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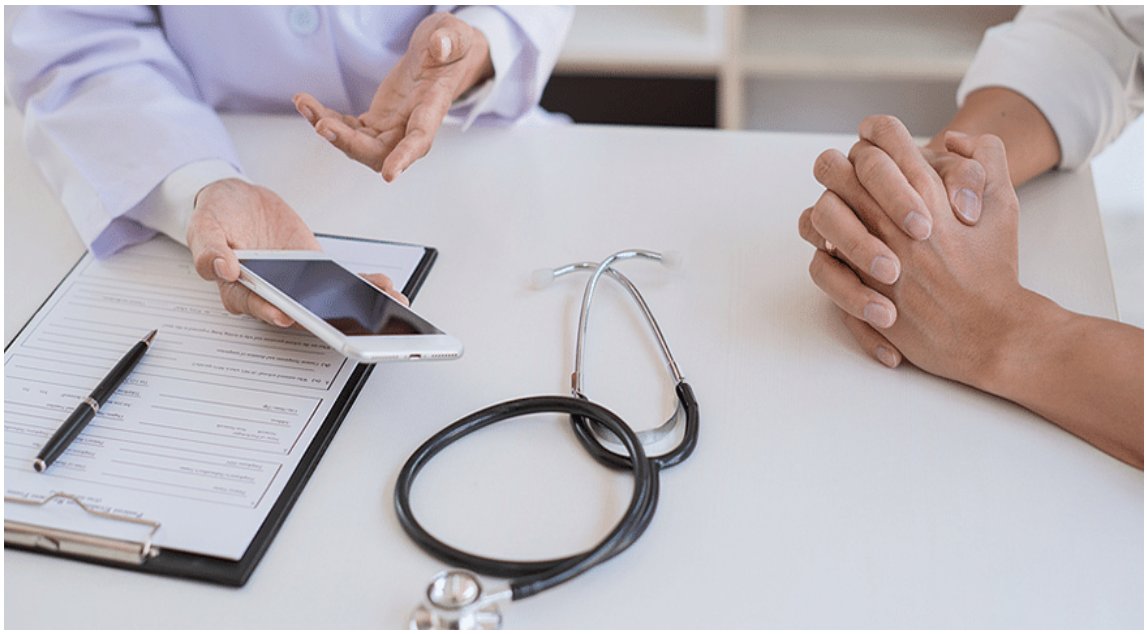
ZAPORIZHZHIA STATE MEDICAL AND PHARMACEUTICAL UNIVERSITY
DEPARTMENT OF GENERAL PRACTICE – FAMILY MEDICINE
AND INTERNAL DISEASES

BASIC SYMPTOMS AND SYNDROMES OF INTERNAL DISEASES

MANUAL

for 2nd years students
speciality 221 «Dentistry»



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Authors:

N. S. Mykhailovska – Doctor of Medical Sciences, Professor, head of General practice – family medicine and internal diseases department, Zaporizhzhia State Medical and Pharmaceutical University;

A. V. Grytsay – PhD, associated professor of General practice – family medicine and internal diseases department, Zaporizhzhia State Medical and Pharmaceutical University;

Y. M. Mykhailovskyi – assistant of Therapy, Cardiology and Neurology department, Zaporizhzhia State Medical and Pharmaceutical University;

I. O. Stetsiuk – assistant of General practice – family medicine and internal diseases department, Zaporizhzhia State Medical and Pharmaceutical University.

Reviewers:

L. V. Lukashenko – Doctor of Medical Sciences, Professor, Head of the Propedeutic of internal medicine, radiation diagnostic and radiation therapy department, Zaporizhzhia State Medical and Pharmaceutical University;

P. P. Bidzilya – Doctor of Medical Sciences, Associate Professor of the Internal Medicine 1 and Simulation Medicine Department, Zaporizhzhia State Medical and Pharmaceutical University.

B29 **Basic symptoms and syndromes of internal diseases** : manual for the practical classes and individual work for 2nd year students of international faculty (speciality 221 «Dentistry») Discipline ««Propedeutics of internal medicine » / N. S. Mykhailovska, A. V. Grytsay, Y. M. Mykhailovskyi [et al.]. – Zaporizhzhia: ZSMPHU, 2023. – 208 p.

Manual compiled in accordance with the program of «Propedeutics of internal medicine». Guidelines are intended to help students prepare for practical classes and learn the material. Can be used for training of 2nd years students of international faculty, discipline «Propedeutics of internal medicine».

Основні симптоми та синдроми внутрішніх хвороб: навчальний посібник до практичних занять та самостійної роботи студентів ІІ курсу міжнародного факультету (спеціальність «Стоматологія») з дисципліни «Пропедевтика внутрішньої медицини» / Н. С. Михайловська, А. В. Грицай, Я.М. Михайловський та співат. - Запоріжжя: ЗДМФУ, 2023. – 208 с.

Навчальний посібник складений відповідно до програми «Пропедевтика внутрішньої медицини». Видання має на меті сприяти кращому засвоєнню теоретичних знань студентами під час підготовки до практичних занять та підсумкового контролю. Посібник рекомендований для використання студентами ІІ курсу міжнародного факультету з дисципліни «Пропедевтика внутрішньої медицини».

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CONTENT

PREFACE

The development of clinical thinking in medical students commences with the study of the propeudeutics of internal diseases. Mastering methods of examination, first appointments with patients, gain of theoretical knowledge are essential for the specialist formation.

This student's manual is designed with the purpose to develop students' skills for synthesising data from the patient's interview, clinical examination, palpation, percussion and auscultation and defining the leading symptom or syndrome of cardiovascular, gastrointestinal diseases, diseases of the urinary and hematopoietic system, for making the presumptive diagnosis, for providing emergency and the prehospital first aid, for forming professional attainments, the basis of clinical thinking, medical ethics and deontology.

This student's manual includes necessary clinical materials for mastering the academic discipline «Propeudeutics of internal diseases» and supposes acquiring of practical knowledge either under the professors' control or individually.

This manual is published for the first time.

The cover image was downloaded from website https://badgut.org/information-centre.

This student's manual provides theoretical material which would improve theoretical knowledge of students of the 2nd international fculty, speciality "Dentistry".

ABBREVIATIONS

ACS – acute coronary syndrome
AF – atrial fi brillation
AH – arterial hypertension
AHA – American Heart Association
ALS – advanced life support
ALT – alanine transaminase or alanine aminotransferase
AST – aspartate transaminase or aspartate aminotransferase
AV – atrioventricular
BMI – body mass index
BLS – basic life support
BP – blood pressure
CBC – complete blood count
CK – creatine phosphokinase
CK–MB – creatine phosphokinase MB isoenzyme
COPD – chronic obstructive pulmonary disease
CPR – cardiopulmonary resuscitation
CT – computed tomography
CVS – cardiovascular system
CXR – chest X-ray
ECG – electrocardiography
ESR – erythrocyte sedimentation rate
ESRD – end-stage renal disease
GFR – glomerular fi ltration rate
GI – gastrointestinal
Hb – hemoglobin
HDL – high density lipoprotein
HF – heart failure
HR – heart rate
IHD – ischemic heart disease
IM – intramuscular
ISH – International Society of Hypertension
IV – intravenous
JVP – jugular venous pressure
LDL – low density lipoprotein
LDH – lactate dehydrogenase
LVH – left ventricular hypertrophy
MI – myocardial infarction
MRI – magnetic resonance imaging
NMU – National Medical University
OSCE – Objective Structured Clinical Exam
PAC – premature atrial contraction
PE – physical examination
PVC – premature ventricular contraction
RBC – red blood cells or erythrocytes
SA – sinoatrial
SC – subcutaneous
SVT – supraventricular tachycardia
UTI – urinary tract infection
VF – ventricular fi brillation
WBC – white blood cells or leucocytes
WHO – World Health Organization

BASIC SYMPTOMS AND SYNDROMES OF INTERNAL DISEASES

BASIC SYMPTOMS AND SYNDROMES OF CARDIOVASCULAR DISEASES

Syndrome of the arterial hypertension

Arterial hypertension is defined as elevation systolic blood pressure (SBP) to 140 mmHg and higher and diastolic blood pressure (DBP) to 90 mmHg and higher in case of stable elevation confirming on repeating measurement blood pressure (2-3 times in different days during 4 weeks).

Classification on etiology

1. Secondary (symptomatic) hypertension.
2. Essential arterial hypertension.

Symptomatic arterial hypertension

Symptomatic arterial hypertension causally related to the diseases with damages of some organs, participating in regulation of arterial pressure.

Causes of secondary hypertension

1. Renal diseases:

- parenchymal and interstitial diseases of kidneys (glomerulonephritis, chronic pyelonephritis, diabetic nephropathy, amyloidosis, hydronephrosis, postradiation nephrosclerosis):

- *renovascular* pathology (atherosclerosis of kidney artery, fibromuscular dysplasia, aortoartentis, vasculitis, endarteritis, thrombosis, embolism, aneurysm of kidney artery, stenosis and thrombosis of veins, trauma of kidney vessels);

- *anomalies* of kidney and urinary tract (polycystosis, hypoplasia, anomalies of urinary system);

- *secondary damage* of kidneys at tuberculosis, bacterial metastases and diffuse diseases of connective tissue (lupus, system sclerodermia).

2. Endocrine hypertension:

- phaeochromocytoma;
- primary hyperaldosteronism (Conn's syndrome);
- idiopathic hyperplasia adrenal cortex (pseudoprimary hyperaldosteronism);
- Cushing's disease (syndrome);

- hyperparathyroidism;
- acromegaly;
- climacteric hypertension.

3. Hemodynamic hypertension:

- atherosclerosis of aorta;
- stenosis of carotid and vertebrobasilar arteries;
- coarctation of aorta;
- aortic regurgitation;
- rheological hypertension (polycythemia vera).

4. Neurogenic hypertension:

- vascular diseases and tumors of brain;
- inflammatory diseases (encephalitis, meningitis, polyomyelitis);
- trauma of brain (postcontusional syndrome);
- polyneuritis.

5. Special forms of second hypertension (after taking some medicines: anabolic steroids and mineralocorticoids, oral contraceptives, containing progesterone and estrogen, sympathomimetic agents, indometacin and other).

Diagnostic criteria of the renoparenhimal hypertension: pointing in anamnesis on the previous pyelonephritis, glomerulonephritis, nephropathy at pregnant, nephrolytiasis and other diseases of kidneys; characteristic changes of laboratory, instrumental and morphological examination of kidneys and also positive hypotensive effect from specific therapy of kidney disease.

Diagnostic criteria of the renovascular hypertension: high systolic hypertension, refractory to treatment; in auscultation - systolic murmur over the abdominal aorta and especially in the area of projection of kidney arteries; small sizes of one kidney (ultrasound and urography); disorders of contrast distribution at kidney (at intravenous urography); high level of renin in plasma of blood; narrowing of the (one or both) kidney arteries (angiography).

Diagnostic criteria of the phaeochromocytoma: transitional arterial hypertension with the signs of activation of the sympathetic nervous system (excitation, trembling, increasing of body temperature), leucocytosis, hyperglicemia. Stable character of arterial hypertension does not exclude phaeochromocytoma; negative effect from therapy with beta-blockers; positive provocative tests (histamine,

injected intravenously in a dose 0,05 mg in 0,5 ml of isotonic solution, causes an increase blood pressure on 60/40 mmHg during the first 4 min; palpation of kidney region provokes hypertensive crisis) and test with alpha-adrenoblockers; enlargement of adrenal glands from data of ultrasonic research, computer tomography; finding out the high level of adrenalin, noradrenalin. Tumor of adrenal gland found out by the instrumental methods.

Diagnostic criteria of the primary hyperaldosteronism (Conn's syndrome): high blood pressure; muscular weakness and neuro-muscular disorders (paraestesia, occasionally tetany because of the metabolic alkalosis with low ionized calcium, transient para- and tetraplegia); polyuria, nicturia, thirst; hypokaliemia, hypernatriemia, increase of potassium level in blood after the test with veroshpiron; alkaline reaction of urine; the low level of plasma renin; diminishing of tolerance to glucose, rarer is obvious diabetes mellitus; finding out the tumor at the adrenal gland by ultrasonic investigation, computer tomography, radioisotope scanning of adrenal glands; level of the aldosteron in blood and urine (their increase to 100 mg/ml and to 150 mg/day, respectively).

ESSENTIAL HYPERTENSION

Essential hypertension (hypertension) is a disease of the cardiovascular system, which develops due to primary dysfunction of the vascular regulatory centers and subsequent involment of neurohumoral and kidney mechanisms, characterized by arterial hypertension, functional, and at the expressed stages - by the organic changes of kidneys, heart and central nervous system. The essential hypertension can be diagnosed after exception of symptomatic (secondary) hypertension.

Factors influencing cardiovascular risk in patients with hypertension

Demographic characteristics and laboratory parameters
Sex (men >women)
Age
Smoking (current or past history)
Total cholesterola and HDL-C

Uric acid
Diabetes
Overweight or obesity
Family history of premature CVD (men aged <55 years and women aged <65 years)
Family or parental history of early-onset hypertension
Early-onset menopause
Sedentary lifestyle
Psychosocial and socioeconomic factors
Heart rate (resting values >80 beats/min)

Classification

Table 1

Classification of hypertension according to blood pressure level

Category	SBP(mmHg)		DBP(mmHg)
Optimal	< 120	and	< 80
Normal BP	120-129	and/or	80-84
High normal	130-139	and/or	85-89
Grade I hypertension	140-159	and/or	90-99
Grade II hypertension	160-179	and/or	100-109
Grade III hypertension	≥180	and/or	≥110
Systolic hypertension	≥140	and	< 90

Table 2

Classification of hypertension by extent of organ damage

Stage I	No objective signs of organic changes
Stage II	At least one of the following signs of organ involvement without symptoms or dysfunction: -left ventricular hypertrophy (electrocardiogram, ultrasound); -generalized and focal narrowing of the retinal arteries; -proteinuria and/or slight elevation of plasma creatinine concentration (1,2- 2,0 mg/dl or to 177 mmol/1); - ultrasound or radiological evidence of atherosclerotic plaque (carotid arteries, aorta, iliac and femoral arteries).
Stage III	Both symptoms and signs have appeared as result of organ damage. These include: - heart (myocardial infarction, heart failure); - brain (stroke, transient ischemic attack, encephalopathy, vascular dimension); - optic fundi (retinal hemorrhages and exudates with or without papillodema); - kidney(plasma creatinine concentration more than 2,0 mg/dl or 177 mmol/1); - vessels (dissecting aneurysm, symptomatic arterial occlusive diseases)

Clinical features

Complaints: pain at the heart, palpitation, headache, dizziness, disorder of vision. At the expressed left ventricular failure - attacks of dyspnea.

Objective examination

General patient condition is usually satisfactory. On progression of disease and appearance of complication general patient's condition may be from middle grave to grave (hypertension crisis, acute and chronic heart failure and cerebral attacks).

The color of the skin may be hyperemic. As usually the patients are overweight. At development of heart failure acrocyanosis and peripheral edema are observed.

Objective examination of the cardiovascular system. Apex beat is displaced to the left and downwards, diffuse, high. Displacement of the left border of the relative cardiac dullness to the left is observed. Increased loudness of the first heart sound at the heart apex and accentuated second heart sound over aorta are heard. At the presence of heart failure the gallop rhythm is heard. Blood pressure > 140/90 mm Hg. Pulse is firm tension (p. durus).

Protocol of diagnostic procedures for patients with hypertension I-II stages

Obligatory examination:

- inquiry;
- physical examination: measurement of blood pressure on both hands, measurement of blood pressure on lower extremities at persons younger 45 years; measurement of body weight of and waist circumference;
- laboratory routine examination hemoglobin and hematocrit, clinical urine analysis, Nechiporenko's test, Zemnicky's test, biochemical blood analysis: serum creatinine, serum potassium, serum total cholesterol, serum low density lipoprotein (LDL) cholesterol, serum high density lipoprotein (HDL) cholesterol, fasting serum triglycerides;
- ECG in 12 standard leads;
- echocardiography;
- fundoscopic examination.

Special examination:

- determination of microalbuminuria;
- daily proteinuria;
- ambulatory blood pressure measurement using monitor;
- ultrasound examination of kidneys.

Protocol of diagnostic procedures for patients with hypertension III stages

Obligatory examination:

- inquiry;
- physical examination: - measurement of blood pressure on both hands, measurement of blood pressure on lower extremities at persons younger 40 years;
- measurement of body weight and waist circumference;
- laboratory routine examination hemoglobin and hematocrit, clinical urine analysis, Nechiporenko's test, Zemnicky's test, biochemical blood analysis: serum creatinine, serum potassium, serum total cholesterol, serum low density lipoprotein

(LDL) cholesterol, serum high density lipoprotein (HDL) cholesterol, fasting serum triglycerides;

- ECG in 12 standard leads;
- echocardiography;
- examination of the eyes;
- X-ray examination of the chest;
- ultrasound examination of kidneys.

Special examination:

- ambulatory blood pressure measurement using monitor;
- doppler-ultrasound scanner of extracranial vessels;
- computer tomography and magnitoresonance tomography of head;
- in case of coronary heart diseases - cardioventnculography.

Additional methods of examination

Clinical blood analysis: at the prolonged course of hypertension occur hypertensive polycytemia - increased hemoglobin and hematocrit are possible.

Biochemical blood analysis: at development of kidney failure there is increasing level of creatinine.

Clinical urine analyses: at development of nephroangiosclerosis and renal failure - proteinuria, microhematuria, hypo-, isostenuria in Zimnitsky's test.

ECG: the left ventricle hypertrophy, depressed ST-segment, inverted or two-phase T-wave in the 1st and 2nd standard, V_5-V_6 chest leads.

X-ray examination of heart. In the initial period of hypertrophy, rounding of apex of the left ventricle is find out. All chambers of heart are dilated in the late stages.

Echocardiography: hypertrophy of the interventricular septum and the posterir wail of the left ventricle, decrease of contractility of the myocardium, increase end systolic and diastolic dimensions of the left ventricle.

Ophthalmoscopy is revealed angioretinopathy.

Hypertensive crisis

Severe elevations in blood pressure (systolic blood pressure ≥ 180 mm Hg or diastolic blood pressure ≥ 120 mm Hg) with impending complications including target end-organ dysfunction.

Types

1. Main categories of hypertensive crises include:
   - hypertensive emergency
     - severe blood pressure elevation plus end-organ damage

- malignant hypertension is term used for patients with severely elevated blood pressure and ischemic end-organ damage usually involving the retina, but may also include the kidneys, heart, arteries, and/or brain

o hypertensive urgency

- severe blood pressure elevation without evidence of end-organ dysfunction
- examples include upper levels of stage II hypertension either asymptomatic or associated with headache, dyspnea, epistaxis, palpitations, or anxiety
- most patients have inadequately treated hypertension or are noncompliant with treatment regimen

2. Additional types of hypertensive crisis include:

o hypertensive emergency in pregnancy

o acute onset of severe hypertension persisting > 15 minutes plus end-organ damage

o end-organ damage may include severe preeclampsia, eclampsia, and hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome

3. False or pseudo hypertensive crisis

o transient blood pressure elevations due to external stimuli (such as pain, anxiety, stress, and urinary retention) without evidence of end-organ dysfunction includes patients with isolated clinical hypertension, white coat hypertension, and errors in blood pressure measurement technique

Clinical signs

Hypertensive emergency means blood pressure is so high that organ damage can occur. Blood pressure must be reduced immediately to prevent imminent organ damage. This is done in an intensive care unit of a hospital.

The most common non-specific symptoms are: chest pain, headache, blurred vision, weight loss.

Less common presenting symptoms include: dizziness, nausea, dyspnea, fatigue, malaise, epigastric pain, polyuria, gross hematuria

Organ damage associated with hypertensive emergency may include:

- Changes in mental status, such as confusion
- Bleeding into the brain (stroke)
- Heart failure
- Chest pain (unstable angina)

- Fluid in the lungs (pulmonary edema)
- Heart attack
- Aneurysm (aortic dissection)
- Eclampsia (occurs during pregnancy)

ISCHEMIC HEART DISEASE

Ischemic (coronary) heart disease (IHD) - define as acute and chronic heart damage, caused due to diminishing or stopping blood delivery to myocardium. Disease of the coronary arteries is almost always due to atheroma and its complications, particularly thrombosis.

Etiology and pathogenesis

Atherosclerosis of coronary arteries; the degree of its expression is different - from small wall affection to complete occlusion of vessel.

Spasm of coronary arteries develops, as a rule, on a background of atherosclerosis of coronary arteries. The physical overloading, mental stress provokes the development of clinical features of IHD.

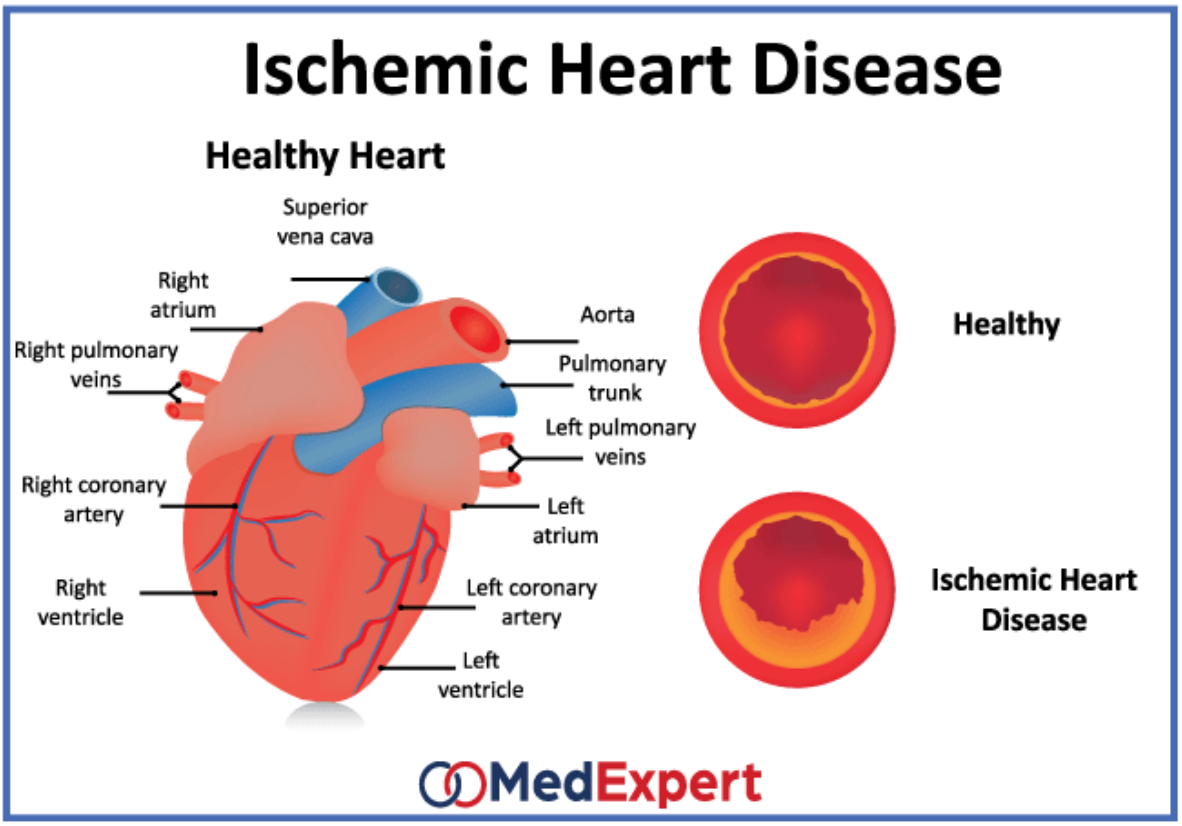


Image 1. Ischemic (coronary) heart disease

The image was downloaded from website https://www.medexpert.sg/en/medical-specialities/cardiothorasic-surgery/ischemic-heart-disease/

The main pathophysiological mechanism of IHD is imbalance between the demand myocardium in oxygen and possibilities of coronary arteries satisfied the myocardium by adequate amount of blood.

The followings mechanisms are involved in pathological process:

- mechanical occlusion of coronary arteries due to an atherosclerotic process;
- dynamic occlusion of coronary arteries due to coronarospasm;
- activation of thrombocytes aggregation with development of microagregates in microcirculation;
- promotion of production the pro-coagulating factors, insufficiently level of prostacyclin and endothelin- derived relaxing factor;
- increasing of demand myocardium in oxygen under influencing of the intensive physical loading, mental stress, resulting in the high level catecholamines in blood caused cardiotoxic action;
- insufficiency of collateral circulation of blood;
- activation of the lipid peroxidation;
- activation of immune mechanisms.

Classification of ischemic heart disease (IHD)

1. Sudden cardiac death.

2. Angina pectoris:

- stable angina pectoris;
- vasospastic angina (Princmetala's);
- unstable angina.

3. Myocardial infarction (MI):

- acute Q-wave MI;
- acute non-Q-wave MI;
-subendocardial MI;
- acute MI (undetected);
- recurrent MI (3-28 days);
- repeated MI (after 28 days).

4. *Postinfarction cardiosclerosis.*

1. *Cardiac arrhythmia.*
2. *Painless form of the IHD.*

STABLE ANGINA

The 2002 American College of Cardiology/American Heart Association (ACC/AHA) guideline update defined chronic stable angina as a clinical syndrome characterized by discomfort in the chest or adjacent areas caused by myocardial ischemia typically aggravated by exertion or emotional stress and relieved by rest or by nitroglycerin. Patients often describe their symptom as discomfort rather than pain.

Clinical features

The main parameters of pain in patients with stable angina are: location, character, intensity, duration, frequency, radiation, associated symptoms and cause of onset, aggravating and relieving factors.

The typical location of angina is mid or lower part of sternum. Less typically, discomfort may occur in the epigastric area. The discomfort is usually described as pressure, tightness, heaviness, strangling, constricting, burning, squeezing, suffocating and crushing. The severity of the discomfort varies greatly. The pain may radiate in arm to the wrist and fingers, lower jaw or teeth, throat, between the shoulder blades. The duration of the discomfort is brief, not more than 10 min in the majority of cases and more commonly even less. Angina equivalents are common and include dyspnea, faintness, and syncope. Chest discomfort may be accompanied by less specific symptoms such as nausea, burping, restlessness, or a sense impending doom. Frequency of the pain may be different.

An important characteristic is the relation to exercise, specific activities, or emotional stress. Symptoms classically triggered by increased levels of exertion, such as walking up an incline or against a breeze, and rapidly disappear within a few minutes, when these causal factors abate. Exacerbations of symptoms after a heavy meal or work are classical features of angina. Buccal or sublingual nitrates rapidly relieve angina.

For patient with stable angina it is useful to classify the symptoms using a grading system which was devised by the Canadian Cardiovascular Society, based on the severity of the angina stressor.

Table 3

Canadian Cardiovascular Society classification of stable angina

Class	Severity of exertional stress including angina	Limitation ordinary activity
I	Strenuous rapid or prolonged exertion at work or recreation	None
II	Walking or climbing stairs rapidly, walking uphill, walking	Slight

	or stair climbing	
III	Walking one to two blocks on the level and climbing one flight of stairs in normal condition and at a normal pace	Marked
IV	Symptoms may be present at rest	Discomfort in all activity performed

Objective examination

During the attack of stable angina the patient's condition is moderate, clear consciousness, standing up right position (if the patient walking), or sitting position with hand placed over sternum. Patient's face is pale with cyanotic tint. Arcus senilis, xanthelasma are revealed. Extremities are cold.

In auscultation of lung may be detected bilateral basal rales. Apex beat displaced outside. The left border of relative cardiac dullness displaced. Both heart sounds are decreased, paradoxically split S, and sometimes may be arrhythmia. premature beat, atrial fibrillation. The clinical features of stable angina are abnormal carotid pulse, decreased peripheral pulse, jugular venous distension. In some patients observe hepatomegaly, pedal edema.

Additional method of examination

Clinical blood analysis is without change.

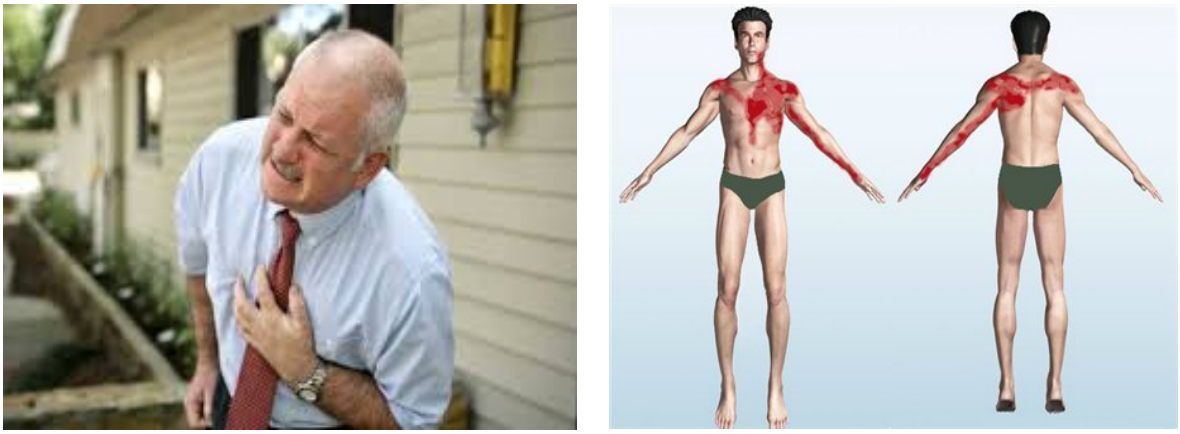
Biochemical analysis in patients with stable angina may show elevated level of cholesterol, triglycerides, decreased high density lipoprotein cholesterol and increased low density lipoprotein cholesterol. Biochemical markers of myocardial damage in stable angina are in a normal range.

X-ray examination in stable angina does not provide specific information for diagnosis.

Resting ECG may show evidence of previous myocardial infarction, left ventricular hyperthrophy, bundle branch block, preexcitation, arrhythmias, or conduction defects, but is normal in most patients. Since 12-lead ECG is normal in 50 % of patients with chronic stable angina it cannot exclude IHD. During chest pain the ECG becomes abnormal in half of the angina patients with a normal resting ECG. ST-segment and T-wave depression or inversion on the resting ECG and their pseudonormalization during pain are observed. Sinus tachycardia is common,

bradyarrhythmia less go. These findings indicate that resting ECG should be performed during episode of chest pain.

Exercise ECG is more sensitive and specific than the resting ECG for detecting myocardial ischemia. Exercise tolerance test is usually performed using a standard treadmill or bicycle ergometer protocol to ensure a progressive and reproducible increase in work load while monitoring the patient's ECG, blood pressure and general condition. Planar and down sloping ST-segment depression of 1 mm or more is indicative of ischemia; up sloping ST-depression is less specific and often occurs in normal individuals. An exercise test should be carried out only after careful clinical evaluation of symptoms and a physical examination including resting ECG. Exercise ECG testing is not of diagnostic value in the presence of left bundle branch block, paced rhythm, and Wolff-Parkinson-White syndrome in which cases the ECG changes cannot be evaluated. Additionally, false positive results are more frequent in patients with abnormal resting ECG in the presence of left ventricular hypertrophy, electrolyte imbalance, intraventricular conduction abnormalities, and use of digitalis. Exercise ECG testing is also less sensitive and specific in women.



A B

Image 2. A – localization of anginal pain behind the sternum; B - irradiation of pain in angina pectoris

The image was downloaded from website https://www.healthline.com/health/sternum

Resting two-dimensional and Doppler echocardiography is useful to detect or rule out the possibility of other disorders such as heart valve disease or hypertrophic cardiomyopathy as a cause of symptoms and to evaluate ventricular function. For

diagnostic purposes, Echo-CG is useful in patients with clinically detected murmurs, history and ECG changes compatible with hypertrophic cardiomyopathy or previous myocardial infarction and symptoms or signs of heart failure. Tissue Doppler imaging allows regional quantification of myocardial motion and strain rate, imaging allows determination of regional deformation thus improve to detect ischemia earlier in the ischemic cascade.

Stress testing in combination with imaging are used in the diagnosis of stable angina. The most well-established stress imaging techniques are echocardiography and perfusion scintigraphy. Both may be used in combination with either exercise stress. Exercise stress echocardiography has been developed as an alternative to "classica" exercise testing with ECG and as an additional investigation to establish the presence or location and extent of myocardial ischaemia during stress. A resting echocardiogram is acquired before a symptom-limited exercise test is performed, most frequently using a bicycle ergometer, with further images acquired where possible during each stage of exercise and at peak exercise.

Exercise testing with myocardial perfusion scintigraphy is required. Thallium-201 and technetium-99m radiopharmaceuticals are the most commonly used tracers, employed with single-photon emission computed tomography in association with a symptom-limited exercise test on either a bicycle ergometer or a treadmill. With this technique myocardial hypoperfusion in patients with stable angina is characterized by reduced tracer uptake during stress in comparison with uptake at rest.

Pharmacological stress testing with imaging techniques. Pharmacological stress testing with either perfusion scintigraphy or echocardiography is indicated in patients who are unable to exercise adequately or may be used as an alternative to exercise stress. Two approaches may be used to achieve this: infusion of short-acting sympathomimetic drugs such as dobutamine in an incremental dose protocol which increases myocardial oxygen consumption and mimics the effect of physical exercise or infusion of coronary vasodilators (adenosine and dipyridamole).

Cardiac magnetic resonance stress testing in conjunction with a dobutamine infusion can be used to detect wall motion abnormalities induced by ischemia or perfusion abnormalities.

ACUTE CORONARY SYNDROME

Acute coronary syndrome (unstable coronary artery disease) includes both ***unstable angina*** and ***non-Q-wave myocardial infarction.***

Clinical features

- increased severity or frequency of the patient's pre-existing angina within the

last month;

- rapidly worsening chronic stable angina (crescendo angina);
- new onset of angina pectoris;
- angina at rest;
- post-infarction angina (more than 24 hours after myocardial infarction);
- non-Q-wave myocardial infarction.

Objective examination

During attack of chest pain the patient's condition is grave, forced sitting position, the face is pale with acrocyanosis. The border of relative cardiac dullness displaced outside.

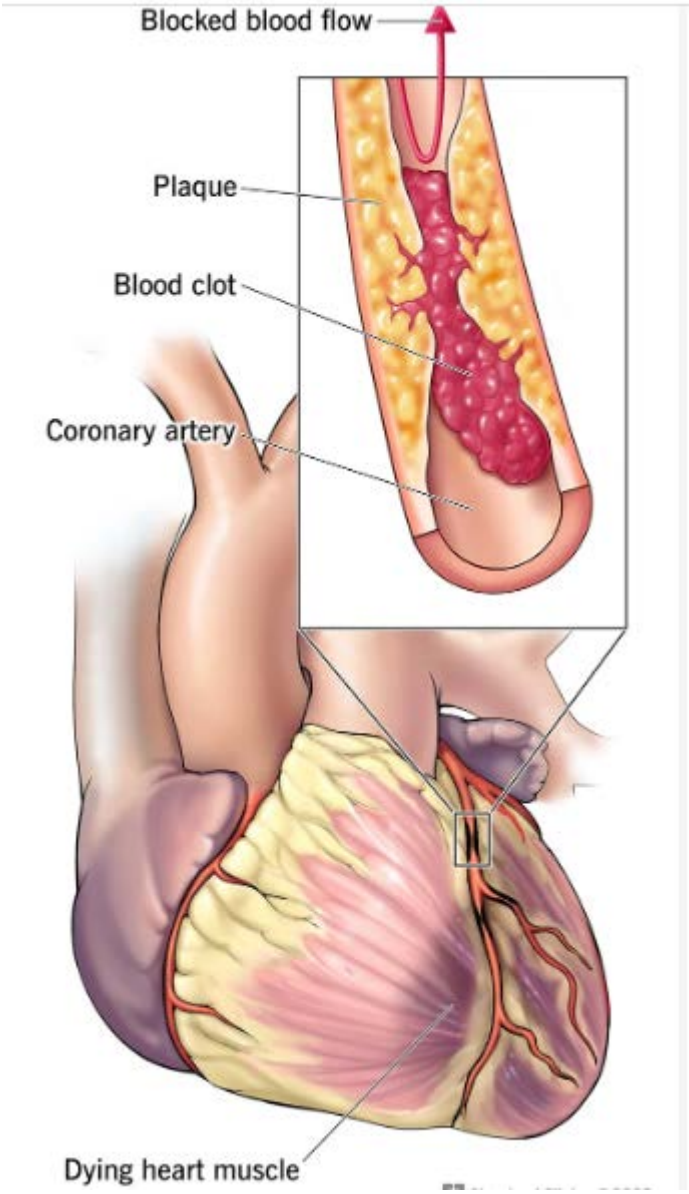


Image 3. Acute coronary syndrome

The image was downloaded from website https://my.clevelandclinic.org/health

In auscultation both heart sounds are decreased, S_3 or S_4 gallop may be detected during an episode of pain. Mitral regurgitation murmur appears. Arrhythmia is often observed. Blood pressure tends to have less level, than in period free of pain. The signs of congestion failure present: enlarged liver, pedal edema.

Additional methods of examination

Clinical blood analysis is without change, seldom may be slight leukocytosis.

Biochemical blood analysis: commonly there are the signs of disorders of lipid profile: increased level total cholesterol, triglycerides, low density lipoprotein cholesterol.

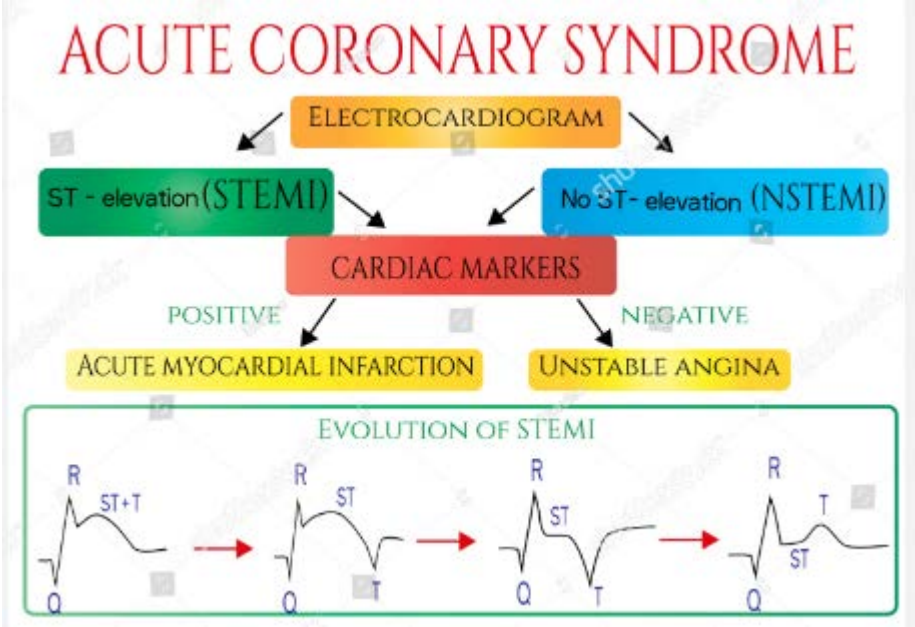


Image 4. Acute coronary syndrome. Schematic Electrocardiogram of myocardial infarction

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Small rises in the serum levels of biochemical markers of cardiac injury (creatine kinase, creatine kinase MB), troponin-T or troponin-I reflect the development of small foci of myocardial necrosis, minor creatine kinase, creatine kinase MB, which are usually accompanied by elevated troponin-T levels, indicate an increased risk of future events, despite stabilization of their clinical condition. Cardiac troponin-I is not detectable in the absence of cardiac injury. Because of the lag period before a rise becomes detectable, at least two samples, taken at an interval of 12-24 hours, should always be tested.

Elevated fibrinogen levels at the time of admission are associated with an increased risk of death, myocardial infarction or spontaneous ischemia in patients with unstable angina.

The acute-phase proteins C-reactive protein is sensitive, but non-specific, markers of inflammation. There is much evidence to suggest a role for inflammation in the etiology of unstable angina and myocardial infarction and level of this protein have been observed to be elevated in some patients with acute coronary syndrome. C-reactive protein levels >3 mg/1, as detected by means of sensitive radioimmunoassay, indicate an increased risk of subsequent cardiac events m patients with acute coronary syndrome.

Instrumental examination. ECG monitoring is regarded as an essential part of routine management. All patients with suspected acute coronary syndrome should be admitted to the coronary unit for 12-24 hours of ECG monitoring (Holter monitoring). Admission ECG finding in acute coronary syndrome: ST-segment depression, ST-segment elevation (transient), T-wave inversion, normal ECG.

A normal ECG recorded when the patient is pain free not exclude the diagnosis of acute coronary syndrome, although a normal ECG recorded during an episode of pain makes the diagnosis unlikely, and is associated with an excellent prognosis. Following abnormalities of ECG support a diagnosis of acute coronary syndrome: ST-segment depression >0,5 mm, ST-segment elevation >1mm, T-wave inversion. Transient elevation of the ST-segment which settles, either spontaneously or in response to nitrate treatment, is fully consistent with the diagnosis acute coronary syndrome. Isolated T-wave inversion on the initial ECG is a relative by benign sign, and is associated with a low risk of future myocardial infarction or death. A total of more than 60 minutes of ischemia during Holter monitoring is associated with a poor prognosis. However, T-wave inversion and change of ST-segment must be considered in the context of the whole clinical picture taking into account the patient's age, presence of other risk factors, levels of biochemical markers of cardiac injury. Exercise testing undertaken either before or shortly after hospital discharge, is a minimum requirement for patients. Once the patient has been pain-free for 24-48 hours and the ECG stable the risks associated with performing an exercise test are very low. Severe ischemia and low exercise tolerance in a patient who has had either unstable angina or non-Q-wave myocardial infarction is associated with a poor short-term prognosis.

Echocardiography should be performed in all patients in order to evaluate the left ventricular function.

Stress echocardiography can be performed either during or immediately after dynamic exercise or under pharmacological stress administration of dipyridamole or dobutamine. Patients who are unable to perform an exercise test can be usefully assessed by pharmacological induced stress echocardiography.

Myocardial perfusion scintigraphy (tallium or technetium scan) may be particularly valuable in patients who are unable to exercise. Such techniques can outline perfusion defects.

MYOCARDIAL INFARCTION

Myocardial infarction is formation of necrotic foci in the heart muscle due to imbalance between upset coronary circulation and myocardial oxygen supply.

There are three pathophysiological events in development of myocardial infarction: rupture of an atheromatous plaque in a coronary artery, thrombus at a site of ruptured or intact plaque, local or generalized vasoconstriction. In myocardial infarction thrombus as a rule is occlusive. Under condition of complete occlusion of coronary artery the myocardial change occur after 20 minute and necrosis is formed for 6 hours. The time of formed necrosis is individual process which depends on presenting collateral circulation.

Diagnostics of myocardial infarction based on clinical features, ECG data and markers of tissue damage.

Clinical features

There are some clinical variants of myocardial infarction: angina (status anginous), abdominal variant, asthmatic variant, arrhythmic variant, cerebral variant, peripheral variant, painless or "silent" variant, combined variant.

Pain is the cardinal symptom of myocardial infarction. The pain resembles angina pectoris in patients with status anginous, but it usually more severe and often described as tightness, squeezing, pressing heaviness or constriction in the chest. The pain is characterized by inconstant character, lasts longer than angina, more than 20-30 minutes, some hours and even days. The pain irradiates in the left arm, throat, teeth, ear, under the left shoulder blade, sometimes in epigastrium. The chest pain is not relieved at rest or taking nitroclycerin. The pain is accompanied by feeling of fear, impending death, excitation, weakness, sweating and palpitation.

Atypical variants of myocardial infarction are particularly common in elderly and diabetic patients.

Abdominal type variant is observed more frequently at posterior diaphragmal myocardial infarction. This variant is characterized by intenstive pain in the epigastrium or in the right hypochondrium, which associated with dyspeptic disorders such as nausea, vomiting, regurgitation by air. Altered intestinal motility leads to diarrhea or constipation, paresis of intestine. On examination there is tenderness of the abdominal wall. Dangerous complication is acute gastrointestinal lesion and ulcer which are responsible for acute hemorrhage. The bleeding is often recurrent and caused shock.

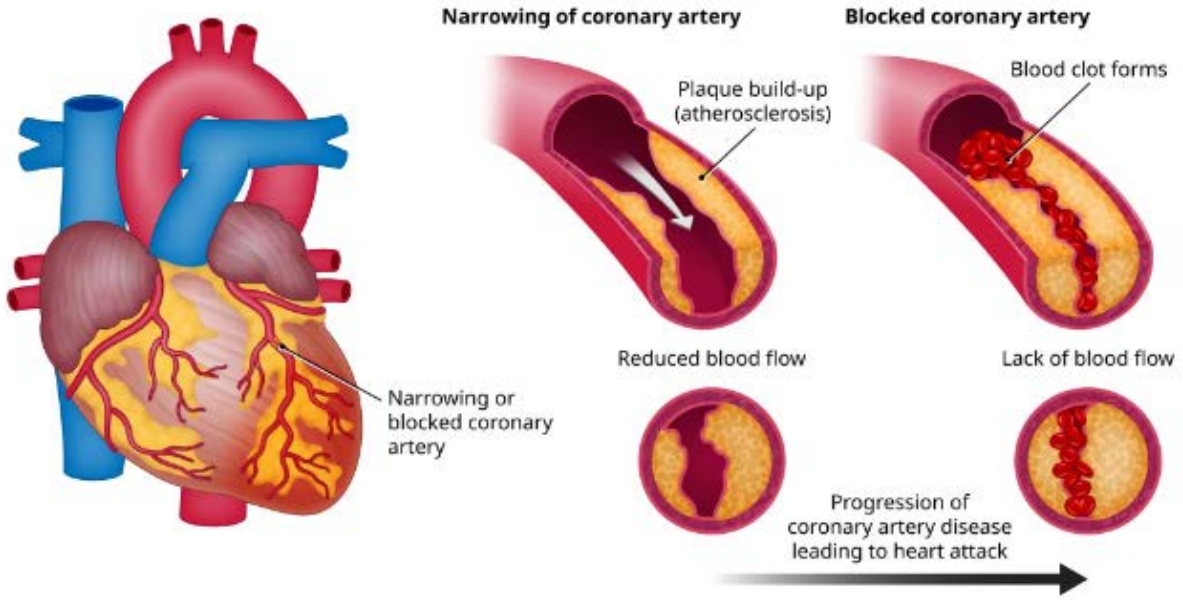

Image 5. Myocardial infarction

The image was downloaded from website https://www.mountelizabeth.com.sg/conditions-diseases/myocardial-infarction

Asthmatic variant is characterized by severe difficulty in breathing, cough with a foamy pink sputum (cardiac asthma, pulmonary edema) and small intensity of chest pain. There gallop rhythm, arrhythmias, decreasing of blood pressure is present. As a rule, this variant is more frequently observed at repeated myocardial infarction, and also at myocardial infarction on background of severe cardiosclerosis and practically always at the myocardial infarction of papillary muscle resulted the relative mitral incompetence.

Arrhythmic variant of myocardial infarction is predominated with disorders of rhythm and cardiac conduction, with slightly pain syndrome. This variant is related mostly with supraventricular or ventricular paroxysmal tachycardia, less frequent - paroxysmal atrial fibrillation or complete atrioventricular block. Arrhytmic variant may be complicated by cardiogenic shock with fall of blood pressure and sharply diminished myocardial perfusion.

Cerebral variant is observed in elderly patients with cerebral atherosclerosis and diminished brain circulation. Simultaneously with myocardial infarction may be spasm or thrombous of cerebral arteries. According to decreased cardiac output relevant with myocardial infarction such symptoms and signs of cerebral ischemia appear: giddiness, nausea and vomiting central origin, syncope, bradycardia, cramps and even, coma. Affection of central nervous system may be in a form of psychomotor anxiety resembles the clinical features of meningitis, epilepsy, polyneuropathy.

Painless, or "silent" variant of myocardial infarction pass unrecognized and may reveal afterwards during ECG recording or Echo-CG examination.

Objective examination

The patient's condition is severe, may be forced sitting position, consciousness is clear, pallor, excessive perspiration, cold peripheries, acrocyanosis. At second-third days of pain the temperature elevation till subfebril or febril level is observed. In percussion of the lung the intermediate sound is revealed in posterior part. Lung crepitation is heard. The borders of cardiac dullness correspond with preceding disease. Tachycardia is appeared as sign sympathetic activation. Decreased first heart sound or decreased both sounds are heard. At mostly patients presystolic and protodiastolic gallop rhythms occur. At 90-95 % of patients the extrasystoles are appeared. In the first listening point is heard loud pansystolic murmur which is explained by sudden onset of severe mitral incompetence with regurgitation due to the myocardial dysfunction or rupture of papillary muscle. A new loud pansystolic murmur may have another origin and caused by rupture of the interventricular septum with left-right shunting through a ventricular septal defect. Temporary, pericardial friction sound may appear at acute period of myocardial infarction as a rule in case of damage of anterior wall of the left ventricle.

Blood pressure can elevate in the period of pain attack. Sign of impaired myocardial function are hypotension, small pulse (pulses porous), oliguria. Sudden death, presumably from ventricular fibrillation or asystole, may occur immediately, within the first hour of chest pain.

According to clinical features and results Additional methods of examination five periods of myocardial infarction are distinguished: very acute, acute, subacute, recovery, stabilization. Acute period lasts approximately two days and characterized by diminished or disappeared chest pain. Nevertheless at this period may be the complications such as acute heart failure, disorders of cardiac rhythm and conduction, cardiogenic shock.

At the peak of first day at patient develops the syndrome related to the resurbtion of necrotic tissue. This syndrome includes elevated temperature, leukocytosis and accelerated ESR.

In case of bening course of disease at the subacute period the patient's condition becomes better, chest pain as usually absent, the heart sound louder, blood pressure remove to normal level. The signs of resorbtion syndrome disappeared. Prolonged leukocytosis and accelerated ECR indicate on accompanied complication, such as postinfarction syndrome or presence of inflammatory process as pneumonia, thromboflibites. At the period of recovery and stabilization the myocardial scar is formatted. The patient's condition is satisfactory, temperature is normal, tolerance to exercise load and physical activity are increased. The loudness of cardiac sound is slight decreased or normal. Heart rate is normal. Arrhythmia may preserve, but a number life-threatening arrhythmia is diminished. Hypertrophy of left ventricle reflects the cardiac remodeling in post infarction period.

Laboratory findings are normalized.

Course and outcomes of myocardial infarction depends on accompanied *complications.* In acute period may be such complications: disorders of rhythm and conduction, acute left ventricular failure (cardiac asthma, pulmonary edema), cardiogenic shock, acute aneurysm of left ventricle, rupture of the ventricle with cardiac tamponade and is usually fatal, pericarditis, thromboembolism, acute lesions and ulcers of gastrointestinal tract. In subacute period may observe: disorders of rhythm and conduction, chronic heart failure, chronic aneurysm of left ventricle, post-infarction angina, thromboembolism, post-infarction remodeling, post-infarction syndrome (Dressler's syndrome).

Nearly all patients with different variants of myocardial infarction have arrhythmias, which may be mild with favorable outcomes, but sometimes cause life threatening events. Ventricular fibrillation occurs in about 5-10 % of patients with myocardial infarction and is the major cause of sudden death. Atrial fibrillation is frequently transient state. Heart block complicating infarction is usually temporary and removes after specific treatment. Heart block complicating arterior infarction has unfavorable prognosis, because asystole may suddenly appear.

Cardiogenic shock - the most severe complication of myocardial infarction. Diagnostic signs of cardigenic shock: deranged consciousness, fall systolic blood pressure less 90 mm Hg, peripheral vasoconstriction and decreased volume of urine less 20 ml/hour. According to the leading mechanism there are three kind of shock: reflectory, arrhythmic, and true cardiogenic shock. Reflectory shock develops at patients with status anginous as a hemodynamic reaction on pain. Arrhythmical shock is resulting from paroxysmal tachycardia or cardiac blockade. True cardiogenic shock is explained by damage of cardiomyocytes, disorders of microcirculation and pronounced decreasing of contractile ability of left ventricle.

Heart failure complicating acute myocardial infarction indicates a bad prognosis. Cardiac asthma and pulmonary edema develop due to the acute left ventricular failure at approximately in up 10-15 % of patients and often lead to death. Classification of the acute heart failure at patients with myocardial infarction was proposed in 1967 by Killip. Four classes of acute heart failure are distinguished: 1 class - absence of pulmonary rales and gallop cardiac rhythm, this class develops at 40-50 % of patients and mortality is till 10 %. 2 class - presence of rales in less 50 % of lung areas or gallop rhythm, this class develops at 30-40 % of patients, mortality is till 20 %. 3 class - presence of rales in more, 50 % of lung areas associated with gallop rhythm, this class develop at 10-15 % of patients, mortality is till 40 %. 4 class - presence of cardiac shock, develops at 5-20 % of patients, mortality is till 50-90 %.

In approximately 10% of patients full thickness myocardial infarction causes thinning of the infracted segment and develops the bulge at the left ventricle so called ***aneurysm,*** revealed during inspection of the heart region as weak restricted pulsation in the III-IV intercostals spaces somewhat laterally from the left sternal edge. ***Post-infarction angina*** occurs in up to 50 % of patients. ***Thromboembolism*** is determined in different vessel sites with clinical features of stroke, pulmonary infarction and ischemic limb. Primary thrombus forms on the endocardial surface of freshly infarcted myocardium and transformed to systemic embolism.

The post-infarction syndrome (Dressler's syndrome) is an autoimmune reaction to necrotic process in myocardium and is characterized by persistent fever, pericarditis and pleurisy. The Dressler's syndrome occurs a few weeks or even month after the myocardial infaction.

Additional methods of examination

Clinical blood analysis - leukocytosis with mild nuclear shift to the left occurs in a few hours after onset of chest pain, reached the peak at 2-4 days and normalized in a week. The degree of leukocytosis depends on amount of damaged myocardial

tissue. Accelerated ESR is observed at 2-3 days from onset of chest pain, reached maximal level till 2 week and normalized at 3-4 weeks.

Markers of myocardial infarction are plasma enzymes, which are normally concentrated within cardiac cells. During the necrosis of cardiomyocytes their membranes destroyed and the enzymes released at first at microcirculation and later at systemic circulation. Thus myocardial infarction causes a detectable rise in the plasma enzymes which serve as laboratory markers of necrosis: creatine kinase, lactate dehydrogenase, aspartate aminotransferase, troponin T and I, myoglobin. Optimal time for estimation of myocardial markers of necrosis depicted at table.

Table 4

Optimal time for estimation of myocardial markers of necrosis

Markers	Optimal time for estimation of myocardial markers of necrosis
Myoglobin	In 1-2 hours after chest pain
Creatine kinase	Every 12 hours 3 time
Creatine kinase MB	In 60-90 minutes after chest pain, every 12 hours 3 time
Lactate dehydrogenase	In 24 hours after chest pain, one time
Troponin T	In 12 hours after chest pain, one time
Troponin I	In 12 hours after chest pain, one time

Baseline and peak elevation of markers of myocardial damage is different. Dynamic of laboratory markers of myocardial infarction is depicted at table below.

Table 5

Dynamic of laboratory markers of myocardial infarction

Markers	Norma	Time from onset of myocardial infarction		
		Baseline elevation hours	Peak elevation hours	Normalization days
Creatine kinase MB	0-4 ME/L	3-6	12-24	1,5-3
Lactate dehydrogenase	15-30%	12-24	24-72	7-14
Aspartate aminotransferase	28-125 mmol/l	8-12	24-48	3-5
Troponin T, I	Less 0,1 mkg/1	3-12	12-48	3-16
Myoglobin	20-66 mkg/1	1-4	6-7	1

ECG: one of the most significant uses of a 12 lead ECG is to aid in determining whether a myocardial infarction has occurred.

The usual first finding in an infarction is elevation of the ST-segment, which occurs some hours after infarction. Hours to days later the T-wave inverts, diminution of the size of the R-wave and the Q-wave becomes deep and wide. The height of the R-wave is directly proportional to the amount of living tissue that escapes death. In case of full thickness myocardial infarction the R-wave is disappeared. Days to weeks later the ST-segment returns to near normal isoilectric line position. Weeks to moths later the T-wave becomes upright again, but Q-wave may remain abnormal. As the infarction heals the Q-wave may remain as the only sign of an old coronary occlusion. Since a deep and wide Q-wave is often indicate of an old infarction. The Q-wave may considered abnormal if it is over 0,03 second wide and if it is greater in depth than one fourth the height of the R-wave.

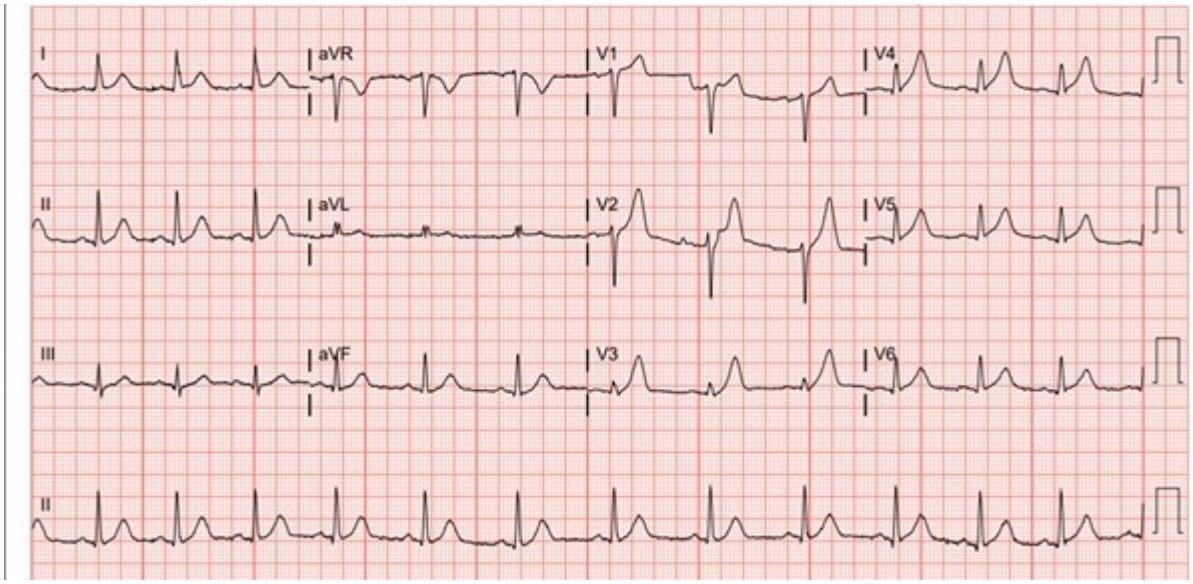

Image 6. Acute Myocardial Infarction in a 29-year-old male
The image was downloaded from website https://www.emra.org/emresident

Echo-CG: two-dimensional echocardiography may assess the cardiac structures, pericardium and ascending aorta, allows identification of regional wall motion abnormalities, valvular abnormalities, global left and right ventricular function and detecting important complications such as cardiac rupture, ventricular septal defect, mitral regurgitation and pericardial effusion.

Radioisotope scintigraphy by technetium-99m-pyrophosphate. Scintigraphy is generally used for the diagnosis of myocardial infarction in patients hospitalized late after the onset of symptoms in which cardiac enzymes are no longer elevated or are

unreliable. Imaging is optimal 2-7 days after myocardial infarction. Focal increases in technetium pyrophosphate uptake are generally diagnostic of infarction. This technique is highly sensitive (>90 %) in detecting large transmural infarctien but is less reliable in the detection of small non-Q-wave myocardial infarction.

Radionuclide ventriculography allows to reveal right and left ventricular ejection fraction and assessment of regional wall motion abnormalities. Because radionuclide ventriculography provides less information regarding the cardiac structures, echocardiography is generally preferred in the initial evaluation of patients with myocardial infarction

SUDDEN CARDIAC DEATH

Sudden cardiac death (SCD) is defined as follows: "Natural death due to cardiac causes, heralded by abrupt loss of consciousness within one hour of the onset of acute symptoms; preexisting heart disease may have been known to the present, but the time and mode of death are unexpected". The key concepts that are central in the definition of sudden death are the non-traumatic nature of the event and the fact that sudden death is unexpected and instantaneous.

The single most important cause of death in the adult population of the industrialized world is SCD due to *ischemic heart disease.* In patients with sudden cardiovascular collapse, the most often recorded rhythm shows that ventricular fibrillation is present in 75-80% of cases, whereas bradyarrhythmias are thought to contribute to a minority of SCD. In about 5% to 10% of cases, SCD occurs in the absence of coronary artery disease or congestive heart failure.

Clinical features

Complains: giddiness, darkening in the eyes, sudden appearance of dyspnea.

Objective examination

grave condition, passive position, loss of consciousness expansion of pupils, appearance of pale-grey tint of skin, apnea, absence of heart sounds, absence of pulse on large arteries.

Program examination for the prevention of sudden coronary death:

Clinical examination of patients with IHD, detection of risk factors, reanimated in the acute period of MI with the heart failure; with angina pectoris at rest after the MI; with the complete blockade of bundle-branches block.

Clinical analysis of blood, urinalysis. Biochemical analysis of blood: total protein, transaminases, creatin-phosphokinase, lactatdehydregenase, cholesterol, triglycerids, coagulogram. ECG-Holter-monitoring.

MAIN DIAGNOSTIC METHODS OF THE EXAMINATION OF THE DIGESTIVE SYSTEM. THE INTERVIEW AND THE EXAMINATION OF PATIENTS WITH GASTROINTESTINAL DISEASES. DIAGNOSTIC METHODS AND THE SEMIOTICS OF THE DIGESTIVE SYSTEM PATHOLOGY. BIOCHEMICAL BLOOD ANALYSES. BASIC SYNDROMES IN THE GASTROENTEROLOGY. CHANGES IN THE ORAL CAVITY IN THE CASE OF GASTROINTESTINAL DISEASES

Patients with the disorders of digestive system complain of poor appetite, perverted taste, regurgitation, heartburn, nausea, vomiting, epigastric pain, haematemesis and the feeling of overfilled stomach after meals. Determining the specific character of each symptom is important during inquiry of the patient.

Deranged (poor or increased) appetite occurs in infectious diseases, metabolic disorders, etc. Poor appetite or its complete absence (anorexia) is usually characteristic of gastric cancer. Appetite often increases in peptic ulcer, especially in duodenal ulcer. Appetite is perverted in pregnant women and in persons suffering from achlorhydria.

Bitter **belching** indicates intensive degradation of proteins. Belching is characteristic of stenosed pylorus with great distention of the stomach and significant congestion in it. Acid regurgitation is usually associated with hypersecretion of gastric juice and occurs mostly during pain attacks in ulcer.

Abdominal pain is the most important symptom.

It can be classified into:

- Somatic (parietal) pain - is caused by irritation of abdominal wall, peritoneum, root of the mesentery and diaphragm. It is a sharp, marked, localised pain, often accompanied by reflex muscle contraction (défense musculaire). It is conducted by sensitive branches of spinal nerves.

- Visceral pain - is caused by irritation of inner organs (tension of organ capsule or muscle wall). The pain is dull, the worst one can describe, usually in medial line; its localisation does not correspond to position of organs. It is conducted by sympathetic nerves.

- Referred pain (shooting) - caused by a strong stimulus or anatomic damage of organs (passage of calculus, intestinal hernia). Pain shoots into places on the body surface, which are innervated from the same spinal roots as the affected organ. Typical direction of pain helps to determine its origin.

In abdominal pain the following can be assessed:

Character - usually dull, compressive, stinging and spastic.

Localisation - of pain does not need to correspond to the position of the organ.

Irradiation - has greater importance than localisation of pain, allows determination of the affected organ.

The most common directions of irradiation are:

- Upward from epigastrium: disorder of lower esophagus, gastric cardia, and upper part of stomach (diagnostically need to differentiate stenocardia).
- Into the right subcostal area: gastroduodenal ulcer, biliary tract, the head of pancreas.
- Under the right shoulder blade: gall bladder disorder.
- Into the left subcostal area and under the left shoulder blade: body and cauda of pancreas, stomach or colon cancer.
- In between shoulder blades: inflammation and ulcer of esophagus, calculus in cystic duct, perforation of gastro-duodenal ulcer.
- Into shoulder: affection of diaphragm and subdiaphragmatic area (subphrenic abscess, spleen infarction, perforation of gastroduodenal ulcer).
- Into groin: kidneys, ureters.

Duration – varies, usually characteristic for the type of disease. Spastic pain lasts seconds, minutes, even hours; irritation of the mucous membrane lasts days but also weeks.

Rhythm – here means changing of periods with and without pain. “Colic” (colic pain) – is rhythmically recurring and repeatedly receding abdominal pain of various duration, caused by peristaltic of hollow organs (spasm and relaxation of smooth muscle tissue trying to overcome an obstacle in the passage); biliary – a calculus in the biliary duct, renal – a calculus in the ureter, intestinal – ileus, dyskinesia.

Triggering and relieving factors:

- Food intake - can improve or provoke pain (duodenal and gastric ulcer).
- Defecation - usually provokes pain in diseases of rectum (carcinoma, proctocolitis) and anal canal (fissure, hemorrhoids).
- Suitable position - usually brings relief in esophageal reflux disease (elevation of the chest) or pancreas carcinoma ("on all fours")

Perception of the pain: depends on the nature and extent of the impuls, as well as on the sensitivity threshold and patient’s interpretation of the sensation. It is always necessary to take into account the possibility of extraabdominal origin of the

pain. It can be radicular, associated with disorders of the abdominal wall, myalgia, myocardial infarction, and general symptoms of other diseases (e.g. decompensation of diabetes mellitus), toxic or infectious causes, and CNS disorders (tabes dorsalis).

Dyspepsia is a term difficult to define. It is used for overall expression of GIT discomfort of functional or organic origin, particularly of extra-gastrointestinal character (metabolism, medications).

Upper (gastric) dyspepsia - represents:

- Nausea (a desire to vomit)
- Vomitting
- Burping
- Pyrosis (heartburn)

Lower (intestinal) dyspepsia - the most common are:

- Defecation disorders
- Flatulence (flatus)
- Bloating (tympanites)

Dysphagia describes feeling of solid bolus stuck in the digestive tube while swallowing. According to localisation we distinguish upper or lower type. The reason can be mainly carcinoma or esophageal ulcer, esophageal reflux disease, or spasms. Paradox dysphagia represents troubles while swallowing some liquid. It usually has a functional character.

Pyrosis is a stinging feeling behind the lower part of sternum related to reflux of gastric or duodenal content to esophagus. Due to the nature of complaints it is necessary to exclude angina pectoris.

Vomiting has a complex reflex character, it is caused by irritation of the vomiting centre.

The following types of vomiting are recognised according to its cause:

- Central vomiting - toxicity (acidosis, uraemia), medication (digoxin, morphine), psychogenic (repulsion), intracranial hypertension (vomiting without nausea).
- Peripheral vomiting - in gastroduodenal diseases, biliary diseases, but also in otogenic diseases and during pregnancy.

Correct diagnosis of vomiting requires evaluation of the contexts of its origin and inspection of vomitus.

Origin - dependence on food intake in context with the time and type of food.

Appearance - color, presence of food (fresh, semi-digested), and/or blood.

Smell - sour indicates the presence of hydrochloric acid, faecal smell is connected with intestinal obstruction.

Constipation and diarrhea

Constipation means difficulty in emptying of rigid stool. Diarrhea is characterised by emptying of runny or watery stools, more often than usual.

Patient's comments in both cases are very subjective; therefore they cannot be relied upon. The following should be evaluated number of stools, quantity, consistence, pathological admixture, and relation to food intake.

The urgent desire to empty the bowel (tenesmus) is also assessed. Causes can be functional, infectious, or organic, they always require careful diagnoses because of possible presence of colorectal carcinoma.

Bleeding into gastrointestinal tract (GIT)

Melena, enterorrhagia. Melena means leaving of runny stool of black color, and tar appearance. It is caused by bleeding in upper part of the digestive tube (esophagus, stomach, duodenum). Evaluating of black colored stool can be made more difficult by previous intake of food containing animal blood, some medications (containing iron, bismuth, or charcoal).

Bleeding from lower part of GIT is manifested by enterorrhagia (blood is not semi-digested). The most common reason can be colorectal carcinoma, internal hemorrhoids, and idiopathic proctocolitis.

Hematemesis represents vomiting of fresh or semi-digested blood. Coloring depends on bleeding intensity, speed of stomach emptying, and presence of hydrochloric acid. Slow emptying and effect of hydrochloric acid causes brown-black coloring, it looks like coffee grounds.

The source of bleeding are usually esophageal varicose, duodenal or gastric ulcers, hemorrhagic gastropathy, and tumors. Presence of blood admixture in repeated forcefull vomiting means high probability of Mallory-Weiss syndrome (laceration – rupture of mucous membrane of distal part of esophagus). Evaluation of hematemesis requires excluding other causes of bleeding (epistasis, hemoptysis), particularly confusion with consumed food (blackberry, beetroot) or some medications (charcoal). Hematemesis may occur together with melena.

Physical Examination. During general inspection of the patient the physician may assess poor nutrition of the patient (cachexia), which is characteristic of stomach cancer and untreated benign pyloric stenosis. Pale skin is observed after gastric haemorrhage. Patients with uncomplicated peptic ulcer look practically healthy.

Next stage is inspection of the abdomen. Physical examination of the abdominal organs is performed in two positions: lying and upright.

The abdominal cavity is divided into several areas. Two parallel horizontal lines, one of which joins the costal arches, the other upper axes of the iliac bones, divide the abdomen into three portions: upper, epigastric region; median, mesogastric region; lower, hypogastric. Two parallel vertical lines, going through the external edges of the abdominal rectal muscle, divide the abdomen into the right and left hypochondriac and epigastric regions, mesogastric region is divided into left and right iliac regions and umbilical region, which is located between them; the hypogastric region is divided into left and right inguinal regions and suprapubic region located between them.

The abdomen is examined in the following way: the shape of the abdomen, symmetrical shape of the both halves, umbilicus, the integument of the abdominal wall, participation of the abdomen in the act of respiration.

Shape of the abdomen is determined by the constitution. In pathologic conditions, the shape of the abdomen may change: first, it may enlarge or diminish, the halves being symmetrical; second, it may be pulled in or stuck out in some regions. General enlargement of the abdomen is seen in pregnant. Pathological enlargement of the abdomen is observed in ascites, obesity, flatulence (accumulation of gases in the intestine). Asymmetrical sticking out, when only one area is prominent, is observed at enlargement of separate organs, e.g. liver, spleen, in tumors from these organs and other abdominal organs (stomach, pancreas, intestine). In case of general retraction, the abdomen is boat-shaped. This is observed in alimentary dystrophy, chronic dysentery, narrowing of the pylorus, cancer cachexia, prolonged diarrhea and vomiting. Retraction of separate areas of abdomen is rare. Thus, retraction in the epigastric area may be seen in gastroptosis or splanchnoptosis.

The state of the abdominal integument. The normal skin of the abdomen is pale rose, smooth, dull. It is necessary to pay attention to the rashes, hernias, development of the subcutaneous veins, separate pulsations, scars, and pigmentations.

Doing inspection it is necessary to pay attention to the movement of the anterior abdominal wall which may be associated with stomach peristalsis, intestine, pulsation of the aorta, right ventricle, liver as well as respiratory excursions.

Palpation of the abdomen. Palpation is the main method of physical examination in diagnosis of diseases of the abdominal organs. Surface and deep palpation are used.

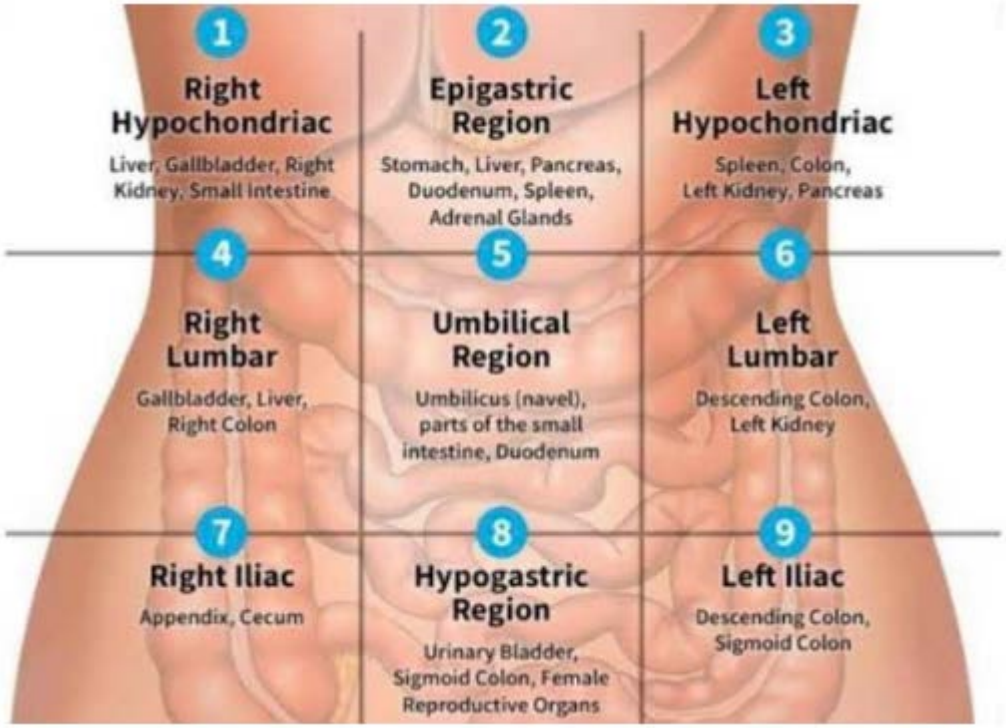

Image 7. Palpation of the abdomen
The image was downloaded from website https://medsim.in/help/Abdomen

Surface tentative palpation. The purpose of surface palpation is to determine the presence of tenderness of the whole abdominal wall or its separate portions, the tone of the abdominal muscles, presence of large tumors and enlargement of the abdominal organs, presence of tumors in the abdominal wall, edema of the abdominal wall, presence of hernias.

The physician assumes his position by the bedside as described above and places his right hand flat on the abdomen of the patient (the fingers may be slightly flexed) to examine carefully and gradually the entire abdomen without trying to penetrate the deep parts of the abdomen. By this examination the physician should establish the strain of the abdomen, its tenderness, and location of the painful site. The left inguinal area should be examined first, provided the patient does not complain of pain in this region. Palpation is then continued by examining symmetrical points of the abdomen on its left and right sides to end in the epigastric region. If the patient complains of pain in the left inguinal area, the sequence of palpation should be so changed that the least painful site on the anterior abdomen should first be examined. The physician should simultaneously assess the condition of the abdominal skin and subcutaneous connective tissue, the strain of the abdominal wall, the zones of superficial and deeper painful areas to locate them accurately. Hernial separation of

muscles and protrusions, and also other anatomical changes should be revealed, if any. Resistance and marked strain of muscles of the abdominal wall are usually palpated over the organ affected by inflammation, especially so if the peritoneum is involved. In the presence of acute inflammation of the peritoneum (local inflammation included, e.g. in appendicitis, cholecystitis, and the like), local pressure causes strong pain but it becomes even more severe when the pressure is released Shchetkin-Blumberg symptom). In the presence of pronounced enlargement of the parenchymatous organs, in strained abdomen or intestinal loops, and also in the presence of large tumors, even surface palpation can give much diagnostic information.

The sign of fluid fluctuation helps to recognize ascites. The palm of the left hand is placed on the lateral surface of the right half of the abdomen, short pushes are made by the finders of the right hand along the lateral surface of the abdomen. When large volumes of free fluid are present in the abdominal cavity, the left hand feels clearly its pushes simultaneously with the movements of the right hand fingers.

Deep sliding methodical palpation of intestine, stomach, liver

Percussion is used to determine the borders, size and configuration of the liver. The superior and inferior borders of the liver are outlined. Two superior borders of liver dullness are distinguished: relative dullness, which is the true upper border of the liver, and the absolute dullness, i.e. the upper border of that part of the anterior surface of the liver which is directly adjacent to the chest and is not covered by the lungs. But in practice only absolute dullness is determined, because the upper border of the liver is covered by the lung and the percussion sphere dose not reach it. The upper border of absolute dullness corresponds to the lower border of the right lung. Deep palpation of the abdomen as an objective methods of investigation of the abdominal organs was suggested by professor V.P. Obraztsov and improved by proffers N.D. Strazhesko and V.H. Vasilenko.

The purpose of deep palpation is to study the topography of intestine, stomach, liver, spleen, kidneys, to determine the size, shape. Location of these organs, their motility, tenderness, consistence, as well as the properties of the wall and the character of the content (for the hollow organs) and palpate the tumors in the abdominal cavity.

The palpation technique includes the following four steps. *First*: proper positioning of the physician's hands. The right hand is placed flat on the anterior abdominal wall, perpendicular to the axis of the examined part or the edge of the examined organ. *Second*: formation of a skin fold to facilitate further movements of the examining hand.

Third: moving the hand inside the abdomen. Deep palpation is when the fingers are moved gradually, with each expiration, into the abdomen when the abdominal wall is relaxed. The examining hand thus reaches the posterior wall of the abdomen or the underlying organ. *Fourth*: sliding movement of the fingertips in the direction perpendicular to the transverse axis of the examined organ. The organ is pressed against the posterior wall and the examining fingers continue moving over the examined intestine or the stomach curvature. Depending on the position of the organ, the sliding movement should be either from inside, in the outward direction (the sigmoid, caecum) or in the downward direction (the stomach, transverse colon); the movements should then be more oblique in accordance with the deviation of the organ from the horizontal or vertical course. The examining hand should always move together with the skin and not over its surface.

By palpating the intestine, the physician establishes its localization, mobility, tenderness, consistency, diameter, the condition of the surface, the absence or presence of rumbling sounds during palpation.

The **sigmoid** is palpated from top right to medial left, downward and laterally, perpendicularly to the axis of the intestine which runs obliquely in the left iliac space at the border of median and the outer third of the linea umbilico-iliacae. Palpation is carried out by four fingers, placed together and slightly flexed, or by the ulnar edge of the right little finger. The fingers are immersed medially of the expected position of the intestine and as soon as the posterior wall of the abdomen is reached, the fingers slide along the intestine in the given direction, i.e. laterally and downward. The intestine is pressed against the posterior wall and first slides along it (to the extent allowed by the mesenteric length) but later it slips from under the examining fingers. The sigmoid can be palpated by the described technique in 90-95 per cent of cases. Normally the sigmoid can be palpated over the length of 20-25 cm as a smooth firm cylinder, its thickness being that of a thumb or an index finger; the sigmoid is painless to palpation, it does not produce rumbling sounds, its peristalsis is rather flaccid and infrequent. The sigmoid can be displaced 3-5 cm to either side.

The **caecum** is palpated by the same technique, except that the direction is different. Since the caecum is situated at the border of the median and lateral third of the umbilico-iliac line (5 cm by the iliac spine), the palpation is carried along this line or parallel to it. A normal caecum can be palpated in 80-85 per cent of cases as a moderately strained cylinder (widening to the round bottom), 2-3 cm in diameter; when

pressed upon, it rumbles. Palpation is painless. It reveals a certain passive mobility of the caecum (to 2-3 cm).

The **ascending** and **descending colons** are palpated by two hands. The left hand is placed under the left and then the right lumbar side, while the fingers of the right hand press on the anterior wall of the abdominal cavity until the examiner feels his right and left hands meet. The examining fingers then slide laterally, perpendicularly to the axis of the intestine.

The **transverse colon** is palpated by four fingers of the right hand held together and slightly flexed. Bimanual palpation can also be used. Since the position of the transverse colon is unstable, it is useful first to determine the lower border of the stomach, and only then to search for the colon some 2-3 cm below this border. The right hand (or both hands) is placed on the sides of the linea alba and the skin is moved slightly upwards. The examining hand is then immersed gradually during relaxation of the prelum at expiration until the posterior wall of the abdomen is felt. Once the posterior wall is reached, the examining hand should slide down to feel the intestine: this is an arching (transverse) cylinder of moderate density (2-2.5 cm thick), easily movable up and down, painless and silent. If the intestine is impalpable in this region, the same technique should be used to examine the lower and lateral regions, the position of the palpating hands being changed accordingly. Normal transverse colon can be palpated in 60-70 per cent of cases.

Methods of definition of the bottom border of a **stomach**.

Deep palpation of the stomach. The examiner pulls up the skin on the abdomen and presses carefully the anterior wall of the abdomen to penetrate the depth until the examining fingers reach the posterior wall. When pressed against the posterior wall of the abdomen, the stomach slips from under the examining fingers. The greater curvature and the pylorus can best of all be examined by this method. The greater curvature can be examined by deep sliding palpation in 50-60 per cent and the pylorus in 20-25 per cent of healthy subjects. The greater curvature is found to either side of the median line, 2-3 cm above the nave.

Percussion is used to determine the inferior border of the stomach. Provided professional skill is high, the inferior border of the stomach can be outlined by light percussion by, differentiating between gastric and intestinal tympany.

Better results are obtained on direct percussion with one finger according to Obraztsov (technique of *percutory palpation*). It consists in determining the location of the lower border of the stomach according to a splashing sound. A splashing

sound is produced by quick tapping with the finger of the right hand on the abdominal wall, the tapping finger should do gathering movements downwards and inwards. A splashing sound appears at the moment of tapping. The fingers gradually move down beginning from the epigastric area. The place, where the splashing sound disappears, corresponds to the border of the stomach. In healthy moderately nourished men the border is 3-4 cm above the umbilicus along the median line, in women 1-2 cm below.

Auscultation of the stomach is used together with palpation of the stomach to outline its inferior border. *Stethacoustic palpation* is performed as follows: a stethoscope is placed beneath the left costal arch, below the Traube's face. The examiner rubs the abdominal wall overlying the stomach by the finger and gradually moves the finger away from the stethoscope bell. As during as the finger rubs the skin overlying the stomach, the physician hears the friction, but when the finger moves outside the stomach borders, the found disappears. This method is very simple but the findings are sometimes inaccurate.

Palpation of the pyloric portion: the palpating fingers are placed in the triangle formed by the lower border of the liver, median line, and transverse line going 3-4 cm above the umbilicus in the area of the right rectal muscle and are moved on the left of this space downward and to the right. A thin moderately movable cylinder is felt, its density varies (from dense to not detected). Sliding along this cylinder may produce borborygmus.

Determination of the lower border of absolute liver dullness (according to Obraztsov and Strazhesko) should be begun from the right part of the abdomen along the right anterior axillary line with the patient in the horizontal position. The plessimeter finger is placed parallel to the expected inferior border of the liver. As the plessimeter finger is then moved upwards, tympany is followed by absolute dullness. The point of disappearance of tympany is marked in each pitied line (right midclavicular, right parasternal, and anterior median line).

When determining the left border of liver dullness, the plessimeter finger is placed perpendicularly to the edge of the left costal arch, at the level of the 8-9th ribs, and percussion is carried out to the right, directly liver the edge of the costal arch, to the point where tympany changes to dullness.

Normally the inferior border of absolute dullness of a lying patient with normosthenic chest passes at the 10th rib in the right anterior axillary line, it the superior edge of the right arch in the midclavicular line, 2 cm below the interior edge

of the right costal arch in the right parasternal line, and 5-6 cm away from the inferior edge of the xiphoid process (at the border of the upper third of the distance from the base of the xiphoid process to the navel) in the anterior median line; on the left the border does not extend beyond the left parasternal line.

The size of the liver can be determined according to M.G. Kurlov. First, the percussion is done downward the right medioclavicular line up to the liver dullness. This place is marked on the skin. After that percussion is done along the same line from the level of the umbilicus upwards until a dull sound appears, this point is also marked on the skin with ink. The distance between the points (normally 9±1-2 cm) is the size of the right lobe of the liver. The third point is marked at the base of the xiphoid process along the median line. Then percussion is done upward from the umbilicus up to the point of dullness, which is also marked on the skin. The distance between the points is the size of the liver in its middle portion (approximately 8±1-2 cm). At last, percussion is done from point 3 along the left costal arch until a tympanic sound appears, the fifth point is also marked. The distance between these points is 1±1-2 cm (the length of the left half of the liver).

Palpation on the liver. The palm of the left finger presses the right costal arch, the palm of the right finger is placed flat on the right side of the abdomen the fingers are parallel to the direction of the lower border of the liver below its supposed level which can be detected by percussion as well as by sliding of the palpating fingers from the lower edge of the costal arch downwards until the consistence becomes soft. The tips of the fingers penetrate 1-2 cm in depth, them without removing the fingers, the patient is asked to breathe deeply and slowly. The edge of the liver, making respiratory excursions, surrounds the palpating fingers, this allows to have an idea about its properties. In 80% of healthy persons the edge of the liver is rounded, thin, elastic, insensitive, and is felt on the costal arch along the medioclavicular line.

The enlargement of the liver often results from various pathological processes (hepatitis, cirrhosis, cancer, echinococcus, blood congestion in heart failure).

Percussion of the spleen allows determining the size of the organ. Only the lower 2/3 of the organ adjacent to the chest wall can be percussed. Low percussion is used, it produces a dull sound over the spleen. As the spleen borders on air-containing organs, even minute increase of percussion force involves them in the percussion sphere and a tympanic sound is added to the dull percussion sound. Percussion is better performed in a vertical position on in right decubitus along the middle axillary line. The patient is asked to breathe normally. Dullness,

corresponding to the location of the spleen, occupies the area of the 9-10th ribs; it does not cross the anterior axillary line. The long axis of the spleen is 5-6 cm, the width of the spleen dullness is 4-8 cm.

Spleen palpation is done in supine and right diagonal position. The patient is supine. The palm of the right hand presses the left costal arch, the left palm is flat on the upper portion of the left half of the abdomen below the left hypochondrium. The fingers are slightly flexed and directed parallel the costal arch. The palpating fingers penetrate 1-2 cm in depth, then the patient is asked to breathe slowly and deeply, the fingers remain still. If the border of the spleen is detected, it suggests its enlargement. Moderate enlargement is observed in acute infections, syphilis, cirrhosis of the liver, bacterial endocarditis, lymphogranulomatosis, hemolytic jaundice.

SYNDROM OF FUNCTIONAL DYSPEPSIA

Syndrome of functional dyspepsia - the complex of the symptoms that includes the pain and feeling of the discomfort in epigastria, heaviness and feeling of overflow after meal, early saturation, swelling of a stomach, nausea, vomiting, eructation, heartburn and other signs at which it is not possible to reveal organic pathology.

Classification

I. According to the type of dyspepsia there are distinguish:

- the ulcer-like type;
- the dysmotor type;
- the nonspecific type.

II. According to the stage of dyspepsia there are distinguish:

- stage of aggravation;
- stage of unstable remission;
- stage of remission.

Clinical features

In patients with functional dyspepsia the clinical picture includes the general neurologic displays - sleeplessness, migraines, irritability, bad mood and special (gastric) that depend on a type of dyspepsia.

Ulcer-like type - is characterized by periodic pain in epigastria, the moderate intensity, as a rule without irradiation, arising on an empty stomach (hungry pains) or at night (night pains), relieved after reception of food and/or antacids.

Dysmotor type - is characterized by the feeling of early saturation, weight, overflow, a swelling in the epigastria; sensation of discomfort after meal; nausea, sometimes vomiting; decrease in appetite.

At a *nonspecific type* there can be various attributes, which difficultly carry to any of described variants.

For functional dyspepsia there are specific three attributes (according to Roman (III) diagnostic criteria):

- constant or recurrent dyspepsia (a pain or the discomfort localized in epigastria), which duration not less than 12 weeks for last 6 months (between aggravations there can be light intervals);

- on the basis of the anamnesis, endoscopic researches of the upper part of a gastrointestinal tract and ultrasound examination of abdominal cavity organs there are absent proofs of organic disease;

- absence of proofs, that dyspepsia is facilitated by defecation or connected with change of frequency of a stool.

Establishment of the diagnosis probably only by exception of disease with a similar clinical picture, especially that connected with the «symptoms of alarm» (a fever, an impurity of blood in stool, an anemia, accelerated ESR, unmotivated behaviors).

IRRITABLE BOWEL SYNDROME

Functional gastrointestinal disorders are defined as disorders of gut function in the absence of structural pathology. Irritable bowel syndrome is a function bowel disorder in which abdominal pain is associated with defaecation or a change in bowel habit with features of disordered defaecation and distension.

Irritable bowel syndrome encompasses a wide range of symptoms and single cause is unlikely. It is generally believed that most patients develop symptoms in response to psychosocial factors, altered gastrointestinal motility, altered visceral sensation or luminal factors.

Clinical features

The most common presentation is that of recurrent abdominal pain. This is usually colicky or “cramping”, is felt in the lower abdomen and is relived by defaecation. Abdominal bloating worsens throughout the day; the cause is unknown but it is not due to excessive intestinal gas. The bowel habit is variable. Most patients alternate between episodes of diarrhea and constipation. The constipated type tend to pass infrequent pellety stools, usually in association with abdominal pain. Those with

diarrhoea have frequent defaecation but produce low-volume stools. Passage of mucus is common.

Despite apparently severe symptoms, patients do not lose weight and are constitutionally well. Many have other “functional” symptoms including dyspepsia, headaches, backache, poor sleep and chronic fatigue syndrome. Physical examination does not reveal any abnormalities.

MALABSORPTION SYNDROMES

Malabsorption refers to impaired nutrient absorption at any point where nutrients are absorbed, and **maldigestion** refers to impaired nutrient digestion within the intestinal lumen or at the brush border.

Malabsorption can arise from any defect in the digestion/absorption process. These defects can result from an inherent disease of the mucosa, conditions that lead to acquired damage of the mucosa, congenital defects in the intestinal membrane transport systems, impaired absorption of specific nutrients, impaired GI motility (decreased peristalsis and stasis), disrupted bacterial flora, infection, or compromised blood flow or compromised lymphatics. The result is either a global impairment of absorption of all nutrients or specific nutrients.

Impaired nutrient absorption is often located somewhere along the small intestine since it provides a substantial surface area maximized by villi and microvilli and space within the lumen. Additional contributors to digestion and absorption are the gall bladder, pancreas, blood vessels, and lymphatics, each having direct relationships with the small intestine. Digestion and absorption occur by a combination of mechanical mixing, enzyme synthesis, enzyme secretion, enzymatic activity, mucosal integrity, blood supply, intestinal motility, and a balanced microbial flora. Presenting symptoms of malabsorption syndromes overlap and some combination of diarrhea, steatorrhea, unintentional weight loss, developmental delay or skeletal deformities (in children), and, in many cases, observable anemia.

There are three stages of nutrient absorption: luminal, mucosal, postabsorptive. Malabsorption syndromes are categorized according to which of these three stages is or are affected.

- The luminal phase involves mechanical mixing and digestive enzymes.
- The mucosal phase requires a properly functioning mucosal membrane for absorption.

- The postabsorptive phase becomes facilitated by an intact blood supply and lymphatic system.

Fat Malabsorption

Fat malabsorption is one of the most common malabsorption syndromes, and it arises from defects in fat digestion and absorption.

Causes

Significant disruption of fat breakdown typically results in steatorrhea.

- Decreased duodenal pH: optimal duodenal pH 6.5.
- Lost absorptive intestinal surface area: lost functional small intestine mucosa results in decreased transit time and reduced exposure to digestive enzymatic activity. The loss occurs through diffuse mucosal injury, enterocyte disease, functional loss, or complete loss of small intestinal mucosa (surgical resection).
- Crohn disease (an inflammatory bowel disease)
- Ulcerative colitis (an inflammatory bowel disease)
- Celiac disease
- Liver disease - liver disease such as hepatic cirrhosis impair bile acid synthesis. In gastrointestinal amyloidosis, the amyloid deposition in liver stellate cells can cause similar pathologies to fibrotic liver disease.
- Cholestasis - decreased or obstructed bile secretion and flow due to intrahepatic and/or extrahepatic pathology.
- Pancreatic exocrine insufficiency: defective production of pancreatic lipase, colipase, and bicarbonate.
- Defective chylomicron/lipoprotein secretion: Abetalipoproteinemia - defective apoproteins impair chylomicron packaging and secretion into the lymphatics. Mutations in the MTP gene cause it.

Carbohydrate Malabsorption

Carbohydrate digestion and absorption often refer to the starch, lactose, and sucrose of the human diet.

Causes

- Pancreatic amylase deficiency
- Inadequate disaccharidase activity:
    - Lactase deficiency (also known as hypolactasia) - the most common disaccharidase deficiency. Adult-onset lactase deficiency is present in the majority of the world’s population. Lactase is located on the surface of small intestinal microvilli and serves to cleave lactose into glucose

and galactose. During early childhood, lactase activity is down-regulated, leaving some individuals completely devoid of lactase enzymes. In this way, lactase deficiency is actually the result of decreased enzyme synthesis rather than a lactase defect. Lactase deficiency can also be congenital, like other disaccharidase deficiencies.

- Lost absorptive intestinal surface area
- Celiac disease (gluten-sensitive enteropathy, gluten-induced enteropathy, celiac sprue, non-tropical sprue)
- Tropical sprue (post-infective tropical malabsorption)
- Autoimmune enteropathy
- Intestinal lymphangiectasia
- Inflammatory bowel disease (IBD) - can create blind loops or cause lymphatic outflow obstruction.
- Crohn disease - a systemic disease that can affect any part of the GI tract and significantly impact the small intestine
- Ulcerative colitis - a condition that typically affects the colon and atypically can also include the terminal ileum.

Protein Malabsorption

Protein digestion and absorption begin as proteolysis in the stomach with proenzymes that become automatically activated at low pH levels (i.e., an acidic environment).

Causes

- Impaired pancreatic bicarbonate and protease secretion and/or activity: Chronic pancreatitis, cystic fibrosis
- Lost absorptive intestinal surface area: Inflammatory bowel disease (IBS), intestinal lymphangiectasia, bowel resection

Vitamin, Mineral, and Trace Element Malabsorption

Various intestinal transport mechanisms accomplish the absorption of vitamins, minerals, and trace elements. Dysfunction at any one of these levels results in malabsorption of that specific vitamin, mineral, trace element, or any nutrient dependant on them to be successfully absorbed. Deficiencies include but are not limited to deficiencies in vitamin B12, calcium iron, folate, vitamin D, magnesium, carotenoids, thiamin, copper, selenium, and more. The effects of malabsorption of these vitamins, minerals, or trace elements depend on which is deficient and the

degree to which they are deficient. Exploring the various mechanisms and covering the numerous etiologies are beyond the scope of this discussion.

Causes

- Pathology of the stomach or proximal small intestine (e.g., vitamin B12 deficiency)
- Fat malabsorption: caused when fatty acids bind calcium, magnesium, and other divalent cations.
- Lost absorptive intestinal surface area.

Bacterial Malabsorption

Whether transient, curable, or permanent sequelae transpire, bacterial malabsorption is most often due to *Giardia lamblia* (giardiasis), *Tropheryma whipplei*, *Cryptosporidium parvum* (cryptosporidiosis), and the Phylum Microspora (microsporidiosis).

History and Physical

*The history and physical a*re invaluable when initiating the evaluation of malabsorption syndromes. A malabsorption syndrome should be suspected when a patient's history includes but is not limited to ongoing or chronic diarrhea, unintentional weight loss despite normal nutrient intake, greasy, voluminous, foul-smelling stools that reportedly float. Additional components of the history may include flatulence, bloating, borborygmi. Abdominal pain might be reported but is less common in most malabsorption syndromes.

Key questions in the history and a focused physical exam help create a more targeted approach to diagnosing the patient's condition. A thorough history boosts cost-effectiveness and saves time. For those patients whose malabsorption syndrome is affected by emotions, early treatment can start through interviews alone. The therapeutic benefit comes from the nurturing of the patient-doctor relationship by empowering the patient and positively impacting the patient's self-esteem in the face of their malabsorption syndrome.

Questioning should include a review of systems, symptom duration, symptom timing, presence or absence of pain/pain radiation, location/location changes, intensity/intensity changes, known precipitating factors, associated symptoms (e.g., change in bowel habits/frequency), the appearance of the stool, whether or not the presenting symptoms have happened previously. Stool description could be of floating, pale, greasy stools, and a patient may report seeing oil droplets in the toilet, stool color, stool bulk, stool consistency, stool smell. Important additional questions

include past medical history (e.g., peptic ulcer disease), family history (especially for systemic and gastrointestinal conditions), medications, surgeries, radiation exposure/treatments, caustic substance ingestion, allergies, and social history (e.g., smoking, drinking, recreational drug use past or present).

Physical exam should include a full abdominal examination and inspection of neighboring systems to consider differential diagnoses that could also account for the patient's clinical presentation. The physical exam may yield findings of hyper/hypoactive bowel sounds, abdominal distention, abdominal tenderness (less common), pallor (suggests anemia), muscle wasting, abnormal deep tendon reflexes, skeletal deformities, rashes, cardiac arrhythmia, delayed growth (in infants and children), poor wound healing, ecchymosis, decreased visual acuity, peripheral neuropathy, auditory disturbances, or cognitive impairment.

General Evaluation for Malabsorption Syndromes

When the history and physical raise suspicion for malabsorption syndromes without strongly supporting a diagnosis requiring more specific testing, general testing may begin. An example is the non-specific symptoms of unintentional weight loss, ongoing diarrhea, or poor wound healing.

Laboratory testing is used to support the diagnosis but is not diagnostic.

Blood tests

- Comprehensive metabolic panel - electrolyte disturbances, hepatic function, renal function
- Complete blood cell count - contributes to evaluating anemia.
- Albumin
- Magnesium
- Zinc
- Phosphorous
- Vitamins (e.g., vitamin B12, folate, vitamin D)
- Iron panel (includes serum iron, total iron-binding capacity, ferritin)

Fecal tests: most sensitive for fat malabsorption syndromes

- Fecal fat - fecal fat is measured from a single specimen; if the test is positive or there remains high clinical suspicion of fat malabsorption syndrome, then testing proceeds to a 72-hour fecal fat excretion evaluation
- 72-hour fecal fat excretion - the gold standard for steatorrhea diagnosis; performed on a 72-hour stool collection, accurate interpretation of fecal fat depends on patient's successful adherence to testing instructions

- Sudan III stain - performed on a spot stool sample, sensitive
- Acid steatocrit
- Near-infrared reflectance analysis (NIRA) - comparable accuracy to a 72-hour fecal fat excretion analysis but faster; it also measures nitrogen and carbohydrates while measuring fecal fat.

SYNDROME OF BILE DUCTS DYSKINESIA
(dysfunctional bile tract disorders)

The syndrome of bile ducts dyskinesia is the complex of clinical symptoms which developing connects with moto-tonic dysfunction of gallbladder, bile ducts and sphincters. Dysfunctional bile tract disorders include not coordinated, untimely, insufficient or excessive reduction of a gallbladder and sphincters (Oddy, Lutkensa and Mirricy).

Classification

Depending on the etiological factor, localization and functional state there are the next forms of dysfunctional bile tract disorders:

I. *According to the etiology*:

1. Primary dysfunctional bile tract disorders (hereditary decrease of muscular tone, decrease of receptors apparatus sensitivity to neurohumoral stimulation).

2. Secondary dysfunctional bile tract disorders.

II. *According to the localization*:

1. Dysfunction of the gall bladder.

2. Dysfunction of the Oddy's sphincter.

III. *According to the functional state*:

1. Hyperfunction.

2. Hypofunction.

In hyperkinetic form of the gall bladder or/and bile ducts dysfunction the main complaints are: acute pain in the abdomen and clinical signs of neurotic syndrome.

Pain in the abdomen - is periodic, recurrent, colic like, localized in the right hypochondrial region with radiation to the back, right scapulae and right shoulder, aggravated more frequent at night-time after improper feeding, alcohol, augment physical or psychical activity.

In hypokinetic form of the gall bladder or/and bile ducts dysfunction the main complaints are: dull pain in the abdomen, clinical signs of neurotic and dyspeptic syndromes.

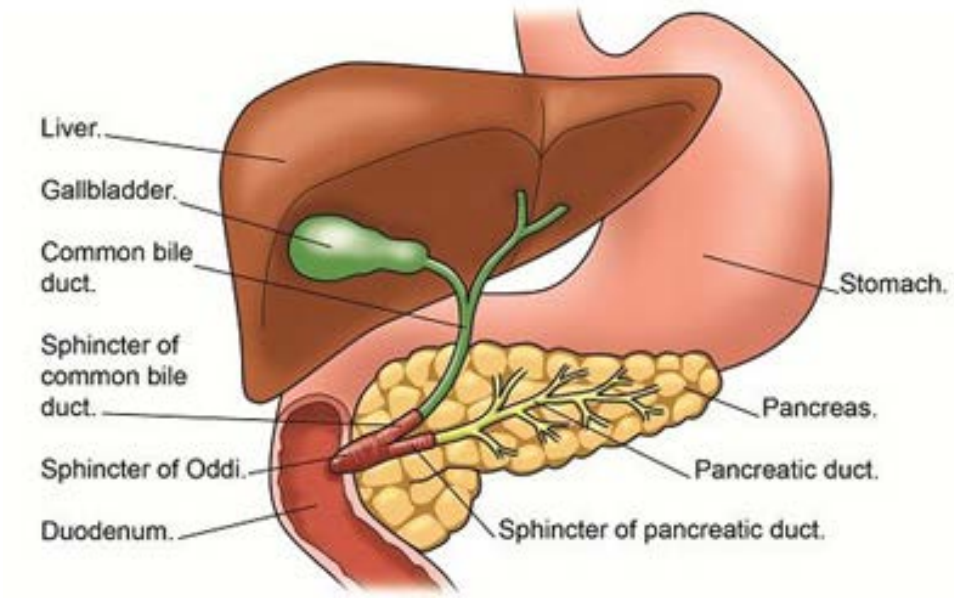

Image 8.Biliary system

The image was downloaded from website https://www.milehighhernia.com

Clinical features

Pain in the abdomen is periodic, recurrent, has dull holding apart character with localization in the right hypochondrial region and radiation to the back, right scapulae and right shoulder, aggravated during bending of body and at night-time after improper feeding, alcohol, augment physical or psychical activity.

The clinical signs of neurotic syndrome include - irritability, fatigue, perspiration, tachycardia, and headache. The clinical signs of dyspeptic syndrome include - bitterness in a mouth, nausea, vomiting and difficult defecation.

Objective examination

General patient's condition as usual satisfactory, consciousness is clear, posture is frequently active or active with restriction in cause of intensive biliar colic.

The color of the skin and visible mucosa has corporeal color *(cutis colons somatici),* without eruption, moderate moisture arid elasticity, preserved turgor, may observe transient subicteria of the skin.

The results of inspection, palpation, percussion and auscultation of respiratory and cardiovascular systems are without particularities.

In superficial tentative oriental palpation of the abdomen detect moderate pain in right hypochondria. Muscular resistance, diastases recti, and fluctuation symptoms are negative.

In penetrative palpation of the abdomen identify tenderness in gall bladder point (Ker point).

Additional methods of examination

Clinical blood analysis: without pathological changes.

Clinical urine analysis: without pathological changes.

Biochemistry blood analysis: increased activity of alkaline phosphotase and aspartate aminotransferases (more than in twice during two-multiple analisis), in combination with pancreatic ferments elevation (amylasa, lipasa), hyperbilirubunemia with predominance of bound fraction.

Medicament test (morphincholeretic test Debrea or morphinneostigmin test Nardy) - provocation of typical bile colic.

Ultrasound examination of the digestive organs. With obligatory evaluation of functional gall bladder state (use of bile discharge stimulated breakfast - 29g sorbitol in 100ml water) - specific constriction of gall bladder less than 40 %, increase of choledoch diameter more than after fat food.

Endoscopy. Endoscopic visualization of the biliary tree is now the best diagnostic procedure for stones, tumors, and strictures of the bile duct and is the only reliable means of diagnosing primary sclerosing cholangitis. Furthermore, it offers the therapeutic procedures of sphincterotomy, stone withdrawal, and the insertion of stents across strictures.

In patients with dysfunctional bile tract disorders the endoscopic sign are: edema and stricture of duodenal papilla.

Study of duodenal secretion. Reduction of gall bladder reflex (amount of bladder bile increase to 100-150ml in norm 30-70ml; the bile excreted by little portions; dilation of bile discharge more than 45min).

JAUNDICE

The syndrome of jaundice is one of the most widespread syndromes of the digestive system pathology that based on the significant hyperbilirubinemia and bilirubin accumulation in the tissue and skin.

Etiology

Depending on the etiological factor there are the next forms of jaundice:

A. Exogenic (false) jaundice or xanthosis.

B. Endogenic (true) jaundice:

I. Suprahepatic (hemolytic):

1. Hereditary hemolytic anemia (talassemia, Minkovskogo-Shofara).

2. Acquired hemolytic anemia (autoimmune, posthemotransfusion).

3. Increased erythrocytes hemolysis on different diseases:

- infections;
- burns;
- tumors;
- hemorrhages (hematoms, infarctions);
- on diseases with deranged erythropoesis (B_{12}-deficiency anemia, primary erythrocytosis, sideroplastic anemia).

II. Hepatic (parenchimatous):

1. Liver disease:

- different types of hepatitis;
- liver cirrhosis;
- tumor of the liver;
- Gilber's syndrome;
- Kriglera-Nayara syndrome;
- Dabina-Dgonsona syndrome;
- Rotor syndrome.

III. Subhepatic (mechanical):

1. Mechanical jaundice with tumor genesis:

- cancer of the pancreas;
- cancer of the major duodenal papilla;
- cancer of the bile bladder;
- cancer of the extra hepatic bile duels

2. Mechanical jaundice with non-tumor genesis:

- calculus cholecystitis.

Pathogenesis

Depending on the causes there are the next mechanisms of jaundice:

A. Exogenic (false) jaundice or xanthosis: xanthosis related with prolonged using of carotin (carrots), oranges, tangerines and administration of ethacridme lactate (rivanol), picric acid.

B. Endogenic (true) jandice:

I. ***Suprahepatic jaundice*** (icterus suprahepatica) occurs due to the excessive hemolysis of erythrocytes in the cells of the reticulohistocytic system (spleen, liver,

bone marrow). Hemoglobin brakes down to the globin and hem. Bilirubin is formed from the released hem and accumulates in blood. Observe in malaria, sepsis, poisoning by hemolytic substances, inherited or acquired hemolytic anemia.

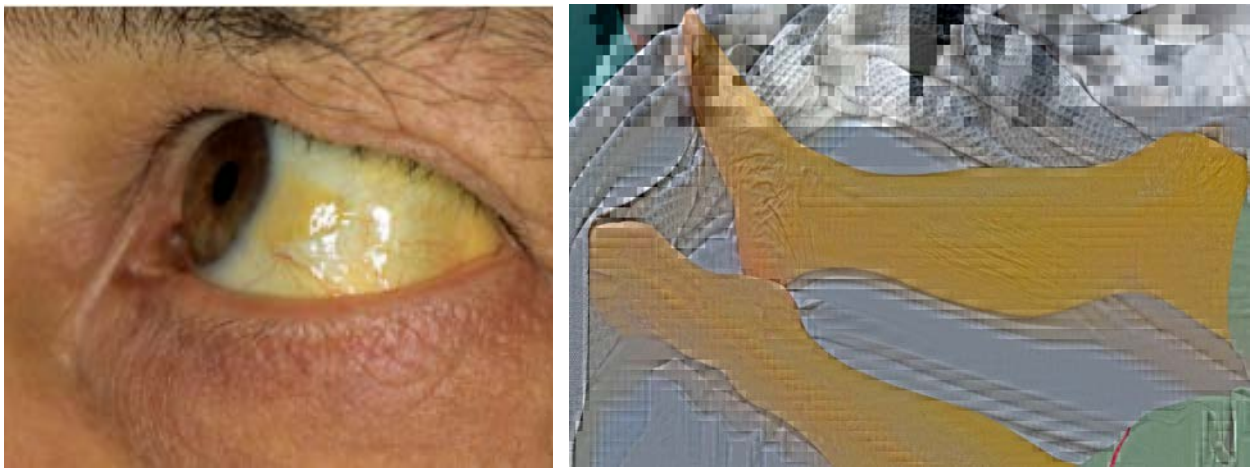

Image 9. Jaundice in adults
The image was downloaded from website https://www.healthdirect.gov.au/jaundice

On suprahepatic jaundice - it is characterized by lemon-yellow tint, moderate intensity without itching of the skin and hematological signs of anemia and hyperbilirubinemia in suprahepatic jaundice: bilirubinemia - increased of total bilirubin mainly due to the unbound bilirubin.

II. ***Hepatic jaundice*** (icterus hepatica) occurs due to the damage of hepatocytes and disorders of their function (inversion of unbound bilirubin to bound), observe in acute and chronic hepatitis, poisoning and other liver diseases. On parenchymatous jaundice it is characterized by orange-yellow tint. In hepatic jaundice: bilirubinemia - increased of total bilirubin due to the unbound and bound fractions.

III. ***Subhepatic jaundice*** (icterus infrahepatica) occurs due to the accumulation of bilirubin (the product of gradual oxidation of bilirubin) resulted from partial or complete obstruction of the common bile duct in patients with stones in the gall bladder, cancer of the head of the pancreas, cancer of the major duodenal papilla. On obstructive jaundice - it is characterized by greenish-yellow tint, with early appearance of skin itching (may be before jaundice manifestation). In subhepatic jaundice - increased of total bilirubin mainly due to the bound bilirubin.

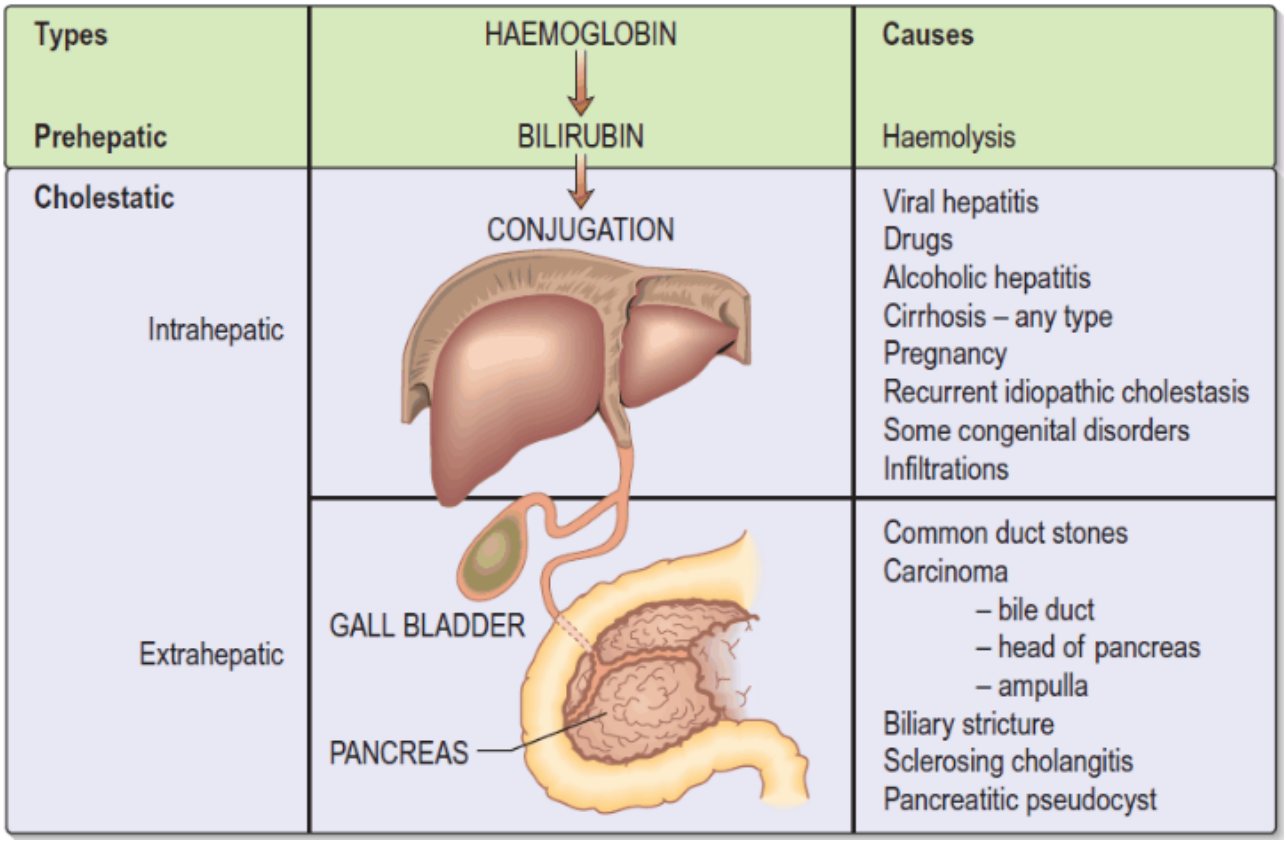

Image 10. Causes of jaundice

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Additional methods of examination

Clinical blood analysis: anemia, leukocytosis, neutrophilia and accelerated ESR.

Clinical urine analysis: the color is greenish-yellow or greenish-brown (beerlike), odorless, bilimbinuria and urobilinogenuria.

Biochemical blood analysis

In suprahepatic jaundice: bilirubinemia - increased of total bilirubin mainly due to the unbound bilirubin; dysproteinemia, positive thymol test; elevated aldolase; alanine aminotransferases;

In hepatic jaundice: bilirubinemia - increased of total bilirubin due to the unbound and bound fractions; dysproteinemia, positive thymol test; elevated prothrombin index (in significant degree of hepatic-cellular failure - decreased), decrease of total cholesterol, increased concentration of aldolase, alanine aminotransferases, aspartate aminotransferases, alkaline phosphatase, lactate dehydrogenase, cholinesterase, sorbitol dehydrogenase and ceruloplasmin.

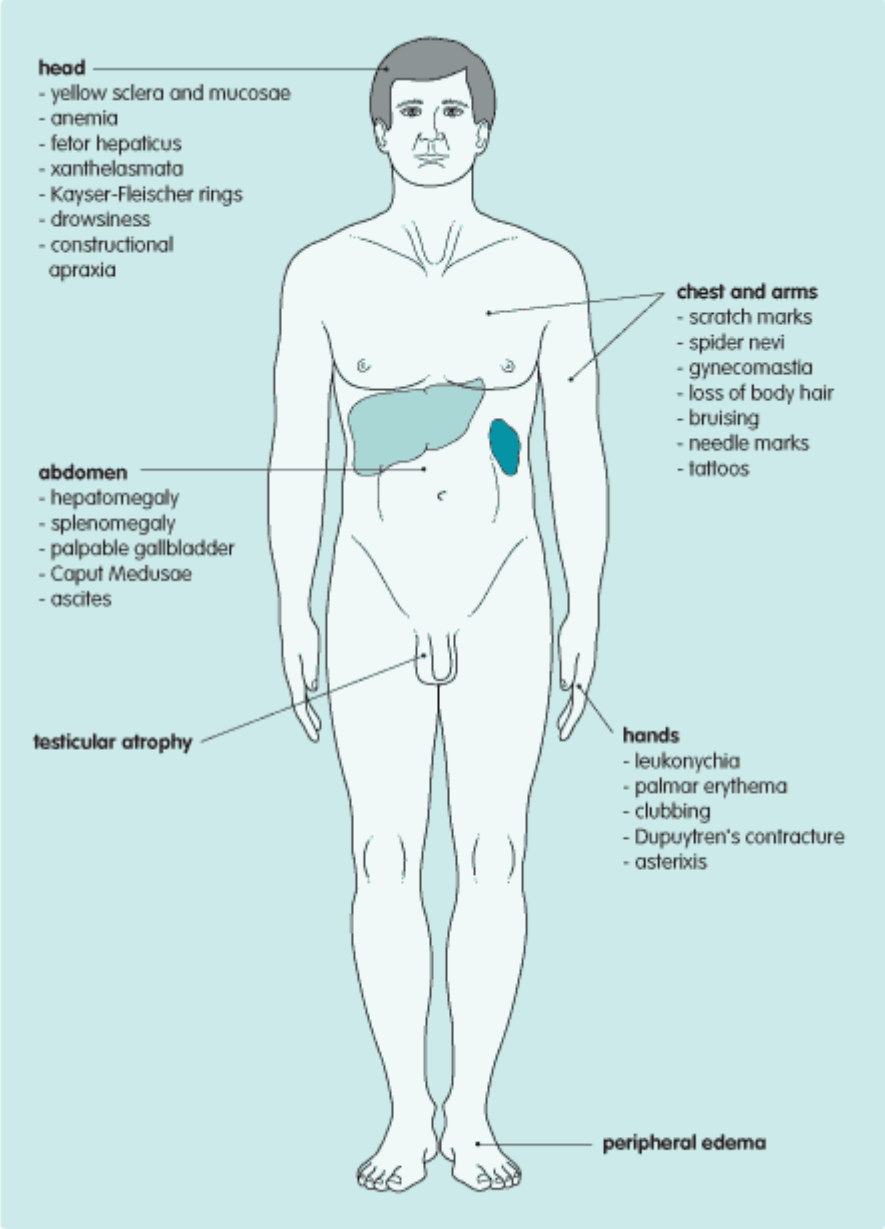

Image 11. Examining the patient with jaundice

The image was downloaded from website https://manualofmedicine.com

In subhepatic jaundice - increased of total bilirubin mainly due to the bound bilirubin; dysproteinemia, negative thymol test; elevation of prothrombin index, significant increase of total cholesterol and β-lipoproteins, moderate (non-obligatory) increase of alanine aminotransferases, aspartate aminotransferases, alkaline phosphatase and ceruloplasmin.

MAIN METHODS OF THE EXAMINATION OF THE URINARY SYSTEM. THE INTERVIEW AND THE EXAMINATION OF PATIENTS WITH THE URINARY SYSTEM DISEASES. LABORATORY AND INSTRUMENTAL TESTS OF THE URINARY SYSTEM. BASIC SYNDROMES IN THE NEPHROLOGY. THE EDEMA SYNDROME. CHANGES IN THE ORAL CAVITY IN THE CASE OF URINARY DISEASES

Interviewing of the patient: complaints

- Thirst
- Itching, easy bruising, and pale skin
- Bleeding
- Numbness in the feet or hands
- Disturbed sleep
- Restless legs syndrome
- Shortness of breath from fluid accumulation in the lungs
- Chest pain due to pericarditis
- Bone pain and fractures
- Muscle twitching or cramping
- Decreased sexual interest and erectile dysfunction
- Kidney' lumbar and abdominal pain
- Disordered urination
- Swelling of the legs and puffiness around the eyes
- Fatigue and weakness
- High blood pressure
- Headache
- Dizziness
- Deranged vision
- Dyspnea
- Loss of appetite, nausea and vomiting
- Changes in the urine -- its color, odor, and consistency
- Hyperthermia

Kidney' lumbar pain

- Kidneys' lumbar pain caused by the kidneys is typically felt in the flank area, which is in the back, just at the lower edge of the ribs on either side of the spine
- This pain caused by the kidneys tends to be sharp and severe, to and occur in waves

• Depending on the cause, it may radiate down the flank to the groin or toward the abdominal area

• Some individuals may develop fever, painful urination (dysuria), blood in the urine, nausea, and vomiting

• The renal tissue is devoid of pain receptors and the pain is felt when the capsule or the pelvis is distended

Kidney' abdominal pain

• Kidney' abdominal pain names renal colic and commonly caused by kidney stones

• Renal colic typically begins in the abdomen and often radiates to the hypochondrium or the groin

• It is typically colicky (comes in waves) due to ureteric peristalsis, but may be constant and is often described as one of the strongest pain sensations known

• The pain occurs when a stone becomes lodged in the ureter, the slender tube that connects the kidney with the bladder

Kidney' pain causes

• Bleeding in kidney (hemorrhage)
• Blood clots in kidney veins (renal vein thrombosis)
• Urinary tract infection
• Arteriosclerosis /atherosclerosis
• Horseshoe kidney
• Kidney tumor
• Kidney infection (pyelonephritis)
• Kidney swelling due to a backup of urine (hydronephrosis)
• Polycystic kidney disease

Table 7

Pain in selected urinary diseases

Disease	**Location** **Radiation**	**Character**
Nephrolithiasis	Loin pain, by the ureters course, more frequent unilateral, downward radiation	Periodic, intense, renal colic
Pyelonephritis	Loin pain, bilateral, without radiation	Dull, constant, increasing in intensity, accompanied by irregular fever
Renal abscess	Loin pain, unilateral	Pain and muscular tension, accompanied by fever, chills,

		headache, and symptoms of bacteriotoxic shock
Renal infarction	Loin pain, unilateral	Occur suddenly, intense, accompanied by excretion of red urine
Nephroptosis (movable kidney)	Loin pain, unilateral, inconstant pain location	Periodic, sometimes renal colic like, intensified in upright position, in physical exertion, in jolting motion, relieved in lying posture at rest
Acute glomerulonephritis	Loin pain, bilateral, without radiation	Dull, of insignificant intensity, in some patients the pain is absent
Congestive kidney	Loin pain, bilateral, without radiation	Dull, depend on degree of edematous syndrome
Cystitis	Suprapubical, increased in palpation	Pain is provoked by urination, most intense and burning at the end of it. Imperative increasing of urination by small portions of urine
Urethritis	Urethra region	Burning pain in urethra, increasing in urination, accompanied by ample, purulent excretions from the urethra and painful and frequent erections

Disordered urination

Dysuria - means stinging and cutting pain when urinating (cystitis, urethritis, hypertrophy of prostate). Dysuria is painful or uncomfortable urination, typically a sharp, burning sensation. Some disorders cause a painful ache over the bladder or perineum. Dysuria is an extremely common symptom in women, but it can occur in men and can occur at any age.

Pollakisuria - represents more often urging to urinating, usually in inflammation or calculus in urinary tract.

Urinary retention (residuum) - is characterised by presence of urine in urinary bladder after urination (prostate hypertrophy).

Paradox ischuria - represents strong urine retention with drop outflow (prostate hypertrophy).

Isuria is an excretion of urine at a uniform rate (about equal intervals with evacuation of about equal portions of urine). The most common cause of isuria is chronic renal insufficiency

Incontinence of urine - spontaneous outflow of urine (cerebral stroke, in advanced arteriosclerosis, functional disorder of cervix sphincter in gynecological diseases).

Urinary frequency

• Urinary frequency is the need to urinate many times during the day, at night (nocturia), or both but in normal or less-than-normal volumes

• Frequency may be accompanied by a sensation of an urgent need to void (urinary urgency)

• Urinary frequency is distinguished from polyuria, which is urine output of >3 L/day

• The most common causes of urinary frequency are urinary tract Infection (UTIs), urinary incontinence, benign prostatic hyperplasia (BPH), urinary tract calculi

Nocturia

• A healthy person urinates during night not more than once

• Nocturia is a condition in which the individual has to wake at night one or more times for voiding

• Nocturia has four major underlying causes: global polyuria, nocturnal polyuria, bladder storage disorders, or mixed etiology

• Causes: Cardiac (after oliguria during day time occurs in cardiac decompensation and is explained by a better renal function at night, i.e at rest); Renal (may concur with polyuria in renal dysfunction, at the final stage of chronic glomerulonephritis, chronic pyelitis, vascular nephrosclerosis and other chronic renal diseases)

Diuresis

• Diuresis is defined as secretion of urine during a certain period of time

• Increased diuresis occurs in diabetes mellitus and diabetes insipidus, acute renal failure, during mild to moderate hypothermia (coldinduced diuresis)

• Coffee, tea, certain foods, diuretic drugs, anxiety, fear, some steroids cause increase diuresis

• Types of diuresis: – Positive (the amount of urine excreted exceeds the volume of liquid taken) – Negative (the reverse ratio).

Table 8

Disorders of urination

Term	Definition	Causes
Polyuria	Urine volume exceed 2l/24h	High fluid intake Diabetes mellitus Renal failure initial stage
Oliguria	Urine volume is less than 500ml/24h	Hot climate Restricted fluid intake Obstruction Acute renal parenchymal diseases Failure of renal perfusion
Anuria	Complete absence of urine secretion and/or excretion	Renal failure Acute glomerulonephritis Nephrosclerosis Sepsis, collapse, shock, poisoning by nephrotoxic substances Dehydration By reflex in severe pain Mechanical obstruction of the urinary tract
Ishuria	Absence of urine excretion	Damage of the spinal cord Loss of consciousness
Nocturia	Passing of more than one third of total 24-h urine volume by night	Chronic renal diseases with renal dysfunction Heart failure Prostate adenoma Diabetes insipidus
Pollakiuria	Frequent more than 6 times a day micturition	High fluid intake Cold climate Cystitis Prostatitis Urethritis Stones in the bladder Prostate adenoma Diuretics taking Decreased volume of the urine bladder
Ollakiuria	Rare micturition	Low fluid intake After much salted food Excessive sweating (hot climate, fever)

		Neuroreflex disorders
Enuresis	Involuntary urination without desire	Organic affection of the central nervous system and spinal cord Urinary tract defects Functional disorders in children
Dysuria	Painful urination	Cystitis Urethritis
Isuria	Urination at about equal intervals of about equal amounts of urine	Chronic renal failure
Stranguria	Passage of small amounts of urine (by drops)	Stricture (after operative) of the bladder cervix Strangulation of the stones or foreign bodies in the urethra Bladder tumor Phimosis

Edema is important and common symptom of the urinary organs diseases. Renal edema has following peculiarities. Patients complain on edema that initially arises on the face. In disease progression renal edema spreads from the face downward, up to anasarca. Edema is characteristic of acute and chronic glomerulonephritis, especially in nephrotic syndrome presence, amyloidosis, and acute renal excretory dysfunction (anuria).

High blood pressure

• High blood pressure caused by the kidneys' hormonal response to narrowing of the arteries supplying the kidneys (renal artery stenosis) called renal (secondary) hypertension

• Due to low local blood flow, the kidneys mistakenly increases blood pressure of the entire circulatory system

• Patients with renal hypertension have a diastolic blood pressure of more than 100 mmHg and are at increased risk of end organ dysfunction, including permanent kidney damage, if inadequate pharmacologic therapies are used to control blood pressure.

Complaints concerning general condition. Patients with chronic renal diseases (glomerulonephritis, pyelonephritis) complain on general weakness, fatigue in development of functional disorders.

Fever can indicate infectious inflammatory affection of the kidneys and the urinary ducts, or can be the sign of the main disease, which cause damage of the kidneys. Hectic fever accompanied by chills and profuse perspiration is typical to acute pyelonephritis or aggravation of chronic pyelonephritis. High temperature (to 39-40˚C) observes in the patients with renal abscess, acute paranephritis. Subfebrile temperature (37-38˚C) can be detected in nephrolithiasis during attack of renal colic. In urinary ducts obstruction and congestion of the urine, the fever is constant. Recurrent fever is the sign of kidney tuberculosis. Insignificant elevation of body temperature arises in the patients with acute glomerulonephritis, in chronic glomerulonephritis fever, usually, is absent.

Itch of the skin occurs in the patients with severe renal failure.

Perspiration arises in the patients with renal inflammatory diseases. Considerable perspiration is common symptom of purulent destructive damage of the kidney and perirenal cellular tissue, and specific tubercular process.

Change of body mass, as a rule, weight loss may occur as a consequence of chronic renal failure, in tuberculosis and tumor of the kidneys, polyps, and in tumor of the urine bladder.

Nervous system. Patients with urinary organs diseases may complain on decreased work capacity, impaired memory and attention, deranged sleep (insomnia), headache, dizziness, flashing lights before eyes, weakness in the extremities. All these symptoms are the result of elevated blood pressure, or encephalopathy and polyneuropathy that arise as complication of the chronic renal failure. Deranged vision and hearing are due to hypertension in the patients with acute and chronic glomerulonephritis, pyelonephritis, nephropathy, and in renal vascular pathology presence.

Respiratory system. The common complaints of the patients with renal diseases are cough with insignificant amount of the sputum and dyspnoe that increase in intensity corresponding to worsening of the renal function. These complaints are characteristic of chronic glomerulonephritis, pyelonephritis, and are due to the accompanied pneumonia. Pronounced breathing disorders observe in the patients with chronic renal failure, so-called “uremic lung” is formed. Patients complain on dyspnoe in insignificant physical exertion, and asthma attacks. In case of uremic pleurisy, dyspnoe develops quickly up to acute respiratory failure with circulatory disorders.

Cardiovascular system. Pain in the heat region, retrosternal pain, palpitation, dyspnoe, suffocation by cardiac asthma type are typical to acute glomerulonephritis,

and also to other diseases, which are accompanied by elevated blood pressure. All these complaints are revealed in chronic renal failure, and are caused by metabolic disorders that lead to formation of cardiomyopathy.

Digestive system. Loss of appetite and pain in the upper part of the abdomen are early signs of renal dysfunction. Dyspeptic disorders, such as dryness and unpleasant taste in the mouth, nausea, vomiting can also be observed. At the final stage of chronic renal failure, meteorism, diarrhea alternated with constipation arises that suggest enterocolitis. These symptoms are the result of uremic gastroenteropathy.

Anamnesis morbi. In acute renal diseases it is necessary to establish time of diseases onset, possible connection with previous in/factious diseases, such as tonsillitis, scarlet fever, otitis, acute respiratory disease, etc. It should be note consequence and dynamic of symptoms occurring. Edema arising, blood pressure elevation, and changes of the clinical urinalysis 2-3 weeks after infectious diseases is typical to acute glomerulonephritis. Dysuria on the base of toxicosis (elevated temperature, chills) after cold is characteristic of pyelonephritis.

It is important to ask patient about possible industrial or domestic poisoning, and taking of nephrotoxic drugs (antibiotics, sulpha preparations, preparations of bismuth, silver, etc).

Chronic affection of the kidneys and urinary ducts can for a long time be latent, and are revealed occasionally. In such cases it is difficult to establish the onset of disease. Therefore the patient should be asked about previous edema, or possible dysuria, and loin pain. In established previously disease, it should noted character of the disease course, frequency and cause of exacerbations, consequence of clinical symptoms, results of previous examination and treatment.

Anamnesis vitae. It necessary to note previous infectious diseases (scarlet fever, influenza, etc), presence of infectious center (otitis, tonsillitis, adnexitis), and diseases with disorders of urine passage (prostate adenoma). Such diseases as diabetes mellitus, tuberculosis, collagenosis, hemoblastosis, and infectious diseases of genitals can cause renal affection. In the patients with long- standing chronic purulent pulmonary diseases, tuberculosis, osteomyelitis, rheumatic arthritis, Bekhterev’s disease secondary amyloidosis of the kidneys can occur. Primary amyloidosis is of congenital character. Nephrolithiasis can be also inherited, thus it is important to know about diseases of the urinary organs and hypertension presence in the relatives of the patient.

Chronic poisoning - narcotics, smoking and alcohol abuse are accompanied by the kidneys damage.

When questioning women, it should be remember that in pregnancy difficult urine passage can observes, and frequently pyelitis and pyelonephritis occur. Women

should be asked about edema and elevation of blood pressure during pregnancy – so-called nephropathy of pregnancy.

Physical examination of the patient

General inspection

• The patient's posture in bed: active, passive (uraemic coma), forced (paranephritis, renal colic, uraemic coma, renal eclampsia, atc.)

• Development of edema of renal origin is quite specific. Initially edema appears on the face in the morning, has descending character, and can develop very quickly (in few hours). Edema spreads on extremities, loin region, then fluid accumulates in cavities (ascitis, hydrothorax, hydropericardium), and general edema (anasarca) can arises. The skin over edema is glossy. Renal edema should be differentiated from cardiac edema

• Pallid oedematous skin in cronic nephritis due to the spasm of arterioles, and anaemia which attends kidney disease

• Wax pallid skin can be detect in amyloidosis and lipoid nephrosis

• Scratches on the skin and coated dry tongue can be find in a patient with chronic nephritis

• An unpleasant odour if ammonia can be felt from the mouth and skin of the patient (factor uremicus)

• Lymphadenopathy; lymph nodes may be enlarged due to metastatic spread from any urological cancer

Table 9

Symptomatic features in the differential diagnosis of renal and cardiac edema

Features	Renal edema	Cardiac edema
Location, character	Descending character, starts from the face and spreads downward	Ascending character, starts from low extremities and spreads upward
Time of arising	More pronounced in the morning	More pronounced in the evening
Colour of the skin	Pallor	Cyanotic
Temperature of the skin over edema	Warm	Cold

Abdominal investigation

• Abdomen may be distended due to large polycystic kidneys or ascites due to nephritic syndrome or nephrotic syndrome

• The kidneys are examined bimanually with a hand posteriorly lifting up the kidney towards the examining abdominally placed hand

• Tenderness over the kidney should be tested by gentle pressure over the renal angle

• Palpation for renal enlargement or masses (an enlarged kidney usually bulges forwards; in polycystic kidney disease, there may also be hepatomegaly from hepatic cysts)

• Percussion for the presence of ascites (shifting dullness) and for an enlarged bladder

• Auscultation for a renal bruit in renal artery stenosis (heard above the umbilicus, 2 cm to the left or right of the midline and also in both flanks with the patient sitting up)**.**

The kidneys should be palpated in the lying and standing position. When the patient is in the horizontal position this kidneys are better palpated because the strain of the prelum is absent. But the movable kidney can be palpated in the standing patient because it hangs by gravity and is displaced downward by the pressure of the low diaphragm.

During palpation of the patient in the lying position his legs, should be stretched and the head placed on a low pillow; the prelum is relaxed and the arms are free placed on the chest. The physician should assume his position by the right side of the patient with, his left hand under the patient’s loin, slightly below the12ribs so that the finger tips are near the spinal column. During palpation of the left kidney, the physician's hand should be moved further, beyond the vertebral column, to reach the left part of the lumbar region. The right hand should be placed on the abdomen, slightly below the corresponding costal arch, perpendicularly to it and somewhat outwardly of the rectus abdominis muscles. The patient is asked to relax the abdominal muscles as much as possible and breathe deeply and regularly. The physician's right hand should press deeper with each expiration to reach the posterior abdominal wall, while the left hand presses the lumbar region to meet the fingers of the right hand. When the examining hands are as close to each other as possible, the patient should be asked to breathe deeply by "the abdomen" without straining the prelum. The lower pole of the kidney (if it is slightly descended or enlarged) descends still further to reach the fingers of the right hand. As the physician feels the passing

kidney, he presses it slightly toward the posterior abdominal wall and makes his fingers slide over the anterior surface of the kidney bypassing its lower pole. If ptosis of the kidney is considerable, both poles and the entire anterior surface of the kidney can be palpated. The physician should assess the shape, size, surface (smooth or tuberous), tenderness, mobility, and consistency of the kidneys. Bimanual palpation of the kidney can also be done with the patient lying on his side. In healthy persons the kidneys are bean-shaped, the borders are rounded, they are dense, elastic. Enlarged kidneys are observed in hydronephrosis, tuberculosis, and tumors.

A method for examination of the kidneys is tapping. The physician places his left hand on the patient's loin and using his right hand taps with a moderate force on the right hand overlying the kidney region on the loin. If the patient feels pain, the symptom is positive (Pasternatsky's symptom). This symptom is also positive in nephrolithiasis, inflammation of the pelvis, paranephritis.

Percussion for the presence of ascites

• Ask the patient or an observer to place their hand longitudinally over the center of the abdomen

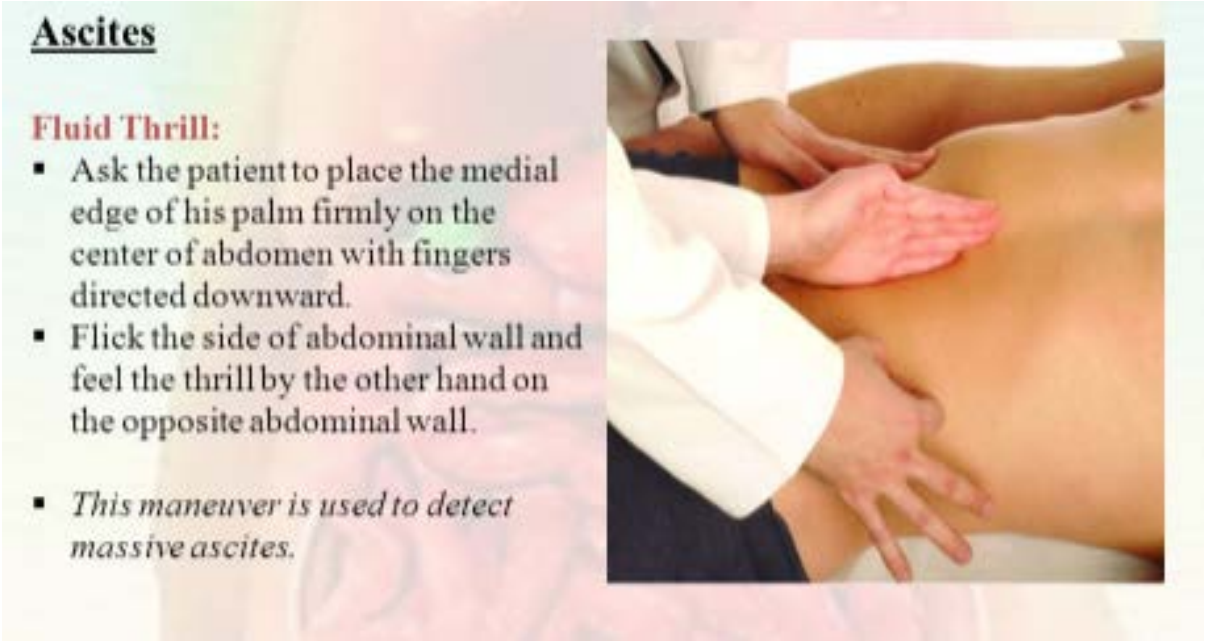

Image 12. Percussion for the presence of ascites

The image was downloaded from website https://slideplayer.com/slide/4091028

• Place your right hand on the left side of the abdomen and your left hand opposite, so that both are equidistant from the umbillicus

• Firmly tap on the abdomen with your right hand while your left remains against the abdominal wall

• If there is a lot of ascites present, you may be able to feel a fluid wave (generated in the ascites by the tapping maneuver) strike against the abdominal wall under your left hand.

Percussion for the urinary bladder

• Percuss your patient's bladder, beginning over symphysis pubis and working toward umbilicus

• A urine-filled bladder produces a dull sound

• A change to tympany indicates the bladder's border

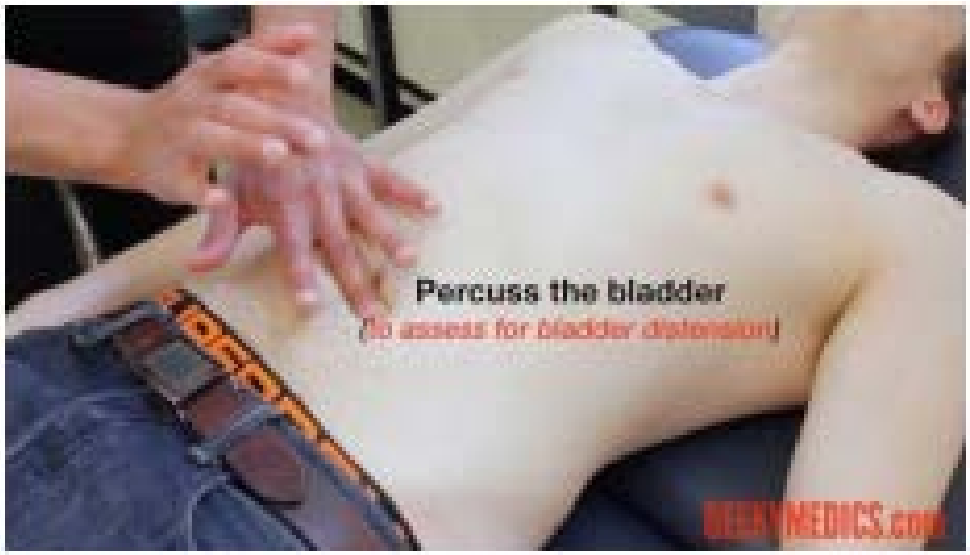

Image 13. Percussion for the presence of ascites

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URINE ANALYSIS

Clinical urine analysis includes: macroscopic (physical properties), chemical, microscopic, bacteriological and bacterioscopic studies.

Collection of the urine

Urine sample is taken after night sleep in the clear and dry container. Urine sample can be collected from males after retraction of the foreskin, and from females with the labia separated by their fingers. Ideally the genitalia should be swabbed with sterile saline but this is often impracticable. Antiseptics should be avoided if the sample is required for culture. The urine sample must be sent promptly to the laboratory to avoid growth of contaminant organisms and the dissolution of cellular elements and casts. It should be cooled in refrigerator at 4˚C if delay is likely to be greater than 2 h.

Macroscopic study

Macroscopic study includes assessment of physical properties of the urine: amount, color, cloudiness, smell, and specific gravity.

Physical properties of the urine

Amount of the urine. In healthy adult the normal amount of excreted urine is between 1000 ml and 2000 ml in 24 h (diurnal diuresis).

Polyuria is defined as a production by an adult of more than 2000 ml of urine/24h.

Olyguria is defined as a production by an adult of less than 500 ml of urine/24h.

Color of the urine depends on the presence of physiologic pigments (urochromes, urobilinoids, uroerythrin, etc) and on its concentration. The color of the normal urine varies from straw yellow to orange-yellow. Different pathological conditions of the urinary organs can cause peculiar changes of the urine color.

Cloudiness of the urine. Normal, freshly excreted urine is clear. Cloudiness of the urine can be cause by the presence of salts, cellular elements (leucocytes, erythrocytes, epithelium cells), bacteria, mucus, and fats.

Smell of the urine. Normally, the urine has not strong specific smell. In bacterial decomposition on air or in urinary ducts (severe cystitis, degradation of malignant tumor) urine smells of ammonia. Peculiar “fruity” or “apple” odor of the urine is characteristic of diabetic coma or diabetes mellitus in decompensation stage. Such specific odor of the urine is a result of ketone bodies presence.

Specific gravity of the urine is proportional to concentration of dissolved in it substances: urea, uric acid, various salts, and depends not only on amount but mainly on their molecular weight.

Specific gravity is measured by urometer, normally it varies from 1.015 to 1.025. In health there is diurnal variation of the specific gravity; in morning, the most concentrated portion of the urine, it can be to 1.020-1.026.

Assessment of the specific gravity of the urine is of great diagnostic significance, because these parameter gives information about concentrating ability of the kidneys. The specific gravity can also be depends on the volume of urine excreted.

Zimnitsky’s test characterize condition of renal concentrating and excretory ability. In order to correct measure urinary concentrating ability, the patient must avoid taking much fluid.

Urine samples are collected each 3 hours in separate container with designation of time – 8 portions during 24 hours. Volume and specific gravity of the urine is measured in each portion.

The advantages of this method are:

- Possibility to measure diurnal diuresis and to detect presence of polyuria or oliguria;
- Possibility to measure separately daily and nightly diuresis and to detect presence of nicturia;
- Possibility to determine diurnal variation of the specific gravity and its maximal value.

Normally, diurnal diuresis is 1000-2000 ml, amount of urine in each portion can vary from 50 to 250 ml, daily diuresis exceeds nocturnal, and specific gravity vary from 1.010 to 1.025. if the maximal mean of specific gravity in Zimnitsky's test exceeds 1.020, renal concentrating ability is considered to be normal.

Low specific gravity in all portions is typical to renal failure.

Isosthenuria is defined as condition when osmotic concentration of urine is equal to osmotic concentration of blood plasma. Maximal osmotic concentration of urine in isosthenuria is 270-330 mmol/l, and maximal specific gravity – 1.010-1.012.

Hyposthenuria is defined as condition when maximal osmotic concentration of urine is less than osmotic concentration of blood plasma. Maximal osmotic concentration of urine in hypusthenuria is 200-250 mmol/l, and specific gravity of urine – 1.005-1.008.

Extrarenal causes of urine specific gravity changes

In diabetes mellitus, polyuria and high specific gravity of the urine (to 1.026-1.050) due to glucosuria is determined. Diabetes insipidus and pituitary insufficiency are characterized by polyuria and low specific gravity of the urine. Renal causes of urine specific gravity changes In acute glomerulonephritis, nephrotic syndrome, and in congestive kidney in heart failure osmotic concentration of urine is elevated to 1200 mosm/l, specific gravity of the urine – to 1.031-1.035, that accompanied by oliguria. Hyposthenuria in normal diuirnal diuresis and nicturia observe in patients with chronic glomerulonephritis, chronic pyelonephritis, and nephrosclerosis. Isosthenuria suggests complete absence of renal concentrating ability. Long standing excretion of urine with low specific gravity, monotonous means in combination with oliguria are the signs of severe chronic renal failure with unfavorable prognosis.

Chemical study

Chemical study includes assessment of reaction of the urine (urine pH), protein, glucose, ketone bodies, and bile pigments.

Reaction of the urine – urine pH can be determined calorimetrically (litmus paper and other indicators) and electrometrically. The urine reaction may vary from pH 5.0 to 7.0 – neutral or feebly acid reaction. Urine pH can be changed in both physiological and pathological conditions.

Protein. The normal amount of protein excreted in the urine per 24 hours is 25-75 mg that cannot be detected by routine tests. More than half of this amount consists of small molecular weight proteins or protein fragments, although albumin is the largest single component.

Proteinuria is the appearance of protein in the urine in cincentration determinable by qualitative methods. The protein content of the urine of normal individuals can rise to about 150 mg/l when the urine is concentrated.

Selective and non-selective proteinuria is distinguished. *Selective proteinuria* is characterized by the presence in the urine of low molecular weight proteins – albumin, ceruloplasmin, and transferrin. *In non-selective proteinuria* high molecular weight proteins – α2- macroglobulib, β2-lipoprotein, and γ-globulin are detected. Moreover, Bence-Jones proteins – low molecular weight proteins, can be revealed in the urine. In some pathological conditions, hemoglobin, hemosiderin, myoglobin, and Tamm-Harsfall proteins are present in the urine.

Depend on protein- amount in the urine, *microalbuminuria* – 30-300 mg/24h, and *proteinuria* (macroalbuminuria) – more than 300 mg/24h are distinguished.

Proteinuria can be functional and organic. Functional proteinuria observed in subjects without renal diseases, has transitory character, does not exceeds 1 g/24h, and are not accompanied by the other urine abnormalities. Postural (orthostatic), effort, and cold proteinuria are differentiated. Healthy adults are found to have proteinuria when up and about, but not after a period of horizontal rest. Standing position can induce significant proteinuria in a substantial proportion of people who do not otherwise show it. Proteinuria can also be observed in subjects without renal diseases after severe exercise, in fever, or on exposure to extremes of cold or heat. These findings do not imply the presence of renal disease and do not require further investigation.

Organic proteinuria can came about in three ways:

1. The glomerular filter becomes more permeable to proteins of large molecular size, as well as permitting those of small molecular weight to pass – ‘glomerular’ proteinuria. This is by far the commonest cause of proteinuria in clinical practice.

2. There is a marked rise in the plasma concentration of protein in circulation, so that amount filtered exceeds the reabsorptive capacity of the proximal tubule – ‘overflow’ proteinuria.

3. The proximal tubule is damaged so that normally reabsorbed proteins, principally of low molecular weight, pass into the urine – ‘tubular’ proteinuria.

Glucose. Excretion of glucose with urine is called glycosuria. Glucose is freely filtered by the glomerulus and reabsorbed actively by the proximal tubule. Under normal circumstances, reabsorption is complete but if the blood glucose rises sufficiently, a plasma level is reached (the threshold) at which the transport mechanism is saturated and glucose starts to spill into the urine. Glycosuria could arise in principle in two different ways. First, if the plasma glucose concentration rises above the threshold level (around 10 mmol/l in man) the unreabsorbed glucose will appear in the urine, and this occurs in uncontrolled diabetes mellitus, the commonest clinical cause of glycosuria. Alternatively, if the tubular mechanism for reabsorption is defective, glucose will appear in the urine even when the plasma glucose is within the normal range. This can occur as a result of an inherited abnormality in the protein mediating glucose transport across the proximal tubular cells, or as a consequence of a disease process interfering with the function of this epithelium, as in cyctinosis or tubular damage by heavy metals and other toxins.

Ketone bodies (acetone, acetoacetic and β2-oxybutyric acid) are normally absent in the urine. Ketonuria is defined as a presence on ketone bodies in the urine. They usually occur in diabetes mellitus, carbohydrate deficit: fasting, grave toxicities, long- standing intestinal disorders, dysentery, and in postoperative period. Ketonuria is important laboratory sign of decompensation of diabetes mellitus with transformation to diabetic coma.

Bilirubin. Normal urine contains minimal quantity of the bilirubin. Increased excretion of bilirubin is pathological condition and is called – bilirubinuria. Bilirubinuria occurs in increased blood level of bound bilirubin more than 0,01-0,02 g/l (“renal threshold of bilirubin”) in parenchymatous jaundice (acute virus, toxic,

toxico-allergic hepatitis, liver cirrhosis), subhepatic jaundice (altered permeability of bile ducts due to inflammation, obstruction by stones, by tumor, or by scars).

Urobilinoids: urobilin (urobilinogens, urobilins) and stercobilin (stercobilinogens, stercobilins) are derivates of bilirubin. They are not determined separately. A large quantity of urobilinoids in urine is called urobilinogenuria. It occurs mainly in: parenchymatous affection of the liver (hepatitis, cirrhosis), hemolytic processes (hemolytic anemia); and in intestinal diseases (enteritis, constipation, etc).

Macroscopic study

Erythrocytes. The urine of healthy person contains single erythrocytes. The presence of erythrocytes in the urine is called haematuria. Determination of erythrocytes in microscope vision area (more than 1000 cells in 1 ml) is defined as microhaematuria; the color of the urine is unchanged in such cases. If erythrocytes amount is 2500 cells in 1 ml, the urine is of red color that is defined as macrohaematuria.

Haematuria can be true (from the kidneys and urinary tract) and false (in man in prostatitis, tuberculosis and tumor of prostate, in woman of genitalia origin). It is important diagnostically to determine location of bleeding source. A three-glasses test is used for this purpose. Patient urinates in three containers.

Macrohaematuria in the first portion suggests bleeding from urethra, in all three portions – from kidneys or ureters, and inn last portion – from urine bladder.

Leucocytes are observed mainly in a form of neutrophils, and sometimes eosinophils and lymphocytes are present. Urine of healthy individuals contains small amount of leucocytes (1-2 in vision area). Leucocyturia is defined as elevated amount (from 5-6 to 20 cells in vision area) of leucocytes in the urine. Pyuria is said to be present when amount of leucocytes increases to 60-100 cells in vision field, and they are seen macroscopically.

Epithelium cells

Tubular (renal) epithelium cells are absent normally in the urine. Their presence indicates acute or chronic affection of the kidneys. They can also be detected in fever, toxicities, and in infectious diseases.

Transitional epithelium cells presence in the urine suggests inflammatory processes in the pelves or bladder.

Squamous epithelium cells originate from genitalia and urethra, and diagnostic their significance is low.

Cylinders (casts). These are cylindrical bodies formed in the lumen of the distal tubule, particularly the collecting tubule. Casts are protein copies of tubules. Appearance of cylinders in urine sediment is called cylinduria - the sign of organic renal diseases.

Hyaline casts are occasionally seen in the urine of normal people, particularly when it is concentrated, or after exercise. Hyaline casts appear in the urine during secondary proteinuria: febrile, congestive, orthostatic, toxic, and after administration of loop diuretics. Constant hyaline casts presence suggests proteinuria of renal genesis: glomerulonephritis, pyelonephritis, and nephropathy.

Granular casts occur in much the same situations as hyaline casts and have similar significance. They are found in the urine of normal subjects after exercise. They appear in many types of renal disease but are particularly characteristic of chronic proliferative or membranous glomerulonephritis, diabetic nephropathy, and amyloidosis.

Waxy casts presence in the urine indicates chronic diseases of the kidneys.

Erythrocytes (unaltered) casts are pathognomic of renal bleeding: nephrolithiasis, tuberculosis and tumor of the kidneys; acute process in the kidneys: acute glomerulonephritis.

Erythrocytes (altered) casts are seen in chronic glomerulonephritis.

Leucocytes casts may appear in considerable numbers during an episode of acute pyelonephritis; a few may be found in the urine in chronic pyelonephritis.

Nechiporenko's method allows counting formed elements in 1 ml of urine, normally:

- Leucocytes – to 4000;
- Erythrocytes – to 1000;
- Casts – to 200.

Crystals. Cystine crystals may be found in freshly passed urine bur are found more consistently if a concentrated sample is acidified and cooled in a refrigerator, their presence is diagnostic of *cystinuria.* Oxalate crystals are common in urine from normal individuals when it has stood for an hour or two. When present in freshly passed urine, in large numbers or aggregates, they may indicate an increased liability to form oxalate stones, but firm conclusions can only be drawn if the urine is kept at 37˚C until examined on a warm-stage microscope.

Mucus. The normal urine practically contains no mucus. Commonly mucus appears in diseases of the urinary tract: urethritis, prostatitis, cystitis, and in stones presence.

It must be emphasized that although urinalysis and microscopy yield valuable information, it is possible for significant renal disease to be present without anything abnormal being detected in the urine.

Bacterioscopic study

Bacteriuria is defined as presence of bacteria in the urine. In quantity not more than 50 000 in 1 ml they may occur in the urine of healthy person. In the presence of bacteriuria, it is important to determine its degree and microorganism sensitivity to various antibiotics.

INSTRUMENTAL METHODS

Ultrasonography. This is now the initial investigation for the majority of patients in renal failure and has displaced conventional radiology as the first structural investigation of the urinary tract. Highresolution real-time (moving picture) scans are standard equipment.

Ultrasound findings are independent of renal function. They can therefore be used to study patients with renal failure, measuring with considerable accuracy the shape, depth from the surface, and internal architecture of the kidney and upper urinary tract. Ultrasound generally detects the dilated calyces, pelvis, and ureter of the obstructed kidney, although in the presence of very recent obstruction the calyceal system may not have dilated sufficiently to make a firm diagnosis on ultrasound, and other investigations such as retrograde ureterography may be necessary. In unexplained renal failure, ultrasound is very useful to assess renal size and cortical thickness, with the presence of small kidneys suggesting chronic renal disease and enabling the renal physician to make appropriate decisions about whether or not renal biopsy is indicated.

Ultrasound is often helpful in identifying the cause of abnormalities detected on the IVU. It may show whether an enlarged kidney is the site of hydronephrosis, an infiltrative process, or a spaceoccupying lesion. It is particularly useful in deciding whether a localized swelling detected on IVU is cystic (and probably benign) or solid (and probably malignant). However, solid lesions may undergo some cystic change and therefore if a cystic lesion is not absolutely classical (unilocular, uniformly thin walls) then further investigation is indicated. This may be by CT scanning, MRI, invasive cyst puncture, or biopsy.

Ultrasonography has replaced excretion urography as the screening test for polycystic disease; the two techniques are comparable in accuracy but ultrasonography is faster, cheaper, and devoid of the risk of contrast injection and irradiation. However, cysts and tumours below 5 mm in diameter are not detected reliably by either ultrasound or excretion urography so polycystic disease cannot be excluded with certainty below the age of about 30 years.

Perinephric lesions are readily displayed by ultrasound; it is used to detect extravasation of blood after trauma or renal biopsy, although CT scanning may provide more accurate information in this regard. Ultrasonography is the first test for radiolucent calculi; it is also used for detecting radio-opaque calculi, but straight radiography remains the first investigation.

Finally, ultrasound is very useful in the assessment of complications of renal transplantation, particularly the surgical complications of extrarenal collections of blood, pus, and lymph, and in the identification of an obstructed transplant kidney. An ultrasoundguided percutaneous nephrostomy can then allow temporary decompression of the obstruction. Doppler ultrasound may have a limited role in the diagnosis of vascular rejection of the transplanted kidney, but at this stage cannot reliably distinguish acute tubular necrosis and cyclosporin nephrotoxicity from acute rejection.

Plain radiography of the urinary tract. A plain radiograph of the kidneys, ureters, and bladder is an essential preliminary to urography. It is often possible to trace the renal outlines and measure the renal size.

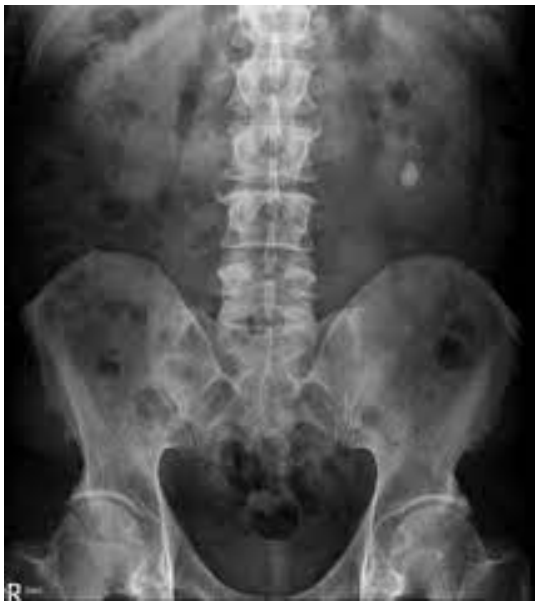

Image 14. Radiography of the urinary tract

The image was downloaded from website https://www.ssregypt.com/Radiology

The left kidney is normally about 1cm longer than the right. The length should be recorded in centimetres for comparison with subsequent films. The other main function of a plain abdominal film is to detect calcification in the kidneys or radiopaque calculi in the ureters or bladder, which may be obscured in the subsequent pyelogram. Oblique views and films taken in inspiration and expiration may be necessary to confirm that suspected calculi are in kidneys. The film may yield other diagnostic information; gallstones are often detected and renal osteodystrophy or myelomatosis may be recognized in the skeleton.

Excretion urography (synonyms: intravenous pyelography; IVP; IVU). The older hyperosmolar contrast media, such as diatrizoate and metrizoate, are now being replaced in many centres by low osmolar, non-ionic compounds such as iopamidol and iohexol. The contrast medium is excreted almost entirely by glomerular filtration. A film at 1min after injection gives the best view of renal outlines, with contrast concentrated in the tubules (the nephrogram). Later images, from 2.5 to 30 min will show excretion of contrast into the collecting system (the pyelogram). If calyceal detail is not adequately visible the pelvis and calyces may be distended by applying compression over the lower ureters with an abdominal belt. A film immediately after release of compression will provide detail of ureteric filling. Pre- and postmicturition films of the bladder will provide information on prostatic indentation, space-occupying lesions, and the presence of bladder diverticula and will assess bladder emptying. However, in many centres ultrasound has replaced the IVU for assessment of prostatic volume, bladder capacity, and residual urine volume. Impaired renal function will cause a delayed pyelogram and extra films will need to be taken as late as 12 to 24 h in this situation or in the presence of severe obstruction.

The IVU is clearly the best choice for anatomical detail and filling defects of the collecting system, but it has been largely replaced by ultrasound and computed tomography (CT) scanning for the investigation of abnormalities of renal anatomy, and by nuclear renal scanning or angiography for the investigation of renovascular hypertension.

Retrograde pyelography/ureterography. This technique is very useful for determining the site of complete obstruction to a ureter and for visualizing the ureter distal to the obstruction. It is particularly useful in cases of poor renal function where the kidneys and ureter show poor opacification on the IVU. A cystoscopy and anaesthetic is required and contrast is injected through a ureteric catheter. If an obstruction, such as sloughed papillae or epithelial tumour, is shown, then the catheter may be left in situ as a temporary drain pending surgery. Complications of the procedure include renal colic, temporary ureteric obstruction from mucosal oedema, infection, and intrarenal or extrapelvic extravasation of contrast.

Renal arteriography. The renal arteries may be opacified either by intra-arterial injection or by peripheral intravenous injection of contrast medium. The latter requires larger doses of contrast and the quality of images obtained is often not sufficient to allow accurate evaluation of renal artery branches and intrarenal vessels. Intra-arterial injection is therefore the preferred method, but is an invasive procedure with a greater risk, including contrast nephrotoxicity, than urography, ultrasound, or nuclear renal scanning. It is performed by retrograde femoral catheterization under local anaesthesia. The narrow catheters now used have reduced the local complication rates substantially, often enabling patients to be discharged from hospital on the same day.

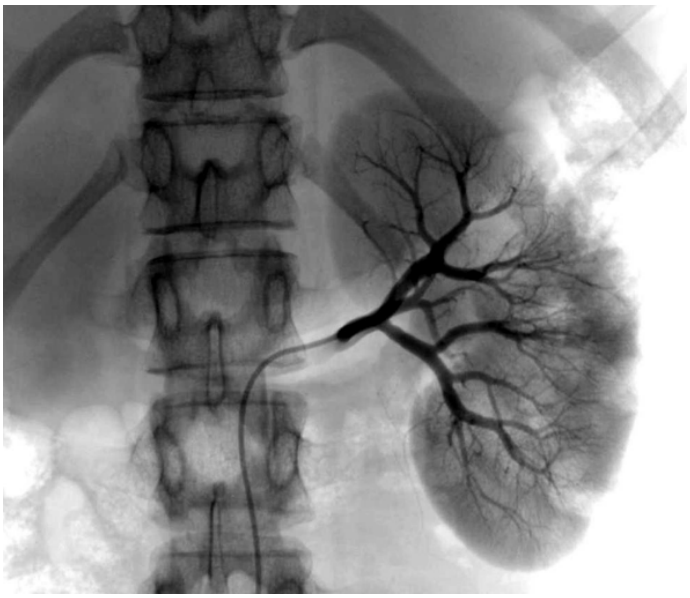

Image 15. Renal angiogram arterial anatomy
The image was downloaded from website https://radiopaedia.org/cases/renal-angiogram

Contrast medium is injected rapidly into the aorta at the level of the renal arteries. Selective catheterization of the renal arteries is often required to evaluate the intrarenal vasculature, particularly in renal tumours and in assessment of living renal transplant donors. Digital techniques have now largely replaced standard angiographic imaging, allowing subtraction of superimposed tissue and contrast enhancement. Digital angiography also allows the use of 50 per cent lower doses of contrast medium, lower flow rates, and smaller catheters.

Current indications for renal arteriography are limited, as refinements of less invasive procedures such as CT scanning and ultrasound may provide appropriate information. The chief use is in the evaluation of renovascular disease. If the renal artery stenosis is amenable to transluminal angioplasty, the dilatation (or renal artery

stenting) can be performed at the same time as the arteriogram. Other indications include suspected renal artery occlusion from thrombus, embolus, dissection or trauma, screening for arterial aneurysms in the diagnosis of classical polyarteritis nodosa, and when an intrarenal vascular lesion is suspected, as in persistent haematuria following a renal biopsy. In the latter situation arteriography can confirm an arteriovenous fistula or false aneurysm, and renal embolization via an endovascular catheter at the same time will prevent further bleeding. Renal angiography is always required in the surgical evaluation of the renal vasculature of potential live donors of kidney grafts. CT and magnetic resonance imaging (MRI) scanning have now largely replaced arteriography in the evaluation of renal tumours.

Renal venography. Few indications now remain for this procedure as new imaging techniques such as MRI and CT allow easier detection of renal vein thrombosis. However, an iliocavagram may be necessary to document caval extension of a renal vein thrombosis. Selective catheterization of the renal veins for renal vein renin levels in renovascular hypertension has now largely been replaced by the more reliable and quicker technique of nuclear renal scanning.

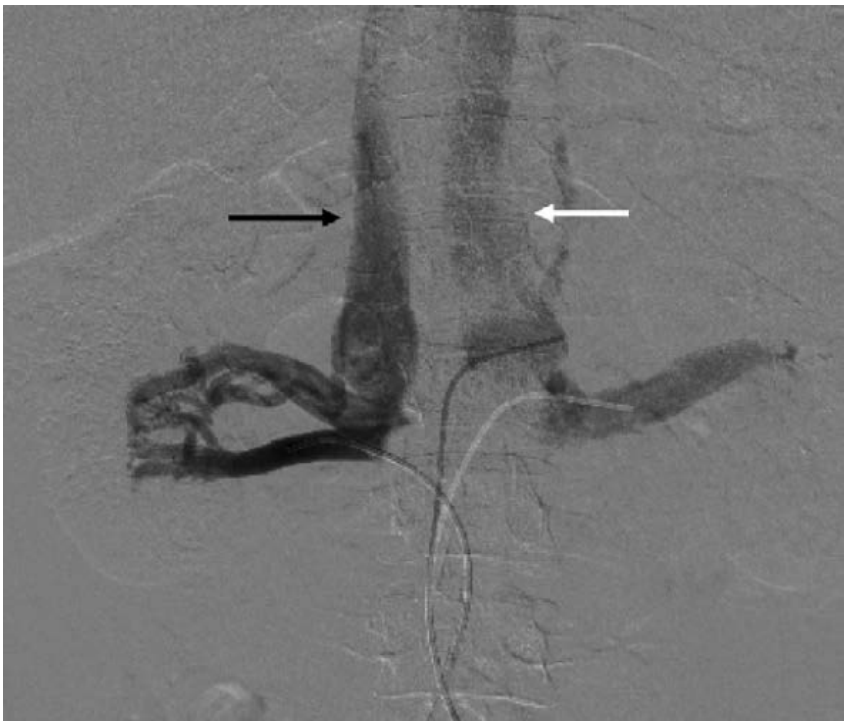

Image 16. Renal venography shows both renal veins draining directly into the thrombosed renal inferior vena cava, the right renal vein (black arrow) drains through a collateral into the right ventricle and the left renal vein drains into the azygous system (white arrow), also through a collateral

The image was downloaded from website https://www.researchgate.net/figure/Renal-venography

Computed tomography (CT scanning) of the trunk displays the kidneys particularly well in contrast to the surrounding perinephric and peripelvic fat. It can reveal abnormalities of the retroperitoneal and perirenal spaces that cannot be shown with conventional techniques. Contrast media used in CT scanning are the same as those used for intravenous urography.

The prime indications for CT scanning of the kidneys are to detect renal mass lesions and suspected renal trauma. Generally, simple renal cysts and polycystic renal disease can be equally well diagnosed with the cheaper technique of ultrasound. However, CT is the method of choice for the diagnosis of renal tumours, since it can confirm the solid nature of the tumour and allow determination of its local extension. Central calcification is very suggestive of a malignancy, as is contrast enhancement due to hypervascularity of the tumour. Extension of renal cell carcinoma has implications for prognosis and surgical intervention. CT is the best technique for documenting tumour thrombus in the renal veins. Lymph node involvement by tumour can be detected if the nodes are greater than about 1 cm in diameter.In renal trauma, CT scanning is clearly the best technique for demonstrating parenchymal damage, subcapsular haematoma, and perirenal urinary collections, as well as assessing damage to other organs such as the liver and spleen.

Finally, CT scanning is useful in the investigation of retroperitoneal fibrosis, which may be idiopathic or secondary to the use of drugs. The appearance of the fibrous plaque, which starts below the level of the aortic bifurcation and extends upwards, often enveloping the ureters, can usually be distinguished from lymphoma or sarcoma involving this region.

Magnetic resonance imaging (MRI) is a digital tomographic imaging system where tissue contrast depends on the manipulation of intrinsic magnetic fields. The technique employs a strong uniform magnetic field combined with transient oscillating magnetic fields to create images without the use of ionizing radiation. MRI offers very superior soft-tissue contrast and the ability to distinguish easily simple renal cysts, complex cysts, and solid renal masses. Like CT scanning, it is particularly useful in detecting tumour (Fig.1.10) extension into veins. MRI angiography of the renal circulation is yet to be assessed but may have a future role in renovascular disease. Presently, MRI is mainly indicated to clarify equivocal CT findings in renal tumours.

Nuclear renal imaging. The value of radiolabelled tracers in the investigation of renal disease lies in the ability to obtain important information about organ

function as opposed to the predominantly structural information obtained from the previously described imaging procedures. In particular, nuclear imaging of the kidneys provides the only non-invasive quantitative assessment of individual kidney function. Radionuclides (such as 123I, 99Tcm) are linked to compounds that depend on either glomerular filtration alone, tubular excretion, or a combination of both for excretion from the body. These compounds can therefore provide quantitative information on these functions of the kidney, in addition to dynamic images.

URINARY SYNDROME

Definition: quantitative and qualitative changes in urine.

Symptoms: changes in the volume and composition of the urine output; changes in the rhythm of urinary excretion; changes in the volume and composition of the blood.

NEPHROTIC SYNDROME

Definition: Clinical and laboratory syndrome characterized by massive proteinuria, which lead to hypoproteinemia (hypoalbuminemia), hyperlipidemia and pitting edema in results from increased permeability of glomerular basement membrane (GBM) to plasma protein.

Criteria:

• hematuria (RBC in urine, gross hematuria)

• hypertension (≥140 /90 mmHg) • azotemia（renal insufficiency - increased level of serum BUN , Cr）

• hypocomplementemia (decreased level of serum c3)

ETIOLOGY OF NEPHROTIC SYNDROME	
PRIMARY CAUSES	SECONDARY CAUSES
Minimal Change Nephrotic Syndrome	Systemic disease (diabetes, lupus)
Focal Segmental Glomerulosclerosis (FSGS)	Infection (HIV, hepatitis B, hepatitis C)
Membranous Nephropathy (MN)	Pre-eclampsia
Membranoproliferative Glomerulonephritis (MPGN)	Certain drugs and toxins
IgA nephropathy	Congenital due to intrauterine infections
Hereditary (Finish-type, Denys-Drash, Frasier)	

Image 17. Etiology of nephrotic syndrome

The image was downloaded from website https://www.maimonidesem.org

Types: • idiopathic (90%) • secondary (10%, anaphylactoid purpura, systemic lupus erythematosus, HBV infection, act.) • congenital.

Degrees of proteinuria:

• mild < 0.5 g/m2/day

• moderate 0.5 – 2 g/m2/day

• severe > 2 g/m2/day

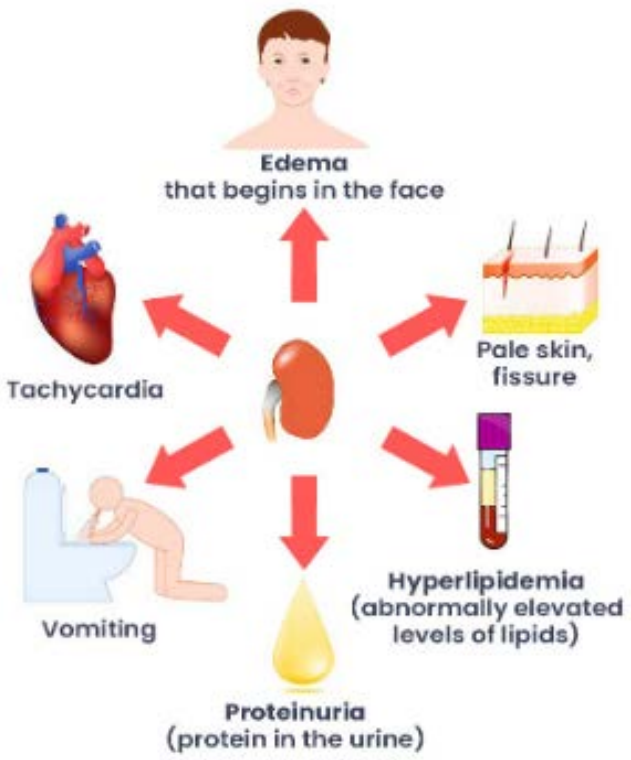

Image 18. Nephrotic syndrome

The image was downloaded from website https://www.aasthakidneyhospital.com

Types of proteinuria:

• Selective (where proteins of low molecular weight, such as albumin, are excreted more readily than protein of HMW (High Molecular Weight))

• Non selective (LMW (Low Molecular Weight)+HMW are lost in urine)

Symptoms:

Edema (varying degrees): local (edema of face (facial edema), edema around eyes (periorbital swelling) , in lower extremities), generalized (anasarca), edema of penis and scrotum.

Other clinical symptoms: fatigue, lethargy, loss of appetite, nausea and vomiting, abdominal pain, diarrhea, body weight increase, urine output decrease, pleural effusion (respiratory distress).

Nephrotic syndrome: tests

Blood tests (serum protein > 5.5 gm/dL , albumin ＜ 2.5 gm/dL, cholesterol ＞220 mg/dl) Urine tests (proteinuria, oliguria (during stage of edema formation), microscopic hematuria 20%, large number of hyaline casts).

Main in nephrOtic syndrome (all words contain letter O)

1. Massive prOteinuria
2. HypOprOteinemia (peeing out albumin)
3. Oedema (Oncotic pressure in the blood goes down)
4. HyperchOlesterolemia (hyperlipidemia/hyperlipiduria)
5. HypercOagulable state (thrOmbotic and thrOmboembolic complications)

NEPHRITIC SYNDROME

Definition: Clinical and laboratory syndrome associated with disorders affecting the kidneys, more specifically glomerular structures, and characterized by having a thin glomerular basement membrane and small pores in the podocytes of the glomerulus, large enough to permit proteins (proteinuria) and red blood cells (hematuria) to pass into the urine.

Criteria:

• hematuria, with red blood cell (RBC) casts present in the urine

• proteinuria (<3,5 g/day)

• hypertension

• uremia, due to retention of waste products

• variable renal insufficiency, with azotemia, oliguria (low urine output <400 mL/day)

Types

• post-streptococcal glomerulonephritis

• crescentic glomerulonephritis (rapidly progressive glomerulonephritis)

Nephritic syndrome (characterized by inflammation; both words contain letter i)

Nephritic syndrome features PHARAOH:

- Proteinuria
- Haematuria
- Azotaemia (elevated blood nitrogen levels)

- Red blood cell casts
- Anti-streptolysin O titres if poststreptococcal infection
- Oliguria (output <0,5 ml/kg/hour)
- Hypertension

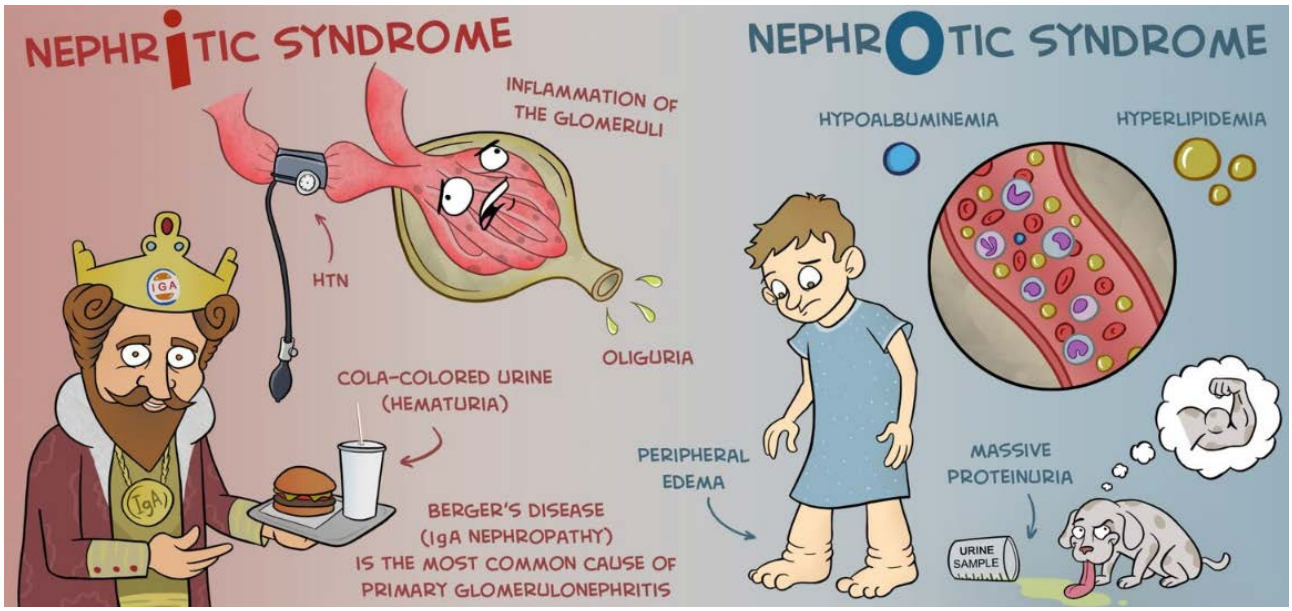

Image 19. Nephritic vs. Nephrotic Syndrome

The image was downloaded from website https://www.medcomic.com

URINARY TRACT OBSTRUCTION SYNDROME

• urinary tract obstruction can occur at any point in the urinary tract, from the kidneys to the urethral meatus

• it can develop secondary to calculi, tumors, strictures, anatomical abnormalities, or functional abnormalities

• obstructive uropathy can result in pain, urinary tract infection, loss in renal function, or, possibly, sepsis or death

Urinary upper tract obstruction

Symptoms are typified by the symptoms of ureteral stricture or ureteral or renal stone The principal complaints are pain in the flank radiating along the course of the ureter, gross total hematuria, gastrointestinal symptoms, chills, fever, burning on urination, and cloudy urine with onset of infection, which is the common consequence of obstruction or vesicoureteral reflux.

Nausea, vomiting, loss of weight and strength, and pallor are due to uremia secondary to bilateral hydronephrosis. Anemia, leukocytosis, microscopic hematuria.

Ureter: in the early stages intravesical pressure is normal; later added stretch effect at the lower end of the ureter induces further hydroureteronephrosis; finally the ureteral wall becomes attenuated.

Urinary mid tract obstruction

Typified by the symptoms of urethral stricture, benign prostatic hyperplasia, neurogenic bladder, and tumor of the bladder involving the vesical neck.

Symptoms: hesitancy in starting urination, lessened force and size of the stream, and terminal dribbling; hematuria, which may be partial; cloudy urine (due to complicating infection), acute urinary retention; anemia, leukocytosis, microscopic hematuria.

Stages:

• compensation - the bladder musculature becomes hypertrophied - the thickness may double or triple, hypertrophied muscle may be seen endoscopically - superimposed with secondary infection;

• decompensation - large obstructing gland can be palpated rectally and observed cystoscopically, may appears as a mild obstruction cystoscopically.

Urinary lower tract obstruction

The principal symptoms are hesitancy in starting urination, lessened force and size of the stream, and terminal dribbling; hematuria, which may be partial, initially, with stricture or total with prostatic obstruction or vesical tumor, cloudy urine (due to complicating infection), acute urinary retention. Anemia, leukocytosis, microscopic hematuria.

Obstruction - Hydrostatic pressure proximal - dilation of the urethra - The wall of the urethra become thin - form of diverticulum - Infected urine + urinary extravasation - periurethral abscess.

Typified by the symptoms of urethral stricture, benign prostatic hyperplasia, neurogenic bladder, and tumor of the bladder involving the vesical neck.

HYPERTENSIVE SYNDROME

• elevated > 140/90 mm Hg blood pressure (renal or renovascular hypertension), caused by a narrowing in the arteries that deliver blood to the kidney (renal artery stenosis)

• when the kidneys receive low blood flow, they respond by releasing hormones that stimulate the body to retain sodium and water, blood vessels fill with additional fluid, and blood pressure increases

• the narrowing in one or both renal arteries is most often caused by atherosclerosis, or hardening of the arteries

• symptoms: headache, confusion, blurred or double vision, bloody (pinkcolored) urine, nosebleed, bruits over affected renal artery

• hypertension can cause chronic kidney disease.

Patient's clinical examination inspection

• General state of health: fatigue, lethargy, diminished alertness, skin- pallor, yellow-gray, excoriations, changes in turgor, bruises, texture(e.g. rough, dry skin)

• Mouth: stomatitis, ammonia breath

• Face, extremities: generalized and peripheral edema, bladder distention, masses, enlarged kidney

• Abdomen: abdominal contour for midline mass in lower abdomen or unilateral mass

• Weight: weight gain secondary to edema, weight loss and muscle wasting in renal failure

Patient's clinical examination percussion, palpation, auscultation

• Kidney: percussion (to detect areas of tenderness by costovertebral test) and palpation (contour, size, tenderness); presence of tenderness and pain indicates a kidney infection or polycystic kidney disease

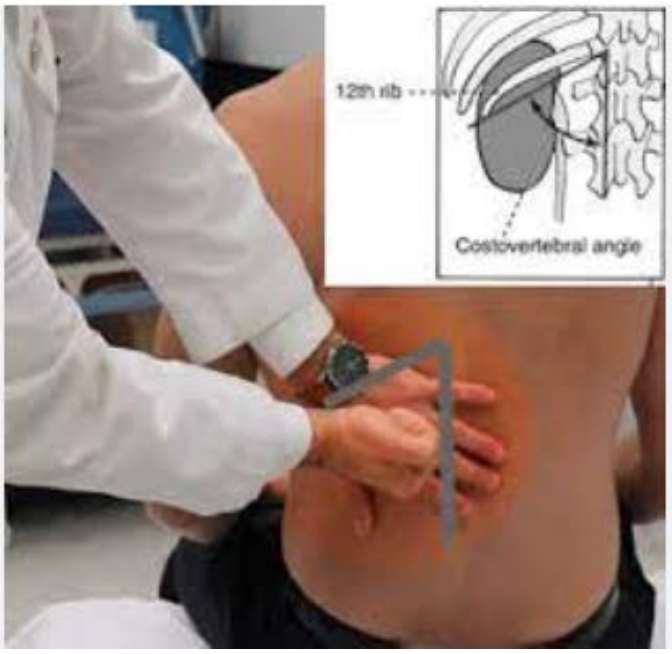

Image 20. Kidney percussion

The image was downloaded from website http://www.nodusstudios.com

• Bladder: percussion of the area over the bladder (5 cm) above the symphysis pubis to detect difference in sound, percussion toward the base of the bladder

• urethral meatus: inspection for swelling, discharge and inflammation

• Auscultation: the abdominal aorta & renal arteries are auscultated for a bruits, which indicate impaired blood flow to the kidneys

MAIN METHODS OF EXAMINATION OF THE HEMATOPOIETIC SYSTEM. THE INTERVIEW AND THE EXAMINATION OF PATIENTS WITH THE DISORDERS OF THE HEMATOPOIETIC SYSTEM. THE COMPLETE BLOOD COUNT. BLOOD CLOTTING TESTS (THE COAGULATION PANEL)

Questioning of patients with blood disorders

Common symptoms in haematologic disorders include:

- Constitutional symptoms - fatigue, lethargy, malaise, weight loss, night sweats
- Symptoms of anaemia - Fatigue, shortness of breath, reduced exercise tolerance, lightheadedness, worsening angina, ankle swelling
- Symptoms of neutropaenia - mouth ulcers, skin infections, other recurrent infections
- Symptoms of bleeding diathesis - easy bruising, epistaxis, gum bleeding, joint pain / swelling
- Symptoms of lymphoma - enlarged / painful lymph nodes, painful splenomegaly, B symptoms
- Symptoms of hyperviscosity - neuropathy, epistaxis, blurred vision, headache
- Symptoms of venous thromboembolism - limb pain / swalling, chest pain, shortness of breath, palpitations

Patients with haematologic disorders are often also referred in because they have abnormal blood tests; they may themselves be asymptomatic.

Complaints of patients with diseases of the hematopoietic system are varied.

In most cases, patients complain of:

- general weakness,
- fatigue,
- loss of appetite,
- headache,
- dizziness,
- fainting,
- palpitations,
- shortness of breath.

In some diseases, the patients complain of bleeding gums, nosebleeds, bloody vomiting and bloody stool, uterine bleeding, the appearance on the skin of different-sized hemorrhages.

In some cases, patients complain of itchy skin, profuse sweating and fever. A peculiar complaint may include a burning sensation in the tip of the tongue.

Sometimes there is a perversion of taste - the patient has a need to eat chalk, clay, coal.

History of Presenting Complaint

The following questions are a good starting point for any type of pain, and may be useful in gaining information about other symptoms:

- Site - localised or generalised; unilateral or bilateral
- Onset - sudden or gradual, and what the situation was (e.g. following trauma)
- Character - sharp, dull, burning or pressure-like
- Radiation - e.g. down the arm or across the back
- Associated symptoms - e.g. fevers, nausea / vomiting, bony pain
- Timing - duration of symptoms, frequency of episodes, changes through the day
- Exacerbating & alleviating factors - e.g. exacerbation with exertion and alleviation with rest
- Severity - on a scale of 1 to 10, with 10 being the worst

When collecting medical history is necessary to ask the patient about recent past diseases, especially infectious diseases, which can cause changes in the blood system. Of particular importance are infections such as malaria, tuberculosis, syphilis.

Matters also detect chronic infection foci: tonsillitis, sinusitis, otitis, cholecystitis and others. Of great importance in the origin of diseases of the hematopoietic system may have a worm infestation.

It should also ask the patient about the presence in the past of bleeding (nasal, uterine, of the gastrointestinal tract), which may be the cause of anemia. It should also be borne in mind that long-term use of certain drugs, such as aspirin, sulfa drugs, methylthiouracil can lead to inhibition of bone marrow function and a reduction in the number of white blood and red blood cells.

It is recommended to pay attention to the nature of the patient's nutrition (lack of food proteins and vitamins). The important thing is picking the professional

history. Since work with some chemicals (benzene, yshyak, phosphorus, lead) as well as X-rays, radioactive isotopes can sometimes cause destruction of the hematopoietic system.

Ask about whether the patient has recieved any transfusions in the past, and whether they recieved red blood cells, platelets or plasma products.

Ask about any previous transfusion reactions (infectious or non-infectious), and whether the patient has any known antibodies.

Patients with certain haematologic disorders will have had an autologous or allogeneic stem cell transplant in the past.

An autologous stem cell transplant involves mobilising and collecting a patient's stem cells, providing chemotherapy to deplete the bone marrow, and then retransfusing their stem cells. This process is less complex and has less potential side effects than an allogeneic stem cell transplant.

An allogeneic stem cell transplant involves depleting a patient's bone marrow using chemotherapy, and then transfusing another (matched) patient's stem cells. This serves purposes of both replacing their haematopoietic cells with normal cells, and providing some degree of graft-vs-disease effect.

Inspection. On examination, the patient first of all should pay attention to the color of the skin and visible mucous membranes. By reducing the amount of red blood cells in the blood and hemoglobin (anemia), skin and mucous membranes become pale. In some forms of anemia, pale skin combined with yellowness. By increasing the amount of hemoglobin in the blood and red blood cells (polycythemia and erythremia) skin becoming dark red in color, sometimes with a bluish tinge.

In a number of diseases of the hematopoietic system in the skin can appear hemorrhages of various sizes and various localization. There may be small petechial hemorrhages - petechiae and more extensive hemorrhages in the skin as blood spots, then converted in bruises. Bleeding can also be found on the oral mucosa, gums and conjunctiva.

On examination of the oral cavity should pay attention to the condition of the gums (swelling, looseness, bleeding), language (language redness, cracks, aphthous eruptions, sometimes smooth shiny tongue with atrophic papillae), oral mucosa, tonsils. In severe lesions of the hematopoietic system (leukemia, agranulocytosis) in the mouth and tonsils develop necrotic changes.

Palpation

A number of diseases of the hematopoietic system is accompanied by multiple enlarged lymph nodes result in lymphoid tissue hyperplasia. On palpation can determine the increase in cervical, supraclavicular, axillary, inguinal lymph nodes, and other. Knots are hard or soft, elastic consistency, mobile on palpation. Sometimes they are fused with each other and with the surrounding tissues, forming a dense conglomerates.

On palpation the abdomen is often found enlarged liver and spleen. In some diseases (chronic leukemias, hemolytic anemia) spleen dostegaet enormous size, becoming a dense, smooth surface and rounded edge.

Changes in other organs and systems. When anemia is often observed tachycardia, increased heart tones sonority and the emergence of a functional systolic murmur at the apex of the heart.

When gastric investigation sometimes reveals Akhil, plays a decisive role in the development of some forms of anemia. When urine study may show hematuria, usually along with other bleeding.

Complete Blood Count (CBC)

In a complete blood count (CBC) a routine hematology screening includes the following determinations: white blood cell count (WBC), red blood cell count (RBC), hematocrit (Hct), hemoglobin (Hgb), and differential white cell count (Diff). The differential states the neutrophils, lymphocytes, monocytes, eosinophils, basophils, and any abnormal cells as a percent of the total WBC count.

A complete hematologic examination also includes the indices, which are mean cell volume (MCV), mean cell hemoglobin (MCH), and mean cell hemoglobin concentration (MCHC). In addition, a careful inspection of the peripheral blood smear is important, as is a sedimentation rate (Sed rate or ESR).

Clinical blood analysis

- RBC: Red Blood Cells 4.2- 5.9 million/mm^3
- Hemoglobin (Hgb): Males: 14- 18g/dL, Females: 12- 16g/dL
- Hematocrit (Hct): Males 40 - 54%, Females: 37- 47%
- MCV: Mean Cell Volume: 86 - 98 fl
- MCH: Mean Cell Hemoglobin: 27 - 32 pg
- MCHC: Mean Cell Hemoglobin Concentration: 31 – 35g/dl
- Platelet Count: 150,000 - 400,000 / mm3
- WBC: White Blood Cells: 4,000-10,000/mm3

Differential: Neutrophils 40-75%, Lymphocytes 15-45%, Monocytes 1-10%, Eosinophils 1-6%, Basophils 0-2%.

Colour index. Once the quantity of erythrocytes and hemoglobin in a given blood specimen is known, it is possible to calculate the hemoglobin content of each erythrocyte. There are many methods by which hemoglobin saturation can be determined. One of them is the calculation of the colour index. This is a conventional value derived from the ratio of hemoglobin to the number of erythrocytes. This value is found by dividing a triplet quantity of hemoglobin in grams by the first three figures expressing the quantity of erythrocytes. Normally this value approaches 0,85-1.1. If it is less than 0,8, the erythrocyte saturation of hemoglobin is insufficient; it the value exceeds 1,1 the volume of erythrocytes is higher than normal.

Red blood cell morphology can be determined from a thin blood film stained with Romanowsky dyes. The three basic features of a red blood cell are its size, its shape and its inclusions.

Size of erythrocytes. Normal erythrocyte is nearly uniform in size with diameter of 7,2 to 7,9 nm. An increasing and decreasing in the size of a red blood cell is known as anisocytosis.

Shape of normal erythrocytes is a biconcave disc, which is thickest at its edges. The presence of many abnormal shapes on a blood smear is known as poikilocytosis.

Inclusions in erythrocytes. The normal red blood cell filled mainly with hemoglobin. In pathological states blood films will show red blood cells with colored spots or rings inside their cytoplasm.

Howell-Jolly bodies. These are small, well-defined, round, densely staining basophilic inclusion bodies about 1 urn in diameter, which usually occur singly but sometimes in multiples. They appear after splenectomy and are also seen in cases of severe anemia from a variety of causes. They contain DNA and may be chromosomal remnants or nuclear fragments.

Cabot rings. These are blue-staining, threadlike inclusions in the red cells in severe anemia. They may appear as rings, or twisted and convoluted in a variety of shapes. They may occupy the entire periphery of the cell but frequently are much smaller. They are not often seen. It has been postulated that they are remnants of the mitotic spindle, but others have found that they contain histone and iron.

Heinz bodies can be seen with special supravital stains such as methylviolet Heinz bodies are granules of precipitated hemoglobin.

Normal WBC count

The normal WBC count is usually between 4500 and 11,000/mm3 and may vary in a particular individual at different times of the day. A minor variation outside the normal range is not significant as long as the differential count and the peripheral blood smear are both normal. However, some early disorder, whether infectious or myeloproliferative, is not necessarily ruled out.

Mild to moderate leukocytosis (11,000-17,000/mm3): mild to moderate elevation of the WBC count usually indicates infectious disease, mainly of bacterial etiology. Usually, the leukocytosis increases with the severity of the infection. However, there are exceptions to this rule, particularly in elderly patients in whom severe sepsis can coexist with only a modest leukocytosis. As mentioned previously, the differential WBC count is of additional help.

Leukemoid reaction: occasionally such massive leukocytosis accompanies a systemic disease that the blood picture of leukemia is simulated. When a blood picture looks like leukemia but is not, the term "leukemoid reaction" is used. Severe sepsis, miliary tuberculosis, and other nonmalignant infectious conditions are among the more common causes.

In the differentiation of myelogenous leukemia versus leukemoid reaction determination of the leukocyte alkaline phosphatase is helpful. This enzyme is high in leukemoid reaction and is decreased in myelogenous leukemia. Also, the presence of Philadelphia antigen is specific for the majority of cases of chronic myeloid leukemia.

Leukopenia: a decreased absolute WBC count (leukopenia) can be mild (3000-5000/mm^3), moderate (1500-3000/mm^3), or extremely severe (<1500/mm^3), and may be associated with diminution of the WBC count as a whole, decreases in neutrophils, or diminution of all the blood particles (pancytopenia).

Table 10

Complete Blood Count (CBC)

Test	Name	Increased/Decreased
WBC	White Blood Cell	May be increased with infections, inflammation, cancer, leukemia; decreased with some medications (such as methotrexate), some autoimmune conditions, some severe infections, bone marrow failure, and congenital marrow aplasia (marrow doesn't develop normally)

% Neutrophil	Neutrophil/Band/Seg/Gran	This is a dynamic population that varies somewhat from day to day depending on what is going on in the body. Significant increases in particular types are associated with different temporary/acute and/or chronic conditions. An example of this is the increased number of lymphocytes seen with lymphocytic leukemia
% Lymphs	Lymphocyte	
% Mono	Monocyte	
% Eos	Eosinophil	
% Baso	Basophil	
RBC	Red Blood Cell	Decreased with anemia; increased when too many made and with fluid loss due to diarrhea, dehydration, burns
Hgb	Hemoglobin	Mirrors RBC results
Hct	Hematocrit	Mirrors RBC results
MCV	Mean Cell Volume	Increased with B12 and Folate deficiency; decreased with iron deficiency and thalassemia
MCH	Mean Cell Hemoglobin	Mirrors MCV results
MCHC	Mean Cell Hemoglobin Concentration	May be decreased when MCV is decreased; increases limited to amount of Hgb that will fit inside a RBC
Platelet	Platelet	Decreased or increased with conditions that affect platelet production; decreased when greater numbers used, as with bleeding; decreased with some inherited disorders (such as Wiskott-Aldrich, Bernard-Soulier), with Systemic lupus erythematosus, pernicious anemia, hypersplenism (spleen takes too many out of circulation), leukemia, and chemotherapy
MPV	Mean Platelet Volume	Vary with platelet production; younger platelets are larger than older ones

Blood clotting tests

The three major components of the hemostatic mechanism are: the platelets, blood vessels, and the plasma protein factors involved in coagulation and fibrinolysis.

The function of platelets in hemostatic process:

- platelet are the instrumental in maintaining the integrity of the endothelial lining of the blood vessels;

- platelet play a major role in repairing any injury in the vascular system, especially at the microcirculatory level;

- platelets take part in regulation of local inflammatory reaction and immune damage initiation;

- platelets are responsible for the specific reaction related to the formation of hemostatic plug.

There are three stages of platelets activation:

- signal transduction from platelet membrane lo the structure responsible for the specific reaction;

- platelet adhesion, release of chemical substances of platelet, aggregation and finally formation a plug or clot in vessel damage.

The chemical substances of platelet include a number of enzyme, epinephrine, norepinephrine, ATP and ATP-ase. Many specific compounds participating in clotting of the blood have been revealed in platelets. There are called thrombocytic or platelet factors and are designated by Arabic numerals.

The liquid state of the blood and the closed uninterrupted system of blood vessels in which blood circulates are the principal conditions for body functioning. They are provided by the system of blood coagulation (hemocoagulation system). It keeps blood in a liquid state and restores the wholeness of the pathways of its circulation by formation of blood thrombi (plugs, clots) in the damaged vessels.

The coagulation blood system comprises blood and tissues which produce, utilize and secrete substances from the body that are indispensable for the process of coagulation. The neurohumoral apparatus also belongs to this system.

The coagulation of blood is the process of clotting of whole blood, which results in the formation of a fibrin clot. Three processes are involved in blood clotting such as formation of prothrombinase, thrombin and fibrin. In addition, the phase preceding and the phase following blood coagulation are distinguished. The primary phase is accompanied by vascular thrombocytic hemostasis (i.e. processes involved in stoppage of bleeding) in which bleeding from the microcirculatory vessels with

low blood pressure is arrested. This process is also known as microcirculatory hemostasis. In the second phase two processes simultaneously occur, i.e. retraction and fibrinolysis of the blood clot. Thus, the process of hemostasis involves three components: vessel walls, formed blood elements, and enzymatic plasma system of blood clotting.

The main methods of laboratory diagnostics of hemorrhagic syndromes

Tests for vascular - platelet factors. Tests for platelet factors include the quantitative platelet count, its morphology, platelet aggregation and adhesiveness tests, bleeding time test, estimation of platelet components in plasma.

Platelet aggregation test. An aggregating agent (activated thrombin, epinephrine, ADP, and collagen) is added to a suspension of platelet rich plasma and the response is measured in a spectrophotometer. Special devices called aggregometers are used to measure platelet aggregation.

Platelet adhesiveness test measures the ability of cells to adhere to glass surface. Adhesiveness can be determined by counting the number of platelet in the anticoagulated blood before they are passed through the column with glass beads, and by counting them again after they have passed through the column.

Bleeding time test measures time required for the cessation of bleeding after a standardized puncture through the skin 3 mm deep. The Duke test involves puncturing the earlobe with a lancet, drops of blood are blotted every 30 second and the time at which bleeding stops is noted. Normal limes for the Duke test are 1 to 3 minutes. The Ivy test have similar procedure but added a blood pressure cuff, which is placed on the upper arm and inflated to 40 mm Hg the skin is pieced with a lancet in the lower forearm. Blood is blotted every 30 second until the bleeding stops. Normal times for the Ivy test are between 2 and 6 minutes.

Tests for plasma factors involved in coagulation and fibrinolisis

Prothrombin time (PT) measures the extrinsic system (factor VII) as well as factors common in both systems (factor X, V, 11 and I). Prothrombin time test is performed by adding tissue extract (factor III = tissue factor) and calcium to the plasma. Normal prothrombin time - 10-17 second.

Activated partial thromboptastin time (APTT or PTTK.) measures the intrinsic system's factors VIII, DC XI and XII, in addition to factors common to both systems. Three substances - phospholipid, a surface activator (Kaolin) and calcium arc added to the plasma. The normal PTTK. is 30-40 seconds.

Fibrinogen determinant test is performed by addition 0,2 ml thromboplastin and 0,1-0,5 % solution of calcium chloride to 1 ml platelet-rich plasma. Formed clot is dried and weighed. The normal fibrinogen levels in the blood are 200 to 400 mg per deciliter of plasma.

Thrombin time or fibrinogen deficiency test is performed by added the activated thrombin to blood plasma and measure the time in takes to form a clot The test reflects fibrinogen-fibrin conversion. Normal thrombin lime - 10-12 second.

BASIC SYNDROMES IN THE HEMATOLOGY. CHANGES IN THE ORAL CAVITY IN DISEASES OF THE HEMATOPOIETIC SYSTEM

SYNDROME OF ANEMIA

Decreases in numbers of RBCs or Hb content caused by blood loss, deficient erythropoiesis, excessive hemolysis, or a combination of these changes.

The term anemia has been used incorrectly as a diagnosis; more properly, it denotes a complex of signs and symptoms. The type of anemia defines its pathophysiologic mechanism and its essential nature, allowing for appropriate therapy. Not investigating mild anemia is a serious error; its presence indicates an underlying disorder, and its severity reveals little about its genesis or true clinical significance.

The symptoms and signs of anemia represent cardiovascular-pulmonary compensatory responses to the severity and duration of tissue hypoxia. Severe anemia (eg, Hb<7 g/dL) can be associated with weakness, vertigo, headache, tinnitus, spots before the eyes, fatigability, drowsiness, irritability.

Anemia results from one or more of three basic mechanisms: blood loss, deficient erythropoiesis (RBC; production), and excessive hemolysis (RBC destruction). Blood loss should be the first consideration. Once it is ruled out, only the other two mechanisms need to be considered. Because RBC survival is 120 days, maintenance of a steady RBC population requires daily renewal of 1/120 of the cells. Complete cessation of erythropoiesis results in a decline of about 10%/wk (1%/day) of RBCs. Deficient erythropoiesis results in relative or absolute reticulocytopenia. When RBC values fall > 10%/wk (500,000 RBCs/uL) without blood loss, hemolysis is a causative factor.

Classification

There are two classifications:

Classification according to the cause

I. Blood loss:

- acute post-hemorrhagic anemia;
- chronic post-hemorrhagic anemia.

II. Impaired red cell formation:

Disturbance of bone marrow function due to deficiency of substances essential for erythropoiesis:

- iron deficiency anemia;

- megalobastic macrocytic anemias due to deficiency of vitamin B12 or folic acid;
- aplastic anemia.

III. Increased red cell destruction (hemolytic anemias):

- hemolytic anemias due to corpuscular defect (intracorpuscular or intrinsic abnormality). The basic defect may in any of three main components of the cell: the membrane, the hemoglobin molecule and the enzymes related to cell metabolism;
- hemolytic anemias due to an abnormal hemolytic mechanism (extracorpuscular or extrinsic abnormality). These are acquired and result from either an immune or non-immune mechanism.

Classification according to the morphology

1. Microcytic (MCV<80 fl) 100fl)
• Iron deficiency anemia;
• Thalassemia minor;
• Sideroblastic anemia;
• Lead poisoning
2. Macrocytic (MCV>100fl)
• Megaloblastic: due to Vit. B12 and folic acid deficiency. Severely macrocytic anemia (MCV>125) is almost always due to megaloblastic anemia);
• Macrocytic without megaloblastic: due to alcohol excess, cirrhosis of liver, hypothyroidism and reticulocytosis, marrow infiltration and myelodysplasia syndrome.
3. Normocytic (80-100 fl)
• Aplastic anemia (bone marrow failure);
• Myelodysplastic syndrome.

IRON DEFICIENCY ANEMIA

Etiology

Blood loss:

Uterine (menorrhagia, metrorrhagia).

Chronic gastrointestinal blood loss:

- esophageal varices;
- hiatus hernia;
- peptic ulcer;
- chronic aspirin ingestion;
- carcinoma of stomach, colon, caecum, rectum;
- ulcerative colitis;

- hemorrhoids;
- diverticulosis;
- hookworm infestation (anemia with eosinophilia).

Urine bladder and kidney:

- glomerulonephritis;
- carcinoma of kidney and urine bladder.

Increased requirements:

- prematurity (diminished iron stores);
- growth (infants and young children);
- females in reproductive age group: menstruation, pregnancy, lactation.

Impaired absorption:

- achlorhydria (especially in middle aged females);
- atrophic gastritis;
- gastrectomy;
- gastroenterostomy;
- tropical sprue or coeliac disease.

Inadequate intake:

- improper feeding in infants and young children;
- poverty;
- dietary fads;
- anorexia (nervosa, of pregnancy or malignancies).

Clinical features

The clinical features include two syndromes: general anemic and specific one due to the iron lack.

Anemic syndrome. The patients complaint on fatigue, tiredness, faintness, easy fatigability, dyspnea, palpitation, heart pain, headache, giddiness, spots before the eyes, lack of concentration, drowsiness, numbness, coldness, tingling of hands and feets. Mild fever 37,2-38,2 °C is observed. Physical examination of the cardiovascular system reveals the displacement of the left relative cardiac border outside, diminished first sound, functional systolic murmurs over sound points with maximal intensity over pulmonary artery, systolic bruits over carotic arteries. ECG changes occurST-segment depression and flattening or inversion of T-wave. Amenorrhoea, menorrhagia in females and loss of libido in the males appear.

Cideropenic syndrome was first described by Basenstrom in 1930. The patient complains on the generalized muscular weakness, disorders of muscular sphincters and disorders of urination.

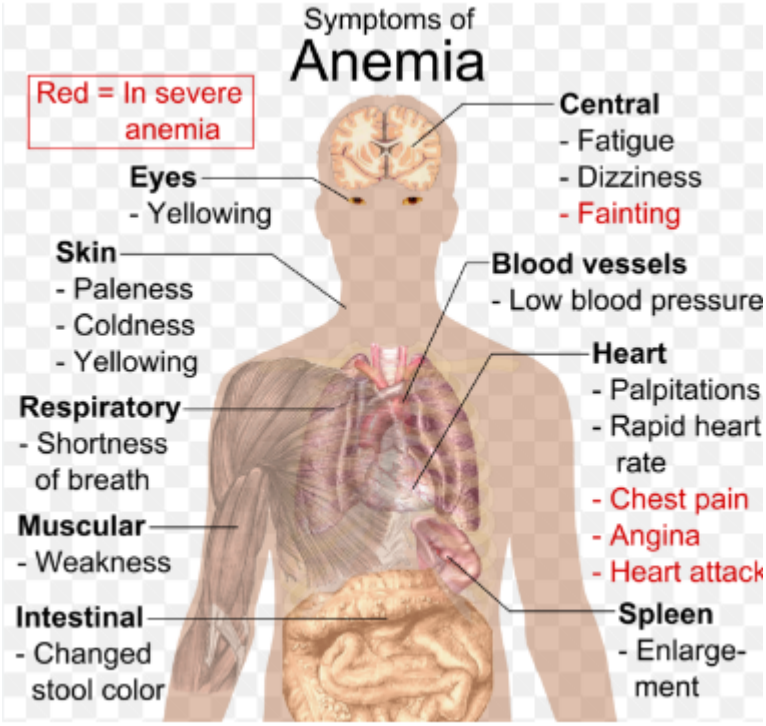

Image 21. Symptoms of Anemia

The image was downloaded from website https://www.phlbi.org/divisions/blood-disorders/anemia

The colour of the skin is pallor with greenish tint. Pallor of the nail beds, mucous membranes of the mouth, conjunctivae, sclerae are revealed. The skin is dry with creak (chirp rattle) on the legs and hands leukoplakia. The nail beds became dry, fragile, with sketch, spoon-shaped named koilonychias. The hair became thin, fragile, and grey.

The gastrointestinal disorders are the specific symptoms and signs of iron deficiency anemia. The patients complain on the difficulties during swallowing solid food - Plummer-Vinson syndrome according to the atrophy of the postcricoid esophageal web. In chronic, severe iron deficiency the patients have specific features - pica chlorotica, which characterized by the eating of unusual items such as coal, earth, chalk, clay, starch, ice (pagophagia) and smell acetone, petroleum.

Nausea, regurgitation, pain and dulling at the epigastric region after meal, diarrhea, anorexia are the specific symptoms of the patients with iron deficiency

anemia. The clinical signs of anemiaglossitis with redness and papillae atrophy, angular stomatitis, inflammation of the gum, cheilosis.

During the endoscopic investigations and biopsy the atrophy esophagitis and gastritis are detected. Sometimes may be splenomegaly.

Additional methods of examination

Clinical blood analysis:

- hemoglobin concentration is decreased;
- red blood cells count decreased normal or slightly decreased;
- mean cell volume (MCV) < 76 fl;
- mean cell hemoglobin (MCH) < 27 pg;
- mean cell hemoglobin concentration (MCHC) < 30 gm%;
- color index < 0,8;
- anisocytosis, microcytic red cells;
- poikilocytosis, pencil shaped cells and target cells;
- hypoehromia, ring or pessary cells;
- few polychromatophils;
- reticulocyte count is variable;
- red blood cells osmotic fragility is slightly decreased;
- hematocrit low.

Bone marrow:

- micronormoblaslic erythroid hyperplasia;
- predominantly intermediate normoblasts;
- cytoplasm decreased and shows differential staining;
- bone marrow iron is reduced or absent.

Biochemical blood analysis:

- serum iron level is reduced;
- total iron binding capacity is increased;
- unsaturated iron binding capacity is also raised; percentage saturation reduced.

VITAMIN B12 DEFICIENCY ANEMIA

Anemia caused by vitamin B12 deficiency anemia is blood disorder, which characterized by abnormalities in the DNA synthesis of the blast cells due to the deficiency of vitamin B12 and/or folic acid.

The vitamin B12 molecule consists of the nucleotide 5,6-dimethylbenzimidazole linked at right angles to a four-pyrrole ring with a cobalt

atom (the corrin nucleus). Several cobalamins (vitamin B12 compounds), which vary only in the ligand attached to the cobalt atom, occur in nature.

Methylcobalamin (MeCbl) and adeno-sylcobalamin (AdoCbl), physiologic cobalamin coenzymes, perform the biochemical roles of B12. MeCbl functions in nucleic acid metabolism and is the cofactor involved in defective DNA synthesis. AdoCbl serves as a scavenger system for catabolism of aliphatic amino acids, lipid membranes, and precursors of propionate; it may be the cofactor involved in altered myelin synthesis and repair.

Vitamin B12 is available in meat and animal protein foods. Its absorption is complex; it occurs in the terminal ileum and requires intrinsic factor, a secretion of parietal cells of the gastric mucosa, for transport across the intestinal mucosa. Vitamin B12 in food binds to binding proteins (R binders) in saliva that protect B12 in the acid milieu of the stomach. When this B12 complex (B12-R binders) enters the small intestine, pancreatic enzymes cleave it, and the vitamin B12 binds to the intrinsic factor.

Etiology of vitamin B12-deficiency anemia

1.Reduced intake: nutritional deficiency.

2.Strict veganism.

3.Impaired absorption:

- gastric cause: total or partial gastrectomy;

- intestinal cause: chronic tropical sprue, intestinal stagnant loop syndrome (e.g. jejunal diverticulosis, blind loop, strictures), scleroderma, Crohn's disease and ileal resection, congenital selective malabsorption with proteinuria, Zollinger Ellison syndrome, severe pancreatitis, coeliac disease;

- hemodialysis;

- transport protein defects: hereditary lack of transcobalamin II, abnormal transcobalamin II, abnormal B12 binding protein.

4. Competition for cobalamin:

- bacterial colonization of the small intenstine;

- fish tapeworm infection;

- bacteria "blind loop" syndrome.

5. Impaired metabolism:

- inhibitors of dihydrofolate reductase;

- purine antagonists;

- pyrimidine antagonists;

- alcohol.

Clinical features

There are three clinical syndromes: anemic, affection of the digestive system and neurological syndrome.

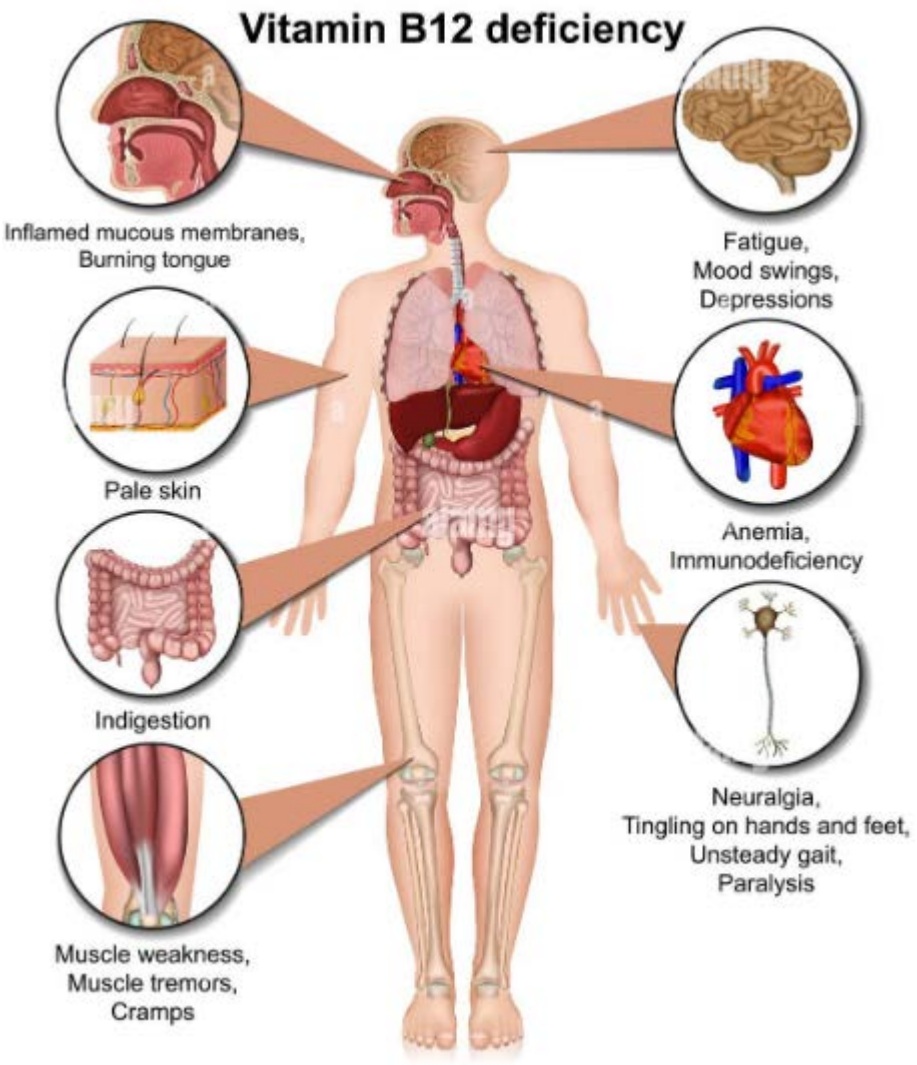

Image 22. Vitamin B12 deficiency

The image was downloaded from website https://www.alamy.com/vitamin-b12-deficiency

Anemic syndrome includes such complaints: fatigue, tiredness, palpitation, dyspnea, giddiness. The skin is pallor with lemon yellow tint, slightly icteric skin and sclerae, swallowing face, slight pedal edema. Physical examination of the cardiovascular system reveals tachycardia, systolic murmur at the apex and pulmonary artery, systolic bruits over carotid arteries, ischemic changes on ECG, heart failure. The symptoms and signs of gastrointestinal affection: anorexia, Hunter's

glossitis (sore, smooth red tongue, with ulcer over the edge), atrophic gastritis, bladder and bowel dysfunction, diarrhea, enlarged liver and sometimes spleen.

Neurological syndrome includes peripheral neuropathy and combined degeneration of the spinal cord where the posterior and lateral columns undergo demyelization. The symptoms and signs are next: numbness, tingling, paresthesia in the extremities, difficulty in walking, ataxia, position and vibration senses are diminished, dumbness. There may be sphincter disturbance. Reflexes may be diminished or increased. The Romberg and Babinski signs may be positive. Affections of the mental state reflect irritability, diminished memory, even severe dementia or psychosis. In young females there may be infertility.

Additional methods of examination

Clinical blood analysis:

- hemoglobin concentration decreased moderately; red blood cell count decreased pronouncly;
- mean cell volume ranging from 100 to 140 fl;
- color index > 1,2;
- moderate leucopenia;
- mild, usually asymptomatic thrombocytopenia;
- anisocytosis - macrocytosis;
- poikilocytosis - ovalocytosis;
- hyperchromia, ring or pessary cells;
- red blood cells may show: Howel-Jolly bodies, Cabot rings;
- hypersegmentes neutrophils;
- macropolycytes (large neutrophils).

Bone marrow:

- hyperplasia of erythroid elements;
- megaloblasts - gigantic cells with large nucleus oval shape and basophilic cytoplasm;
- gigantic metamyelocytes;
- megakaryocytes.

Biochemical blood analysis:

- increased level of unconjugated bilirubin;
- increased level faeces stercobilin;
- increased level of lactatdehydrogenasa.

Special tests for diagnosing vitamin B12 deficiency:

- low serum vitamin B12 assay;
- increased urinary excretion of methylmalonic acid;
- low radioactive vitamin B12 absorption test (Schilling's test);
- reticulocyte response to vitamin B12 administration.

HEMOLYTIC ANEMIA

Hemolytic anemias are the geterogenous group of anemias, which characterized by shortened life span of erythrocytes in the circulation resulting from their accelerated destruction.

At the end of their normal life span (about 120 days), RBCs are removed by components of the mononuclear phagocyte system, principally in the spleen, where Hb catabolism takes place. The essential feature of hemolysis is a shortened RBC life span; hemolytic anemia results when bone marrow production can no longer compensate for the shortened RBC survival.

Classification of hemolytic anemias

Hereditary hemolytic anemias

Defects of the cell membrane:

- hereditary spherocytic anemia;
- hereditary elliptocytic anemia.

Defects of erythrocytic metabolism:

- glucose-6-phosphate dehydrogenase (G-6-PD) deficiency anemia. Abnormal hemoglobins:
- sickle cell anemia;
-thalassemia.

Acquired hemolytic anemia

Immunological destruction of red blood cells:

- transfusion with incompatible blood;
- hemolytic disease of the newborn;
- autoimmune hemolytic anemia (AIHA) (warm-active AIHA and cold-active AIHA).

Physical destruction of red blood cells:

-march hemoglobinuria;
- traumatic cardiac hemolytic anemia.

Hemolytic anemia induced by chemical agents.

Hemolytic anemia caused by microorganism:

- anemia of malaria;
- anemia of Clostridia.

Hemolytic anemia secondary to other disease.

Paroxysmal nocturnal hemoglobinuria.

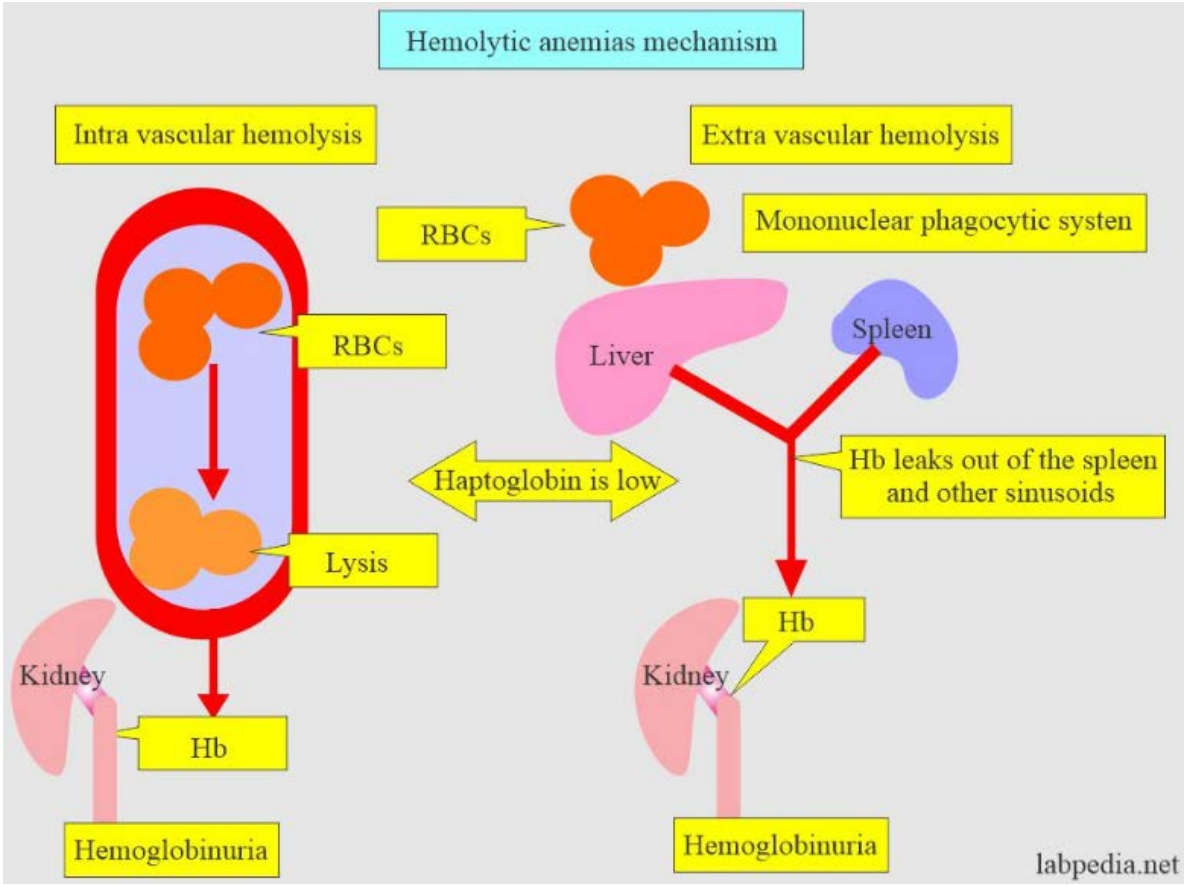

Image 23. Hemolytic anemias mechanism

The image was downloaded from website https://labpedia.net

Table 11

Causes of hemolytic anemia

Congenital causes of hemolytic anemia (inherited)	**Acquired causes of hemolytic anemia**
1. Hemoglobinopathies: 1. Sickle cell anemia (Hb S) 2. Hb C 3. Thalassemia 2. RBC Membrane defects: 1. Hereditary spherocytosis 2. Hereditary	1. Autoimmune: 1. Cold antibody 1. Infections like mycoplasma pneumonia 2. Lymphoma 3. Infectious mononucleosis 4. Paroxysmal cold hemoglobinuria 2. Warm antibody

acanthocytosis 3. Hereditary elliptocytosis 4. Hereditary stomatocytosis 3. Enzyme deficiency (metabolic defect): 1. G6PD deficiency 2. Pyruvate kinase deficiency	1. SLE 2. Drugs (methyldopa) 3. Lymphoma 4. CLL 2. Alloimmune: 1. Hemolytic disease of the newborn 2. Blood transfusion reaction 3. Marrow transplantation rejection (allograft rejection) 3. Non-immune: 1. Paroxysmal nocturnal hemoglobinuria 4. Chemical agents: 1. Drugs 2. Industrial chemicals 3. Domestic substances 5. Infectious agents: 1. Malaria 2. Clostridia 6. Physical trauma: 1. Burn 2. Valve prosthesis 7. Microangiopathic hemolytic anemia 8. Secondary causes: 1. Liver diseases 2. Renal diseases 9. Hemolytic transfusion reaction

Clinical features

Clinical features include three indications: anemia, jaundice and splenomegalia. The symptoms of anemia are common as most other one: weakness, fatigue, dyspnea, palpation, headache, dizziness, inability to concentrate. The most important sign of hemolytic anemia is jaundice, which differ from slightly yellow tint to intense lemon color of mucosa membrane, sclera and skin. Splenomegaly is specific sign, explained by hyperplasia of cells, which take part in phagocytosis. Commonly spleen is enlarged moderately.

Latent compensated hemolytic anemia explained by capacity of bone marrow to produce increased number of reticulocytes and in the peripheral circulation red blood cell counts may be fairly normal.

However the bone marrow will no longer be able to compensate and breakdown rate of erythrocytes becomes greater than the production rate of new erythrocytes. In acute cases is developed the hemolytic crisis with abrupt onset, high temperature, severe fatigue, nausea, vomiting pain in the abdomen, pronounced pallor with yellow color of mucosa and skin, hemorrhage lesions. Patient has grave condition, may be occur hemolytic coma. Tachycardia, systolic murmur, hypotension are observed. During palpation of abdomen the hepatosplenomegalia is detected.

Hemolysis may be acute, chronic, or episodic. Hemolytic crisis (acute, severe hemolysis) is uncommon; it may be accompanied by chills, fever, pain in the back and abdomen, prostration, and shock. In severe cases, hemolysis increases (jaundice, splenomegaly, and, in certain types of hemolysis, hemoglobinuria and hemosiderinuria), and erythropoiesis increases (reticulocytosis, hyperactive bone marrow). In chronic hemolysis, anemia may be exacerbated by aplastic crisis (temporary failure of erythropoiesis); this is usually related to an infection, often parvovirus.

Additional methods of examination

Clinical blood analysis:

- hemoglobin concentration decreased;
- red blood cells count decreased;
- reticulocytes increased;
- macrocytosis;
- polychromasia;
- polymorphonuclear.

Bone marrow:

- compensatory erythroid hyperplasia.

Biochemical blood analysis:

- increased plasma unconjugated bilirubin;
- increased urinary urobilinogen; increased faecal urobilinogen;
- increased plasma lactatdehydrogenasa.

Findings of intravascular hemolysis:

- reduced or absence of haptoglobin in the blood;
- presence of free hemoglobin in the blood;
- presence of free hemoglobin in the urine;
- presence of methemalbumemia.

HEMORRHAGIC SYNDROME

The bleeding disorders are a heterogeneous group of syndromes characterized by easy bruising and spontaneous bleeding from the blood vessels.

Classification:

I. Disorders of coagulation (coagulopathy) - hemophilia.

II. Disorders of platelets (thrombocytopenia) - Werlhoff's disease.

Ill. Vascular disorders (vasopathy) Henoch-Schoenlein purpura.

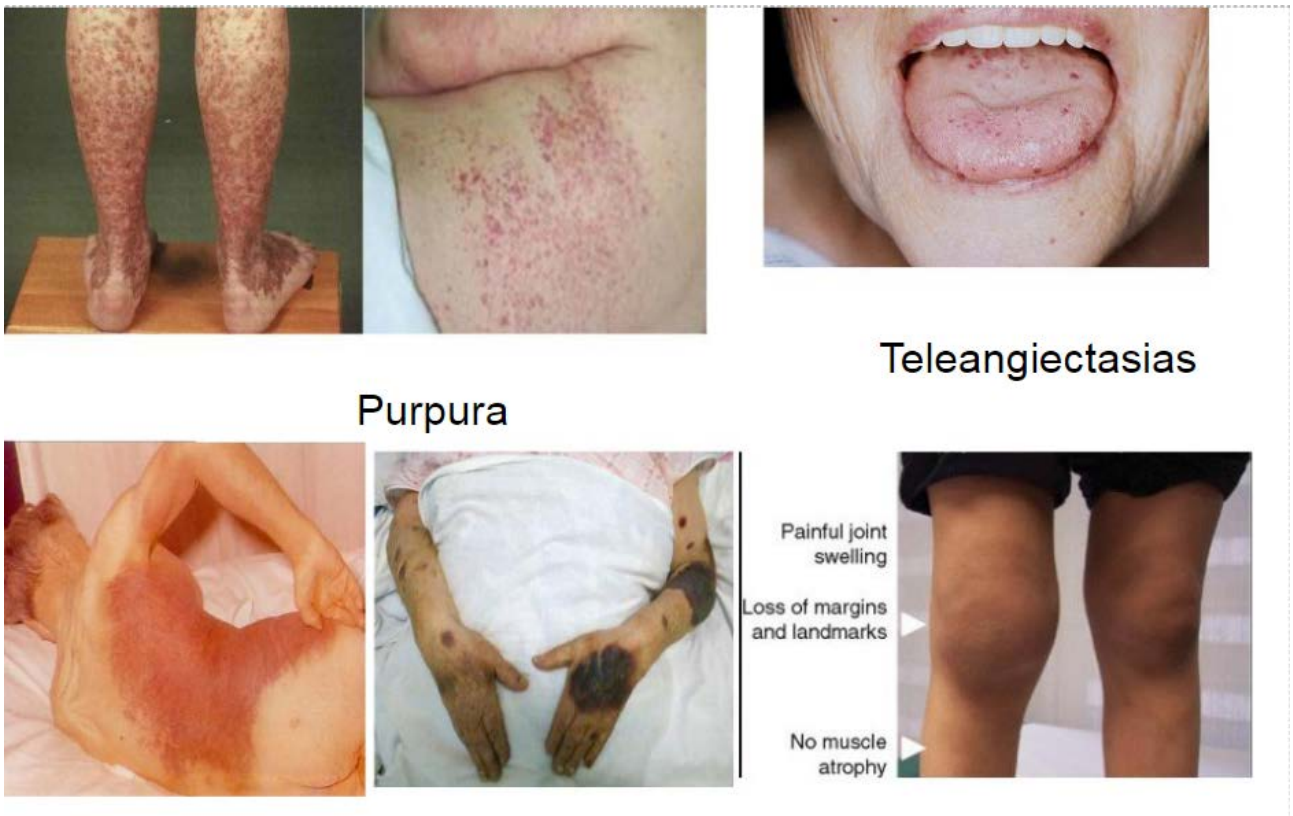

Image 24. Hemorrhagic syndrome

The image was downloaded from website https://www.slideshare.net

HEMOPHILIA

Etiology

- congenital blood coagulation disorder;
- inheritance is sex linked, males are affected while females act as carrier;
- some cases do not have any family history and presumably result from spontaneous genetic mutations.

Clinical feature

The main patients' complaints: spontaneous bleeding after trauma, dental extraction, surgery manipulation. Sometimes may be nasal, pulmonary hemorrhage

and from gastrointestinal, genitourinary systems. The patient complains of the joint enlargement.

Objective examination

General patient's condition is usually satisfactory. In case of prolonged and recurrent hemorrhages and loss of large amount of blood general condition may be middle grave or grave. The posture of the patients is active with restriction due to the pain and walking difficulties in affected joints and muscles caused by spontaneous bleeding.

The color of the skin and visible mucosa as a rule is pallor, with hemorrhages lesions: petechia, ecchymoses and hematoma. Bleeding into the joints is known as hemarthrosis begin spontaneously without apparent trauma. The joints most commonly affected are knees, elbows, ankles and hips. Bone destruction occurs due to repeated subperioctal hemorrhages. The defects undergo
neoossification causing expansion and pathological fractures in the bones. The deformities of joints and bones are specific signs of hemophilic patients. Muscle hemotomas are also characteristic of hemophilia secondary to hematomas appears atrophy of muscles. These occur most commonly in the calf and psoas muscles but they can arise in almost any muscle and cause the pressing on the nerve with consequent parasthesia and weakness in the extremities, progressive muscle and nerve damage resulting neuropathy. Hemophilic pseudotumours may occur in long bones, pelvis, ringers and toes.

The course of disease is characterized by early onset in babies about 6 months old, when superficial bruising or a hemarthrosis may occur. The spontaneous bleeding episodes, joint deformity and crippling are observed entire the patient life. Hematuria is more frequently than gastrointestinal bleeding. Intracranial hemorrhage is rare, but in severe and prompt case it may be fatal outcome. Operative and postoperative hemorrhage is dangerous.

Additional methods of examination

Clinical blood analysis:

- activated partial thromboplastin time increased;
- whole blood coagulation time is raised;
- factor VIII dolling assay (VIII C) reduced;
- immunological methods show normal VIII R, AG;
- bleeding time and prothrombin time tests normal;

- carrier females have half the clotting activity (VIII C) expected for the level of VIII R, G.

X-ray examination:

- broadening of femoral epicondyles;
- sclerosis, osteophyte and bony cists;
- atrophy of muscles.

The computer tomography scan: intracerebal hematoma.

HEMOPHILIA B (Christinas' disease)

Hemophilia B (Christinas disease) occurs as a result of a deficiency of factor IX. Like Hemophilia A it is also X-linked recessive trail. The clinical feature similar to the hemophilia A but bleeding is usually not as severe because factor IX is more stable than factor VIII C.

Additional methods of examination

Clinical blood analysis

- activated partial thromboplastin time is raised;
- whole blood clotting time (severe cases) is raised;
- factor IX clotting assay is reduced;
- both bleeding time and prothrombin time tests are normal.

HEMOPHILIA C

Hemophilia C - may be defined as a bleeding disease caused by a deficiency of factor XI. It is inherited as a recessive trait. The symptoms and signs are similar to other type of hemophilia.

IDIOPATHIC THROMBOCYTOPENIC PURPURA (Werlhoff's disease)

Thrombocytopenia is most common form of bleeding disorders due to the quantitative abnormalities of platelets. Because a number of platelets reduce in the blood stream, their function is impaired.

Etiology

Causes of decreased platelet production:

- selective megakaryocytic depression in bone marrow: drug-induced, chemicals.

Infiltration of bone marrow:

- aplastic anemia;
- leukemia;
- myelosclerosis;
- multiple myeloma;

- megaloblastic anemia;
- carcinoma.

Increased destruction of platelets:

- disseminated intravascular coagulation;
- idiopathic thrombocytopenic purpura;
- viral infections - Epstein-Barr virus, HIV;
- bacterial infections - septicemia.

Clinical feature

Idiopathic thrombocytopenic purpura more commonly affects females at an early age. The main complaints are easy bruising in skin and bleeding from mucosa with sudden onset after easy trauma and sometimes spontaneously. Very often symptoms are the bleeding from nose, gastrointestinal tract. lung and kidney hemorrhage, in women - menorrhagia. The course of disease is chronic, with remissions and relapses.

Objective examination. General patient's condition is satisfactory. If bleeding persists for more than some days resulted acute posthemorrhage anemia the patient's condition become grave and required immediately treatment. The main clinical signs are the presence features of skin bruising different size: petechiae, purpura and even hematoma, which located at the anterior part of trunk and extremities. According to the term of bruising appearance may be change of color with different tint: read, blue, green and yellow.

Skin bruising sometimes accompanied with profuse mucosa bleeding and become insidious character because occur posthemorrhage anemia. Spontaneous bleeding docs not usually occur until the platelet count falls below about $30x10^9$/l.

Severe thrombocytopenia results in eye-ground hemorrhage, but intracranial hemorrhage israre.

Splenomegaly is observered in about 10 % of the cases.

Additional methods of examination

Clinical blood analysis: the platelet count is usually $10\text{-}50xl0^9$/l; the blood film shows reduced numbers of platelets.

The bone marrow usually shows increased number of megakaryocytes; sensitive tests can demonstrate antiplatelet IgG either alone or with complement, on the platelet surface or in the serum in most patients.

HENOCH-SCHOENLEIN SYNDROME

The vascular disorders are a heterogeneous group of syndromes characterized by easy bruising and spontaneous bleeding from the blood vessels.

Vascular disorders resulting in abnormal hemostasis are classified into two major groups: inherited and acquired.

Henoch-Schoenlein syndrome belongs to acquired vascular disorders.

Etiology

Etiology is still unknown, but it was observed that this disease often begin after the ingestion of certain drugs or as a result of a group A streptococcal infection.

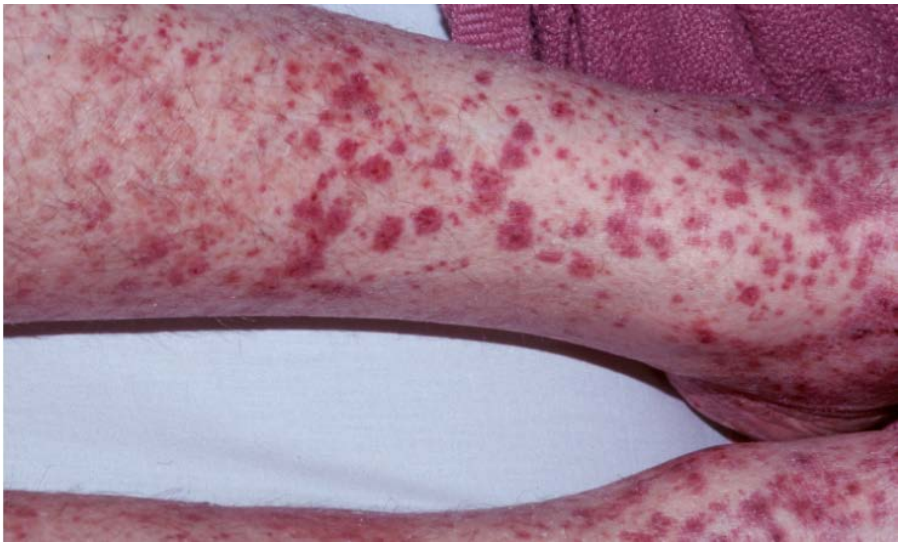

Image 25. Henoch Schonlein purpura

The image was downloaded from website https://healthjade.net

Clinical features

This disease is most common in children, although it also may occur in adults. The abrupt onset with pain in the joints and elevated temperature arc the first features. The specific signs are the appearance on the legs and arms small pinpoint hemorrhages at the skin known as petechial accompanied with itching. The mucosa doesn’t affect in adults. During severe course of disease appear the additional points anywhere in the body with swelling and necrosis. The hematuria may be the additional sign of disease. After two weeks the lesions disappeared without skin changing.

Additional methods of examination

Clinical blood analysis: normal erythrocytes and platelets count; leucocytes count increased; regenerative nuclear shift to the left; ESR accelerated.

EUCOSIS (Hemoblastosis)

Hemoblastosis is a disease of the whole blood system characterized by:

1) progressive cell hyperplasia in the hemopoietic organs with pronounced prevalence of proliferation of certain cells;

2) metaplasia of these pathological cells instead of normal cells to hemopoietic organs;

3) development of pathological foci of hemopoiesis in various organs.

Table 12

Classification of hemoblastosis

Primary affection of the bone marrow		Tumor growth outsides the marrow bone
Myeloproliferative disorders	Lymphoproliferative disorders	
Acute myeloblastic leukemia Chronic myelocytic leukemia Polycythemia vera Myelofibrosis leukemia	Acute lymphoblastic leukemia Chronic lymphocytic leukemia Multiple myeloma	Hodgkin's disease Malignant lymphoma Reticulosarcoma Limphosarcoma

Acute myeloblastic leukemia

Acute myeloblastic leukemia is characterized by profuse proliferation of the blast clement of blood with their subsequent disturbed differentiation, with development of foci pathological hemopoiesis in various organs.

Acute myeloblastic leukemia occurs in all age groups but commonly in adults and less in children. Acute myeloblastic leukemia is predominantly a disease of adults with two peaks, one at 15 to 20 years of age and another peak after 50 years of age.

Etiology

The reason of the appearance of leukemia is still unknown. Most authors regard hemoblastosis as tumors whose morphological basis are hemopoietic cells of various organs.

Some factors can provoke acute myeloblastic leukemia:

1) chemical concerogenous substances (benzpyrence, benzol);

2) radiaionizing;

3) viruses theory connect the appearance of acute myeloblastic leukemia with DNA or RNA damage, but only animal experimental studies support this point of view;

4)genetic theory: according to this theory, acute leukemia develops due to the congenital or acquired damage to the chromosome structures of low differentiated cells of the hemopoietic organs.

Classification

French-American-British Group (FAB)

Ml - undifferentiated

M2 - differentiated

M3 - promyelocytic

M4 - myelomonocytic

M5 - monocytic

M6 - erythroleukemia

M7 - megakaryoblastic

Clinical features

The onset of the disease is in most cases acute or subacute. In some eases the onset disease is gradually with non specific general symptoms: weakness, fatigue, subfebrile temperature, weight loss.

There ate some syndromes of acute leukemia: intoxication, ulcerative necrotic, infections, bleeding, anemia, splenomegaly and hepatomegaly, bone pain, neurological syndrome:

Syndrome of intoxication are as follows: high temperature (remittent or hectic), profuse sweating, chills, pronounced weakness, reduced exercise tolerance, general loss of strength. Fever chills and sweating are explained by the pyrogenic effects of purenes released in great quantity during the decomposition of immature leucocytes.

Ulcerous - necrotic syndrome is characterized pain in the throat, swallowing becomes painful. Ulcerous of the oral mucosa occurs commonly in acute myeloblastic leukemia. There may be infiltration of the gums with swelling and bleeding. Ulcerous and necrotic tonsillitis, gingivitis and stomatitis are quite characteristic of this disease.

Despite the markedly increased production of white blood cells, their function is inadequate. This fact is explained such complications as secondary infections due to the pathogenetic agents: gram negative bacteria, staphylococci and streptococci, viral - herpes simplex and zoster, fungal - Candida, protozoal - pneumocystitis

carinii. The infections of skin, mouth, throat, respiratory and urinary tract including septicemia are common usually. Pericarditis and pleuritis arc possible.

Bleeding syndrome: traces of subcutaneous and imracutaneuos hemorrhages can be seen. The lesions vary in size from small pointed hemorrhages (petechiae) to large black and blue spots (ecchymosed) which appear spontaneously or at points of injections. Spontaneous bruises, purpura, bleeding gums and bleeding from venepuncture sites because of thrombocytopenia are common. Occasionally there may be major internal hemorrhage.

Syndrome of anemia is explained by depressed erythropoiesis; increased bleeding; accelerated destruction of red blood cells. The degree of anemia depends of the speed of the development of acute myeloblastic leukemia as well as on iron and folic acid stores. There are general symptoms of anemia: fatigue, dizziness and dyspnea. The mucous membranes and nail beds are pallor.

Lymphadenopathy is rare sign in patients with acute myeloblastic leukemia. Sometimes enlarged cervical and supraclavicular lymph nodes are detected in the superficial areas by palpation. Tenderness of the sternum may be quite pronounced. Blast infiltration of meningeal membranes lead to neurological disorders with clinical features of meningitis.

Additional methods of examination

Clinical blood analysis: leucocytosis 30-300xl0^9/l; the white blood cells count may be normal or even decreased; red blood cells count decreased; hemoglobin concentration decreased; severe thrombocytopenia; blast cells - 95%.

Blood film examination show variable numbers of blast cells. In patients with acute myeloblastic leukemia the blast cells are the myeloblasts or erythroblasts. The blasts may show Auer rods and other abnormal cells may be present: promyelocytes, myelocytes, agranular neutrophils; absence of eoisinophyls and basophils.

Bone morrow: bone marrow is hypercellular with a marked proliferation of blast cells which typically amount to over 75 % of the marrow cell total.

CHRONIC MYELOCYTIC LEUKEMIA

Chronic myelocytic leukemia - is defined as the myeloproliferative disorders. Chronic myelocytic leukemia is as a neoplastic disease of bone marrow stem cell - precursor of myelopoiesis, which is common for granulocytes, erythrocytes and megakariocytes with excessive production of granulocytes in the bone marrow and other hematopoietic organs.

Etiology

The specific factors haven't been established. The causative agents of chronic myelocytic leukemia arc suspected such as ionizing radiation, exposure some chemical carcinogens, which damage bone marrow.

Clinical features

The presence of neoplastic bone marrow element shows the following consequences. Increased nonfunctional white blood cell production and decreased normal white blood cell production result in infections. Decreased red blood cell production leads to anemia. Decreased platelet production will result in a greater tendency to bleeding. There are three clinical stages of disease: stage I - initial, stage II - accelerated phase, stage III - dystrophy and blast crisis. The disease develops gradually. The initial symptoms and signs are not specific such as general malaise, fatigue, weight loss, low-grade fever. These disorders are detected accidentally as a rule. Some patients are symptomatic at diagnosis. In the pronounced stage weakness becomes considerable, night sweating profuse, elevation of temperature periodically to 37,5-39°C, pain in the left hypochondrium, abdominal fullness and discomfort. Myeloid infiltration in the lung can be caused some additional symptoms, such as coughing. Many patients will complain on pain of the bones especially the sternum and ribs, which are the major sites of blood cell production.

Objectivel examination reveals pallid skin with yellowish or grayish tint due to the anemia. The specific sign of disease is skin leukemic infiltration and local lesions. Infiltrations of the bones and the joints may cause localized lesions. Features of anemia may include dyspnea and tachycardia, lethargy. Chronic myelocytic leukemia is associated with increased susceptibility to infections such as pneumonia, pleuritis, pyelonephritis.

In patients occurs considerable nonsymmetrical enlargement of abdomen predominantly in the left hypochondrium, due to the marked enlarged spleen. In about 10 % patients the enlargement is massive, extending to over 15 cm below the costal margin. The spleen is usually firm, smooth and painless. The presence of splenomegaly may be explained by excessive work to eliminate senescent and abnormal white blood cells. Enlarged liver is fairly common also. Less common neurological presentations include dizziness, visual disturbances, convulsions, paralysis resulting from the affection of the brain and spinal cord.

In patients is common bleeding syndrome with bruising, epitasis, menorrhagia or hemorrhage from other sites.

In stage III may observe cachexia, secondary prolonged infections, progressive anemia, great tendency to bleeding. Finally, this chronic condition may transform to blast crises similar to an acute form of leukemia with the production of large number of immature myeloblasts in the bone marrow and the bloodstream. This new blastic phase is fatal.

Additional methods of examination

Clinical blood analysis:

- the number of blood cells is usually between $50x10^9$/l and $300x10^9$/l;
- the number of red blood cells decreased;
- the number of platelet decreased;
- ESR accelerated;
- complete spectrum of myeloid cells is seen: blast cells, myelocytes, metamyelocytes, band cell, nature polymorphonuclear neutrophils;
- myeloblasts are usually less than 10 %;
- increased count of eosinophils and basophils.

Bone marrow:

- hypercellular with granulopoietic predominance;
- Phyladelphia chromosome in bone marrow cells is detected during cytogenetic analysis.

CHRONIC LYMPHOCYTIC LEUKEMIA

Chronic lymphocytic leukemia is now regarded as a tumor of the immunocompetent lymphatic tissue.

Etiology

Some environmental factors such ionizing radiation, mutagenic chemicals have been implicated at the onset of disease.

Clinical features

Chronic lymphocytic leukemia is a disease of middle-aged and elderly persons. There is peak occurrence between 50 and 60 years of age. This disease has slowly onset with non specific complatains on loss of weight, decreased appetite and fatigue. The first specific clinical finding at the beginning of the disease is symmetrical, discrete, non tender peripheral lymphadenopathy, which observes at about 80 % patients. Palpation is used to assess the enlargement of the lymph nodes and their properties. The lymph nodes are elastic, they do not fuse with the skin or with one another; they are painless in most cases. The lymph nodes never ulcerate or suppurate.

Under condition of benign process the initial stage may last for a long time. As the disease progresses the peripheral lymph nodes become enormous, firm. Lymphadenopathy processes becomes generalized character with involvement of cervical, submandibular, supraclavicular, axillary, inguinal lymph nodes. They fuse together with formation of conglomerates. Dyspnea and attacks of asphyxia are observed related lo the enlargement of mediaslinal lymph nodes and compression of trachea and bronchi. Diffuse swelling of the neck and face may occur with obstruction of the superior vena cava due to lymphous. Enlarged mesenterial lymph nodes cause compression of vena cava. Abdominal fullness, belching discomfort, abdominal pain may arise from intestinal obstruction by lymph nodes. Pronounced enlarged lymph nodes may obstruct the gallbladder, urinary tract, upper respiratory tract.

The progression of the disease is characterized by high temperature, intoxication, dispnoe, skin itching. In some patients may observe the appearance on skin the specific signs – lymphoma and non-specific signs such as herpetic lesions, weals. Widespread erythroderma occurs in some cases. Skin leukemic lymphoderma on the face made in like ”lion face”.

Affection of the gastro-intestinal tract by lymphoid infiltration: dyspepsia, diarrhea. The fiver and the spleen are enlarged and consolidated. Infraction of the spleen can occur; its palpation then becomes tender.

There may be an increased incidence of bacterial, viral or fungal infections due to a lack of functional white blood cells.

In thrombocytopenic patients appear bruising or purpura. Features of anemia are pallor skin and mucosa, tachycardia.

At terminal stages observe bleeding complications, intoxication, hyperthermia, heart and renal failure.

Additional methods of examination

Clinical blood analysis

- leucocytosis 3 x 10^{10}/l-3 x 10^{11}/l;
- red blood cell count decreased;
- platelet count decreased;
- between 70 and 90% of white cells on blood film appear as mature lymphocytes;
- the structure of their nuclea and cytoplasm is sometimes quite peculiar;
- the cells are very soft and arc easily destroyed, when preparing a smear;

- specific Botkin-Gymprecht shadows are formed.

Bone marrow: bone marrow aspiration shows lymphocyte replacement of normal marrow elements. Lymphocytes comprise 25 - 95% of all the cells in early stage; in terminal stage total lymphoid metaplasia.

Enlargement of mediastinal lymph nodes can be detected by standard X-ray examination or by tomography.

MAIN METHODS OF THE EXAMINATION OF THE ENDOCRINE SYSTEM. LABORATORY AND INSTRUMENTAL RESEARCH METHODS OF THE ENDOCRINE SYSTEM. BASIC SYNDROMES IN THE ENDOCRINOLOGY

Symptoms of endocrine disturbance are frequently varied and non-specific, and affect many body systems. Endocrine conditions may be picked up by chance: for example, hypothyroidism discovered on blood test screening, goitre found during routine medical examination or acromegaly recognized when the doctor meets a patient not seen for several years. Remember that, apart from diabetes mellitus, thyroid disease and some reproductive disorders, endocrine diseases are uncommon; most patients with tiredness or excessive sweating, for example, will not have an underlying endocrine cause.

While each endocrine disorder has its own set of symptoms, some of the most common symptoms found among many of them include:

- Mood swings
- Fatigue
- Weakness
- Unintended weight fluctuations
- Changes in blood glucose levels or cholesterol levels

Regardless of whether there is an obvious problem, treat each patient as an unknown in order to avoid missing an endocrine disorder. A patient with one endocrine disease (e.g., Hashimoto's thyroiditis) is at greater risk for the development of other endocrine disorders (e.g., adrenal, testicular, or ovarian failure). A patient may harbor more than one endocrinopathy, which could be overlooked if subtle historical and clinical clues are not heeded.

Always allow patients to express themselves. Ask patients how they feel and let them answer. Often, within the first few minutes of the history an endocrine cause becomes apparent. I find it most useful to review the patient's complaints literally from head to toe. The patient's vocal pitch may give a clue. A hypogonadal male has a high-pitched voice, while an androgenized female may have a deeper voice than expected. Body fat distribution gives important clues to the presence of adrenal steroid excess, while excessive wasting may imply adrenal steroid insufficiency or hyperthyroidism. A eunuchoid habitus suggests hypogonadism. Observation of skin

color, pattern of wrinkling, distribution of skin pigment, and body hair can yield useful historical clues.

Hair growth is an important piece of information. Ask the patient how often he shaves, and if the frequency has decreased. In the adult male the presence or absence of facial hair and the frequency of shaving give important information as to gonadal status; for example, hypogonadal males with primary (Klinefelter's or Kallman's syndrome) or secondary gonadal insufficiency (atrophic testicles following trauma, mumps, autoimmune diseases, etc.). Family history can be a clue because many families display sparse facial hair growth. Females may complain of excessive body hair, which should lead you to investigate causes of excessive androgens.

The pituitary gland should be investigated through history, physical, and radiographs. If you think of the hormones secreted by the pituitary, appropriate questions can be asked. Adrenocorticotrophic hormone (ACTH) controls glucocorticoid production. Excess ACTH produces the classic Cushing's appearance. Mental changes, fatigue, muscle weakness, easy bruising, infections, stretch marks, and acne are but a few of the findings related to steroid excess. Deficiency of these hormones can produce complaints ranging from fatigue and apathy to dizziness, shock, coma, unexplained fever, joint and abdominal complaints. These findings, coupled with hyperpigmentation, would lead one to suspect primary hypoadrenalism. The absence of hyperpigmentation would lead one to suspect a primary ACTH deficiency. Chapter 144 outlines the tests of endocrine function and demonstrates how one can relate the above findings to the laboratory.

Follicle stimulating hormone (FSH) and luteinizing hormone (LH) control testicular and ovarian steroid synthesis. In the female, the appropriate sequence of adenarche, thelarche, and menarche should be obtained. Amenorrhea is an important clue in a breakdown in the hypothalamic-pituitary–ovarian axis.

Male sexual development and function require a normal hypothalamic-testicular axis. The history helps assure adequacy of FSH, LH, and testosterone. Certainly a male with a full beard who has fathered children recently does not have a primary hypogonadal process. The presence of normal erections, adequate libido, and a full beard with a normal male body habitus helps exclude hypogonadism without the need for extensive testing.

Growth hormone plays little role in the adult when it is deficient. Growth hormone excess produces acromegaly. History often reveals enlargement of acral

parts, tightly fitting rings on the fingers, and an increase in shoe and hat size. Photographs will often demonstrate marked changes in appearance over the years.

Prolactin can produce galactorrhea in the female patient. Any woman who complains of breast secretions deserves an evaluation. The presence of menstrual periods with galactorrhea often implies a benign etiology, while amenorrhea—galactorrhea with elevated prolactin suggests a pituitary tumor.

Thyroid disease also displays protean presenting manifestations. Thyroid dysfunction can be so mild as to be unnoticed by the patient or examiner. Local effects of thyroid gland enlargement may produce only a goiter. Pain and compression of the surrounding structures can occur, however.

Hyperthyroidism in the elderly may cause few complaints other than lassitude, fatigue, weight loss, and constipation. Younger patients often complain of overactivity, nervousness, jitterness, tremulousness, intolerance to extremes in heat, difficulty concentrating, and insomnia. These symptoms may develop so insidiously that the patient does not recognize them until they are specifically quizzed.

Hypothyroidism may present as loss of interest, depression, fatigue, cool dry skin, constipation, mild degree of weight gain, or simply difficulty losing weight. The disorder can progress to the point of extreme and overwhelming hypothermia, coma, and death. The presence of an enlarged thyroid gland is useful in assessing both hyperthyroidism and hypothyroidism. Neck pain, tenderness, and trouble swallowing are important clues to the cause of an enlarged thyroid gland. Severe tenderness heralded by an antecedent viral illness should lead the clinician to think of thyroiditis.

Diabetes often presents insidiously with the gradual onset of excessive thirst, urination, nocturnal frequency, weight loss, and increased appetite. These manifestations occur frequently in type II, or non-insulin-requiring adult-onset, diabetes. The more acute development of these symptoms occurs in the type I, or insulin-requiring, diabetes. Blurring of vision, frequent infections, numb or painful extremities, and nonhealing extremity ulcers are important clues that should lead to a diabetic evaluation.

Extremely short stature with failure to undergo a pubertal growth spurt are clues of growth hormone deficiency. Hypothyroidism plus other hormone deficits often coexist. Individuals who are disproportionately tall in relation to their parents and siblings with complaints of sexual difficulties and gynecomastia may have Klinefelter's or another form of gonadal disturbance. A eunuchoid or female habitus helps in making this assessment.

The symptoms of diabetes mellitus may be those of a fulminant illness characterized by extreme thirst, blurring of vision, and nocturia. This presentation is more common for a type I, or insulin-requiring, diabetic as opposed to the insidious complaints of a type II diabetic. Less commonly, the patient may present with complaints of end organ damage. Swelling of the feet secondary to urinary protein loss or renal insufficiency, neuropathic complaints as numbness of the feet or hands, pain in an extremity or in a dermatomal distribution of the body may occur together or separately. A vascular event such as leg cramps on walking (claudication), ulcers of the extremities, or more dramatically stroke and coronary disease may be the initial finding.

Table 13

Common clinical features in endocrine disease

Symptom, sign or problem	**Differential diagnoses**
Weight gain	Hypothyroidism, polycystic ovary syndrome (PCOS), Cushing's syndrome
Weight loss	Hyperthyroidism, diabetes mellitus, adrenal insufficiency
Short stature	Constitutional, non-endocrine systemic disease, e.g. coeliac disease, growth hormone deficiency
Delayed puberty	Constitutional, non-endocrine systemic disease, hypothyroidism, hypopituitarism, primary gonadal failure
Menstrual disturbance	PCOS, hyperprolactinaemia, thyroid dysfunction
Diffuse neck swelling	Simple goitre, Graves ' disease, Hashimoto's thyroiditis
Excessive thirst	Diabetes mellitus or insipidus, hyperparathyroidism, Conn's syndrome
Hirsutism	Idiopathic, PCOS, Cushing's syndrome, congenital adrenal hyperplasia
"Funny turns"	Hypoglycaemia, phaeochromocytoma, neuroendocrine tumour
Sweating	Hyperthyroidism, hypogonadism, acromegaly, phaeochromocytoma
Flushing	Hypogonadism (especially menopause), carcinoid

	syndrome
Resistant hypertension	Conn’s syndrome, Cushing’s syndrome, phaeochromocytoma, acromegaly, renal artery stenosis
Erectile dysfunction	Primary or secondary hypogonadism, diabetes mellitus, non-endocrine systemic disease
Muscle weakness	Cushing’s syndrome, hyperthyroidism, hyperparathyroidism, osteomalacia
Bone fragility and fractures	Cushing’s syndrome, hypogonadism, hyperthyroidism
Altered facial appearance	Hypothyroidism, Cushing’s syndrome, acromegaly, PCOS

Physical examination

With the patient undressed, observe the body size and habitus. The distribution of body fat may reveal information as to nutrition, thyroid and adrenal status, important clues as to the presence of Cushing's disease. The combination of supraclavicular fullness, moon facies, violaceous striae, dorsal cervical fat pad, and a centripetal truncal obesity is often diagnostic. The penguinoid habitus of the Klinefelter's patient is often recognized at first glance.

Scalp and facial hair as well as the balding pattern are useful clues in assessing the patient's gonadal status. Decreased quantities of facial hair, perioral and periorbital wrinkling may be subtle signs of hypogonadism. In the female, excessive hair, acne, male-pattern balding, and central scalp hair loss are signs of androgen excess.

The presence of retinal changes characteristic of diabetes range from subtle vascular anomalies to microaneurysms, hemorrhages, exudates, retinal buckling or detachment, and proliferative changes. Optic atrophy manifested by disk pallor suggests a pituitary tumor and mandates careful visual field examination. Graves" disease displays classic eye findings. Hyperthyroid eyes may range from redness to protrusion with extraocular muscle and optic nerve dysfunction.

The thyroid gland is both visible and palpable. The skilled examiner can often visualize a thyroid nodule or outline a diffusely enlarged gland. The palpable characteristics of the gland may differentiate multinodular goiter, Hashimoto's thyroiditis, nontoxic goiter, and Graves" disease. The thyroid's morphology coupled

with the clinical finding of thyroid disease often suggests a diagnosis prior to the return of laboratory tests.

The presence of galactorrhea should lead one to assess for other pituitary disturbances. Gynecomastia in the male may have important clinical significance ranging from hypogonadism to malignancy.

In the male, the genital examination together with peripheral manifestations of gonadal disease may be of high diagnostic yield. One should carefully inspect for the presence of testicles within the scrotum and palpate for size and consistency. In both the male and female, pubic hair patterns are important. Examination of the perineum may yield important information as clitoromegaly or other labial or urogenital abnormalities are noted.

Careful inspection of the hands and feet, especially in diabetics, is important. Diabetic cheiropathy with classic periarticular tightening suggests the presence of vascular disease in other organs and portends a high risk for heart disease. Shiny thin skin with absence of hair on the lower extremities and absent pulses in the feet suggest the presence of macrovascular or microvascular disease of diabetes mellitus.

Examination of the neuromuscular system is of equal importance. The absence of ankle jerks, vibratory sensation, pinprick or light touch, abnormalities injoint position sense, and muscle atrophy in a diabetic indicates diabetic neuropathy.

Proximal muscle weakness is common to other endocrine disorders, such as hyperthyroidism and Cushing's disease.

The thyroid gland

- Inspect the neck from the front.
- Look for a swelling while the patient swallows a sip of water. The thyroid (or a thyroglossal cyst) moves upwards on swallowing since it is enveloped in the pre-tracheal fascia which is attached to the cricoid cartilage.
- Ask the patient to sit with the neck muscles relaxed and stand behind him.
- Place your hands gently on the front of the patient’s neck, with your index fi ngers just touching. Ask the patient to swallow a sip of water while you feel over the gland as it moves upwards. Some patients fi nd neck palpation uncomfortable, so be alert for any signs of distress.
- Note the size, shape and consistency of any goitre and feel for any thrill. Measure any discrete nodules with calipers. With large goitres, record the maximum neck circumference using a tape measure (an objective measurement for long-term follow-up).

- Listen with your stethoscope for a thyroid bruit.

Abnormal findings

Shape and surface

Simple goitres are relatively symmetrical in their earlier stages but often become nodular with time. In Graves ’ disease the surface of the thyroid gland is usually smooth and diffuse, whereas it is irregular in uninodular or multinodular goitre.

Mobility

Most goitres move upwards with swallowing. Very large goitres may be immobile, and invasive thyroid cancer may fi x the gland to surrounding structures.

Consistency

Nodules in the substance of the gland may be large or small, and single or multiple, and are usually benign. A very hard consistency suggests malignant change in the gland. Large, fi rm lymph nodes near a goitre suggest thyroid cancer.

Tenderness

Diffuse tenderness is typical of viral thyroiditis, whereas localized tenderness may follow bleeding into a thyroid cyst.

Thyroid bruit

This indicates abnormally high blood fl ow and can be associated with a palpable thrill. It occurs in hyperthyroidism. A thyroid bruit may be confused with other sounds. A bruit arising from the carotid artery or transmitted from the aorta will be louder along the line of the artery. Transient gentle pressure over the root of the neck will interrupt a venous hum from the internal jugular vein.

Table 14

Investigations in endocrine disease

Investigation	Indication/comment
Bedside	
Urinalysis	Glycosuria in diabetes mellitus Proteinuria in hypertensive renal damage
Capillary blood glucose	High in diabetes mellitus
Blood	
Calcium	High in hyperparathyroidism
Free thyroxine	High in hyperthyroidism Low in hypothyroidism
TSH	Undetectable in hyperthyroidism

	High in primary hypothyroidism
Serum cortisol	Low in hypoadrenalism, usually with reduced Synacthen response Loss of diurnal rhythm in Cushing's Reduced dexamethasone suppressibility in Cushing's
Gonadotrophins	High in primary hypogonadism in both sexes
Imaging	
Ultrasound	Thyroid, parathyroid, ovary, testis
MRI	Pituitary, pancreas
CT	Pancreas, adrenal
Radionuclide	Thyroid (^{123}I), parathyroid (^{99m}Tc-sesta-MIBI), adrenal (^{123}I-mIBG), neuroendocrine tumours (^{123}I-octreotide)
Positron emission tomography (PET) CT	Thyroid and neuroendocrine tumours
Invasive	
Fine needle aspiration cytology	Thyroid nodule
Inferior petrosal sinus sampling for	ACTH ACTH-dependent Cushing's

DIABETES MELLITUS

Diabetes mellitus is a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat, metabolism resulting from defects of insulin secretion, insulin action, or a combination of both. There are two types of diabetes mellitus: insulin dependent diabetes mellitus (IDDM) called type I diabetes and non-insulin dependent diabetes mellitus (INDDM) called type 2 diabetes.

Etiological classification of glycemia disorders

Type 1 (β-cell destruction, usually leading to absolute insulin deficiency)

• Autoimmune

• Idiopatic

Type 2 (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with or without insulin resistance)

Other specific type

- Genetic defects of β-cell function;

- Genetic defect in insulin action;

- Diseases of the exocrine pancreas: pancreatitis, trauma/pancreatectomy, neoplasia, cystic fibrosis.

Endocrinophaties: Cushing's syndrome, acromegaly, phaeochromocytoma, hyperthyroidism.

Drug or chemical-induced: cortisone, anti-depressant drugs, beta-blockers, thiazide, infections: cytomegalovirus.

Uncommon forms of immune-mediated diabetes.

Other genetic syndromes sometimes associated with diabetes: Down's syndrome, Friederich's ataxia, Klinefelter`s syndrome, Wolfram's syndrome.

Gestational diabetes.

Classification according to clinical feature

Severity of diabetes:

- mild (I degree),
- moderate (II degree),
- severe (III degree).

Compensation state:

- compensated,
- subcompensated,
- decompensated.

Complications:

- ketoacidotic coma, hyperosmolar coma, lactacidotic coma, hypoglycemic coma;
- microangiopathy - retinopary, nephropaty;
- macroangiopathy,
- neuropathy.

The type I diabetes, it is due to a lack of endogenous pancreatic insulin production, whereas in type 2 diabetes, the rising blood glucose results from a combination of genetic predisposition, unhealthy diet, physical inactivity, and increasing weight with a central distribution resulting in complex pathophysiological processes.

Clinical features

The symptoms and signs of diabetes may be divided into three group regards to main metabolic consequences of lack of insulin (hyperglycemia); specific long-term

complications of diabetes (microangiopathy); including retinopathy with potential blindness, nephropathy with a risk of progression to renal failure, nephropathy with a risk for foot ulcers, amputation, and Charcot joints and autonomic dysfunction such as sexual impairment; acceleration of comorbid pathology due to diabetes (atherosclerosis, infections). Thus DM is associated with development of specific long-term organ damage (diabetes complication).

Symptoms of hyperglycemia. When the concentration of glucose in the plasma exceeds the renal threshold glucosuria occurs. In case of consistent glucosuria (generally >180 mg/dl or 10,0 mM throughout the day and night) the classical symptoms of diabetes appear: polydipsia, polyuria and polyphagia which is related directly to the degree of glucosuria. Polydipsia is accompanied by thirst and dryness in the mouth. In the period decompensation patient can drink more than 5 liters of water in day, quite often he drink a lot of water at night.

Characteristic of diabetes is increased appetite (polyphagia). Nevertheless inspite the increased of food intake, such patients lose weight because of the loss of glucose in the urine. Weight loss is specific features for patients with IDDM and not expressed or absent at NIDDM which, as a rule, is accompanied by obesity. Polyphagia goes down sharply during severe decompensation, commonly at ketoacidosis. Frequent and abundant urination (polyuria and pollakiuria) both in the day and night time present at diabetic patients. Osmotic diuresis due to lack of insulin may contribute to pathophysiology of polydipsia and polyuria. Increased catabolism lead to augmentation of glycogenolysis, gluconeogenesis, lipolysis result in protein wasting and increased urinary nitrogen loss. These changes in protein and fat metabolism contribute to wasting, loss of weight, growth retardation in children. Protein wasting in patients with uncontrolled diabetes may be responsible for general and muscle weakness, poor wound healing. Sharp changes of glucose concentration and plasma osmolarity may cause visual blurring. Persistent glucosuria is frequently accompanied by skin itching, in women in region of genitals due to vulvovaginitis with odorous vaginal discharge.

The specific symptoms related 10 diabetic macroangiopathy correspond with affection of retina, kidneys, nervous system. The main complaints are partial an temporary impairment of vision and even blindness, appearance of edema due to the nephritic syndrome as evidence of diabetic nephrophaty, change of diuresis at initial stage in a form of polyuria, later oliguria. In stage of renal failure - appear anuria. Involvement of the nervous system in diabetes gives such clinical manifestations:

numbness, tingling, parcsthesias, burning and sharp pain in the distal portions of the lower extremities, less frequently of the upper extremities. Abnormalities of the autonomic nervous system occur in patients with long-standing diabetes with involvement cardiovascular, gastrointestinal, urogenital systems. The patients complain on palpitation escape beat, nausea, vomiting, dysphagia, diarrhea, urinary incontinence, failure to empty the urinary bladder fully. Impotence presents in 40 % of diabetic patients.

At early stage of diabetes are there metabolic abnormalities which serve as pathophysiological basis for increased predisposition to atherosclerosis of different vessels: coronary, peripheral. Coronary artery disease occurs more frequently in diabetic patients compared with general population. Clinical manifestation of comorbid pathology is chest pain different duration and intensity, arrhythmia. Atherosclerotic affection of peripheral vessels commonly low extremities is characterized by intermitted claudication and in more severe vessel occlusion, pain at rest.

Objective examination

The patient condition depends on stage of disease and evidence of complications. In early stage of disease the patient' condition is satisfactory. As a result of diabetic nephropathy, renal failure, visual impairment, clinical signs of neuropathy, cardiovascular disorders the condition becomes grave and even extremely grave in case of diabetic ketoacidosis, which characterized by passive position and unconsciousness. There are some features of diabetic dermopathy as a direct result of metabolic abnormalities: dryness of skin, decreased turgor and elasticity, shiny spots, scaly patches, diabetic bullae which located in the pretibial area. In diabetic patients with marked hypertryglyceridemia may observe eruptive xanthomas, which located in the elbow, shin; knees, buttocks and posterior thigh areas. In area of eyelids quite often it is possible to

find xantelasm yellow spots with content of lipid. Red-brown papulae are observed on the skin of shins, later transformed in pigmental atrophy spots. In case of dilation of skin capillaries the hyperemia of skin in area of cheek and neck are appeared so called diabetic blush. Infectious complications of skin lead to furuncules which in diabetic patients progress to disseminated process with formation carbuncules. Some factors ischemia, peripheral polyneuropathy and infections cause fool under, cellulitis and gangrene. Neuropathic ulcers may appear in the areas of callus formation. Changes of joints related lo neuropathic arthrophaty occur at the ankle or in the foot

at the tarsometatarsal or metatarsophalangeal joints. So called Charcot`s joints are characterized by unilateral painless swelling, erythema in association with joint instability.

Affection of the respiratory system in diabetes may assume progressive and threatening forms due to the infections. Patients with diabetes are predisposed to tuberculosis which progresses very rapidly. Prognosis for diabetic patients is worse than for nondiabetic person in case of tuberculosis. Infections of various types lead to complications such as nasal sinusitis with purulent process and gangrene of the nasal mucous membrane, bronchitis, pneumonia.

Affection of the cardiovascular system may take the form of diabetic cardio-myopathy and coronary heart disease due to the acceleration of atherosclerotic process. Clinically diabetic cardiomyopathy may manifests as chest pain and features of congestive heart failure: dyspnea, cough, and edema. Decreased ventricular ejection fraction is revealed by echocardiography and radionuclide ventriculography.

Arterial hypertension as a rule has secondary origin as a sign of diabetic nephropathy, chronic pyelonephritis, atherosclerosis of kidney arteries, cerebral atherosclerosis. Patients with diabetes are at a particularly high risk for cardiovascular, cerebrovascular and peripheral artery disease relevant to atherosclerosis. The risk of myocardial infarction and sudden death are higher twofold in diabetic patients as compare with nondiabetic population. Myocardial infarction occurs at young age, has severe course and poor outcomes, complicated by cardiogenic shock, thromboembolism of pulmonary artery, aneurism of left ventricle. Period of rehabilitation lasts longer and myocardial remodeling more frequent results in development of heart failure. A greater prevalence of “silent” myocardial infarction among diabetic patients have been revealed. Death rate relevant to myocardial infarction account on the average 38-50 % at patients with diabetes.

The factors responsible for the accelerated atherosclerosis in the diabetic population are hypercholesterolemia, hypertriglyceridemia, increased concentration of low density lipoproteins, reduced concentration of high density lipoproteins, increased adhesiveness and sensitivity to aggregating agents. Cluster of impaired glucose homeostasis, abdominal obesity, hyperlipidemia and hypertension have been described as metabolic syndrome with specific entity "dead quartet". This term considered the meaning of metabolic abnormalities as crucial factors for atherosclerosis and vascular complication more commonly in NIDDM. It seems likely that insulin resistance being the primary defect of metabolic syndrome.

Signs of peripheral atherosclerosis may include diminished or impalpable pulses in the feel, bruits over the carotid or femoral arteries. According to the atherosclerotic occlusion of tibiae and popliteal arteries occurs vascular impairment in the leg and/or foot with development of ulcer and gangrene. Infected necrotic lesions, complicated by cellulites, osteomylitis and generalized septicemia required surgical amputation.

Gastrointestinal disorders at diabetes are explained by decreased motility with distension of stomach and gallbladder which clinically are manifested by poor esophageal contraction, diarrhea, "blind loop" syndrome, malabsorption. Hepatomegaly due to marked fatty infiltration of the liver is observed in patients with decompensated diabetes.

The most dangerous complication of both IDDM and NIDDM is diabetic nephropathy, which responsible for development or renal failure and is a major cause of morbidity and mortality in the diabetic population. The earliest clinical manifestation is microalbuminuria which is defined as an increase in urinary albumin measurable by radioimmune assay. Further progression from early stage to overt diabetic nephropathy is manifested by gross proteinuria in excess of 500 mg/24 h. The proteinuria may reach massive proportions, resulting in the nephritic syndrome with hypoalbuminemia and edema. The course of diabetic nephropathy is complicated by the presence of symptomatic hypertension. The outcomes of nephropathy are renal failure.

Urogenital dysfunction results from incompetence of internal vesicle sphincter, dilation of urine bladder, accompanied by chronic recurrent urinary tract infections: pyelonephritis, cystitis. In women the vulvovaginitis is detected. The women in fertile age are predisposed to reproductive dysfunction and have an increased incidence of stillborn, abnormally large and heavy babies and babies with congenital defects. Involvement of the nervous system in diabetes has been described as clinical specific syndrome of diabetic neuropathy. Another reason of nervous dysfunction is a consequence of accelerated atherosclerosis leading to infarction of a spinal or cerebral artery. The various forms of diabetic neuropathy may be divided into three major clinical groups: symmetric peripheral polyneuropathy, mononeuropathy and autonomic neuropathy. The main signs of diabetic neuropathy are loss of vibratory sensation dislally in the legs, depression or loss of the tendon reflexes at the ankles. Deep and penetrating neuropathic ulcers at the feet may develop. In case of mononeurupathy muscle atrophy may arise.

One of the serious complications of diabetes is retinopathy as the leading cause of blindness. Diabetic patients are prediposided to the development of glaucoma. Metabolic cataract is most commonly observed in patients with uncontrolled diabetes with high hyperglycemia.

The classical clinical features of the two main types of diabetes as regard to family history, peculiarities of symptoms, age at onset of disease are differ.

Table 15

Comparative clinical features of IDDM and NIDDM

Clinical features	**IDDM**	**NIDDM**
Age of onset	<40 years	>50 years
Genetic prediposition	Moderate, requires environmental	Strong -80-100%
Family history	-	+
Duration of	Weeks	Months - years
Precipitating factors	Viral, other trigger	Obesity, age
Autoantibodies	+	-
Insulin resistance	-	+
Ketonuria Response to stress withdrawal of	+, Ketoacidosis	-, Hyperglycemia without ketoacidosis
Treatment	Diet, insulin	Diet, oral antidiabetic
Rapid death drugs without treatment with insulin	+	-

HYPOGLYCEMIA

Causes:

• Imbalance between injected insulin and patients normal diet, activity and basal insulin requirement.

• Irregular eating habits, unusual exertion and alcohol excess may precipitate episodes.

• Impaired ability to counter - regulate glucose levels after hypoglycemia in diabetic patient is also responsible for episode. Glucagon response is lost. Adrenaline response may also fail in patients with a long duration of diabetes.

Clinical features

Symptoms of hypoglycemia begin at plasma glucose 60mg/dl; brain impairment develops at approximately 50mg/dl. Brain damage after prolonged severe hypoglycemia is not reversible.

Features of hypoglycemia are:

• Pallor, tachycardia, palpitation, sweating, nausea and tumor (due to stimulation of sympathetic system as a counter regulatory mechanism which increases blood glucose by increasing glycogenolysis);

• Hunger due to parasympathetic stimulation;

• Mental confusion, aggression or convulsion;

• Some patients with long duration of diabetes have not such symptoms and go into severe hypoglycemia. Patients become pale, drowsy. Mental confusion or convulation rapidly occurring hypoglycemic coma (due to decreased supply of glucose to the brain).

DIABETIC KETOACIDOSIS

Diabetic ketoacidosis is a medical emergency with mortality rate about 5%. It may be the initial manifestation of type I diabetes or may result from increased insulin requirement in type I diabetes patients during the course of stress such as infection, trauma, surgery or myocardial infarction. Type II diabetics may develop ketoacidosis under severe stress such as infection or trauma.

Precipitation factors:

- Acute infection: bacterial or viral;
- Omission or drastically reduction the dose of insulin;
- New onset type I diabetes (about 25% patients of type I are first time diagnosed when they present with ketoacidosis).

Clinical feature

Features of dehydration and acidosis: intense thirst, polyuria, nausea, vomiting, abdominal pain.

Objective examination

1. Level of consciousness is variable, patient with severe ketoacidosis may be conscious and alert, drowsiness is usual but coma is uncommon. Level of consciousness depends on serum osmolality, not on level of acidosis. When serum osmolality exceeds 320-330 mosm/L, CNS depression or coma develops (normal value is 280-300 mosm/L).

2. Dry tongue, inelastic skin, sunken eyes

3. Hypothermia
4. Kussmaul's respiration (rapid and deep breathing)
5. Hypotension
6. Rapid weak pulse
7. Fruity breath odor of acetone
8. Abdominal tenderness

Additional methods of examination

Determination of glucose: hyperglycemia (usually > 250mg/dl). The magnitude of hyperglycemia does not correlate with the severity of metabolic acidosis: moderate elevation of blood glucose may be associated with life-threatening ketoacidosis. In some cases hyperglycemia predominates with minimal acidosis.

Biochemical blood analysis. Metabolic acidosis (blood pH < 7.3, serum bicarbonate < 15 mEq/L). Hyperketonemia.

Clinical urine analysis: ketonuria (urinary ketones strongly positive ++++). There is ++++ glycosuria.

HYPEROSMOLAR NON-KETOTIC COMA

This condition, in which severe hyperglycemia develops without significant ketosis, is the metabolic emergency characteristic of uncontrolled type II diabetes. Patients present in middle or later life, often with mild or previously undiagnosed diabetes. Infection, myocardial infarction, stroke, or recent surgery is the precipitating factors.

Clinical features

Clinical features are dehydration and stupor or coma due to hyperosmolality. Nausea, vomiting and abdominal pain are much less common because there is no acidosis.

Additional methods of examination

• Severe hyperglycemia, blood sugar 600-2400mg/dl.
• Serum osmolality 330-340 mosm/L.
• Pre-renal azotemia with raised urea.
• ABGs show normal pH.

Additional methods of examination DM

Clinical blood analysis reveals inflammatory changes (leukocytosis, neutrophilia in case of infections complication). Anemia may be detected in patients with renal failure.

Clinical urine analysis may identify the kidney function during examination of physical properties of the urine. Poiyuria or oligyria, low specific urine gravity indicate to appearance of renal failure.

Chemical study of urine includes assessment of glucose, ketone bodies and protein. Glucosuria is a specific sign of diabetes. Ketone bodies are determined in patients with decompensation and presence of ketoacidosis. Microalbuminuria and proteinuria indicate to development of diabetic nephropathy. Patients with diabetes should be screened for albuminuria. Given the insidious onset. INDDM patients should be screened for albuminuria at the time of the initial diagnosis. Patients with IDDM should be screened within 5 years of diagnosis.

Microalbuminuria is defined as a urinary albumin excretion (UAE) of 30-300 mg in a 24-hour collection period; albuminuria is defined as a UAE >300 mg/24 hours. Albuminuria is the clinical hallmark of the development of nephropathy.

Biochemical blood analysis. According to modern determination of glucose should be performed in venous plasma for diagnostics of diabetes.

Criteria of diabetes: fasting plasma glucose ≥7,0 mmol/L. A standardized oral glucose tolerance test (OGTT) performed in the morning, after an overnight fast (8-14 h); one blood sample should be taken before and one 120 min after intake of 75 g glucose dissolved in 250-300 mL water in a course of 5 min (note: timing of the test is from the beginning of the drink). Impaired glucose tolerance (IGT) can be recognized by the result of OGTT only: 2-h post-load plasma glucose (2hPG) ≥7,8 and < 11,1 mmol/L (≥ 140 and <200 mg/dL).

Special test for diagnostic of diabetes is glycated hemoglobin. Glycated hemoglobin (HbAlc), a useful measure of metabolic control and the efficacy of glucose-lowering treatment, is an integrated summary of circadian blood glucose during the preceding 6-8 weeks, equivalent to the lifespan of erythrocytes. It provides a mean value but does not reveal any information on the extent and frequency of blood glucose excursions. HbA1c has never been recommended as a diagnostic test for diabetes. A primary reason is the lack of a standardized analytical method and therefore lack of a uniform, non-diabetic reference level between various laboratories. A high HbA1c may only identify a fraction of asymptomatic people with diabetes. HbA1c is insensitive in the low range and a normal HbA1C cannot exclude the presence of diabetes or IGT.

Serum creatinin concentration increased in patients with diabetic nephropathy.

ECG is revealed the signs of ischemia (inverted T), arrhythmia (extrasystole).

Echo-CG- sign of left ventricular hypertrophy, decreased ejection fraction.

Renal biopsy in patient with end-stage renal disease should be directed at the detection of primary kidney disease or renal complication of diabetes.

Ophtalmoscopic examination of the fundus is required for evaluation of diabetic retinopathy.

Instrumental invasive examination of the coronary, kidney, peripheral arteries is required for detecting the macroangiopathy.

HYPERTHYRIDISM

Hyperthyroidism (hyperthyroid syndrome) - complex of symptoms, which results from hyperfunction of thyroid gland with increased secretion of thyroid hormones and expose them on the body tissues.

Etiology

In over 90% of patients with hyperthyroidism is due to Graves' disease. Other causes of excess production thyroid hormones are thyroiditis, multinodular goiter, iodide-induced after lingering taking some drugs (e.g. amiodarone). Extra thyroidal source of thyroid hormone excess is due struma ovary or excess secretion of TSH which may originate from pituitary in case of tumor - choriocarcinoma or hydatidiform mole.

The factors which provoke the development hyperthyroidism include:

- inherited predisposition;
- acute and chronic psychical traumas;
- acute and chronic infections (flu, quinsy, measles, whooping-cough, tuberculosis, chronic tonsillitis, encephalitis, rheumatism);
- immunological disturbances;
- neuro-endocrine alteration in woman (pubertal period, pregnancy, lactation, climax);
- chronic disease of liver and kidneys, attended with disorders of metabolism of thyroid hormones.

Clinical feature

The main symptoms of the hyperthyroidism: excitability, anxiety, nervousness, inability; increased sweating, heat intolerancy; fatigue, muscular weakness; despite normal or increased appetite loss of weight; dyspnea on exertion; exacerbation of asthma; palpitation, pains in heart region; escaped beat; thirst, anorexia, vomiting, diarrhea; loss of libido, impotence.

Objective examination

The condition of patient is satisfactory. In case of hyperthyroid crises may be life-threatening condition. The consciousness is clear, posture is active. The patient is characterized by fast changing of mood, impossibility to be concentrated, motor, emotional and vocal lability. Patient looks younger his age.

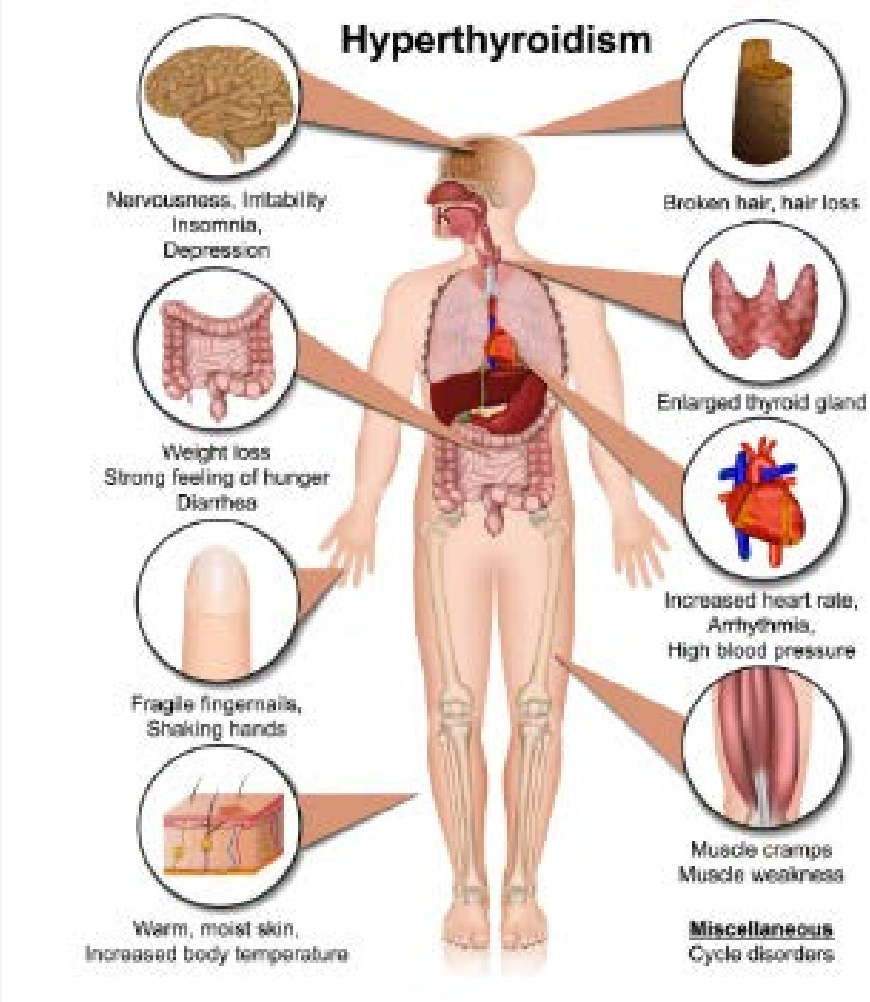

Image 26. Symptoms of hyperthyroidism

The image was downloaded from website https://medicdrive.org/thyroid-disease/hyperthyroidism

The face has specific signs: lively with widened eye slits, exophtalmos, excessive lacrimation, corneal ulceration, hyperemia of conjunctiva.

There are specific eye signs in patients with hyperthyroidism:

- upper lids are symmetrically retracted so that some sclera is visible;
- Kraus' sign (abnormally sparkling eyes);
- Ellinec' sign (pigmentation of eyelids related to adrenal insufficiency);
- Rosenbach` sign (shallow tremor of the closed eyelids);

- Greffe' sign (lid lag during fixing of slowly downward moving object);

- Mebius' sign (weakness of convergence or loss of ability to fix a object at short distance);

- Stelvag` sign (rare blinking, less than 6-8 times in a minute).

Dermopathy is characterized by moist, hyperemic skin with palmar erythema, spider naive, sometimes appearance pigmentation, vitiligo and giblet clubbing. The hair may become thin and fine in texture and alopecia can occur. The nail is soft and separated from the nail bed - onchyolysis. Perspiration is increased. In patient may be pretibial myxoedema in the form of pink coloured or purplish plagues on the anterior part of the leg, accompanied with itching. The muscles are atrophic, their force and tone are reduced.

Thyroid enlargement of some type is a common sign.

Classification of diffuse toxic goitre according to degree of enlargement of thyroid gland:

0 - there are no thyroid gland at palpation;

1 - at palpation enlarged isthmus of gland and slightly lateral lobes;

2 - thyroid gland is noticeable at swallowing, at palpation determined well;

3 – “thin neck” (enlarged thyroid gland is well noticeable at examination);

4 - the expressed goitre, sharply changing configuration of neck;

5 - degree is goitre of largeness.

The size and consistency varies according to the pathology caused hyperthyroidism. In Graves' disease the thyroid is twofold to fourfold enlarged slightly tender and the surface is usually smooth. The thyroid bruit or thrill related to increased thyroid blood flow are heard. Thyroiditis usually characterized by slight diffuse thyroid enlargement. The affection of respiratory system in patient is uncommon. In severe hyperthyroidism may be pneumonia and abnormalities in respiratory function. Decreased vital capacity decreased pulmonary compliance, respiratory muscle weakness cause dyspnea, aggravation of bronchial asthma.

The Jeading signs of affection of cardiovascular system, which accompanied the hyperthyroidism at every stage are defined as thyroidtoxic heart. The apex beat displaced to the left, diffuse, high and strong. The main sign of hyperthyroidism is stable arrhythmic tachycardia more than 90 beats per minute. The heart sounds are loud. Functional systolic murmur can appear over all auscultative points. Pulse is high and fast (altus et celer). Functional murmur can be heard over a. carotis and v. jugularis. Systolic blood pressure is increased, diastolic blood pressure is decreased,

pulse pressure is elevated. In case of constant longstanding atrial fibrillation in patients with hyperthyroidism may be complication in the form of heart failure with congestion in lesser and grater circulation.

Due to the increased motility of stomach and intestine appear the pain and hyperdefecation. Intestinal hypermotility lead to more rapid small and large intestinal transport, resulting in steatorrhea. Inactivation of thyroid hormones takes place in liver hence in condition of their excess circulation develop hepatic dysfunction with raised concentrations of enzymes. In severe course of disease the enlarged liver and jaundice are observed. Renal blood flow, glomerular filtration rate and secretory capacities are increased. The common sign are polydipsia and polyuria. Urine concentrating ability may be impaired due to the dehydratation. Neuromuscular signs of the hyperthyroidism: shallow symmetrical tremor of fingers when the hands are extended, but it may involve the arms, legs, tongue and head. The movements are rapid and low amplitude. Instability in the Romberg' posture, hyperreflexia, muscle weakness, proximal myophaty, increased reflexes of tendons are observed. Myopathy can also involve the respiratory and oropharyngeal musculature, causing difficulties in swallowing or hoarseness. After exercise may be the attacks of periodic paralysis. The signs of central nervous system dysfunction are anxiety, irritability, episodes of paranoia, impairment of cognitive function.

Disorders of endocrine system include gonadal dysfunction. In women menstrual cycles are normal, although some of them have oligomenorrhea or amenorrhea accompanied with infertility.

In men hyperthyroidism results in decreased potency and loss of libido. Gynecomastia may be observed.

Additional methods of examination

Clinical blood analysis: normochromic anemia, reduction of hemoglobin values, leucopenia, relative lymphocytosis, granulocytopenia, easy thrombocytopenia.

Biochemical blood analysis: oral glucose tolerance is impaired, modest reduction in serum total and LDL cholesterol concentrations, serum triglyceride concentration is normal, hepatic lipase activity and plasma free fatty acid concentration are increased. Serum alanine and aspartate aminotransferase, bilirubin concentrations are increased.

Immunological examination: decreased of T-lymphocytes and T-lymphocytes-supressors, increased of level of immunoglobulins, antibodies to thyroglobulin; appearance of thyrostimulating immunoglobulins.

Radioimmunological examination: increased serum total and free T4 and T3 concentrations and decreased TSH concentration. Thyroid radioiodine uptake is increased in most patients. ECG: atrial fibrillation, depresses ST-segment and inverted T-wave.

HYPOTHYROIDISM

Hypothyroidism (hypothyroid syndrome) is pathological condition which resulted from insufficient secretion the thyroid hormones by thyroid gland.

Etiology

- inherited disorder of thyroid hormones biosynthesis;
- defects of embryonic development, resulting to hypo- or aplasia of thyroid gland;
- infectious-inflammatory processes, including chronic infections (tuberculosis, syphilis), attended with the degenerative changes of gland parenchyma;
- residence in endemic region with the deficit of iodine in environment;
- Hashimoto's thyroiditis;
- jatrogenic hypothyroidism due to thyroidectomy or radioactive iodine therapy;
- outcomes of treatment the diffuse toxic goiter with antithyroide drugs; pathology of the hypotaiamo-hypophysal system, relevant with decreasing of thyrotrophin-releasing hormone.

Clinical features

The complaints are general weakness, tiredness, somnolence, cold intolerance, poor hearing, disorders of mental abilities, dyspnea, constipation, weight gain, impairment of sexual function, headache and dizziness. Subjective muscle dysfunction is the myalgia, muscle cramps and stiffness. The complaints of muscle weakness and fatigability are common. Hypothyroid patients may complain of arthralgia and joint stiffness.

Objective examination

the condition of the patient is satisfactory. In case of prolonged hypothyroidism and accompanying changes of organs the conditions becomes grave and even extremely grave if the coma occurs. The patient with hypothyroidism as a rule is adynamic. Patient has specific features of face, so called myxoedematous face (facies myxoedemica): periorbital pufliness narrowing of the eye slit, poor mimic, purplish lips, the hair is thinned or absent on the outward portions of the eyebrows. The patient looks older his real age.

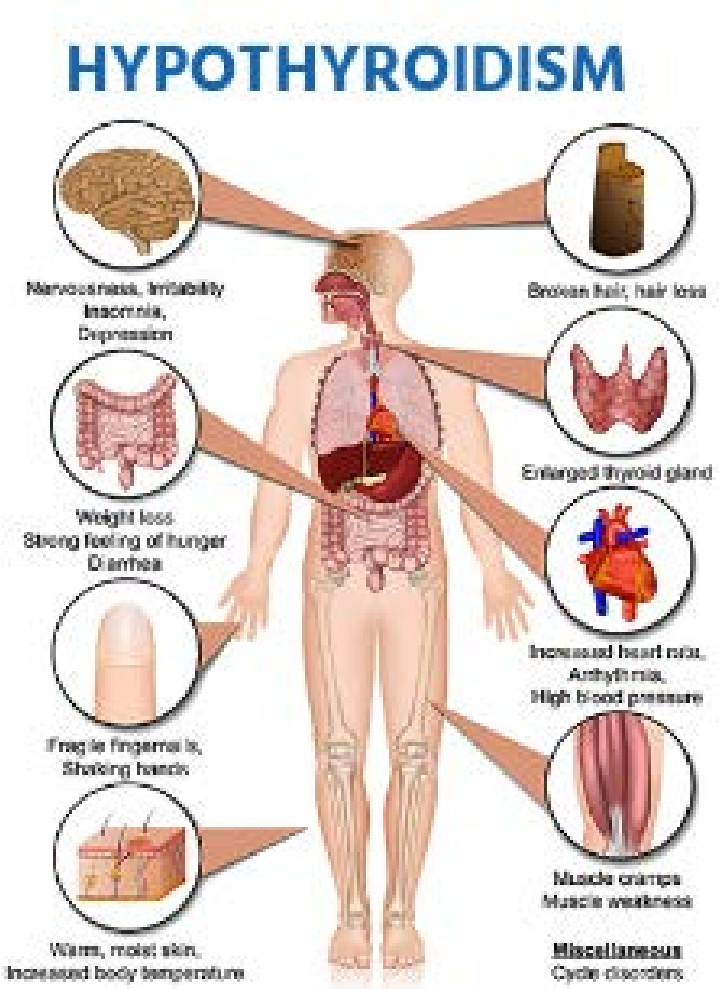

Image 27. Symptoms of Hypothyroidism

The image was downloaded from website

https://www.medicoverhospitals.in/diseases/hypothyroidism

The skin of patient is pale with icterus tint. Pallor develops due to vasoconstriclion and anemia. Yellow color is explained by carotinemia resulted from delayed turnover of carotin to vitamin A. The skin becomes rough, scaly and thickened. Trophic disorders of the skin and its derivates are characterized by such signs: dryness. Fragility and loss of hairs, nails are thin, brittle with transvered lines, grow slowly, infiltration of the skin with specific substances which content mucopolysaccharides leads to edema which does not pit with pressure. The edema is most marked in the skin of the hands, feet. The periorbital edema is observed. As a rule edema is nonpitting. If the edema is pitting, especially in the legs, should suspect the presence of complication as heart failure as a result of myxoedematous heart.

The skin is cold due to the both thickening and decreased blood flow, poor peripheral circulations. The patients are usually overweight.

Signs of muscular affection are dystrophy, muscle stiffness, mainly at the proximal part of extremities, muscular weakness and painful spasms, myotonia. Chronic hypothyroid myopathy occurs due to increased muscle mass (pseudohyperthrophy). Movements may be slow and clumsy. Some patients have synovial thickening and synovial effusions, usually of the knees.

Respiratory system. The signs related to the upper airways and respiratory system include chronic nasal congection, shortness of breath and sleep apnea. Complaints referable to the airways are explained by mutinous edema of the nasal mucosa and larynx. Shortness of breath may inducate on the presence of pleural effusion. The patient has low-pitched hoarse voice due to the edema of vocal cords. Simultaneously with enlarged tongue and lips therefore speech become very slowly with lingering intervals. The course of hypothyroidism is characterized by frequent attacks vasomotor rhinitis, pneumonia.

Disorders of *the cardiovascular system* are characterized so-called, myxoedematous heart due to the interstitial myocardial edema, dystrophy of its fibers. The apex beat is displaced to the left, diffuse and weak. In percussion the borders of relative cardiac dullness are displaced outside. In auscultation decreased loudness of both sounds over in all listening points are revealed. In case of pericardial effusion the loudness of cardiac sounds extremely decreased or even disappears. Constant and stable bradycardia less than 60 beats per minute is typical sign of hypothyroidism. Appearance of premature beat is possible. Blood pressure mainly systolic is decreased, pulse pressure diminished. Hypothyroidism promotes and accelerates the development of atherosclerosis with affection different vessels. These patients as usually have clinical features of ischemic heart disease.

Changes from the *digestive system* occur due lo the edema of gastrointestinal tract, which associated with motor and secretory dysfunction. These alterations appear as persistent constipation, flatulence, paresis of intestine. Decreased intestinal motility may cause abdominal distension and constipation, produce paralytic ileus or megacolon with the clinical feature of intestinal obstruction. Sometimes is observed the propensity to parodontosis. The liver usually is unaffected. Ascitis is uncommon sign of hypothyroidism.

Renal blood flow is reduced according to the decrease in cardiac output. The glomerular filtration rate is usually reduced and mild proteinuria is revealed. Due to the hypotension develops oliguria till anuria.

Neurological dysfunction manifested by carpal tunnel syndrome due to the edema of the flexor of the wrist. Patient has slow deep tendon reflexes with prolonged contraction and relaxation phases. Cerebellar dysfunction includes such

signs as ataxia, intention tremor and nystagmus. Disorders thermoregulation may present in a form of cold intolerance.

Hypothyroid patients have the signs of mental dysfunction due to chronic insufficiency of cerebral circulation, hypoxia and brain edema. The main features are somnolence, and even lethargy. The patient may sleep longer at night or may go to asleep frequently during the day.

The patient becomes physically and mentally slow: the speech is slow, memory loss, significant limitation of activity, adynamia, and apathy. In some patients may observe depression, indifference to surrounding or severe anxiety and agitation, maniac state. Lingering hypothyroidism leads to cognitive impairment and overt dementia. Outcomes of hypothyroidism may be disorders of pituitary gland. In men observe decreased sexual potential till impotence, deranged spermatogenesis. In women appears amenorrhea or menorrhagia, infertility. In patients of both gender groups occur diminished libido, no pubic and armpit hair. One of the dangerous complications of disease may be hypothyroid coma. The patient's condition is grave, unconsciousness, passive posture, declining body temperature till 23°C, deep and slow breating sinus bradycardia till 30 beats per minute, hypotension. Accumulation of fluid in pericardial cavity may cause the compression of the heart with acute heart failure. Constant and severe constipation resemble ileus.

Additional methods of examination

Clinical blood analysis: normocytic, microcytic or macrocytic anemia (pernicious-like). Macrocytic anemia is associated with vitamin B12 malabsorption. Leukocyte, lymphocyte and platelet count are normal, accelerated ESR.

Biochemical blood analysis: elevated serum creatine kinase (MM fraction) concentration due to the release from skeletal muscle as a result of increased sarcolemmal permeability.

The serum concentration of total and low density lipoprotein cholesterol and sometimes triglycerides are elevated; hypoalbuinmemia with hyperglobulinemia.

Elevated serum lactate dehydrogenase, aminotransferase concentrations iron deficiency in premenopausal women.

Radioimmunologocal method: diminishing of thyroxin level (T4) and triiodothyronin (T3). Thyroidal radioiodine uptake is reduced in most patients with hypothyroidism.

ECG: bradycardia, low amplitude P wave and QRS complex, conduction disturbances, depressed ST-segment and inverted T-wave. Echo-CG: septal and wall thickening, decreased myocardial contractility and relaxation, pericardial effusion.

Ultrasound examination of thyroid gland allows reveal the changes at echogenic density.

Radioisotope scanning by thechnetium-99 gives the information about functional activity of gland, size, form, presence of "cold" and "hot" zones.

HYPOPITUITARISM

Anterior hypopituitarism may be due to compression of the pituitary by a macroadenoma, infarction after childbirth (Sheehan's syndrome), severe head trauma or cranial radiotherapy. Extreme skin pallor (a combination of mild anaemia and melanocytestimulating hormone defi ciency), reduced/absent secondary sexual hair and testicular atrophy. Absence of axillary hair is abnormal after puberty.

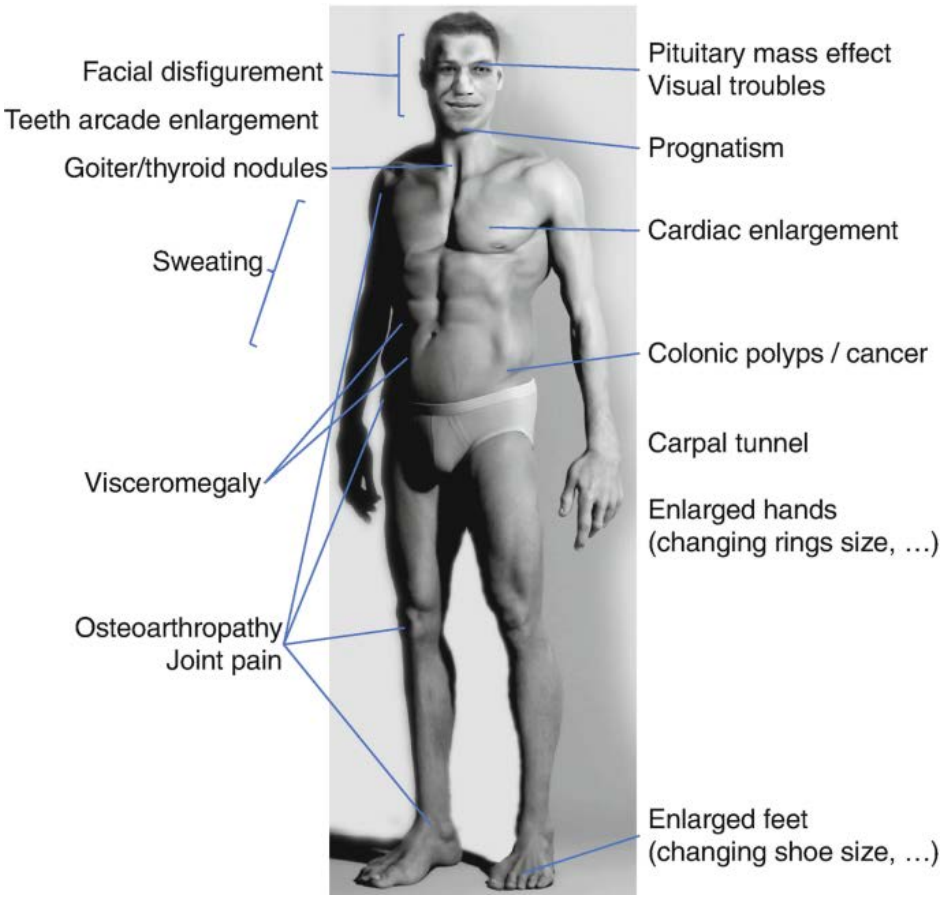

Image 28. Symptoms of Acromegaly
The image was downloaded from website https://link.springer.com

ACROMEGALY

Acromegaly is caused by a GH-secreting pituitary tumour. GH stimulates excessive insulin-like growth factor-1 production by the liver, and this hormone is responsible for most of the clinical manifestations. The characteristic facial changes,

including coarsening of features, thick greasy skin, enlargement of the nose, prognathism (protrusion of the mandible) and separation of the lower teeth. Expansion of the soft tissues of the hands and feet causes tight fi tting of rings, gloves and footwear. Expansion of the tumour can cause pressure on the optic chiasm, resulting in visual fi eld defects, especially bitemporal hemianopia.

CUSHING'S SYNDROME

Cushing's syndrome is caused by excess exogenous or endogenous corticosteroid exposure. Most cases of Cushing's are iatrogenic, due to side-effects of corticosteroid therapy. 'Endogenous' Cushing's usually results from an ACTH-secreting pituitary microadenoma. Other causes include a primary adrenal tumour or 'ectopic' ACTH secretion. The catabolic effects of steroids cause widespread tissue breakdown (particularly in skin, muscle and bone) with central accumulation of body fat. Proximal myopathy, fragility fractures, spontaneous purpura, skin thinning and susceptibility to infection are common.

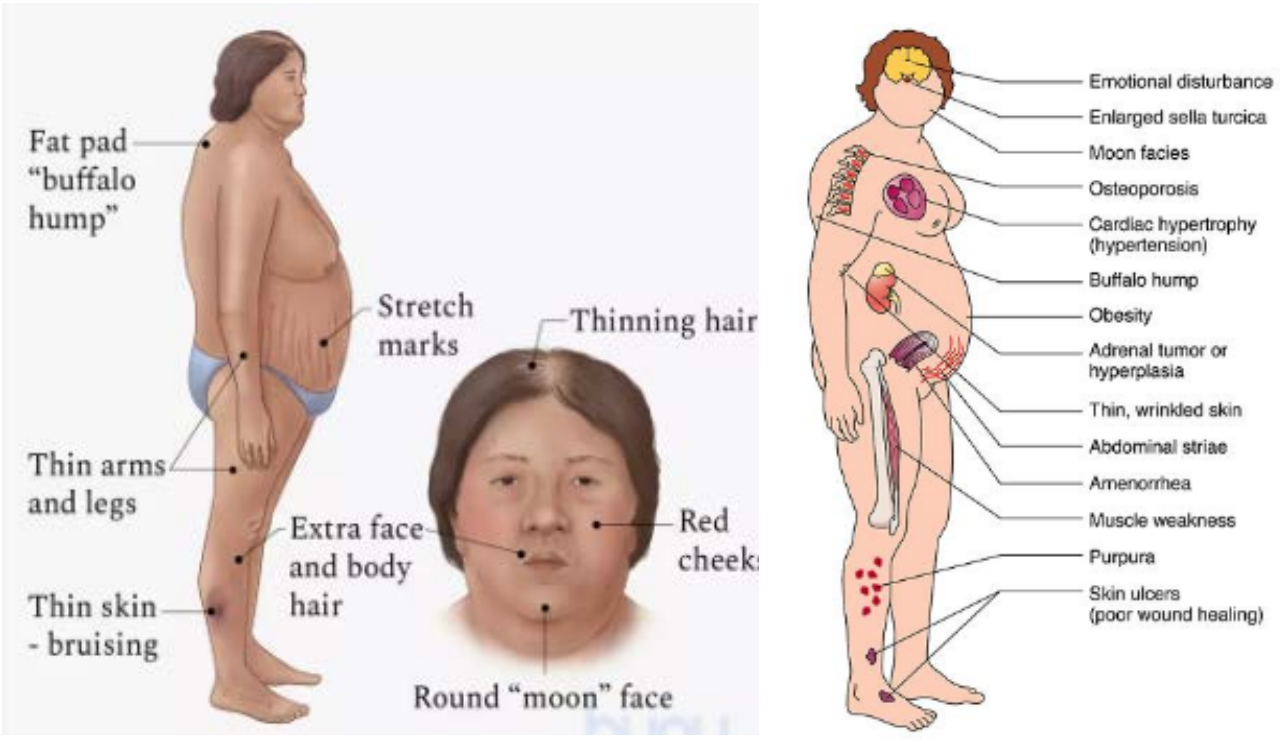

Image 29. Symptoms of Cushing's syndrome

The image was downloaded from website https://www.buoyhealth.com

ADDISON'S DISEASE

Addison's disease is due to inadequate secretion of cortisol, usually secondary to autoimmune destruction of the adrenal cortex. The melanocyte-stimulating hormone-dependent brown pigmentation of Addison's disease (primary adrenal insuffi ciency) is most striking in white Caucasians.

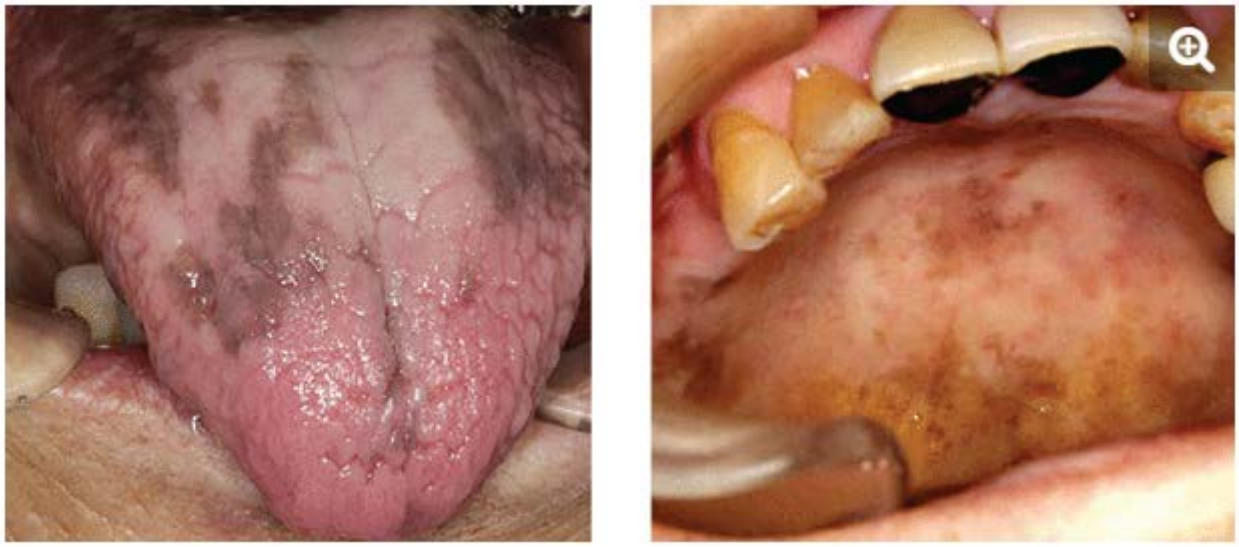

Image 30. Addison's disease: Skin pigmentation in the patient's tongue (left) and on the soft palate (right).
The image was downloaded from website
https://www.ccjm.org/content/89/9/498

It is most prominent in surface epithelia subject to trauma: that is, skin creases, pressure areas, buccal mucosa and healing scars; areas of depigmented skin known as vitiligo in patients with Addison's disease.

MAIN METHODS OF EXAMINATION OF PATIENTS WITH ALLERGIC DISEASES. LABORATORY AND INSTRUMENTAL TESTS IN ALLERGOLOGY. BASIC SYNDROMES IN THE ALLERGOLOGY

Allergic (including atopic) and other hypersensitivity disorders are inappropriate or exaggerated immune reactions to foreign antigens. Inappropriate immune reactions include those that are misdirected against intrinsic body components (self), leading to autoimmune disorders This topic focuses on type I hypersensitivity reactions.

Classification of Hypersensitivity Reactions

Hypersensitivity reactions are divided into 4 types (I through IV) by the Gell and Coombs classification. Hypersensitivity disorders often involve more than 1 type.

Type I

Type I reactions (immediate hypersensitivity) are IgE-mediated. Antigen binds to IgE that is bound to tissue mast cells and blood basophils, triggering release of preformed mediators (eg, histamine, proteases, chemotactic factors) and synthesis of other mediators (eg, prostaglandins, leukotrienes, platelet-activating factor, cytokines). These mediators cause vasodilation, increased capillary permeability, mucus hypersecretion, smooth muscle spasm, and tissue infiltration with eosinophils, type 2 helper T (TH2) cells, and other inflammatory cells.

Type I hypersensitivity reactions develop < 1 hour after exposure to antigen.

Type I reactions underlie all atopic disorders (eg, atopic dermatitis, allergic asthma, rhinitis, conjunctivitis) and many allergic disorders (eg, anaphylaxis, some cases of angioedema, urticaria, latex and some food allergies). The terms atopy and allergy are often used interchangeably but are different:

- **Atopy** is an exaggerated IgE-mediated immune response; all atopic disorders are type I hypersensitivity disorders.
- **Allergy** is any exaggerated immune response to a foreign antigen regardless of mechanism.

Thus, all atopic disorders are considered allergic, but many allergic disorders (eg, hypersensitivity pneumonitis) are not atopic.

Atopic disorders most commonly affect the nose, eyes, skin, and lungs. These disorders include conjunctivitis, extrinsic atopic dermatitis (the most common type of eczema), immune-mediated urticaria, some forms of angioedema, acute latex allergy, some allergic lung disorders (eg, allergic asthma, IgE-mediated

components of allergic bronchopulmonary aspergillosis), allergic rhinitis, and allergic reactions to venomous stings.

Type II

Type II reactions (antibody-dependent cytotoxic hypersensitivity) result when antibody binds to cell surface antigens or to a molecule coupled to a cell surface. The surface-bound antigen-antibody structure (as opposed to the circulating antigen-antibody complex in type III hypersensitivity) activates cells that participate in antibody-dependent cell-mediated cytotoxicity (eg, natural killer cells, eosinophils, macrophages), complement, or both. The result is cell and tissue damage.

Disorders involving type II reactions include hyperacute graft rejection of an organ transplant, Coombs-positive hemolytic anemias, Hashimoto thyroiditis, and anti–glomerular basement membrane disease (eg, Goodpasture syndrome).

Type III

Type III reactions (immune complex disease) cause inflammation in response to circulating antigen-antibody immune complexes deposited in vessels or tissue. These complexes can activate the complement system or bind to and activate certain immune cells, resulting in release of inflammatory mediators.

Consequences of immune complex formation depend in part on the relative proportions of antigen and antibody in the immune complex. Early in the immune response, there is excess antigen with small antigen-antibody complexes, which do not activate complement. Later, when antigen and antibody are more balanced, immune complexes are larger and tend to be deposited in various tissues (eg, glomeruli, blood vessels), causing systemic reactions. The isotype of induced antibodies changes during an immune response, and the isotype, glycosylation, size, and charge of the complex’s components contribute to the clinical response.

Type III disorders include serum sickness, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), leukocytoclastic vasculitis, cryoglobulinemia, acute hypersensitivity pneumonitis, and several types of glomerulonephritis.

Type III reactions develop 4 to 10 days after exposure to antigen and, if exposure to the antigen continues, can become chronic.

Type IV

Type IV reactions (delayed hypersensitivity) do not involve antibodies but are mediated by T cells.

T cells, sensitized after contact with a specific antigen, are activated by continued exposure or reexposure to the antigen; they damage tissue by direct toxic effects or through release of cytokines, which activate eosinophils, monocytes and macrophages, neutrophils, or natural killer cells.

Disorders involving type IV reactions include Stevens-Johnson syndrome, toxic epidermal necrolysis (SJS/TEN), drug rash with eosinophilia and systemic symptoms (DRESS) , contact dermatitis (eg, poison ivy), subacute and chronic hypersensitivity pneumonitis, acute and chronic allograft rejection, the immune response to tuberculosis, and many forms of drug hypersensitivity.

Etiology of Allergic and Atopic Disorders

Complex genetic, environmental, and site-specific factors contribute to development of IgE-mediated allergies.

Genetic factors may be involved, as suggested by familial inheritance of disease, association between atopy and specific human leukocyte antigen (HLA) loci, and polymorphisms of several genes, including those for the high-affinity IgE receptor beta-chain, IL-4 receptor alpha-chain, interleukin (IL)-4, IL-13, CD14, dipeptidyl-peptidase 10 (DPP10), and a disintegrin and metalloprotease domain 33 (*ADAM33*).

Environmental factors interact with genetic factors to maintain type 2 helper T (TH2) cell–directed immune responses. TH2 cells activate eosinophils, promote IgE production, and are proallergic. Early childhood exposure to bacterial and viral infections and endotoxins (eg, lipopolysaccharide) may normally shift native TH2-cell responses to type 1 helper T (TH1)–cell responses, which suppress TH2 cells and therefore discourage allergic responses. Regulatory T (Treg) cells (eg, CD4+CD25+Foxp3+), which are capable of suppressing TH2-cell responses, and IL-12–secreting dendritic cells, which drive TH1-cell responses, are perhaps also involved. Trends in developed countries toward smaller families with fewer children, cleaner indoor environments, and early use of antibiotics may limit children's exposure to the infectious agents that drive a predominantly TH1-cell response; such trends may explain the increased prevalence of some allergic disorders.

Other factors thought to contribute to allergy development include chronic allergen exposure and sensitization, diet, and environmental pollutants.

Site-specific factors include adhesion molecules in bronchial epithelium and skin and molecules in the gastrointestinal (GI) tract that direct TH2 cells to target tissues. The composition of the GI tract, respiratory tract, and skin microbiota appears

to strongly influence the development of allergy. These microbiota may provide new targets for allergy therapy.

Allergens

By definition, an allergen induces type I IgE-mediated or type IV T-cell–mediated immune responses. Allergic triggers are almost always low molecular weight proteins; many of them can become attached to airborne particles.

Allergens that are the most common causes of acute and chronic allergic reactions (type I and type IV) include

- House dust mite feces
- Animal dander
- Pollens (tree, grass, weed)
- Molds
- Foods
- Insect saliva and venom (transmitted by bites and stings)
- Drugs
- Latex
- Household chemicals (eg, hydroxyisohexyl 3-cyclohexene carboxaldehyde, cinnamal, eugenol)

For type IV hypersensitivity reactions, drugs are the most common cause.

Pathophysiology of Allergic and Atopic Disorders

When allergen binds to IgE-sensitized mast cells and basophils, histamine is released from their intracellular granules. Mast cells are widely distributed but are most concentrated in skin, lungs, and gastrointestinal (GI) mucosa; histamine facilitates inflammation and is the primary mediator of clinical atopy. Physical disruption of tissue and various substances (eg, tissue irritants, opiates, surface-active agents, complement components C3a and C5a) can trigger histamine release directly, independent of IgE.

Histamine causes the following:

- Local vasodilation (causing erythema)
- Increased capillary permeability and edema (producing a wheal)
- Vasodilation of surrounding arterioles mediated by neuronal reflex mechanisms (causing flare—the redness around a wheal)
- Stimulation of sensory nerves (causing itching)
- Smooth muscle contraction in the airways (bronchoconstriction) and in the GI tract (increasing GI motility)

- Increased nasal, salivary, and bronchial gland secretions

When released systemically, histamine is a potent arteriolar dilator and can cause extensive peripheral pooling of blood and hypotension; cerebral vasodilation may be a factor in vascular headache. Histamine increases capillary permeability; the resulting loss of plasma and plasma proteins from the vascular space can worsen circulatory shock. This loss triggers a compensatory catecholamine surge from adrenal chromaffin cells.

Common symptoms of type I hypersensitivity allergic disorders include

- Rhinorrhea, sneezing, and nasal congestion (upper respiratory tract)
- Wheezing and dyspnea (lower respiratory tract)
- Itching (eyes, nose, skin)

Signs may include nasal turbinate edema, sinus pain during palpation, wheezing, conjunctival hyperemia and edema, urticaria, angioedema, dermatitis, and skin lichenification.

Stridor, wheezing, and hypotension are life-threatening signs of anaphylaxis.

Diagnosis of Allergic and Atopic Disorders

- Clinical evaluation
- Sometimes complete blood count (to check for eosinophilia) and occasionally serum IgE levels (nonspecific tests)
- Often skin testing and allergen-specific serum IgE testing (specific tests)
- Rarely provocative testing

A thorough history is generally more reliable than testing or screening. History should include:

- Questions about frequency and duration of attacks and changes over time
- Triggering factors if identifiable
- Relation to seasonal or situational settings (eg, predictably occurring during pollen seasons; after exposure to animals, hay, or dust; during exercise; or in particular places)
- Family history of similar symptoms or of atopic disorders
- Responses to attempted treatments

Age at onset may be important in asthma because childhood asthma is likely to be atopic and asthma beginning after age 30 is not.

Nonspecific tests

Certain tests can suggest but not confirm an allergic origin of symptoms.

Complete blood count (CBC) may be done to detect eosinophilia if patients are not taking corticosteroids, which reduce the eosinophil count. However, CBC is of limited value because although eosinophils may be increased in atopy or other conditions (eg, drug hypersensitivity, cancer, inflammatory bowel disease, parasitic infection), a normal eosinophil count does not exclude allergy. Total white blood cell count is usually normal. Anemia and thrombocytosis are not typical of allergic responses and should prompt consideration of a systemic inflammatory disorder.

Conjunctival or nasal secretions or sputum can be examined for leukocytes; finding any eosinophils suggests that TH2-mediated inflammation is likely.

Serum IgE levels are elevated in atopic disorders but are of little help in diagnosis because they may also be elevated in parasitic infections, infectious mononucleosis, some autoimmune disorders, drug reactions, immunodeficiency disorders (hyper-IgE syndrome and Wiskott-Aldrich syndrome), IgG4-related disease, and in some forms of multiple myeloma. IgE levels are probably most helpful for following response to therapy in allergic bronchopulmonary aspergillosis.

Specific tests

Skin testing uses standardized concentrations of antigen introduced directly into skin and is indicated when a detailed history and physical examination do not identify the cause and triggers for persistent or severe symptoms. Skin testing has higher positive predictive values for diagnosing allergic rhinitis and conjunctivitis than for diagnosing allergic asthma or food allergy; negative predictive value for food allergy is high.

The most commonly used antigens are pollens (tree, grass, weed), molds, house dust mite feces, animal danders and sera, insect venom, foods, and beta-lactam antibiotics. Choice of antigens to include is based on patient history and geographic prevalence.

Two skin test techniques can be used:

- Percutaneous (prick)
- Intradermal

The prick test can detect most common allergies; it is usually done first. The intradermal test is more sensitive but less specific; it can be used to evaluate sensitivity to allergens when prick test results are negative or equivocal.

For the **prick test,** a drop of antigen extract is placed on the skin, which is then tented up and pricked or punctured through the extract with the tip of a 27-gauge needle held at a 20° angle or with a commercially available prick device.

If no allergen is identified in the prick test, an intradermal test is done.

For the **intradermal test,** just enough extract to produce a 1- or 2-mm bleb (typically 0.02 mL) is injected intradermally with a 0.5- or 1-mL syringe and a 27-gauge short-bevel needle.

Prick and intradermal skin testing should include the diluent alone as a negative control and histamine (10 mg/mL for prick tests, 0.01 mL of a 1:1000 solution for intradermal tests) as a positive control. For patients who have had a recent (< 1 year) generalized reaction to the test antigen, testing begins with the standard reagent diluted 100-fold, then 10-fold, and then the standard concentration.

A test is considered positive if a wheal and flare reaction occurs and wheal diameter is 3 to 5 mm greater than that of the negative control after 15 to 20 minutes.

False positives occur in dermatographism (a wheal and flare reaction provoked by stroking or scraping the skin). False negatives occur when allergen extracts have been stored incorrectly or are outdated.

Certain drugs can also interfere with results and should be stopped a few days to a week before testing. These drugs include over-the-counter (OTC) and prescription antihistamines, tricyclic antidepressants, omalizumab, and monoamine oxidase inhibitors. Some clinicians suggest that testing should be avoided in patients taking beta-blockers because these patients are more likely to have risk factors for severe reactions. These risk factors tend to predict limited cardiopulmonary reserve and include coronary artery disease, arrhythmias, and older age. Also, beta-blockers can interfere with treatment of severe reactions by blocking response to beta-adrenergic agonists such as epinephrine.

Allergen-specific serum IgE tests use an enzyme-labeled anti-IgE antibody to detect binding of serum IgE to a known allergen. These tests are done when skin testing might be ineffective or risky—for example, when drugs that interfere with test results cannot be temporarily stopped before testing or when a skin disorder such as eczema or psoriasis would make skin testing difficult. For allergen-specific serum IgE tests, the allergen is immobilized on a synthetic surface. After incubation with patient serum and enzyme-labeled anti-IgE antibody, a substrate for the enzyme is added; the substrate provides colorimetric, fluorescent, or chemiluminescent detection of binding. Allergen-specific IgE tests have replaced radioallergosorbent testing (RAST), which used 125-I-labeled anti-IgE antibody. Although the allergen-

specific serum IgE tests are not radioactive, they are still sometimes referred to as RAST.

Provocative testing includes an oral challenge, which involves direct exposure of the mucosae to allergen; it is indicated for patients who must document their reaction (eg, for occupational or disability claims) and for excluding an IgE-mediated allergy in patients thought to be at low risk of allergy. This test is frequently done to exclude food and drug allergy. Other types of provocative testing include asking patients to exercise to diagnose exercise-induced asthma. Various provocative tests for physical urticaria can be done in the office; they include placing an ice cube on the skin for 4 minutes to diagnose cold-induced urticaria, asking patients to exercise to increase body temperature and thus confirm cholinergic urticaria, and placing a vortex (laboratory vibratory device) on a patient's arm or hand to identify mast-cell mediated vibratory urticaria.

Ophthalmic testing has no advantage over skin testing and is rarely used.

Nasal and bronchial challenge are primarily research tools, but bronchial challenge is sometimes used when the clinical significance of a positive skin test is unclear or when no antigen extracts are available (eg, for occupation-related asthma).

Prevention of Allergic and Atopic Disorders

Allergic triggers should be removed or avoided. Strategies include the following:

- Using synthetic fiber pillows and impermeable mattress covers
- Frequently washing bed sheets, pillowcases, and blankets in hot water
- Frequently cleaning the house, including dusting, vacuuming, and wet-mopping
- Removing upholstered furniture, soft toys, and carpets or frequently vacuuming upholstered furniture and carpets
- Exterminating cockroaches to eliminate exposure
- Using dehumidifiers in basements and other poorly aerated, damp rooms
- Using high-efficiency particulate air (HEPA) vacuums and filters
- Avoiding food triggers
- Limiting pets to certain rooms or keeping them out of the house
- For people with severe seasonal allergies, possibly moving to an area that does not have the allergen

ANGIOEDEMA

Angioedema is edema of the deep dermis and subcutaneous tissues. It is usually an acute but sometimes a chronic mast cell–mediated reaction caused by exposure to a drug (eg, angiotensin-converting enzyme inhibitors), venom, dietary, pollen, or animal dander allergens, or it can be idiopathic. Angioedema can also be a hereditary or an acquired disorder characterized by an abnormal complement response. The main symptom is swelling, often of the face, mouth, and upper airways, which can be severe. Diagnosis is by examination. Treatment is with airway management as needed, elimination or avoidance of the allergen, and drugs to minimize swelling (eg, H1 blockers).

Angioedema is swelling (usually localized) of the subcutaneous tissues due to increased vascular permeability and extravasation of intravascular fluid. Known mediators of increased vascular permeability include the following:

- Mast cell–derived mediators (eg, histamine, leukotrienes, prostaglandins)
- Bradykinin and complement-derived mediators

Mast cell–derived mediators tend to also affect layers superficial to subcutaneous tissue, including the dermal-epidermal junction. There, these mediators cause urticaria and pruritus, which thus usually accompany mast cell–mediated angioedema.

In bradykinin-mediated angioedema, the dermis is usually spared, so urticaria and pruritus are absent.

In some cases, the mechanism and cause of angioedema are unknown. Several causes (eg, calcium channel blockers, fibrinolytic drugs) have no identified mechanism; sometimes a cause (eg, muscle relaxants) with a known mechanism is overlooked clinically.

Angioedema is usually acute or but can be chronic (> 6 weeks).

There are hereditary and acquired forms characterized by an abnormal complement response.

Acute angioedema

Acute angioedema is mast cell–mediated in > 90% of cases. Mast cell–mediated mechanisms include acute allergic, typically IgE-mediated reactions. IgE-mediated angioedema is usually accompanied by acute urticaria (local wheals and erythema in the skin) and itching. It may often be caused by the same allergens (eg, drug, venom, dietary, extracted allergens) that are responsible for acute IgE-mediated urticaria.

Acute angioedema can also result from agents that directly stimulate mast cells without involving IgE. Causes can include opiates, radiopaque contrast agents, aspirin, and nonsteroidal anti-inflammatory drugs (NSAIDs).

Angiotensin-converting enzyme (ACE) inhibitors cause up to 30% of cases of acute angioedema seen in emergency departments. ACE inhibitors can directly increase levels of bradykinin. The face and upper airways are most commonly affected, but the intestine may be affected. Urticaria does not occur. Angioedema may occur soon or years after therapy begins.

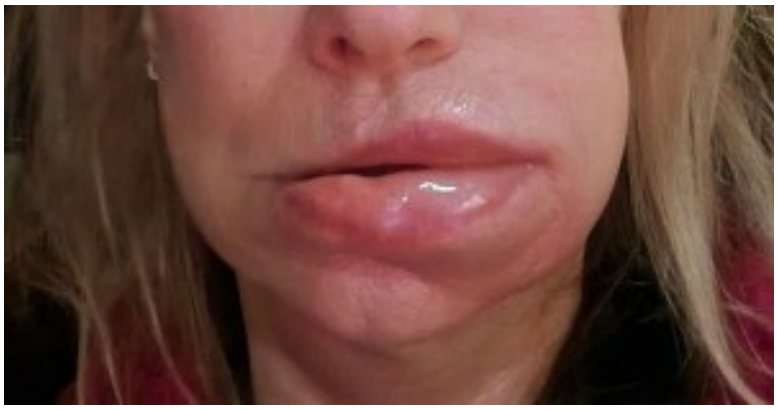

Image 31. Angioedema

The image was downloaded from website https://www.bauersmiles.com

Chronic angioedema

The cause of chronic (> 6 weeks) angioedema is usually unknown. IgE-mediated mechanisms are rare, but chronic ingestion of an unsuspected drug or chemical (eg, penicillin in milk, a nonprescription drug, preservatives, other food additives) is sometimes the cause. A few cases are due to hereditary or acquired C1 inhibitor deficiency.

Idiopathic angioedema is angioedema that occurs without urticaria, is chronic and recurrent, and has no identifiable cause.

Hereditary and acquired angioedema

Hereditary angioedema and acquired angioedema are disorders that are characterized by abnormal complement responses and caused by deficiency or dysfunction of C1 inhibitor. Symptoms are those of bradykinin-mediated angioedema.

Symptoms and Signs of Angioedema

In angioedema, edema is often asymmetric and mildly painful. It often involves the face, lips, and/or tongue and may also occur on the back of hands or feet, on the

genitals, or in the abdomen. Edema of the upper airways may cause respiratory distress and stridor; the stridor may be mistaken for asthma. The airways may be completely obstructed. Edema of the intestine may cause nausea, vomiting, colicky abdominal pain, and/or diarrhea.

Other manifestations of angioedema depend on the mediator.

Mast cell–mediated angioedema

- Tends to develop over minutes to several hours
- May be accompanied by other manifestations of acute allergic reactions (eg, pruritus, urticaria, flushing, bronchospasm, anaphylactic shock)

Bradykinin-mediated angioedema

- Tends to develop over hours to a few days
- Is not accompanied by other manifestations of allergic reactions

Diagnosis of Angioedema

Patients with localized swelling but no urticaria are asked specifically about use of ACE inhibitors.

The cause of angioedema is often obvious, and diagnostic tests are seldom required because most reactions are self-limited and do not recur. When angioedema is acute, no test is particularly useful. When it is chronic, thorough drug and dietary evaluation is warranted.

If no cause is obvious or if family members have urticaria, clinicians should consider measuring C1 inhibitor levels to check for C1 inhibitor deficiency and C4 levels to check for hereditary or acquired angioedema. Low levels of C4, even between episodes, may help confirm a diagnosis of hereditary angioedema (types 1 and 2) or acquired C1 inhibitor deficiency.

Erythropoietic protoporphyria may mimic allergic forms of angioedema; both can cause edema and erythema after exposure to sunlight. The two can be distinguished by measuring blood and fecal porphyrins.

URTICARIA

Urticaria consists of migratory, well-circumscribed, erythematous, pruritic plaques on the skin.

Urticaria also may be accompanied by angioedema, which results from mast cell and basophil activation in the deeper dermis and subcutaneous tissues and manifests as edema of the face and lips, extremities, or genitals. Angioedema can occur in the bowel and present as colicky abdominal pain. Angioedema can be life-

threatening if airway obstruction occurs because of laryngeal edema or tongue swelling.

Pathophysiology of Urticaria

Urticaria results from the release of histamine, bradykinin, kallikrein, and other vasoactive substances from mast cells and basophils in the superficial dermis, resulting in intradermal edema caused by capillary and venous vasodilation and occasionally caused by leukocyte infiltration.

The process can be immune mediated or nonimmune mediated.

Immune-mediated mast cell activation includes

- Type I hypersensitivity reactions, in which allergen-bound IgE antibodies bind to high-affinity cell surface receptors on mast cells and basophils
- Autoimmune disorders, in which antibodies to an IgE receptor functionally cross-link IgE receptors and cause mast cell degranulation

Nonimmune-mediated mast cell activation includes

- Direct nonallergic activation of mast cells by certain drugs
- Drug-induced cyclooxygenase inhibition that activates mast cells by poorly understood mechanisms
- Activation by physical or emotional stimuli; mechanism is poorly understood but possibly involves the release of neuropeptides that interact with mast cells

Etiology of Urticaria

Urticaria is classified as acute (< 6 weeks) or chronic (> 6 weeks); acute cases (70%) are more common than chronic (30%).

Acute urticaria most often results from

- Type I hypersensitivity reactions

A presumptive trigger (eg, drug, food ingestion, insect bite or sting, infection) occasionally can be identified.

Chronic urticaria most often results from

- Idiopathic causes
- Autoimmune disorders

Chronic urticaria often lasts months to years, eventually resolving without a cause being found.

Evaluation of Urticaria

Because there are no definitive diagnostic tests for urticaria, evaluation largely relies on history and physical examination.

History

History of present illness should include a detailed account of the individual episodes of urticaria, including distribution, size, and appearance of lesions; frequency of occurrence; duration of individual lesions; and any prior episodes. Activities and exposures during, immediately before, and within the past 24 hours of the appearance of urticaria should be noted. Clinicians specifically should ask about recent exercise; exposure to potential allergens (see Table: Some Causes of Urticaria), insects, or animals; new laundry detergent or soaps; new foods; recent infections; or recent stressful life events. The patient should be asked about the duration between any suspected trigger and the appearance of urticaria and which particular triggers are suspected. Important associated symptoms include pruritus, rhinorrhea, swelling of the face and tongue, and dyspnea.

Review of systems should seek symptoms of causative disorders, including fever, fatigue, abdominal pain, and diarrhea (infection); heat or cold intolerance, tremor, or weight change (autoimmune thyroiditis); joint pain (cryoglobulinemia, systemic lupus erythematosus [SLE]); malar rash (SLE); dry eyes and dry mouth (Sjögren syndrome); cutaneous ulcers and hyperpigmented lesions after resolution of urticaria (urticarial vasculitis); small pigmented papules (mastocytosis); lymphadenopathy (viral illness, cancer, serum sickness); acute or chronic diarrhea (viral or parasitic enterocolitis); and fevers, night sweats, or weight loss (cancer).

Past medical history should include a detailed allergy history, including known atopic conditions (eg, allergies, asthma, eczema) and known possible causes (eg, autoimmune disorders, cancer). All drug use should be reviewed, including over-the-counter drugs and herbal products, specifically any agents particularly associated with urticaria (see Table: Some Causes of Urticaria). Family history should elicit any history of rheumatoid disease, autoimmune disorders, or cancer. Social history should cover any recent travel and any risk factors for transmission of infectious disease (eg, hepatitis, HIV).

Physical examination

Vital signs should note the presence of bradycardia or tachycardia and tachypnea. General examination should immediately seek any signs of respiratory distress and also note cachexia, jaundice, or agitation.

Examination of the head should note any swelling of the face, lips, or tongue; scleral icterus; malar rash; tender and enlarged thyroid; lymphadenopathy; or dry

eyes and dry mouth. The oropharynx should be inspected and the sinuses should be palpated and transilluminated for signs of occult infection (eg, sinus infection, tooth abscess).

Abdominal examination should note any masses, hepatomegaly, splenomegaly, or tenderness. Neurologic examination should note any tremor or hyperreflexia or hyporeflexia. Musculoskeletal examination should note the presence of any inflamed or deformed joints.

Skin examination should note the presence and distribution of urticarial lesions as well as any cutaneous ulceration, hyperpigmentation, small papules, or jaundice. Urticarial lesions usually appear as well-demarcated transient swellings involving the dermis. These swellings are typically red and vary in size from pinprick to covering wide areas. Some lesions can be very large. In other cases, smaller urticarial lesions may become confluent. However, skin lesions also may be absent at the time of the visit. Maneuvers to evoke physical urticaria can be done during the examination, including exposure to vibration (tuning fork), warmth (tuning fork held under warm water), cold (stethoscope or chilled tuning fork), water, or pressure (lightly scratching an unaffected area with a fingernail).

Image 32. Urticaria

The image was downloaded from website https://healthjade.net/urticaria

Red flags

The following findings are of particular concern:

- Angioedema (swelling of the face, lips, or tongue)
- Stridor, wheezing, or other respiratory distress
- Hyperpigmented lesions, ulcers, or urticaria that persist > 48 hours

- Signs of systemic illness (eg, fever, lymphadenopathy, jaundice, cachexia)

Interpretation of findings

Acute urticaria is nearly always due to some defined exposure to a drug or physical stimulus or an acute infectious illness. However, the trigger is not always clear from the history, particularly because allergy may develop without warning to a previously tolerated substance.

Most **chronic urticaria** is idiopathic. The next most common cause is an autoimmune disorder. The causative autoimmune disease is sometimes clinically apparent. Urticarial vasculitis sometimes is associated with connective tissue disorders (particularly SLE or Sjögren syndrome). In urticarial vasculitis, urticaria is accompanied by findings of cutaneous vasculitis; it should be considered when the urticaria is painful rather than pruritic, lasts > 48 hours, does not blanch, or is accompanied by vesicles or purpura.

Testing

Usually, no testing is needed for an isolated episode of urticaria unless symptoms and signs suggest a specific disorder (eg, infection).

Unusual, recurrent, or persistent cases warrant further evaluation. Referral for allergy skin testing should be done, and routine laboratory tests should consist of complete blood count, blood chemistries, liver tests, and thyroid-stimulating hormone (TSH). Further testing should be guided by symptoms and signs (eg, of autoimmune disorders) and any abnormalities on the screening tests (eg, hepatitis serologies and ultrasonography for abnormal liver tests; ova and parasites for eosinophilia; cryoglobulin titer for elevated liver tests or elevated creatinine; thyroid autoantibodies for abnormal TSH).

Skin biopsy should be done if there is any uncertainty as to the diagnosis or if wheals persist > 48 hours (to rule out urticarial vasculitis).

Clinicians should be cautious when recommending the patient do an empiric challenge (eg, “Try such and such again and see whether you get a reaction”) because subsequent reactions may be more severe.

DRUG HYPERSENSITIVITY

Drug hypersensitivity is an immune-mediated reaction to a drug. Symptoms range from mild to severe and include rash, anaphylaxis, and serum sickness. Diagnosis is clinical; skin testing is occasionally useful. Treatment is drug

discontinuation, supportive treatment (eg, with antihistamines), and sometimes desensitization.

Drug hypersensitivity differs from toxic and adverse effects that may result from the drug and from problems due to drug interactions.

Pathophysiology of Drug Hypersensitivity

Some protein and large polypeptide drugs (eg, insulin, therapeutic antibodies) can directly stimulate antibody production. However, most drugs act as haptens, binding covalently to serum or cell-bound proteins, including peptides embedded in major histocompatibility complex (MHC) molecules. The binding makes the protein-drug complex immunogenic, stimulating antidrug antibody production, T-cell responses against the drug, or both. Haptens may also bind directly to class II MHC molecules, directly activating T cells. Some drugs act as prohaptens. When metabolized, prohaptens become haptens; eg, penicillin itself is not antigenic, but its main degradation product, benzylpenicilloic acid, can combine with tissue proteins to form benzylpenicilloyl (BPO), a major antigenic determinant. Some drugs bind and stimulate T-cell receptors (TCR) directly; the clinical significance of nonhapten TCR binding is being determined.

How primary sensitization occurs and how the immune system is initially involved is unclear, but once a drug stimulates an immune response, cross-reactions with other drugs within and between drug classes can occur. For example, penicillin-sensitive patients are highly likely to react to semisynthetic penicillins (eg, amoxicillin, carbenicillin, ticarcillin). In early, poorly designed studies, about 10% of patients who had a vague history of penicillin sensitivity reacted to cephalosporins, which have a similar beta-lactam structure; this finding has been cited as evidence of cross-reactivity between these drug classes. However, in recent, better-designed studies, only about 2% of patients with a penicillin allergy detected during skin testing react to cephalosporins; about the same percentage of patients react to structurally unrelated antibiotics (eg, sulfa drugs). Sometimes this and other apparent cross-reactions (eg, between sulfonamide antibiotics and nonantibiotics) are due to a predisposition to allergic reactions rather than to specific immune cross-reactivity.

Symptoms and Signs of Drug Hypersensitivity

Symptoms and signs of drug allergies vary by patient and drug, and a single drug may cause different reactions in different patients. The most serious is anaphylaxis (type I hypersensitivity reaction); exanthema (eg, morbilliform

eruption), urticaria, and fever are common. Fixed drug reactions—reactions that recur at the same body site each time a patient is exposed to the same drug—are uncommon.

Some distinct clinical syndromes can involve other types of hypersensitivity reactions:

- Serum sickness
- Drug-induced immune hemolytic anemia
- DRESS (drug rash with eosinophilia and systemic symptoms)
- Pulmonary effects
- Renal effects
- Other autoimmune phenomena

Serum sickness typically occurs 7 to 10 days after exposure and causes fever, arthralgias, and rash. Mechanism is a type III hypersensitivity reaction due to drug-antibody complexes and complement activation. Some patients have frank arthritis, edema, or gastrointestinal symptoms. Symptoms are self-limited, lasting 1 to 2 weeks. Beta-lactam and sulfonamide antibiotics, iron-dextran, and carbamazepine are most commonly implicated.

Drug-induced immune hemolytic anemia may develop when an antibody-drug-red blood cell (RBC) interaction occurs (eg, with cephalosporins and with cefotetan) or when a drug (eg, fludarabine, methyldopa) alters the RBC membrane in a way that induces autoantibody production. These reactions are type II hypersensitivity reactions.

DRESS (drug rash with eosinophilia and systemic symptoms), also called drug-induced hypersensitivity syndrome (DHS), is a type IV hypersensitivity reaction that can start up to 12 weeks after initiation of drug treatment and can occur after a dose increase. Symptoms may persist or recur for several weeks after stopping drug treatment. Patients have prominent eosinophilia and often develop hepatitis, exanthema, facial swelling, generalized edema, and lymphadenopathy. Carbamazepine, phenytoin, allopurinol, and lamotrigine are frequently implicated.

Pulmonary effects may be caused by some drugs (eg, bleomycin, amiodarone, nitrofurantoin, amphotericin B, sulphonamides, sulfasalazine). These drugs can induce respiratory symptoms (distinct from the wheezing that may occur with type I hypersensitivity), deterioration in pulmonary function, and other pulmonary changes (called drug-induced pulmonary disease, most commonly

interstitial lung disease). These effects are thought to be primarily type III and type IV hypersensitivity reactions.

The most common allergic **renal effect** is tubulointerstitial nephritis; NSAIDs (including COX-2 inhibitors), methicillin, antimicrobials, and cimetidine are commonly implicated. Types I, III, and/or IV hypersensitivity reactions can be involved.

Other autoimmune phenomena may occur. Hydralazine, propylthiouracil, and procainamide can cause a systemic lupus erythematosus (SLE)-like syndrome, which is a type III hypersensitivity reaction. The syndrome may be mild (with arthralgias, fever, and rash) or fairly dramatic (with serositis, high fevers, and malaise), but it tends to spare the kidneys and central nervous system. The antinuclear antibody test is positive. Penicillamine can cause SLE and other autoimmune disorders (eg, myasthenia gravis, which is a type II hypersensitivity reaction). Some drugs can cause perinuclear antineutrophil cytoplasmic autoantibodies (p-ANCA)–associated vasculitis. Common drugs associated with drug-induced perinuclear antineutrophil cytoplasmic autoantibodies (p-ANCA)–associated vasculitis include antithyroid drugs, antituberculosis drugs, certain antibiotics, allopurinol, hydralazine, and atorvastatin. These autoantibodies are directed against myeloperoxidase (MPO), causing type II hypersensitivity reactions. Immune checkpoint inhibitors, a commonly used class of cancer immunotherapy, can have immune-related adverse effects. These effects result from nonspecific immune activation and can affect almost any organ system; however, they most commonly affect the skin, liver, gastrointestinal tract, and endocrine system.

Diagnosis of Drug Hypersensitivity

- Patient’s report of a reaction soon after taking a drug
- Skin testing
- Sometimes drug provocation testing
- Sometimes direct and indirect antiglobulin assays

The following can help differentiate drug hypersensitivity from toxic and adverse drug effects and from problems due to drug interactions.

- Time of onset
- Known effects of a drug
- Results of a repeat drug challenge

For example, a dose-related reaction is often drug toxicity, not drug hypersensitivity.

Drug hypersensitivity is suggested when a reaction occurs within minutes to hours after drug administration. However, many patients report a past reaction of uncertain nature. In such cases, if there is no equivalent substitute (eg, when penicillin is needed to treat syphilis), testing should be considered.

Skin testing

Tests for type I (IgE-mediated) hypersensitivity help identify reactions to beta-lactam antibiotics, foreign (xenogeneic) serum, and some vaccines and polypeptide hormones. However, typically, only 10 to 20% of patients who report a penicillin allergy have a positive reaction on skin tests. Also, for most drugs (including cephalosporins), skin tests are unreliable and, because they detect only IgE-mediated reactions, do not predict the occurrence of morbilliform eruptions, hemolytic anemia, or nephritis.

Penicillin skin testing can be done if patients with a history of an immediate hypersensitivity reaction must take a penicillin. BPO-polylysine conjugate and penicillin G are used with histamine and saline as controls. The prick test is used first. If patients have a history of a severe anaphylactic reaction, reagents should be diluted 100-fold for initial testing. If prick tests are negative, intradermal testing may follow. If skin tests are positive, patients should be given penicillin only as part of a drug desensitization protocol. If tests are negative, a serious reaction is extremely unlikely but not excluded. Therefore, an oral challenge with amoxicillin is often done after a negative skin test result to completely eliminate the possibility of an IgE-mediated allergy.

For **xenogeneic serum skin testing,** patients who are not atopic and who have not previously received xenogeneic (eg, horse) serum should first be given a prick test with a 1:10 dilution; if this test is negative, 0.02 mL of a 1:1000 dilution is injected intradermally. A wheal > 0.5 cm in diameter develops within 15 minutes in sensitive patients. Initially, for all patients who may have previously received serum—whether or not they reacted—and for those with a suspected allergic history, a prick test should be done using a 1:1000 dilution; if results are negative, 1:100 is used, and if results are again negative, 1:10 is used as above. A negative result rules out the possibility of anaphylaxis but does not predict incidence of subsequent serum sickness.

ANAPHYLAXIS

Anaphylaxis is an acute, potentially life-threatening, IgE-mediated allergic reaction that occurs in previously sensitized people when they are reexposed to the sensitizing antigen. Symptoms can include stridor, dyspnea, wheezing, and hypotension. Diagnosis is clinical. Treatment is with epinephrine. Bronchospasm and upper airway edema may require inhaled or injected beta-agonists and sometimes endotracheal intubation. Persistent hypotension requires IV fluids and sometimes vasopressors.

The prevalence of anaphylaxis is difficult to ascertain, but one study using 2 nationwide public surveys suggested that it was about 1.6% in the general adult population. Fatal anaphylaxis is far less common; it occurs in < 1 per million population.

Etiology of Anaphylaxis

Anaphylaxis is typically triggered by

- Drugs (eg, beta-lactam antibiotics, insulin, streptokinase, allergen extracts)
- Foods (eg, nuts, eggs, seafood)
- Proteins (eg, tetanus antitoxin, blood transfusions)
- Animal venoms
- Latex

Peanut and latex allergens may be airborne. Occasionally, exercise or cold exposure can trigger or contribute to an anaphylactic reaction.

History of atopy does not increase risk of anaphylaxis but increases risk of death when anaphylaxis occurs.

Pathophysiology of Anaphylaxis

Interaction of antigen with IgE on basophils and mast cells triggers release of histamine, leukotrienes, and other mediators that cause diffuse smooth muscle contraction (eg, resulting in bronchoconstriction, vomiting, or diarrhea) and vasodilation with plasma leakage.

Anaphylactoid reactions

Anaphylactoid reactions are clinically indistinguishable from anaphylaxis but do not involve IgE and do not require prior sensitization. They occur via direct stimulation of mast cells or via immune complexes that activate complement.

The most common triggers of anaphylactoid reactions are:

- Iodinated radiopaque contrast agents
- Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs)

- Opioids
- Monoclonal antibodies
- Exercise

Symptoms and Signs of Anaphylaxis

Symptoms of anaphylaxis typically begin within 15 minutes of exposure and involve the skin, upper or lower airways, cardiovascular system, and/or gastrointestinal (GI) tract. One or more areas may be affected, and symptoms do not necessarily progress from mild (eg, urticaria) to severe (eg, airway obstruction, refractory shock), although each patient typically manifests the same reaction to subsequent exposure.

Symptoms range from mild to severe and include flushing, pruritus, urticaria, sneezing, rhinorrhea, nausea, abdominal cramps, diarrhea, a sense of choking or dyspnea, palpitations, and dizziness.

Signs of anaphylaxis include hypotension, tachycardia, urticaria, angioedema, wheezing, stridor, cyanosis, and syncope. Shock can develop within minutes, and patients may have seizures, become unresponsive, and die. Cardiovascular collapse can occur without respiratory or other symptoms.

Late-phase reactions may occur 4 to 8 hours after the exposure or later. Symptoms and signs are usually less severe than they were initially and may be limited to urticaria; however, they may be more severe or fatal. Therefore, patients who have an anaphylactic reaction should be observed in an acute care setting for several hours after the initial reaction.

Diagnosis of Anaphylaxis

- Clinical evaluation
- Sometimes measurement of serum levels of tryptase

Diagnosis of anaphylaxis is clinical. Anaphylaxis should be suspected if any of the following suddenly occur without explanation:

- Shock
- Respiratory symptoms (eg, dyspnea, stridor, wheezing)
- Two or more other manifestations of possible anaphylaxis (eg, angioedema, rhinorrhea, GI symptoms)

Risk of rapid progression to shock leaves no time for testing, although mild equivocal cases can be confirmed by measuring serum levels of tryptase (preferably within 2 hours of the reaction). During anaphylaxis, these levels are elevated, and

measuring them can help confirm the diagnosis if it is unclear or if the symptoms recur (eg, after treatment with IV drugs).

The cause is usually easily recognized based on history. If health care workers have unexplained anaphylactic symptoms, latex allergy should be considered.

Treatment of Anaphylaxis

- Epinephrine given immediately
- Sometimes intubation
- IV fluids and sometimes vasopressors for persistent hypotension
- Antihistamines
- Inhaled beta-agonists for bronchoconstriction

Anaphylactoid reactions are treated similarly to anaphylactic reactions.

Epinephrine

Epinephrine is the cornerstone of treatment for anaphylaxis; it may help relieve all symptoms and signs and should be given immediately.

Epinephrine can be given subcutaneously or IM (usual dose is 0.3 to 0.5 mL of a 1:1000 [0.1%] solution in adults or 0.01 mL/kg in children, repeated every 5 to 15 minutes). Maximal absorption occurs when the drug is given IM in the anterolateral (mid-outer) aspect of the thigh.

Management of cardiac arrest is as per standard protocols. Patients with hypotension or severe airway obstruction may be given epinephrine IV or intraosseously (IO). A continuous drip using an infusion pump is preferred, but if the delay to prepare the drip and pump is unacceptable, epinephrine can be given as a single slow IV bolus dose of 0.05 to 0.1 mg (0.5 to 1 mL of a 0.1 mg/mL[1:10,000] solution over 1 to 2 minutes). For a continuous drip, 1 mg epinephrine is mixed in 250 mL 5% D/W or 0.9% normal saline for a concentration of 4 mcg/mL and is started at 0.1 mcg/kg/minute and titrate up by 0.05 mcg/kg/min every 2 to 3 minutes as needed based on blood pressure, heart rate, and oxygenation. If the patient's weight cannot be estimated accurately, the recommended starting dose for adults is 1 to 2 mcg/minute, titrated upward by 2 to 4 mcg/min every 2 to 3 minutes. If an initial bolus is desired but IV access is delayed, 0.2 to 0.25 mg epinephrine may also be given through an endotracheal tube (2 to 2.5 mL of a 0.1 mg/mL solution diluted to 5 to 10 mL with sterile water or saline); alternatively, a second IM dose of epinephrine may be given.

Glucagon 1 to 5 mg IV over 5 minutes (20 to 30 mcg/kg in children) followed by a 5 to 15 mcg/minute infusion has been recommended for patients taking oral

beta-blockers, which attenuate the effect of epinephrine. However, some evidence suggests that patients taking beta blockers are no less responsive to epinephrine. Rapid administration of glucagon can cause vomiting.

Other treatments

Patients who have stridor and wheezing unresponsive to epinephrine should be given oxygen and be intubated. Early intubation is recommended because waiting for a response to epinephrine may allow upper airway edema to progress sufficiently to prevent endotracheal intubation and require cricothyrotomy.

Hypotension often resolves after epinephrine is given. Persistent hypotension can usually be treated with 1 to 2 L (20 to 40 mL/kg in children) of isotonic IV fluids (eg, 0.9% saline). Hypotension refractory to fluids and IV epinephrine may require vasopressors (eg, dopamine 5 mcg/kg/minute).

Antihistamines – both H1 blockers (eg, diphenhydramine 50 to 100 mg IV) and H2 blockers (eg, cimetidine 300 mg IV) – should be given every 6 hours until symptoms resolve.

Inhaled beta-agonists are useful for managing bronchoconstriction that persists after treatment with epinephrine; albuterol 5 to 10 mg by continuous nebulization can be given.

Corticosteroids have no proven role but may help prevent a late-phase reaction; methylprednisolone 125 mg IV initially is adequate.

THE PRINCIPLES OF THE EMERGENCY. THE PRINCIPLES OF THE PREHOSPITAL FIRST AID

First Aid means initiating life support treatment for people suffering from an injury or sudden illness. We have to understand that First Aid has its own limitations and cannot be substituted for professional medical treatment. Assistance given by a First Aider helps in saving the life of a patient.

The primary purpose of giving First Aid is to sustain the life of a person before the arrival of a qualified medical expert, reduce her/his discomfort due to pain, help in early recovery and prevent her/his condition from worsening.

The basic principles of First Aid are as follows:

• Preserve life: This includes preserving the life of the casualty and the rescuer.

• Ensure protection of the casualty from further harm: The treatment area needs to be safe and must not have excess people.

• Provide pain relief: This includes the use of ice packs or applying a sling.

• Prevent the condition from worsening: Ensure that the First Aid procedures do not worsen the patient's condition.

Rules of First Aid

• Check: Find out what has happened and what is wrong with the person.

• Call: Arrange for a professional medical aid.

• Care: Help the victim, preferably without moving her/him.

Observe ABC

A → Airway

B → Breathing

C → Circulation

Airway: Ensure that the tongue or any foreign body does not obstruct the airway.

Breathing: Make sure the victim is breathing. If you are trained to give mouth-tomouth respiration, then facilitate breathing.

Circulation: Check for the pulse to ensure that the heart is beating normally. Check the heartbeat or pulse of the victim. If there is no pulse and you are trained to do Cardio Pulmonary Resuscitation (CPR), then begin CPR immediately.

CARDIAC ARREST

Cardiac arrest refers to cessation of cardiac mechanical function characterized by the absence of palpable pulse, lack of the patient's response to stimulation, and apnea or agonal respirations. If not rapidly reversed, cardiac arrest progresses to death.

Primary cardiac arrest is caused by or associated with a principal cardiac condition, such as:

1) Coronary artery disease (eg, acute coronary syndrome [ACS]/ ischemic heart disease, coronary vasospasm, spontaneous coronary artery dissection).

2) Cardiomyopathies (eg, ischemic cardiomyopathy, nonischemic dilated cardiomyopathy, hypertrophic cardiomyopathy, infiltrative disorders such as amyloidosis or sarcoidosis, arrhythmogenic right ventricular cardiomyopathy, ventricular noncompaction, myocarditis).

3) Congenital arrhythmogenic heart diseases (eg, long QT syndrome, short QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, idiopathic ventricular fibrillation).

4) Structural heart disease (eg, severe aortic stenosis, mitral valve prolapse, anomalous coronary artery circulation, Wolff-Parkinson-White syndrome, sinus node disturbances, atrioventricular conduction disturbances).

5) Other (eg, cardiac tamponade, commotio cordis, aortic dissection).

Secondary cardiac arrest occurs due to noncardiac causes, such as pulmonary embolism, respiratory arrest, multisystem trauma, hemorrhage, acute intracerebral hemorrhage, intoxication, seizures, or near-drowning.

Rhythms in cardiac arrest:

1) Ventricular fibrillation (VF).

2) Pulseless ventricular tachycardia (pVT) or ventricular flutter.

3) Asystole: Lack of electrical and mechanical activity of the heart (also diagnosed at a heart rate <10 beats/min).

4) Pulseless electrical activity (PEA): Lack of a hemodynamically effective mechanical contraction of the heart despite preserved organized electrical activity.

Asystole and PEA commonly result from secondary cardiac arrest or more prolonged primary cardiac arrest (degenerated from VF or pVT) and therefore always require a search for reversible causes.

Basic Life Support (BLS)

Cardiopulmonary resuscitation (CPR) refers to interventions (chest compressions and ventilation) aimed at maintaining circulation and oxygenation of blood in an individual with cardiac arrest. High-quality CPR is essential to improving survival rates. The steps described below refer to nontraumatic cardiac arrest in adults when help is provided by a health-care professional.

1. Make sure the patient and you (as well as other rescuers) are safe. Control possible hazards (as necessary, call the police, fire department, or other emergency agency for additional assistance).

2. Assess the patient's consciousness. If the patient does not respond to voice and gentle shaking, assume that they are unconscious.

3. Shout or phone for help.

4. Clear/open the airway. Place the unconscious patient on their back. Then tilt the head backwards (this maneuver is contraindicated in individuals with suspected cervical spine injury) and examine the mouth, removing any visible foreign bodies. Proceed to chin lift or jaw thrust; these two maneuvers may be performed in patients with suspected cervical spine injury, provided that the head is stabilized in a neutral position without tilting.

5. Assess respirations. Look for chest movements, listen at the patient's mouth for the sounds of inspiration and expiration, place your cheek near the patient's mouth to feel for air movement, and check for pulse at the carotid (or femoral) artery for a maximum of 10 seconds. The lack of chest movements, respiratory sounds, and perceptible air movement indicates apnea, which may be caused by a primary cardiac arrest or by complete airway obstruction, respiratory depression, or respiratory diseases. Agonal respirations (residual, single sighs) are treated as apnea. Other sounds accompanying respiration may indicate partial obstruction of the respiratory tract: (1) gurgling due to liquid or semiliquid content in the airways (ie, vomit, blood, respiratory tract secretions); (2) snoring due a partial closure of the throat by the tongue, palate, or foreign body; (3) stridor due to obstruction or swelling at the level of the glottis.

In some cases it may be necessary to clear/open the airway. If the patient is breathing spontaneously, place them in the recovery position. If a pulse is definitely present in a patient who is not breathing spontaneously, deliver ventilations at the rate of 10 breaths/min without chest compressions (see below). Every 2 minutes check the pulse and look for signs of circulation. Absence of signs of circulation (ie,

spontaneous movements, coughing, breathing) and of carotid pulse indicate cardiac arrest and require immediate CPR. During CPR check for signs of circulation and pulse every 2 minutes.

6. Call for help. If you are alone, immediately upon discovering apnea, grossly abnormal breathing, or lack of pulse call for expert assistance if at all practical, even if you have to briefly leave the patient for this purpose. When away from the hospital, call local emergency services. Hospitals should have an emergency extension or phone number known to and available for all employees. Exception: In the case of children and infants, before calling for help proceed with CPR for ~1 minute (perform 5 rescue breaths, then 15 sternal compressions, then another 2 breaths and 15 compressions).

7. Start chest compressions. Place the patient in the supine position on a hard surface and compress the center of the sternum. In adults compress from 5 to 6 cm deep at a rate of 100 to 120 compressions/min (~2 compressions/s). In children compress the sternum with one hand, and in infants compress with 2 fingers to one-third the depth of the sagittal dimension of the chest (or 4 cm deep for infants and 5 cm deep for children). To perform compressions in adults, place the heel of one hand in the center of the patient's chest and the heel of your other hand on the top of the first hand, interlock the fingers of your hands, and keep your arms straight and your shoulders directly over the patient's chest, all without leaning on the patient's ribs. Completely release the pressure without taking your hands off the chest; the duration of a compression and a release should be identical. In adults start with 30 chest compressions followed by 2 rescue breaths, then continue with chest compressions and rescue breaths, maintaining a ratio of 30:2 in nonintubated adult patients. In pediatric patients the optimum ratio of compressions to respirations is not clear, but the American Heart Association (AHA) guidelines propose 30:2 for a single rescuer and 15:2 when the second rescuer is available as reasonable suggestions.

8. Continue ventilation, giving mouth-to-mouth rescue breaths while pinching the patient's nose if more than one responder is available. In infants perform mouth-to-mouth-and-nose rescue breaths. A lone rescuer should focus on compressions and should avoid excessive interruptions of chest compressions to provide rescue breaths. One breath should last ~1 second (2 rescue breaths [inspiration plus expiration] should last <5 seconds). Make sure the chest rises during inspiration and allow for its complete fall during exhalation. Chest compressions should not be interrupted for

>10 seconds while rescue breaths are being delivered. If the rescue breaths are ineffective (ie, the chest does not rise), change the position of the head and jaw and repeat a maximum of 2 ventilation attempts.

9. Defibrillate using an automated external defibrillator (AED). Use an AED immediately when available. Defibrillation of a shockable rhythm within 3 to 5 minutes of a cardiac arrest can increase survival rates by up to 50% to 70%. For each minute that defibrillation is delayed, the likelihood of survival to hospital discharge is reduced by 10% to 12%. Switch on the AED and attach the pads to the chest (one below the right clavicle along the sternum and the other below and to the left of the left nipple in the midaxillary line: Figure 3.3-5). Keep away from the patient for the time the AED is assessing the rhythm and when the shock is being delivered. Charge the AED and trigger the shock whenever indicated by the AED. After 1 defibrillation immediately start CPR and continue for 2 minutes before the AED reevaluates the heart rhythm.

SYNCOPE

Syncope is a transient loss of consciousness caused by global cerebral hypoperfusion. It is characterized as a loss of postural tone with a rapid onset, short duration, and spontaneous recovery without neurologic deficits. **In presyncope** (a syncopal prodrome) the patient has a sensation of imminent loss of consciousness but true syncope does not occur.

Other causes of symptoms that can mimic syncope include sudden-onset conditions not associated with loss of consciousness, such as a fall or psychogenic pseudosyncope (appearance of a transient loss of consciousness in the absence of true loss of consciousness), or conditions associated with a partial or complete loss of consciousness not primarily related to cerebral hypoperfusion (metabolic disturbances [eg, hypoglycemia], hypoxia, hyperventilation with hypocapnia, seizure, drug or alcohol intoxication).

Initial Evaluation of a Patient with Syncope

1. Detailed and comprehensive history:

1) Context at the onset of symptoms: After standing; with dehydration (decreased oral intake, bleeding, diarrhea, vomiting); with drug administration (suggestive of an orthostatic cause); related to strong emotions like fear, pain, or sight of blood (vasovagal); related to specific situations such as micturition, defecation,

coughing, sneezing, or exercise (situational); on exertion; with head turning (carotid artery occlusion); or when supine.

2) Prodromal symptoms: Weakness, presyncope, visual blurring, diaphoresis, nausea, terminal warmth (vasovagal), palpitation, or lack of prodromal symptoms (cardiac).

3) Symptoms following the event: Rapid return of consciousness (cardiac) versus confusion, focal weakness, or delayed return to baseline (seizure).

4) Collateral history of the event: Appearance during the event, including the overall duration, presence of seizure symptoms, signs of pseudosyncope (slumping to the floor, lack of trauma, closed eyes, lack of diaphoresis).

5) Associated conditions: Primary autonomic failure (Parkinson disease, dementia with Lewy bodies, pure autonomic failure, multiple system atrophy) or secondary autonomic failure (diabetes mellitus, amyloidosis, spinal cord injuries, autoimmune autonomic neuropathy, paraneoplastic autonomic neuropathy, kidney failure); bradyarrhythmias such as sinus node dysfunction or heart block; tachyarrhythmias such as atrial fibrillation, long QT syndrome, Brugada syndrome, and other supraventricular tachyarrhythmias; structural heart disease like history of myocardial infarction and cardiomyopathy; valvular heart diseases like aortic stenosis; pulmonary embolism.

2. Physical examination:

1) Vital signs including orthostatic blood pressure and heart rate.

2) Neurologic examination: Screening examination for focal deficits. Examination of the lateral aspects of the tongue for signs of tongue biting indicating a seizure.

3) Cardiovascular examination: Jugular veins, enlarged/displaced apical beat, murmurs, bruits, signs of congestive heart failure.

4) Carotid sinus massage: Indicated in all patients aged >40 years with syncope of unknown origin compatible with a reflex mechanism. Carotid sinus hypersensitivity is defined as a ventricular pause lasting >3 seconds, a decrease in systolic blood pressure >50 mm Hg, or both. Check for carotid bruits before doing this manoeuver. Do not perform carotid sinus massage if bruits are present.

5) Other: Signs of pulmonary embolism such as parasternal heave, unilateral leg swelling, tenderness, and erythema.

3. Investigations:

1) 12-lead electrocardiography (ECG) is performed in all patients to look for signs of conduction disturbances, ischemia, preexcitation syndromes (long QT, delta wave, or Brugada syndrome [right bundle branch block with ST-segment elevation in leads V1-V3]).

2) Echocardiography is performed in patients with signs of possible structural heart disease including aortic stenosis, hypertrophic cardiomyopathy, pulmonary embolism, pulmonary hypertension, and ischemia.

3) Other investigations are used to identify etiology of the syncopal event as dictated by the history, physical examination, and ECG. These include tilt table testing (orthostatic hypotension), extended ECG monitoring and electrophysiologic study (arrhythmia-related cardiac syncope), and in-hospital video recording (seizure).

First Aid Guide

In the event of fainting, attempt the following self-care measures:

- If possible, try to prevent someone who is fainting from hitting the ground.
- Lay the person down on the ground, face up, and elevate his/her feet 8–12 inches.
- Loosen any constrictive clothing.
- Apply a cool, wet compress to the person's forehead.
- Attempt to keep the person from standing up until fully recovered.

DRUG-INDUCED HYPOGLYCEMIA

Drug-induced hypoglycemia is a plasma glucose level <3.9 mmol/L (70 mg/dL) regardless of symptoms of hypoglycemia. Symptoms may first appear in patients with lower blood glucose levels (eg, in those with long-standing well-controlled type 1 diabetes mellitus (DM) [hypoglycemia unawareness]) or in patients with blood glucose levels still >5.6 mmol/L (100 mg/dL) when the level has rapidly decreased, that is, in relative hypoglycemia.

Hypoglycemia is an important treatment-related complication of DM. Repeated episodes of hypoglycemia increase the risk of cardiovascular and all-cause mortality and hypoglycemia unawareness in diabetes.

Causes:

1) An excessively high dose of antidiabetic therapy (insulin, sulfonylureas, or meglitinides) in relation to food intake and physical activity levels.

2) Impaired physiologic mechanisms preventing hypoglycemia recognition, such as in autonomic dysfunction.

3) Decreased insulin or medication clearance, such as in patients with renal impairment.

4) Decreased endogenous glucose production (eg, after alcohol intake or in hepatic dysfunction).

5) Increased insulin sensitivity (eg, after a decrease in body weight, as a delayed effect of exercise, or as a result of improved diabetes control).

6) Erratic glucose control, such as in gastroparesis associated with diabetes and in patients with associated adrenal insufficiency.

Hypoglycemia classification:

1) **Level 1**: Blood glucose levels <3.9 mmol/L (70 mg/dL) and ≥3.0 mmol/L (54 mg/dL).

2) **Level 2**: Blood glucose levels <3.0 mmol/L (54 mg/dL), sufficiently low to indicate serious, clinically important hypoglycemia.

3) **Level 3** (defined by symptoms): A severe event characterized by altered mental and/or physical status requiring assistance of a third party for recovery. Repeated level 3 hypoglycemia may cause cognitive impairment in the long term.

Clinical features:

1) Autonomic symptoms: Dizziness, blurred vision, pallor, hunger, nausea, lightheadedness, palpitations, tremor, hunger, anxiety, and profuse perspiration are caused by sympathetic and vagal stimulation. These develop in patients with blood glucose levels of ~3.0 mmol/L (54 mg/dL).

2) Neuroglycopenic symptoms: Confusion, somnolence, dysarthria, abnormal coordination, atypical behavior, visual disturbances, migrant paresthesia, seizures, loss of consciousness, coma, and death. These symptoms may develop in patients with blood glucose levels <2.8 mmol/L (50 mg/dL), leading to glucose deficit in the central nervous system. They are usually seen in patients with level 3 hypoglycemia.

In some patients symptoms and signs of hypoglycemia may be absent despite very low glucose levels. This is referred to as **hypoglycemia unawareness**. Causes:

1) Autonomic nervous system dysfunction in patients with long-standing DM causes a loss of warning signs related to adrenergic stimulation. This leads to features of neuroglycopenia appearing without warning autonomic symptoms.

2) Other factors that increase the risk of hypoglycemia unawareness include repeated episodes of hypoglycemia, which may require temporary adoption of less

stringent criteria of glycemic control, and the use of certain drugs, for example, beta-blockers.

Acute Treatment

1. Level 1 and 2 hypoglycemia (conscious patients): Intake of fast-acting carbohydrates should be recommended at a blood glucose alert value of 3.9 mmol/L (70 mg/dL). Glucose (10-15 g) is the preferred treatment, although any foods or fluids that contain glucose (fruit juice, hard candy bar) will raise blood glucose levels; this may be repeated as necessary. Ingestion of fatty foods may delay and then prolong acute glycemic response. Subsequently, the patient should consume a meal or snack with complex (long-lasting) carbohydrates and added fat to prevent recurrent hypoglycemia (eg, bread, potatoes, cereal, nuts, peanuts). All patients, and particularly patients using insulin pumps or treated with insulin analogues as part of an intensive insulin therapy regimen, should consume 15 g of glucose and measure their blood glucose level after 15 minutes (the 15/15 rule; see Diabetes Mellitus); this should be repeated in case of persistent hypoglycemia. Glucagon should be prescribed for all individuals with level 2 hypoglycemia to have it available if needed.

2. Level 3 hypoglycemia (unconscious or impaired patients): In patients with altered mental status or those unable or unwilling to consume carbohydrates by mouth, administer 20% glucose (dextrose) IV solution (0.2 g of glucose/kg, even up to 80-100 mL of the solution; in Canada up to 50 mL of a 50% glucose solution is used), followed by an IV infusion of a 10% glucose solution until the mental status improves and the patient is able to tolerate oral carbohydrates.

In case of level 3 hypoglycemia in patients with DM in whom it is difficult to establish IV access, administer glucagon 0.5 to 1 mg as an IM or subcutaneous injection; if there is no improvement, repeat the injection after 10 minutes. There is a new intranasal formulation of glucagon available, called Baqsimi, which can also be used for level 3 out-of-hospital hypoglycemic episodes by care providers. Glucagon should be used with caution in patients with type 2 diabetes. Do not use glucagon in patients with hypoglycemia caused by sulfonylureas (as it may paradoxically stimulate the secretion of endogenous insulin and worsen the hypoglycemic episode). Glucagon is also contraindicated in patients with recent alcohol use.

ACUTE RESPIRATORY FAILURE

Acute respiratory failure develops suddenly (usually over hours or days to a few weeks) and is potentially reversible.

Anatomical approach to acute hypoxemia:

1) Diffuse lung parenchymal disease:

a) Pulmonary edema caused by increased hydrostatic pressure in the pulmonary vessels (left ventricular failure, fluid overload), increased permeability of the alveolar-capillary barrier (acute respiratory distress syndrome [ARDS]), drowning, lung reperfusion [after lung transplant or arterial embolectomy]); of unclear or complex mechanism (decompression [eg, pneumothorax], postobstructive [following the elimination of the cause of atelectasis], neurogenic, following stroke, after tocolytic therapy).

b) Alveolar bleeding: Vasculitis and connective tissue diseases (including anti-glomerular basement membrane disease [formerly known as Goodpasture syndrome]), disorders of hemostasis (particularly disseminated intravascular coagulation).

2) Focal lung parenchymal disease: Severe pneumonia, atelectasis (resulting from airway obstruction by a foreign body, tumor, or exudate), pulmonary contusion.

3) Pleural disease: Pneumothorax (particularly tension or large pneumothorax), massive pleural effusions.

4) Reduced pulmonary perfusion: Pulmonary embolism, shock.

Clinical features

1. Symptoms: Dyspnea is a relatively uniform finding in acute respiratory failure. Depending on the cause, the following may also occur: cough, fever, chest pain, hemoptysis, and other symptoms.

2. Signs include signs of acute hypoxia (cyanosis, tachycardia, tachypnea) and acute hypercapnia (headache, altered mental status) as well as signs of the underlying condition. In more advanced states the use of accessory respiratory muscles and paradoxical movements of the chest wall and abdomen may be observed. Paradoxical abdominal indrawing on inspiration suggests that respiratory collapse is imminent. Untreated acute respiratory failure can be fatal.

Diagnostic Tests

1. Pulse oximetry: Low oxygen saturation of hemoglobin (SpO2).

2. Blood tests:

1) Arterial blood gas analysis: Hypoxemia, hypercapnia (respiratory acidosis), and metabolic acidosis may be present in various combinations. Blood gas analysis provides measurement of blood pH, oxygen tension (PaO2), carbon dioxide tension (PaCO2), bicarbonate concentration, as well as SaO2, allowing interpretation of oxygenation, ventilation, and acid-base balance. While an arterial blood gas (ABG) sample accurately reflects oxygenation and pulmonary gas exchange, central venous blood is more accurate at detecting the acid-base status and hypercapnia at the tissue level if severe hypoperfusion is present (ie, circulatory failure). Peripheral venous blood gas (VBG) analysis is a simpler, less painful, and more convenient alternative to ABG. While it is likely sufficient to estimate arterial pH, VBG may not be sufficient to estimate arterial pCO2, especially at highly abnormal values. In the absence of circulatory failure or shock, venous pH, bicarbonate, and base excess have sufficient agreement with arterial values and, while the relationship between venous and arterial pCO2 remains to a degree unpredictable, it may still be of value as a screening test for arterial hypercapnia or to monitor changes in respiratory function.

2) Complete blood count (CBC) and biochemical tests: Abnormalities may suggest specific etiologies (eg, leukocytosis, anemia, or eosinophilia; elevated serum brain natriuretic peptide or troponin, elevated D-dimers).

3. Microbiology: Because acute respiratory failure is frequently caused by infections, attempt to identify the etiologic agent (microbiological tests of respiratory secretions [eg, during flexible bronchoscopy], blood, or other clinically relevant material).

4. Imaging studies:

1) Plain chest radiography: Specific abnormalities may suggest the etiology (eg, various patterns of interstitial or air-space opacification in the lungs, volume loss, pneumothorax, pleural effusion).

2) Chest ultrasonography or computed tomography (CT) may further help in delineating the etiology of acute respiratory failure.

5. Electrocardiography (ECG) may reveal features of myocardial ischemia or pulmonary hypertension.

Treatment

1. Clearing the upper airway, as the situation requires: Noninstrumental; insertion of an oropharyngeal tube or other device; intubation; cricothyrotomy;

tracheostomy (the procedure of choice in patients with massive laryngeal edema or prolonged mechanical ventilation).

2. Oxygen therapy with a fraction of inspired oxygen (FiO2 100%) as required. Consider the possibility of hypoxic respiratory drive in chronic lung diseases. Consider oxygen supplementation with a lower FiO2 or a lower target of arterial oxygenation, because a higher FiO2 or higher target of oxygenation may increase the rates of mortality and serious adverse events.

3. High-flow nasal cannula compared with conventional oxygen therapy in the setting of acute hypoxemic respiratory failure decreases the need for noninvasive or invasive ventilation. There is some evidence that it may be preferred to noninvasive ventilation maneuver in such situations.

The ratio of SpO2 measured by oximeter to FiO2 (higher levels indicate less hypoxia) divided by RR is kown as the ROX index and may be of some use in estimating risk of failure of therapy. A ROX of ~5 provides the best cutoff.

4. Treatment of the underlying condition: Pharmacologic (eg, epinephrine for anaphylaxis, bronchodilators, antibiotics) or invasive (eg, decompression of pneumothorax, thoracentesis).

5. Mechanical ventilation:

1) Noninvasive positive pressure ventilation should be an early consideration for patients with an acute exacerbation of COPD or cardiogenic pulmonary edema (in the absence of shock or an acute coronary syndrome). It may also be beneficial in other situations of acute respiratory failure.

2) Invasive mechanical ventilation may be required.

3) When a patient no longer requires invasive mechanical ventilation, there is some evidence that the use of high-flow nasal cannula alternating with noninvasive ventilation may prevent postextubation respiratory failure in patients at high risk of extubation failure (aged >65 years, with underlying chronic heart or lung disease).

6. Respiratory physiotherapy, including postural drainage.

7. Nutrition support to prevent malnutrition.

FIRST AID FOR SEVERE BLEEDING

Severe bleeding demands special attention that can mean the difference between life and death. Scrapes, cuts, amputations and puncture wounds can all result in uncontrolled bleeding, which can quickly develop into a life-threatening situation.

While you wait for medical help to arrive, follow these steps to increase the person's chances of survival:

1. If at all possible, wash your hands or put on latex gloves before attempting to aid the person.
2. Have the person lie flat and cover him or her to prevent loss of body heat.
3. If possible, elevate the legs and/or the wound.
4. Remove dirt or debris from the wound, but leave large or deeply embedded objects in place.
5. Apply pressure to the wound until it stops bleeding. Use a clean cloth or bandage to apply 20 minutes of continuous pressure before looking to see if the bleeding has subsided.
6. Don't remove the bandage or gauze, even if blood is seeping through. Instead, simply apply more bandages over the top.
7. If necessary, apply pressure to the main artery delivering blood to the wound. For arm wounds, target the area inside the arm just below the armpit or right above the elbow. For leg wounds, target the area in the groin or just behind the knee.
8. Once you've stopped the bleeding, immobilize the body part and leave bandages in place until the person receives medical attention.

PROMPT MEDICAL HELP OF INTERNAL BLEEDING

1. Check for danger before approaching the person.
2. If possible, send someone else to call triple zero (000) for an ambulance.
3. Check that the person is conscious.
4. Lie the person down.
5. Cover them with a blanket or something to keep them warm.
6. If possible, raise the person's legs above the level of their heart.
7. Don't give the person anything to eat or drink.
8. Offer reassurance. Manage any other injuries, if possible.
9. If the person becomes unconscious, place them on their side. Check breathing frequently. Begin cardiopulmonary resuscitation (CPR) if necessary.

ANAPHYLAXIS AND ANAPHYLACTIC SHOCK

Anaphylaxis is a severe, life-threatening, generalized or systemic rapid-onset hypersensitivity reaction (allergic or nonallergic).

Anaphylactic shock is a severe rapidly progressing anaphylactic reaction (anaphylaxis) resulting in a life-threatening drop in blood pressure.

The most frequent causes of anaphylaxis:

1) Allergic:

a) Drugs: Most commonly beta-lactam antibiotics, paralytic drugs, barbiturates, biologic drugs, and cytotoxic agents.

b) Hymenoptera venoms (honeybee, bumblebee, yellow jacket, hornet, fire ant).

c) Proteins administered via parenteral routes, including blood and its products, enzymes (eg, streptokinase), sera (eg, tetanus immunoglobulin), allergens used for in vivo diagnosis and immunotherapy.

d) Foods: In adults most commonly fish, seafood, peanuts, cow's milk, chicken egg, and mammalian meat proteins (delayed anaphylaxis may occur 3-6 hours after consumption of mammalian meat products, eg, beef or pork).

e) Inhaled allergens, for instance, animal dander.

f) Latex.

g) Dialysis membranes sterilized with ethylene oxide.

h) Vaccines.

i) Disinfectants from the biguanide group (eg, chlorhexidine).

2) Nonallergic:

a) Direct release of mediators from mast cells: Opioids, muscle relaxants, colloids (eg, dextran, hydroxyethyl starch, human albumin), hypertonic solutions (eg, mannitol), physical exercise, low temperature.

b) Immunologic complexes: Blood and its products, immunoglobulins, animal sera, vaccines, dialysis membranes.

c) Alterations of arachidonic acid metabolism: Hypersensitivity to acetylsalicylic acid (ASA) and other nonsteroidal anti-inflammatory drugs (NSAIDs).

d) Histamine and tyramine present in foods (this makes an anaphylactic reaction more severe).

e) Other mechanisms: Radiologic contrast media, food contaminants and preservatives, or unknown causes.

Risk factors for anaphylaxis include a previous episode of anaphylaxis and re-exposure to the triggering factor (beta-lactam antibiotics, hymenoptera venoms, radiographic contrast agents), adult age, female sex (anaphylaxis is more common and severe in women than in men), atopy, allergen entry site (after administration of the antigen parenterally, especially IV, reactions are frequent and severe), mastocytosis, mast cell and basophil activation syndromes, simultaneous exposure to

the allergen administered parenterally and occurring in the environment (eg, allergen immunotherapy during the pollen season), medical procedures (eg, administration of diagnostic agents, in vivo tests, provocation tests, surgery under local or general anesthesia).

The most common causes of anaphylaxis in adults are drugs (~35%), food (~30%), and insect venoms (20%), while in children, food (70%), insect venoms (20%), and medications (7%). In ~30% of adults and ~15% of children, the cause of anaphylaxis (idiopathic) cannot be identified. Occasionally anaphylaxis requires ≥2 factors (eg, exposure to the sensitizing allergen and exercise) to be close in time for anaphylaxis to occur.

Clinical features and natural history

Signs and symptoms of anaphylaxis most often occur within seconds or minutes of exposure to a trigger (although in some cases they may develop later, even after several hours):

1) Skin and subcutaneous tissue: Urticaria/angioedema and erythema occur in up to 90% of patients.

2) Respiratory system: Upper airway edema, hoarseness, stridor, cough, wheezing, respiratory compromise, rhinitis.

3) GI system: Nausea, vomiting, abdominal pain, diarrhea.

4) Systemic reactions: Hypotension and other symptoms of shock occur in 30% of patients; they may occur simultaneously with other signs and symptoms of anaphylaxis or (usually) develop shortly after their onset.

5) Less frequent: Dizziness or headache, uterine cramps, anxiety, feeling of impending doom.

The more rapidly the symptoms develop, the higher the risk of severe and life-threatening anaphylaxis; however, it should be noted that symptoms that are initially mild (eg, limited to the skin and subcutaneous tissue) may also rapidly become life-threatening if adequate treatment is not started promptly. Delayed or biphasic reactions may occur, with symptoms developing or relapsing over 3 to 8 hours. Symptoms of anaphylaxis may last for hours or even days despite adequate treatment.

Signs and symptoms of anaphylactic shock (regardless of the trigger) include cold and pale skin, sweating, collapsed subcutaneous veins, hypotension, tachycardia, oliguria or anuria, loss of bowel control, and loss of consciousness. Circulatory arrest may occur.

Diagnosis

According to the 2011 World Allergy Organization guidelines, anaphylaxis is highly likely when any of the following **criteria is fulfilled:**

1) Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, urticaria, itching, lips-tongue-uvula edema), which is accompanied by either (or both):

a) Respiratory compromise (eg, dyspnea, stridor, wheeze-bronchospasm, hypoxemia).

b) Reduced blood pressure or associated symptoms of end-organ dysfunction (eg, hypotonia, syncope, incontinence).

2) Exposure to a likely allergen for a patient is rapidly **followed by ≥2 of the following** (within minutes to several hours):

a) Involvement of the skin-mucosal tissue (eg, urticaria, itching, lips-tongue-uvula edema).

b) Respiratory compromise (eg, dyspnea, stridor, wheeze-bronchospasm, hypoxemia).

c) Reduced blood pressure or associated symptoms (eg, hypotonia, syncope, incontinence).

d) Persistent GI symptoms (crampy abdominal pain, vomiting).

3) Decreased blood pressure following exposure to a “known allergen” (within minutes to several hours):

a) Infants and children: Low systolic pressure (age-related) or a decrease >30% in systolic blood pressure (in children low systolic blood pressure is defined as <70 mm Hg from 1 month to 1 year; <[70 mm Hg + 2 × age] from 1-10 years; and <90 mm Hg from 11-17 years).

b) Adults: A systolic blood pressure <90 mm Hg or >30% compared with baseline.

Infants are more likely to have respiratory compromise than hypotension or shock, and in this age group, shock is more likely to be manifested initially by tachycardia than by hypotension.

Diagnostic Tests

1. Assays measuring levels of histamine or methylhistamine are not widely available, not specific for anaphylaxis, and not routinely used.

2. Assaying **total tryptase levels** has become more common. Tryptase should be measured within 2 hours of the onset of symptoms and then repeated 24 hours

after the symptoms have resolved to get a basal level. The minimal elevation in the acute total tryptase level that is considered to be clinically significant has been suggested as ≥2 + 1.2 × baseline tryptase levels. However, tryptase may not be elevated in a third of patients and its usefulness in excluding diagnosis is thus limited, if any.

3. Where there is a clear causative agent, it is best to simply avoid exposure rather than confirm the cause by performing a challenge test. Often sensitivity may be lost over time, and where alternative agents cannot be used, cautious challenge under close observation and after a full discussion with the patient could be considered. Such an attempt to establish the allergic cause of anaphylaxis with skin tests should be made, if considered essential, no earlier than 3 to 4 weeks after the episode. Generally, challenge tests are not recommended after anaphylactic shock. Assessing the levels of IgE specific to suspected allergens may be helpful.

Immediate Treatment

1. Assess airway, breathing, circulation (ABC), and level of consciousness. Establish and maintain the airway if necessary. In case of respiratory or cardiac arrest, start cardiopulmonary resuscitation (see Cardiac Arrest). In patients with stridor or significant edema of the face and upper airways (tongue, oral and throat mucosa, hoarseness), consider immediate endotracheal intubation. If delayed, it may be progressively more difficult, and unsuccessful intubation attempts may further aggravate the edema. If the edema causes life-threatening airway obstruction and attempts of endotracheal intubation have been unsuccessful, perform cricothyroidotomy.

2. Stop exposure to the suspected antigen (eg, stop infusion of a drug or blood transfusion).

3. Call for help.

4. **Administer epinephrine as soon as possible once anaphylaxis is recognized (or even suspected)**:

1) In patients with a history of anaphylaxis who carry an epinephrine autoinjector, immediately administer 1 dose of IM epinephrine in the lateral thigh in case of even minor symptoms suggestive of anaphylaxis.

2) In patients without cardiac arrest, **administer IM epinephrine in the lateral thigh in a dose of 0.01 mg/kg of a 1:1000 (1 mg/mL) solution to a maximum of 0.5 mg in adults (0.3 mg in children weighing >25 kg).**

Record the time of injection and repeat in 5 to 15 minutes as necessary. Most patients respond to 1 to 2 doses. Patients who do not respond to an IM injection of epinephrine and fluid resuscitation (shock is imminent or has already developed) should receive epinephrine in a slow IV infusion; the dose should be titrated on the basis of the effect of treatment on blood pressure assessed using continuous noninvasive monitoring. In adults the starting dose is 1 to 10 microg/min in an IV infusion (0.1 mg/mL; 1:10,000 solution contains 100 microg/mL or 1000 microg in a 10-mL syringe). Do not use IV epinephrine bolus (unless required during cardiac arrest).

5**. Place the patient on the back,** or in a different position of comfort and safety if there is respiratory distress or vomiting, and elevate the lower extremities, as this may be helpful in the management of hypotension. Do not let the patient sit or stand up suddenly or be placed in an upright position.

6. Administer oxygen 6 to 8 L/min via a face mask. This is indicated in patients in whom it was necessary to administer several doses of epinephrine, patients with respiratory distress, signs and symptoms of myocardial ischemia, or chronic diseases of the respiratory system.

7. Establish peripheral IV access with 2 large-bore needles (optimally ≥1.6-1.8 mm [16-14 gauge]) and use infusion kits allowing for rapid fluid administration.

8. Administer IV fluids: In patients with a substantial decrease in blood pressure who do not respond to IM epinephrine, administer a rapid IV infusion of 1 to 2 L of isotonic crystalloid (eg, in adults 5-10 mL/kg of 0.9% saline over the first 5 to 10 minutes [10 mL/kg in children]).

9. Monitor blood pressure and, depending on the clinical situation, also electrocardiography (ECG), oxygen saturation (SpO2), or arterial blood gases.

LIST OF FINAL CONTROL QUESTIONS

Basic symptoms and syndromes of diseases of the internal organs

1. Syndrome of pulmonary tissue compaction: causes, clinical, laboratory and instrumental methods of diagnosis.
2. Pulmonary airflow syndrome: causes, clinical , laboratory and instrumental methods of diagnosis.
3. Syndrome of accumulation of fluid in the pleural cavity: causes, clinical, laboratory and instrumental methods of diagnosis.
4. Syndrome of accumulation of air in the pleural cavity: causes, clinical, laboratory and instrumental methods of diagnosis.
5. Bronchial obstruction syndrome: causes, clinical, laboratory and instrumental methods of diagnosis.
6. Heart pain syndrome: etiology, pathogenesis, clinical, laboratory and instrumental methods of diagnosis.
7. Heart failure syndrome: etiology, pathogenesis, classification, clinical, laboratory and instrumental methods of diagnosis.
8. Vascular insufficiency syndrome: etiology, pathogenesis, clinical, laboratory and instrumental methods of diagnosis.
9. Hypertension syndrome: etiology, pathogenesis, clinical, laboratory and instrumental methods of diagnosis.
10. Dyspeptic syndrome: etiology, pathogenesis , clinical, laboratory and instrumental methods of diagnosis.
11. Dysphagic syndrome; etiology, pathogenesis, clinical, laboratory and instrumental methods of diagnosis.
12. Types of dyskinesia of the biliary tract: the main clinical manifestations, laboratory and instrumental methods of diagnosis.
13. Portal hypertension syndrome: etiology, pathogenesis, clinical, laboratory and instrumental methods of diagnosis.
14. Jaundice syndrome: etiology, pathogenesis, clinical, laboratory and instrumental methods of diagnosis.
15. Syndrome of gastrointestinal bleeding: etiology, pathogenesis, clinical, laboratory and instrumental methods of diagnosis.

16. Nephrotic syndrome: etiology, pathogenesis, clinical, laboratory and instrumental methods of diagnosis.

17. Urinary syndrome: etiology, pathogenesis, clinical, laboratory and instrumental methods of diagnosis.

18. Syndrome of acute renal failure: etiology, pathogenesis, clinical, laboratory and instrumental methods of diagnosis.

19. Chronic renal failure syndrome: etiology, pathogenesis, clinical , laboratory and instrumental methods of diagnosis.

20. Anemic syndrome; etiology, pathogenesis, clinical, laboratory and instrumental methods of diagnosis.

21. Hyperplastic syndrome in diseases of the hematopoietic organs: etiology, pathogenesis, clinical, laboratory and instrumental methods of diagnosis.

22. Hemorrhagic syndromes: classification, pathogenesis, clinical and laboratory methods of diagnosis.

23. Hyperthyroid syndrome: the main causes, clinical manifestations, laboratory and instrumental methods of diagnosis.

24. Hypothyroidism : the main causes, clinical manifestations, laboratory and instrumental methods of diagnosis.

TASKS FOR FINAL CONTROL

Basic symptoms and syndromes of cardiovascular diseases

1. The main ECG sign of intraventricular block:
   A. Extending the P-Q interval;
   B. The increase in the QRS complex with deformation
   C. The increase in the QRS complex without deformation
   D. Reducing the length of the P-Q segment
   E. S-T segment displacement
2. What ECG interval is used to determine heart rate?
   A. P-Q;
   B. QRS;
   C. QRST;
   D. R-R;
   E. P-P.
3. What registers R-R interval on ECG?
   A. intraatrial conductivity;
   B. intraventricular conduction;
   C. atrioventricular conduction;
   D. ventricular systole;
   E. duration of cardiac cycle.
4. What is normal heart rate?
   A. 30-40 for 1 minute;
   B. 40-60 for 1 minute;
   C. 60-80 C. for 1 minute;
   D. 80-100 for 1 minute;
   E. 90-110 for 1 minute.
5. What registers R wave on ECG?
   A. Excitation of atria;
   B. Excitation of ventricles;
   C. atrial systole;
   D. ventricular systole;
   E. Excitation of Hiss bundle.
6. What conductavity registers complex QRS?
   A. atrioventricular;
   B. intraatrial;
   C. Intraventricular;
   D. The conductivity of the left Hiss bundle branch;
   E. Conductivity on the right Hiss bundle branch.
7. What registers T wave on the ECG?
   A. Excitation of atria;
   B. Excitation of ventricles;
   C. Reduction fibrillation;
   D. Shifting of electrical axis of the heart;
   E. ventricular repolarization.
8. In which lead wave P must always be negative?
   A. I standard;
   B. II standard;
   C. III standard;
   D. AVR;
   E. AVF.
9. I standard registers mostly potential of:
   A. Right atrium;
   B. Right ventricle;
   C. Anterior wall of the left ventricle;
   D. Interventricular septum;
   E. posterior wall of the left ventricle.

10. W standard allotment registers mostly potential:

A. Right atrium;
B. Right ventricle;
C. Anterior wall of the left ventricle;
D. Interventricular septum;
E. posterior wall of the left ventricle.

Answers

1	2	3	4	5	6	7	8	9	10
B	D	E	C	A	C	E	D	C	E

Main diagnostic methods of the examination of the digestive system. Basic syndromes in the gastroenterology

1. The patient, 38 years has arrived with complaints to difficulty of swallowing of firm food, vomiting, decrease in body weight. In the anamnesis - a poisoning with a alkali. Inspection: pallor skin, an exhaustion. At superficial palpation the abdomen is soft and painless. What organ defeat it is possible to think of?

A. Stomach
B. Pancreas
C. Oesophagus
D. Intestines
E. Liver

2. The patient, 33 years complaints to a heartburn, a pain in epigastrium that arises right after food, tarry [currant jelly] stool during 2 days, fainting fit, weakness. In the anamnesis - a stomach ulcer. Inspection - pallor skin. What complication is it possible to think of?

A. Perforation
B. Penetration
C. Malignization
D. A bleeding
E. Pilorostenosis

3. Patient P. 60 years is disturbed heavy sense epigastral site, with disgust for meat food, vomiting by the food eaten on the eve, decrease in body weight. In the anamnesis - a stomach. Inspection: - pallor skin, the expressed growing thin, above left clavicle a dense lymph nod is palpate. Detonation of abdomen wall in epigastral site is determined. At palpation in epigastral site it is more than stomach to the left of a median line, palpable formation in the size 3x4 cm. Your previous

diagnosis?

A Pilorostenosis

B. Bleeding.

C. Stomach cancer

D. Atrophic gastritis

E. Ulcer

4. The patient, 42 years, complains of dyspnea, increase of abdomen. In the anamnesis - abusing alcohol. Abdomen inspection – is increased, umbilicus is protruding by formation of a hernia, - behind the umbilicus « the head of a jellyfish». Your diagnostic assumptions?

A. Flatting

B. Obesity

S. Tumor

D. Ascitis

E. Cyst

5. The patient, 48 years, complains of weight in right hypochondrium, increase abdomen. During 10 years suffers on chronic persistent hepatitis. At abdomen inspection in vertical position -is loose-hanging, umbilicus is protruding a little. In horizontal position detonation of lateral departments abdomen is marked. Your diagnostic assumptions?

A. Flatting

B. Obesity

S. Tumor

D. Ascitis

E. Cyst

6. The patient, 70 years has arrived in clinic with complaints on sharp knife-like pain in the top of the abdomen that has appear after rise heavy. In the anamnesis - a stomach ulcer during 4 years. Inspection. Position of the patient is forced - lays with the pressed to a breast legs, features are aggravated, pale skin, covered sticky then. Superficial palpation: the poured pressur of abdomen wall muscles, sharp painess in epigastral part is marked. What pathology is it possible to think of?

A. Stomach ulcer exacerbation

B. Ulcer perforation

C.Acute cholecystitis

D. Peritonitis

E. Bleeding

7. The patient, 35 years complains of a pain in epigastrium, that appears in 30 minutes after food, a heartburn, decrease of appetite, tarry [currant jelly] stool. The anamnesis. 4 year of stomach ulcer. The beginning of disease connects with stress, an aggravation during the autumn-spring period. Inspection tongue is covered by white patch near root. Superficial palpation: moderate plainness in epigastral part. Your diagnostic assumptions?

A. Ulcer penetration

B. Ulcer perforation

C. Ulcer malignization

D. Peritonitis

E. Bleeding

8. The patient, 70 years, has arrived in clinic with complaints to a constant pain and sensation of spreading in paraumbilical site that amplify after reception even a small amount of food. The simplification comes after vomiting. In the anamnesis - stomach ulcer. Last aggravation about three months ago. Inspection – skin is dry, the patient of lowered feed, visible peristaltics of stomach in the form of deep waves which go from left hypochondrium to right is determined. Your diagnosis?

A. Flatting

B. Perforation

C. Pilirostenosis

D. Ascitis

E. Tumor of stomach

9. The patient, 19 years, complains on colicky [cramping] pain that arises after fat food and attend by heartburn, an eructation sour. Objectively: tongue is densely imposed white patch. At palpation – moderate painness in epigastrium. Your diagnosis?

A. Atrophy gastritis

B. Stomach ulcer

C. Calculous cholecystitis

D. Chronic gastritis

E. Pilorostenosis

10. Patient, 35 years, complains of a pain in epigastrium that arises shortly after food, faintness. An eructation, stool instability. Diseases developed gradually, first attributes has been appears about three years ago. Inspection: patient is satisfactory fatness, tongue is imposed white patch, crude with reflections teeth on edges. Moderate palpatory tenderness is defined at epigastric region. Your previous diagnosis?

A. Acute gastritis

B. Chronic cholecystitis

C. Stomach ulcer

D. Chronic pancreatitis

E. Chronic gastritis

Answers

1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
C	D	C	D	D	B	E	C	D	E

Main methods of the examination of the urinary system. Basic syndromes in the nephrology. The edema syndrome

1. A 20-year old patient developed edema of the face, pain in the lumbar area 3 days after tonsillitis. Changes in the urine were revealed. Which system can be involved?

A. Nervous

B. Respiratory
C. Cardiovascular
D. Genitourinary
E. Digestive

2. A 50-year old patient has been suffering from kidney disease for 15 years. Examination revealed paleness, dryness of the skin, ammonia odor from the mouth, the pupils are narrow. What diagnosis can be supposed?

A. Uremia
B. Atropine poisoning
C. Myxedema
D. Thyrotoxicosis
E. Itsenko-Cushing syndrome

3. Morning edema of the face is typical in:

A. Pericarditis
B. Acute glomerulonephritis
C. Heart failure
D. Liver cirrhosis
E. Thyrotoxicosis

4. The patient, 19 years, the mechanic, complains of a blunt pain in right lumbar region, frequent urination, rising temperature up to 37,8◦C. A condition become worth 2 days ago after overcooling. At the review a lumbar site symmetric, skin hyperemy, oedema are absent. Positive Pasternaysky symptom. Your previous diagnosis?

A. Acute pyelonephritis
B. Acute glomerulonephritis
C. Acute cystitis
D. Intercostal neuralgia
E. Nephrotic syndrome

5. The patient, 22 years, complains of face and eyelid oedema, general weakness, rise in temperature of a body up to 37,2C. Anamnesis: was ill sharply, 2 weeks ago has carried quinsy. Inspection: face is pale, bloated, eyelid oedema, shins and fingers of hands. Arterial pressure is 140/95 mm hg. Pasternatsky symptom is negative from both sides. Your suggested diagnosis?

A. Acute pyelonephritis
B. Acute glomerulonephritis
C. Acute cystitis
D. Intercostal neuralgia
E. Nephrotic syndrome

6. Leukocyteuria is more typical for:

A. Tumor of urine bladder
B. Paranephritis
C. Pyelonephritis
D. Acute glomerulonephritis
E. Renal amiloidosis

7. Presence of unchanged erhythrocytes in urine is typical for the patients with:

A. Acute pyelonephritis
B. Chronic pyelonephritis
C. Glomerulonephritis
D. Nephrotic syndrome
E. Urethritis

8. Positive Pasternatsky' syndrome is typical for the patients with:

A. Acute glomerulonephritis
B. Chronic glomerulonephritis
C. Uremia
D. Cystitis
E. Renal colics

9. For the patients with Chronic glomerulonephritis is typical following changes in the urine:

A. Leukocyteuria and proteinuria
B. Cylindruria and leukocyuria
C. Hematuria and leukocyteuria
D. Proteiunuria and hematuria
E. Leukocyteuria and hematuria

10. What isPolyuria ?

A. arbitrarily defined as the production by an adult of less than 500 ml of urine/24h.
B. traditionally defined as frequent, more than 6 times a day, urination.
C. defined as complete absence of urine secretion and/or excretion.
D. describes the excretion of larger than normal volume of urine (exceed 2l/24 h).
E. is defined as passing of more than one-third of the total 24-h urine volume by night.

Answers

1	2	3	4	5	6	7	8	9	10
D	A	B	A	B	C	C	A	B	D

Main methods of examination of the hematopoietic system. The interview and the examination of patients with the disorders of the hematopoietic system

1. Iron deficiency anaemia is characterized by the following:

A. Hypochromia, microcytosis, sideroblasts in the sternal punctate;
B. Hypochromia, microcytosis, target-like erythrocytes;
C. Hypochromia, microcytosis, elevated iron-binding capacity of serum;
D. Hypochromia, microcytosis, reduced iron-binding capacity of serum;
E. Hypochromia, microcytosis, positive Desferal test.

2. Which abdominal organ is often enlarged in the case of diseases of the hematopoietic system?

A. Pancreas
B. Spleen
C. Stomach
D. Left kidney
E. Right kidney

3. Which test should be used to diagnose haemophilia?

A. coagulation time;
B. determination of bleeding time;
C. plasminogen.
D. Desferal test
E. fibrinogen

4. The reference range of erythrocytes in the healthy individual is as the following:

A. 2.0-3.0 $x10^{12}$ / l
B. 3.9-5.0 x 10^{12} / l

C. 5.0-6.0 x10^{12} / l

D. 3.0-3.9 x10^{12} / l

E. 10.0 x10^{12} / l

5. The hemolysis is defined by the following:

A. reduced leukocytes in the peripheral blood

B. elevated bilirubin in the blood

C. reduced leukocytes in the peripheral blood

D. elevated ESR

E. elevated basophils in the blood

6. Where are blood cells formed?

A. In the liver

B. In the spleen

C. In the bone marrow

D. In the lymph nodes

E. In the thymus

7. The leukocyte formula is described as the following:

A. elevated leukocytes in the peripheral blood

B. elevated lymphocytes in the peripheral blood

C. elevated band-shaped neutrophils and juvenile neutrophils in the peripheral blood

D. the ratio of particular types of leukocytes

E. low leukocytes in the peripheral blood

8. Which lymph nodes are enlarged in the case of haematological diseases?

A. only axillary

B. axillary and anterior cervical

C. occipital

D. all palpable lymph nodes

E. inguinal

9. Which bones should be punctured to obtain the bone marrow sample?

A. frontal

B. the shin

C. IV thoracic vertebra

D. the sternum

E. ribs

10. Reticulocytosis in the peripheral blood may be a sign of the following:

A. Lymphogranulomatosis

B. Haemophilia

C. Haemolytic anaemia

D. Werlhof's disease

E. Myeloma disease

Answers

1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
C	B	A	B	B	C	D	D	D	D

Basic syndromes in the hematology. Changes in the oral cavity in diseases of the hematopoietic system

1. The erythraemia is distinguished from the erythrocytosis by the following:
   A. thrombocytopenia;
   B. elevated alkaline phosphatase in neutrophils;
   C. elevated basophils;
   D. all of mentioned above;
   E. options B and C.

2. Chronic myeloid leukaemia is characterised by the following:
   A. the onset in patients with acute myeloblastic leukaemia;
   B. refers to myeloproliferative diseases;
   C. is characterised by pancytopenia;
   D. elevated basophils;
   E. no correct option

3. The Philadelphia chromosome in patients with leukaemia is characterised as the following:
   A. a mandatory sign of the disease;
   B. is found only in granulocytes;
   C. is found only in progenitor cells of the megakaryocytic lineage;
   D. is found only in the myeloid lineage;
   E. no correct option

4. Treatment of subleukemic myelosis consists in the following:
   A. begins just after making the diagnosis;
   B. cytostatics are prescribed in the combination with prednisolone;
   C. the mandatory radiation therapy;
   D. the splenectomy is not indicated;
   E. correct options C and D.

5. Chronic lymphocytic leukaemia is characterised by the following:
   A. the most common type of heamoblastosis;
   B. the benign clinical course;
   C. occurs in elderly and advanced ages, mostly does not require cytostatic therapy;
   D. does not require cytostatic therapy
   E. all of mentioned above.

6. Which form of chronic lymphocytic leukaemia is characterised by significantly enlarged lymph nodes with low leucocytosis?
   A. with splenomegaly;
   B. classical;
   C. benign;
   D. with the bone marrow involvement;
   E. tumorous.

7. Which complications are typical for chronic lymphocytic leukaemia?

A. thrombotic;
B. infectious;
C. bleeding;
D. hepatic failure;
E. no correct options.

8. The patient X. has the daily proteinuria of more than 3.5 m, the positive Bence-Jones protein and the hyperproteinaemia. Which clinical condition should be suspected?

A. the nephrotic syndrome;
B. myeloma disease;
C. Waldenström's macroglobulinemia;
D. acute lymphocytic leukaemia;
E. chronic lymphocytic leukaemia.

9. The syndrome of increased viscosity in myeloma is characterized by the following:

A. the mucous membranes bleeding;
B. the proteinuria;
C. the dyslipidaemia;
D. the hyperbilirubinemia;
E. correct B and C.

10. The hypercalcemia in the case of myeloma is characterized by the following:

A. associated with the myeloma osteolysis;
B. decreases with the azotemia;
C. does not have a negative impact on the renal tubular system;
D. a secondary reaction of kidneys;
E. all of mentioned above.

11. Lymphogranulomatosis is characterised by the following signs:

A. the selective involvement of lymph nodes;
B. the early lymphocytopenia;
C. positive Berezovsky-Sternberg cells in biopsies;
D. correct A and B;
E. all of mentioned above.

Answers

1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
B	B	C	B	B	E	B	B	A	A	C

Main methods of the examination of the endocrine system. Laboratory and instrumental research methods of the endocrine system. Basic syndromes in the endocrinology

1. A 35-year-old woman has a one-year history of an arterial hypertension with hypertensive crisis. She was not treated. After an intense house work she felt the fear, excitement, palpitation, intense headache, chest and abdominal pains, the low back pain, frequent urinations, the nausea, and vomiting. Upon the physical examination: her skin was moist, the face was pale, the pulse was regular with the rate of 170 beats/min; her heart sounds were normal; the blood pressure was 220/110 mmHg. Laboratory tests revealed the blood sugar 7.2 mmol/l, leucocytosis, and erythrocytosis. What was the preliminary diagnosis?

A. Pheochromocytoma's crisis;
B. The hypertensive crisis;
C. Myocardial infarction;
D. The thyrotoxic crisis;
E. The hypothalamic crisis.

2. On a regular medical check-up a 28-year-old woman was diagnosed with the arterial hypertension. During the deep abdominal palpation, the patient noticed the acute diffuse abdominal pain, nausea, vomiting, headache, agitation, feeling of fear, irritability, sweating, palpitations, and paraesthesia. Upon the physical examination: her skin was pale, moist; her pupils were dilated; the pulse was regular with the rate of 160/min, her heart sounds were normal; the blood pressure was 220/120 mmHg. Laboratory tests revealed the blood sugar 8.00 mmol/l and leucocytosis. She was given a nifidipine tablet SL without a positive effect. Which drug should be prescribed as an emergency?

A. Phentolamine.
B. Papaverine.
C. Furasemid.
D. Verapamil.
E. Anaprilin.

3. A 48-year-old man had a three-years history of the arterial hypertension with the reference range of blood pressure 220/120–240/140 mmHg. The hypotensive therapy was ineffective. He presented complaining for a muscle weakness, dry mouth, polyuria, and headache. Laboratory tests revealed the sodium of 155 mmol/l and potassium of 3.6 mmol/l. Which was the likeliest cause of the arterial hypertension?

A. Primary hyperaldosteronism
B. Pheochromocytoma
C. Hypertensive heart disease
D. The renal hypertension

E. Itsenko-Cushing's disease

4. A 36-year-old woman complained of the headache, muscle weakness, periodic jerks, episodes of acute general weakness, thirst, polyuria, and increased blood pressure. She had been unwell for 2 years. Upon the physical examination: her height was 170 cm, her body weight was 68 kg, her pulse was 78 beats/min, regular; her heart sounds were muffled, with the II tone's accent over the aorta, her blood pressure was 170/100 mmHg, no oedema. Laboratory tests revealed the potassium of 2.9 mmol/l, sodium of 158 mmol/l, blood glucose of 5.3 mmol/l; the urinalysis - the alkaline reaction, protein was 0.033 g/l, l-3-4 in view; hypoisostenuria. What was the preliminary diagnosis?

A. Primary hyperaldosteronism.
B. Hypertensive disease.
C. Chronic pyelonephritis.
D. Itsenko-Cushing's disease.
E. Pheochromocytoma.

5. A 32-year-old woman complained of the dizziness, headache, palpitations, and tremors. For several months she had been under the family doctor's supervision due to her high blood pressure. Gradually, such attacks had become more frequent and more severe. Upon the physical examination: her skin was sweaty and sticky, with limbs' tremors; her heart rate was 110/min, the blood pressure was 220/140 mmHg; her heart tones were weak. Laboratory tests revealed leukocytes of 9.8×10^9/l, ESR of 22 mm/h, the blood glucose of 9.8 mmol/l. Which was the likeliest cause of the crisis?

A. Diabetic glomerulosclerosis;
B. Hypertensive heart disease;
C. Preeclampsia;
D. Primary hyperaldosteronism;
E. Pheochromocytoma.

6. The woman complained of paroxysms of the headache with vomiting, chills, nausea, and palpitations. She was unwell for 15 years. The patient had lost 17 kg. Upon the physical examination: she was withdrawn, her heart sounds were rhythmic, with the II tone's accent over the aorta, the systolic murmur over the apex and the aorta, her pulse was 96/min, the blood pressure was 300/170 mmHg. Laboratory tests revealed leukocytes of 18×10^9/l, the fasting glucose was 6.8 mmol/l, during the crisis it was 21 mmol/l, the vanillin-mandelic acid (+++); the urinalysis - 1% glucose; adrenaline in the urine was 320 nmol/day. What was the preliminary diagnosis?

A. Autonomic crisis;
B. Cerebrovascular arterial hypertension;
S. Hypertensive disease;
D. Pheochromocytoma;

E. Conn's syndrome.

7. A 32-year-old woman complained of fits of dizziness, headache, palpitations, and tremors. Over the last months such attacks had become more frequent and severe. Upon the physical examination: her skin was sweaty, the limbs' tremors, her heart rate was 110/min, her blood pressure was 210/110 mmHg; her heart sounds were normal. Laboratory tests revealed leukocytes of 9.8×10^9/l, ESR of 22 mm/h, the blood glucose of 9.8 mmol/l. Which of the following diagnostic methods should be recommended for establishing a diagnosis?

A. the urinary aldosterone test;

B. Dipyridamole tests;

C. Atropine test;

D. urinary catecholamine's test;

E. blood sodium and potassium.

8. A 30-year-old woman complained of the increased blood pressure, severe weakness, seizures, transient paresis, palpitations, dizziness, and headache. She had been suffering from arterial hypertension for 3 years. The ECG showed: the sinus tachycardia, the prolongation of the Q-T interval, the ST depression in V1-V6, the negative T wave in V3-V6. The urinalysis: the alkaline reaction, the relative density was 1010, transparent, negative protein and sugar. The blood potassium was 2.9 mmol/l, sodium was 160 mmol/l. What pathology did cause the arterial hypertension?

A. Itsenko-Cushing's disease;

B. the hypertensive disease, II stage;

C. the hypertensive disease, III stage;

D. Kohn's syndrome;

E. Chronic pyelonephritis.

9. A 45-year-old man complained of an acute weakness, polyuria, the increased blood pressure till 210/120 mmHg. Laboratory tests revealed potassium of 3.12 mmol/l, sodium of 148 mmol/l, aldosterone of 715 nmol/l. What was the preliminary diagnosis?

A. Hypertensive disease, III stage, HF IIB;

B. Kohn's syndrome;

C. Chronic pyelonephritis, CKF;

D. Diabetic glomerulosclerosis, CKD;

E. Itsenko-Cushing syndrome.

10. A 42-year-old man complained of periodic squeezing chest pains, severe proximal limbs weakness and convulsions, and dizziness. He was unwell for 2 years. Upon the physical examination: her height was 176 cm, her weight was 80 kg, the heart's borders were shifted to the left; her HR was 92 beats/min, the blood pressure was 190/100 mmHg. The ECG showed: the sinus rhythm,

oblique-descending shift of the ST segment in all leads. The Zimnytsky urinalysis: polyuria, nocturia with isosthenuria, hyporeninaemia. Laboratory tests revealed potassium of 2.8 mmol/l. What was the preliminary diagnosis?

A. Hyperparathyroidism;
B. Itsenko-Cushing syndrome;
C. Primary hyperaldosteronism;
D. Essential hypertension;
E. Pheochromocytoma.

Answers

1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
A	D	A	E	E	D	D	D	B	C

Main methods of examination of patients with allergic diseases. Laboratory and instrumental tests in allergology. Basic syndromes in the allergology

1. Clinical manifestations of pathology of immediate hypersensitivity reactions are as following:

A. Allergic rhinitis
B. allergic rhinoconjunctivitis
C. allergic asthma
D. urticaria
E. All of mentioned above

2. An antigen is characterised by the following properties:

A. Foreignness.
B. Antigenicity.
C. Immunogenicity.
D. Specificity.
E. All of mentioned above.

3. What does occur during the release of mast cell mediators?

A. Increasing in cAMP
B. Bronchospasm
C. Arteriolar spasm and tissue swelling
D. Bronchospasm and tissue swelling
E. Increasing in cAMP, bronchospasm and tissue swelling

4. What does result from the simultaneous ingestion intake of the allergens and alcohol?

A. Accelerates the manifestation of allergic reactions
B. Slows down the manifestation of allergic reactions
C. does not produce symptoms

D. does not produce symptoms when ingested without subsequent exercise

E. produce only skin symptoms

5. Which chemical mediators are released during degranulation of mast cells?

A. Bradykinin

B. Hemotoxic factor of eosinophils

C. Histamine

D. Hemotoxic factor of eosinophils and slowly reacting substance of anaphylaxis

E. Bradykinin, chemotaxic factor of eosinophils, histamine and slowly reacting substance of anaphylaxis

6. An 8-year-old child had dyspeptic symptoms and diarrhoea after the ingestion of non-pasteurised cow's milk. He tolerates boiled milk, as well as goat's milk. What is the preliminary diagnosis?

A. Pseudoallergy;

B. Food allergy to cow's milk;

C. Lactose intolerance;

D. Chronic gastritis with low secretory function of the stomach;

E. chronic pancreatitis.

7. Which is the urgent treatment in the case of the angioedema of the laryngopharynx?

A. Intravenous administration of glucocorticoids

B. Oral administration of antihistamines

C. Parenteral administration of epinephrine

D. Hot foot baths

E. izadrin or novodrin inhalation

8. The patient had an angioedema as a result of the contact with the daphnia fish food. What type of food allergies can be expected in this patient?

A. For meat

B. For boiled fish

C. For dried fish

D. On crayfish and crabs

E. For iodine preparations

9. Which antibodies are produced during an attack of atopic asthma?

A. IgA

B. IgM

C. IgG

D. IgE

E. all of mentioned above

10. Which cells produce immunoglobulins?

A. Plasmocytes;

B. T-lymphocytes;
C. Smooth cells;
D. Macrophages;
E. Stem cells.

Answers

1	2	3	4	5	6	7	8	9	10
E	E	D	A	E	B	B	A	D	D

The principles of the emergency. The principles of the prehospital first aid

1. The basic emergency measures, the alleviation of the victim's suffering and the prevention of possible complications can be classified as the followings?
   A. Qualified medical help;
   B. Specialised medical help;
   C. First aid;
   D. All of mentioned above;
   E. Options A and B.
2. What is the algorithm of the initial patient's assessment:
   A. A (airway);
   B. B (breathing);
   C. C (circulation);
   D. D (disability);
   E. All of mentioned above.
3. Which is the recommended target level of BP in the case of the complicated hypertensive crisis with intracranial haemorrhage or subarachnoid haemorrhage?
   A. 120/80 mmHg;
   B. 90/60 mmHg;
   C. should exceed by 15-20% the normal value;
   D. should exceed by 5-10% the normal value;
   E. The level depends on the patient's well-being.
4. Which mechanisms of the cardiac arrest can you pinpoint?
   A. ventricular fibrillation or fluttering;
   B. pulseless ventricular tachycardia;
   C. Asystole;
   D. pulseless electrical activity;
   E. All of mentioned above.
5. What is the normal compression-to-ventilation ratio of CPR?
   A. 2:30
   B. 30:2.
   C. 15:10
   D. 30:3
   E. 25:5
6. What is the clinical trend of the syncope?
   A. duration longer than 2 minutes;
   B. resolve spontaneously within <20 s;

C. accompanied by the chest pain;

D. options A and C;

E. All of mentioned above.

7. Define the right place of electrodes for defibrillation?

A. Apex-anterior;

B. On both sides;

C. Apical-posterior;

D. Anterior-posterior;

E. All of mentioned above.

8. What is the first aid in the case of respiratory failure?

A. Restoration of airway patency;

B. CPR with a ratio of 25:15;

C. Oxygen therapy;

D. HBO;

E. All of mentioned above.

9. A pulsating bright red blood escaping from the circulatory system from damaged blood vessels, sometimes intermittent is typical for the following?

A. Arterial bleeding.

B. Venous bleeding.

C. Capillary bleeding.

D. Internal bleeding.

E. All of mentioned above.

10. How long a tourniquet should not be used on a patient's limb in the case of bleeding?

A. No longer than 1 hour in the warm weather and no longer than 2 hours in the cold weather;

B. No longer than 1 hour in the cold weather and no longer than 2 hours in the warm weather.

C. for 1 hour;

D. for 15 minutes in the warm weather, for 30 minutes in the cold weather.

E. so long as it is needed.

Answers

1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
C	E	D	E	B	B	E	A	A	B

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