors for GC are heredity, obesity, psycho-emotional overload, salt abuse and others. GC can lead to disability, complications such as cerebral hemorrhage, hypertensive heart, angina pectoris (ST), myocardial infarction (MI), acute and chronic heart failure, arrhythmias, sudden coronary death, hypertensive encephalopathy and nephropathy, with the development of chronic renal failure. In this regard, the problem of detection, adequate treatment and prevention is very important for doctors of different specialties.

The social significance of neurocirculatory dystonia (NCD) is very high, as this pathology is one of the common diseases. Among patients of therapeutic and cardiological profiles, according to various authors, this pathology is found in 30-50% of cases. The disease occurs most often at a young age, mainly in women. NCDs are especially often encountered by general practitioners, cardiologists, neurologists.

2. **The aims of the training course:**
   **To Know:**
   1. Differential diagnosis of arterial hypertensions: essentially and secondary (renal, endocrine, hemodynamic, central origin, etc.).
   2. Risk stratification of cardiovascular complications and determining prognosis.
   3. Plan survey.
   4. Tactics of the patient curation.
   **To be able to:**
   - Conduct surveys and patients examination with major cardiological syndromes
   - To draft survey the patients with heart diseases, to justify the use of major invasive and non-invasive diagnostic techniques witch are using in cardiology, to identify indications and contraindications for their conduction, possible complications
   - Identify different options for the course and complications of heart disease
   - Carry out differential diagnosis, justify and formulate diagnoses for major cardiac syndromes based on laboratory analysis and test tool
   • Prescribe treatment, determine prognosis, to conduct primary and secondary prevention in heart disease
   • Register and interpret the ECG in 12 assignments
   • Measure and interpret blood pressure
   • Diagnose and assist in syncope
   • Diagnose and assist in hypertensive crisis
   • Diagnose and assist with arterial hypotension
   • Diagnose and assist in the paroxysmal disorders of cardiac rhythm
   • Diagnose and assist syndrome Morhany-Edems-Stoks
   • Conduct pulmonary heart reanimation
   • Demonstrate knowledge of moral principles medical specialist and professional principles of subordination

**COMPETENCIES:**
- **integral:**
  Ability to solve typical and complex specialized problems and practical problems in the learning process, which involves research and / or innovation and is characterized by complexity and uncertainty of conditions and requirements
- **general:**
  - Ability to apply knowledge of internal medicine in practical situations
  - Knowledge and understanding of internal medicine
  - Ability to choose communication; ability to work in a team; interpersonal skills
- Ability to communicate in a foreign language (English) both orally and in writing;
- Skills in the use of information and communication technologies
- Ability to abstract thinking, analysis and synthesis, the ability to learn and be modernly trained
- Ability to evaluate and ensure the quality of work performed;
- Definiteness and perseverance in terms of tasks and responsibilities
  - special (professional, subject):
- Ability to evaluate the results of clinical examination of the patient, laboratory and instrumental studies.
- Ability to analyze the etiopathogenesis and clinical picture of internal diseases.
- Ability to analyze the clinical manifestations of the disease.
- Ability to analyze the structural basis of the development of diseases and their clinical manifestations, the structural basis of recovery, complications and consequences.
- Ability to master the methods of laboratory and instrumental research.

3. Basic knowledge, skills, abilities necessary for studying the topic (interdisciplinary integration)

<table>
<thead>
<tr>
<th>Names of previous disciplines</th>
<th>Acquired skills</th>
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<tr>
<td>Normal anatomy</td>
<td>To know the features of the anatomical structure of the cardiovascular system</td>
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<tr>
<td>Normal physiology</td>
<td>Knowledge of the physiology of the circulatory system, regulation of blood pressure</td>
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<tr>
<td>Pathological physiology</td>
<td>Representation of primary arterial hypertension, etiology and pathogenesis of arterial hypertension, neurocirculatory dystonia.</td>
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<tr>
<td>Pathological anatomy</td>
<td>Representation of the main pathomorphological changes in the internal organs in hypertension</td>
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<tr>
<td>Pharmacology</td>
<td>To know the clinical pharmacology of the main groups of drugs used to treat hypertension, NCDs</td>
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<tr>
<td>Biochemistry</td>
<td>To evaluate the data of laboratory methods of examination of patients with pathology of the cardiovascular system</td>
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<tr>
<td>Propaedeutics of internal diseases</td>
<td>To know the scheme of writing a medical history. Be able to collect complaints. Have a method of physical examination of a patient with hypertension, neurocirculatory dystonia. Identify changes on the ECG. Measure blood pressure and interpret the data.</td>
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<td>Faculty therapy</td>
<td>The concept of essential hypertension, neurocirculatory dystonia.</td>
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<tr>
<td>Department of Nervous Diseases</td>
<td>Assess neurological status. Classify and compare the signs of predominance of the sympathetic and parasympathetic divisions of the nervous system.</td>
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4. Tasks for independent work in preparation for the lesson.
### 4.1 The list of the basic terms, parameters, characteristics which the student should master at preparation for employment

<table>
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<tr>
<th>Term</th>
<th>Definition</th>
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<tr>
<td>1. Arterial hypertension</td>
<td>persistently elevated systolic (SAT) over 140 and / or diastolic blood pressure (BP) over 90 mm Hg</td>
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<td>2. Essential hypertension</td>
<td>elevated blood pressure in the absence of an obvious reason for its increase</td>
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<td>3. Risk factors</td>
<td>age, sex, heredity, overweight, hypodynamics, smoking, alcohol abuse, coffee, salt, animal fats, stress</td>
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<td>4. Secondary hypertension</td>
<td>hypertension, the cause of which can be identified</td>
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<td>5. Malignant hypertension</td>
<td>Syndrome characterized by high blood pressure (over 220/120 mm Hg) with hemorrhages and exudates in the retina, often with optic nerve edema, cerebral hemorrhage, kidney damage with the development of uremia, cardiac complications.</td>
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<td>6. Hypertensive crisis</td>
<td>a sudden increase in blood pressure above the usual normal figures, which is accompanied by the appearance or intensification of disorders of the target organs or the autonomic nervous system.</td>
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<td>7. Neurocirculatory dystonia</td>
<td>Polymetiological functional neurogenic disease of the cardiovascular system, which is based on disorders of neuroendocrine regulation with multiple and diverse clinical symptoms</td>
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<td>8. Autonomic crisis: Sympatho-adrenal crisis (type 1):</td>
<td>● Sudden onset, anxiety, unconscious fear, severe headache, throbbing in the head, discomfort in the heart, severe heart failure, palpitations, tachycardia, increased blood pressure, mydriasis, chin hyperkinesis, numbness of the extremities, sharp excitement, body temperature 38-39 °C, sudden termination with polyuria (urine light), general weakness;</td>
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<td>9. Vagoinsular (parasympathetic) crisis (2nd type):</td>
<td>●General weakness, heaviness in the head, dizziness, &quot;hot flashes to the face&quot;, low blood pressure, bradycardia, heart failure, extrasystole, respiratory disorders, shortness of breath, gastrointestinal dyskinesia, sometimes allergic reactions - urticaria, severe post-crisis asthenia;</td>
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<td>10. Mixed crisis (type 3):</td>
<td>●Expressed range of vegetative-vascular manifestations and disorders of thermoregulation. Exit from the crisis is accompanied by weakness, lethargy, brokenness, depressed mood, discomfort in the heart, polyuria, thirst, increased appetite, a combination of symptoms of type 1 and 2 crisis.</td>
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### 4.2 Theoretical questions for the lesson.

**Essential hypertension.**

1. Definition. The role of disorders of central and renal mechanisms of regulation of blood pressure, endothelial function and other factors.
4. Diagnosis and diagnostic criteria of essential arterial hypertension.
5. Differential diagnosis of essential arterial hypertension.
7. Complicated and uncomplicated hypertensive crises, features of treatment tactics.
8. Primary and secondary prevention of hypertension.

**Neurocirculatory dystonia**
1) Definition. Etiology and pathogenesis.
2) Classification.
3) Features of clinical syndromes.
5) Differentiated therapy.
6) Primary and secondary prevention.
7) Forecast and efficiency

**4.3. Practical work (tasks) performed in class:**

**List of typical tasks and skills:**
1. Work with the patient
   - Collect complaints, medical history, life history.
   - Collect information about the general condition of the patient (consciousness, constitution, fatness) and assess the appearance (examination of the skin, subcutaneous fat, palpation of lymph nodes, thyroid and mammary glands), examine the condition of the musculoskeletal system, joints.
   - Examine the condition of the respiratory organs (chest examination, chest palpation, percussion and lung auscultation).
   - Examine the condition of the cardiovascular system (examination and palpation of the heart and blood vessels, percussion of the heart and auscultation of the heart and blood vessels).
   - Examine the condition of the digestive organs (examination, percussion, superficial and deep palpation).
   - Examine the condition of the urinary system (examination of the lumbar region, palpation of the kidneys).
2. To make a probable (preliminary) diagnosis of the disease (Essential arterial hypertension (hypertension). Neurocirculatory dystonia.).
3. To appoint and substantiate laboratory and/or instrumental examination of a patient with diseases.
5. Carry out differential diagnosis in diseases accompanied by hypertension and NCDs.
6. To make a clinical diagnosis of diseases.
7. To determine the necessary regime and diet of a patient with diseases accompanied by hypertension and NCDs.
8. Determine the principles and nature of treatment (conservative, operative) of the patient.
9. Diagnose and provide assistance in hypertensive and autonomic crises.
10. Perform medical manipulations (Measure blood pressure. Register an ECG in 12 leads. Perform artificial lung ventilation and perform indirect heart massage).
11. To determine the tactics of secondary prevention of patients subject to dispensary supervision.
13. Know the clinical pharmacology of the main groups of drugs used to treat hypertension, NCDs.
14. To be able to draw up medical documentation. Medical card of an inpatient. Extract from the medical card of an inpatient. Procedural sheet (form B №28). Referral to MSEC. Medical certificate of death. Incapacity certificate. .).

4.4 The contents of topic:
Text

Definition
Defining abnormally high blood pressure is extremely difficult and arbitrary. Furthermore, the relationship between systemic arterial pressure and morbidity appears to be quantitative rather than qualitative. A level for high blood pressure must be agreed upon in clinical practice for screening patients with hypertension and for instituting diagnostic evaluation and initiating therapy. Because the risk to an individual patient may correlate with the severity of hypertension, a classification system is essential for making decisions about aggressiveness of treatment or therapeutic interventions.

Based on recommendations of the Seventh Report of the Joint National Committee of Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII), the classification of blood pressure (expressed in mm Hg) for adults aged 18 years or older is as follows*:

- Normal† - Systolic lower than 120, diastolic lower than 80
- Prehypertension - Systolic 120-139, diastolic 80-99
- Stage 1 - Systolic 140-159, diastolic 90-99
- Stage 2 - Systolic equal to or more than 160, diastolic equal to or more than 100

*Based on the average of 2 or more readings taken at each of 2 or more visits after initial screening

†Normal blood pressure with respect to cardiovascular risk is less than 120/80 mm Hg. However, unusually low readings should be evaluated for clinical significance.

Prehypertension, a new category designated in the JNC VII report, emphasizes that patients with prehypertension are at risk for progression to hypertension and that lifestyle modifications are important preventive strategies.

Hypertension may be either essential or secondary. Essential hypertension is diagnosed in the absence of an identifiable secondary cause. Approximately 95% of American adults have essential hypertension, while secondary hypertension accounts for fewer than 5% of the cases.

Pathophysiology
Arterial blood pressure is a product of cardiac output and systemic vascular resistance. Therefore, determinants of blood pressure include factors that affect both cardiac output and arteriolar vascular physiology. There is potential relevance of blood viscosity, vascular wall
sheer conditions (rate and stress), and blood flow velocity (mean and pulsatile components) on vascular and endothelial function regulating blood pressure in humans. Furthermore, changes in vascular wall thickness affect the amplification of peripheral vascular resistance in hypertensive patients and result in reflection of waves back to the aorta, increasing systolic blood pressure.

Regulation of blood pressure

Regulation of normal blood pressure is a complex process. Although a function of cardiac output and peripheral vascular resistance, both of these variables are influenced by multiple factors.

The factors affecting cardiac output include sodium intake, renal function, and mineralocorticoids; the inotropic effects occur via extracellular fluid volume augmentation and an increase in heart rate and contractility. Peripheral vascular resistance is dependent upon the sympathetic nervous system, humoral factors, and local autoregulation. The sympathetic nervous system produces its effects via the vasoconstrictor alpha effect or the vasodilator beta effect. The humoral actions on peripheral resistance are also mediated by other mediators such as vasoconstrictors (angiotensin and catecholamines) or vasodilators (prostaglandins and kinins). For additional resource, please visit Angiotensin II Receptor Blockade.

Autoregulation of blood pressure occurs by way of intravascular volume contraction and expansion, as well as by transfer of transcapillary fluid. Interactions between cardiac output and peripheral resistance are autoregulated to maintain a set blood pressure in an individual. For example, constriction of the arterioles elevates arterial pressure by increasing total peripheral resistance, whereas venular constriction leads to redistribution of the peripheral intravascular volume to the central circulation, thereby increasing preload and cardiac output.

Pathogenesis of hypertension

The pathogenesis of essential hypertension is multifactorial and highly complex. Multiple factors modulate the blood pressure for adequate tissue perfusion and include humoral mediators, vascular reactivity, circulating blood volume, vascular caliber, blood viscosity, cardiac output, blood vessel elasticity, and neural stimulation. A possible pathogenesis of essential hypertension has been proposed in which multiple factors, including genetic predisposition, excess dietary salt intake, and adrenergic tone, may interact to produce hypertension. Although genetics appears to contribute to essential hypertension, the exact mechanism has not been established.

The natural history of essential hypertension evolves from occasional to established hypotension. After a long invariable asymptomatic period, persistent hypertension develops into complicated hypertension, in which target organ damage to the aorta and small arteries, heart, kidneys, retina, and central nervous system is evident. The progression begins with prehypertension in persons aged 10-30 years (by increased cardiac output) to early hypertension in persons aged 20-40 years (in which increased peripheral resistance is prominent) to established hypertension in persons aged 30-50 years, and, finally, to complicated hypertension in persons aged 40-60 years.

The early stage of hypertension has been described as high-output hypertension. High-output hypertension results from decreased peripheral vascular resistance and concomitant cardiac stimulation by adrenergic hyperactivity and altered calcium homeostasis. In contrast, the chronic phase of essential hypertension characteristically has normal or reduced cardiac output and elevated systemic vascular resistance.

The vasoreactivity of the vascular bed, an important phenomenon mediating changes of hypertension, is influenced by the activity of vasoactive factors, reactivity of the smooth muscle
cells, and structural changes in the vessel wall and vessel caliber, expressed by a lumen-to-wall ratio. Patients who develop hypertension are known to develop a systemic hypertensive response secondary to vasoconstrictive stimuli. Alterations in structural and physical properties of resistance arteries, as well as changes in endothelial function, are probably responsible for this abnormal behavior of vasculature. Furthermore, vascular remodeling occurs over the years as hypertension evolves, thereby maintaining increased vascular resistance irrespective of the initial hemodynamic pattern.

**Genetic factors**

Hypertension is likely to be related to multiple genes. Hypertension develops secondary to multiple environmental factors, as well as to several genes, whose inheritance appears to be complex. Very rare secondary causes are related to single genes.

**Role of the vascular endothelium**

The vascular endothelium is presently considered a vital organ, where synthesis of various vasodilating and constricting mediators occurs. The interaction of autocrine and paracrine factors takes place in the vascular endothelium, leading to growth and remodeling of the vessel wall and to the hemodynamic regulation of blood pressure.

Numerous hormonal, humeral vasoactive, and growth and regulating peptides are produced in the vascular endothelium. These mediators include angiotensin II, bradykinin, endothelin, nitric oxide, and several other growth factors. Endothelin is a potent vasoconstrictor and growth factor that likely plays a major role in the pathogenesis of hypertension. Angiotensin II is a potent vasoconstrictor synthesized from angiotensin I with the help of an angiotensin-converting enzyme (ACE). Another vasoactive substance manufactured in the endothelium is nitric oxide. Nitric oxide is an extremely potent vasodilator that influences local autoregulation and other vital organ functions. Additionally, several growth factors are manufactured in the vascular endothelium; each of these plays an important role in atherogenesis and target organ damage. These factors include platelet-derived growth factor, fibroblast growth factor, insulin growth factor, and many others.

**Pathophysiology of target organ damage**

**Hypertension and the cardiovascular system**

Cardiac involvement in hypertension manifests as LVH, left atrial enlargement, aortic root dilatation, atrial and ventricular arrhythmias, systolic and diastolic heart failure, and ischemic heart disease. LVH is associated with an increased risk of premature death and morbidity. A higher frequency of cardiac atrial and ventricular dysrhythmias and sudden cardiac death may exist. Possibly, increased coronary arterial resistance leads to reduced blood flow to the hypertrophied myocardium, resulting in angina despite clean coronary arteries. Hypertension, along with reduced oxygen supply and other risk factors, accelerates the process of atherogenesis, thereby further reducing oxygen delivery to the myocardium.

Hypertension remains the most common cause of congestive heart failure. Antihypertensive therapy has been demonstrated to significantly reduce the risk of death from stroke and coronary heart disease. Two published meta-analyses have shown 14% and 26% reductions in cardiovascular mortality rates.

**Left ventricular hypertrophy**
The myocardium undergoes structural changes in response to increased afterload. Cardiac myocytes respond by hypertrophy, allowing the heart to pump more strongly against the elevated pressure. However, the contractile function of the left ventricle remains normal until later stages. Eventually, LVH lessens the chamber lumen, limiting diastolic filling and stroke volume. The left ventricular diastolic function is markedly compromised in long-standing hypertension.

The mechanisms of diastolic dysfunction have been elucidated only recently. An aberration in the passive relaxation of the left ventricle during diastole appears to exist. Over time, fibrosis may occur, further contributing to the poor compliance of the ventricle. As the left ventricle does not relax during early diastole, left ventricular end-diastolic pressure increases, further increasing left atrial pressure in late diastole. The exact determinants of left ventricular diastolic dysfunction have not been well studied; possibly, the abnormality is governed by abnormal calcium kinetics.

The central nervous system

Long-standing hypertension may manifest as hemorrhagic and atheroembolic stroke or encephalopathy. Both the high systolic and diastolic pressures are harmful; a diastolic pressure of more than 100 mm Hg and a systolic pressure of more than 160 mm Hg have led to a significant incidence of strokes. Other cerebrovascular manifestations of complicated hypertension include hypertensive hemorrhage, hypertensive encephalopathy, lacunar-type infarctions, and dementia.

Mortality/Morbidity

- In the Framingham Heart Study, the age-adjusted risk of congestive heart failure was 2.3 times higher in men and 3 times higher in women when highest blood pressure was compared to the lowest. Multiple Risk Factor Intervention Trial (MRFIT) data showed that the relative risk for coronary heart disease mortality varied from 2.3-6.9 times higher for persons with mild-to-severe hypertension compared to persons with normal blood pressure.
- The relative risk for stroke ranged from 3.6-19.2. The population-attributable risk percentage for coronary artery disease varied from 2.3-25.6%, whereas the population-attributable risk for stroke ranged from 6.8-40%.

Race

Blacks have a higher prevalence and incidence of hypertension than whites. The prevalence of hypertension was increased by 50% in African Americans. In Mexican Americans, the prevalence and incidence of hypertension is similar to or lower than in whites. The National Health and Nutrition Examination Survey (NHANES) III reported an age-adjusted prevalence of hypertension at 20.6% in Mexican Americans and 23.3% in non-Hispanic whites.

- Are there ethnic differences in the pathogenesis of hypertension, and do these differences influence the choice of treatment? To understand ethnic influence, an understanding of the renin angiotensin system is essential. Renin secretion is suppressed when the kidney detects that the amount of sodium excretion is increased; thus, a clue to the excess sodium in the circulation. Black people tend to develop hypertension at an earlier age and have lower rennin activity; target organ damage also differs in black people from that in white people.
- Most studies in the United Kingdom and the United States report a higher prevalence and lower awareness of hypertension in black people than in white people. Mortality from
hypertension in African-Caribbean–born people is 3.5 times the national rate; similar data have been published for African American citizens. Strokes are more common in black people, but coronary heart disease is more common in Asians. Both groups have a higher incidence of chronic renal failure than white people, but this is more due to hypertension in black people and diabetes in Asians.

- Black people have a poorer response to treatment with ACE inhibitors compared to white people; the evidence for beta-blockers being less effective in black people is also clear. However, diuretics are more effective at a young age in black people.

Sex

The age-adjusted prevalence of hypertension was 34%, 25.4%, and 23.2% for men and 31%, 21%, and 21.6% for women among African Americans, whites, and Mexican Americans, respectively. In the NHANES III study, the prevalence of hypertension was 12% for white men and 5% for white women aged 18-49 years. However, the age-related blood pressure rise for women exceeds that of men. The prevalence of hypertension was reported at 50% for white men and 55% for white women aged 70 years or older.

Age

A progressive rise in blood pressure with increasing age is observed. The third NHANES survey reported that the prevalence of hypertension grows significantly with increasing age in all sex and race groups. The age-specific prevalence was 3.3% in white men (aged 18-29 y); this increased to 13.2% in the group aged 30-39 years. The prevalence further increased to 22% in the group aged 40-49 years, to 37.5% in the group aged 50-59 years, and to 51% in the group aged 60-74 years. In another study, the incidence of hypertension appeared to increase approximately 5% for each 10-year interval of age. Age-related hypertension appears to be predominantly systolic rather than diastolic. The systolic blood pressure rises into the eighth or ninth decade, while the diastolic blood pressure remains constant or declines after age 40 years.\(^1\)

History

- Following the documentation of hypertension, which is confirmed after an elevated blood pressure, properly measured, has been documented on at least 3 separate occasions (based on the average of 2 or more readings taken at each of 2 or more visits after initial screening), a detailed history should extract the following information:
  - Extent of target organ damage
  - Assessment of patients’ cardiovascular risk status
  - Exclusion of secondary causes of hypertension
- Patients may have undiagnosed hypertension for years without having had their blood pressure checked. Therefore, a careful history of end organ damage should be obtained.
- A history of cardiovascular risk factors includes hypercholesterolemia, diabetes mellitus, and tobacco use (including chewing tobacco).
- Obtain a history of over-the-counter medication use, current and previous unsuccessful antihypertensive medication trials, and ethanol intake.
- The historical and physical findings that suggest the possibility of secondary hypertension are a history of known renal disease, abdominal masses, anemia, and urochrome pigmentation.
- A history of sweating, labile hypertension, and palpitations suggests the diagnosis of pheochromocytoma.
- A history of cold or heat tolerance, sweating, lack of energy, and bradycardia or tachycardia may indicate hypothyroidism or hyperthyroidism.
- Kidney stones raise the possibility of hyperparathyroidism. The presence of papilledema and other neurologic signs raises the possibility of increased intracranial pressure. A history of drug ingestion, including oral contraceptives, licorice, and sympathomimetics, should be obtained.

**Physical**

An accurate measurement of blood pressure is the key to diagnosis. Several determinations should be made over a period of several weeks.

At any given visit, an average of 3 blood pressure readings taken 2 minutes apart using a mercury manometer is preferable. Blood pressure should be measured in both the supine and sitting positions, auscultating with the bell of the stethoscope. On the first visit, blood pressure should be checked in both arms and in one leg to avoid missing the diagnosis of coarctation of aorta or subclavian artery stenosis.

As the improper cuff size may influence blood pressure measurement, a wider cuff is preferable, particularly if the patient's arm circumference exceeds 30 cm.

The patient should rest quietly for at least 5 minutes before the measurement.

Although somewhat controversial, the common practice is to document phase V (a disappearance of all sounds) of Korotkoff sounds as the diastolic pressure.

- A funduscopic evaluation of the eyes should be performed to detect any evidence of hypertensive retinopathy. These are flame-shaped hemorrhages and cotton wool exudates.
- Palpation of all peripheral pulses should be performed.
- Look for renal artery bruit over the upper abdomen; the presence of a unilateral bruit with both a systolic and diastolic component suggests renal artery stenosis.
- A careful cardiac examination is performed to evaluate signs of LVH. These include displacement of apex, a sustained and enlarged apical impulse, and the presence of an S4. Occasionally, a tambour S2 is heard with aortic root dilatation.

**Lab Studies**

- Unless a secondary cause for hypertension is suspected, only the following routine laboratory studies should be performed:
  - CBC count, serum electrolytes, serum creatinine, serum glucose, uric acid, and urinalysis
  - Lipid profile (total cholesterol, low-density lipoprotein [LDL] and high-density lipoprotein [HDL], and triglycerides)
- Additional tests described below are indicated when specific clinical situations warrant further investigation.
Microalbuminuria is an early indication of hypertensive nephrosclerosis and is also a marker for a higher risk of cardiovascular morbidity and mortality. Present recommendations suggest that individuals with type I diabetes should be screened for microalbuminuria. Usefulness of this screening in hypertensive patients without diabetes has not been established.

Plasma renin activity (PRA) is performed to detect evidence of primary hyperaldosteronism. Low renin values confirm the diagnosis of primary hyperaldosteronism; however, hypokalemia may be associated with a form of hypertension, but it is not often present.

Determination of sensitive thyroid-stimulating hormone (TSH) level excludes hypothyroidism or hyperthyroidism as a cause of hypertension.

Imaging Studies

- Echocardiography: The limited echocardiography study, rather than the complete examination, may detect LVH more frequently than electrocardiography. The main indication for limited echocardiography is evaluation for end organ damage in a patient with borderline high blood pressure. Therefore, the presence of LVH despite normal or borderline high blood pressure measurements requires antihypertensive therapy.
- Imaging studies for renovascular stenosis: If the history suggests renal artery stenosis and if a corrective procedure is considered, further radiologic investigations are performed.

Other Tests

- Routine testing includes electrocardiograms.
- Ambulatory blood pressure monitoring: Indications for ambulatory blood pressure monitoring include labile blood pressure, a discrepancy between blood pressure measurement inside and outside the physician's office, and poor blood pressure control. Ambulatory monitoring also identifies patients who have the distinct syndrome called white coat hypertension.

Hypertension Risk Stratification

Risk Group A: Low Cardiovascular Risk

A. Criteria
   1. No Cardiovascular Risks (See Risk Group B)
   2. No Target organ damage or Cardiovascular Disease
B. Prehypertension (120-139 / 80-89)
   1. Lifestyle Modification in Hypertension
C. Stage 1 Hypertension (140-159 / 90-99)
   1. Lifestyle Modification in Hypertension
   2. Consider Antihypertensive after up to 6-12 months
      a. Hydrochlorothiazide first choice in most patients
      D. Stage 2 Hypertension or greater (>159/99)
        1. Lifestyle Modification in Hypertension
        2. Hypertension Combination Therapy

Risk Group B: Moderate Cardiovascular Risk
A. Criteria
1. Tobacco Abuse
2. Dyslipidemia
3. Renal insufficiency
4. Patient age over 60 years
5. Male gender of postmenopausal women
6. Cardiovascular Family History
7. No Diabetes Mellitus
8. No Target organ damage or Cardiovascular Disease

B. Prehypertension (120-139 / 80-89)
   1. Lifestyle Modification in Hypertension

C. Stage 1 Hypertension (140-159 / 90-99)
   1. Lifestyle Modification in Hypertension
   2. Antihypertensive (e.g. Hydrochlorothiazide)

D. Stage 2 Hypertension or greater (>159/99)
   1. Lifestyle Modification in Hypertension
   2. Hypertension Combination Therapy

Risk Group C: High Cardiovascular Risk

A. Criteria
   1. Target organ damage or Cardiovascular Disease
      a. Left Ventricular Hypertrophy
      b. Angina or prior Myocardial Infarction
      c. Prior coronary revascularization
      d. Cerebrovascular Accident (Stroke or CVA)
      e. Transient Ischemic Attack (TIA)
      f. Nephropathy or Chronic Kidney Disease
      g. Peripheral Vascular Disease
      h. Retinopathy
   2. Cardiovascular Risks (See Risk Group B)

B. Prehypertension (120-139 / 80-89) or greater
   1. Lifestyle Modification in Hypertension
   2. Antihypertensive
   3. Hypertension Combination Therapy if >20/10 over goal

Hypertension Criteria

I. Criteria: Hypertension in Adults
A. Goal Blood Pressures for Hypertensive Patients
   1. Hypertension without Co-morbidity: <140/90
   2. Diabetes Mellitus: <130/80
   3. Congestive Heart Failure: <130/80
   4. Renal Insufficiency: <130/80
   5. Renal Failure and >1gProteinuria/24 hours: <125/75

B. JNC-7 Blood Pressure definitions
   1. Optimal Blood Pressure: <115/80
   2. Normal Blood Pressure: <120/80
   3. Pre-Hypertension: 120-139/80-89
   4. Stage 1 Hypertension: 140-159/90-99
   5. Stage 2 Hypertension: >160/100

C. Stages eliminated in JNC-7
1. Stage 3 Hypertension: 180-209/110-119
2. Stage 4 Hypertension: >210/120

D. Isolated Systolic Hypertension
   1. Systolic Blood Pressure: >140 mmHg
   2. Diastolic Blood Pressure: <90 mmHg

II. Criteria: Hypertension in Adolescents
   . Age 16-18 years
   1. Significant Hypertension: BP> 142/92
   2. Severe Hypertension: BP> 150/98
   A. Age: 13-15 years
   1. Significant Hypertension: BP> 136/86
   2. Severe Hypertension: BP> 144/92

Antihypertensive Selection

Step 1: Determine when and how to intervene

A. Review Hypertension Risk Stratification
B. Determine Hypertension Reduction Goal

Step 2

A. Consider Hypertension Combination Therapy
   1. For Refractory Hypertensive Populations
B. Monotherapy
   1. Standard initial monotherapy choices
      a. Diuretics (e.g. Hydrochlorothiazide)
         i. If Diuretic is not first, it should be second
         ii. Excellent adjunct to other antihypertensives
         iii. Better outcomes than Lisinopril and Amlodipine
            i. Reduced risk of CVA, MI, CHF over other agents
      b. Beta Blocker
      c. ACE Inhibitor
      d. Angiotensin Receptor Blocker
   2. Compelling reason for other antihypertensive
      . AntiHypertensives for Specific Comorbid Diseases
         a. Antihypertensives for Specific Populations
   3. Agents to avoid for monotherapy
      . Alpha blockers
         a. Hydralazine
         b. Minoxidil
         c. Calcium Channel Blockers
   4. Avoid if non-compliant (rebound Hypertension)
      . Beta Blockers
      a. Clonidine

Step 3

A. Consider Hypertension Combination Therapy

Hypertension Combination Therapy

Indications for Combination Antihypertensive Therapy
A. Failed Hypertension Monotherapy
B. Hypertension

**Protocol**

A. Consider reasons for resistant Hypertension (see below)
B. Review Hypertension Risk Stratification
C. Determine Hypertension Reduction Goal
D. Advance to next step if BP>15/10 above goal
E. Consolidate medications into combination agents

**Causes: Resistant Hypertension**

A. Noncompliance with current regimen (most common)
   1. Recent drug holiday
   2. Unfilled prescription
B. Inaccurate Blood Pressure measurement (see BP Examination regarding pitfalls)
C. White coat Hypertension (consider Ambulatory Blood Pressure Monitoring)
D. Progression of disease
E. Treatment program not optimized
   1. Example: Thiazide Diuretics are ineffective at GFR <30 ml/min (use Loop Diuretics instead)
F. Medications or drugs counteracting antihypertensive (e.g. NSAIDS, Sympathomimetics)
G. Comorbid condition (e.g. Sleep Apnea, morbid Obesity, Alcohol Abuse, anxiety, Chronic Pain)
H. Secondary Hypertension
   1. Hyperaldosteronism represents 20% of refractory cases (consider if Hypokalemia)

**Preparations: Combinations (assist with cost and compliance)**

A. Prinizide (Lisinopril 10-20 mg with Hydrochlorothiazide 12.5-25 mg)
B. Diovan-Hct (Valsartan 80-160 mg with Hydrochlorothiazide 12.5 mg)
C. Ziac (Bisoprolol with Hydrochlorothiazide 6.25)
D. Lotrel (Benzapril 10-20 mg with Amlodipine 2.5-10 mg)
E. Tarka (Trandolopril 1-2 mg with Verapamil 180-240 mg)
F. Exforge (Valsartan and Amlodipine)
G. Reserpine 1.25-2.5 mg with Hydrochlorothiazide 25 mg
H. Tenoretic (Atenolol 50-100 mg with Chlorthalidone 25 mg)

**Protocol: Combinations that add 4 drugs in 2 pills for $50-60**

A. Tenoretic 100/25 with Lotrel 10/20
B. Tenoretic 100/25 with Prinizide 20/12.5

**Protocol: Step 1**

A. Serum Creatinine <1.8 mg/dl
   1. ACE Inhibitor and Thiazide Diuretic
B. Serum Creatinine >1.8 mg/dl
   1. ACE Inhibitor and Loop Diuretic
Protocol: Step 2

A. Add Non-Dihydropyridine Calcium Channel Blocker

Protocol: Step 3

B. Heart Rate >83
   1. Add Low dose Beta Blocker
   2. Caution regarding Atrioventricular Block
C. Heart Rate <84
   1. Add Dihydropyridine Calcium Channel Blocker

Protocol: Step 4

D. Add long acting Alpha adrenergic blocker (at night)
E. Add Spironolactone 12.5 to 50 mg po qd
F. Consult Nephrology or Cardiology

Protocol: Additional Measures

G. Consider Tekturna (Aliskiren), a Direct renin inhibitor

Self preparation at class:
Listen information;
Work with patients (with cardiac pathology);
Ask about the problems that have not been found in information given.

Self preparation at home:
Compose the plan of your answer;
Answer the questions to the topic;
Do the test given above.

Question 1
A man aged 45 years with treated moderate hypertension left for a business trip. About 36 hours after leaving home he attended a casualty department complaining of headache, agitation, sweating and palpitations. The blood pressure was 220/145 mmHg. He was admitted and investigation showed a urinary catecholamine excretion of 15 μmol/24 hours (274 mg/24 hours).

(a) What was the differential diagnosis?
(b) What hypotensive agent had he left at home?
(c) What is the treatment of this condition and with what drug?

Question 2
A woman of 19 years was found to have a blood pressure of 180/125 mmHg. IVP normal; peripheral venous rennin 3490 pg ml-1 h-1; blood urea 12 mmol/l (72 mg/100ml); GFR 48 ml/min; urine microscopy no abnormality; proteinuria 1.9 g/day.

(a) What was the diagnosis?
She was successfully treated with oral diazoxide and frusemide. One week later the peripheral venous renin was found to have approximately doubled in concentration and the GFR had fallen to 33 ml/min.
(b) Comment upon the increase in the renin and the fall in GFR.
(c) Comment upon the drug treatment.

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**Recommended Books**

**I. Basic**


**II. Additional:**

2. CURRENT Medical Diagnosis and Treatment 2012, Fifty-First Edition (LANGE CURRENT Series) by Stephen McPhee, Maxine Papadakis and Michael W. Rabow (Paperback - Sep 12, 2011)
3. Davidson's Principles and Practice of Medicine: With STUDENT CONSULT Online Access, 21e (Principles & Practice of Medicine (Davidson's)) by Nicki R. Colledge BSc FRCP(Ed), Brian R. Walker BSc MD FRCP(Ed) and Stuart H. Ralston MB ChB MD FRCP FMedSci FRSE (Paperback - Mar 11, 2010)Kumar and Clark's Clinical Medicine, 7e (Kumar, Kumar and Clark's Clinical Medicine) by Parveen J. Kumar (Paperback - Jul 2, 2009)
4. 1000 Questions and Answers from Kumar & Clark's Clinical Medicine, 2e [Paperback] Parveen Kumar CBE BSc MD FRCP FRCP(Edin) (Editor), Michael L Clark MD FRCP (Editor)
5. Differential Diagnosis in Internal Medicine: From Symptom to Diagnosis by Walter Siegenthaler (Mar 21, 2007)
7. CURRENT Diagnosis and Treatment Emergency Medicine, Seventh Edition (LANGE CURRENT Series) by C. Keith Stone (May 23, 2011)

**Electronic resources**

[http://www.rheumatologyclinic.ca/imagebank/#close](http://www.rheumatologyclinic.ca/imagebank/#close)
[https://images.rheumatology.org/bp/#/](https://images.rheumatology.org/bp/#/)
Answer 1

(a) The symptoms and high urinary catecholamine levels suggest either a pheochromocytoma or the rebound phenomenon which occurs in some patients who withdraw their regular doses of clonidine abruptly.

(b) This man had left his supply of clonidine at home. The explanation of this phenomenon is not known but it is believed that during clonidine treatment there is increased storage of catecholamine in nerve terminals by the stimulation of inhibitory α-receptors. If the drug is suddenly stopped the stored amines are released, producing pheochromocytoma – like symptoms, and their urinary excretion increases.

(c) In the acute phase probably the treatment of choice is clonidine - symptoms subside rapidly and blood pressure is lowered. Alternatively labetalol may be used which has α- and β-blocking properties and can also be given parenterally.

Answer 2

(a) This woman had accelerated (malignant) hypertension. The normal urine microscopy and IPV virtually exclude primary renal disease. High concentration of circulating renin are usually found in accelerated hypertension and are thought to be a reflection of renal damage secondary to the high pressure rather than a primary phenomenon.

(b) The increase in plasma renin is to be expected: frusemide causes renin release secondary to the sodium depletion it produces. Diazoxide causes renin release as a result of the increase in circulating volume consequent upon the peripheral vascular dilatation it produces. A fall in GFR after aggressive hypotensive therapy is also to be expected; with stabilization of the blood pressure the GFR usually returns to, or may rise above, the pretreatment level.

(c) Diazoxide is a very potent hypotensive drug but has two important side-effects: intense sodium retention and a diabetogenic action. All patient taking diazoxide should receive a potent “loop” diuretic and also a hypoglycaemic agent. Without these patient taking diazoxide will very probably develop hyperosmolar non-ketotic diabetic coma.