Arterial Hypertension
Methodic materials for international students (IV-VI year)

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I. Definitions

According to WHO definition (1980) **arterial hypertension** is chronic rise of systolic and/or diastolic BP. AH is stated when SBP is 140 mm Hg and higher and diastolic - 90 mm Hg and higher in persons, who don't receive any antihypertensive treatment at that moment.

Hypertensive (vascular) disease (=???) (=primary=essential=idiopatic hypertension) – chronic disease with syndrome of arterial hypertension being the main syndrome in case if this syndrome is not caused by certain pathological conditions (symptomatic=secondary hypertensions).

Classification:

1. Aethiology

Essential	Classified according to the BP level, stage (target organs affection) and risk grade (risk of cardiovascular complications)	
Secondary		
	Types	Causes
Renal*	Parenchymal	Glomerulonephritis, pyelonephritis, polycystic renal disease, diabetic nephropathy, renin-producing tumors
	Renovascular	Renovascular stenosis of different aethiology: fibromuscular dysplasia, Takayasu syndrome, atheromatous plaque, inborn anomalities
	Obturation –related	Impairment of urine flow due to obturation: hydronephrosis, reflux nephropathy, anomalities
*** in case of nephroptosis all 3 mechanisms are involved:** impairment of urine flow due to renal dystopia (obturation), vascular (renal dystopia leads to abnormal position of a.renalis, so that blood flow may be reduced); parenchymal mechanism develops as a result of ascendant infection (pyelonephritis development).		
Endoc-rine	Cushing disease and syndrome (increased cortizol level)	Hypohysis tumors or ectopic ACTH-syndrome, adenoma or carcinoma of adrenal cortex, adrenal cortex hyperplasia etc. Medicamentous Cushing syndrome (intake of oral glucocorticosteroids – asthma, connective tissue diseases etc

		is included into drug-induced SAH)
	Primary hyper-aldosteronism	Solitar adenoma, carcinoma, 1-side or both sides hyperplasia, glucocorticosteroid-reducable hyperaldosteronism
	Pheochromacy-toma	Adrenal (constant, paroxysmal); non-adrenal (gangliomas, neuroblastoma, paraganglioma)
	Acromegaly	
	Congenital or hereditary adrenogenital syndromes (17α- and 11β-hydroxylases deficiency)	
	E.Braunwald also includes in this group hypertension, occurring in patients with **Myxedema** and in women, taking **Oral contraceptives**.	
Hemodynamic	Coarctation of aorta, aortitis, tyrotoxicosis, increased intravascular volume (polycytemia etc)	According to classification, given by **E.Braunwald**, these types are included in 2 groups: systolic **Hypertenstion with wide pulse pressure** and **Miscellaneous hypertension**
Neurogenic	"Dienchephalic syndrome", brain tumors, encephalitis, neuritis, injure of n.glossopharyngeous; familial disautonomia (Riley-Day), poliomyelitis (bulbar), polyneuritis (acute porphyria, lead poisoning), increased intracranial pressure (acute), spinal cord section (acute); psychogenic	
Caused by medicaments	Glucocorticosteroids, oral contraceptives, erythropoietin, sandimun	
Isolated systolic hypertension (in geriatric patients)		
"WCH" (White-coat)-hypertension (transient situation hypertension)		

According to classification, given by E.Braunwald:

I. Systolic hypertension with wide pulse pressure

A. Decreased compliance of aorta (arteriosclerosis)

B. Increased stroke volume

1. Aortic regurgitation
2. Thyrotoxicosis
3. Hyperkinetic heart syndrome
4. Fever
5. Arteriovenous fistula
6. Patent ductus arteriosus

II. Systolic and diastolic hypertension (increased peripheral vascular resistance)

A. Renal (cases mentioned in table above)

B. Endocrine (cases mentioned in table above)

C. Neurogenic (cases mentioned in table above)

D. Miscellaneous

1. Coarctation of aorta
2. Increased intravascular volume (excessive transfusion, polycytemia vera)
3. Polyarteriitis nodosa
4. Hypercalciemia

E. Unknown aethiology

1. Essential hypertension
2. Toxemia of pregnancy
3. Acute intermittent porphyria

2. Level of Blood Pressure

Classification of High Blood Pressure (The VI report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI)).

Category	Systolic Blood Pressure (mm Hg)	Diastolic Blood Pressure (mm Hg)
Optimal	<120	<80
Normal	<130	<85
High normal	130-139	85-89
Degree 1 hypertension	140-159	90-99
Degree 2 hypertension	160-179	100-110
Degree 3 hypertension	180-209	110-119
Degree 4 hypertension	≤ 210	≥120

4. Stage

Target organs involvement

Organs	Stage 1	Stage 2 (affection of target organs without clinical symptoms)	Stage 3 (clinical symptoms relating target organs)
Heart	-	Left ventricle hypertrophy (ECG, Ultrasonic, X-ray)	Myocardial infarction Stenocardia Coronary vessels revascularization Congestive cardiac failure
Kidneys	-	Microalbuminuria (???)	Proteinuria, renal failure (???) Nephropathia related to diabetus mellitus
Vessels	-	Ultrasonic or X-ray signs of aorta dissection; atheromatic plaques of aa. Carotes, iliacae, femorales, aorta	Clinical symptoms related to these cases
Retina	-	Angiopathia	Haemorrhages or excudation, oedema of сосок (???) n.opticus (high grade retinopathia)
Nervous system	-		Ischemic or haemorrhagic stroke, transient blood flow disturbances

4. Risk of cardiovascular complications

Pathogenetic classifications: see Natural course of the disease

II. Epidemiology

Prevalence of arterial hypertension

In average, elevation of BP are revealed in 25% of adults. In USA its is revealed in 45 million of people.

According to the results of Framingham Study (white suburban population) nearly ½ have pressures greater than 140/90; and over 160/95 – about 1/5 population.

Age dependence:

- The proportion of individuals who are hypertensive increases with age: before 20 years old – 10%; 20-29 years old – 10%; over 60 – about 50%.

Race dependence:

- AH prevalence is greater in blacks than in whites; AH course is more severe in blacks than in whites.

Complications, morbidity and mortality:

AH is associated with high rate of cardiovascular complications, leading to high mortality. Thus, in Russia every second person is dying from the diseases of cardiovascular system. Direct links exist between BP level and cerebral insult rate. Although, as it was shown in a prospective follow-up of 18,700 physicians (USA), even borderline elevations of systolic blood pressure (140–159 mm Hg) were associated with a 42% increase in strokes and a 56% increase in cardiovascular deaths.

AH is also associated with atherosclerosis, IHD and cardiac failure development.

AH and its control: only 25% of AH patients in USA are controlled to a goal of normotension. Due to more successful treatment of AH in USA, the mortality rates for stroke and coronary heart disease, the major complications of hypertension, have declined 40–60% over the past 2–3 decades.

Secondary AH: the prevalence of different types of SAH depends on the cause of hypertension, nature of population and how extensive the evaluation is (in specialized clinics SAHs are more often revealed):

Diagnosis	General population,%	Specialized clinics, %
Essential	92-94	65-85
Renal: Renoparenchymal Renovascular	 2-3 1-2	 4-5 4-16
Endocrine Primary aldosteronism Cushing syndrome Pheochromacytoma Oral contraceptive-induced	 0.3 <0.1 <0.1 2-4	 0.5-12 0.2 0.2 1-2
Miscellaneous	0.2	1

III. Morhology, Aethiology and Pathogenesis:

Morphology

Remodeling of resistive vessels and myocardium (proliferation and migration of smooth muscular cells, myocardium hypertrophy and fibrosis) , small arteries and arterioles hyalinosis. These changes are due to the influence of tissue Angiotensin-2 on AT-1 receptors. Nephrosclerosis (primary).

Primary=Essential hypertension is a multifactorial disease, in which both intrinsic (including genetic ones) and environmental factors are significant.

Secondary=symptomatic hypertension: aethiology depends on the aethiology of the disease causing AH.

1. Aethiology of essential hypertension:

1.1. Hereditary factors:

In 80% of EH patients cases of EH in families are revealed. In healthy relatives of EH patients high rate of biological defects, predisposing to the onset of the diseases, are found:

- instability of vascular tone regulation
- high threshold of salt-sensitivity
- dyslipoproteidemia
- disturbances of univalent kations transport through the plasmatic membrane
- phenilalanin metabolism changes, leading to sympathetic nervous system hyperfunction

Confirmed genetic factors

- changes of Renin gene structure (13 chromosome)
- presence of different types of ACE and ACE receptors
- in mice other loci influencing BP level were found: (HYP-1 locus stimulates aldosterone secretion; HYP-2 – controls vascular smooth muscles contraction as a response to cobalt)
- proved links between AH development and HLA-system.
- higher prevalence and more severe course of EH in USA negroids (probably due to higher sodium retain)

Role of genetic factors had been proved in different studies (including studies of relatives, twins and adopted children). In general, genetic factors contribute about 30 per cent to blood pressure variance, when blood pressure is measured under screening conditions.

1.2. Risk factors

Genetic predisposition is realized in persons having risk factors.

Risk factors are following:

1.2.1. Genetic ones (can't be removed):

- see 1.1.
- age and gender (in 30-45 years old higher prevalence of the disease is revealed in men; over 45 – in women)

1.2.2. Removable risk factors (elimination of these is included into the EH treatment program):

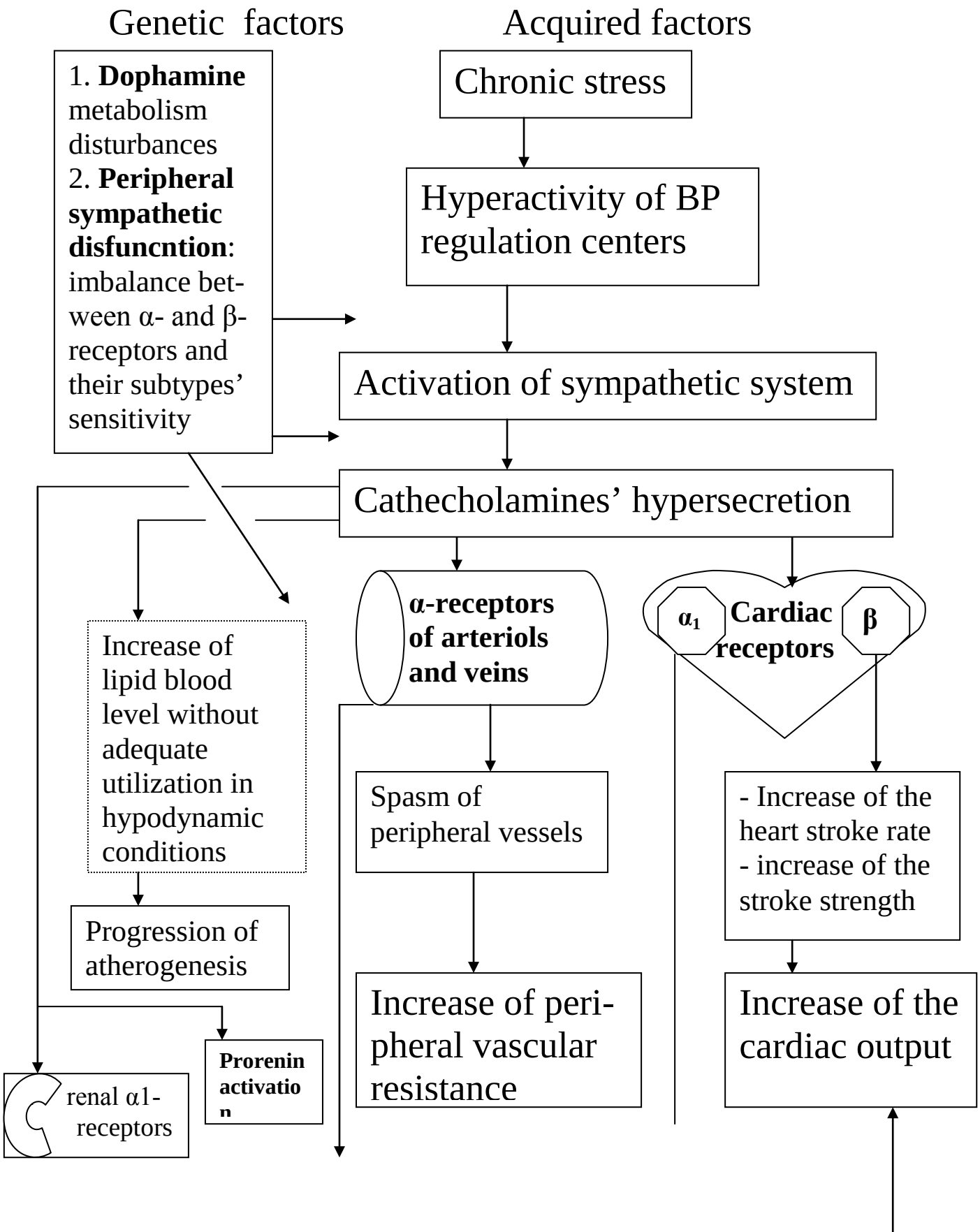
- obesity
- hypodynamia
- stress (including unrealized anger)
- disturbances of circadian rhytmes
- smoking
- alcohol intake
- salt intake

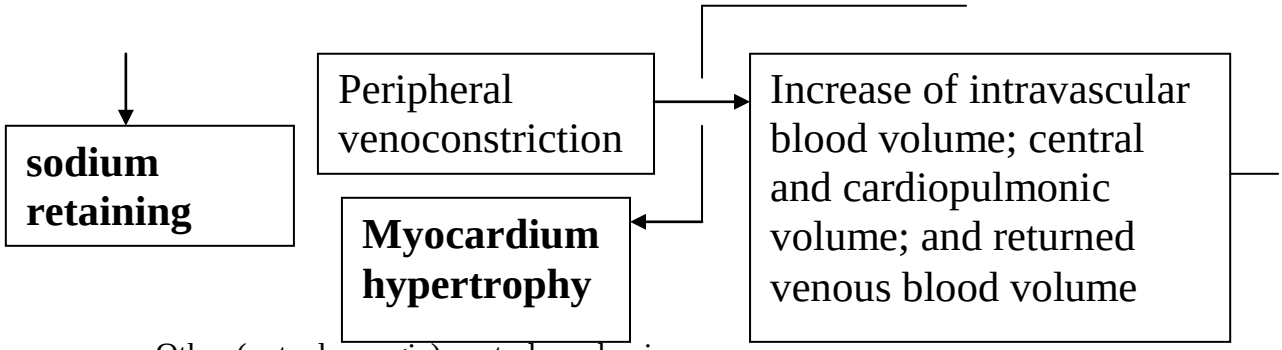
Thus, all the factors, determining modern urban lifestyle, play patogenetic role in EH development. In several cases it has been shown that when individuals migrate to an urban environment blood pressure rises; from the other hand, when Australian aborigines return from an urban to a rural mode of life a substantial fall in blood pressure is associated with reduced body mass and alcohol intake, and with improved glucose tolerance and serum lipids.

2. Pathogenesis of EH.

2.1. Central mechanisms

During the long-time period in Russia and Soviet Union the role of central mechanisms (central regulation disturbances, caused by direct influence of emotional factor) was considered to be the most important (G.Lung, A.Myasnikov). And, even now, when this point of view is not overestimated, central regulation disturbances are thought to play important role in EH pathogenesis (chronic job strain, emotional stress, unrealized muscular reaction on stress, where catecholamines' secretion is not accompanied by growth of muscular activity).


Genetic factors
Acquired factors
1. **Dophamine** metabolism disturbances
2. **Peripheral sympathetic disfuncntion**: imbalance between α- and β-receptors and their subtypes' sensitivity
Chronic stress
Hyperactivity of BP regulation centers
Activation of sympathetic system
Cathecholamines' hypersecretion
α-receptors of arteriols and veins
α_1 **Cardiac receptors** β
Increase of lipid blood level without adequate utilization in hypodynamic conditions
Progression of atherogenesis
Spasm of peripheral vessels
- Increase of the heart stroke rate
- increase of the stroke strength
Increase of peripheral vascular resistance
Increase of the cardiac output
renal α1-receptors
Prorenin activation



Other (not adrenergic) central mechanisms:

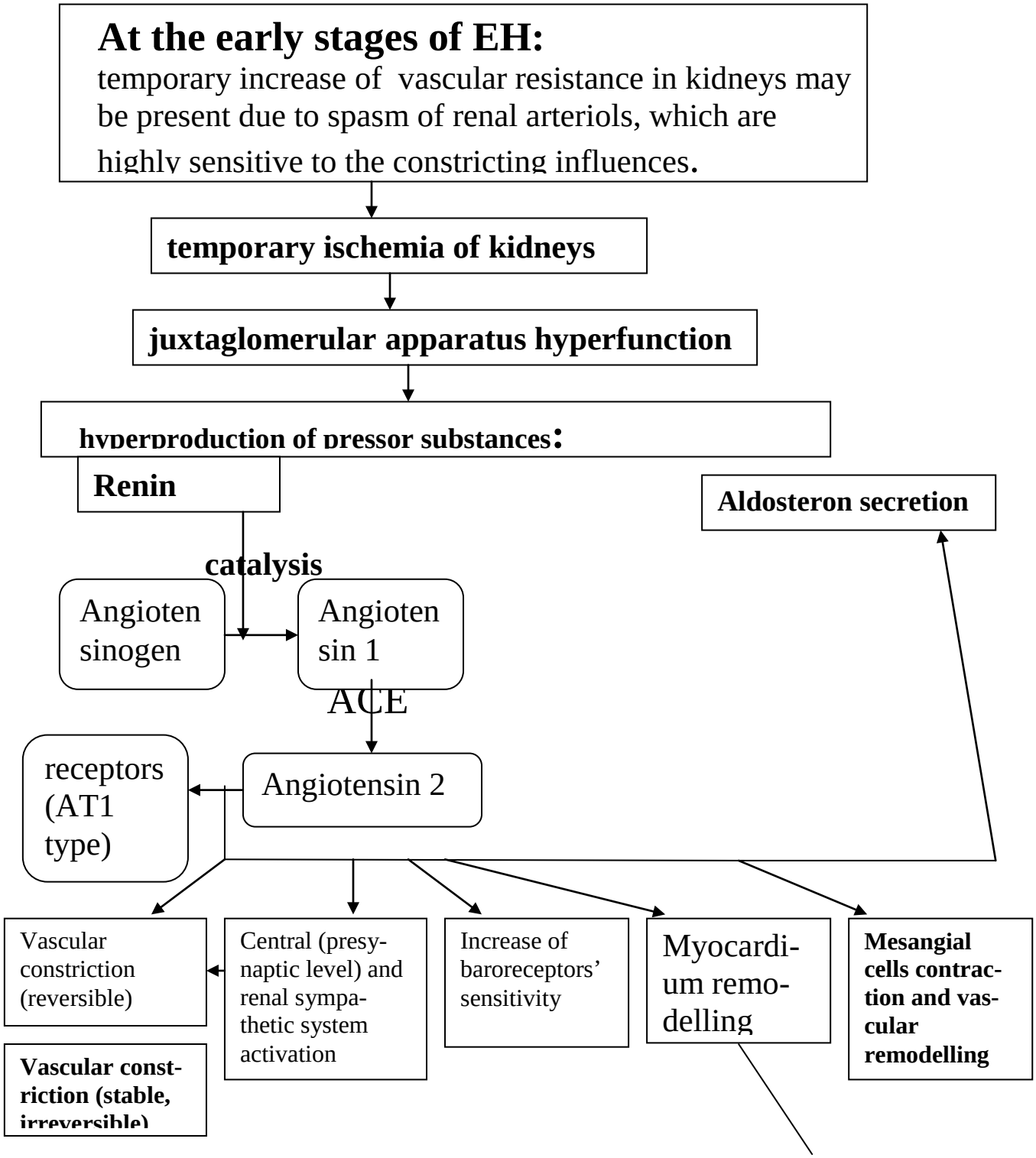
- **Andidiuretic hormone (ADH):** stimulation of adrenals' mineralcorticoid function; stimulation of water reabsorbtion in kidneys; causes oedema and narrowing of the vessels' walls and increase of vessels reactivity to catecholamines.
- **Opiates** (endorphins, enkephalines)

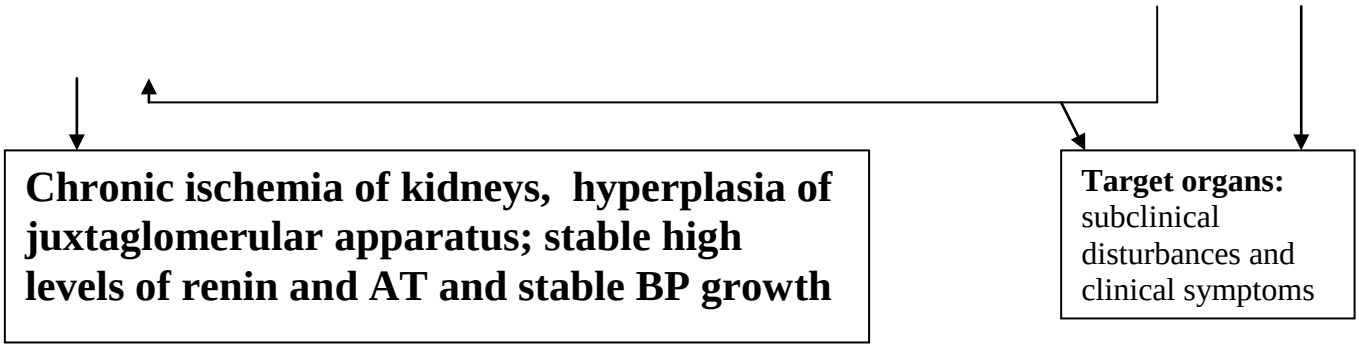
Central mechanisms dominate in the early stages of essential hypertension (especially in young people).

What is typical for this period:

- **labile mild hypertension with marked BP fluctuations**
- **increase of cardiac output**
- **tachycardia**
- **as a rule, peripheral vascular resistance doesn't change significantly (a short-time increase of vascular resistance in kidneys may be present)**

Renal mechanisms. System “renin-angiotensin-aldosteron”.





Endothelium and EH

Imbalance between secretion of vasodilators and vasoconstrictors by endothelial cells. The most important are:

- endothelin – the most active pressor peptide
- nitric oxide – vasodilator
- vascular RAS

Vascular renin-angiotensin system

First of all, determines **long-time action**:

- myocardium hypertrophy
- vascular remodeling
- intraglomerular hypertension,

while the **circulating (renal) RAS is responsible for short-time effects**:

- aldosterone secretion stimulation
- retaining of sodium and water
- vascular constriction
- positive chronotropic and arythmogenic action

Salt-dependent mechanisms:

Angiotensin-2: stimulation of salt and water consumption due to central effects (increase of "salt appetite")

Aldosteron:

- increase of sodium reabsorbtion in canals of kidneys and in gut
- increase of sodium in plasma leads to the increase of circulating fluids (sodium-volume-dependent mechanism)
- vasopressin secretion
- sodium retention in walls of arteriols and increase of their sensitivity to pressor factors
- diffusion of calcium into the cell (together with sodium, in depolarization phase), leading to the smooth muscles hypertonus and thus to further increase of vascular resistance

Intracellular sodium and calcium metabolism:

- abnormalities in Na+-K+ exchange and other Na+ transport mechanisms
- intracellular Na+ is elevated in blood cells and other tissues in essential hypertension.
- An increase in intracellular Na+ may lead to increased intracellular Ca2+ concentrations as a result of facilitated exchange.
- This could explain the increase in vascular smooth muscle tone that is characteristic of established hypertension.

Decrease of depressor mechanisms:

Renal:

- prostaglandin E2α
- prostaglandin D
- prostaglandin A
- prostacyclin J2

Prostoglandins are formed from arachidonic acid by interstitium cells and собирательные tubules epitheliocytes in сосочки пирамид.

Prostoglandins improve renal blood circulation, inhibit sodium and chloride reabsorbtion from ascendant part of Genle loop, reduce antidiuretic hormone possibility to improve permeability of собирательных трубок for water. Prostoglandins participate in diuretic and natriuretic action of kallikrein.

- phospholypid peptide – renin inhibitor
- depression if kinins system

Vascular

- Atrial natriuretic peptide - 1000 times more active than Furosemid. Leads to transient improvement of renal flow, blocks renal vasoconstriction and indirectly (through improvement of blood flow to medullar zone of kidneys) causes natriuresis. Some authors report about its possibility to reduce basal renin secretion through renal dophaminergic system.

- baroreceptors synocarotid zone and aorta: stimulation of baroreceptors in case of BP increase, which causes (through stimulation of respective zones of brain) to reducing of the heart work, vasodilatation and thus decrease of BP.

Involvement of RAS, aldosterone and, especially, impairment of depressor mechanisms, lead to chronic, stable increase of BP. Remodelling of heart and vascular system cause changes of the target organs, including heart, and appearance of clinical symptoms, caused by the affection of the target organs.

Removable risk factors in EH patogenesis:

Obesity:

- increase of total body fluid
- increase of natriuretic factor secretion
- hyperinsulinemia (especially in case of masculine-type=trunk obesity), which stimulates sympathetic system activity
- trend to sodium retaining

Hypodinamia

- development of obesity
- intensive muscular work leads to sodium loss during perspiration, utilization of lipids, growth of high density lipoproteins level, metabolits, forming during muscular work in tissues lead to vasodilatation and hypotension.

Stress: see above. Similar effect have conditions, where hypermobilization is necessary: exams, activity, connected with high psychological concentration and/or struggle situations at the working place, high responsibility, excessive information; the extreme situation is war. All these factors are sympathetic system activators.

High sodium level in food or changing of sodium/potassium ratio with the increase of sodium or decrease of potassium

Smoking

- sympathetic system activation
- growth of cadmium concentration in body

Alcohol

- taking in 6 or more standard doses of alcohol (1 dose=15 ml of pure ethanol)

Other risk factors (which are not fully confirmed from the points of view of evidence-based medicine):

- work connected with contact with cadmium
- work connected with contact with plumbum, noise, vibration
- disturbance of annual and circadian rhythmes (night working, changing of climate, work in conditions of polar winter and polar summer)

The role of following factors is been discussed:

- cervical spondilosis (in 30-40% of EH patients, its active treatment leads to lowering of BP)
- concentrated tee or coffee (coffein leads to increase of renin level)
- oral contraceptives (symptomatic AH)

Secondary=symptomatic hypertension are connected with disturbances of one or more above mentioned mechanisms. For example:

- Pheochromacytoma – excessive catecholamines secretion by tumor
- Konn syndrome: excessive aldosterone secretion by tumor
- Diseases of kidneys' parenchyme: RAS involvement and impairment of renal depressing mechanisms
- Renovascular: RAS activation
- Etc.

From the point of view of pathogenesis, secondary AHs are either hypertrophy of one or more pressor systems (tumor of the hypophysis, adrenals, brain), or loss of one or more depressor functions (pyelonephritis, interstitial nephritis, aorta atherosclerosis) or compensatory reaction in case of lack of vitally important organs' blood supply (vasorenal, cerebral in case of cerebral ischemia).

Target organs in AH: pathogenesis and clinical signs

All the clinical sighs of AH is due to the reaction of the target organs on the hypertensive syndrom. These are caused by affection of heart and vasculature (reaction on high BP and remodeling processes).

Target organs are:

- Heart
- Brain
- Retina
- Kidneys
- Vessels

Heart:

- Left ventricle hypertrophy (hypertrophic heart remodeling: growth of size of cardiomyocytes; increase, sometimes 3-4 times, of heart mass)
- Reduction of intramural blood flow due to pressure of hyperthrophic remodeled muscle on small subendocardial branches of coronary arteries
- Myocardial fibrosis(due to chronic hypoxia).
- Impairment of diastolic relaxation of rigid remodeled myocardium.

Clinical signs of:

LV hypertrophy (its presence is associated with several-fold in cardiovascular complications risk)

- *Objective:* heaving apex beat without changing of the left border of relative cardiac dullness

- *X-ray:* round cardiac apex
- *Ultrasonic:* LV thickness more than 10-12 mm; impairment of diastolic function of the heart due to hyperthrophy and calcium increase in cardiomyocytes' cytoplasm (at the early stages systolic function may be either normal or increased); septum hyperthrophia
- *ECG-signs of left ventricular hypertrophy:*

*shift of the electric axis to the left (α from 0 to -30)
* shift of the equation zone (??? -R=S) to the right (V2)
* Abnormally high R V5-V6 (≥25 mm)
* Abnormally deep SV1-V2 (≥25 mm)
* RV6+SV1≥35 mm in aged and 45 mm in young
* relative coronary insufficiency: changes of T and ST (left ventricle strain – downsloping ST and asymmetrically inverted T in left chest leads, I, II, aVL; these changes reflect intramural blood flow reducing in hypertrophycally remodeled myocardium)
* Ventricular activation time > 0.05 s in V5–6.
* QRS interval may be prolonged over 0.1 s.

LVH in patients with different heart position:

II. Frontal Plane Leads:

A. Horizontal Heart: R wave of 11 mm or more in aVL (except when frontal plane axis is superior to –30°; VAT, ORS interval, and ST–T changes as described for precordial leads. R1 + S3 > 26 mm; pattern in I similar to aVL.

B. Vertical Heart: R wave of over 20 mm in aVF; VAT, QRS interval, and ST–T changes as described for precordial leads. Unless confirmed by precordial leads, this pattern in aVF is not diagnostic of left ventricular hypertrophy (since right ventricular hypertrophy can give a similar pattern in aVF).

Minimal Criteria

R in aVL greater than 11 mm; or R in V5–6 greater than 27 ram; or S in V1 + R in V5–6 greater than 35 mm.

At the later stages of AH signs of LV dilatation are present:

- *Objective:* moving of the apex beat and left border of relative cardiac dullness to the left; apex beat may be diffused (thrusting)
- *X-ray and Ultrasonic signs* of LV dilatation; systolic function is impaired.

Clinical symptoms: stenocardia; infarction, cardiac failure.

Vessels

- accentuated aortic closure sound
- presence of murmurs (due to atherosclerosis changes: aortic stenosis or insufficiency; murmurs on carotids, iliac arteries etc)
- X-ray: changes of aorta configuration
- Ultrasonic examination of vessels: atherosclerotic plaques revealed.

Retina:

Its changes causes typical complains in AH patients: flying black dots; vision disturbances may be present.

Stages of angio- and retinopathy:

1. Angiopathy with dominating functional changes:
- narrowing of arteriols (transient or stable)
- dilatation and tortuosity of veins
- Salus-Gune symptom: depression of vein by arteria at the AV crossing place

2. Angiosclerosis: dominating of organic changes:
- "copper wire" syndrome (veins dilatation); arteriols hyalinosis and lipids retention in walls, reddish color due to the fact that blood can be seen)
- later – "silver wire" arterial wall is more dense due to the organic changes

- sclerosis of arteriols

3. Retinopathia: affection of retina itself
- hemorrhages
- white spots of lipid infiltration
- oedema of соска of n.opticus
- in severe cases: отслойка сетчатки
- retina infarctions

For more detailed evaluation of retina condition Keith-Wagener-Barker classification can be used

degree	Hypertension					arteriosclerosis	
	Arterioles		retina				
	General narrow-ing AV ratio*	Focal spasm**	Haemor-rhages	Exccu-dates	Papil-ledema	Arteriolar light reflex	AV cros-sing*** defects
Normal	3:4	1:1	0	0	0	Fine yellow line, red blood column	0
Grade I	1:2	1:1	0	0	0	Broadened yellow line, red blood column	Mild depression of vein
Grade II	1:3	2:3	0	0	0	Broad yellow line, “copper wire”, blood column not visible	Depression or humping of vein
Grade III	1:4	1:3	+	+	0	Broad white line, “silver wire”, blood column not visible	Right-angle deviation, tapering and disappearance of vein under arteriole; distal dilatation of vein
Grade IV	Fine, fibrous cords	Obliter ation of distal flow	+	+	+	Fibrous cords, blood column not visible	Same as grade III

5. Brain:
- As usual, headache (frequently in occipital region) is present
- Stroke (haemorrhagic)
- Transient attacks

Also, hypertension is associated with a higher incidence of subsequent dementia, both the vascular and the Alzheimer types.

5. Kidneys:
Morphologically: hyalinosis, then – sclerosis of arteriols.
Clinically: at the early stages – microalbuminuria, later – proteinuria; BP stabilizes at high levels due to more active involvement of renal mechanism; at final stages – chronic renal failure (neprosclerosis).

Case taking and examination of patient with AH
Goals:
1. Differentiation between essential and symptomatic AH
2. Evaluation of target organs affection grade

3. Evaluation of AH severity (BL level)
4. Evaluation of cardiovascular complications risk factors and clinical conditions, influencing prognosis and treatment of AH and determining risk grade.

Complains

1. *Reflecting brain involvement:*
- headache (most common – in the occipital region), which is usually associated with BP increase; the pain is more severe in the morning and while lying in bed
- neurotic disturbances (irritation, easy fatigability, dizziness, sleep disorders, unstable mood)
- episodes of weakness and dizziness due to transient cerebral ishemia
- symptoms of complications (stroke, transient disturbances of cerebral blood flow)

2. Symptoms, reflecting eye affection: vision disturbances, flying black dots; in severe cases – loss of vision may be present (central retinal artery thrombosis)

3. Heart involvement:
- non-specific pain sensation in left side (more often in the apex zone), appearing after emotional stress, which are not related to physical exertion and which are not relieved by nitrates. This pain is related to lowering of impulses perceptibility threshold.
- non-specific pain appearing during BP rise and relieving after BP lowering (sensation of pressure)
- stenocardic pain
- infarction pain
- palpitation
- congestive heart failure symptoms

5. Vessels involvement:
- nasal bleedings (often recurrent bleedings during BP rises)
- aorta dissection or leaking aneurism
- signs of atherosclerosis of aa. iliacae et femoralis may be present

6. In case of symptomatic AH – presence of signs, related to the main disease

Case history:

An. Morbi:
- AH course in patient: age of the onset of the disease, level of BP rise (dynamics from the beginning of the disease to the present time, progression of the disease in time), systolic/diastolic BP ratio, stability or lability of BP, meteotropism, presence of cerebral symptoms (dizziness, black dots, typical headache); presence and symptoms of crises; presence of symptoms typical for secondary AH.
- treatment: regular or unregular drugs use, character of treatment and its efficacy (controlled or undercontrolled AH), side effects of the used drugs
- clinical symptoms reflecting the affection of the target organs
- clinical symptoms, reflecting presence of metabolic disorders (obesity, diabetus mellitus, podagra, disturbances of lipid metabolism)
- intake of drugs which can lead to BP rise (oral contraceptives, non-steroid antiiflammatory drugs, cocain, amphethamin, erythropoietin, cyclosporine, steroids)

Anamnesis vitae
- family history (AH, diabetus mellitus, IHD, strokes or transient cerebral attacks, diseases of kidneys, lipids metabolism disturbances)
- way of life: risk factors, salt appetites, growth of weight beginning from the beginning of the adult life

- personal and psychological peculiarities, marital life, level of education, situation at the working place, social and economic status (these factors also may influence the course and outcome of AH)

Objective examination

1. **BP measuring**

- Blood pressure should be measured with a well-calibrated sphygmomanometer with a correctly sized cuff (bladder width approximately 20% greater than arm diameter), after the patient has been resting comfortably in the sitting or supine position.
- BP is measured after 5 minutes of rest, before use of sympathomimetics (including inhaled, eye or nasal drops), smoking (15 minutes before BP measuring), coffee (1 hour before)

- for BP evaluation it must be measured **3 times** with no less than **1 min interval**; if the difference is more than 5 mm Hg, additional measurements should be performed. For the AH diagnosis, 3 measurements with no less than 1 week intervals should be performed

- **Indications for ambulatory 24-hour blood pressure monitoring** (taking into attention its cost – in USA -$200.00–$300.00): suspected WCH, borderline hypertension, variability of BP during several office visits; resistant hypertension; possible treatment-related hypotensive symptoms.

3. **WCH (white coat hypertension) or isolated clinical hypertension** is caused by worrying reaction connected with BP measurement. BP rise may be 20-30 mm Hg higher than real BP level. It occurs in 20% of patients, more often women, during the 1st BP measurement; gradual decrease of BP is observed when BP is measured with 2-3 minutes intervals; no target organs involvement is observed; BP monitoring results are normal; BP is also normal if the patient measures it himself at home. However, discussion concerning the influence of WCH on cardiovascular complications risk is still continuing. Thus, long-time observation should take place if WHC is revealed.

- **BP changing during the day:** the highest levels are observed usually at 6-7 in the morning and 17-18 in the evening; minimal BP is detected at 2-4 at night. According to the ratio daily BP/nightly BP all patients are divided to **dippers** (adequate BP lowering at night); **non-dippers** (BP lowering is insignificant); **over-dippers** (excessive BP lowering) and **night-peakers** (at night BP is higher). The last group (20%) have the highest complications risk.

Other objective signs important in patient with AH:

1. Body mass index: weight (kg)/(height (m))^2
2. Cardiovascular system (including pulsations of peripheral arteries, murmurs on these vessels, changes of wall of the arteries – more dense wall due to atherosclerosis; heart borders, heart tones and their accents, heart murmurs; presence of signs of heart failure etc)
3. Presence of signs, typical for symptomatic AH.

Laboratory and instrumental methods

Obligatory analyses:

1. Urine analysis – 3 times or more; in case of renoparenhyme AH protein, casts, RBC (glomerulo-nephritis) or WBC, bacteria (pyelonephritis) may be revealed.
2. Biochemical blood analysis (venous blood): potassium, glucose (after night fasting), creatinin, cholesterol. Lypid spectrum investigation (lipoproteins of high, low and very low density, triglycerids, atherogenity coefficient) is strongly recommended (indications

to medicamentous treatment of atherosclerosis, which can strongly influence on risk of cardiovascular complications development).
3. ECG
4. Ophthalmoscopy
5. X-ray of chest
6. Ultrasonic examination of kidneys
7. Ultrasonic heart examination is strongly recommended
8. Haemogram as a part of obligatory clinical examination of all admitted patients.
9. Reberg test or complex functional investigation of kidneys including filtration, reabsorbion, daily proteinuria etc; Zimnitsky test (concentration function of kidneys); bacteriological investigation of urine (3 times or more) with investigation of sensitivity to antibiotics in case of positive result

Recommended:
- system haemodynamic investigation (see pathogenetic AH classification) – in order to improve treatment

If after these investigation secondary AH is suspected, additional investigations are to be performed:

Type of hypertension	Used methods
Renal	
Renoparenchymatous	Excretory urogram, scintigraphy, radioisotope renogram, biopsy
Renovascular	Doppler of renal arteries; excretory urogram, radioisotope renogram (vascular segment of the curve); CT in vascular regimen, renal arteriograms; if nephroptosis is suspected – ultrasonic kidneys investigation in lying and standing position; urogram
Obstructive	Excretory urograms
Endocrine	
Konn syndrome	Aldosteron level (increase); plasma renin level (decrease); CT of adrenals
Cushing syndrome	Serum cortizole, urine 17-hydroxicorticosterone; hydrocortisone test, CT of adrenals
Pheochromacytoma	Catecholamines in urine; blood glucose during the crisis; CT of adrenals and suspected zones (paraaortic ganglii etc)
Others	
Haemodynamic (aorta coarctation, aortitis)	Aortography
Central	Neurological examination
Drug-related	Case history

Differential diagnosis of EH and SAHs:

Symptom	EH	SH

Complains		
Cerebral symptoms	Typical	Usually not present, good tolerance even of high BP
Factors causing AH exacerbations	Emotional stress, meteotropism	Exacerbation of the main disease (pyelonephritis, glomerulonephritis etc)
Systolic/Diastolic BP	Both	Diastolic more
Level of BP	Mild or moderate	Severe; malign hypertensive syndrome
Crises	Typical	Not typical (except paroxysmal pheochromacytoma)
Case history		
Onset of the disease (age)	30-50	Earlier than 30 or older than 50
BP at the time of the onset	Labile BP just after the onset with spontaneous BP normalization (dominating of central mechanisms); crises	Stable BP; onset with high BP level; crises not present
BP changes in time	Gradual increase of BP with a trend to further stabilization at the high levels (RAS involve-ment; gradual increase of the disease severity); complications at the late stages	Stable BP (except paroxysmal pheochromacytoma); complications may be present at the early stages
Reaction to therapy	At the beginning – good control (by changing of way of life of or monoterapy); uncontrolled disease only at the late stages	Difficulties in disease control even in case of good patient's compliance; use of drugs combinations from the beginning of the disease
Life history		
Hereditary factors	Typical: AH family history (80%, more often – from mother's side)	AH family history not present
Risk factors	Present	Not typical
Salt appetites	High	Normal
Psychological factors (job strain etc)	Present	Not significant
Complains, history and objective signs, which are typical for diseases, which are accompanied by symptomatic AH	Not present	Typical

Signs of different symptomatic AHs:

Disease	Complains	History	Objective; instrumental
Renal			

Parenchymal			
Glomerulo-nephritis	In clinically marked cases -oedemas, hematuria; in latent cases – only complains related to AH; back pain (bilateral) may be present	Early age of onset (often - childhood), onset after “cold” situations or Streptococcus infection; changes in urinanalysis (RBC, casts, protein) may not be found if urinanalysis is not performed	Urinanalysis (RBC, casts, protein); Reberg test (filtration), daily proteinuria; diagnosis is proved by renal biopsy.
Pyelonephritis	Back pain (more intensive at one side); disuria may be present a result of cystitis (ascending infection); episodes of increase of body temperature; appearance of all these symptoms coincides with BP rise	Same episodes in case history; coinciding of exacerbations with BP rise	Urinanalysis (WBC, bacteria); urine concentration disturbances may be present; positive results of bacteriological urine examination; changes revealed by i.v.pyelograms and (only as a suspecting factor – ultrasonic inv-n)
Vasorenal			
fibromuscular displa-sia;stenosis or hypopla-sia or other inborn ano-malities of a.renalis and its branches	No signs except severe BP with stable high diastolic pressure		Bruits revealed 2sm below and lateral the navel; at the back side – at the place of junction between 12 rib and vertebrum; at the i.v.pyelograms and renograms – the delay of contrast appearance at the affected kidney; Doppler, CT in vascular regimen and aortography prove the diagnosis
Atherosclerosis (plaque in the begin-ning of a.renalis)	Complains and history, confirming presence of atherosclerosis; more often in men		Same picture; plaque may be revealed by ultrasonic investigation and aortography; lipid spectrum changes
Vasculites (Takayasu)	Subfebrile fever; headache; syn-copes; arthralgia; signs of extre-mities ischemia; weight loss	More often in young women; usually the history is not long; such complications as blindness or ischemic strokes may be due to affection of a.carotis	Pulse weakness at one of the hands (affectted); BP difference at the hands is more than 10 mm Hg; systolic bruits on aorta or a.sub-clavia; Doppler

			and aortographic signs
Tumor, lymphatic nodes, compressing a.renalis: signs of tumor; ultrasonic and CT confirmation			
Endocrine			
Pheochromacytoma (paroxysm-mal form)	Hypertensive crises with chills, trembling, weakness, dizzi-ness, cold sensation; sensation of pulsation in whole body; pallor; tachypnoe; BP rise up to 300/160; aggressiveness; quick normalization of BP with sensation of warmness; the face becomes reddish		Cathecholamines in blood and/or urine; CT of adre-nals; hypergly-cemia during the paroxysm
Konn syndrome	Muscular weakness; paresthesias; cramps		Hypopotassiemia; high circulating blood volume; high extracellular fluid volume; left ventricle hyper-trophy usually is not present
Cushing syndrome			
Coarctation of aorta			
Aorta valve insufficience			
Isolated systolic hy-pertension	Aged patients with atherosclerosis; hypertension is due to rigid aorta and main arteries; rise of systolic BP and low or normal diastolic BP; signs of atherosclerosis		

Orienting signs of symptomatic AH:

- onset at age before 20 or over 50 years old
- acute onset and/or stable BP rise
- moderate or severe AH
- malign AH syndrome (rapid development of severe target organs affection; high and stable BP rise with high diastolic BP)
- onset with crise
- crises with signs of activation of sympathetic system
- relative resistance to traditional therapy
- kidneys disease in case history; onset during pregnancy
- presence of even minimal urinanalysis changes (cells, casts, proteinuria) at the time of AH diagnosis statement
- diabetus mellitus
- marked muscular weakness
- hyperthyreosis
- climacteric period
- Cushingoid features
- Suspection of acromegalia
- Big or small difference between systolic and diastolic BP
- Marked bradycardia
- Hypothrophy of lower trunk
- Clinical picture of a.carotis stenosis
- Cranial trauma; meningoencephalitis or other neurological disease in case history

Age and AH onset

Age	Type of AH	Disease
5-15 years old	Renoparenchymal	Glomerulonephritis
	Haemodynamic	Aorta coarctation
	Endocrine	Pheochromacytoma, Konn syndrome
	Neurogenic	
	Severe hereditary AH	
15-30	Neurocirculatory dystonia (hypertensive type)	
30-50	Essential AH	
Over 50	renoparenchymal	Loss of renal depressive functions (due to pyelonephritis; tubulointerstitional nephritis; diabetus mellitus)
	Isolated systolic AH	
	Combination of variants: picture of isolated systolic+renoparenchymal AH combination is almost similar to that of essential one.	

Natural history. Types. Complications. Crises.

As it was mentioned before, EH usually starts as a labile, mild, caused by predominantly central mechanisms. Sometimes patient even can't fix the time of the disease onset (so, in order to differentiate between EH and SH the attention in case taking should be paid to reminding of this period). Later, when RAS involvement, and, especially loss of depression functions takes place, AH becomes stable and BP – high. At that time complications usually develop.

Pathogenetic variants of EH course

Haemodynamics changes

Hyperkinetic: growth of cardiac index (usually at the onset of the disease) without significant changes of peripheral vascular resistance.

Hypokinetic: growth of peripheral vascular resistance (usually at the later stages after RAS involvement and depressive mechanisms failure)

Eukinetic: proportional growth of both indices

From point of view of main pathogenetic mechanisms

Low-renin EH (volume-salt dependent) approximately 20% of EH; in USA - more frequently in black patients; in whites (in Russia) – in women in menopausal and postmenopausal periods. Main features (in white postmenopausal and menopausal women):

- BP increase is associated with water and salt intake
- Oedema of lids, puffiness of face, paresthesias and numbness of fingers
- Rare – myocardium infarction and stroke

are sodium retention and low plasma renin activity.

- low plasma renin and sodium retention (also in black Americans)

Differential diagnosis: Konn syndrome

High-renin EH (angiotensin-dependent)– 15% of AH:

- stable high diastolic BP; trend to arteriolar spasms
- severe course with affection of target organs (severe angio- and retinopathy; myocardium infarction, stroke)
- high plasma renin level

Differential diagnosis: renovascular AH; malignant AH
Treatment: combination of
- ACE or sartanes
- Alpha-blockers or prolonged calcium antagonists

If malignant AH is suspected, diuretic administration should be very carefull.

Hyperadrenergic EH

with dominating central mechanisms, more often in young patients; the crises may look like these in pheochromacytoma:
- lability of BP
- marked hyperkinetic type of haemodynamics (increase of stroke volume and minute volume)
- palpitations, sensation of pulsation in a head, reddish face, perspiration, chills, anxiety
- as a rule, plasma renin level is normal

Differential diagnosis: dystonia; thyrotoxicosis, pheochromacytoma and other hyperkinetic conditions.
Recommended treatment: β-blockers

Malignant AH syndrome: according to WHO definition, it is rapidly progressing AH, which from morphological point of view is characterized by nectrotizing angiitis with fibrinoid changes, and from clinical one – by high BP, retinal haemorrhages and, sometimes discus oedema, as well as progressive uremia due to secondary affection of kidneys. Malignant AH is not a nosological form; it is defined as a separate condition only due to its extremely severe course with progressive affection of target organs and malign prognosis, so active treatment should be administered.
Epidemiology: more often in middle-aged men (below 45 years old; men:women=7:1)
Classification:
- primary
- secondary (with preceding EH, kidneys diseases – pyelo- and glomerulonephritis; the last one – more often extracapillar; renal vessels affection, periarteriitis nodosa or scleroderma, coarctation of aorta, pheochromacytoma or Konn syndrome, contraceptives use). Variants of syndrome were described in cases of Lithium intoxication and 17-alpha-hydroxilase deficiency.

Pathogenesis
- severe affection of kidneys' arteriols (their ischemia, thrombotic microangiopathia, endoartheriitis and intima smooth muscle cells proliferation)
- these changes lead to RAS activation with hypertrophy and hyperplasia of renin-producu\ing cells and 8-times and higher stable plasma renin increase.
- so, general vascular resistance is becoming very high
- high levels of angiotensin2 and other vasoactive substances (antidiuretic hormone, norepinephrin) causes endothelium affection and its separation from the vascular wall
- adhesion of platelets to the vascular wall defects, causing tromboxan, serotonin and histamine deliberation; so that microangiopatic haemolytic anemia and disseminated intravascular coagulation syndrome are developing
- endothelium changes activate vascular wall remodeling, which leads to further RAS activation and rapid progression of symptoms.

Sodium metabolism in malignant AH:
- marked excretion of sodium in urine
- decrease of sodium plasma level
- hypovolemia

These also stimulate RAS, secretion of ADH and norepinephrine; so, increase of sodium excretion by diuretics may lead to further RAS stimulation and AH progression

Clinical features:

- rapid progression
- BP is extremely high from the onset of the disease (220/130-140 and higher)
- Absence of stages
- Early target organs changes, which are typical for the late stages of EH (discus and retina oedema and haemorrhages, encephalopathy, strokes, kidneys arteriosclerosis and arteriolonecrosis with renal failure development; acute left ventricle failure, haemolytic anemia)
- Inefficacy of traditional treatment
- Letal outcome is frequent and early (1-2 years after first symptoms appearance) if active treatment is not used.

3 signs can be mentioned as malign AH criteria (Arabidze):

- BP higher than 220/130-140 mm Hg
- severe retinopathia with exccudates and haemorrhages
- severe kidneys affection with renal failure

Complications

I. Crises

Definition: sudden BP growth accompanied by appearance or increasing of the severity of complains and clinical signs (cardiovascular, cerebral, nervous). *Prevalence of crises:* is 25-30% of AH patients.

Crises and BP level: BP level, causing crise, depends on individual brain blood flow regulation, so in some patients crise may appear in moderate BP increase, the others don't feel even severe BP rise.

Clinical features of crises:

1. Syndrome of BP increase (headache, flying dots, unpleasant sensation in precordial region)
2. Syndrome of cerebral blood flow changes and cerebral oedema (severe headache, nausea, vomiting, dizziness etc)

Classification of crises (Kushakovski)

Type	
Neuro-autonomic	Sympathetic system activation: anxiety, tremor, agitation, tachycardia, face hyperemia, skin humidity; the crise develops rapidly; usually treatment is effective
Salt-water rela-ted (oedematous)	Sensation of heaviness in head, nausea; Заторможенность, Disorientation in time and space, puffiness of face; tachycardia is not present; slow development of crise with (sometimes) preceding decreased urination volume; slow BP decrease after beginning of treatment
With cramps (hypertensive encephalopathia)	Usually in patients with high BP. May be the outcome of 2 preceding variants (especially oedematous) in case of the delay of treatment. Consciousness disturbances or loss, which is preceded by nausea, vomiting, clonic or tonic cramps. Objective

	examination reveals high BP, congestion (left ventricle type), discus oedema, neurological symptoms. The most dangerous is progressive oedema of brain with вклинивание ствола мозга

II. Stroke.

- *Haemorrhagic:* rupture of Sharkot-Bushar microaneurisms (which are formed in small arteries as a result of morphological changes due to AH), rupture of minimally affected vessels
- *Ishemic*: *trombosis* of vessel, affected by atherosclerosis; brain arteries *embolism* (embols are forming in atrium or ventricle in case IHD or atrial fibrillation)
- Subarachnoid bleeding
- Transient neurological symptoms as a result of brain hypoperfusion due to quick BP fall

III. Other bleedings and haemorrhages

1. Nasal bleeding (rupture of small vessels)
2. Retinal haemorrhages
3. Aorta dissection

IV. Other vascular complications

1. *Microangiopathias:* chronic blood flow disturbances with fibrosis (nephrosclerosis, chronic encephalopathy, retinal angiopathia)

2. macroangiopathia: progression of atherosclerotioc changes of aorta and arteries due to haemodynamic factor (endothelium affection, remodelling) and endocrine peculiarities typical for AH (increase of insuline and cathecholamines). Progression of ischemic heart disease and ischemic disease of lower extremities, atheromatic plaques in aa.renalis with vasorenal mechanism of AH development.

V. Cardiac failure (chronic or acute): disturbances of contractility due to haemodynamic overload and heart fibrosis. IHD presence and rhythm disorders accelerate development of cardiac failure.

Prognosis and outcomes

Factors, indicating an adverse prognosis in AH:

1. Black race
2. Youth
3. Male
4. Persistent diastolic pressure over 115 mm Hg
5. Smoking
6. Diabetus mellitus
7. Hypercholesterolemia
8. Obesity
9. Evidence of target organs damage

A. Cardiac:
- enlargement
- ECG changes of ischemic or left ventricular strain
- myocardial infarction
- congestive heart failure

B. Eyes:
- retinal excudates and haemorrhages
- papilledema

C. Renal
- impaired renal fucntion

D. Nervous system

- cerebrovascular accident
10. High-renin hypertension

Modern diagnostic formulas include indication of cardiovascular complications risk grade.

Treatment

Guidelines for management of Hypertension (1999):

1. **In patients with high and very high risk:** immediately beginning of treatment of AH, risk factors and accompanying diseases.
2. **In patients with moderate and low risk:** way of life modification as a first ("zero") step of treatment. Beginning of drug treatment is determined by level of BP after these measurements and level of other risk factors control.
3. **In patient with moderate risk BP** monitoring is possible (weeks-3-6 months); if BP remains higher than 140/90, drugs are used. But, taking into attention heterogeneity of this group, concrete time of drugs administration is stated taking into attention individual picture peculiarities (BP, risk factors etc)
4. In patients with low risk: way of life modification during 6-12 month. Drug administration if BP is 150/95 mm Hg and higher for 6 months.

Way of life modification (non-drug treatment)
1. Is a part of treatment in all patients (also receiving drugs) independently from risk grade.
2. Constructive plan should be worked out, it should include the plan of consultations and long-time observation and be adapted for a certain patient. Modern methods of patient education should be used.
3. Parts of way of life modification:

- smoking cessation	including special treatment
- lowering of body mass	5 kg loss is accompanied by 10% BP lowering; as a first step 5 kg loss is recommended; further strategy is formed individually
- alcohol cessation	Maximal daily intake (but: patients should be oriented on alcohol cessation, preferable drinks shouldn't be discussed): Males – 20-30 g ethanol Females – 10-20 g (equal beer 700ml, vine 250, strong drinks 60) Neurotic subjects – cessation.
- increase of physical activity	Mild or moderate regular activity (walking or swimming 30-45 min 3-4 times a week); intensive activity, connected with tension cause rise of BP
- lowering of salt intake	3-4 g daily (maximum 6)
- complex nutrition changes	Increase of fruits and vegetables, decrease of saturated fats; potassium and magnesium increase in food. Fish (lipid spectrum improvement). Tea and coffe are not recommended
- psychotherapy	Efficacy hadn't been proved from point of

	view of evidence-based medicine. But these methods, however, are recommended to be used.

Antihypertensive drugs classification

I group - diuretics
II group – beta-blockers
III group – alpha-blockers
IV group - ACE
V group – calcium antagonists
VI group – central alpha2-receptors antagonists
1) Guanfacin (estulik)
2) Clonidin (clophelin)
3) Methyldopa (dopegit)
4) Moxidonin
VII Peripheral sympatholytocs
1) Guanetidin (isobarin)
2) Rauvolfia (reserpin)
VIII Direct vasodilators
1) hydralazin
2) Minoxidin
IX AT-receptors antagonists (sartanes): volsartan (diovan), losartan (kosaar), aprovel

Special group:
1) Combined drugs
2) MgSO4
3) Dibasol

Drugs groups

	Positive	Side effects	Dose
Diuretics	Cheep, effective, well tolerated, are proved to prevent complications Special indications: black, climacteric women, systolic AH; sodium-volume-dependent variant (low rennin level)	High doses: hypokaliemia (use of combinations with triamterene); lowering of glucose tolerance; ventricular rhythm disorders; impo-tence; triglyceri-des' level rise	Thiasides – 12.5 mg hydrochlorothiazide (maximum – 25 mg)
Diuretics: indapamid	Direct vasodilator activity which is much higher than diuretic effect itself; prostoglandines E2, J2 synthesis stimulation, influence on Na and Ca cellular metabolism; preventing vessels remodeling; modulating vasoconstrictors (lowering) and vasodilators (increase) effect; antioxidant	Minimal	1.5 - 2.5 mg, retard forms are preferred
Beta-blockers	Safe, cheep, effective as monotherapy and in combinations, suppress plasma renin level, diminish LV hypertrophy	Bronchial spasm; peripheral vascular spasm; lipid spectrum changes towards atherogenigy; lowering	Preferable: selective (atenolol – 50 mg daily; stable effect is reached in 2-4

	Preferrable: In young (less than 50), with tachycardia, supraventricular rhythm disorders and IHD.	of glucose tolerance; rhythm disorders (automatism, conductivity and irritability depression); negative inotrope function of non-selective blockers Contrindications: bradycardia, conductivity disorders, bronchial obstruction, Reinauld syndrome, exacerbation of peptic ulcer, obliteration diseases of lower extremities	weeks) or with sympathomimetic activity (trasikor, visken, cordanum). Modern drugs: **sotalol** – also antiarrhythmic drug, **nebivolol** (prevention of cardiosclerosis after myocar-dium infarct-tion); **carvedilol:** can be used in treatment of congestive heart failure
ACE	Lowering of peripheral vascular resistance; should be used in high-renin hypertension; in elevated diastolic BP; prevents kidneys vasculature remodeling; can be used in case of cardiac failure	Dry cough; angioneurotic oedema Contrindication: bilateral a.renalis stenosis	Captopril (750-150 mg daily; 2-3 times) Enalapril 10-20 daily; 1-2 tims Lysinapril 20 once; Ramipril – 5-10 once; Perinidopril (prestarium4-12 once); cilasapril 2.5-5 once etc
Sartans (AT receptors antagonists)	Same	Doesn't influence on respiratory system	Losartane 25-150 daily; valsartan 80-160 mg daily; ibesartan 150-300 mg daily
Calcium antagonists: Niphedipine; dilthiazem, amlodipin groups	Influence on vascular resistance	Short-time of action: rapid BP fall leads to brain ischemia (and swoons in aged patients) as well as to activation of compensatory mechanisms aimed on further BP rise. Retard- forms: better tolerated (tachycardia, slight oedema of feet)	Niphedipin-retard Amlodipin Dilthiazem As an emergency care short-time of action drugs can be used: Niphedipin 20 mg sublingual + 20 mg per os
Alpha-blockers	Peripheral resistance lowering; safe and effective; Special indications: dislypidemia and lowering of glucose tolerance (where beta-blockers and diuretcs	Orthostasis hypotension	Preferable: retard-forms: prasosin (pratsiol) – 5-10 mg daily; doxasosin

	can't be used)		(cardura – 2-4 mg daily)
Selective imidasolin-I-1 receptors inhibitors (selective clophelin analogues)	Lowering of plasma renin, effective BP control; lowering of cholesterole and triglycerides; positive influence on LV hypertrophy	These effects hadn't been proved in multicentric investigations	Moxidonin (retard-form)

General approaches:

Aim of treatment: maximal control of the disease and minimization of risk of cardiovascular complications and death due to them.

Level of BP that should be reached: normal or at least high normal level – 140/90 (diabetus mellitus – 135/95). Higher BP is associates with higher risk of complications!!! In order to improve the tolerance of BP lowering gradual BP decrease is recommended with 25% initial lowering with subsequent reaching of normal BP.

Drug combinations

Moderate AH: monotherapy
Long-time stable AH: usually 2 (second is diuretic)
Severe AH: DBP higher than 115 – 3 drugs

Factors, influencing individual drugs choice:

- risk factors presence
- target organs changes
- indications, contrindications and side effects (including in case of long-time use)
- proved prevention of letal outcomes
- positive influence on other diseases of the patient
- absence of negative psychological reaction of patient on the drug
- optimal life quality reaching
- optimal economic effect

Emergency situations in AH (crises) treatment:

2 groups

1. treatment must begin in first minutes and hours, parenteral use of drugs:

- target organs symptoms appearance or exacerbation during crisis: unstable stenocardia, infarction, acute cardiac failure, aorta dissection, stroke, papilledema

Drugs used:

Vasodilators:
sodium nitroprusside (but: increase of intracranial pressure)
nitroglycerine (preferable in IHD)
ACE - enalapril (preferable in cardiac failure)
Antiadrenergic:
Esmolol
Phentolamin (if pheochromacytoma is suspected)
Diuretics
Loop diuretics - Furosemid (Lasix)
Ganglioblockers
Neuroleptics – droperidol

Frequency of BP measurements: every 15-30 min in case BP is higher than 180/120

Velocity of BP decrease: 25% from initial level – first 2 hours; then during 2-6 hours – till 160/100. Rapid BP decrease leads to CNS, kidneys and myocardium ischemia.

2. Gradual decrease in several hours can be used

Short-time oral drugs should be used: beta-blockers; nifedipin (sublingual and per os), clophelin, loop diuretics, prasosin. At home monitoring can tale place, but if the crisis state remains or complications appear, patient should be admitted to the hospital.

Indication to emergency hospitalization in AH:

- crise if home treatment is ineffective
- crise with marked signs of encephalopathia
- complications, which need constant monitoring by the physician: stroke, acute vision disorders, pulmonary oedema

Indications to hospitalization in AH (delay of admission is possible)

- unclear diagnosis and necessity of special methods of investigation
- difficulties in AH control (frequent crises, resistant AH)
- malignant AH syndrome

Standard crises treatment:

Neural-authonomic variant:

Not severe:

Niphidipin sublingual 10 mg; then per os every 30 min or clonidin 0.15 per os, then 0.075 mg every hour until the effect can be reached

Or: anaprilin 40 mg

If the effect is not reached – furosemid 20-0 mg per os

Severe

Clonidin 0.1 mg i.v. slowly or labetalol 50 mg or pentamin up to 50 mg infusion or sodium nitroprusside 30-50 mg in 300-500 ml 5% glucose (initial velocity 0.1 mkg/kg/min). Pentamin should be used only in life threatening cases (stroke, infarction, lung oedema, aorta dissection) because of difficulties to control its effect. Instead of pentamine arfonade can be used – 250 mg in 250 mg 5% glucose infusion beginning from 1 mg/min.

If effect is not reached – furosemid 40 mg i.v.

If marked emotional stress is present – diazepam 5-10 mg per os or droperidol 2.5-5 mg

Salt-dependent variant:

Not severe:

Furosemid 40-80 per os once

+ nifedipin 10 mg every 30 min till the effect is seen

OR

Furosemid 20 mg per os once+ captopril 6.25-25 sublingual every 30-60 min till the effect is seen.

Severe

Furosemid 20-40 mg i.v.

Labetalol 50 mg i.v. every 5 min or 200 mg in 200 mg 0.9%NaCl

Or pentamin or sodium nitroprusside

In case of marked neurological symptoms: 240 mg euphyllin i.v.

In case of marked diuresis: potassium p.os or i.v.

Cramps variant

- Diasepam 10-20 mg i.v. slowly till the relieve of the cramps + MgSo4 2.5 g i.v. very slowly
- Labetalol (see above) or pentamin or nitroprussid (see above)

Furosemid 40-80 mg i.v. slowly