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

INTERNAL MEDICINE

MANUAL

for 3rd year students
speciality 221 «Dentistry»

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I-69 **Internal medicine** : manual for the practical classes and individual work for 3rd year students of international faculty (speciality 221 «Dentistry») Discipline «Internal medicine (with infectious diseases, epidemiology, and clinical pharmacology)» / N. S. Mykhailovska, A. V. Grytsay, M.O. Konovalova et al. – Zaporizhzhia: ZSMPHU, 2023. – 213 p.

Manual compiled in accordance with the program of «Internal medicine (with infectious diseases, epidemiology, and clinical pharmacology». Guidelines are intended to help students prepare for practical classes and learn the material. Can be used for training of 3rd year students of international faculty, discipline «Internal medicine (with infectious diseases, epidemiology, and clinical pharmacology».

Внутрішня медицини : навчальний посібник до практичних занять та самостійної роботи студентів III курсу міжнародного факультету (спеціальність «Стоматологія») з дисципліни «Внутрішня медицина (у тому числі інфекційні хвороби, епідеміологія та клінічна фармакологія)» / Н. С. Михайловська, А. В. Грицай, М.О. Коновалова та співат. – Запоріжжя: ЗДМФУ, 2023. – 213 с.

Навчальний посібник складений відповідно до програми «Внутрішня медицина (у тому числі інфекційні хвороби, епідеміологія та клінічна фармакологія)». Видання має на меті сприяти кращому засвоєнню теоретичних знань студентами під час підготовки до практичних занять та підсумкового контролю. Посібник рекомендований для використання студентами III курсу міжнародного факультету з дисципліни «Внутрішня медицина (у тому числі інфекційні хвороби, епідеміологія та клінічна фармакологія)».

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CONTENT

PREFACE

Mastering the academic discipline «Internal medicine», students of the speciality «Dentistry» have to form their clinical thinking, to be able to assess the the connection between the oral cavity changes and interanl organ pathology, to recognise the widespread intrernal diseases and their life-threatening complications, to know the dentist's tactics towards patients with somatic pathology, provide emergency during an appointment at the dentist's.

This manual was prepared by the department of general practice – family medicine and internal diseases of Zaporizhzhia State Medical and Pharmaceutical University in accordance with requirements of the program of the educational discipline «Internal medicine (with infectious diseases, epidemiology, and clinical pharmacology» for 3rd studying year students, the speciality 221 «Dentistry». This manual encompasses such fields of internal diseases as pulmonary, cardiovascular, gastrointestinal, and rheumatic diseases. There were highlighted current apparoach to internal diseases, their etiology and pathogenesis, classifications, clinical presentation, diagnostic considerations based on the American, European and local protocols of medical care.

This manual is published for the first time.

The cover image was downloaded from website https://www.issuewire.com/lavanya-a-kodavali-md-internal-medicin

This book tends to improve theoretical knowledge of 3rd studying year students, the 2nd international faculty, speciality 221 «Dentistry» during their preparation for practical classes.

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

INTERNAL MEDICINE

TOPIC 1

COPD. ASTHMA. EMPHYSEMA. PULMONARY INSUFFICIENCY. DENTAL ASPECTS

Modern classification of chronic obstructive pulmonary disease. Definition and the basic mechanisms of the development of chronic bronchitis and bronchial asthma. Chronic bronchitis and bronchial asthma, the basic complaints and physical examination of the patients. A syndrome of bronchial obstruction, mucocellular insufficiency and the increased lightness of the lungs. The basic methods of instrumental diagnostics. Laboratory findings of bronchial asthma according to the general blood tests and sputum examination. Bronchiectasis, definition and the basic clinical syndroms.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

A disease characterized by chronic bronchitis or emphysema and airflow obstruction that is generally progressive, may be accompanied by airway hyperreactivity, and may be partially reversible.

Patients who have features of chronic bronchitis or emphysema without airflow obstruction have one or both of those diseases but not COPD. Most patients with COPD, who by definition have airflow obstruction, have features of both chronic bronchitis and emphysema. Patients whose asthma is characterized by incomplete reversibility of airway obstruction are considered to have a form of COPD (called asthmatic bronchitis or asthmatic COPD in the USA), because they often cannot be differentiated from those who have chronic bronchitis and emphysema with reversible airway obstruction and airway hyperreactivity. Those with completely reversible airflow obstruction without features of chronic bronchitis or emphysema have asthma but not COPD.

Etiology

Smoking is the dominant risk factor for the development and progression of COPD; however, not all smokers develop COPD, and COPD does occur in persons who have never smoked, suggesting that other factors are important in the etiology of COPD. Occupational and environmental exposures to various pollutants (eg, particulate matter, agricultural dusts) are also important factors in the development of COPD. α_1-antitrypsin deficiency is an important cause of COPD in a very small

percentage of cases. Other undefined genetic factors certainly play an important role in COPD development. The role of infections in both the development and progression of COPD is receiving increased attention, including the role of adenoviral infections in emphysema and the role of intracellular infections (eg, mycoplasma) in asthma.

Table 1

Classification of Chronic Obstructive Pulmonary Disease by Severity

Stage	Characteristics
I (mild COPD)	Chronic symptoms (cough, sputum production) FEV1/FVC < 70% FEV1 ≥ 80% of predicted
II (moderate COPD)	With or without chronic symptoms FEV1/FVC < 70% 50% of predicted ≤ FEV1 < 80% of predicted
III (severe COPD)	With or without chronic symptoms FEV1/FVC < 70% 30% of predicted ≤ FEV1 < 50% of predicted
IV (very severe COPD)	With or without chronic symptoms FEV1/FVC < 70% FEV1 < 30% of predicted or < 50% of predicted plus the presence of respiratory failure or clinical signs of right heart failure increase.

Note: FEV_1 - forced expiratory volume in 1 second; FVC - forced vital capacity.

Clinical features

Patients who have smoked > 20 cigarettes per day for > 20 yr may develop a productive cough in their 40s or early 50s. Exertional dyspnea usually does not become severe enough to warrant a visit to a physician until COPD patients are in their 50s or mid-60s. Sputum production is insidious in onset, initially occurring only in the morning. Daily volume rarely exceeds 60 mL. Sputum is usually mucoid but becomes purulent during an exacerbation.

Acute chest illnesses-characterized by increased cough, purulent sputum, wheezing, dyspnea, and occasionally fever-may occur from time to time. (A history of wheezing and dyspnea may lead to the erroneous diagnosis of asthma.) As COPD progresses, the intervals between acute exacerbations tend to become shorter. Late in the disease, an exacerbation may cause severe hypoxemia with cyanosis, which is accentuated if erythrocytosis is present. Morning headache may indicate hypercapnia. Hypercapnia with more severe hypoxemia, sometimes with

erythrocytosis, is common in end-stage disease. Weight loss occurs in some patients.

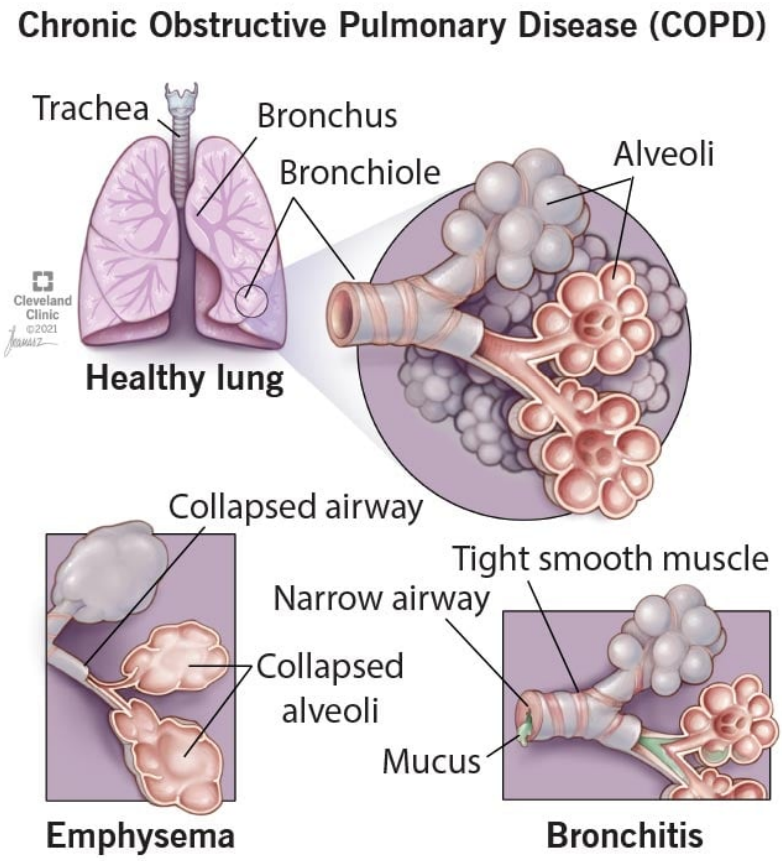

Image 1. Healthy lungs have open airways versus the collapsed and narrow airways of emphysema and bronchitis, conditions grouped under COPD
This image was downloaded from website https://my.clevelandclinic.org

Objective examination

Early in COPD, physical examination of the chest may not be remarkable except for auscultation of expiratory wheezes. As airway obstruction progresses, hyperinflation of the lungs becomes evident. Cyanosis may be present. The anteroposterior diameter of the chest increases because the lungs are near full inspiration and because emphysema increases total lung capacity (barrel chest). The diaphragm is depressed, and its motion limited. Breath sounds are decreased, and heart sounds become distant. Signs of pulmonary hypertension and right ventricular hypertrophy are usually not detectable because emphysematous lung tissue is interposed between the heart and anterior chest wall. A few coarse crackles are often

heard at the lung bases. An enlarged, tender liver indicates heart failure. Neck vein distention, especially during expiration, may occur in the absence of heart failure because of increased intrathoracic pressure. Asterixis may accompany severe hypercapnia.

The patient with end-stage COPD is often a dramatic sight - standing before a counter leaning forward with arms outstretched and weight supported on the palms. The accessory respiratory muscles of the neck and shoulder girdle are in full use. Expiration often occurs through pursed lips. The chest appears overinflated, often with paradoxic in drawing of the lower interspaces. Cyanosis may be present.

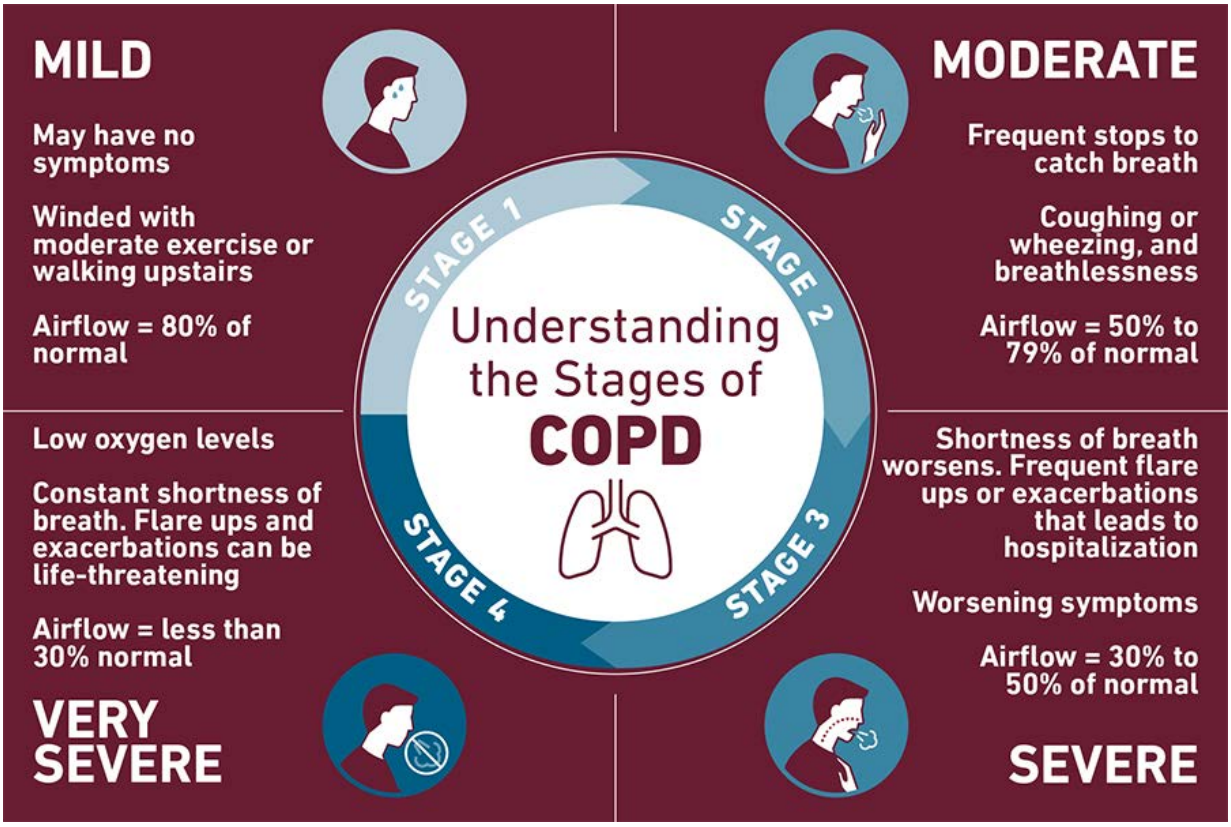

Image 2. Healthy lungs have open airways versus the collapsed and narrow airways of emphysema and bronchitis, conditions grouped under COPD

This image was downloaded from website https://www.templehealth.org

Additional methods of examination

Clinical blood analysis: without significant changes, sometimes secondary erythrocytosis; in progression assess leukocytosis, neutrophilia, accelerated ESR.

Sputum analysis: sputum in patients with stable chronic bronchitis is mucoid. During an exacerbation, sputum usually becomes purulent, with an influx of neutrophils.

X-ray examination: in severe disease, persistent, marked overdistention of the lungs is indicated in the frontal view by a low, flat diaphragm and in .the lateral view by widening of the retrosternal airspace and an increase in the angle formed by the sternum and diaphragm from acute to ≥ 90°. The heart shadow tends to be long and narrow.

Test of ventilatory function (spirometric recording and pneumotachymetry): pulmonary function tests are helpful in diagnosing COPD, in assessing its severity, and in following its progress. Forced expiratory spirometry quantifies airway obstruction. Airflow obstruction is an important indicator of symptomatic respiratory insufficiency and of the likelihood of blood gas abnormalities. The FEV_1 and the FEV_1/FVC fall progressively as the severity of COPD increases. The FEV_1 is less variable than other measurements of airway dynamics and can be predicted more accurately from age, sex, and height. Functional residual capacity and residual volume are increased; vital capacity is decreased. Roughly comparable information can be obtained from the forced expiratory flow-volume loop.

ECG: diagnosing pulmonary hypertension and cor pulmonale in COPD is difficult without right-sided heart catheterization. On the ECG, an R or R' wave as large as or larger than the S wave in lead V_1 and R wave smaller than the S wave in lead V_6 and right-axis deviation >110° without right bundle branch block support the diagnosis of cor pulmonale.

Echocardiography: especially with an esophageal transducer, and pulsed Doppler techniques to estimate mean pulmonary arterial pressure can be used to assess pulmonary hypertension and right ventricular function. Left ventricular size and performance are generally normal inpatients with COPD and no other associated cardiac abnormalities. The right ventricular ejection fraction is frequently abnormal, especially during exercise.

Blood gas analysis: arterial blood gas measurements detect hypoxemia and hypercapnia and determine their severity. In the early stages of COPD, measuring arterial blood gases reveals mild or moderate hypoxemia without hypercapnia. As the disease progresses, hypoxemia becomes more severe and hypercapnia supervenes. Hypercapnia occurs with increasing frequency as the FEV_1 falls below 1L. Blood gas abnormalities worsen during acute exacerbations and may worsen during exercise and sleep.

CHRONIC BRONCHITIS

Chronic bronchitis is chronic inflammation of the bronchi and bronchioles.

Etiology

- smoking, pollution of the environment by products of incomplete fuel substances combustion, organic and inorganic dust;
- infection (bacterial, viral, micoplasms, fungus);
- congenital occurrences in lesser circulation on heart failure;
- exposure of metabolic products on renal failure;
- result of acute bronchitis.

Classification of chronic bronchitis (by N.R Paleev, 1990)

I. According to the character of inflammatory process:

- simple (catarrhally);
- purulent;
- muco-purulent;
- special forms: hemorrhagic and fibrinous.

II. According to the presence of bronchial obstruction:

- obstructive bronchitis (stages: I, II, III; duration: simple, moderate grave, grave);
- non obstructive bronchitis.

III. According to the level of bronchi injury:

- proximal;
- distal;
- diffuse.

IV. According to the duration:

- latently;
- with infrequent aggravations;
- with frequent aggravations;
- continuously progress.

V. According to the phases:

- progress;
- remission.

VI. According to the complications:

- emphysema of the lungs;
- hemoptysis;
- pneumonia;
- respiratory failure;
- "Cor pulmonale".

Pathogenesis

On chronic bronchitis occurs development of classic pathogenetic triad*:*

- hypercrinia (mucous hyperproduction);
- dyscrinia (increased sputum viscosity);
- mucostasis (overcrowding of the sputum in bronchi).

Approaching to the bronchi of infection agent leads to the sensebilization and autosensebilization of the organism.

There are the next mechanisms of the bronchial obstruction development:

- brochospasm;
- inflammatory edema and bronchial wall infiltration;
- hyper- and dyscrinia;
- hypotonic dyskinesia of large bronchi;
- collapse of small bronchi during expiration;
- mucus lays hyperplasic reaction.

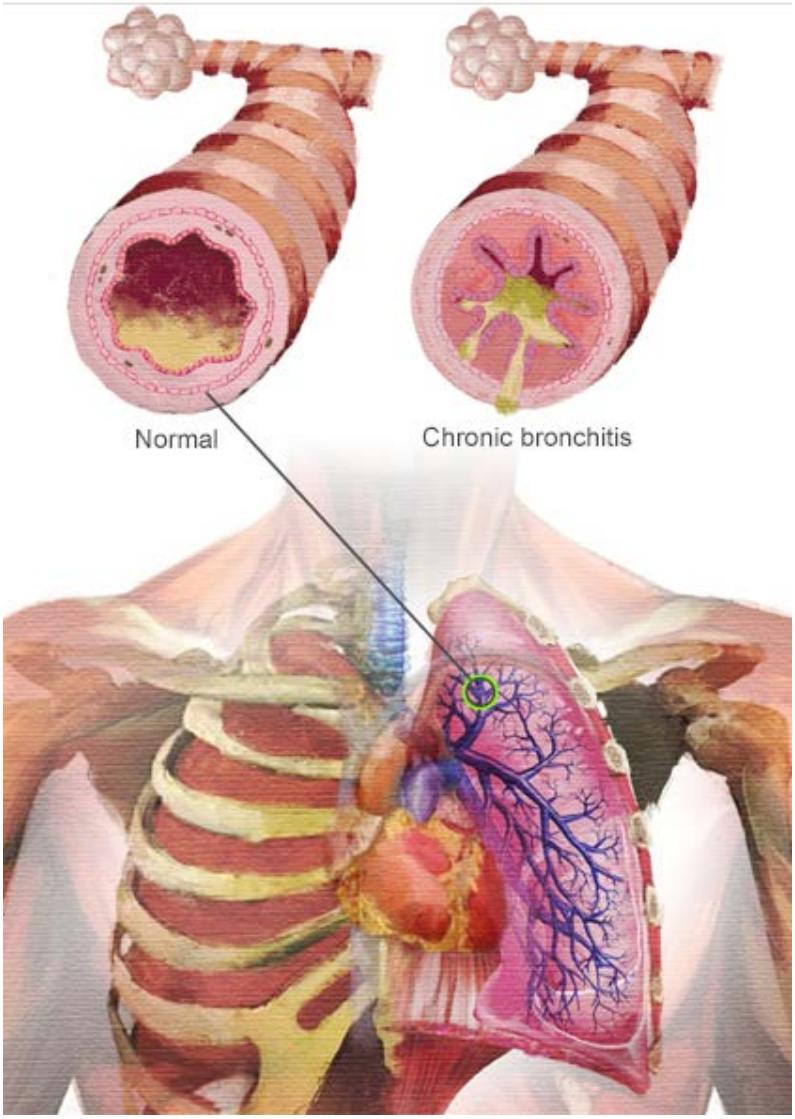

Image 3. Chronic bronchitis

This image was downloaded from website https://www.respelearning.scot

Clinical features

The main complaints in patients with chronic bronchitis are moist cough, general weakness, perspiration and dyspnea in cause of bronchium obstruction.

Cough is commonly periodic, moist with difficult sputum expectoration.

Sputum expectoration is the most important symptom of chronic bronchitis. On early stages of the disease the sputum may be mucous, tenacious consistency, glass-like, for the period of progression becomes mucopurulant or purulent. The 24-hours amount of sputum is usually 50-70 ml, due to development of bronchiectasis significantly increase to 100-200 ml.

Dyspnea - commonly has expiratory character and its appearing indicates presence of bronchial obstruction and emphysema.

Objective examination

General patient's condition is usually satisfactory. On progression and complications advance general patient's condition may be from middle grave to grave. Due to gradual chronic hypoxia and intoxication possibly will be observed perspiration and subfebrile or febrile temperature.

The posture of the patients is frequently active. On progression and complications advance is forced in form of orthopnea - sitting position fixing the shoulder girdle in order to reduce dyspnea via assists the accessory muscles and diaphragm to take part in respiration.

The color of the skin and visible mucous depends on the stage and variant of obstruction. In initial stage the color of the skin and visible mucous is without any particularities. Due to the chronic bronchitis progression observe diffuse cyanosis with peripheral edema via to the "cor pulmonale" development. In obstructive emphysema bronchi spasm occurs during expiration therefore alveolar air is a little change and in spite for constant dyspnea the skin and visible mucous cyanosis isn't specific. In purulent chronic bronchitis detect the form of the Hippocratic nails.

The data of chest inspection, palpation and percussion include clinical features of bronchium obstruction: emphysematous form of the chest with accessory respiratory muscles participation in the breathing act, decreased excursion of the chest, badly transmitted vocal fremitus and generalized bandbox sound over the lungs during percussion.

Auscultation of the lungs. Auscultative data in patients with chronic bronchitis is characterized by sibilant and sonorous dry rales of different tone and intensity over the pathologically increased vesicular breathing. In localized affection of medium and

large bronchi insignificant amount of low pitched and soft rales are heard. Accumulation of the viscous secret in bronchi via active inflammation, are accompanied by coarse and medium bubbling rales that can be altered by coughing or deep inspiration.

Additional methods of examination

Clinical blood analysis: without significant changes, sometimes secondary erythrocytosis; in progression assess leukocytosis, neutrophilia, accelerated ESR, eosinophilia (allergic reaction).

Sputum analysis: the character of the sputum depends on the stage of disease: in initial stage the sputum is mucous; in progression or later stage - muco-purulant, tenacious or tenacious thick consistency, glass-like or with yellow traces, odorless and absent of layersness. In microscopic study are revealed a lot of columns ciliated epithelium, leucocytes, alveolar macrophages, eosinophils, fibrin fibers, Charcot-Leyden crystals and large amount of microorganisms (bacterial flora).

X-ray examination: augment and deformity of lung picture over increased in transparent lung tissue.

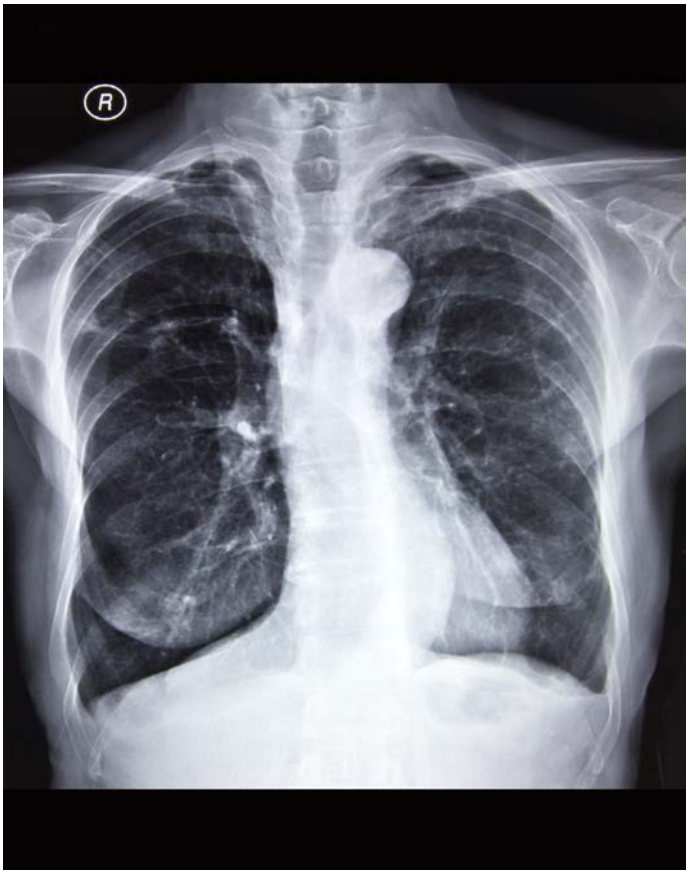

Image 3. X-ray of Chronic bronchitis

This image was downloaded from website https://lungdiseasenews.com

Test of ventilatory function (spirometric recording and pneumotachymetry): in patients with no obstructive bronchitis results of spirometric recording is comparable with healthy subjects; in patients with bronchial obstruction assess decreased respiratory reserve (75 % of maximum lung ventilation and lower), and decreased Votchal-Tiffeneau index.

ECG: deviation of electric axis of the heart to the right, P-pulmonale in II, III, AVF leads.

BRONCHIAL ASTHMA

A pulmonary disease characterized by reversible airway obstruction, airway inflammation, and increased airway responsiveness to a variety of stimuli. Obstruction persisting for days or weeks is known as status asthmaticus.

In the base of the disease lays chronic inflammatory process in bronchi due to the bronchi smooth muscles spasm (acute obstruction), mucus edema (subacute obstruction) and bronchi obstruction by tenacious secret (chronic obstruction). On longterm duration of disease via fibrosis in bronchial wall develops sclerotic obstruction**.**

Etiology

I. The risk factors:

- genetic factors;
- atopia (ability of the organism to the increased production of IgE owing to the allergens);
- bronchi hyperreactivity.

II. The cause factors:

- allergens;
- endogenous factors;
- impaired arachidonic acid metabolism;
- bronchi hyper reactivity to physical load;
- nervous and psychological factors;
- dyshormonal state.

III. The initiate factors:

- respiratory infections;
- airs pollutants;
- smoking.

Classification

Bronchial asthma is classificated according to the complex of clinical and functional signs of bronchial obstruction.

Table 2

Bronchial asthma classification

Category	Symptoms	Pulmonary Function
Mild intermittent	Symptoms ≤ 1 times a week No symptoms and normal PEF between exacerbations Exacerbations brief (from a few hours to a few days); intensity may vary Nighttime symptoms ≤ 2 times a month	FEV1 or PEF ≥ 80% predicted PEF variability < 20%
Mild persistent	Symptoms > 1 times a week but not daily Exacerbations that sometimes limit activity Nighttime symptoms > 2 times a month	FEV1 or PEF ≥ 80% predicted PEF variability 20-30%
Moderate persistent	Daily symptoms Daily use of inhaled short-acting β2-agonist Exacerbations that limit activity Exacerbations ≥ 2 times a week; may last days Nighttime symptoms > 1 time a week	FEV1 or PEF > 60% predicted PEF variability > 30%
Severe persistent	Continual symptoms Limited physical activity Frequent exacerbations Frequent nighttime symptoms	FEV1 or PEF ≤ 60% predicted PEF variability > 30%

Note: FEV_1 - forced expiratory volume in 1 second; PEF - peak expiratory flow.

Classification of the bronchial asthma aggravations (according to the anamnesis, intensity of the clinical signs, respiratory and cardiovascular dysfunction):

Degree I- effortless;

Degree II- moderate grave;

Degree III - grave;

Degree IV- risk of breathing stop.

Table 3

Bronchial asthma classification

Symptoms	Effortless	Moderate grave	Grave	Risk of breathing stop
Dyspnoea	At walking	At speaking	At rest	-
Conversation	Sentences	Phrases	Words	-
Consciousness	Normal	Exiting	Exiting	Deranged
Breathing rate	Increase	Increase	>30/min	-
Participation of the additional muscles	Absent	Present	Present	Paradox thoracoabdominal breathing
Whistling breathing	At the end of expiration	Loud	Loud	Absent
Pulse/min.	<100	100-120	>120	Bradycardia
FEV_1 after taking broncholytic, % from normal level	> 80 %	60-80 %	< 60 %	Absent
PaO_2	Normal	>60 mm Hg	<60 mm Hg	-
$PaCO_2$	<45 mm Hg	<45 mm Hg	>45 mm Hg	-

Clinical features

The main complaints in patients with bronchial asthma are bronchial asthma attacks: dyspnea, asphyxia, episodic breathlessness and cough. In attacks development there are divide 3 periods: prodromal, manifestation, reverse.

I. The prodromal period: starts at several minutes, hours or sometimes days before asthma attack and characterized by sneezing, itchiness of the skin and eyes, hypersecretion from nose, paroxysmal coughing, breathlessness, headache, weakness and changes of mood.

II. The period of clinical manifestation (bronchial asthma attack): appears feeling of difficult breathing, significant dyspnea (expiratory type) with changes in respiratory rate (tachypnea), depth (shallow respiration) and noisy distant rales. *General patients condition* is from middle grave to extremely grave. Due to the acute hypoxia may be observed depressed or exited deranged consciousness. During asthma attack the patients take the *forced posture* in form of orthopnea - sitting position fixing the shoulder girdle in order to reduce dyspnea. *The color of the skin* is pale with central or diffuse cyanosis. The form of the chest is emphysematous with accessory muscles participate in the breathing act, observed decreased excursion of the chest. The vocal fremitus is badly transmitted and generalized bandbox sound assessed over the lungs during percussion. *Anscultative data* are characterized by sibilant and sonorous dry rales over the pathologically decreased vesicular breathing.

III. The period of asthma attack reverse: the duration of attack is differing and its final may come quickly without any complications through sputum discharge; or may continue for several hours or days accompanied by permanent dyspnea, headache and weakness.

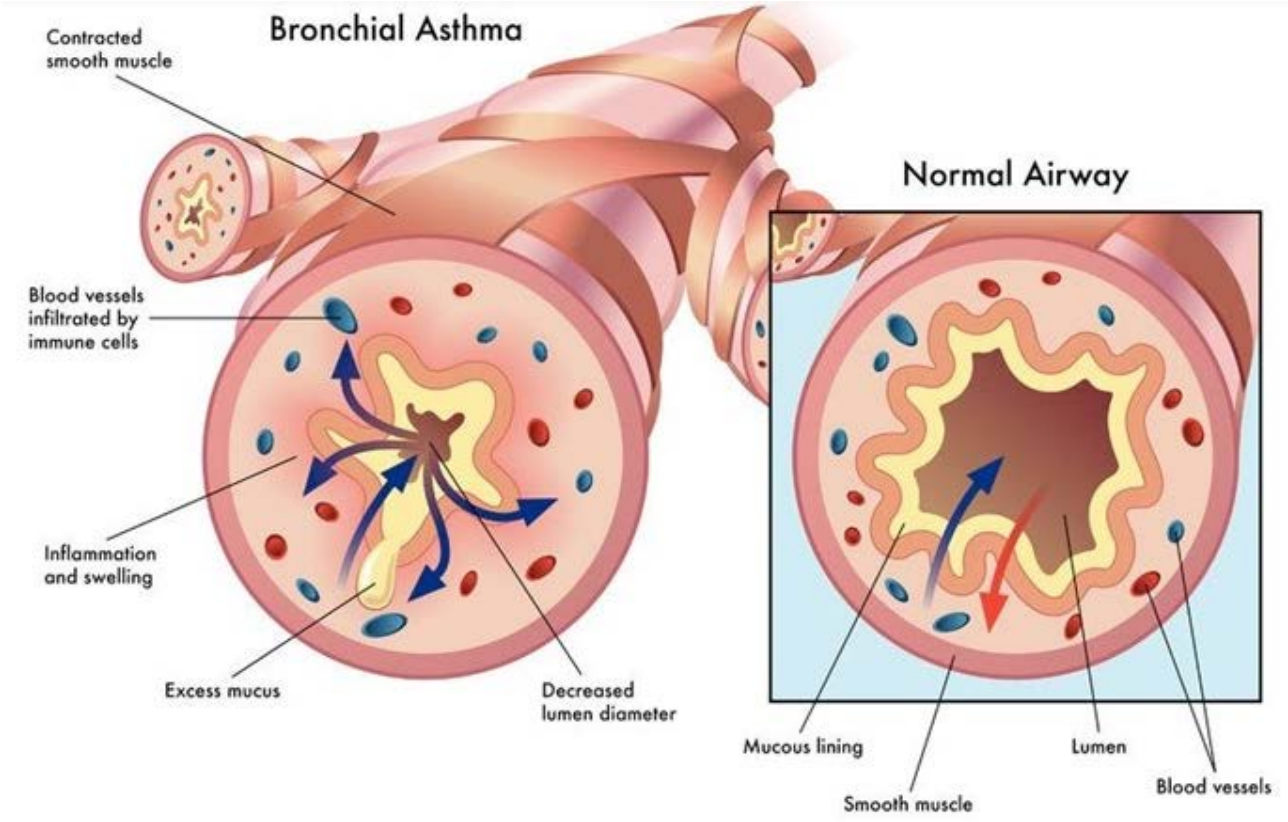

Image 4. Bronchial asthma

This image was downloaded from website https://www.mymed.com

In severe causes bronchial asthma attacks may transform at asthmatic status - lingering bronchial asthma attack that characterized by shallow quick respiration (significant tachypnea), constant dyspnea and formation of "dumb lung". Severity of asthmatic status is characterized by degree of respiratory failure, acidosis, hypercapnia, level of hypoxemic coma and respiratory center paralysis.

In period of stable remission the general patients condition commonly satisfactory or middle grave, however the clinical signs of emphysema are stay be present, particularly in causes of long disease duration and recurrently asthma attacks.

Additional methods of examination

Clinical blood analysis: secondary erythrocytosis; eosinophilia, accelerated ESR.

Sputum analysis: the character of the sputum is mucous, tenacious or tenacious thick consistency, glass-like color and odorless. In microscopic study are revealed columns ciliated epithelium, leucocytes, alveolar macrophages, eosinophils, Charcot-Leyden crystals and Kurshman spirals.

X-ray examination: in initial stages the specific data are absent. During asthma attack and according to the repeatedly periods of progression assess transparent lung tissue, horizontal position of the ribs, dilation of the intercostals spaces, low diaphragm position. In cause of inflammatory and allergic etiology of bronchial asthma observed augment and deformity of lung picture.

Test of ventilatory function (spirometric recording and pneumotachymetry): assess decreased respiratory reserve (75 % of maximum lung ventilation and lower), and decreased Votchal-Tiffeneau index.

Dynamic lung volumes and capacities are reduced but return toward normal after inhalation of an aerosolized bronchodilator. In patients with mild asymptomatic asthma, results may be normal. Because expiratory flow is determined by the diameter of the airways and by the elastic recoil forces of the lung, flow at large lung volumes exceeds flow at small lung volumes. Tests that measure flow at relatively large lung volumes (the forced expiratory volume during the first 1 sec (FEV1) and peak expiratory flow) are largely effort-dependent and are less satisfactory than tests that measure flow over a range of lung volumes. Expiratory flow measurements at large lung volumes are insensitive to changes in peripheral airway resistance and reflect abnormalities principally in central airways. Early in an acute attack, forced expiratory flow between 25 and 75% of the vital capacity (FEF25-75%) may decrease only modestly. As the attack progresses, the FVC and FEV1 progressively

decrease; associated air trapping and increased residual volume result in hyperinflation of the lungs.

Allergen identification: Inhalational bronchial provocation testing can be used with allergens to establish the clinical significance of positive skin tests or with methacholine or histamine to assess the degree of airway hyperresponsiveness in known asthmatics. It also aids in diagnosis when the symptoms are atypical (a persistent cough but no wheeze, as in cough-variant asthma).

SYNDROME OF BRONCHIUM OBSTRUCTION
(Bronchospastic syndrome)

Bronchospastic syndrome - the grouping of symptoms that developed due to the impaired air entrance to the pulmonary tissue through bronchus and accompanied by decreased lung's ventilation, enlargement of residual air volume in them, clinically manifests by intensive cough and resulted in emphysema.

Etiology

Spasm of the smooth muscles; inflammatory infiltration and edema of the tracheobronchial tree mucus; non-uniform swelling of the bronchial mucus due to the inflammation or viscous sputum narrows the lumen of bronchi; deformity of the bronchial tree; expiratory bronchi collapse; external compression of bronchi by diffuse peribronchial fibrosis.

Pathogenesis

In syndrome of bronchium obstruction at first modify air passage in small bronchi and bronchioles due to the inflammatory edema and swelling of their mucosa (chronic bronchitis), spasm in the smooth muscles (bronchial asthma) and the external compression by peribronchial diffuse fibrosis.

Affection of the air passage through the bronchi (in all causes and pathogenetic mechanisms) leads to the alveoli hypoventilation, hypoxemia, hypercapnia, pulmonary hypertension and "cor pulmonale" development.

Clinical features

The main complaints in patients with bronchium obstruction are dyspnea and cough. Dyspnea commonly has expiratory character, gradually increased (chronic obstructive pulmonary diseases) and frequently transformed to periods of asthma (bronchial asthma). Cough is commonly periodic, moist with difficult sputum expectoration that has mucous or mucopurulant character, tenacious consistency, glass-like or glass like with yellow- traces color.

Objective examination

General patients condition is from middle grave to grave. Due to the acute or gradual chronic hypoxia may be observed the deranged consciousness.

The posture of the patients is frequently forced in form of orthopnea - sitting position fixing the shoulder girdle in order to reduce dyspnea via assistance of accessory muscles and diaphragm to take part in respiration.

The color of the skin depends on the variant of obstruction. In chronic bronchitis observe diffuse cyanosis with peripheral edema due to the "cor pulmonale" development. In obstructive emphysema bronchi spasm occurs during expiration therefore alveolar air is a little change and inspite for constant dyspnea the skin and visible mucous cyanosis isn't specific.

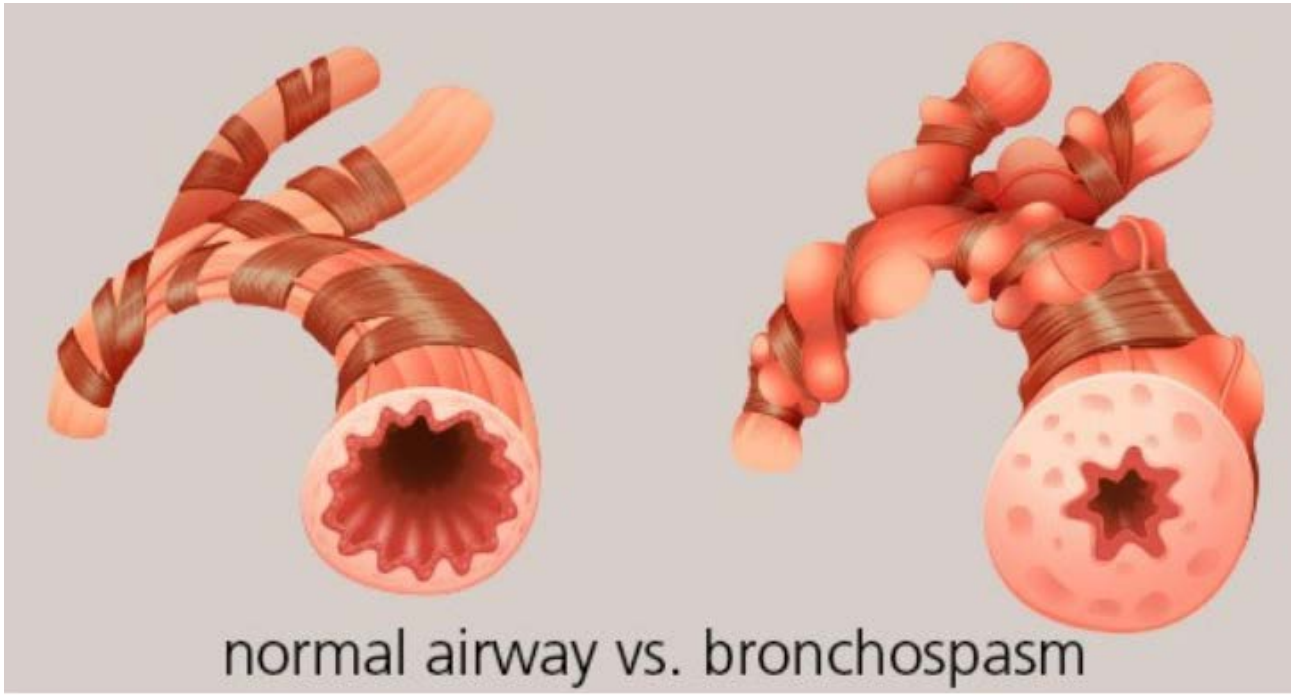

Image 5. Bronchospasm

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The data of chest inspection, palpation and percussion include clinical features of bronchium obstruction complications: emphysematous form of the chest with accessory respiratory muscles participation in the breathing act, decreased excursion of the chest, badly transmitted vocal fremitus and generalized bandbox sound over the lungs during percussion.

Auscultative data are the main specific in patients with bronchospastic syndrome: they characterized by dry rales over the pathologically increased vesicular

breathing. Moreover, the particularities of the rales give possibility to evaluate the cause of the obstruction, the size and depth of the affected bronchi:

- in localized affection of medium and large bronchi insignificant amount of low pitched and soft rales are heard;

- widespread bronchi inflammation or bronchospasm in asthma attack both sibilant and sonorous rales of different tone and intensity are heard;

- accumulation of the viscous secretions in the lumen of bronchi accompanied by dry rales that can be altered by coughing or deep inspiration.

Additional methods of examination

Clinical blood analysis: secondary erythrocytosis; leukocytosis, neutrophilia, accelerated ESR (during progression of chronic diseases), eosinophilia (bronchial asthma).

Sputum analysis: the character of the sputum is mucous or muco-purulant, tenacious or tenacious thick consistency, glass-like or glass like with yellow traces color, odorless and absent of layers ness. In microscopic study are revealed columnar, ciliary epithelium, leucocytes, alveolar macrophages, eosinophils, fibrin fibers, Charcot-Leyden crystals and large amount of microorganisms (bacterial flora).

X-ray examination: augment and deformity of lung picture over increased in transparent lung tissue.

Test of ventilatory function: Forced expiratory spirometry quantifies airway obstruction. The FEV_1 and the FEV_1/FVC fall progressively as the severity of bronchium obstruction increases. The FEV_1 is less variable than other measurements of airway dynamics and can be predicted more accurately from age, sex, and height. Roughly comparable information can be obtained from the forced expiratory flow-volume loop. These tests cannot distinguish between chronic bronchitis and emphysema. Arterial blood gas measurements detect hypoxemia and hypercapnia and determine their severity.

SYNDROME OF INCREASED AIRINESS OF THE PULMONARY TISSUE (LUNG EMPHYSEMA)

The syndrome of increased airiness of the pulmonary tissue is based on the protracted enlargement of residual air volume in the lung that clinically manifests by emphysema.

Etiology

Chronic bronchial obstruction; decreased of the pulmonary tissue elasticity; compensatory reaction on the advance of destructive process in the lung and diffuse fibrosis.

Pathogenesis

Depending on the character and mechanism there are the next forms of increased airiness of the pulmonary tissue:

I. According to the widespread:

- local (one sided injury);
- diffuse (both lungs injury).

II. According to the development:

- destructive (chronic obstructive lung diseases, bronchiectatic disease);
- nondestructive (bronchial asthma).

Usually of bronchial obstruction has diffuse character, lung emphysema is most frequently bilateral process and assessed as complication of chronic lung diseases.

Clinical features

The main complaints in patients with increased airiness of the pulmonary tissue are dyspnea and cough. Dyspnea - has expiratory or mixed character and increased during physical activity. Cough - commonly dry and has reflex character, on destructive processes - with purulent sputum discharge.

Objective examination

General patient's condition may be satisfactory (early stage of the disease, the stage of remission); may be middle grave, moderate grave or grave (progression of bronchiectatic disease, destructive process in the lung, bronchial asthma attacks). Due to the acute or gradual chronic hypoxia may be observed the deranged consciousness.

The posture of the patients is frequently active. May be observed the forced posture - orthopnea (spasm of bronchi, attacks of bronchial asthma, decreasing the breath surface).

The color of the skin is characterized by central or diffuse cyanosis due to the accumulation of the carbon dioxide and reduced restored hemoglobin.

Inspection of the chest may reveal barrel-like (emphysematous) form of the chest with protruded supra- and subclavicular fosses, horizontal direction of the ribs, smoothed and narrow intercostals spaces, increased anteroposterior diameter. As usual the chest is symmetrical, the type of respiration is mixed or thoracic, accessory respiratory muscles active participate in the breathing act. especially m.

sternocleidomastoideus and m. trapezius with evident elevation and lowering of the entire chest during breathing. May be observed tachypnea with shallow respiration depth.

Palpation of the chest. Elasticity of the chest is decreased (rigid chest), the chest is painless. Vocal fremitus is badly transmitted.

Percussion of the lungs. In comparative percussion of the lungs generalized hyperresonance (bandbox sound) may be heard over the hyperinflated lungs of emphysema. In topographic percussion of the lungs is observed bilateral lowering of the lower lungs edges, respiratory mobility of the lower borders of the lungs is decreased.

Auscultation of the lungs. In auscultation of the lungs may be observed pathologically decreased vesicular breathing and dry rales.

Additional methods of examination

Clinical blood analysis: secondary erythrocytosis; leukocytosis, neutrophilia, accelerated ESR (during progression of chronic diseases), eosinophilia (bronchial asthma).

Sputum analysis: data depends on the main disease.

X-ray examination: the signs of increased airiness of the pulmonary tissue, low diaphragm's position.

Spirometry shows decreased vital lung capacity.

TOPIC 2
PNEUMONIA. PLEURAL SYNDROME. DENTAL ASPECTS

Definition and modern classification of pneumonias (hospital-acquired, non-hospital-acquired, aspiration, pneumonia at immunodeficiency persons), classification by character of affection of the lungs (pleuropneumonia, bronchopneumonia, interstitial pneumonia). The basic etiology factors of pneumonias. Lobar and bronchopneumonia: complaints and physical methods of examination of the patients. Criteria of heavy current of pneumonia. Instrumental diagnostics of consolidation of pulmonary tissue. Laboratory findings of an inflammatory syndrome at pneumonias. Principal causes of development of pneumosclerosis. Pneumosclerosis, physical and instrumental examination of a patient. The basic clinical forms of tumors of the lungs: clinical features in the central and peripheral localization of tumor. A syndrome of consolidation of pulmonary tissue. The reasons of the development of inflammation of the pleura. Ways of occurrence and circulation of intrapleural fluid both in norm and pathologies. Complaints of a patient in dry pleurisy and pleural effusion, differences of the results of physical examination (palpation, percussion, auscultation of the lungs). Syndromes of accumulation of fluid and air in the pleural cavity. Opportunities of instrumental diagnostics. Pleural puncture: pleural fluid examination. Differences between exudates and transudates due to the results of physical and laboratory examination. The basic clinical syndromes and stages of the syndrome of respiratory failure in lung diseases.

PNEUMONIA

Pneumonia – acute inflammatory lung disease with obligatory alveoli involment and exudative formation in them.

Classification

I. Acceding to the particularities of infection:

- nonhospital pneumonia;
- pneumonia in outpatients;
- pneumonia in innnpatients;
- intrahospital pneumonia;
- asperities pneumonia;
- pneumonia at severe immunodeficiency persons.

II. The category of the patients with nonhospital pneumonia:

1 category – pneumonia in patients without associated pathology and other modified factor;

2 category – pneumonia in patients with associated pathology and/or other modified factor;

3 category – pneumonia that needs hospitalization (without intensive treatment);

4 category – severe pneumonia that needs intensive treatment (reanimation).

III. The groups with intrahospital pneumonia:

1 group (A) – patients with mild or moderate pneumonia severity (without risk factors) that develops in different period of hospitalization or grave pneumonia with early manifestation (less than 5 days of hospitalization);

2 group (B) – patients with slight or moderate pneumonia severity (with specific risk factors) that develops in different period of hospitalization or grave pneumonia with early manifestation (less than 5 days of hospitalization);

3 group (C) – patients with grave in presence risk factors) or pneumonia with late manifestation (more than 5 days of hospitalization).

Nonhospital pneumonia means pneumonia that develops outside from hospital (in conditions of life).

Intrahospital pneumonia means pneumonia that develops in first 48-72 hours after hospitalization in condition of reject infectious in incubation period on the moment of admission to the hospital.

The main risk factors:

- smoking;
- taking of alcohol;
- chronic left ventricular heart failure;
- chronic obstructive pulmonary disease;
- influence of toxic ecologic and professional factors;
- innate defects of bronchopulmonary system;
- chronic infection in nosepharynx;
- the state of immunodeficiency and treatment with immune depressants;
- the status after operation;
- general exhaustion;
- long confinement to bed;
- old age.

The main pathogenic links:

- entrancing of the pathologic agent to the pulmonary tissue;

- impaired local bronchopulmonary resistance;
- development of the local inflammatory process and its overspreading in lung tissue;
- sensebilization advance to infectious agents and input of proinflammatory reactions;
- impaired microcirculation;
- activation of oxidative stress and proteolysis in lung tissue;
- antibody and immune complexes formation.

ACUTE LOBAR PNEUMONIA

All authors who studied the etiology of acute lobar pneumonia (pleuropneumonia, croupous pneumonia), discovered Frenkel pneumococci (mostly types I and II, less frequently types III and IV) in about 95 per cent of cases. Fridlaender diplobacillus, streptococcus, staphylococcus, etc. are found less frequently.

Acute lobar pneumonia occurs mostly after severe overcooling. The main portal of infection is bronchogenic, less frequently lymphogenic and haematogenic. Congestion in the lungs in cardiac failure, chronic and acute diseases of the upper airways, avitaminosis, overstrain and other factors promote the onset of pneumonia. Acute lobar pneumonia is relatively frequent in patients who had pneumonia in their past history (it recurs in 30- 40 per cent of cases which is another evidence of the hyperergic character of the disease).

Pathological anatomy

Four stages are distinguished in the course of acute lobar pneumonia. The stage of *congestion* is characterized by acute hyperemia of the lung tissue, exudation, obstruction of capillary patency, and stasis of the blood. It lasts from 12 hours to 3 days. The stage of *red hepatization* continues from 1 to 3 days. The alveoli are filled with plasma rich in fibrinogen and erythrocytes. The stage of *grey hepatization* is characterized by cessation of erythrocyte diapedesis; the erythrocytes contained in the exudate decompose and their hemoglobin converts into haemosiderin. The alveoli (containing fibrin) become filled with leucocytes. The lungs become grey. The stage lasts from 2 to 6 days. The last stage is *resolution*. Fibrin is liquefied by proteolytic enzymes and exudate is gradually resorbed.

Clinical features

The onset of the disease. Typical acute lobar pneumonia begins abruptly with shaking chills, severe headache, and fever, to 39-40°C. The chills usually persist for 1-3 hours, then pain appears in the affected side; sometimes it may arise below the costal arch in the abdomen to simulate acute appendicitis, hepatic colics, etc. (this usually occurs in inflammation of the lower lobe of the lung, when the diaphragmal pleura becomes involved in the process). Cough is first dry and in 1-2 days dusty sputum is expectorated.

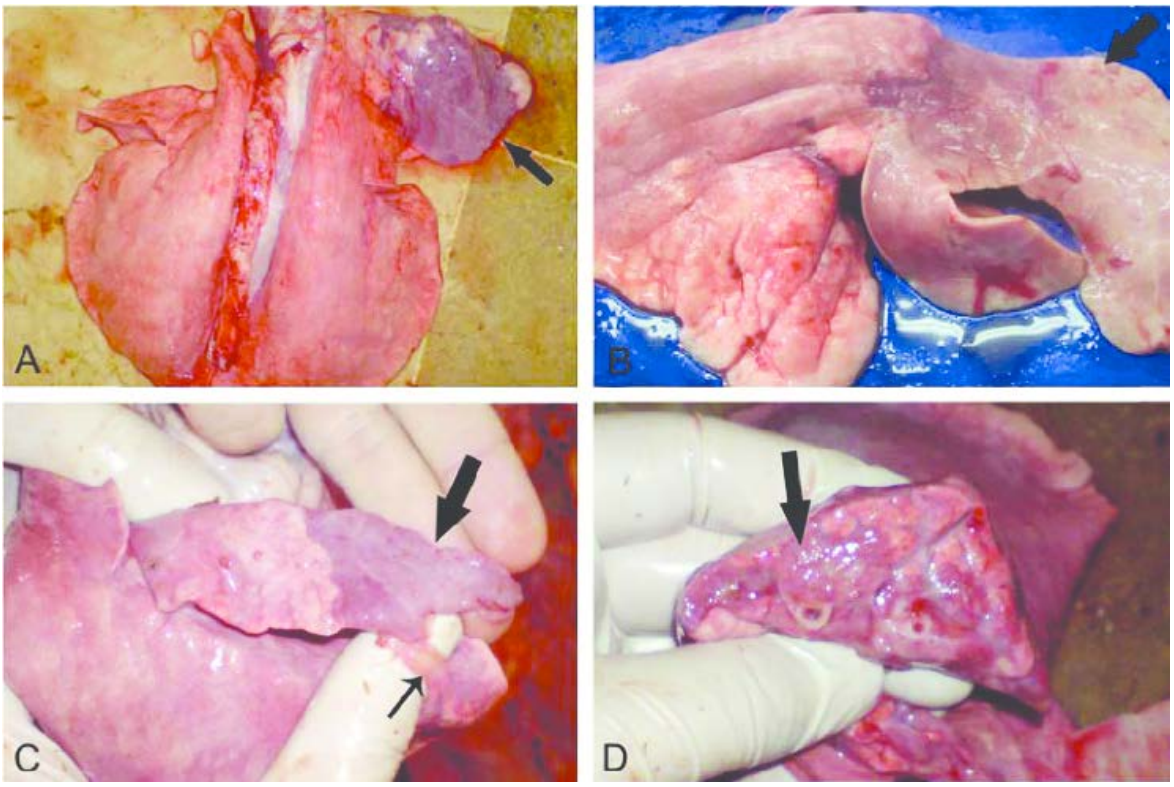

Image 6. A-Right cranial lobe, lobar pneumonia (arrow), dorsal appearance, B-Right cranial lobe with medial lobe, lobar pneumonia (arrow), dorsal appearance, C-Medial lobe lobular pneumonia (arrow), adhesion on visceral pleura (thin arrow), dorsal appearance, D-The cut section of pneumonic areas

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Objective examination

The patient's general condition is grave. General examination shows hyperemia of the cheeks, more pronounced on the affected side, dyspnea, cyanosis, often herpes on the lips and nose; the affected side of the chest lags behind in the respiratory act. Vocal fremitus is slightly exaggerated over the affected lobe. Sounds over the lungs are quite varied and depend on the distribution of the process, the stage of the disease,

and other factors. At the onset of the disease, shortened percussion sound can be heard over the affected lobe, often with tympanic effect because liquid and air are simultaneously contained in the alveoli; the vesicular breathing is decreased while bronchophony is increasing; the so-called initial crepitation (crepitus indux) is present.

The height of the disease (classified by pathologists as the red and grey hepatization stages) is characterized by the grave general condition. It can be explained not only by the size of the affected area of the lung which thus does not take part in respiration but also by general toxicosis. Respiration is accelerated and superficial (30-40 per min) and tachycardia (100-200 beats per min) is characteristic. Dullness is heard over the affected lobe of the lung; bronchial respiration is revealed by auscultation. Vocal fremitus and bronchophony are exaggerated. Vocal fremitus is in some cases either absent or enfeebled (in combination with pleurisy with effusion, and also in massive acute lobar pneumonia, in which the inflammatory exudate fills large bronchi); bronchial breathing is inaudible. Before the antibiotic era, the patient with acute lobar pneumonia would often develop vascular failure with a marked drop in the arterial pressure due to toxic sis. Vascular collapse is attended by general asthenia, drop of temperature, increased dyspnea, cyanosis and accelerated small pulse. The nervous system is also affected (sleep is deranged; hallucinations and delirium are possible, especially in alcoholic patients). The heart, liver, kidneys and other organs are also affected. Fever persists for 9-11 days if antibiotics are not given. The temperature then drops abruptly during 12-24 hours or lytically during more than 2-3 days. Resolution stage. The exudate thins, air again fills the alveoli to decrease dullness of the percussion sound, tympany increases, and bronchial breathing lessens. Crepitation is heard again (crepitus redux) because the alveolar walls separate as air fills them. Moist rales are heard. Exaggerated vocal fremitus, then bronchophony, and finally bronchial breathing disappear.

Additional methods of examination

General blood analysis. The leukocyte count in the blood increases to 15-25 x 109 per liter (15000-25000 per microlitre); neutrophils account for 80-90 per cent of the leucocytes; a shift to the left with the appearance of juvenile forms is sometimes observed. The number of eosinophils increases and they can disappear completely in grave cases. Relative lymphopenia and monocitosis are observed. The ESR increases, the red blood does not change.

Sputum is tenacious during the congestion period; it is slightly crimson and contains much protein, a small number of leucocytes, erythrocytes, alveolar

cells, and macrophages. In the stage of red hepatization sputum is variant and rusty; it contains fibrin and a higher number of formed elements. In the stage of grey hepatization leucocyte count in the sputum increases significantly; the sputum becomes mucopurulent. In the resolution stage, leucocytes are converted into detritus, which is found in the sputum; many macrophages are also found. Pneumococci, staphylococci, Friedlaender diplobacilli can be detected in the sputum.

X-Ray changes in the lungs depend on the stage of the disease. The lung pattern is first intensified, then dense foci develop, which later fuse. The shadow usually corresponds to the lung lobe. The lungs become normally clear in two or three weeks. Dynamics of the X-ray changes spends on the tune when the therapy is begun.

BRONCHOPNEUMONIA (FOCAL PNEUMONIA)

Separate lobules of the lungs are affected in bronchopneumonia, hence another name, lobular pneumonia. Inflammatory foci may be multiple, or they may fuse (confluent pneumonia); the foci may be located in various parts of both lungs simultaneously (mostly in the lower parts of the lungs).

Quite varied bacterial flora would be normally found in bronchopneumonia. The importance of pneumococcus has significantly decreased while the role of other microorganisms, especially of streptococci and staphylococci, has increased. Acute pneumonia is caused in many cases by viruses (in influenza, ornithosis, and psittacosis).

Development of bronchopneumonia is associated with the extension of the inflammatory process from the bronchi and bronchioles to the pulmonary tissue (hence another name of bronchopneumonia - catarrhal pneumonia, which reflects the transition of inflammation and infection with the mucous secretion from the inflamed bronchi into the alveoli). Infection gets inside the pulmonary tissue via the bronchi, and more frequently peribronchially, i.e. by lymph ducts and interalveolar septa. Local atelectasis that occurs in obstruction of the bronchus by a "mucopurulent plug" is important in the pathogenesis of bronchopneumonia. Obstruction of bronchial patency can be caused by a sudden bronchospasm and edema of the bronchial mucosa, inflammation (bronchitis), etc. Recently bronchopneumonia occurs mostly in children and the aged, usually during cold seasons (spring, autumn, winter).

Clinical features

The onset of the disease is usually overlooked because the often develops against the background of bronchitis or catarrh of the up air airways. But if a patient with

clinical signs of acute bronchitis develops high temperature and has symptoms of a more severe disease, he should be considered to have bronchopneumonia. The most typical signs of bronchopneumonia are cough, fever and dyspnea. If the inflammatory focus at the periphery of the lung and the inflammation involves the pleura pain in the chest during coughing and deep breathing may occur. Fever may persist for various terms in bronchopneumonia. Usually fever is remittent and irregular. The temperature is often subfebrile or it may even be normal in the middle-aged or old patients.

Objective examination

Can sometimes reveal moderate hyperemia of face and cyanosis of the lips. Respiration accelerates to 25-30 per min; respiratory lagging of the affected side of the chest may be observed. Percussion and auscultation may prove ineffective if the inflammatory foci are small and deeply located. In the presence of a large focus, especially if it is located at the periphery of the lung tissue, and also in confluent pneumonia, the percussion sounds lose resonance (or become completely full), and auscultation reveals vesiculobronchial or bronchial breathing. Vocal fremitus and bronchophony are characteristic of such cases. Dry and moist rales are frequent, but consonating moist rales and crepitation that are heard over a limited part of the chest are especially informative.

Additional methods of examination

Clinical blood analysis: leukocytosis, neutrophilia, shift of leukocyte formula to the left, accelerated ESR.

Sputum analysis: in focal pneumonia the sputum is mucopurulant, tenacious or tenacious thick consistency, glass-like with yellow traces color, odorless. In microscopic study are revealed a lot of columns ciliated epithelium, leucocytes, alveolar macrophages.

X-ray examination: in focal pneumonia- the signs of focal pulmonary tissue consolidation (darkening limited by the lung's segment).

TUMORS OF THE LUNGS

Tumors of the lungs may be benign or malignant primary tumors or metastases from primary cancers of many other organs and tissues. Primary lung tumors include bronchogenic carcinoma (the most common type of lung cancer), bronchial carcinoid, and a number of rarer types.

Bronchial carcinoid (formerly called bronchial adenoma) may be benign or malignant and occurs equally in both sexes. Its course is prolonged. The endobronchial portion of the tumor may obstruct the lumen of major bronchi. Risk bleeding from the overlying mucous membrane often occurs. Recurrent pneumonia within the same lung zone and localized overlying pleural pain are common. Metastases are uncommon but may occur to regional lymph nodes.

Etiology

Cigarette smoking is the principal cause of bronchogenic carcinoma, accounting for >90% of cases in men and > 80% of cases m women, with 87% of all lung cancers attributed to tobacco exposure. A strong dose-response relationship occurs in the three most common types of bronchogenic carcinoma: squamous cell, small cell, and adeno carcinoma; the slope of the curve is steepest for small cell carcinoma and least steep for adenocarcinoma. A small proportion of lung cancers (15% in men and 5% in women) are related to occupational agents, often overlapping with smoking: asbestos, radiation, arsenic, chromates, nickel, chloromethyl ethers, mustard (poison war) gas, and coke oven emissions. The exact role of air pollution is uncertain.

The TNM (tumor, node, metastasis) system is a standard staging classification for non-small cell carcinoma. Small cell carcinoma has usually metastasized by the time it is diagnosed; it is staged as either limited (confined to one hemithorax with or without involvement of mediastinal and ipsilateral supraclavicular lymph nodes) or extensive (spread beyond this point).

Clinical features

Manifestations depend on the tumor's location and type of spread. Because most *bronchogenic carcinomas* are endobronchial, patients typically present with cough, with or without hemoptysis. In patients with chronic bronchitis, increased intensity and intractability of preexisting cough suggest a neoplasm. Sputum arising from an ulcerated bronchial tumor usually is not excessive (although occasionally sputum may be profuse and watery with bronchioloalveolar carcinomas), but it contains inflammatory exudate and is often blood-streaked. Hemoptysis is uncommon in small cell carcinoma. Copious bleeding is uncommon and strongly suggests invasion of large underlying blood vessels. Bronchial narrowing may cause air trapping with localized wheezing and commonly causes atelectasis with ipsilateral mediastinal shift, diminished expansion, dullness to percussion, and loss of breath sounds. Infection of an obstructed lung produces fever, chest pain, and weight loss. Persistent localized chest pain suggests neoplastic invasion of the chest wall.

Peripheral nodular tumors are asymptomatic until they invade the pleura or chest wall and cause pain or until they metastasize to distant organs. Late symptoms include fatigue, weakness, decreased activity, worsening cough, dyspnea, decreased appetite, weight loss, and pain. Malignant serosanguineous pleural effusions are common and are often large and recurrent. *Horner's syndrome* (due to invasion of the cervical thoracic sympathetic nerves) consists of enophthalmos, miosis, ptosis, and ipsilateral facial anhidrosis. *Pancoast syndrome* (due to infiltration of the brachial plexus and neighboring ribs and vertebrae) consists of pain, numbness, and weakness of the affected arm. The two syndromes may coexist. A tumor may extend directly into the esophagus, producing obstruction, sometimes complicated by a fistula. Phrenic nerve invasion usually causes diaphragmatic paralysis.

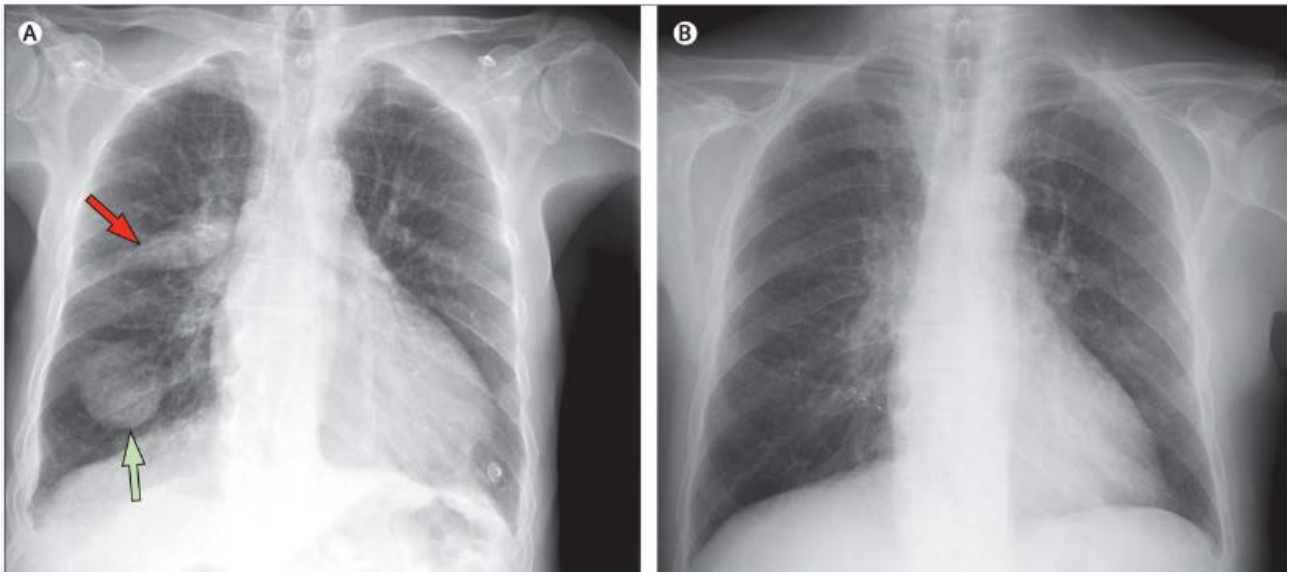

Image 7. Phantom Tumors of the lungs
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Clinical features of cardiac involvement include arrhythmias, cardiomegaly, and pericardial effusion. *Superior vena cava obstruction* and left recurrent laryngeal nerve paralysis (causing hoarseness) are produced by direct extension of the tumor or by extension of the tumor from neighboring lymph nodes. In the superior vena cava syndrome, obstruction of venous drainage leads to dilation of collateral veins in the upper part of the chest and neck; edema and plethora of the face, neck, and upper part of the torso, including the breasts; suffusion and edema of the conjunctiva; breathlessness when supine. Intrapulmonary spread of primary or secondary cancer may cause lymphangitic carcinomatosis with subacute cor pulmonale, worsening

hypoxemia, and severe dyspnea. Secondary hematogenous nodular metastases within the lungs are common, but secondary bronchial invasion is rare. Hematogenous metastatic spread to the liver, brain, adrenals, and bone is common and may occur early, resulting in symptoms at those sites before obvious pulmonary symptoms.

Paraneoplastic syndromes of lung cancer, which are numerous, are extrapulmonary, remote effects of tumors. They lead to metabolic and neuromuscular disturbances unrelated to the primary tumor or metastases. They may be the first sign of occurrence or recurrence, but they do not necessarily indicate that a tumor has spread outside the chest In hypertrophic pulmonary osteoarthropathy (the best known), clubbing of the fingers and toes and periosteal elevation of the distal parts of long bones occur. Hematologic disorders, including thrombocytopenic purpura, leukemoid reaction, myelophthisic anemia, polycythemia, and marantic thrombosis, may also occur.

Additional methods of examination

X-ray. The principal sources of diagnostic information are the history, which raises the suspicion of tumor and provides early localizing information, and the chest x-ray, which shows the lesion, its location, and its anatomic effects. However, large-scale studies at several cancer centers did not demonstrate any advantages for lung cancer screening using chest x-rays and sputum sample analysis. Although cancers were occasionally detected earner using these methods, early detection did not appear to affect the overall survival of patients.

Bronchoscopy is used to visualize and biopsy bronchial tumors. With a flexible bronchoscope, the subsegmental bronchi can be explored to demonstrate and to sample tumors by washings, brushings, and biopsy. Many surgeons perform a preoperative mediastinoscopy to evaluate the mediastinal and hilar lymph nodes, to confirm the diagnosis, and to separate operable from inoperable tumors.

Exploratory thoracotomy is required in < 10% of cases to establish the diagnosis and resectability of lung cancer. Contraindications include distant or mediastinal metastases and cardiorespiratory insufficiency. Exploration is unnecessary when metastases are demonstrated by mediastinoscopy, by parasternal mediastinotomy (which has largely replaced scalene node exploration), or by pleural or liver biopsy. Palpable lymph nodes and metastatic skin nodules provide important diagnostic material.

PLEURISY

Most diseases of the pleura (pleurisy included) are secondary to disease of the lung. Pleurisy usually develops as a reaction of the pleura to pathological changes in the adjacent organs, in the lungs in the first instance, and less frequently as a symptom of a systemic disease. Serous pleurisy often arises as an allergic reaction. Purulent pleurisy is often a complication of bronchopneumonia: inflammation may extend onto the pleura, or an inflammatory focus may turn into an abscess, which opens into the pleural cavity. Inflammation of the pleura is always attended by markedly increased permeability of the wall of the affected capillaries of the pulmonary pleura.

In the presence of purulent processes in the lungs or adjacent organs (pericarditis, perioesophagitis, etc.), purulent pleurisy often develops abruptly. The affection of the pleura in tumours, which in most cases are metastatic (less frequently primary), decreases its absorptive function to promote accumulation of pleural effusion (haemorrhagic effusion in most cases).

DRY PLEURISY

Dry pleurisy (adhesive, fibrinous) is the pathology of the respiratory system that characterized by bands and commissures formation between pleural layers and increase of their thickness due to the inflammation.

Etiology

- infection (tuberculosis, bacterial infection, fungus, viral infection);
- dissemination of the tumor cells to pleura;
- reactive pleuritis (uremia);
- dehydrotation (profuse bleeding, vomiting, diarrhea).

Pathogenesis

- dilation of lymphatic capillaries;
- increased vessels penetration;
- pleural inflammation;
- pleural infiltration;
- fibrin accumulation on visceral and parietal pleura;
- fibrosis development;
- anatomic and functional block of resorbtion apparatus.

Clinical features

Intensity of clinical features depends on the pathologic process spreading. The main complaints in patients with dry pleurisy are: cough, pain in the chest and dyspnea.

Cough - most commonly dry and has reflectivity character.

Pain in the chest - connecting with pleura injury, occurs suddenly on the affected side, intensive and increases during deep inspiration or coughing.

Dyspnea - intensity depends on process spreading.

Objective examination

General patient's condition may be from middle grave to grave.

The posture of the patients is forced (lie on the affected side in order to relieve the pain).

The color of the skin and visible mucosa is without changes.

In inspection occur superficial, rapid breathing (via intensive pain); participation of the accessory respiratory muscles in the breathing act or even mixed type of respiration. In static inspection as usual the chest is symmetrical, on dynamic - detect poor movement of the chest expansion on one side.

In palpation the chest is painful on the damage side, elasticity is saved, vocal fremitus is equal transmitted.

In comparative percussion of the lungs may be observed dull sound over pathological region.

In topographic percussion of the lungs the normal lower borders are revealed, respiratory mobility of the lower border on the affected side is decreased.

In auscultation of the lungs over the region with decreased vesicular breathing detect pleural friction sound.

Additional methods of examination

Clinical blood analysis: leukocytosis, neutrophilia, shift of leukocyte formula to the left, accelerated ESR.

X-ray examination: - the signs of pleura injury and fibrin deposition.

PLEURISY WITH EFFUSION

Pleurisy with effusion is characterized by the presence of exudate in the pleural cavity, mostly in the outer costal-diaphragmatic sinus. Parietal, supradiaphragmatic and interlobar pleurisy also occur. After abatement of inflammation, effusion (serous, serofibrinous, haemorrhagic, purulent) usually resolves but the pleura remains thickened, its membranes adhere to one another, and the pleural cavity is completely

obliterated in some cases. Effusion sometimes remains between adhesions to stimulate encapsulated pleurisy.

Etiology

- infection (tuberculosis, bacterial infection, fungus, viral infection);
- dissemination of the tumor cells to pleura;
- allergic and autoimmune pleurisy;
- pleurisy in diffuse connective tissue pathology;
- posttraumatic pleurisy.

Pathogenesis

- direct pleura injury (trauma, operation, tumor, infection through lymph or blood);
- contact way of process spreading;
- infection and allergic mechanism;
- inflammatory exudation to the pleural cavity;
- impaired lymph and blood circulation;
- oncotic pressure disturbance;
- impaired resorbtion;
- fluid accumulation in pleural cavity.

Clinical features

Intensity of clinical features depends on the pathologic process spreading, etiology, amount and character of exudates. The main complaints in patients with exudative pleurisy are: cough, dyspnea, pain and feeling of heaviness in the chest, supplementary - general weakness, hyperthemia, loss of appetite and perspiration.

Cough - most commonly in initial stage dry and has reflectivity character, along disease progression becomes moist.

Pain in the chest - one of the fist symptoms and connecting with pleura injury, may be different in its intensity (from moderate to acute) and increases during deep inspiration or coughing. In cause of diaphragmatic pleurisy localization the pain can irradiate to the upper abdominal region or via the n. diaphragmatic to the neck. For the period of exudates volume intensity the pain becomes duller but dyspnoea increase.

Dyspnea - has mixed character and its intensity depends on the exudates volume and speed of its accumulation, degree of affected lung ventilation via compression by fluid and mediastenum organs displacement.

Objective examination

General patient's condition may be from middle grave to grave.

The posture of the patients is forced (lie on the affected side in order to revile the pain).

The color of the skin and visible mucosa are characterized by diffuse cyanosis. In case of mediastenum fluid localization observed edema of the face and neck, dysphagia and voice changes.

In inspection observe superficial, rapid breathing (via intensive pain); mixed type of dyspnea. In static inspection as usual the chest is asymmetrical, on dynamic - detect poor movement of the chest expansion on the affected side.

In palpation the chest is painful, rigid with badly vocal fremitus transmission on the damaged side.

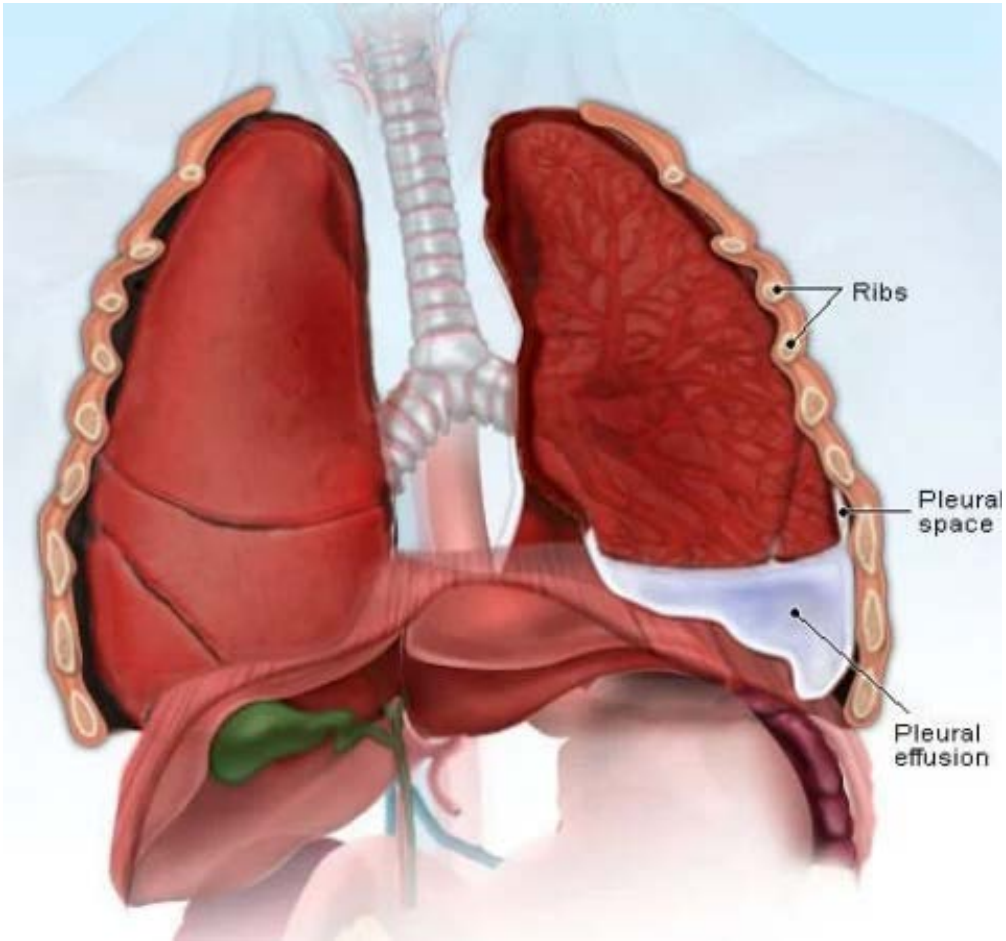

Image 8. Lung scarring and a permanent decrease in lung function are associated with chronic pleural effusion

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In comparative percussion of the lungs detect dull sound over the pathological region.

In topographic percussion of the lungs the lower edge on the affected side is elevated, respiratory mobility is increased. In large exudates amount over the lung there are 5 clinical-diagnostic zones (for more detail information seen syndrome of fluid accumulation in pleural cavity).

In auscultation of the lungs in the initial stage on the affected side over the region with decreased vesicular breathing detect pleural friction sound. In large exudates amount according to the five clinical-diagnostic zones there are distinguished: over exudates - the zone with significant decreased vesicular breathing or full absent of breathing sounds; over consolidate pulmonary tissue - the zone with pathological bronchial breathing; over the free from fluid and healthy side - the zone with increased vesicular breathing.

Additional methods of examination

Clinical blood analysis: leukocytosis, neutrophilia, shift of leukocyte formula to the left, accelerated ESR.

X-ray examination: - the signs of pleura affection, significant darkness with slanting upper border of the fluid and dislocation of mediastenum to the healthy side.

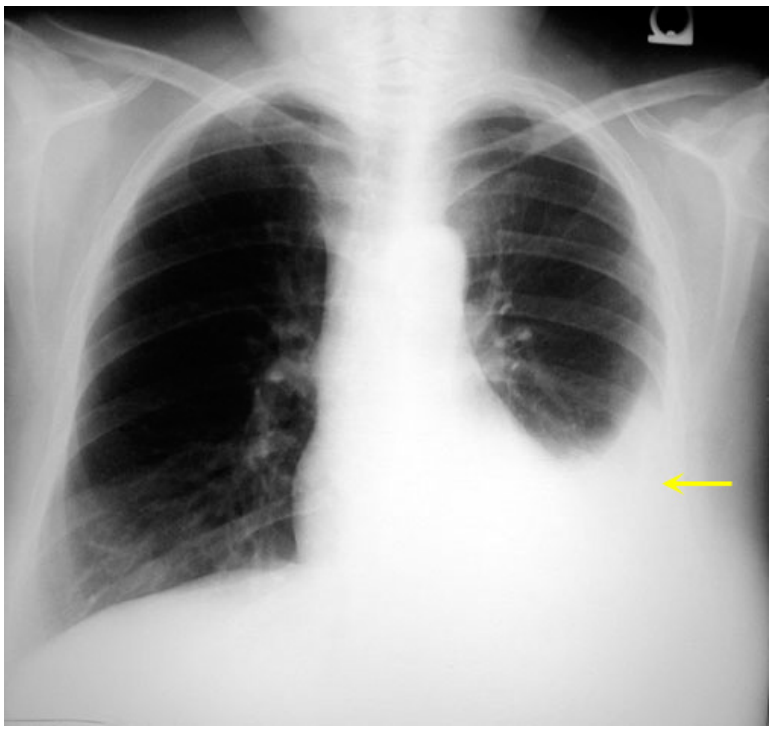

Image 9. Pleurisy with effusion X-ray examination

This image was downloaded from website https://www.meddean.luc.edu

Pleural fluid analysis includes: assessment of macroscopic characteristics (character, transparency, color, consistency, odor, relative density); chemical study (protein, Rivalts's reaction); microscopic study (cellular composition); bacterioscopic study.

RESPIRATORY INSUFFICIENCY

The function of the external respiratory apparatus is to supply the body with oxygen and to remove carbon dioxide formed by exchange reactions. This function is realized firstly by ventilation, i.e. gas exchange between the outer and alveolar air. This insures the required oxygen and carbon dioxide pressure in the alveoli (an important factor is intrapulmonary distribution of the inspired air). Secondly, this function is realized by diffusion of carbon dioxide and oxygen through the walls of the alveoli and lung capillaries (oxygen is supplied from the alveoli to the blood and carbon dioxide is diffused from the blood to the alveoli). Many acute and chronic diseases of the bronchi and the lungs cause respiratory insufficiency (Wintrich, 1854). The degree of morphological changes in the lungs does not always correspond to the degree of their dysfunction.

Respiratory insufficiency is now defined as the condition with abnormal gas composition of the blood, or this abnormality is compensated for by intense work of the external respiratory apparatus and higher load on the heart. This decreases functional abilities of the body. It should be noted that the external respiratory function is closely connected with the blood circulatory function: the heart work is intensified during external respiratory insufficiency, which is an important compensatory element of the heart function.

Respiratory insufficiency is manifested clinically by dyspnea and cyanosis; at later stages, when cardiac failure joins the process, edema occurs.

The patient with respiratory insufficiency employs the same compensatory reserves as a healthy person does during heavy exercise. But the compensatory mechanisms of a sick person are actuated much earlier and it loads under which a healthy person would feel no discomfort (e.g. dyspnea and tachypnea can develop in a patient with lung emphysema given during slow walking).

Among the first signs of respiratory insufficiency are inadequate changes in ventilation (rapid and deep breathing) at comparatively light roads for a healthy individual; the minute volume increases. In certain bases (bronchial asthma, lung emphysema, etc.) respiratory insufficiency is compensated by intensified work of the

respiratory muscles, i.e. by the filtered respiratory mechanics. In other words, in patients with pathology if the respiratory system, the external respiratory function is maintained at he required level by mobilizing compensatory mechanisms (i.e. by efforts greater than required for healthy persons), and by minimizing the respiratory reserves: the maximum lung ventilation decreases, the coefficient of oxygen consumption drops, etc.

Various mechanisms are involved gradually to compensate for progressive respiratory insufficiency depending on its degree. At the early stages of respiratory insufficiency the external respiratory function at rest is realized in normal way. The compensatory mechanisms are only actuated during exercise in a sick person. In other words, only reserves of the external respiratory apparatus are decreased at this stage. As insufficiency further progresses, tachypnea, tachycardia, and signs of intensified work of the respiratory muscles (during both inspiration and expiration), with involvement of accessory muscles, develop during light exercise and even at test. At the later stages of respiratory insufficiency, when the body compensatory reserves are exhausted, arterial hypoxaemia and hypercapnia develop. In addition to the growing vivid arterial hypoxaemia, signs of latent oxygen deficit also develop; underoxidized products (lactic acid, etc.) are accumulated in the blood and tissues.

Still at later stages, right ventricular incompetence joins pulmonary insufficiency because of the developing hypertension in the lesser circulation, which is attended by increased load on the right ventricle, and also because of dystrophic changes in the myocardium occurring as a result of its constant overload and insufficient oxygen supply. Hypertension in the vessels of the lesser circulation in diffuse affections of the lungs arises by reflex mechanisms in response to insufficient lung ventilation and alveolar hypoxia- the Euler-Liliestrand reflex (this reflex mechanism is an important adaptation means in focal lung affections; it limits blood supply to insufficiently ventilated alveoli). Further, in chronic inflammatory diseases of the lungs due to cicatricial and sclerotic changes in the lungs (and due to affections in the lung vessels) blood passage through the lesser circulation becomes even more difficult. Increased load on the myocardium of the right ventricle stimulates gradual development of its insufficiency to cause congestion in the greater circulation (pulmonary heart).

Depending on the cause and mechanism of developing respiratory insufficiency, three types of disordered lung ventilation are distinguished: *obstructive, restrictive and mixed* (combined).

The obstructive type is characterized by difficult passage of air through the bronchi (because of bronchitis, bronchospasm, contraction or compression of the trachea or large bronchi, e.g. by a tumor, etc.). Spirography shows marked decrease in the MLV and PVC, the VC being decreased insignificantly. Obstruction of the air passage increases the load on the respiratory muscles. The ability of the respiratory apparatus to perform additional functional load decreases (fast inspiration, and especially expiration, and also rapid breathing become impossible).

The restrictive type of ventilation disorder occurs in limited ability of the lungs to expand and to collapse, i.e. in pneumosclerosis, hydro- and pneumothorax, massive pleural adhesions, kyphoscoliosis, ossification of the costal cartilages, limited mobility of the ribs, etc. These conditions are in the first instance attended by a limited depth of the maximum possible inspiration. In other words, the vital capacity of the lungs decreases together with the maximum lung ventilation), but the dynamics of the respiratory act is not affected: no obstacles to the rate of normal breathing and whenever necessary, to significant acceleration of respiration) are imposed.

The mixed or combined type includes the signs of the two previous disorders, often with prevalence of one of them; this type of disorder occurs in long-standing diseases of the lungs and the heart.

External respiratory dysfunction occurs also when the anatomical dead pace increases (in the presence of large cavities inside the lung, caverns, abscesses, and also in multiple large bronchiectasis). Similar to this type is the respiratory insufficiency due to circulatory disorders (e.g. in thromboembolism, etc.) during which part of the lung is excluded from gas exchange, while its ventilation is to a certain degree maintained. Finally, respiratory insufficiency arises during uneven distribution of air in the mgs (distribution disorders), when a part of the lung is not ventilated (in pneumonia, atelectasis), with preservation of blood circulation. Part of venous blood is not oxygenated before it enters pulmonary veins and the left chambers of the heart. Similar to this type of respiratory insufficiency with regard to pathogenesis) is the so-called vascular bypass or shunting (from right to left), during which part of the venous blood from the pulmonary artery system enters directly the pulmonary vein (bypassing the capillaries) to mix with oxygenated arterial blood. Oxygenation of blood in le lungs is thus upset but hypercapnia may be absent due to compensatory intensification of ventilation in the intact parts of the lung. This is partial respiratory insufficiency (as distinct from total insufficiency where hypoxemia and hypercapnia are present).

Respiratory insufficiency is characterized by upset gas exchange through the alveolar-capillary membrane of the lungs. It occurs when this membrane is thickened to interfere with normal gas diffusion through it he so-called pneumonoses, alveolar-capillary block). It is not accompanied by hypercapnia either since the rate of CO_2 diffusion is 20 times higher than that of oxygen. This form of respiratory insufficiency is, in the first instance, characterized by arterial hypoxaemia and cyanosis. Lung ventilation is intensified.

Respiratory insufficiency associated with toxic inhibition of the respiratory centre, anaemia, or oxygen deficit in the inhaled air, is not connected directly with the pathology of the lungs.

Acute and chronic respiratory insufficiencies are differentiated. The former occurs in attacks of bronchial asthma.

Three degrees and three stages of respiratory insufficiency are also distinguished. The degrees of respiratory insufficiency reflect the gravity of the disease at a given moment.

The first degree of respiratory insufficiency (dyspnea, in the first instance) becomes evident only at moderate or significant physical load.

Dyspnea develops during light exercise in *the second degree* of insufficiency; the compensatory mechanisms are involved when the patient is at rest and functional diagnosis can reveal some deviations from the normal indices.

The *third degree* is characterized by dyspnea at rest and cyanosis as a manifestation of arterial hypoxaemia; deviations from the normal indices during functional pulmonary tests are significant.

Stages of respiratory insufficiency in chronic diseases of the lungs reflect the changes occurring during the progress of the disease. Stages of latent pulmonary, pronounced pulmonary and cardiopulmonary insufficiency are normally differentiated.

TOPIC 3
ARTERIAL HYPERTENSION. SYMPTOMATIC ARTERIAL HYPERTENSION. HYPERTENSIVE CRISIS. DENTAL ASPECTS

Arterial hypertension, essential hypertension, secondary hypertension. The risk main factors of arterial hypertension and mechanism of the development. Modern classification of arterial hypertension. The main complaints of the patients with arterial hypertension, external examination, palpation, percussion, auscultation of the patients with arterial hypertension. ECG-signs of the changes in myocardium in the patients with arterial hypertension. Secondary hypertension. Hypertonic crisis.

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).

Clinical features

Among all hypertensive states secondary arterial hypertension make approximately 20 %.

Chronic glomerulonephritis meets more frequent in young and middle ages. In anamnesis is acute glomerulonephritis. Clinical features of the glomerulonephritis - proteinuria more than 1 g/day, hematuria, impairment of renal function (early onset with hypo- and isostenuria) and hypertension (mostly increasing of diastolic pressure). Angina pectoris, myocardial infarction and stroke are rare. Rethinopathy develops comparatively lately, arteries are only slightly narrowed, veins are normal. But anemia, which atypical for essential hypertension, is often marked. Final establishment of diagnosis based at the result of isotopic renovasography and biopsy of kidneys, which finds out fibrioblastic, proliferative, membranouse and sclerotic changes in glomerules, tubes and vessels of kidneys.

Chronic pyelonephritis - is a chronic interstitial nephritis resulting from urinary tract infection associated with vesico-uretric reflux. In anamnesis are nephrolitiasis, pyelitis, anomalies of development at kidneys and other diseases of urinary tract. The

most important among the morphological features is presence of coarse scars, which is associated with contraction of the related papilla and dilatation of the corresponding calyx. In the half of cases pyelonephritis is accompanied by arterial hypertension. Difficulty of diagnostics of chronic pyelonephritis consists of that in 1/3 cases the signs of inflammatory process in urinary ways are not observed. Diagnosis based at the following signs: hypostenuria, polyuria, pyuria, proteinuria, information of isotopic reno-, urography, ultrasound examination (diminishing of sizes of kidneys, deformation of the tubular system), biopsy of kidneys and angiography. From the general features of course of disease: young age, primary increase of diastolic pressure, absence of coronary and cerebral complications.

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).

Phaeochromocytoma - is a rare tumor of the chromaffin tissue which secretes catecholamines and is responsible for less than 0,1 % of causes of hypertension. The tumors are usually benign (10 % malignant) and may arise from any part of the sympathetic chain. In over 90 % of causes the tumor is found in the adrenal medulla.

Clinical features: hypertension usually paroxysmal.

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.

Primary hyperaldosteronism *(Conn's syndrome)* is characterized by overproduction of aldosterone, the main salt-retaining hormone, may be due to a primary abnormality in the zone glomerulosa or secondary to stimulation of aldosterone secretion by angiotensin II following activation of the renin-angiotensin system.

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).

Cushing's syndrome — is defined as the symptoms and signs associated with prolonged inappropriate elevation of free corticosteroide level. Patients with Cushing's syndrome can be classified into two groups on the basis of whether the condition is adrenocorticotropic hormone (ACTH)-depended or independed:

1. *ACTH-depended:*
   iatrogenic (ACTH-therapy);
   pituitary-depended bilateral adrenal hyperplasia (Cushng's disease);
   ectopic ACTH syndrome (benign or malignant non-endocrine tumour).
2. *non-ACTH-depended:*
   iatrogenic (prednisolone therapy);
   adrenal adenoma;
   adrenal carcinoma.

Diagnostic criteria of the dishing s syndrome: general inspection: persons with overweight, obesity, thinning hair, hirsutism, acne, plethora, moon face, presence of purple-violet striates on the skin of abdomen, thighs, in area of armpits; examination of organs and systems: arterial hypertension, psychosis, cataracts, peptic ulcer, osteoporosis, exuberant callus with fractures, wasting and weakness of the proximal thigh muscles, menstrual disorders; disorder of tolerance to glucose, hyperglycemia;

changing in the normal day's rhythm of secretion of ACTH and Cortisol (in a norm in the morning higher, than in the evening), increasing the level of Cortisol and 17-OKS is in blood.

Hemodynamic arterial hypertension is associated with demanding of the heart and large vessels and subdivides into:

- systolic hypertension at atherosclerosis, aortic regurgitation;
- regional hypertension at aorta caorctation;
- hyperkinetic circulatory syndrome at arteriovenouse fistulas.

Diagnostic criteria of the hemodynamic arterial hypertension: Arterial hypertension as a result of atherosclerosis of aorta is diagnosed on the basis of the followings signs: elderly patients, accented of second heart sound and its metallic tint over the aorta, systolic murmur over the aorta, increased systolic arterial pressure, presence the signs of atherosclerosis of peripheral arteries; expansion of aorta detected by ultrasound and X-ray examination.

Arterial hypertension under aortic regurgitation characterized by increased of systolic blood pressure and the decreased diastolic with high pulse pressure.

Arterial hypertension as a result of aorta coarctation is characterized by increasing of blood pressure at the upper extremities and it's decreasing at the lower extremities. In palpation - over the intercostal arteries intensification of pulsation is marked, loosening the pulsation at the peripheral arteries of lower extremities is observed; in auscultation - rough systolic murmur is heard at heart base, over the pectoral aorta (at the anterior chest wall and in interscaspular region), irradiated along the large vessels (carotid, subclavia).

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.

Table 4

Factors influencing cardiovascular risk in patients with hypertension

Demographic characteristics and laboratory parameters
Sex(men >women)
Age
Smoking (current or past history)a
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)

Pathogenesis

Elevation of blood pressure arise due to the imbalance between pressor and depressor factors which lead to development of changes in arterioles and precapillares, changing structure and function of cellular membranes, including smooth muscular cells of arterioles, disorders of activity of sodium-calcium pumps, increasing concentration of the ionized calcium in cytoplasm and finally excessive vascular resistance.

Classification

Table 5

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 6

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).

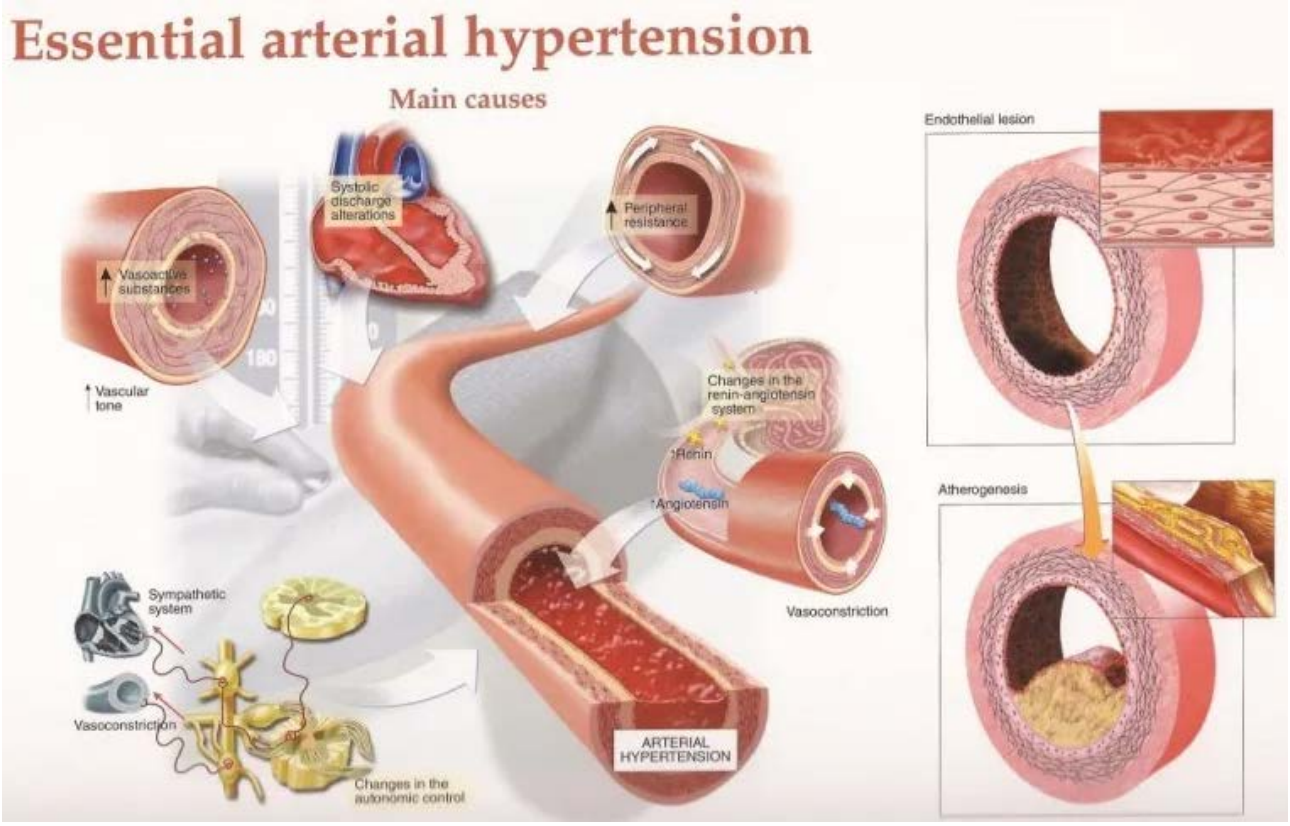

Image 9. Main causes of Essential hypertension

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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
   - 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:
   - hypertensive emergency in pregnancy
   - acute onset of severe hypertension persisting > 15 minutes plus end-organ damage
   - end-organ damage may include severe preeclampsia, eclampsia, and hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome

3. False or pseudo hypertensive crisis
    - 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)

TOPIC 4
ATHEROSCLEROSIS. IHD. ANGINA PECTORIS. ACUTE MYOCARDIAL INFARCTION. DENTAL ASPECTS

Determination of Ischemic Heart Diseases. Main pathogenesis mechanisms of Ischemic Heart Diseases, Basic risk factors of Ischemic Heart Diseases. Modern classification of Ischemic Heart Diseases. Determination and main symptoms of angina pectoris. Functional classes of angina pectoris. Objective diagnostic methods of angina pectoris (ECG, Monitor- controlling 24 hours –ECG, Exercise test, Scintigraphy of heart, Coranarigraphy). Unstable angina pectoris, definition of unstable angina pectoris and main clinical signs and symptoms of unstable angina pectoris. Determination of acute coronary symptoms. Determination of main clinical signs of acute myocardial infraction. Physical examination methods of patients with acute myocardial infraction. Stages of myocardial infraction. ECG-changes in different forms of myocardial infraction. Modern bio-markers of necrosis of myocardium.

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.

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.

Thus the pathological substrate of IHD is almost atheroma narrowing of the coronary arteries. Atheroma or atherosclerosis is a focal disease of the arterial intima. There are some stages of evolution of atherosclerotic process. Initial stage is fatty streaks, which develop as circulating monocytes migrate into the intima take up oxidized low density lipoprotein from the plasma and become lipid foam cells. As these foams cells die extracellular lipid pools appear. Smooth muscle cells then migrate into and proliferate within the plaque. A mature fibrinolipid plaque has a core extracellular lipid, separated from the lumen by a thick cap of a collagen-rich fibrous tissue. Such plaque may narrow the lumen of the vessel and often precipitate local vasospasm and thrombosis. The luminal diameter of a coronary artery must be decreased by at least 50 % to 70 % before blood flows becomes inadequate to meet the metabolic demands of the heart during exercise or stress.

The evolution of the atheromatous plague corresponds with clinical forms of IHD. The principal cause of *stable angina* is atherosclerosis involving at least one large epicardial artery that limited coronary flow under some condition. Stable angina is related to a fixed obstruction and it is usually precipitated by an increase in myocardial oxyden demand (demanded ischemia).

Unstable angina is defined as an obstruction of at least one major epicardial artery that occupies at least 70 % of the artery's cross-sectional diameter or an obstruction of the left main coronary artery that occupies at last 50 % of its diameter. Episodes of myocardial ischemia are due to abrupt reduction in coronary blood flow results from plaque rupture, rapid growth of the lesion or incomplete occlusion of the vessel. Unstable angina is a transitory condition. A platelet rich thrombus forms rapidly around the site of the rupture, reducing, but not usually occluding the blood flow in the vessel.

Myocardial infarction is almost always due to the formation of occlusive thrombus at the site of rupture of an atheromatous plaque in a coronary artery. The affected artery is more commonly completely occluded, usually by a fibrin-rich "red" thrombus.

Sudden death in most cases is attributable to IHD and is usually due to arrhitmia or asystole (ventricular fibrillation, sinoatrial block, complete AV-block) related to acute coronary syndrome, heart failure or scarring from a previous myocardial infarction.

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 7

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 or stair climbing	Slight
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.

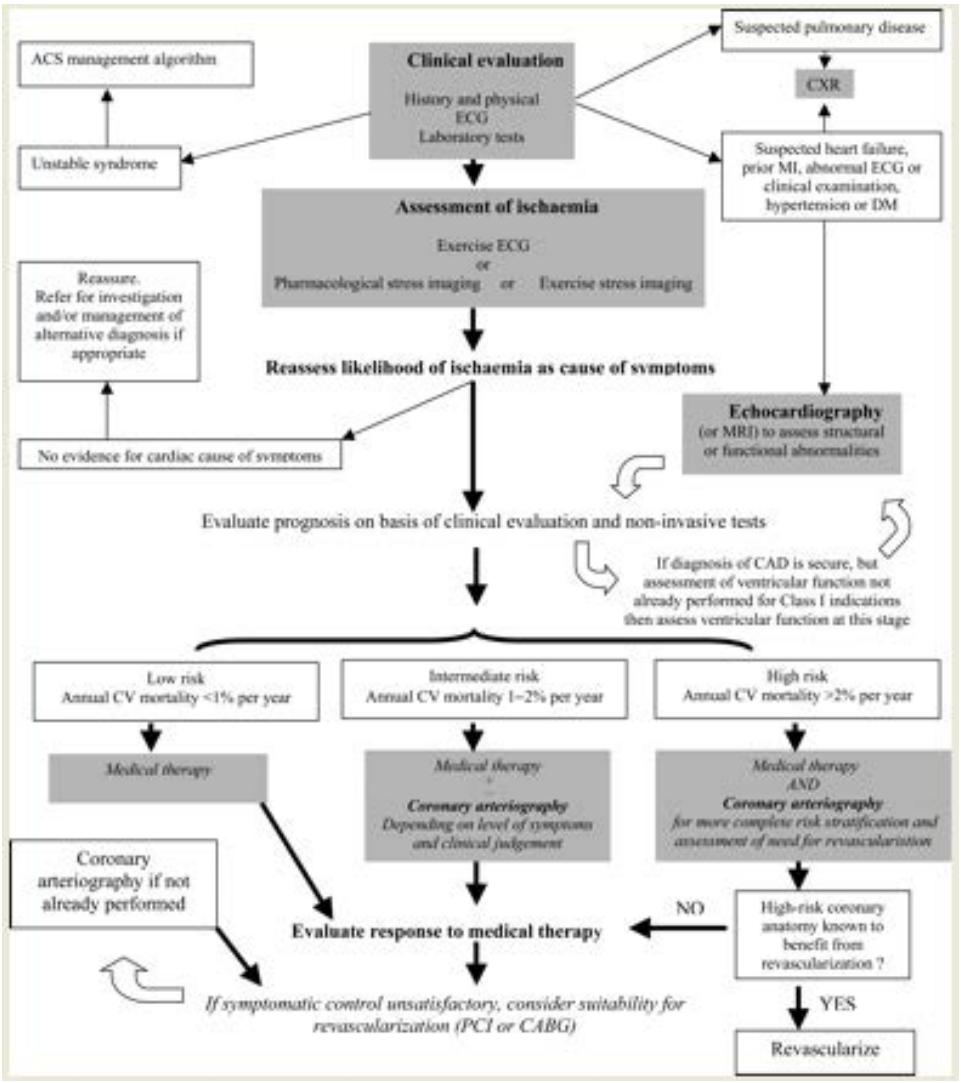

Image 10. An algorithm for the initial evaluation of patients with clinical symptoms suggestive of angina

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Additional methods 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.

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.

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.

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.

UNSTABLE ANGINA

Classification of unstable angina was proposed by E. Braunwald.

Braunwald classification system for unstable angina (UA)

Patients are assessed according to each of the following sets of criteria:

Severity of angina

Class I - New onset of severe angina or increased frequency of attacks

No rest pain

Class II- Angina at rest, sub-acute

Angina at rest within the past month, but not within the preceding 48 hours

Class III-Angina at rest, acute

Angina at rest during the preceding 48 hours

Clinical circumstances

Class A -- Secondary UA

Symptoms secondary to an identified condition reducing myocardial oxyden suplly or increasing demand

Class B - Primary UA

Class C - Post-infarction UA

Intensity of treatment

Class I - Minimal or no therapy

Class II - Therapy for chronic stable angina

Class III - Maximum anti-anginal therapy, including intravenous nitrates

ECG changes

Presence or absence of transient ST, T abnormalities

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.

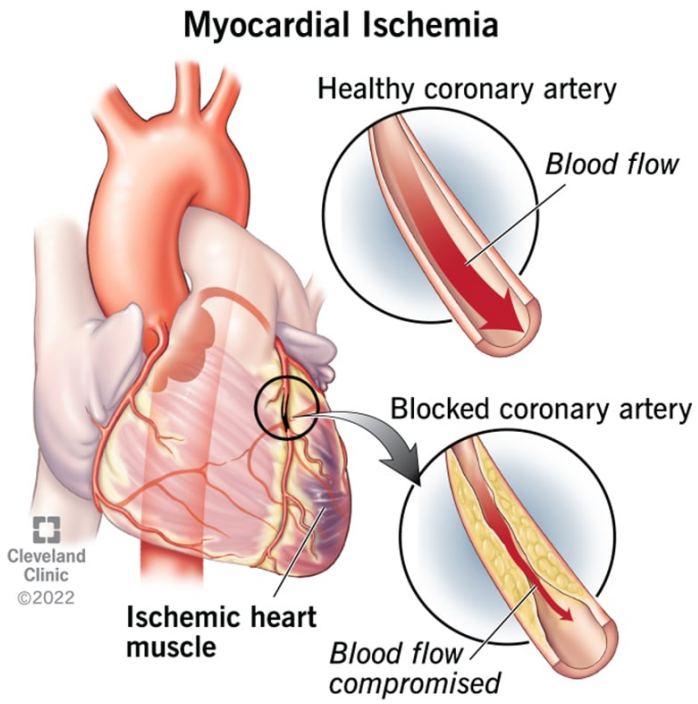

Image 11. Effects of myocardial ischemia

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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.

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.

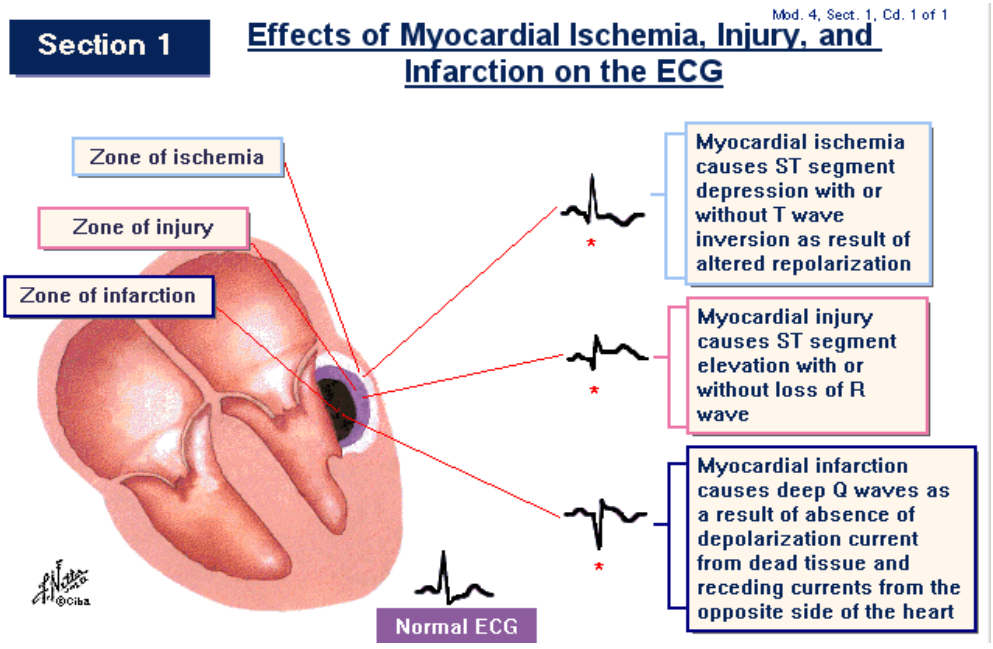

Image 12. Effects of myocardial ischemia

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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 8

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.

Table 9

Dynamic of laboratory markers of myocardial infarction

Markers	Norma	Time from onset of myocardial infarction		
		Baseline elevation	Peak elevation	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.

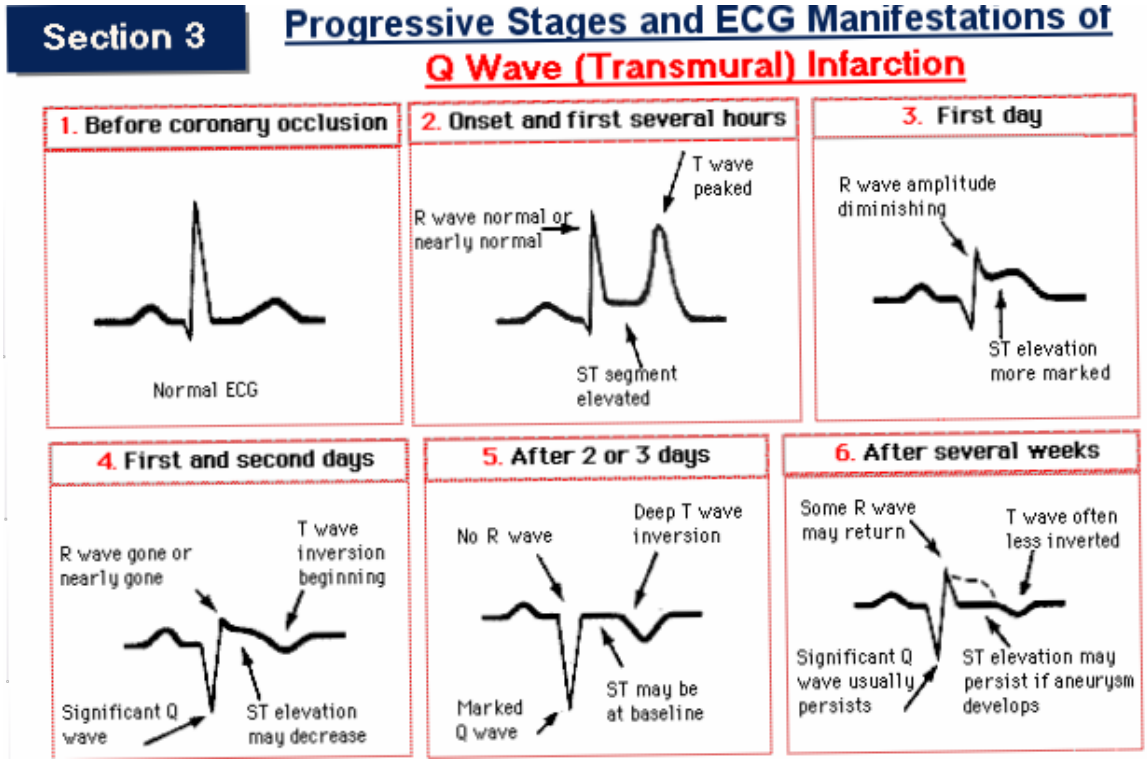

Image 13. Progressive stages and ECG manifestation of Q wave (transmural) infarction
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Echo-CG: two-dimensional echocardiography may assess the cardiac structures, pericardium and ascending aorta, allows identification of regional wall motion abnormalities, valvular abnormalities, global left and right ventricular function and

detecting important complications such as cardiac rupture, ventricular septal defect, mitral regurgitation and pericardial effusion.

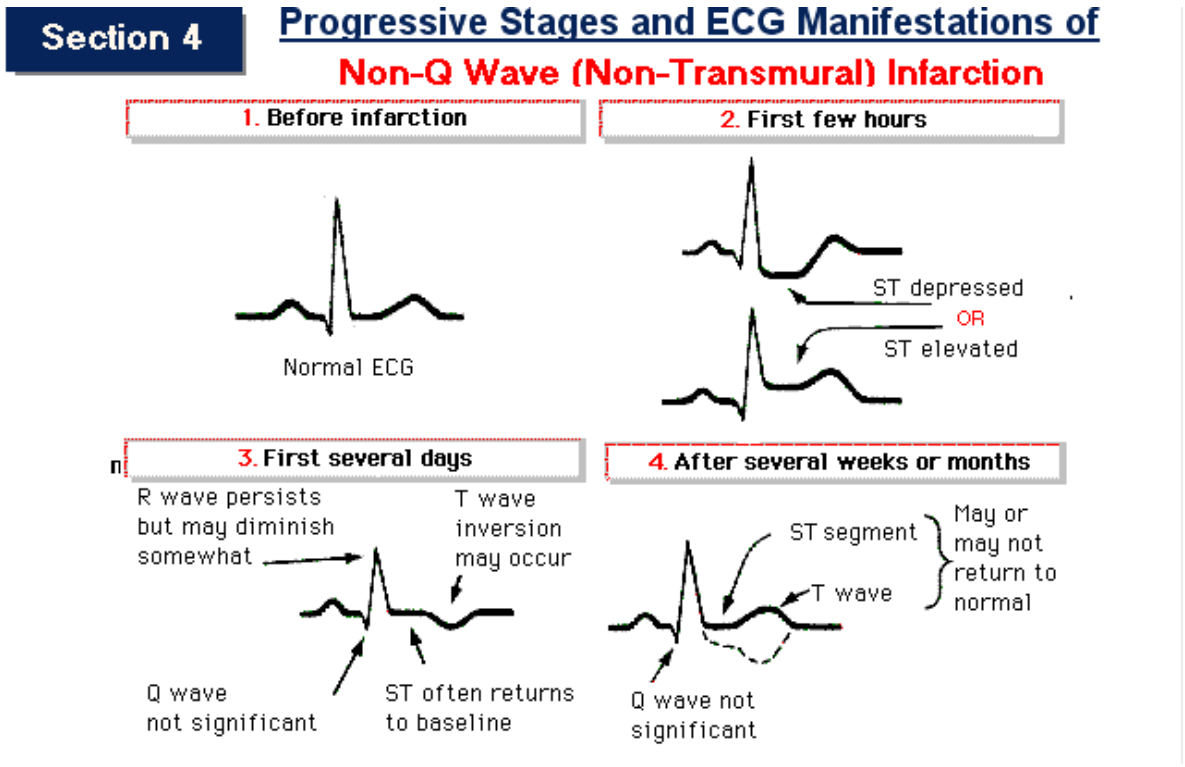

Image 14. Progressive stages and ECG manifestation of non-Q wave (non-transmural) infarction

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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.

TOPIC 5
ACUTE HEART FAILURE. ACUTE VASCULAR INSUFFICIENCY. CHRONIC HEART FAILURE. DENTAL ASPECTS

HEART FAILURE

Heart failure *(HF) is a clinical syndrome caused by abnormal cardiac structure or function resulting in reduced cardiac output or elevated intracardiac pressures at rest or during exercise.*

To support a diagnosis of HF, there must be a presence of symptoms (eg, dyspnea, orthopnea, bendopnea, ankle and/or abdominal swelling, fatigue) and/or signs (eg, elevated jugular venous pressure, pulmonary crackles) of pulmonary or systemic congestion.

In addition, these findings must be validated by elevated natriuretic peptide levels or objective evidence of pulmonary or systemic congestion through diagnostic modalities including imaging (eg, chest radiography, elevated filling pressures on echocardiography) or hemodynamic measurements (eg, right heart catheterization) at rest or during exercise.

The stages of HF can be classified as a continuum:

1) **At risk of HF (Stage A)**: Patients who are without structural heart disease, elevated biomarker levels, signs and/or symptoms of HF, but have significant risk factors for HF development. This group includes patients with hypertension, coronary artery disease, diabetes, obesity, a family history of cardiomyopathy, and/or known exposure to cardiotoxins.

Importantly, not all patients with risk factors will go on to develop HF, but primary prevention through modifying risk factors may reduce the development of symptomatic HF. These interventions include regular physical activity, maintaining a healthy diet and weight, limiting alcohol intake, and managing existing comorbidities with evidence-based pharmacotherapies that prevent cardiovascular events including HF.

2) **Pre-HF (Stage B)**: Patients without previous or current symptoms and/or signs of HF, and with the presence of one of the following: structural heart disease (eg, left ventricular hypertrophy, cardiac chamber enlargement), abnormal cardiac function (eg, reduced ventricular systolic function, increased filling pressures), or elevated levels of cardiac biomarkers (eg, natriuretic peptide levels, cardiac troponins).

3) **Symptomatic HF (Stage C)**: Patients with structural heart disease functional heart abnormality, or both, with previous or current signs and/or symptoms of HF.

4) **Advanced HF (Stage D)**: Patients with HF refractory or intolerant to guideline-directed medical therapy, severe signs and/or symptoms of HF at rest, recurrent hospitalizations, requiring advanced interventions, including transplant, mechanical circulatory support, or palliative care.

For therapeutic and prognostic purposes, HF is also classified according to left ventricular ejection fraction (LVEF), which is defined as stroke volume (end-diastolic minus end-systolic volume) divided by the end-diastolic volume.

1) **HF with reduced ejection fraction (HFrEF)** is typically defined as clinical HF with LVEF ≤40%.

2) **HF with mildly reduced ejection fraction (HFmrEF)**: The LVEF threshold for the diagnosis of HFrEF and heart failure with preserved ejection fraction (HFpEF) has varied across clinical trials and clinical practice guidelines. LVEF between 41% and 49% is considered to be in the gray zone, referred to as mildly reduced ejection fraction.

3) **HFpEF** is typically defined as clinical HF with LVEF ≥50%.

4) **HF with improved ejection fraction (HFimpEF)** is typically defined as HF with an LVEF baseline of ≤40%, followed by a ≥10-point increase from baseline, and a subsequent measurement of LVEF >40%.

Clinically, HF may also be classified as **left ventricular**, **right ventricular**, or **biventricular failure**, depending on whether the predominant symptoms of congestion are pulmonary, systemic, or both.

High-output HF refers to clinical HF occurring due to increased cardiac output and hyperdynamic states, which may not always be associated with an underlying structural heart disease.

ACUTE HEART FAILURE

Acute heart failure - a syndrome that includes the rapid onset of symptoms and signs of impaired functional state of the heart, developing against the background of a previous illness or without it (de novo) and manifests itself as systolic and diastolic dysfunction, cardiac arrhythmias that threaten life and need emergency treatment)

- acute heart failure, which developed for the first time in patients without prior dysfunction of the heart

- decompensation of chronic heart failure

-left ventricular

-right ventricular

On the basis of clinical and hemodynamic data distinguish:

-decompensated acute heart failure (de novo or decompensated CHF), which has mild symptoms of this syndrome, but does not meet the criteria for cardiogenic shock, pulmonary edema, or hypertensive crisis;

-right ventricular acute heart failure

-hypertensive acute heart failure

-Pulmonary edema

-Cardiogenic shock

-high heart rate acute heart failure

Cardiogenic shock is a clinical syndrome that is characterized by a decrease in systolic AT below 90 mm Hg. Art. signs of decreased perfusion of organs and tissues (cold moisture, pale skin, oligoanuria). The pulse in the peripheral arteries is frequent, soft, filiform, may not be detected, at the same time, pulsation of large arteries (carotid, femoral) due to centralization of blood circulation is relatively good. A decrease in pulse pressure is characteristic. Tachypnea is noted, in some patients - dry or wet rales in the lungs. At the same time, cardiac output, MOS, and, unlike hypovolemia, significantly increased pressure in the pulmonary capillaries (pressure of jamming of the pulmonary artery) are significantly reduced - usually more than 18 mm Hg. Art.

The main pathogenetic link of cardiogenic shock is a decrease in cardiac output, which cannot be compensated by peripheral vasoconstriction and leads to a significant decrease in AT and hypoperfusion.

Cardiogenic shock due to acute left ventricular failure should be differentiated from a state of low cardiac output associated with an absolute or, more often, relative decrease in left ventricular filling. The hemodynamically significant right ventricular myocardial infarction in patients with left ventricular myocardial infarction of the posterior (lower) localization, cardiac tamponade, and thromboembolism of the branches of the pulmonary artery belongs to the last.

Cardiogenic pulmonary edema - acute left ventricular or atrial atrial insufficiency, accompanied by severe respiratory failure and decreased arterial blood

oxygen saturation <90%. It develops due to a decrease in the discharge of the left ventricle (or atrium) and blood stasis on the blood flow paths to the left heart, an increase in hydrostatic pressure in the capillaries of the lungs, which leads to the release of the liquid part of the blood into the interstitial space and alveoli. Left ventricular failure is characteristic of hemodynamic overload of the ventricle (hypertensive crisis, aortic heart defects, mitral insufficiency) or primary myocardial damage (CHD), and liver-atrial - mitral stenosis and myxoma of the left atrium. In a hypertensive crisis, pulmonary edema develops against a background of high AT with relatively preserved left ventricular function.

Acute right ventricular failure is characterized by a decrease in ejection of the right ventricle with stagnation of blood and an increase in pressure on the bloodstream to it, that is, in the veins of a large circle of blood circulation. Isolated acute right ventricular failure develops in the event of a sharp overload of the right ventricle with pressure during thromboembolism of the branches of the pulmonary artery, and overwhelming with hemodynamically significant myocardial infarction of the right ventricle in patients with myocardial infarction of the posterior (lower) wall of the left ventricle. The cause of atrial insufficiency may be a mix of the right atrium.

Biventricular (total) heart failure develops in the case of simultaneous damage to both ventricles (for example, myocarditis) or the left heart, which leads to a persistent increase in pressure in the left atrium, pulmonary hypertension and overload of the right ventricle with resistance and, as a consequence, right ventricular failure.

In contrast to the specified:

Decompensation of chronic heart failure is characterized by the sudden onset of symptoms of chronic heart failure of a higher functional class or left ventricular (more often) or right ventricular acute heart failure.

Diagnostics

• Acute heart failure is a life-threatening condition and requires urgent treatment, so diagnostic measures should be carried out quickly.

• Electrocardiography in 12 leads can detect ischemia and myocardial necrosis, as well as cardiac arrhythmias and conduction.

• An echocardiographic study allows you to assess the state of systolic and diastolic function of the ventricles of the heart, to detect damage to the heart valves

and the presence of regurgitation, external or internal (in the area of the interventricular septum) myocardial rupture, effusion into the pericardial cavity.

• Doppler examination of blood flow through the tricuspid valve is important for indirect assessment of systolic pressure in the pulmonary artery.

• X-ray examination (including radiopaque methods) of the chest organs allows you to evaluate the size of the heart, its shape, to identify venous congestion in the lungs, to conduct differential diagnosis of left ventricular failure and lung diseases that have similar clinical manifestations (pneumonia, thromboembolism of the branches of the pulmonary artery), and also aortic dissection.

• In some patients, arterial blood gases and acid-base conditions (CBS) need to be determined. Acute heart failure is characterized by a decrease in pCO2 of arterial blood. pCO2 of arterial blood is first reduced (through hyperventilation), and in advanced stages it is increased. To evaluate CBS, metabolic acidosis with compensatory respiratory alkalosis (in relatively early stages) or respiratory acidosis (in late) is determined. Possible increase in creatinine, aspartic and alanine transaminases, bilirubin. In the coagulogram - signs of disseminated intravascular coagulation. In relatively mild cases, it is sufficient to evaluate the saturation of arterial blood with oxygen using pulse oximetry. In some patients, to clarify the leading pathogenetic mechanism of acute heart failure, it is necessary to evaluate hemodynamic parameters - the pressure of jamming of the pulmonary artery and cardiac output (using a floating balloon catheter of Svan-Hansa).

ACUTE VASCULAR INSUFFICIENCY

Fainting (Syncope)

Syncope is a sudden, brief loss of consciousness with loss of postural tone followed by spontaneous revival. The patient is motionless and limp and usually has cool extremities, a weak pulse, and shallow breathing. Sometimes brief involuntary muscle jerks occur, resembling a seizure.

Near-syncope is light-headedness and a sense of an impending faint without loss of consciousness. It is usually classified and discussed with syncope because the causes are the same.

Seizures can cause sudden loss of consciousness but are not considered syncope. However, seizures must be considered in patients presenting for apparent syncope because history may be unclear or unavailable, and some seizures do not

cause tonic-clonic convulsions. Furthermore, a brief (< 5 second) seizure sometimes occurs with true syncope.

Diagnosis depends on a careful history, eyewitness accounts, or fortuitous examination during the event.

Pathophysiology of Syncope

Most syncope results from insufficient cerebral blood flow. Some cases involve adequate flow but with insufficient cerebral substrate (oxygen, glucose, or both).

Insufficient cerebral blood flow

Most deficiencies in cerebral blood flow result from decreased cardiac output (CO).

Decreased CO can be caused by

- Cardiac disorders that obstruct outflow
- Cardiac disorders of systolic dysfunction
- Cardiac disorders of diastolic dysfunction
- Arrhythmias (too fast or too slow)
- Conditions that decrease venous return

Outflow obstruction can be exacerbated by exercise, vasodilation, and hypovolemia (particularly in aortic stenosis and hypertrophic cardiomyopathy), which may precipitate syncope.

Arrhythmias cause syncope when the heart rate is too fast to allow adequate ventricular filling (eg > 150 to 180 beats/minute) or too slow to provide adequate output (eg, < 30 to 35 beats/minute).

Venous return can be decreased by hemorrhage, increased intrathoracic pressure, increased vagal tone (which can also decrease heart rate), and loss of sympathetic tone (eg, from drugs, carotid sinus pressure, autonomic dysfunction). Syncope involving these mechanisms (except for hemorrhage) is often termed **vasovagal** or neurocardiogenic and is common and benign.

Orthostatic hypotension, a common benign cause of syncope, results from failure of normal mechanisms (eg, sinus tachycardia, vasoconstriction, or both) to compensate for the temporary decrease in venous return that occurs with standing.

Cerebrovascular disorders (eg, strokes, transient ischemic attacks) rarely cause syncope because most of them do not involve the centrencephalic structures that must be affected to cause loss of consciousness. However, basilar artery ischemia, due to transient ischemic attack, stroke, or migraine, may cause syncope.

Rarely, patients with severe cervical arthritis or spondylosis develop vertebrobasilar insufficiency with syncope when the head is moved in certain positions.

Insufficient cerebral substrate

The central nervous system (CNS) requires oxygen and glucose to function. Even with normal cerebral blood flow, a significant deficit of either will cause loss of consciousness . In practice, hypoglycemia is the primary cause because hypoxia rarely develops in a manner causing abrupt loss of consciousness (other than in flying or diving incidents). Loss of consciousness due to hypoglycemia is seldom as abrupt as in syncope or seizures because warning symptoms occur (except in patients taking beta-blockers); however, the onset may be unclear to the examiner unless the event was witnessed.

Etiology of Syncope

Causes are usually classified by the mechanism (see table Some Causes of Syncope).

The most common causes are

- Vasovagal (neurocardiogenic)
- Idiopathic

Many cases of syncope never have a firm diagnosis but lead to no apparent harm. A smaller number of cases have a serious cause, usually cardiac.

Evaluation of Syncope

Evaluation should be done as soon as possible after the event. The more remote the syncopal event, the more difficult the diagnosis. Information from witnesses is quite helpful and best obtained as soon as possible.

History of present illness should ascertain events leading up to the syncope, including the patient's activity (eg, exercising, arguing, in a potentially emotional situation), position (eg, lying or standing), and, if standing, for how long. Important associated symptoms immediately before or after the event include whether there was a sense of impending loss of consciousness, nausea, sweating, blurred or tunnel vision, tingling of lips or fingertips, chest pain, or palpitations. Length of time recovering should also be ascertained. Witnesses, if any, should be sought and asked to describe events, particularly the presence and duration of any seizure activity.

Review of systems should ask about any areas of pain or injury, episodes of dizziness or near-syncope upon arising, and episodes of palpitations or chest pain with exertion. Patients should be asked about symptoms suggesting possible causes,

including bloody or tarry stools, heavy menses (anemia); vomiting, diarrhea, or excess urination (dehydration or electrolyte abnormalities); and risk factors for pulmonary embolism (recent surgery or immobilization, known cancer, previous clots or hypercoagulable state).

Past medical history should ask about previous syncopal events, known cardiovascular disease, and known seizure disorders. Drugs used should be identified (particularly antihypertensives, diuretics, vasodilators, and antiarrhythmics—see table Some Drug Causes of Syncope). Family history should note presence at a young age of heart disease or sudden death in any family member.

Physical examination

Vital signs are essential. Heart rate and blood pressure are measured with the patient supine and after 3 minutes of standing. Pulse is palpated for irregularity.

General examination notes patient's mental status, including any confusion or hesitancy suggesting a postictal state and any signs of injury (eg, bruising, swelling, tenderness, tongue bite).

The heart is auscultated for murmurs; if present, any change in the murmur with a Valsalva maneuver, standing, or squatting is noted.

Careful evaluation of the jugular venous waves while palpating the carotid or auscultating the heart may allow diagnosis of an arrhythmia if an ECG is not available. For example, cannon "a" waves occur when the atria contraction takes place against a closed tricuspid valve and indicate atrial-ventricular dissociation.

Abdomen is palpated for tenderness, and a rectal examination is done to check for gross or occult blood.

A neurologic examination is done to identify any focal abnormalities, which suggest a central nervous system cause (eg, seizure disorder).

Red flags

Certain findings suggest a more serious etiology:

- Syncope during exertion
- Multiple recurrences within a short time
- Heart murmur or other findings suggesting structural heart disease (eg, chest pain)
- Older age
- Significant injury during syncope

- Family history of sudden unexpected death, exertional syncope, or unexplained recurrent syncope or seizures

Interpretation of findings

Although the cause is often benign, it is important to identify the occasional life-threatening cause (eg, tachyarrhythmia, heart block) because sudden death is a risk. Clinical findings help suggest a cause in 40 to 50% of cases. A few generalizations are useful.

Benign causes often lead to syncope.

- Syncope precipitated by unpleasant physical or emotional stimuli (eg, pain, fright), usually occurring in the upright position and often preceded by vagally mediated warning symptoms (eg, nausea, weakness, yawning, apprehension, blurred vision, diaphoresis), suggests vasovagal syncope.
- Syncope that occurs most often when assuming an upright position (particularly in elderly patients after prolonged bed rest or in patients taking drugs in certain classes) suggests orthostatic syncope.
- Syncope that occurs after standing for long periods without moving is usually due to venous pooling.

Dangerous causes are suggested by red flag findings.

- Syncope with exertion suggests cardiac outflow obstruction or exercise-induced arrhythmia. Such patients sometimes also have chest pain, palpitations, or both. Cardiac findings may help identify a cause. A harsh, late-peaking, basal murmur radiating to the carotid arteries suggests aortic stenosis; a systolic murmur that increases with the Valsalva maneuver and disappears with squatting suggests hypertrophic cardiomyopathy.
- Syncope that begins and ends suddenly and spontaneously is typical of cardiac causes, most commonly an arrhythmia.
- Syncope while lying down also suggests an arrhythmia because vasovagal and orthostatic mechanisms do not cause syncope in the recumbent position.
- Syncope accompanied by injury during the episode increases the likelihood of a cardiac cause or seizure, and therefore the event is of greater concern. The warning signs and slower loss of consciousness that accompany benign vasovagal syncope somewhat reduce the likelihood of injury.

Loss of consciousness during a seizure or postictal confusion can sometimes be confused with syncope, but muscular jerking or convulsions that last more than a

few seconds, incontinence, drooling, or tongue biting, if present, usually point to a seizure.

Testing

Testing typically is done.

- ECG
- Pulse oximetry
- Sometimes echocardiography
- Sometimes tilt table testing
- Blood tests only if clinically indicated
- Central nervous system imaging rarely indicated

In general, if syncope results in an injury or is recurrent (particularly within a brief period), more intensive evaluation is warranted. Cardiac and brain imaging are not done unless indicated by clinical findings (suspected cardiac etiology or neurologic deficits).

Patients with suspected arrhythmia, myocarditis, or ischemia should be evaluated as inpatients. Others may be evaluated as outpatients.

ECG is done for all patients. The ECG may reveal arrhythmia, a conduction abnormality, ventricular hypertrophy, pre-excitation, QT prolongation, pacemaker malfunction, myocardial ischemia, or myocardial infarction. If the diagnosis is questionable after this basic evaluation, measuring cardiac markers and obtaining serial ECGs to rule out MI in older patients plus ECG monitoring for at least 24 hours are prudent. Any detected arrhythmia must be associated with altered consciousness in order to be implicated as the cause, but most patients do not experience syncope during monitoring. On the other hand, the presence of symptoms in the absence of rhythm disturbance helps rule out a cardiac cause. An event recorder (which can record cardiac rhythm for longer periods) may be useful if warning symptoms precede syncope. A signal-averaged ECG may identify predisposition to ventricular arrhythmias in patients with ischemic heart disease or in post-myocardial infarction patients. If syncopal episodes are infrequent (eg, < 1/month), an implantable loop recorder can be used for longer term recording. This device continuously records the rhythm and can be interrogated by an external machine that allows the cardiac rhythm to be printed.

Pulse oximetry should be done during or immediately after an episode to identify hypoxemia (which may indicate pulmonary embolism). If hypoxemia is present, CT angiography is indicated to rule out pulmonary embolism.

Laboratory tests are done based on clinical suspicion; reflexively obtained laboratory panels are of little use. However, all females of childbearing age should have a pregnancy test. Hematocrit is measured if anemia is suspected. Electrolytes are measured only if an abnormality is clinically suspected (eg, by symptoms or drug use). Serum troponin is measured if acute myocardial infarction is suspected.

Echocardiography is indicated for patients with clinically unexplained syncope, exercise-induced syncope, cardiac murmurs, or suspected intracardiac tumors (eg, those with positional syncope).

Tilt table testing may be done if history and physical examination indicate vasodepressor or other reflex-induced syncope. It is also used to evaluate exercise-induced syncope if echocardiography or exercise stress testing is negative.

Stress testing (exercise or pharmacologic) is done when intermittent myocardial ischemia is suspected. It is often done for patients with exercise-induced symptoms. Exercise testing is less valuable unless physical activity precipitated syncope.

Invasive electrophysiologic testing is considered if noninvasive testing does not identify arrhythmia in patients with any of the following:

- Unexplained recurrent syncope
- Unexplained red flag findings
- Ischemic cardiomyopathy, non-ischemic cardiomyopathy, and adult congenital disease, or unexplained syncope that does not otherwise meet criteria for an ICD used for primary prevention

A negative response defines a low-risk subgroup with a high rate of remission of syncope. The use of electrophysiologic testing is controversial in other patients.

EEG is warranted if a seizure disorder is suspected.

CT and **MRI** of the head and brain are indicated only if signs and symptoms suggest a focal CNS disorder.

Treatment of Syncope

In witnessed syncope, pulses are checked immediately. If the patient is pulseless, CPR is begun. If pulses are present, severe bradycardia is treated with atropine or external transthoracic pacing. Isoproterenol can be used to maintain adequate heart rate while a temporary pacemaker is placed.

Tachyarrhythmias are treated; a direct-current synchronized shock is quicker and safer than drugs for unstable patients. Inadequate venous return is treated by keeping the patient supine, raising the legs, and giving IV normal saline.

Tamponade is relieved by pericardiocentesis. Tension pneumothorax requires insertion of a pleural cannula and drainage. Anaphylaxis is treated with parenteral epinephrine.

Placing the patient in a horizontal position with legs elevated typically ends the syncopal episode if life-threatening disorders are ruled out. If the patient sits upright too rapidly, syncope may recur; propping the patient upright or transporting the patient in an upright position may prolong cerebral hypoperfusion and prevent recovery.

Specific treatment depends on the cause and its pathophysiology. Driving and use of machinery should be prohibited until the cause is determined and treated.

CHRONIC HEART FAILURE

Epidemiology, etiology, pathophysiology

Heart failure with reduced ejection fraction (HFrEF) is better understood than heart failure with preserved ejection fraction (HFpEF) and represents approximately half of all HF cases. The most common etiology of HFrEF is coronary artery disease (CAD) and arterial hypertension. Other causes include viral infection, alcohol abuse, valvular heart disease, chemotherapy (eg, doxorubicin or trastuzumab), peripartum cardiomyopathy, “idiopathic” dilated cardiomyopathy, and genetic cardiomyopathies.

In HFrEF, maladaptive changes after myocardial injury lead to pathologic remodeling of the ventricle with dilatation and impaired contractility. This is mediated by:

1) Maladaptive left ventricle (LV) hypertrophy associated with the reexpression of fetal isoforms of contractile proteins and progressive loss of cardiomyocytes via apoptosis or necrosis.

2) Abnormal calcium homeostasis and depressed beta-receptor density in cardiomyocytes.

3) Myocardial fibrosis.

4) Progression of mitral insufficiency and pulmonary hypertension.

5) Neurohormonal activation involving the renin-angiotensin-aldosterone system (RAAS), the sympathetic nervous system, and enhanced vasopressin secretion accompanied by impaired vasodilatory and renal responses to natriuretic peptides, which increases preload and afterload. These systemic neurohormonal responses are triggered by cardiac output lowering, have detrimental long-term effects on the heart

and systemic vasculature, and create a vicious cycle of further myocardial injury and remodeling, which in turn exacerbates neurohormonal activation.

Additionally, the following systemic abnormalities both underlie HF symptoms and contribute to HF progression: depressed sensitivity of baroreceptors, enhanced reactivity of chemoreceptors and muscular ergoreceptors, vascular endothelial dysfunction and impaired vasodilatory reserve, renal dysfunction, skeletal muscle dysfunction, functional or absolute iron deficiency with or without anemia, chronic inflammatory activation, and neuroendocrine dysfunction favoring catabolic pathways.

HFpEF is less understood and is increasing in prevalence. Patients are more likely to be older, female, and obese, and have a better prognosis than those with HFrEF. They are less likely to have coronary heart disease and more likely to have hypertension, atrial fibrillation (AF), and sleep apnea. Pathophysiology involves heterogeneous factors, such as impaired LV relaxation due to excessive afterload (owing to elevated blood pressure, aortic stenosis, increased arterial stiffness, and impaired peripheral vasodilatory reserve), decreased passive LV compliance (mediated by changes in the extracellular matrix associated with concentric LV hypertrophy), chronotropic incompetence, microvascular coronary dysfunction, and accompanying myocardial oxidative stress with consequent stimulation of proinflammatory and profibrotic pathways.

Causes of high-output HF include conditions associated with hyperdynamic circulation: severe anemia, thyrotoxicosis, large systemic arteriovenous fistulas, advanced cirrhosis, polycythemia or secondary erythrocytosis, Paget disease, beriberi, carcinoid syndrome, or pregnancy. HF usually develops in patients with hyperdynamic circulation superimposed on an underlying heart disease, although it can occur in absence of structural heart disease.

Cardiomyopathies (abnormalities in cardiac myocytes that result in impaired function) are a predisposing condition for clinical HF but may not always be associated with clinical HF. The World Health Organization categorizes the etiology of HF based on the type of underlying cardiomyopathy, which is defined as pathologic myocardial processes and dysfunction that are a direct consequence of cardiovascular abnormalities other than valvular heart disease, systemic hypertension, congenital heart disease, and atherosclerotic coronary artery disease. For example, dilated cardiomyopathy may be due to toxins (eg, alcohol, cocaine, and chemotherapeutic agents such as anthracyclines, fluorouracil, and trastuzumab),

myocarditis, Chagas disease, peripartum cardiomyopathy, and familial cardiomyopathies (eg, Becker or Duchenne muscular dystrophy), among others.

Causes of HF exacerbations: Patients with chronic HF may develop exacerbations due to the following reasons:

1) Acute coronary syndrome.

2) Poorly controlled hypertension.

3) Tachyarrhythmia (most commonly AF) or bradyarrhythmia.

4) Pulmonary embolism.

5) Endocarditis, myocarditis.

6) Conditions associated with hyperdynamic circulation.

7) Infections (particularly pneumonia).

8) Renal dysfunction.

9) Dietary indiscretion (high sodium intake).

10) Nonadherence to prescribed medications.

11) Iatrogenic: Intravenous fluids, use of medications with negative chronotropic or inotropic effects (eg, verapamil, diltiazem, or inappropriate doses of beta-blockers), cardiotoxic agents (eg, anthracyclines), drugs causing sodium and/or water retention (eg, glucocorticoids, estrogens, nonsteroidal anti-inflammatory drugs [NSAIDs]).

12) Abnormalities in thyroid function (eg, caused by amiodarone).

13) Alcohol abuse, cocaine use.

14) Untreated sleep apnea.

Clinical features

Symptoms of HF are a combination of pulmonary and/or systemic congestion with or without low output. The New York Heart Association (NYHA) classification of the severity of HF (functional status) is based on the assessment of fatigue, dyspnea, and palpitations, which are caused by physical activity. A validated scale, such as that by the NYHA, is commonly used to document functional capacity.

1. **Clinical manifestations of LV failure** (pulmonary congestion):

1) **Symptoms**: Dyspnea (at rest or on exertion); orthopnea (occurs 1-2 minutes after lying down and resolves within a few minutes of sitting or standing up); paroxysmal nocturnal dyspnea, which unlike orthopnea occurs much later after lying down, wakes the patient up, and takes much more time (usually ≥30 minutes) to resolve; cough (an equivalent of exertional dyspnea or orthopnea), generally dry,

occasionally producing pink sputum (usually in patients with pulmonary edema); fatigue.

2) **Signs**: Dilated LV or displaced apex with a third heart sound; crackles over the lung fields (typically audible in the basal regions, although they may extend up to the apical regions), which may be accompanied by wheezing and rhonchi (caused in part by edema of the bronchial mucosa).

2. **Clinical manifestations of right ventricular failure** (systemic congestion):

1) **Symptoms**: Peripheral dependent edema (most commonly affecting the feet and ankles, or the sacral area in bedridden patients), abdominal pain or discomfort caused by liver congestion, or nocturia. The symptoms may also include anorexia, nausea, and constipation caused by venous congestion of the gastric and intestinal mucosa and by reduced cardiac output, which in some cases may lead to malabsorption and subsequent malnutrition or even cachexia in patients with advanced HF.

2) **Signs**: Exudates, including pleural effusions (usually bilateral; when unilateral, they occur more frequently on the right) or ascites; right ventricular heave or a right ventricle that is palpable in the subxiphoid region; an enlarged and tender liver (tenderness is due to stretching of the hepatic capsule and occurs when congestion develops rapidly); a firm and atrophic liver may be observed in a long-standing (several years-long) HF. Other signs include mild jaundice, jugular vein distention with or without sustained elevation, and in some patients Kussmaul sign (increased jugular venous pressure during inspiration, similar to that observed in constrictive pericarditis).

3. **Manifestations common to right and left ventricular failure** (including manifestations of low cardiac output):

1) **Symptoms**: Impaired exercise tolerance, oliguria (in advanced HF).

2) **Signs**: Pale and cool skin of the extremities, diaphoresis, rarely acrocyanosis (features of sympathetic stimulation); tachycardia, third heart sound (often audible in patients with systolic LV dysfunction) or fourth heart sound (more suggestive of isolated diastolic HF), an accentuated pulmonary component of the second heart sound; occasionally murmurs associated with valvular heart disease, which is a cause of HF or is secondary to ventricular dilatation; low pulse pressure, mild elevation of diastolic blood pressure; Cheyne-Stokes respiration; symptoms of abnormal cerebral perfusion, especially in the elderly.

4. **Symptoms and signs of HF with an increased cardiac output** caused by hyperdynamic circulation: High pulse pressure (reduction in diastolic blood pressure); increased precordial pulsation; pulsus altus et celer (bounding and rapid), capillary pulsation (Quincke pulse); tachycardia; abnormal features on auscultation (hyperdynamic heart sounds, sometimes a third or fourth heart sound, midsystolic ejection murmur audible along the left sternal border, sometimes midsystolic murmur over the mitral or tricuspid valve and constant venous hum, carotid bruit); warming and erythema of the skin (not present in patients with ischemia; it may be local, eg, in patients with Paget disease or arteriovenous fistulas). In patients with arteriovenous fistulas, applying pressure on a fistula causes a decrease in heart rate.

5. **Clinical features of HFpEF** are similar to those of HFrEF and include exertional dyspnea and other symptoms of pulmonary congestion, while the features of peripheral hypoperfusion are usually absent.

Table 10

Symptoms and signs typical of heart failure

Symptoms	
Typical	**Less typical**
Breathlessness	Nocturnal cough
Orthopnoea	Wheezing
Paroxysmal nocturnal dyspnoea	Weight gain (>2 kg/week)
Reduced exercise tolerance	Weight loss (in advanced heart failure)
Fatigue, tiredness, increased time to recover after exercise	Bloated feeling
Ankle swelling	Loss of appetite
	Confusion (especially in older people)
	Depression
	Palpitations
	Syncope
Signs	
More specific	Less specific
Elevated jugular venous pressure	Peripheral oedema (ankle, sacral, scrotal)
Hepatojugular reflux	Pulmonary crepitations
Third heart sound (gallop rhythm)	Reduced air entry and dullness to percussion at lung

	bases (pleural effusion)
Laterally displaced apical impulse	Tachycardia
Cardiac murmur	Irregular pulse
	Tachypnoea (>16 breaths/min)
	Hepatomegaly
	Ascites
	Tissue wasting (cachexia)

Further investigations

Following clinical examination and basic investigations, a decision must be made as to whether the patient should undergo an echocardiogram. To help make this decision, the patient should undergo either an electrocardiogram or measurement of B-type natriuretic peptide or N terminal-pro-BNP levels, or both depending on local circumstances. If either test is abnormal, there is sufficient likelihood of HF to warrant echocardiography to confirm a diagnosis. If both tests are normal, HF is unlikely and alternative tests for the symptoms should be considered.

If echocardiography suggests a diagnosis of HF, an ECG should be done (if it has not already been done) to help identify the underlying cause of the heart failure.

Pulmonary-function tests should be considered in selected patients, ie in those whom HF is excluded and also in those with HF and comorbid lung disease which may contribute to dyspnoea.

Electrocardiography

The ECG can be used firstly as a screening test to assess the likelihood of HF and the need for subsequent echocardiography to confirm or refute a diagnosis. It is unusual for a patient with HF to have a normal ECG, so it is a good tool to rule out HF. The ECG abnormalities reported in HF are all non-specific, and relatively common in older patients. The specificity of an abnormal ECG is relatively poor (around 60% at best).

Electrocardiographic abnormalities in patients with HF include:

- pathological Q waves
- left bundle branch block
- left ventricular hypertrophy (LVH)
- atrial fibrillation
- non-specific ST and/or T-wave changes.

Electrocardiography is also useful once HF has been confirmed as it may help to determine the cause (eg Q waves indicate previous myocardial infarction, LVH is seen in patients with hypertension and aortic valve disease) and it is important to exclude atrial fibrillation.

Natriuretic peptides

B-type natriuretic peptide (BNP) and N terminal-pro-B-type natriuretic peptide (NT-proBNP) are peptide hormones produced in the heart by breakdown of a precursor protein (pre-pro-BNP). BNP causes natriuresis, diuresis and vasodilation; NT-proBNP is inactive.

Plasma BNP and NT-proBNP concentrations are raised in patients with both HF-REF and HF-PEF and the concentrations tend to rise with deteriorating NYHA class.

There is evidence of clinical effectiveness of using measurement of BNP or NT-proBNP as a diagnostic tool for heart failure from a health technology appraisal carried out by NHS Quality Improvement Scotland, which included 19 observational studies (11 using BNP, eight using NT-proBNP). Pooled sensitivity for the diagnosis of HF using BNP testing was 0.91 (95% confidence intervals (CI), 0.90 to 0.93), specificity was 0.73 (0.71 to 0.75). Pooled sensitivity for the diagnosis of HF using NT-proBNP testing was 0.91 (95% CI 0.88 to 0.93) and specificity was 0.76 (95% CI 0.75 to 0.77). Although simple single value cut offs for the diagnosis of HF have been proposed, a more realistic interpretation of BNP and NT-proBNP levels is to suggest that very low values rule out a diagnosis of HF, very high values make the diagnosis of HF likely in the absence of other causes of a raised BNP, whilst intermediate to high values should be regarded as indeterminate necessitating further investigation. The upper limit of normal is also age, sex and race dependent, and must be determined locally depending on the assay used.

BNP and NT-proBNP tests are suitable for widespread screening in patients with suspected HF presenting in the community, assuming appropriate quality control of the assay and selection of appropriate cut-off values for the patients tested. BNP levels fall after commencing therapy for HF, for example diuretics, so the sensitivity is lower in patients who have already started treatment.

No evidence was identified on whether early referral of people with suspected HF and high or moderate BNP levels improves outcome. NICE considered that because BNP levels can predict risk of hospitalisation and mortality, people presenting with signs and symptoms of HF in the community setting and who have

very high natriuretic peptide levels should be treated more urgently than those with lower, but still abnormal, levels of natriuretic peptides. NICE devised the following thresholds, based on the expert opinion of the guideline development group:

- BNP >400 pg/ml (>116 pmol/l) or NT-proBNP >2,000 pg/ml (>236 pmol/l): echocardiogram and specialist clinical assessment no longer than two weeks from the time of presentation.
- BNP 100–400 pg/ml (29–116 pmol/l) or NT-proBNP 400–2,000 pg/ml (47–236 pmol/l): echocardiogram and specialised clinical assessment within six weeks from the time of presentation.
- BNP <100 pg/ml (<29 pmol/l) or NT-proBNP <400 pg/ml (<47 pmol/l), in the absence of HF therapy: HF is an unlikely cause for the presentation.

Echocardiography

Echocardiography is a safe and relatively inexpensive investigation which is very helpful in diagnosing HF and determining the cause. It provides a quantitative and semiquantitative assessment of left ventricular systolic and diastolic function, valve disorders can usually be accurately delineated, and pulmonary artery systolic pressure can be estimated. The limitation of poor image quality due to obesity or lung disease is minimised by the skilled use of modern imaging equipment and echocardiographic contrast agents.

Echocardiography is recommended in patients with suspected heart failure who have either a raised BNP or NT-proBNP level or abnormal electrocardiograph result to confirm the diagnosis and establish the underlying cause. The investigation should include:

- a description of overall left ventricular systolic function (preferably measured by the LVEF) together with any wall-motion abnormalities
- Doppler assessment of any significant valve disease
- estimation of pulmonary artery systolic pressure, where possible.

Chest x-ray

The chest X-ray (CXR) is important to help exclude other causes of shortness of breath and to look for supportive evidence for a possible diagnosis of HF. On its own it cannot be used to diagnose HF and must be used in combination with other sources of clinical evidence.

In one systematic review pulmonary venous redistribution with upper lobe blood diversion on CXR was shown to have 65% sensitivity (67% specificity) for increased preload in patients with HF. Cardiomegaly on CXR had 51% sensitivity

(79% specificity) for decreased ejection fraction in patients with HF. However, neither finding alone can adequately confirm or refute left ventricular dysfunction.

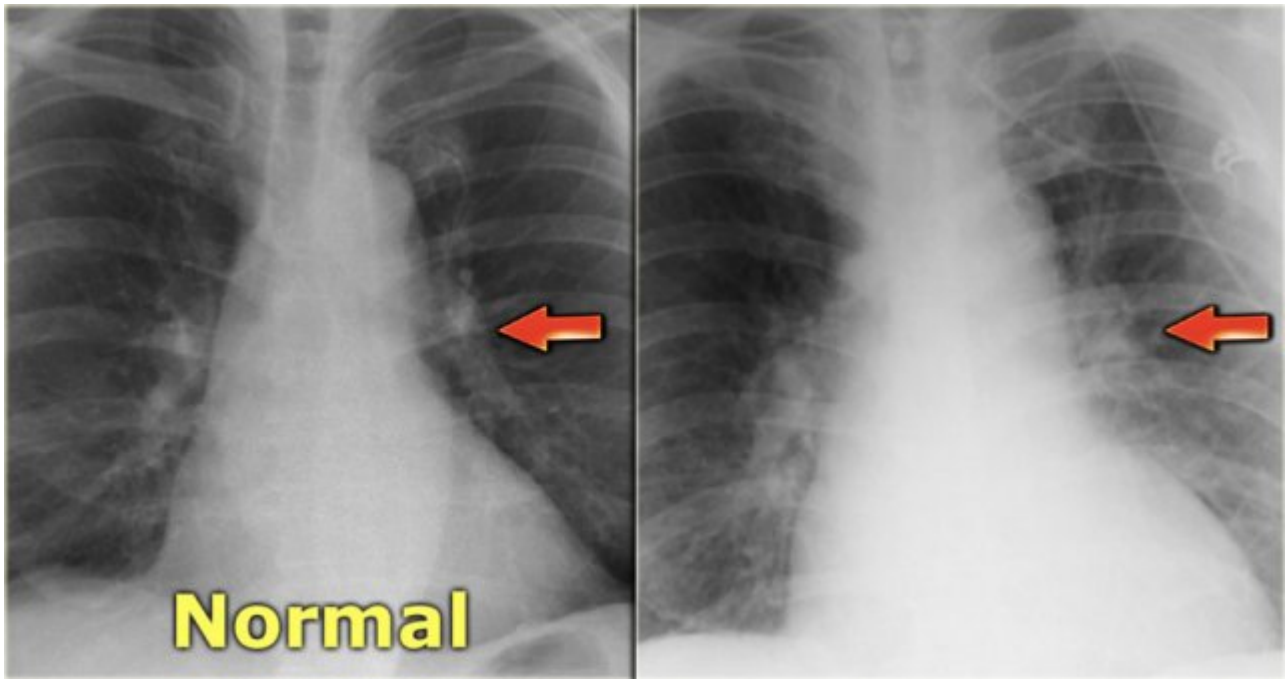

Image 15. Chest X-ray of Heart Failure
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A chest X-ray is recommended early in the diagnostic pathway to look for supportive evidence of heart failure and to investigate other potential causes of breathlessness.

Imaging techniques

In addition to echocardiography, a number of other imaging techniques can be used for the assessment of patients with suspected or diagnosed HF.

Cardiac magnetic resonance (CMR) is regarded as the gold standard for assessment of ventricular volumes, ejection fractions and regional wall motion. It enables assessment of valvular function and provides high image quality in most patients. It is useful for assessing ventricular function when echocardiography images are inadequate. It is also indicated for patients with HF with a background of complex congenital heart disease, patients with suspected cardiomyopathy, or where the differential diagnosis includes active myocarditis or infiltrative myocardial disease, for example amyloidosis, scaroidosis, cardiac haemosiderosis.

Radionuclide blood pool-multiple gated acquisition (MUGA)-scanning can provide an accurate measure of the left ventricular ejection fraction, but it exposes the

patient to ionising radiation, does not allow visualisation of the heart valves and provides less additional information regarding cardiac structure and function than CMR.

Potentially viable myocardium can be detected by single-photon emission computed tomography (SPECT), radionuclide positron emission tomography (PET), magnetic resonance imaging and dobutamine stress echocardiography (DSE). Studies of these imaging modalities have been pooled together in one metaanalysis and one systematic review. Each of these techniques appears capable of detecting ischaemic, viable myocardium.

Laboratory investigations

1) Hyponatremia caused by volume overload may be observed in patients with advanced HF or those who are treated with thiazide diuretics.

2) Hypokalemia or hyperkalemia and increased serum creatinine levels may be caused by diuresis, kidney injury, and/or adverse effects of drugs (see below).

3) Elevated serum aminotransferase, lactate dehydrogenase, and bilirubin levels are observed in patients with hepatic congestion.

4) Anemia (worsening or triggering HF) or high hematocrit values (eg, in chronic obstructive pulmonary disease and congenital heart disease with right-to-left shunt).

TOPIC 6
INFECTIOUS ENDOCARDITIS. RHEUMATIC DISEASE. CONGENITAL HEART DISORDER. DENTAL ASPECTS

INFECTIVE ENDOCARDITIS (IE)

Definition, etiology, pathogenesis

Infective endocarditis (IE) is an infection of the endocardium, most frequently involving the heart valves, although the disease can occur in other areas covered with endocardium such as ventricles, atria, or endothelium of vessels (eg, in patients with coarctation of the aorta). IE can manifest in patients with cardiovascular implantable electronic devices (CIEDs) through affecting electrode leads, valves, or endocardial surface. Most frequently IE affects the mitral and aortic valves; less frequently the tricuspid valve may be involved. IE can involve >1 valve and the proportion of these patients varies in reported literature. IE is preceded by bacteremia, which can last from <2 weeks (80% of patients) to several months (in particular in patients with IE involving a prosthetic valve).

Etiologic agents

1) Bacteria (>90% of cases). Most frequent pathogens:

a) Staphylococci (*Staphylococcus aureus*, the most common cause of IE in high-income countries; *Staphylococcus epidermidis;* coagulase-negative staphylococci).

b) Streptococci (viridans-group streptococci; until recently the most frequent cause of native valve infections).

c) Enterococci.

d) The HACEK group of fastidious gram-negative organisms (*Haemophilus* spp, *Aggregatibacter* [formerly *Actinobacillus*] spp, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* spp).

e) Non-HACEK gram-negative bacteria.

f) Mixed bacterial etiology is frequently found among IV drug abusers.

2) Fungi (<1%).

3) Very rare: Chlamydia, rickettsia, or mycoplasma.

Depending on criteria definitions for IE, etiology cannot be established in 5% to 20% of patients.

Etiologic agents in patients with negative blood cultures

Culture-negative IE may be seen in the context of antimicrobial use prior to blood cultures being drawn or infections caused by fastidious organisms. These organisms include:

1) Nutritionally variant streptococci.
2) *Coxiella burnetii*.
3) *Bartonella* spp.
4) *Mycoplasma pneumoniae*.
5) *Brucella* spp.
6) *Legionella pneumophila*.
7) Fungi (eg, *Aspergillus* spp).
8) *Tropheryma whipplei*.

Diseases and conditions predisposing to native valve endocarditis (NVE): Certain heart diseases predisposing to IE are indications for antibiotic prophylaxis. Other risk factors include history of rheumatic disease, mitral valve prolapse with regurgitation, hypertrophic cardiomyopathy, valvular or congenital heart disease (particularly affecting the aortic valve, eg, bicuspid aortic valve, coarctation of the aorta), degenerative cardiac lesions, prolonged maintenance of indwelling central venous catheters, foreign bodies in the heart (eg, intracardiac electrodes, vascular patches), chronic hemodialysis, and IV drug use (IVDU) (associated with involvement of right-sided heart valves).

Prosthetic valve endocarditis (PVE) accounts for 10% to 30% of all cases of IE. It most frequently develops within 5 to 6 weeks of surgery. IE occurring within 12 months of surgery is considered a postoperative complication. In the first 2 months after surgery, PVE is most frequently caused by *S aureus* followed by coagulase-negative staphylococci (mainly methicillin-resistant strains) and *Candida* spp. In PVE developing >1 year after surgery, etiologic agents are similar to those seen in NVE.

Cardiac device-related infective endocarditis (CDRIE) is most frequently caused by coagulase-negative staphylococci and *S aureus*.

Clinical features

IE presentation is highly variable and differential diagnosis is often broad, sometimes leading to delay in establishing diagnosis. IE is manifested mainly by nonspecific symptoms, including high-grade fever with chills or prolonged low-grade fever (the most frequent feature), malaise, weakness, arthralgia, myalgia, loss of appetite, weight loss, headache, and nausea.

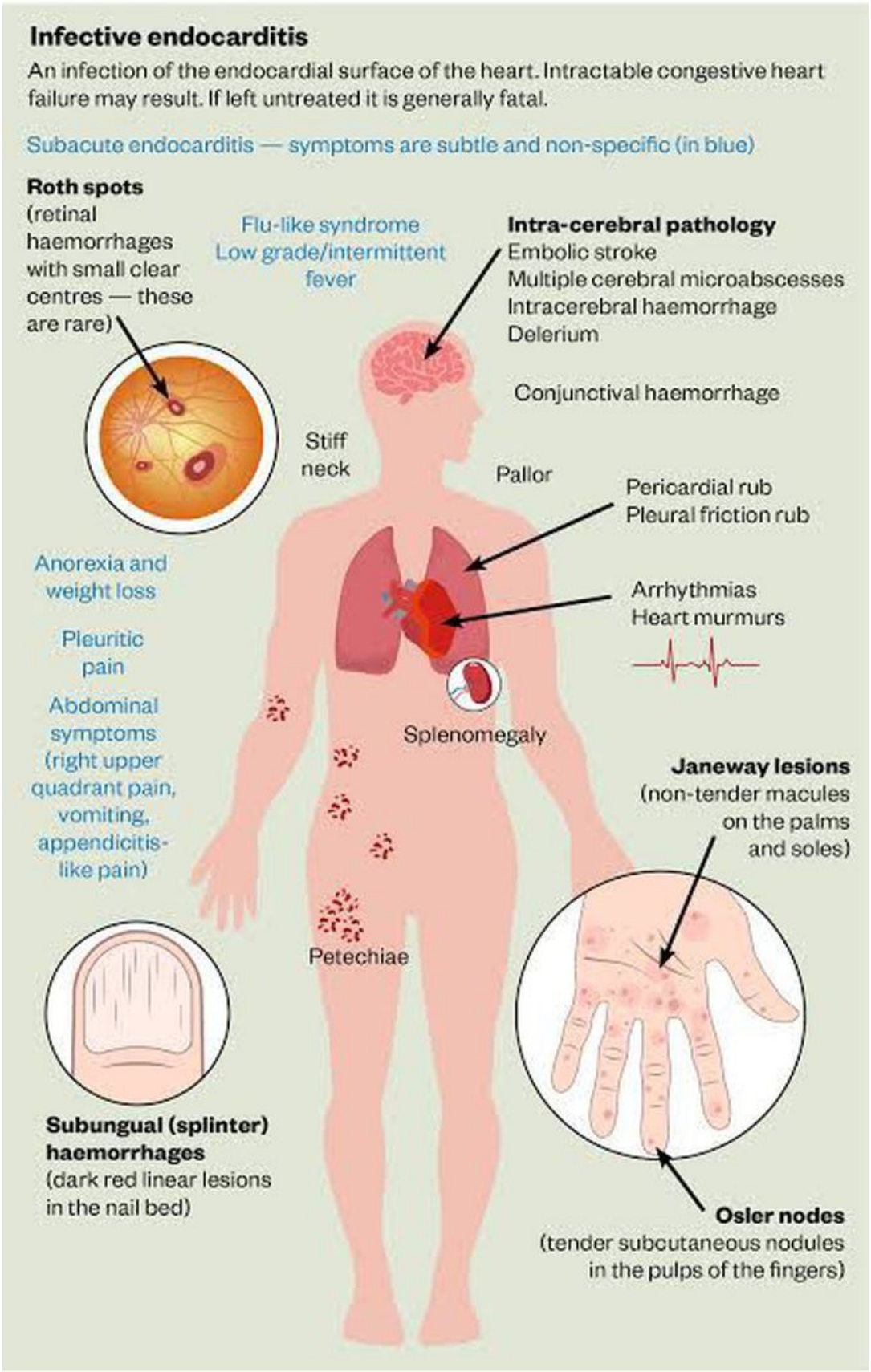

Image 16. Infective endocarditis

This image was downloaded from website https://medizzy.com

1. **Left-sided endocarditis** may also cause symptoms associated with:

1) Regurgitation murmur over the affected valve.

2) Features of heart failure, including pulmonary edema in patients with no prior history of valvular disease.

3) Conduction abnormalities.

4) Rarely large vegetations leading to functional mitral stenosis.

5) Embolic phenomena (most frequently associated with *S aureus*), including:

a) Central nervous system (CNS) symptoms (30%-40% of patients; hemiparesis, aphasia; behavioral changes in those with microembolism).

b) Rarely intracranial hemorrhage due to ruptured mycotic aneurysm.

c) Renal, splenic, or mesenteric embolism, which may lead to adynamic ileus resulting in abdominal pain or back pain.

d) Coronary artery embolism (rare) manifesting as chest pain.

e) Ocular disturbances associated with retinal artery embolism.

f) Peripheral vascular and inflammation symptoms (petechiae on skin and under nail plates, Osler nodes [painful red nodules located mainly on fingers and toes due to deposition of immune complexes], Janeway lesions [painless hemorrhagic lesions on palms and soles], Roth spots [retinal hemorrhages with pale centers]).

g) Splenomegaly and hepatomegaly (more frequent in patients with long-standing IE).

2. **Right-sided endocarditis** may also cause symptoms associated with:

1) Pulmonary embolism, with associated cough and pleuritic chest pain (caused by septic pulmonary emboli): This is the most common manifestation.

2) Murmur caused by tricuspid or pulmonary regurgitation: This is often absent or seen in advanced disease.

3) Features of right ventricular failure in patients with long-standing IE.

4) Often recurrent right-sided IE in the case of IVDU, frequently in the absence of other predisposing heart conditions.

Note: IE must always be excluded in patients with embolism and fever.

Diagnosis

The following studies should be performed in every patient with suspected IE.

1. **Blood cultures** are critical for the diagnosis of IE and treatment planning. Obtain ≥3 blood culture sets from separate venipuncture sites before starting antimicrobial treatment, with the first and last samples being drawn ≥1 hour apart, regardless of body temperature. Each sample should contain 10 mL of blood

collected to an aerobic tube and another 10 mL collected to an anaerobic tube. Mark the order form as suspected IE. In all patients undergoing cardiac surgery, and particularly those with negative results of previous cultures, perform specimen cultures and pathologic examination and, if needed, use molecular identification methods, to identify the etiologic agent.

2. **Serologic studies**: Perform these in the case of suspected infection with *C burnetii, Bartonella* spp, *Brucella* spp, *Histoplasma capsulatum*, *Legionella* spp, or *Chlamydia* spp.

3. **Echocardiography**: In suspected endocarditis it is important to evaluate for vegetations (mobile echogenic structures attached to the endocardium or intracardiac prosthetic material), valvular damage (regurgitation of the infected valve due to vegetations, leaflet perforation, or rupture of chordae tendineae), and perivalvular complications (abscess, pseudoaneurysm, intracardiac fistula).

In all patients without prosthetic valves with IE suspected on the basis of clinical criteria, transthoracic echocardiography (TTE) should be performed. In those with a low clinical probability of IE and a negative TTE result (provided that good-quality images are obtained), IE is unlikely and another diagnosis should be considered. If good-quality TTE images cannot be obtained, transesophageal echocardiography (TEE) should be performed. TEE should be also performed in:

1) Patients with a high clinical probability of IE and a negative TTE result.

2) Patients with suspected IE and a prosthetic valve or intracardiac device.

3) Patients with suspected IE affecting the aortic valve.

4) Patients with IE and significant valvular regurgitation.

5) Patients with a TTE result suggestive of IE (except for those with IE affecting right-sided native heart valves and unequivocal TTE findings). In the case of a negative TEE result and reasonable suspicion of IE, repeat TEE after 5 to 7 days.

Although the mainstay for diagnosis of IE, echocardiography has limitations (it cannot reliably differentiate between active and healed IE, and TTE and TEE sensitivity and specificity are not 100%). As such, results must be interpreted in the context of clinical presentation.

4. **Laboratory tests**: There are no biochemical parameters that have been proven to be sensitive or specific for the diagnosis of IE; however, laboratory evaluation is part of standard workup of IE. IE has been associated with elevated erythrocyte sedimentation rate (ESR), increased levels of C-reactive protein (CRP)

and fibrinogen, leukocytosis with neutrophilia (most frequent in acute IE), anemia (usually normocytic and normochromic), hematuria, and minor proteinuria.

5. **Electrocardiography**: Nonspecific findings and conduction abnormalities.

6. **Chest radiography**: Nonspecific findings, which may include congestive heart failure findings and signs of pulmonary complications.

7. **Multislice computed tomography (CT) and magnetic resonance imaging (MRI)**: CT provides a valuable addition to echocardiography in the diagnosis of perivalvular lesions: abscesses, pseudoaneurysms, and fistulas. It may be also used in patients with prosthetic valves. Multislice CT is useful in the anatomical assessment of the aortic valve (eg, leaflet perforation) and aorta and in the diagnosis of pulmonary embolism in patients with right-side IE, metastatic abscesses (eg, in the spleen), and CNS-related emboli. CT has lower sensitivity than MRI but is more available.

8. **Nuclear imaging**: Nuclear imaging techniques, such as ^{18}Ffluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) have demonstrated potential as a supplementary method for selected patients in the case of difficulties in the diagnosis and management of IE, especially in those with prosthetic valves.

Diagnostic Criteria

The diagnosis of IE can be made in a patient with sepsis or generalized infection and objective features of endocardial involvement. Relevant diagnostic terminology includes:

1) **Definite IE**: Table 1.

2) **Possible IE**: Table 1.

3) **Active IE**:

a) Positive blood cultures or positive intraoperative specimens.

b) Intraoperative confirmation of features of endocarditis.

c) Unfinished course of antimicrobial treatment for IE.

4) **Relapse**: IE caused by the same microorganism within <6 months of a confirmed episode of IE.

5) **Reinfection**: IE caused by the same microorganism after >6 months of a previous episode of IE or caused by a different microorganism.

6) **CDRIE**: CDRIE is difficult to differentiate from local infection of the device. It should be suspected in the case of fever of unknown origin in a patient with a cardiac implantable electronic device. The key diagnostic procedures are

echocardiography (TEE has superior sensitivity and specificity but TTE should be performed first) and blood cultures.

Table 11

The Duke criteria for diagnosis of infective endocarditis modified by the European Society of Cardiology (2015)

Pathologic criteria
1) Microorganisms demonstrated by culture or on histologic examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or 2) Pathologic lesions; vegetation or intracardiac abscess confirmed by histologic examination showing active endocarditis.
Clinical criteria
Major criteria 1) Blood cultures positive for IE: a) Typical microorganisms consistent with IE from 2 separate blood cultures: Viridans-group streptococci, *Streptococcus gallolyticus* (formerly *bovis*), HACEK group, *Staphylococcus aureus*; or community-acquired enterococci in the absence of a primary focus; or b) Microorganisms consistent with IE from persistently positive blood cultures: ≥2 positive blood cultures of samples drawn >12 h apart or all of 3 or a majority of ≥4 separate cultures of blood (with first and last samples drawn ≥1 h apart); or c) Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titer >1:800. 2) Imaging studies positive for IE: a) Echocardiography positive for IE: Vegetation; abscess, pseudoaneurysm, intracardiac fistula; valvular perforation or aneurysm; new partial dehiscence of a prosthetic valve. b) Abnormal activity around the site of prosthetic valve implantation detected by F-FDG PET/CT (only if the prosthesis was implanted for >3 months) or radiolabeled leukocyte SPECT/CT. c) Definite paravalvular lesions on cardiac CT. **Minor criteria** 1) Predisposition, such as predisposing heart condition or injection drug use. 2) Fever defined as temperature >38°C.

3) Vascular phenomena (including those detected by imaging only): Major arterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway lesions. 4) Immunologic phenomena: Glomerulonephritis, Osler nodes, Roth spots, and rheumatoid factor. 5) Microbiological evidence: Positive blood culture but not meeting a major criterion as noted above or serologic evidence of active infection with an organism consistent with IE.
Definite IE: 2 major criteria; 1 major criterion and 3 minor criteria; or 5 minor criteria. **Possible IE**: 1 major criterion and 1 minor criterion; or 3 minor criteria. **Rejected IE**: 1) Firm alternative diagnosis; or 2) Resolution of symptoms suggesting IE with antibiotic therapy for ≤4 days; or 3) No pathologic evidence of IE at surgery or autopsy with antibiotic therapy for ≤4 days; or 4) Not fulfilling the criteria for possible IE, as defined above.

RHEUMATIC FEVER

Definition, etiology, pathogenesis

Acute rheumatic fever (ARF) is an autoimmune disease caused by an excessive immune response to group A beta-hemolytic streptococcus (GABHS) infection, which occurs in ~3% of patients with untreated streptococcal pharyngitis and tonsillitis. The immune response is directed against epitopes similar to proteins found in the myocardium, heart valves, synovia, skin, hypothalamus, and caudate nucleus. The disease is rare in developed countries, but the incidence is higher in low- and middle-income countries, in particular in Africa, and in some Indigenous populations, such as those in Australia and New Zealand. It is usually diagnosed in children aged between 5 and 15 years.

Clinical features and natural history

1. Signs and symptoms of streptococcal pharyngitis.

2. Signs and symptoms of rheumatic fever usually develop 2 to 3 weeks after pharyngitis:

1) Polyarthritis affecting large joints (35%-66% of patients) is always asymmetric and accompanied by characteristic swelling, severe pain, tenderness, and

erythema. Untreated arthritis persists for 2 to 3 weeks and does not lead to permanent joint damage.

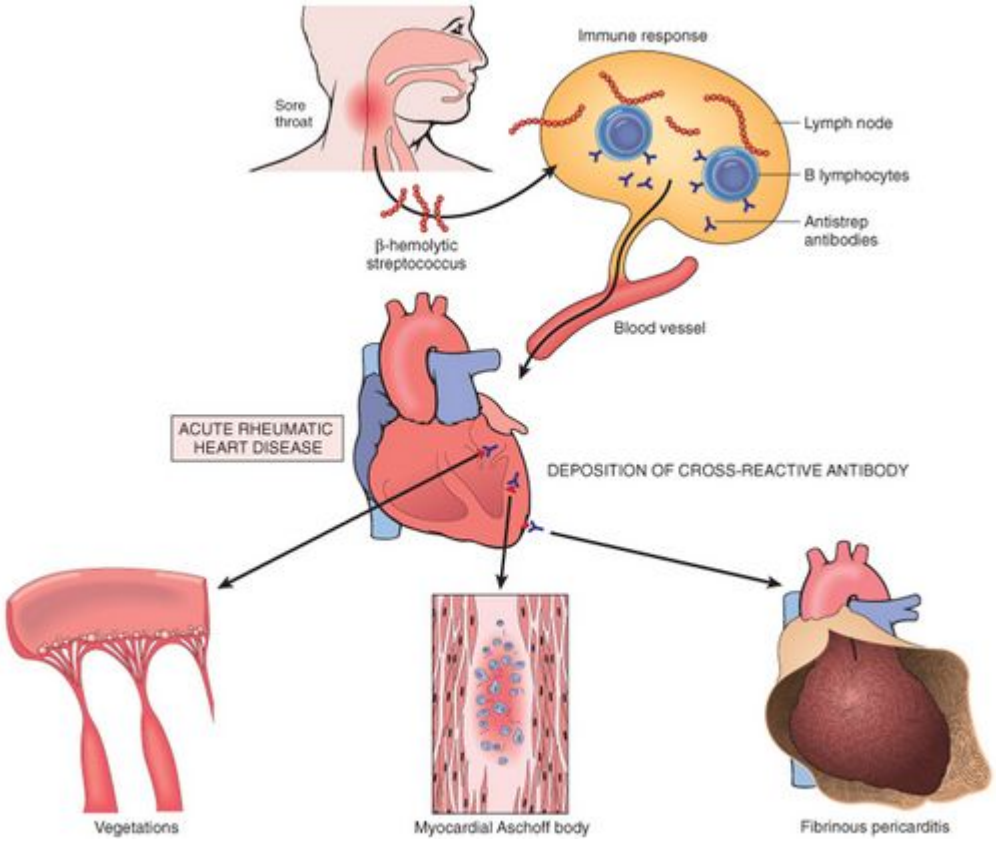

Image 17. Pathophysiology of rheumatic fever
This image was downloaded from website https://www.stepwards.com

Migratory polyarthritis is the most common manifestation of acute rheumatic fever, occurring in about 35 to 66% of children; it is often accompanied by fever. "Migratory" means the arthritis appears in one or a few joints, resolves but then appears in others, thus seeming to move from one joint to another. Occasionally monarthritis occurs in high-risk indigenous populations (eg, in Australia, India, Fiji) but very rarely in the US. Joints become extremely painful and tender; these symptoms are often out of proportion to the modest warmth and swelling present on examination (this is in contrast to the arthritis of Lyme disease, in which the examination findings tend to be more severe than the symptoms).

Ankles, knees, elbows, and wrists are usually involved. Shoulders, hips, and small joints of the hands and feet also may be involved, but almost never alone. If vertebral joints are affected, another disorder should be suspected.

Arthralgia-like symptoms may be due to nonspecific myalgia or tenodynia in the periarticular zone; tenosynovitis may develop at the site of muscle insertions. Joint pain and fever usually subside within 2 weeks and seldom last > 1 month.

2) Carditis (50%-70% of patients) may involve the endocardium, myocardium, and pericardium, but valvulitis is the most common feature. Although murmurs of aortic or mitral regurgitation may be heard, diagnosis by echocardiography in the absence of auscultatory findings is increasingly being recognized.

Carditis can occur alone or in combination with pericardial rub, murmurs, cardiac enlargement, or heart failure. In the first episode of acute rheumatic fever, carditis occurs in about 50 to 70%. Patients may have high fever, chest pain, or both; tachycardia is common, especially during sleep. In about 50% of cases, cardiac damage (ie, persistent valve dysfunction) occurs much later.

Although the carditis of ARF is considered to be a pancarditis (involving the endocardium, myocardium, and pericardium), valvulitis is the most consistent feature of ARF, and if it is not present, the diagnosis should be reconsidered. The diagnosis of valvulitis has classically been made by auscultation of murmurs, but subclinical cases (ie, valvular dysfunction not manifested by murmurs but recognized on echocardiography and Doppler studies) may occur in up to 18% of cases of ARF.

Heart murmurs are common and, although usually evident early, may not be heard at initial examination; in such cases, repeated clinical examinations as well as echocardiography are recommended to determine the presence of carditis. Mitral regurgitation is characterized by an apical pansystolic blowing murmur radiating to the axilla. The soft diastolic blow at the left sternal border of aortic regurgitation, and the presystolic murmur of mitral stenosis, may be difficult to detect. Murmurs often persist indefinitely. If no worsening occurs during the next 2 to 3 weeks, new manifestations of carditis seldom follow. ARF typically does not cause chronic, smoldering carditis. Scars left by acute valvular damage may contract and change, and secondary hemodynamic difficulties may develop in the myocardium without persistence of acute inflammation.

Pericarditis may be manifested by chest pain and a pericardial rub.

Heart failure caused by the combination of carditis and valvular dysfunction may cause dyspnea without rales, nausea and vomiting, a right upper quadrant or epigastric ache, and a hacking, nonproductive cough. Marked lethargy and fatigue may be early manifestations of heart failure.

3) Sydenham chorea (10%-30% of patients) manifests as involuntary movements of the trunk or extremities. It is associated with muscle weakness and emotional lability.

Sydenham chorea occurs in about 10 to 30% of children. It may develop along with other manifestations but frequently arises after the other manifestations have subsided (often months after the acute streptococcal infection) and thus may be overlooked as an indicator of acute rheumatic fever. Onset of chorea is typically insidious and may be preceded by inappropriate laughing or crying. Chorea consists of rapid and irregular jerking movements that may begin in the hands but often becomes generalized, involving the feet and face.

Characteristic findings include fluctuating grip strength (milkmaid's grip), tongue fasciculations or tongue darting (the tongue cannot protrude without darting in and out), facial grimacing, and explosive speech with or without tongue clucking. Associated motor symptoms include loss of fine motor control, and weakness and hypotonia (that can be severe enough to be mistaken for paralysis).

Previously undiagnosed obsessive-compulsive behavior may be unmasked in many patients.

4) Erythema marginatum (<6% of patients) is a pink rash that develops on the trunk and proximal parts of extremities.

Erythema marginatum is a serpiginous, flat or slightly raised, nonscarring, and painless rash. Fewer than 6% of children have this rash. The rash usually appears on the trunk and proximal extremities but not the face. It sometimes lasts < 1 day. Its appearance is often delayed after the inciting streptococcal infection; it may appear with or after the other manifestations of rheumatic inflammation.

5) Painless subcutaneous nodules (0%-10% of patients) on the extensor surfaces of elbows and knees are usually seen in patients with heart involvement.

Subcutaneous nodules, which occur most frequently on the extensor surfaces of large joints (eg, knees, elbows, wrists), usually coexist with arthritis and carditis. Fewer than 10% of children with acute rheumatic fever have nodules. Ordinarily, the nodules are painless and transitory and respond to treatment of joint or heart inflammation.

3. **Natural history**: In patients without cardiac involvement, the disease has a mild course. The majority of relapses occur within 2 years of the first episode. Each recurrence of rheumatic fever increases the risk of mitral or aortic valve disease.

Diagnosis

Diagnostic Tests

1. **Laboratory tests**:

1) A positive throat swab or rapid antigen test for acute GABHS infection.

2) Elevations in the erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) levels, which persist for up to several months.

3) Increasing antistreptolysin O (ASO) or other streptococcal antibodies (anti-deoxyribonuclease B [anti-DNase B]).

2. **Echocardiography** to detect evidence of valvular dysfunction, most commonly mitral or aortic regurgitation (valvular stenosis is usually a late sequelae).

Diagnostic Criteria

1. **Jones criteria**:

1) **Major manifestations**: Carditis, polyarthritis, chorea, erythema marginatum, subcutaneous nodules.

2) **Minor manifestations**: Polyarthralgia, fever, elevated ESR or serum CRP levels, a prolonged PR interval.

2. The **first episode of rheumatic fever** is diagnosed in patients with a documented prior GABHS infection (most frequently diagnosed on the basis of elevated ASO titers) and ≥2 positive major Jones criteria or 1 major + 2 minor Jones criteria.

CONGENITAL HEART DISORDER

Any heart valve can become stenotic or insufficient (also termed regurgitant or incompetent), causing hemodynamic changes long before symptoms. Most often, valvular stenosis or insufficiency occurs in isolation in individual valves, but multiple valvular disorders may coexist, and a single valve may be both stenosed and insufficient.

Heart valve disorders include

- Aortic regurgitation: Insufficiency of the aortic valve causing backflow of blood from the aorta into the left ventricle during diastole
- Aortic stenosis: Narrowing of the aortic valve, obstructing blood flow from the left ventricle to the ascending aorta during systole
- Mitral regurgitation: Insufficiency of the mitral valve causing flow of blood from the left ventricle (LV) into the left atrium during ventricular systole.

- Mitral stenosis: Narrowing of the mitral orifice that impedes blood flow from the left atrium to the left ventricle
- Mitral valve prolapse: Billowing of mitral valve leaflets into the left atrium during systole
- Pulmonic regurgitation: Insufficiency of the pulmonic valve causing blood flow from the pulmonary artery into the right ventricle during diastole
- Pulmonic stenosis: Narrowing of the pulmonary outflow tract causing obstruction of blood flow from the right ventricle to the pulmonary artery during systole
- Tricuspid regurgitation: Insufficiency of the tricuspid valve causing blood flow from the right ventricle to the right atrium during systole
- Tricuspid stenosis: Narrowing of the tricuspid orifice that obstructs blood flow from the right atrium to the right ventricle

Historically, diagnosis of valvular disorders by observation, palpation, and auscultation was a tough test for aspiring clinicians. Today, with the physical examination supplemented by cardiac ultrasonography (including sometimes handheld ultrasonography done by the examining clinician), diagnosis is comparatively straightforward. Standard 2-dimensional studies show the anatomy. Doppler echocardiography evaluates pressure gradients and blood flow. Evaluation also includes ECG (to detect heart rhythm and chamber alterations) and chest x-ray (to detect chamber alterations, pulmonary congestion, and other lung pathology).

AORTIC REGURGITATION

Definition, etiology, pathogenesis

Aortic regurgitation (AR) is a reversal of blood flow from the aorta into the left ventricle (LV) due to incomplete closure of the aortic valve leaflets. **Primary regurgitation** is caused by damage to or a congenital abnormality of the leaflets, with subsequent dilation of the left ventricular outflow tract, aortic annulus, and ascending aorta. **Secondary regurgitation** is caused by dilation of the aortic annulus and the ascending aorta (secondarily causing malcoaptation of the aortic valve leaflets) in the absence of significant aortic valve leaflet pathology.

Etiology

1) **Primary**: Congenital (bicuspid aortic valve, quadricuspid aortic valve, valve damage in subaortic stenosis); degenerative (calcifications, fibrosis); infective

endocarditis (active or healed); rheumatic; drug-induced (fenfluramine, phentermine) damage of the leaflets.

2) **Secondary**: Idiopathic aortic dilation; hypertensive aortic dilation; systemic connective tissue diseases (rheumatic disease, rheumatoid arthritis, aortic stenosis); dilation or dissection of the ascending aorta (hypertension, Marfan or Marfan-like syndrome, atherosclerosis, inflammation, trauma, myxomatous degeneration); aortopathy associated with bicuspid aortic valve; syphilitic aortic disease.

Clinical features and natural history

1. **Symptoms**: In acute AR, a sudden-onset tachycardia and increasing dyspnea (in AR caused by aortic dissection, symptoms of the underlying condition predominate). Chronic AR may be asymptomatic for years, and even in severe AR, the symptoms are at times mild, often involving fatigue.

2. **Signs**: A wide (high) pulse pressure (with elevated systolic blood pressure and low, at times undetectable diastolic blood pressure), rapidly rising and rapidly collapsing pulse (so-called water hammer pulse or Corrigan pulse); sometimes a bisferiens pulse (more easily recognized on the brachial or femoral arteries than on the carotid arteries). The first heart sound is usually normal (although it may be silent in acute AR due to mitral valve preclosure). The aortic component of the second heart sound may be accentuated (in the case of aortic pathology) or soft (in the case of pathology of the leaflets). A holodiastolic decrescendo murmur is audible, frequently most prominent at the left sternal border (in the case of pathology of the ascending aorta, it is frequently better audible at the right sternal border); the Austin Flint murmur—a diastolic rumble due to relative mitral stenosis from preclosure of the mitral valve—may also be present. Frequently, a systolic ejection murmur is audible over the aortic valve (due to increased stroke volume, resulting in increased transaortic valve gradients).

3. **Natural history** of acute AR depends on the underlying condition. Chronic AR is usually asymptomatic for several years; in patients with a normal left ventricular ejection fraction (LVEF), the sudden cardiac death risk is <0.2% per year. The prevalence of cardiovascular events is ~5% per year in patients with severe AR and preserved LV function, and 25% per year in patients with New York Heart Association (NYHA) class III/IV symptoms. Some patients with asymptomatic severe AR may develop irreversible LV dysfunction; thus, early detection and appropriate treatment of severe AR is paramount.

Diagnosis

Diagnosis is based on typical clinical features and echocardiography.

Diagnostic Tests

1. **Electrocardiography (ECG)**: Features of LV hypertrophy and strain pattern; features of left atrial enlargement (P mitrale). Ventricular arrhythmias can occur.

2. **Chest radiographs**: LV hypertrophy, dilation of the ascending aorta and the aortic arch. In acute AR, pulmonary congestion with a normal cardiac silhouette is observed.

3. **Doppler echocardiography** allows for detection of a regurgitation jet and its quantitative and qualitative assessment.

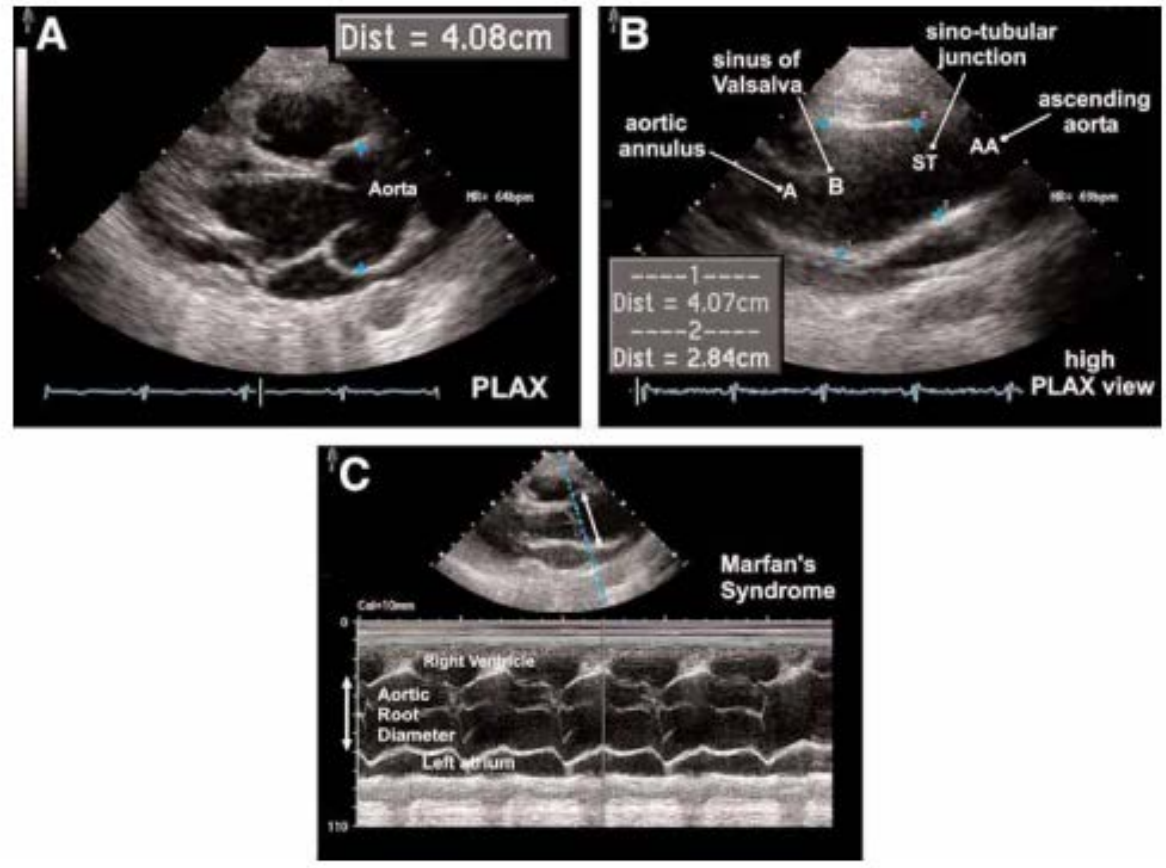

Image 18. Aortic regurgitation secondary to aortic root dilatation in a 26-yr-old female with Marfan syndrome. Annular dilatation can lead to inadequate central coaptation of valve leaflets and aortic regurgitation

This image was downloaded from website http://eknygos.lsmuni.lt

4. **Gated computed tomography (CT)** is best for aortic dilation measurement using the inner-edge-to-inner-edge technique.

AORTIC STENOSIS

Definition, etiology, pathogenesis

Aortic stenosis (AS) results from thickened or calcified valve leaflets leading to restricted leaflet motion, reduced aortic valve area (AVA), and transvalvular flow obstruction. AS is most frequently an acquired disease (age-related degenerative valve disease, with rheumatic disease rarely seen) but may also be congenital (most frequently a bicuspid aortic valve).

Clinical features and natural history

1. **Symptoms**: AS remains asymptomatic for a long time. It may cause angina, palpitations, dizziness, presyncope or syncope, dyspnea, and in more advanced disease, resting dyspnea.

2. **Signs**: Cardiac impulse is diffuse, sustained, and displaced laterally and inferiorly. A systolic thrill may be palpable at the base of the heart and transmitted to the carotid arteries (in patients with severe stenosis). An ejection systolic murmur is present, although its intensity may not reflect the severity of stenosis; the murmur radiates to the carotid arteries and the later the murmur peaks, the more severe the stenosis. An aortic ejection click is audible in patients with elastic leaflets (commonly bicuspid valves). The aortic component of the second heart sound is soft, reverse split, or absent (in severe stenosis); sometimes a fourth heart sound is audible. The pulse is low-amplitude and slow-rising—"parvus and tardus" (in elderly patients these pulse features may be absent due to systemic arteriosclerosis). Patients may have a brachial-radial delay.

3. **Natural history**: The rate of progression of AS is highly variable. In asymptomatic patients the risk of sudden cardiac death is low but rapidly increases with the onset of the 3 cardinal symptoms: syncope, angina, and heart failure. The average survival of untreated patients with such symptoms is 2 to 3 years.

Diagnosis

Diagnosis is based on typical clinical features and echocardiography results.

Diagnostic Tests

1. **Electrocardiography (ECG)** is usually normal in mild to moderate AS. In severe AS, features of left ventricular (LV) hypertrophy with strain pattern are commonly present.

2. **Chest radiography** remains normal for many years. In severe AS, LV hypertrophy and poststenotic dilation of the ascending aorta are observed. Calcifications of the aortic valve may be seen.

3. **Doppler echocardiography** is used to confirm the diagnosis of AS, assess its severity, evaluate LV structure and function, assess valve morphology, aortic root, and ascending aorta, and monitor the course of the disease. A thickened, calcified aortic valve with reduced leaflet excursion is seen. Doppler echocardiography allows for determination of the severity of stenosis by measuring the aortic jet velocity, peak and mean transvalvular pressure gradients, and AVA. In patients with low-flow low-gradient AS (AVA <1 cm^2, but a mean aortic valve gradient <40 mm Hg and/or peak aortic valve velocity <4.0 cm/s), the most common cause is depressed left ventricular ejection fraction (LVEF) (ejection fraction <40%) resulting in low transvalvular flow; in such cases cardiac computed tomography (CT) (see below) and dobutamine stress echocardiography can be performed to distinguish true severe AS from "pseudosevere AS" and to help predict perioperative mortality (expert input usually required).

4. **Noncontrast gated cardiac CT**: Aortic valve calcium scoring can provide a morphologic estimation of the severity of AS and risk of adverse outcomes with medical therapy. Severe AS is unlikely with calcium scores <800 in women and <1600 in men but likely with calcium scores >1200 in women and >2000 in men. CT is the preferred modality to assess valve anatomy, annulus dimensions, root dimensions, and feasibility of vascular access when intervention is being considered.

5. **Cardiac catheterization** may be considered in cases of inconsistent clinical and echocardiographic findings, and to exclude significant coronary artery stenosis before aortic valve surgery. Coronary angiography is recommended before surgical treatment of AS in patients with severe valvular heart disease and one of the following:

1) A history of coronary artery disease (CAD).

2) Suspected myocardial ischemia (chest pain, abnormal results of noninvasive investigations).

3) LV systolic dysfunction.

4) Men >40 years of age, postmenopausal women.

5) ≥1 cardiovascular risk factor (in patients at low risk of atherosclerosis, the diagnosis of CAD may be excluded using coronary CT angiography).

MITRAL REGURGITATION

Definition, etiology, pathogenesis

Mitral regurgitation (MR) is a backward blood flow from the left ventricle (LV) to the left atrium (LA) due to an incomplete closure of the mitral valve leaflets. In 10% to 40% of people in whom Doppler echocardiography is performed results show a mild regurgitant jet with no evident abnormalities of the valve apparatus (so-called physiologic regurgitation).

Primary (organic) MR is due to a primary damage of the valve apparatus (leaflets, chordae tendineae, papillary muscles, or a combination of these). **Secondary (functional) MR** is due to changes in LV/LA size and function (eg, in ischemic or dilated cardiomyopathy) in the presence of structurally normal valve apparatus.

Etiology of chronic MR:

1) Primary: Degenerative lesions (myxomatous mitral valve disease [variable extent with bileaflet involvement known as the “Barlow valve”], idiopathic rupture of the chordae tendineae [fibroelastic deficiency]), systemic connective tissue disorders (Marfan syndrome, Ehlers-Danlos syndrome), calcification of the mitral annulus, infective endocarditis (infectious or noninfectious-eg, associated with antiphospholipid syndrome), rheumatic disease, drug mediated (ergotamines, appetite suppressants [eg, fenfluramine; currently withdrawn]), radiation mediated, congenital (eg, mitral valve clefts).

2) Secondary: Diseases of the myocardium (ischemic heart disease, nonischemic dilated cardiomyopathy, storage and infiltrative diseases [amyloidosis, eosinophilic cardiomyopathy, carcinoid syndrome, endomyocardial fibrosis]), left atrial enlargement (“atriogenic” MR).

Etiology of acute MR:

1) Primary (organic): Lesions of the valve leaflets (infective endocarditis, leaflet trauma, eg, after balloon valvotomy), rupture of the chordae tendineae (idiopathic, myxomatous degeneration, infective endocarditis, acute rheumatic fever, leaflet trauma), papillary muscle rupture (most commonly following inferior ST-segment elevation myocardial infarction [STEMI]).

2) Secondary (functional): Acute leaflet restriction with or without reduction in closing forces (acute myocardial infarction [MI], acute LV dilation, [eg, acute myocarditis]).

Clinical features and natural history

1. **Symptoms**: Mild or moderate chronic MR is usually asymptomatic (in the case of slow progression of regurgitation—even if it is severe—the symptoms may be minor). With time, patients develop symptoms related to changes in LV function and filling pressure, left atrial compliance, pulmonary artery pressure, and right ventricular function, with increased risk of arrhythmias (most commonly atrial fibrillation [AF] and less commonly ventricular arrhythmias). In acute MR, sudden dyspnea and hypotension or cardiogenic shock may occur.

2. **Signs**: A holosystolic murmur, whose loudness is usually correlated with the size of the regurgitant volume (except for ischemic regurgitation); a possible short diastolic rumble (in severe MR); duration can be variable with late systolic murmur preceded by a systolic click associated with mitral valve prolapse; a diminished first heart sound (in clinically significant MR); splitting of the second heart sound; third heart sound (correlating with the regurgitant volume and with LV enlargement); laterally displaced apex. Pulmonary crepitations may occur. In patients with severe MR and pulmonary hypertension, symptoms of right ventricular failure may be present.

3. **Natural history**: In functional MR, disease progression is related to the underlying condition (LV disease). Acute MR is rapidly progressive and usually fatal when left without surgical treatment: 25% of patients with moderate or severe MR related to acute MI die within 30 days, and 50% die within one year. In the case of papillary muscle rupture in the course of acute MI, 95% of patients die within two weeks. Chronic MR may remain asymptomatic for over a decade. The regurgitant volume is of a significant prognostic value in asymptomatic patients. Uncorrected severe MR may lead to irreversible asymptomatic LV dysfunction.

Diagnosis

Diagnosis is based on clinical features (if present) and echocardiography.

Diagnostic Tests:

1. **Electrocardiography (ECG)** is usually normal; the most frequent abnormalities include AF and atrial flutter. Patients with preserved sinus rhythm may have features of left atrial enlargement (or enlargement of both atria in patients with coexisting tricuspid regurgitation). Signs of LV hypertrophy and pulmonary hypertension may be present in chronic severe MR.

2. **Chest radiographs**: Significant LV and left atrial enlargement; right ventricular and right atrial enlargement in patients with coexisting tricuspid regurgitation and pulmonary hypertension. Patients with acute MR have features of

pulmonary congestion with a normal cardiac silhouette. Calcifications of the mitral annulus may be present.

3. **Echocardiography** is the primary diagnostic modality used to detect and classify the severity of regurgitation, define the mechanism of regurgitation, detect secondary structural changes (effects on LV and LA), and estimate pulmonary artery pressures. In the case of equivocal results of transthoracic imaging, transesophageal echocardiography is often helpful.

4. **Exercise stress testing** is helpful for objective evaluation of exercise tolerance. Echocardiographic stress test can be used for noninvasive assessment of exertional increase in pulmonary artery systolic pressures and potential dynamic regurgitation severity changes.

5. **Cardiac catheterization and coronary angiography** are rarely performed in MR, except to assess for concomitant coronary artery disease in patients referred for mitral valve surgery in whom coronary disease is a clinical concern (>40 years of age, coronary disease risk factors).

6. **Magnetic resonance imaging (MRI)** can further define MR severity if the echocardiographic image is equivocal. It can also serve as a more reliable determination of LV volumes and ejection fraction, and potentially add prognostic information (late gadolinium enhancement of the myocardium).

MITRAL STENOSIS

Definition, etiology, pathogenesis

Mitral stenosis (MS) is a reduction of the mitral valve orifice area causing obstruction of blood flow from the left atrium to the left ventricle (LV).

Classification based on etiology

1) **Structural MS**: Limited mobility of the leaflets and chordae tendineae due to organic lesions. Etiology: rheumatic (most frequently, especially if more than mild), degenerative/nonrheumatic/calcific (due to severe mitral annular calcification, increasingly common in aging populations), infective endocarditis; rarely, systemic lupus erythematosus, rheumatoid arthritis, carcinoid syndrome, or storage diseases.

2) **Functional MS**: Inhibited opening of structurally normal valve leaflets. Etiology: aortic regurgitation, left atrial thrombus, tumor (usually left atrial myxoma).

Clinical features and natural history

1. **Symptoms**: Impaired exercise tolerance, fatigue, exertional dyspnea, sometimes cough with expectoration of frothy sputum, hemoptysis, recurrent

respiratory tract infections, palpitations, right upper abdominal quadrant discomfort, rarely hoarseness (due to compression of the left recurrent laryngeal nerve by an enlarged left atrium [Ortner syndrome]), chest pain (in 15% of patients due to high right ventricular pressures or coexisting coronary artery disease).

2. **Signs**: An accentuated first heart sound, opening snap (OS) of the mitral valve, a low-pitched decrescendo diastolic rumble with presystolic accentuation in sinus rhythm (the timing of onset and loudness of the OS vary with left atrial pressure and compliance of leaflets). A Graham Steell murmur caused by pulmonary regurgitation in patients with severe pulmonary hypertension and dilation of the main pulmonary artery. In advanced MS, pinkish-purple patches on the cheeks, peripheral cyanosis, systolic pulsation in the epigastrium, displacement of the apical impulse to the left, symptoms of right ventricular failure.

3. **Natural history**: The severity of MS gradually increases. The first symptoms usually develop approximately 15 to 20 years after an episode of rheumatic fever. The usual presenting symptoms are exertional dyspnea; supraventricular arrhythmias (particularly atrial fibrillation [AF]; the risk increases with age and with progressive left atrial enlargement); and thromboembolic events (up to 6/100 patients); risk factors: age, AF, small mitral valve orifice area, spontaneous left atrial contrast on echocardiography).

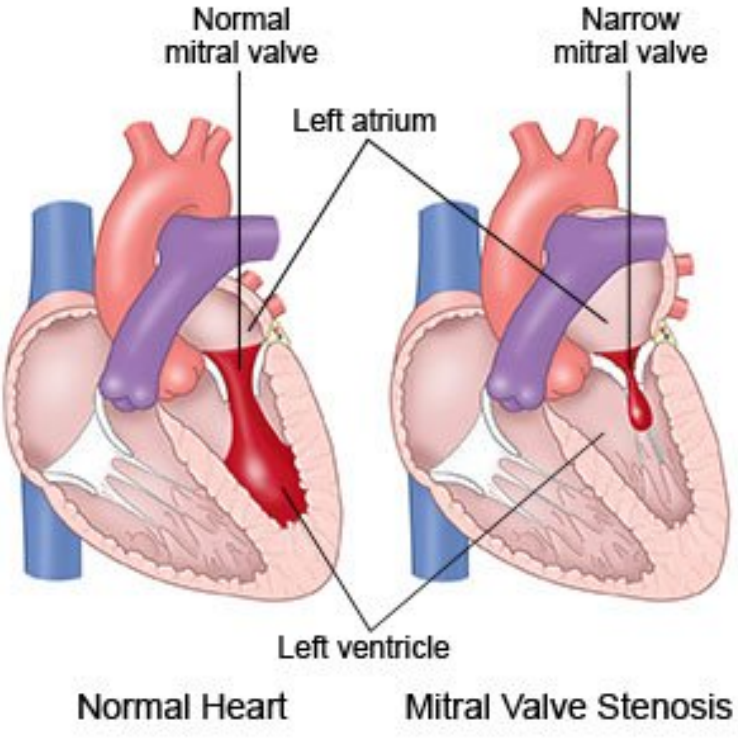

Image 19. Mitral stenosis

This image was downloaded from website https://www.drugs.com/cg/mitral-stenosis.html

Diagnosis

Diagnosis is based on typical clinical features and echocardiography results.

Diagnostic Tests:

1. **Electrocardiography (ECG)**: Features of left atrial enlargement, often P mitrale, frequently atrial arrhythmias, particularly AF. In patients with pulmonary hypertension, right axis deviation, incomplete right bundle branch block (less frequently other features of right ventricular hypertrophy and overload), P mitrale that may evolve into P cardiale or P pulmonale.

2. **Chest radiographs**: Left atrial enlargement, dilation of the upper lobe pulmonary veins, dilation of the main pulmonary artery, pulmonary alveolar edema, pulmonary interstitial edema, right ventricular enlargement, calcifications of the mitral valve (rare).

3. **Echocardiography** is used to evaluate the anatomic features of the valve (define the mechanism and suitability of percutaneous mitral balloon commissurotomy), detect left atrial thrombi (transesophageal echocardiography is useful as most thrombi occur in the left atrial appendage, which is not well-visualized on transthoracic echocardiography), define the severity (measure the mean transvalvular gradient, calculate the mitral valve area [MVA]), estimate the pulmonary artery pressure, and detect concurrent mitral regurgitation or the presence of other structural heart disease.

4. **Exercise stress testing** is used to assess exercise tolerance, with stress echocardiography performed to assess associated changes in pulmonary artery pressures and mean gradients (especially important for management of patients with moderate MS at rest and disproportionate exertional symptoms).

5. **Cardiac catheterization and coronary angiography** are infrequently used in cases that are equivocal by clinical and echocardiographic criteria to confirm the severity of MS and to measure pulmonary artery pressures. Coronary angiography is recommended in patients >40 years of age who are undergoing intervention for MS, or in younger patients with LV dysfunction or suspected coronary artery disease.

TOPIC 7
CONNECTIVE TISSUE DISEASES. SYSTEMIC VASCULITIS. DENTAL ASPECTS

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Systemic lupus erythematosus *is a chronic, multisystem, inflammatory disorder of autoimmune etiology, occurring predominantly in young women. Common manifestations may include arthralgias and arthritis, Raynaud syndrome, malar and other rashes, pleuritis or pericarditis, renal or central nervous system involvement, and autoimmune cytopenias.*

Of all cases, 70 to 90% occur in women (usually of child-bearing age). Systemic lupus erythematosus (SLE) is more common and severe among Black and Asian patients than among White patients. It can affect patients of any age, including neonates. In some countries, the prevalence of SLE rivals that of rheumatoid arthritis. SLE may be precipitated by currently unknown environmental triggers that cause autoimmune reactions in genetically predisposed people. Some drugs (eg, hydralazine, procainamide, isoniazid, anti-tumor necrosis factor [TNF] drugs) cause a reversible lupus-like syndrome.

Symptoms and Signs of SLE

Clinical findings vary greatly. SLE may develop abruptly with fever or insidiously over months or years with episodes of arthralgias and malaise. Vascular headaches, epilepsy, or psychoses may be initial findings. Manifestations referable to any organ system may appear. Periodic exacerbations (flares) may occur.

Joint manifestations

Joint symptoms, ranging from intermittent arthralgias to acute polyarthritis, occur in about 90% of patients and may precede other manifestations by years. Most lupus polyarthritis is nondestructive and nondeforming. However, in long-standing disease, deformities without bone erosions may develop (eg, the metacarpophalangeal and interphalangeal joints may rarely develop reducible ulnar drift or swan-neck deformities without bony or cartilaginous erosions [Jaccoud arthritis]). As in many other chronic diseases, the prevalence of fibromyalgia is increased, which may cause diagnostic confusion in patients with periarticular and generalized pain and fatigue.

Skin and mucous membrane manifestations

Skin lesions include malar butterfly erythema (flat or raised) that generally spares the nasolabial folds. The absence of papules and pustules and presence of skin atrophy help distinguish SLE from rosacea. A variety of other erythematous, firm, maculopapular lesions can occur elsewhere, including exposed areas of the face and neck, upper chest, and elbows. Skin blistering and ulceration are rare, although recurrent ulcers on mucous membranes (particularly the central portion of the hard palate near the junction of the hard and soft palate, the buccal and gum mucosa, and the anterior nasal septum) are common (sometimes called mucosal lupus); findings can sometimes mimic toxic epidermal necrolysis.

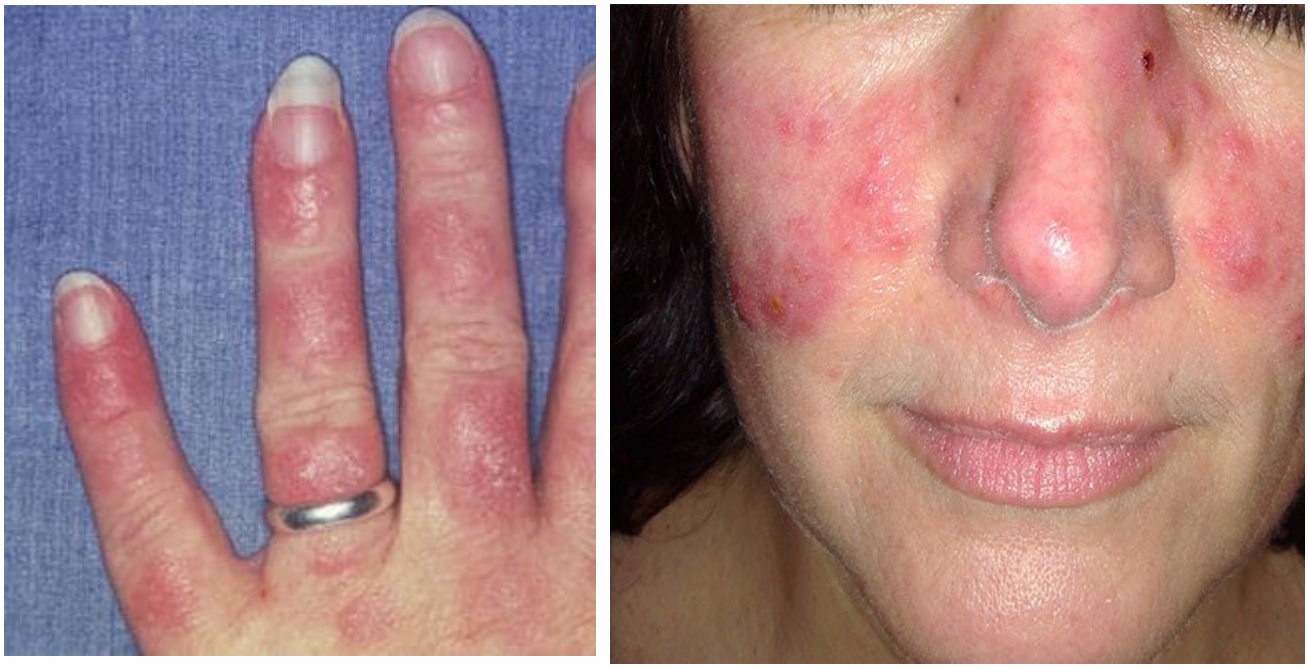

Image 20. Systemic lupus erythematosus
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Generalized or focal alopecia is common during active phases of SLE. Panniculitis can cause subcutaneous nodular lesions (sometimes called lupus panniculitis or profundus). Vasculitic skin lesions may include mottled erythema on the palms and fingers, periungual erythema, nail-fold infarcts, urticaria, and palpable purpura. Petechiae may develop secondary to thrombocytopenia. Photosensitivity occurs in some patients.

Lupus erythematosus tumidus is characterized by pink to violaceous urticarial nonscarring plaques and/or nodules, some annular, in light-exposed areas.

Chilblain lupus is characterized by tender, bright red to reddish blue nodules on the toes, fingers, nose, or ears that occur in cold weather. Some patients with SLE have features of lichen planus.

Raynaud syndrome due to vasospasm in the fingers and toes causes characteristic blanching and cyanosis.

Cardiopulmonary manifestations

Cardiopulmonary symptoms commonly include recurrent pleurisy, with or without pleural effusion. Pneumonitis is rare, although minor impairments in pulmonary function are common. Diffuse alveolar hemorrhage occasionally occurs. Prognosis has traditionally been poor. Other complications include pulmonary emboli, pulmonary hypertension, and shrinking lung syndrome. Cardiac complications include pericarditis (most commonly) and myocarditis. Serious, rare complications are coronary artery vasculitis, valvular involvement, and Libman-Sacks endocarditis. Accelerated atherosclerosis is an increasing cause of morbidity and mortality. Congenital heart block can develop in neonates whose mother has the antibodies against Ro (SSA) or La (SSB).

Lymphoid tissue

Generalized adenopathy is common, particularly among children, young adults, and Black people; however, mediastinal adenopathy is not common. Splenomegaly occurs in 10% of patients.

Neurologic manifestations

Neurologic symptoms can result from involvement of any part of the central or peripheral nervous system or meninges. Mild cognitive impairment is common. There may also be headaches, personality changes, ischemic stroke, subarachnoid hemorrhage, seizures, psychoses, aseptic meningitis, peripheral and cranial neuropathies, transverse myelitis, choreoathetosis, or cerebellar dysfunction.

Renal manifestations

Renal involvement can develop at any time and may be the only manifestation of SLE (see Lupus Nephritis). It may be benign and asymptomatic or progressive and fatal. Renal lesions can range in severity from a focal, usually benign, glomerulitis to a diffuse, potentially fatal, membranoproliferative glomerulonephritis. Common manifestations include proteinuria (most often), an abnormal urinary sediment manifested by red blood cell casts and leukocytes, hypertension, and edema. Early lupus glomerulonephritis may be misdiagnosed as asymptomatic urinary tract infection.

Obstetric manifestations

Obstetric manifestations include early and late fetal loss. In patients with antiphospholipid antibodies, the risk of recurrent miscarriages is increased. Pregnancy can be successful (see SLE in Pregnancy), particularly after 6 to 12 months of remission, but SLE flares are common during pregnancy and especially during the postpartum period. Pregnancy should be timed for when disease is in remission. During pregnancy, the patient should be monitored closely for any disease flare or thrombotic events by a multidisciplinary team that includes an obstetrician who specializes in high-risk pregnancies. Women who are SSA antibody-positive should have weekly fetal ultrasonography between week 18 and week 26 to assess for congenital heart block.

Hematologic manifestations

Hematologic manifestations include anemia (anemia of chronic disease, autoimmune hemolytic anemia), leukopenia (usually lymphocytopenia, with < 1500 cells/mcL), and thrombocytopenia (usually mild but sometimes life-threatening autoimmune thrombocytopenia). Recurrent arterial or venous thrombosis, thrombocytopenia, and a high probability of obstetric complications occur in patients with antiphospholipid antibodies. Thromboses probably account for many of the complications of SLE, including obstetric complications. Macrophage activation syndrome can occur.

Gastrointestinal manifestations

Gastrointestinal manifestations can result from bowel vasculitis or impaired bowel motility. In addition, pancreatitis can rarely result from SLE. Manifestations may include abdominal pain resulting from serositis, nausea, vomiting, manifestations of bowel perforation, and pseudo-obstruction. SLE rarely causes parenchymal liver disease.

Diagnosis

Diagnostic Criteria

Diagnosis is based on the typical clinical features and results of diagnostic tests. Negative antinuclear antibody (ANA) tests by immunofluorescence make the diagnosis of SLE much less likely (they are positive in >95% of patients), while positive anti–double-stranded DNA (dsDNA) or anti-Sm antibodies usually confirm the diagnosis. In 2019, new SLE classification criteria were published by the European League Against Rheumatism (EULAR) and ACR. Note that classification

criteria are designed mostly to classify patients for research purposes and may clinically misclassify some patients diagnosed in routine clinical practice.

Diagnostic Tests

1. **Laboratory tests**:

1) **Serum biochemistry**:

a) **Inflammatory markers**: Neither the erythrocyte sedimentation rate (ESR) nor C-reactive protein (CRP) is a reliable indicator of disease activity in SLE. In patients with polyclonal gammopathy, the ESR can be chronically elevated even in the absence of disease activity.

b) **Hemoglobin**: An inflammatory anemia (anemia of chronic disease) is commonly found in patients with SLE, characterized by elevated ferritin levels with low serum iron, iron saturation, and total iron-binding capacity. Hemolytic anemia with a positive Coombs test result is characteristic of SLE and is an indication for systemic glucocorticoid and/or immunomodulatory therapy.

c) **White blood cells**: Leukopenia (15%-20% of patients) and lymphopenia $<1.5\times10^9$/L are common in SLE and usually do not require specific therapy. Severe neutropenia may require therapy.

d) **Platelets**: Thrombocytopenia is common and can be caused either by immunologic disturbances associated with SLE or by secondary antiphospholipid syndrome.

e) **Creatinine**: Creatinine levels can be elevated in class III, IV, or V lupus nephritis.

f) **Hypergammaglobulinemia**: Hypergammaglobulinemia is generally polyclonal. It may or may not be associated with active disease.

2) **Urinalysis**: Proteinuria is generally present in class III, IV, and V lupus nephritis; hematuria or pyuria can also be present, particularly in class III and IV nephritis. Urine sediment examination in class III and IV lupus nephritis can reveal dysmorphic erythrocyte, leukocyte, and erythrocyte casts.

3) **Immunology**: More than 95% of patients with SLE have ANAs, including extractable nuclear antigens (ENAs) by immunofluorescence or newer immunoassays (BioPlex). ANAs/ENAs represent a group of autoreactive antibodies directed against the nucleus. ENAs constitute antibodies to specific nuclear components, and these reactivities may predict clinical subtypes/phenotypes of lupus. The anti-dsDNA and anti-Sm antibodies are highly specific (95%-97%) for SLE diagnosis. Drug-induced

SLE is associated with antihistone antibodies in >95% of people. Some autoantibodies are more specific to the involvement of certain organs, for instance: anti-dsDNA, lupus nephritis; anti-RNP, myositis; anti-SSA/anti-Ro, lymphopenia, lymphadenopathy, SCLE, sicca complex. Higher disease activity can correlate with low levels of C3 or C4 complement components and elevated levels of anti-dsDNA; in particular, all these can accompany activity of lupus nephritis. Antiphospholipid antibodies (anticardiolipin, anti–beta$_2$-glycoprotein I, nonspecific inhibitor) are found in ~30% of patients with SLE.

2. **Biopsies**:

1) **Skin**: Skin biopsy samples taken from the areas with evident erythematous lesions or even from apparently healthy skin can reveal immunoglobulin and complement deposits along the border of the epidermis and dermis, although these may also occur in other skin conditions as well as in 20% of healthy individuals.

2) **Renal**: Kidney biopsy is indicated in the majority of patients with features of lupus nephritis. Biopsy results identify the type of glomerular lesions as well as the activity and chronic character of renal involvement, which has implications for both management and prognosis.

SYSTEMIC SCLEROSIS

Systemic sclerosis is a rare chronic disease of unknown cause characterized by diffuse fibrosis and vascular abnormalities in the skin, joints, and internal organs (especially the esophagus, lower gastrointestinal tract, lungs, heart, and kidneys). Common symptoms include Raynaud syndrome, polyarthralgia, dysphagia, heartburn, and swelling and eventually skin tightening and contractures of the fingers. Lung, heart, and kidney involvement accounts for most deaths.

Systemic sclerosis is about 4 times more common among women than men. It is most common among people aged 20 to 50 and is rare in children. The etiology is unknown.

Classification of Systemic Sclerosis

Systemic sclerosis is classified as

- Limited systemic sclerosis (CREST syndrome)
- Generalized systemic sclerosis (with diffuse skin involvement)
- Systemic sclerosis sine scleroderma

In limited systemic sclerosis (CREST syndrome—calcinosis cutis, Raynaud syndrome, esophageal dysmotility, sclerodactyly, telangiectasias), patients develop

skin tightening over the face and distal to the elbows and knees and may also have gastroesophageal reflux disease. This type is characterized by slow progression and is often complicated by pulmonary hypertension.

In generalized systemic sclerosis with diffuse skin involvement, patients have Raynaud syndrome and gastrointestinal (GI) complications. This type typically evolves rapidly. Interstitial lung disease and scleroderma renal crisis are the major complications.

In systemic sclerosis sine scleroderma, patients have systemic sclerosis–related antibodies and visceral manifestations of the disease but no skin tightening.

Symptoms and Signs of Systemic Sclerosis

The most common initial symptoms and signs of systemic sclerosis are Raynaud syndrome and insidious swelling of the distal extremities with gradual thickening of the skin of the fingers. Polyarthralgia is also prominent. Gastrointestinal disturbances (eg, heartburn, dysphagia) or respiratory complaints (eg, dyspnea) are occasionally the first manifestations.

Skin and nail manifestations

Swelling of the skin is usually symmetric and progresses to induration. It may be confined to the fingers (sclerodactyly) and hands, or it may affect most or all of the body. The skin eventually becomes taut, shiny, and hypopigmented or hyperpigmented; the face becomes masklike; and telangiectases may appear on the fingers, chest, face, lips, and tongue. However, in some patients, skin can soften to variable degrees. Subcutaneous calcifications may develop, usually on the fingertips (pulps) and over bony eminences. Digital ulcers are common, especially on the fingertips, overlying the finger joints, or over calcinotic nodules. Abnormal capillary and microvascular loops in the nails can be seen with an ophthalmoscope or dissecting microscope.

Joint manifestations

Polyarthralgias or mild arthritis can be prominent. Flexion contractures may develop in the fingers, wrists, and elbows. Friction rubs may develop over the joints, tendon sheaths, and large bursae.

Gastrointestinal manifestations

Esophageal dysfunction is the most frequent visceral disturbance and occurs in most patients. Dysphagia (usually retrosternal) usually develops first. Acid reflux can cause heartburn and stricture. Barrett esophagus occurs in one third of patients and predisposes to complications (eg, adenocarcinoma). Hypomotility of the small bowel causes bacterial overgrowth that can lead to malabsorption. Air may penetrate the

damaged bowel wall and be visible on x-rays (pneumatosis intestinalis). Leakage of bowel contents into the peritoneal cavity can cause peritonitis. Distinctive wide-mouthed pseudodiverticula can develop in the colon. Biliary cirrhosis may develop in patients with limited systemic sclerosis (CREST syndrome).

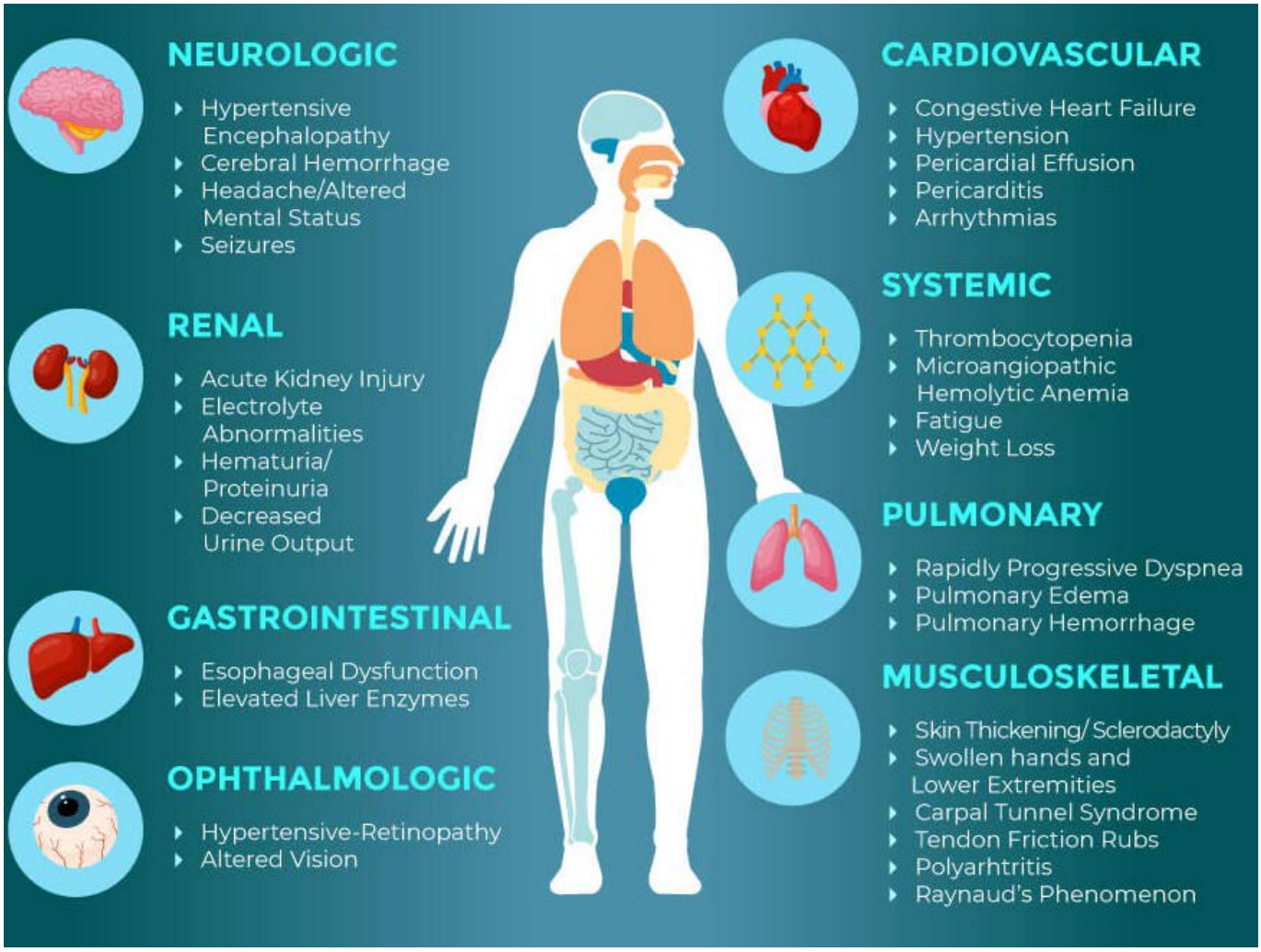

Image 21. Clinical manifistations of Systemic Scleroderma

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Cardiopulmonary manifestations

Lung involvement generally progresses indolently, with substantial individual variability, but is a common cause of death. Lung fibrosis and interstitial lung disease are common and can impair gas exchange, leading to exertional dyspnea and restrictive disease with eventual respiratory failure. Acute alveolitis (potentially responsive to therapy) can develop. Esophageal dysfunction can lead to aspiration pneumonia. Pulmonary hypertension may develop, as can heart failure, both of which

are poor prognostic findings. Pericarditis with effusion or pleurisy can occur. Cardiac arrhythmias are common.

Renal manifestations

Severe, often sudden onset renal disease (scleroderma renal crisis) may occur, most commonly in the first 4 to 5 years in patients who usually have diffuse scleroderma and the RNA polymerase III antibody. It is often heralded by sudden, severe hypertension with features of thrombotic microangiopathic hemolytic anemia. It can also occur without acute hypertension or in systemic sclerosis sine scleroderma, and therefore clinical suspicion is required to make the diagnosis. Corticosteroid use is a risk factor for development of scleroderma renal crisis.

Diagnosis

Diagnostic Tests

1. Laboratory tests:

1) Blood tests: A normal or mildly elevated erythrocyte sedimentation rate (ESR) (a significantly elevated ESR is usually associated with organ involvement or concomitant infection), anemia (usually mild, worsens in patients with malabsorption and progressive renal involvement), hypergammaglobulinemia (increased IgG and IgM levels), positive serum rheumatoid factor (in 20%-30% of patients), elevated serum B-type natriuretic peptide (BNP) or N-terminal pro–B-type natriuretic peptide (NT-proBNP) levels if heart failure and/or advanced PH are suspected.

2) Immunologic studies: Positive ANAs (in 90% of patients), antitopoisomerase-I antibodies (Scl-70, typically in dcSSc [in 30% of patients]), ACAs typically in lcSSc (in 70%-80% of patients), antinucleolar antibodies (nucleolar immunofluorescence), for instance, to RNA polymerase I, RNA polymerase III, Th/To, fibrillarin.

2. Radiologic studies: Hand radiographs may reveal osteolysis of the distal phalanges (or total resorption of the distal phalanx in more advanced disease) and calcifications; less frequently, similar lesions are observed on feet radiographs**. Contrast-enhanced radiography** of the GI tract reveals impaired esophageal motility (in advanced SSc, dilation and pipe-like appearance of the entire esophagus), impaired motor function of the small intestine (alternating segments of strictures and dilations, hypersegmentation) and large intestine (diverticulosis, occasionally significant colonic distention). **Chest radiographs and high-resolution computed tomography** (HRCT) reveal features of ILD, that is, ground-glass linear and reticular opacifications, mainly in the basal peripheral and subpleural areas of the lung,

traction bronchiectases, and bronchial (honeycomb) cysts. **Magnetic resonance imaging (MRI) and single-photon emission computed tomography (SPECT)-CT** may be useful in the diagnosis of cardiac involvement.

3. Doppler echocardiography reveals features of PH (increased right ventricular systolic pressure >35 mm Hg), pericardial effusion, as well as systolic and diastolic dysfunction. Even in asymptomatic patients, echocardiography should be performed annually to facilitate early diagnosis and treatment of PH.

4. Upper GI endoscopy: In the esophagus there are features of gastroesophageal reflux and telangiectasias; in the stomach, diffuse vascular lesions, particularly in the cardia, are observed (solitary or multiple telangiectasias described as a “watermelon stomach” or GAVE).

5. Pulmonary function tests may reveal a low carbon monoxide diffusing capacity of the lungs (DLCO). If there is an isolated reduced DLCO, or if there is a mismatch of DLCO and forced vital capacity (FVC) (FVC%/DLCO% >1.6), consider PH as the cause and investigate with echocardiography. Even in asymptomatic patients, pulmonary function tests and echocardiography should be performed annually to facilitate early diagnosis and management of pulmonary fibrosis or PH.

6. Nail-fold capillaroscopy reveals typical (though not pathognomonic) features of so-called megacapillaries or giant loops (more common in lcSSc) and avascular areas, known as “drop-outs” (predominantly in dcSSc or in late-stage disease).

7. Other studies:

1) Stress tests (6-minute walk test, cardio-respiratory exercise test): These may be used for monitoring the performance status of the patient and progression of SSc-related ILD or PH.

2) Electrocardiography (ECG) (arrhythmias and conduction disturbances).

3) Cardiac catheterization should be considered in patients with high right ventricular systolic pressure on echocardiography, those with symptoms or signs of right heart failure, and in those with isolated declining DLCO on pulmonary function tests (diagnosis of PH).

8. Skin biopsy is of limited use in patients with early SSc due to the high rate of false-negative results. In patients with typical clinical manifestations, the diagnosis is straightforward, which makes the skin biopsy unnecessary. Nevertheless, it is indicated in patients suspected of having other diseases characterized by skin thickening, such as eosinophilic fasciitis or scleredema or scleromyxedema.

SJÖGREN SYNDROME

Sjögren syndrome is a relatively common chronic, autoimmune, systemic, inflammatory disorder of unknown cause. It is characterized by dryness of the mouth, eyes, and other mucous membranes (sicca syndrome) due to lymphocytic infiltration of exocrine glands and secondary gland dysfunction. Sjögren syndrome can affect various exocrine glands or other organs. Diagnosis is by specific criteria relating to eye, mouth, and salivary gland involvement, autoantibodies, and (occasionally) histopathology.

Sjögren syndrome occurs most frequently among middle-aged women. The disease is classified as primary when there is no other associated disease. In about 30% of patients with autoimmune disorders such as rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, mixed connective tissue disease, Hashimoto thyroiditis, primary biliary cirrhosis, or chronic autoimmune hepatitis, Sjögren syndrome develops and, in such cases, is classified as secondary. Genetic associations have been found (eg, HLA-DR3 antigens in White people with primary Sjögren syndrome) but are not necessary for diagnosis or clinical management.

Symptoms and Signs of Sjögren Syndrome

Glandular manifestations

Sjögren syndrome often affects the eyes or mouth initially and sometimes exclusively (sicca syndrome). Dry eyes can cause a sandy, gritty sensation without pruritus. In advanced cases, the cornea is severely damaged, epithelial strands hang from the corneal surface (keratitis filiformis), and vision can be impaired. Diminished saliva (xerostomia) results in difficulty chewing and swallowing, secondary Candida infection, tooth decay, and calculi in the salivary ducts. Taste and smell may be diminished. Dryness may also develop in the skin and in mucous membranes of the nose, throat, larynx, bronchi, vulva, and vagina. Dryness of the respiratory tract may cause cough.

Parotid glands enlarge in 33% of patients and are usually firm, smooth, and mildly tender. Enlargement can be asymmetric, but highly disproportionate; persistent enlargement of one gland may indicate a tumor and should be evaluated. Chronic salivary gland enlargement is rarely painful unless there is obstruction or infection.

Extraglandular manifestations

Joint disease in Sjögren syndrome is typically nonerosive and nondeforming. Arthralgias occur in about 50% of patients. Arthritis occurs in about 33% of patients and is similar in distribution to rheumatoid arthritis but is not erosive.

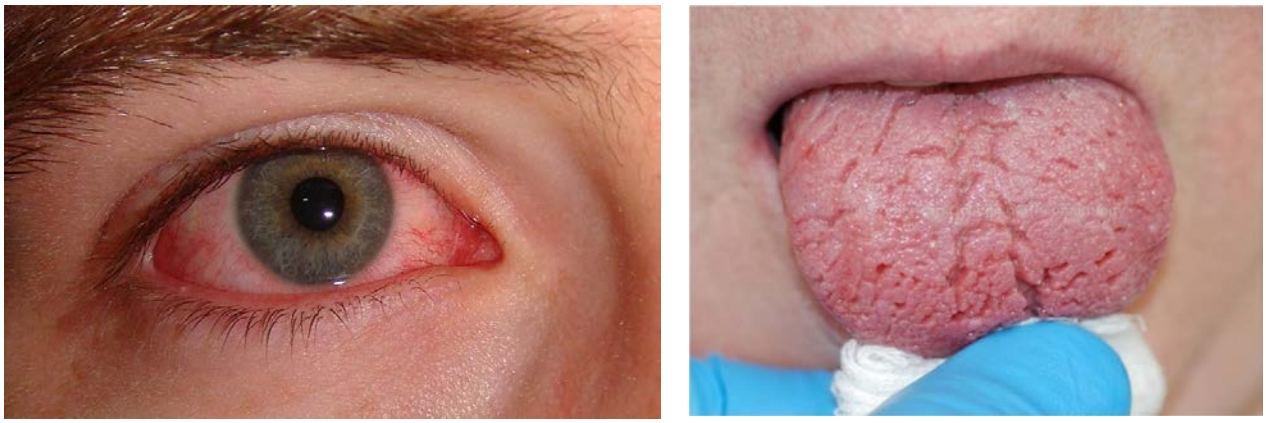

Image 22. Symptoms and Signs of Sjögren Syndrome
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Other extraglandular manifestations include generalized lymphadenopathy, Raynaud syndrome, interstitial lung involvement (which is common but infrequently serious), pancreatic insufficiency, and vasculitis. Vasculitis can occasionally affect the peripheral nerves (causing sensory peripheral polyneuropathy or multiple mononeuropathy) or the central nervous system. It may cause rashes (including purpura) and glomerulonephritis. Kidney involvement can also cause renal tubular acidosis, impaired concentrating ability, kidney stones, or interstitial nephritis. Pseudolymphoma, B-cell lymphoma, or Waldenström macroglobulinemia can develop; patients develop non-Hodgkin lymphoma at 40 times the normal rate. Chronic hepatobiliary disease and pancreatitis (exocrine pancreatic tissue is similar to that of salivary glands) may also occur.

Alopecia may occur. Fatigue is often present.

Diagnosis

Diagnostic Tests

1. Blood tests: Hypergammaglobulinemia (in 80% of patients), cryoglobulins (30%), antinuclear antibodies (ANAs) at a titer >1:80 (90%), anti-Ro/SSA (55%) and anti-La/SSB (40%) antibodies, rheumatoid factor at a titer >1:40 (60%); anemia (25%), leukopenia (10%).

2. Imaging studies: Sialography reveals irregular dilations and strictures of the glandular ducts (a “cherry blossom” appearance). Salivary scintigraphy reveals a delayed uptake, decreased accumulation, and delayed excretion of the radiolabeled marker following stimulation. Ultrasonography (the most useful test) is used to assess the size and structure of the parotid and submandibular salivary glands, as well as to detect cysts or local lymphadenopathy. Ultrasonography of the salivary gland is a simple and cost-effective procedure to evaluate the gland; biopsy can be reserved for those in whom an alternative diagnosis or lymphoma is suspected.

3. Ophthalmologic examination: The Schirmer test is helpful in estimating tear production: a strip of filter paper 5 × 30 mm with a rounded edge at one end is placed under the lower eyelid in such a way that it does not touch the cornea. After 5 minutes, more than 5 mm of the filter paper should be moistened by tears. The rose Bengal stain (or a test using another dye) is used to assess the corneal surface.

4. Assessment of saliva production (without stimulation) using the Saxon test: The patient chews a piece of a sterile gauze (5 × 5 cm) for 2 minutes; the weight of the gauze should increase by ≥2.75 g.

5. Histologic examination of salivary gland biopsy specimens: Assessment of the number of lymphocytic infiltrates.

SYSTEMIC VASCULITIS

Vasculitis is inflammation of blood vessels, often with ischemia, necrosis, and organ inflammation. Vasculitis can affect any blood vessel—arteries, arterioles, veins, venules, or capillaries. Clinical manifestations of specific vasculitic disorders are diverse and depend on the size and location of the involved vessels, the extent of the organ involvement, and the degree and pattern of extravascular inflammation.c

Etiology of Vasculitis

Vasculitis may be:

- Primary
- Secondary

Primary vasculitis has no known cause.

Secondary vasculitis may be triggered by an infection, a drug, or a toxin or may occur as part of another inflammatory disorder or cancer.

Pathophysiology of Vasculitis

Histologic description of an affected vessel should include the following:

- A description of vessel wall damage (eg, type and location of inflammatory infiltrate, extent and type of damage, presence or absence of fibrinoid necrosis)
- A description of healing responses (eg, intimal hypertrophy, fibrosis)

Certain features (eg, predominant inflammatory cell type, location of inflammation) suggest particular vasculitic processes and may aid in the diagnosis. For example, in many acute lesions, the predominant inflammatory cells are polymorphonuclear leukocytes; in chronic lesions, lymphocytes predominate.

Inflammation may be segmental or involve the entire vessel. At sites of inflammation, varying degrees of cellular inflammation and necrosis or scarring occur in one or more layers of the vessel wall. Inflammation in the media of a muscular artery tends to destroy the internal elastic lamina. Some forms of vasculitis are characterized by giant cells in the vessel wall. In some vasculitic disorders, such as granulomatosis with polyangiitis or Kawasaki disease, the vessel inflammation (true vasculitis) is only part of the pathophysiology and there is predominant parenchymal inflammation in a characteristic pattern that involves specific organs.

Leukocytoclastic vasculitis is a histopathologic term used to describe findings in small-vessel vasculitis. It refers to breakdown of inflammatory cells that leaves small nuclear fragments (nuclear debris) in and around the vessels. Inflammation is transmural and nongranulomatous. Polymorphonuclear leukocytes predominate early; later, lymphocytes predominate. Resolution of the inflammation tends to result in fibrosis and intimal hypertrophy. Intimal hypertrophy or secondary clot formation can narrow the vessel lumen and cause tissue ischemia or necrosis.

Classification of Vasculitis

Vasculitic disorders can be classified according to the size of the predominant vessel affected.

Table 12

Classification of Vasculitic Disorders

Size of Predominant Affected Vessels	Disorders	Symptoms and Signs
Large	• Behçet disease • Giant cell arteritis • Takayasu arteritis	Limb claudication Unequal blood pressure measurements or unequal pulse strength/absent pulse in the limbs

		Central nervous system and retinal ischemic symptoms (eg, strokes)
Medium	• Medium-vessel cutaneous vasculitis • Polyarteritis nodosa • Kawasaki disease	Symptoms of tissue infarction in affected organs, such as • Muscles: Myalgias • Nerves: Numbness, paresthesias, and/or weakness. Multiple mononeuropathy (mononeuritis multiplex) or polyneuropathy • Gastrointestinal tract: Abdominal pain, weight loss, and/or diarrhea. Mesenteric ischemia • Kidneys: New-onset hypertension (with renal artery involvement) • Skin: Ulcers, nodules, and livedo reticularis Symptoms and signs in Kawasaki disease: Fever, rash, lymphadenopathy, conjunctivitis, and coronary artery aneurysms
Small	• Eosinophilic granulomatosis with polyangiitis • Cryoglobulinemic vasculitis • Granulomatosis with polyangiitis • Immunoglobulin A–associated vasculitis (formerly called Henoch-Schönlein purpura) • Microscopic polyangiitis • Small-vessel cutaneous vasculitis	Symptoms of tissue infarction in affected organs similar to those for medium-sized vessels, except skin lesions more likely to be purpuric In kidneys: Glomerulonephritis (usually asymptomatic)

POLYARTERITIS NODOSA (PAN)

Polyarteritis nodosa (PAN) is a necrotizing antineutrophil cytoplasmic antibody (ANCA)-negative vasculitis involving medium and small arteries. It can be distinguished from other vasculitides (mainly from microscopic polyangiitis) by the absence of pulmonary involvement, features of glomerulonephritis, or involvement of arterioles, capillaries, or venules. PAN is strongly associated with hepatitis B virus (HBV) infection (10%-80% of patients, according to various sources). A cutaneous form of PAN may also be associated with hepatitis C virus (HCV) infection. PAN usually affects patients aged 40 to 60 years and is more frequent in men than in women.

Symptoms and Signs of PAN

PAN mimics many disorders. The course may be acute and prolonged, subacute and fatal after several months, or insidious, chronic, and debilitating. Symptoms of PAN depend mainly on location and severity of the arteritis and extent of secondary ischemia. Only one organ or organ system may be affected.

Patients typically present with fever, fatigue, night sweats, loss of appetite, weight loss, and generalized weakness. Myalgias with areas of focal ischemic myositis and arthralgias are common. Affected muscles are tender and may be weak. Arthritis may occur.

Symptoms and signs vary, depending on the organ or organ system predominantly affected:

Peripheral nervous system: Patients usually present with asymmetric peripheral neuropathy, such as multiple mononeuropathy (mononeuritis multiplex) with signs of motor and sensory involvement of the peroneal, median, or ulnar nerves. As additional nerve branches are affected, patients may appear to have a distal symmetric polyneuropathy.

Central nervous system: Headache and seizures can result. In a few patients, ischemic stroke and cerebral hemorrhage occur, sometimes resulting from hypertension.

Renal: If small- and medium-sized arteries in the kidneys are affected, patients may have hypertension, oliguria, uremia, and a nonspecific urinary sediment with hematuria, proteinuria, and no cellular casts. Hypertension may worsen rapidly. Rupture of renal arterial aneurysms can cause perirenal hematomas. In severe cases, multiple renal infarcts with lumbar pain and gross hematuria may occur. Renal ischemia and infarction can lead to renal failure.

Gastrointestinal: Vasculitis of the liver or gallbladder causes right upper quadrant pain. Perforation of the gallbladder with acute abdomen may occur. Vasculitis of medium-sized mesenteric arteries causes abdominal pain, nausea, vomiting (with or without bloody diarrhea), malabsorption, intestinal perforation, and acute abdomen. Aneurysms may develop in hepatic or celiac arteries.

Cardiac: Some patients have coronary artery disease, which is usually asymptomatic, but may cause angina. Heart failure may result from ischemic or hypertensive cardiomyopathy.

Cutaneous: Livedo reticularis, skin ulcers, tender erythematous nodules, bullous or vesicular eruptions, infarction and gangrene of fingers or toes, or a combination may occur. The nodules in PAN resemble erythema nodosum, but, unlike nodules in erythema nodosum, the nodules in PAN can ulcerate, and have necrotizing vasculitis that is visible on biopsy within the walls of medium-sized arteries, usually located in the deep dermis and subcutaneous fat.

Genital: Orchitis with testicular pain and tenderness can occur.

Diagnosis

Diagnosis is based on clinical manifestations and histologic findings from biopsies of the involved organs.

Diagnostic Tests

Laboratory test results often reveal elevations in the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels as well as anemia (usually normocytic). In patients with renal involvement there can be elevated serum creatinine levels and rarely moderate proteinuria and microscopic hematuria. Angiography of the visceral arteries reveals dilations (microaneurysms) of medium arteries, for instance, kidney, liver, or intestinal arteries.

EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA) (Churg-Strauss Syndrome; Allergic Granulomatosis and Angiitis)

Eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome) (EGPA) is a multisystem necrotizing granulomatous inflammation with eosinophilic infiltration of various tissues and organs. The lung is the most commonly involved organ, followed by the skin. EGPA can affect any other organ in the cardiovascular, gastrointestinal (GI), renal, and central nervous systems. In the respiratory tract, necrotizing inflammation affects predominantly small-sized and medium-sized vessels and is associated with concomitant asthma and eosinophilia. Nasal polyps as

well as granulomatous and nongranulomatous extravascular inflammation (eg, nongranulomatous eosinophil-rich infiltrates of the lungs, myocardium, and GI tract) are often observed.

Symptoms and Signs of EGPA

The syndrome has 3 phases, which may overlap:

- Prodromal: This phase may persist for years. Patients have allergic rhinitis, nasal polyposis, asthma, or a combination.
- 2nd phase: Peripheral blood and tissue eosinophilia is typical. Clinical presentation, which may resemble Löffler syndrome, includes chronic eosinophilic pneumonia and eosinophilic gastroenteritis.
- 3rd phase: Potentially life-threatening vasculitis develops. Organ dysfunction and systemic symptoms (eg, fever, malaise, weight loss, fatigue) are common in this phase.

However, the phases do not necessarily follow one another consecutively, and the time interval between them varies greatly.

Various organs and systems may be affected:

Respiratory: Asthma, often with onset during adulthood, occurs in most patients and tends to be severe and corticosteroid-dependent. Sinusitis is common, but not destructive, without severe necrotizing inflammation. Patients may be short of breath. Transient patchy pulmonary infiltrates are common.

Neurologic: Neurologic manifestations are very common. Multiple mononeuropathy (mononeuritis multiplex) occurs in up to three fourths of patients. Central nervous system involvement is rare but can include hemiparesis, confusion, seizures, and coma, with or without cranial nerve palsies or evidence of cerebral infarction.

Cutaneous: The skin is affected in about one half of patients. Nodules and papules appear on extensor surfaces of extremities. They are caused by extravascular palisading granulomatous lesions with central necrosis. Purpura or erythematous papules, due to leukocytoclastic vasculitis with or without prominent eosinophilic infiltration, may develop.

Musculoskeletal: Arthralgias, myalgias, or even arthritis can occur.

Cardiac: Cardiac involvement, a major cause of mortality, includes heart failure due to myocarditis and endomyocardial fibrosis, coronary artery vasculitis (possibly with myocardial infarction), valvular disorders, and pericarditis. The predominant histopathologic finding is eosinophilic myocarditis.

Gastrointestinal: Up to one third of patients present with gastrointestinal symptoms (eg, abdominal pain, diarrhea, bleeding, acalculous cholecystitis) due to eosinophilic gastroenteritis or mesenteric ischemia due to vasculitis.

Renal: The kidneys are affected less often than in other vasculitic disorders associated with antineutrophil cytoplasmic autoantibodies. Typically, pauci-immune (few if any immune complexes), focal segmental necrotizing glomerulonephritis with crescent formation is present; eosinophilic or granulomatous inflammation of the kidneys is rare.

Renal, cardiac, or neurologic involvement indicates a worse prognosis.

Diagnostic Tests

1. Laboratory tests: Eosinophilia in peripheral blood (often >1.5×109/L or >10% of white blood cells), elevation in the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels, normocytic anemia, features of renal involvement (microscopic hematuria, proteinuria), a positive myeloperoxidase (MPO) antineutrophil cytoplasmic antibody (ANCA) test result (in ~60% of patients).

2. Imaging studies: Radiography and computed tomography (CT) reveal signs of chronic sinusitis and alveolar hemorrhage.

3. Pulmonary function tests: Features characteristic of asthma.

4. Histologic examination of samples of the involved organs (usually of the respiratory tract, skin, or kidneys): Patchy necrotizing vasculitis affecting small and medium vessels, necrotizing granulomatous inflammation with extensive eosinophilic infiltrates (nongranulomatous inflammation with eosinophilic infiltrates may also be present).

IMMUNOGLOBULIN A–ASSOCIATED VASCULITIS (IgAV) (Henoch-Schönlein Purpura)

IgA vasculitis (IgAV) (formerly Henoch-Schönlein purpura) is a small-vessel vasculitis characterized by the presence of immune deposits (mainly IgA1), which involves small vessels (predominantly capillaries, venules, or arterioles). It primarily affects children (~75% cases in children aged 2-11 years), although it can also present in adults, where the prognosis is generally worse.

Symptoms and Signs of IgAV

The disease begins with a sudden palpable purpuric rash typically occurring on the feet, legs, and, occasionally, the trunk and arms. The purpura may start as small areas of urticaria that become palpable and sometimes hemorrhagic and confluent.

Crops of new lesions may appear over days to several weeks. Many patients also have fever and polyarthralgia with periarticular tenderness and swelling of the ankles, knees, hips, wrists, and elbows.

Gastrointestinal symptoms are common and include colicky abdominal pain, abdominal tenderness, and melena. Intussusception occasionally develops in children. Stool may test positive for occult blood.

Symptoms of immunoglobulin A–associated vasculitis usually remit after about 4 weeks but often recur at least once after a disease-free interval of several weeks. In most patients, the disorder subsides without serious sequelae; however, although rare, some patients develop chronic kidney disease.

In adults, intussusception is rare and chronic kidney disease is more common than in children.

Diagnosis

Diagnosis is based on clinical symptoms and histologic examination of skin biopsy specimens (perivascular and vascular IgA deposits in small vessels). The disease may be limited to skin or kidneys (in the latter case IgA nephropathy is diagnosed). Kidney biopsy should only be considered in patients with severe proteinuria, hematuria, active sediment, or with renal failure.

GRANULOMATOSIS WITH POLYANGIITIS (GPA)

(Previously known as Wegener's Granulomatosis)

Granulomatosis with polyangiitis (GPA), previously referred to as Wegener granulomatosis, is a granulomatous vasculitis that usually involves the upper and lower respiratory tracts and the kidneys. It is a necrotizing vasculitis affecting mainly small-sized and medium-sized vessels (ie, capillaries, venules, arterioles, arteries, and veins). GPA frequently leads to necrotizing glomerulonephritis, ocular vasculitis, pulmonary capillaritis with hemorrhage, and granulomatous and nongranulomatous extravascular inflammation, leading to systemic manifestations such as fever and weight loss.

GPA may also be limited to the upper or lower respiratory tract or to the eye. In these cases, features of systemic vasculitis may not be identified; however, in patients with clinical and histologic abnormalities identical to those seen in GPA, and particularly with a positive antineutrophil cytoplasmic antibody (ANCA) test result, the diagnosis of GPA should be made.

Symptoms and Signs of GPA

Onset of granulomatosis with polyangiitis may be insidious or acute; the full spectrum of the disease may take years to evolve. Some patients present initially with upper and lower respiratory tract symptoms; at some point later, the kidneys are affected. In other patients, onset of systemic manifestations is relatively acute; several organs and systems, such as the upper respiratory tract, peripheral nervous system (causing multiple mononeuropathy [mononeuritis multiplex]), kidneys (causing glomerulonephritis), and lower respiratory tract (causing hemorrhage, lung nodules, cavities, or a combination), are simultaneously affected.

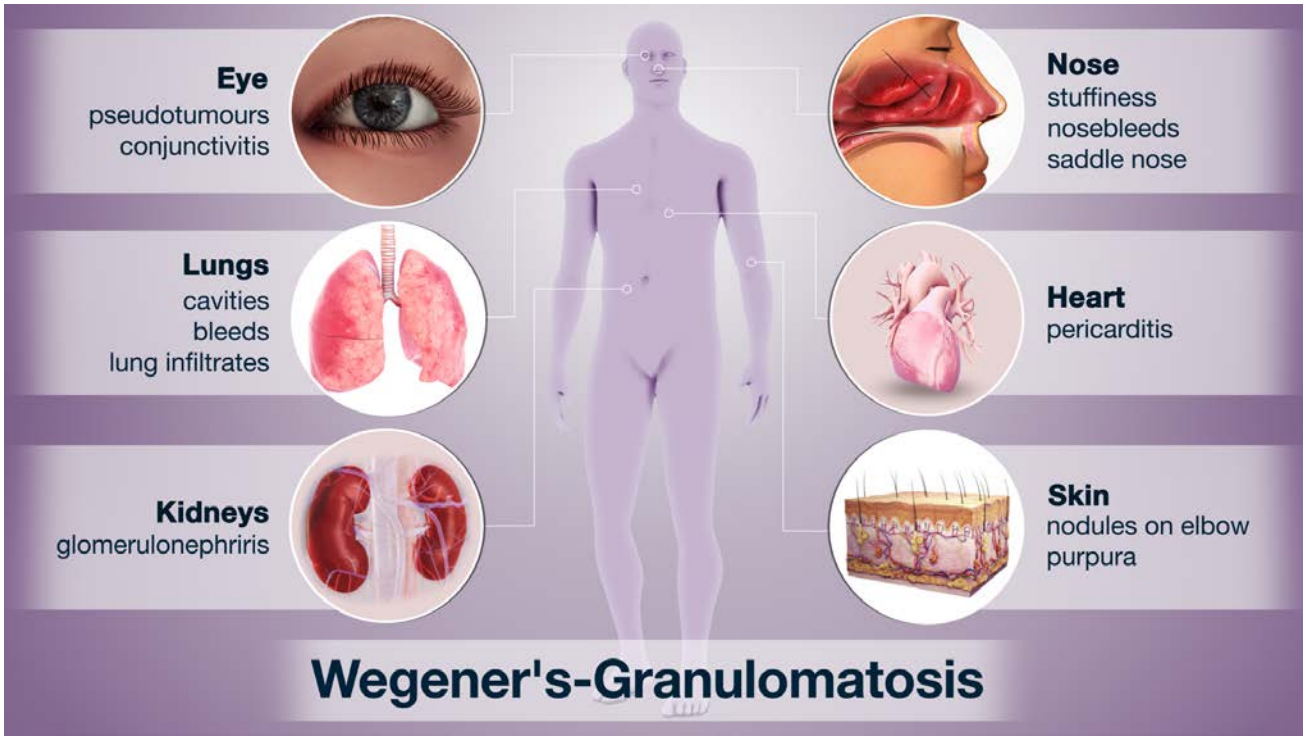

Image 23. Symptoms and Signs of GPA

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Upper respiratory tract: Sinus pain, serosanguineous or purulent discharge, and epistaxis may occur. The mucosa appears granular (like cobblestones) and is friable; ulcers, thick dark crusts, and septal perforation are common. Nasal chondritis can occur with swelling, pain, and collapse of the nasal bridge (saddle nose). Patients may report recurrent sinusitis that has responded inadequately to multiple antibiotic regimens and has required one or more sinus operations before diagnosis. Secondary infections (eg, due to Staphylococcus aureus) may develop. Subglottic stenosis may

develop, causing symptoms such as pain in the larynx, hoarseness, dyspnea, wheezing, and stridor.

Ears: Otitis, sensorineural hearing loss, vertigo, and chondritis may occur. The middle ear, inner ear, and mastoids are often affected.

Eyes: Eyes may appear red and swollen. Nasolacrimal duct inflammation and obstruction, conjunctivitis, scleritis, uveitis, or retinal vasculitis may also occur. Inflammatory infiltrates in the retro-orbital space (orbital pseudotumor) can cause proptosis, compression of the optic nerve, and blindness. Extension into the extraocular muscles leads to diplopia. If serious eye symptoms develop, evaluation and treatment are required immediately to prevent permanent vision loss.

Lower respiratory tract: Respiratory manifestations are common. Inflammation of the major bronchi and branches can cause localized wheezing, postobstructive pneumonia, and atelectasis. Single or multiple pulmonary nodules, with or without cavitation, and parenchymal infiltrates, sometimes cause symptoms, such as chest pain, shortness of breath, and productive cough. Dyspnea with bilateral infiltrates, with or without hemoptysis, may indicate alveolar hemorrhage and must be evaluated immediately.

Heart: Coronary artery disease may occur but rarely.

Musculoskeletal system: Patients frequently present with myalgias, arthralgias, or nonerosive inflammatory arthritis.

Skin: Palpable purpura, tender subcutaneous nodules, papules, livedo reticularis, or ulcers may develop.

Nervous system: Vasculitis may cause ischemic peripheral neuropathy, brain lesions, or extension of inflammation into neural tissue from contiguous sites. Lesions that originate in the sinuses or middle ear may extend directly to the retropharyngeal area and base of the skull, leading to cranial neuropathy, proptosis, diabetes insipidus, or meningitis.

Kidneys: Symptoms and signs of glomerulonephritis develop. Urinary sediment is frequently abnormal, and serum creatinine may increase rapidly. Edema and hypertension may result. Rapidly progressive glomerulonephritis, which is life threatening, can develop.

Venous system: Deep venous thrombosis can affect the lower extremities mostly when granulomatosis with polyangiitis is active.

Other organs: Occasionally, an inflammatory mass occurs in the breasts, kidneys, prostate, or other organs.

Diagnostic Tests

1. Laboratory tests: Positive serum proteinase 3 (PR3) ANCA (in 80%-90% of patients; specificity, 98%). Additionally, there are often elevations in the erythrocyte sedimentation rate and C-protein levels, normocytic anemia, leukocytosis (in some cases >20×109/L), thrombocytosis, and features of glomerulonephritis.

2. Imaging studies: Radiographs and computed tomography (CT) reveal features of chronic sinusitis, frequently accompanied by bone destruction. In the lungs, disseminated infiltrates (these may resolve or change their locations), necrotic nodules, and interstitial lesions (presenting as linear opacifications) are usually observed.

3. Histologic examination: Granulomatous inflammation, necrosis, and inflammatory lesions in vessel walls. Biopsy specimens are taken from an involved organ, ideally the upper respiratory tract or kidney. Usually it is difficult to establish the diagnosis of GPA solely on the basis of histology.

GIANT CELL ARTERITIS

(Temporal Arteritis; Cranial Arteritis; Horton Disease)

Giant cell arteritis (GCA) is an inflammation of predominantly large- and medium-sized arteries that is frequently granulomatous and develops almost exclusively after the age of 50 years. It is characterized by involvement of the arteries branching from the aortic arch. Most often branches of the external carotid artery are involved, but any of the following arteries may be affected (in order of frequency): temporal arteries, vertebral arteries, posterior ciliary arteries, ophthalmic artery, internal carotid artery, external carotid artery, and central retinal artery. The name “temporal arteritis” is misleading, as temporal arteries are not always affected in patients with GCA and may be involved in patients with other vasculitides.

In general terms, large-vessel vasculitis (LVV) occurring in patients aged >50 years is usually diagnosed as or has a clinical form of GCA or more specifically, if temporal arteries are involved, of temporal arteritis. In younger people (<50 years and more so <40 years) the clinical presentation and diagnosis is usually that of Takayasu arteritis.

Symptoms and Signs of Giant Cell Arteritis

Symptoms of giant cell arteritis may begin gradually over several weeks or abruptly.

Patients may present with systemic symptoms such as fever (usually low-grade), fatigue, malaise, unexplained weight loss, and sweats. Some patients are initially diagnosed as having fever of unknown origin. Eventually, most patients develop symptoms related to the affected arteries.

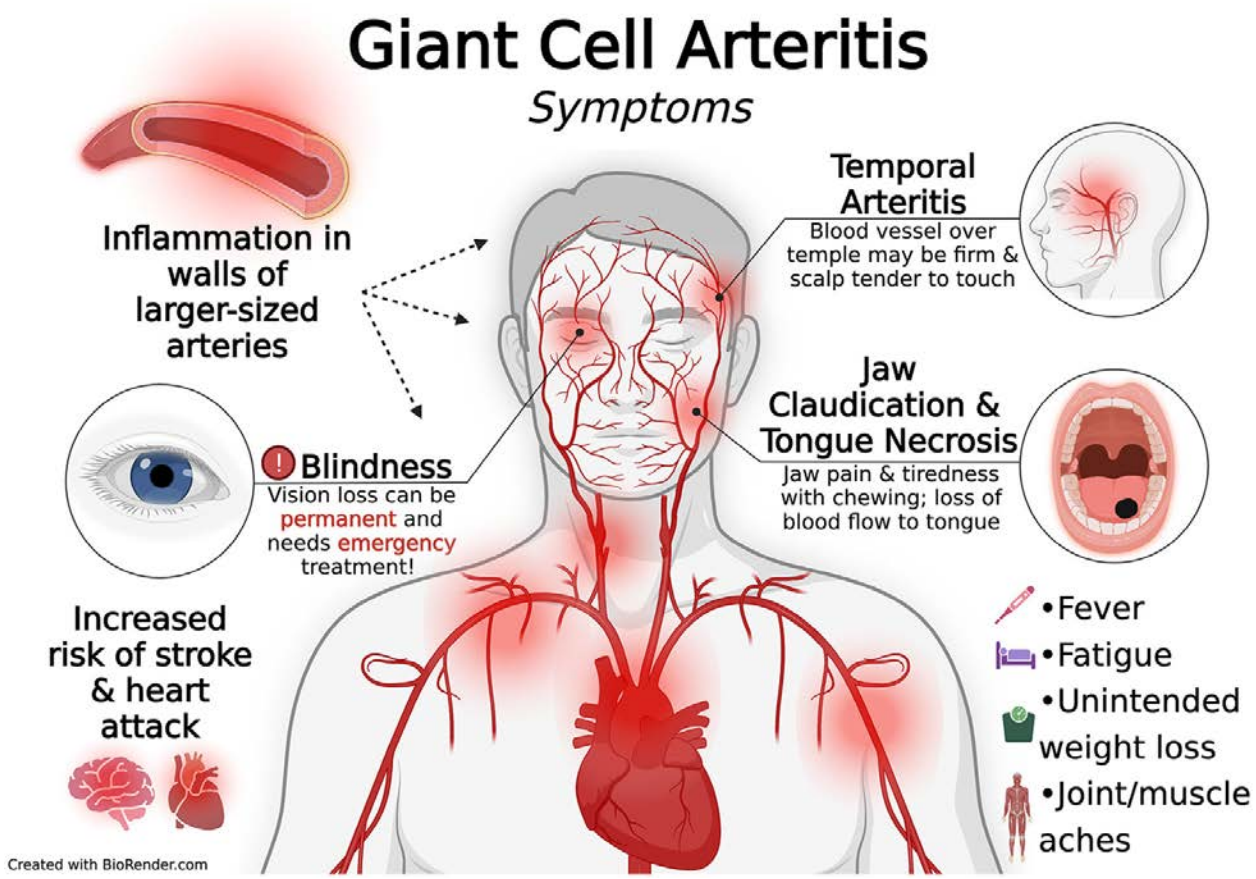

Image 24. Symptoms of giant cell arteritis

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Severe, sometimes throbbing headache (temporal, occipital, frontal, or diffuse) is the most common symptom. It may be accompanied by scalp pain elicited by touching the scalp or combing the hair.

Visual disturbances include diplopia, scotomas, ptosis, blurred vision, and loss of vision (which is an ominous sign). Brief periods of partial or complete vision loss (amaurosis fugax) in one eye may be rapidly followed by permanent irreversible loss of vision. If untreated, the other eye may also be affected. However, complete bilateral blindness is uncommon. Vision loss is caused by arteritis of branches of the ophthalmic artery or posterior ciliary arteries, which leads to ischemia of the optic nerve. Funduscopic findings may include ischemic optic neuritis with pallor and edema of the optic disk, scattered cotton-wool patches, and small hemorrhages. Later,

the optic nerve atrophies. Rarely, central blindness results from infarction in the occipital cortex caused by arterial lesions in the distal cervical region or base of the brain. The incidence of visual disturbances has declined over the past 5 decades, likely because giant cell arteritis is recognized and treated before visual disturbances develop.

Intermittent claudication (ischemic muscle pain) may occur in jaw muscles and muscles of the tongue or extremities. Jaw claudication is noted especially when firm foods are chewed. Jaw claudication and diplopia are associated with a higher risk of blindness.

Neurologic manifestations, such as strokes and transient ischemic attacks, can result when the carotid or vertebrobasilar arteries or branches are narrowed or occluded.

Thoracic aortic aneurysms and dissection of the aorta are serious, often late complications of aortitis and may progress in the absence of other symptoms.

Diagnostic Tests

1. Blood tests: Increased erythrocyte sedimentation rate (ESR) (usually >100 mm after 1 hour, but ESR within the reference range does not exclude the diagnosis of GCA, as <5% of patients have a normal ESR); elevated serum levels of acute phase proteins (C-reactive protein [CRP], fibrinogen); anemia of chronic disease; reactive thrombocytosis; a minor increase in liver function tests, particularly alkaline phosphatase (in ~30% of patients).

2. Imaging studies: Results depend on the location of lesions. Doppler ultrasonography and magnetic resonance imaging (MRI) may reveal inflammatory lesions in the temporal artery. Ultrasonography, conventional arteriography, computed tomography (CT), MRI, computed tomography (CTA) and magnetic resonance angiography (MRA), and 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) scanning may reveal lesions in the large arteries. Imaging studies also allow for detection of complications: aneurysms or arterial dissection.

3. Histologic examination of temporal artery biopsy specimens is the diagnostic gold standard, which in symptomatic patients may remain positive for months despite glucocorticoid treatment. It is usually performed within a few weeks (ideally no later than 14 days) after starting glucocorticoid treatment. A negative result does not exclude the diagnosis of GCA; however, patients rarely have a negative biopsy result and normal ESR.

TAKAYASU ARTERITIS

(Takayasu's Arteritis; Pulseless Disease; Occlusive Thromboaortopathy; Aortic Arch Syndrome)

Takayasu arteritis (TA) is a granulomatous vasculitis of large and medium vessels of unknown etiology that affects mostly the aorta and its branches. Less frequently it may involve other arteries, such as the pulmonary arteries.

TA typically causes numerous segmental stenoses of the aortic branches. Thrombi may form in the stenotic segments and sometimes cause peripheral thromboembolism. Aneurysms usually occur distal to the stenosis. TA rarely leads to aortic dissection or rupture.

In general terms, large-vessel vasculitis occurring in patients aged >50 years is usually diagnosed as or takes the clinical form of giant cell arteritis (GCA)/temporal arteritis. In younger people (<50 years and more so <40 years) the clinical presentation and diagnosis is usually that of TA.

Symptoms and Signs of Takayasu Arteritis

Most patients present with only focal symptoms that reflect hypoperfusion of the affected organ or limb.

About 50% of patients report constitutional symptoms such as fever, malaise, night sweats, weight loss, fatigue, and/or arthralgias.

Repetitive arm movements and sustained arm elevation may cause pain and fatigue. Arterial pulses in arms and legs may be diminished and asymmetric. Extremities may have findings of ischemia (eg, coolness, leg claudication). Bruits are often audible over the subclavian arteries (above the clavicle in the supraclavicular fossa), brachial arteries, carotid arteries, abdominal aorta, or femoral arteries. Reduced blood pressure in one or both arms is common.

Involvement of the carotid and vertebral arteries results in reduced cerebral blood flow manifested by dizziness, syncope, orthostatic hypotension, headaches, transient visual disturbances, transient ischemic attacks, or strokes.

Stenotic lesions in a subclavian artery near the origin of a patent vertebral artery can cause posterior circulation ischemic neurologic symptoms or syncope when the arm is used (called subclavian steal syndrome). The mechanisms are retrograde flow through the vertebral artery to supply the subclavian artery distal to the stenosis and vasodilation of the arterial bed in the upper limb during exercise.

Angina pectoris or myocardial infarction may result from narrowing of the coronary artery orifice due to aortitis or coronary arteritis. Aortic regurgitation may occur if the ascending aorta is markedly dilated. Heart failure can develop.

Obstruction of the descending thoracic aorta sometimes causes signs of aortic coarctation (eg, hypertension, headache, leg claudication). Renovascular hypertension may develop if the abdominal aorta or renal arteries are narrowed. Intermittent arm or leg claudication can develop.

Pulmonary arteries are affected, sometimes causing pulmonary hypertension. Involvement of the medium-sized branches of the pulmonary arteries can cause pulmonary infarcts. Because Takayasu arteritis is chronic, collateral circulation can develop. Thus, ischemic ulcerations or gangrene due to obstruction of the arteries to the extremities is rare.

Diagnostic Tests

1. Blood tests: Laboratory findings in patients with TA are not specific and reflect the underlying inflammation. A normochromic normocytic anemia is common. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) can reflect disease activity, but values within reference ranges alone are not sensitive enough to exclude active disease. Other laboratory abnormalities may include an elevated fibrinogen concentration, hypoalbuminemia, and polyclonal hypergammaglobulinemia.

2. Imaging studies: Magnetic resonance angiography (MRA), computed tomography angiography (CTA), and angiography of the affected vessels demonstrate smooth luminal narrowing and possibly occlusion. CTA and MRA also have the added benefit of demonstrating wall thickening of the affected vessels. Positron emission tomography (PET) is being investigated as an imaging technique to monitor disease activity. Transthoracic echocardiography (TTE) is useful to assess for proximal aortic abnormalities and concomitant aortic insufficiency. Ultrasonography of other affected vessels can also be useful if available.

TOPIC 8
GASTRITIS. GASTRIC AND DUODENAL ULCER. INTESTINAL DISEASES (CHRONIC COLITIS, COLITIS, NONSPECIFIC ULCERATIVE COLITIS). DENTAL ASPECTS

Definition and modern classifications of gastritis, gastric and duodenal ulcer. Etiology of these diseases. Epidemiology of Helicobacter pylori, conditions of damage of a mucosa of a stomach and duodenum. Main complaints of the patients with gastritis and peptic ulcer. Instrumental and laboratory examination of the patients. Complications of peptic ulcer disease. Acute upper gastrointestinal bleeding: clinical features.

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).

CHRONIC GASTRITIS

Chronic gastritis - chronic inflammatory-dystrophic process in the stomach mucous with recurrent duration that passing with cells regeneration disturbances, progressive atrophies of secretory epithelium, impairment secretory, motoric and incretory functions of the stomach.

Chronic gastritis is morphologic concept with stereotypic reactions in the stomach mucosa: inflammation, atrophy, impaired cells regulation with metaplasia and dysplasia.

Etiology

- the leading role in development of the chronic gastritis belongs to Helicobacter pylori;

- genetic predisposition;

- influence of other infectious factors (parasites invasions, virus infectious, fungus damage);

- autoimmune factors;

- particularities of nutrition;

- food allergy; influence of harmful factors of an environment;

- radiating irradiation;

- influence of drugs therapy.

Classification

Table 13

The international classification of chronic gastritis, 1996

The type of gastritis	Synonyms	Etiologic factors
Non-atrophy	Type B Superficial Antral gastritis Chronic antral gastritis Hypersecretory	Helicobacter pylori Other factors
Atrophy	Type A Autoimmune Associated with pernicious anemia	Autoimmune Helicobacter pylori Particularities of nutrition Influence of harmful factors of an environment
The special forms		
Chemical	Type C Reactive reflux-gastritis	Contents of duodenum
Radiating		Radiating irradiation
Lymphocytary	Variolomorphy Associated with celiakia	Idiopathic mechanisms Autoimmune mechanisms Helicobacter pylori
Non-infective granulomatous	Isolated granulomatous	Crone's disease Sarcoidosis
Eoshynophily	Food allergy Other allergens	Allergic
Other infections		Bacteria Viruses Fungus Parasites

Clinical features

The signs of chronic gastritis are difficult to describe because the course and symptomatology of the disease are quite variable. Some patients do not complain of anything during remissions; the disease may also develop for a long time without any manifestations and it is therefore difficult to establish the time of its onset.

The main syndrome of chronic gastritis is gastric dyspepsia: heaviness in abdomen after the meal, earlier saturation, deterioration of appetite, nausea, eructation

and vomiting. It may combine with intestinal dyspepsia characterized by meteorism, rumbling sounds in the abdomen, constipation, and diarrhoea.

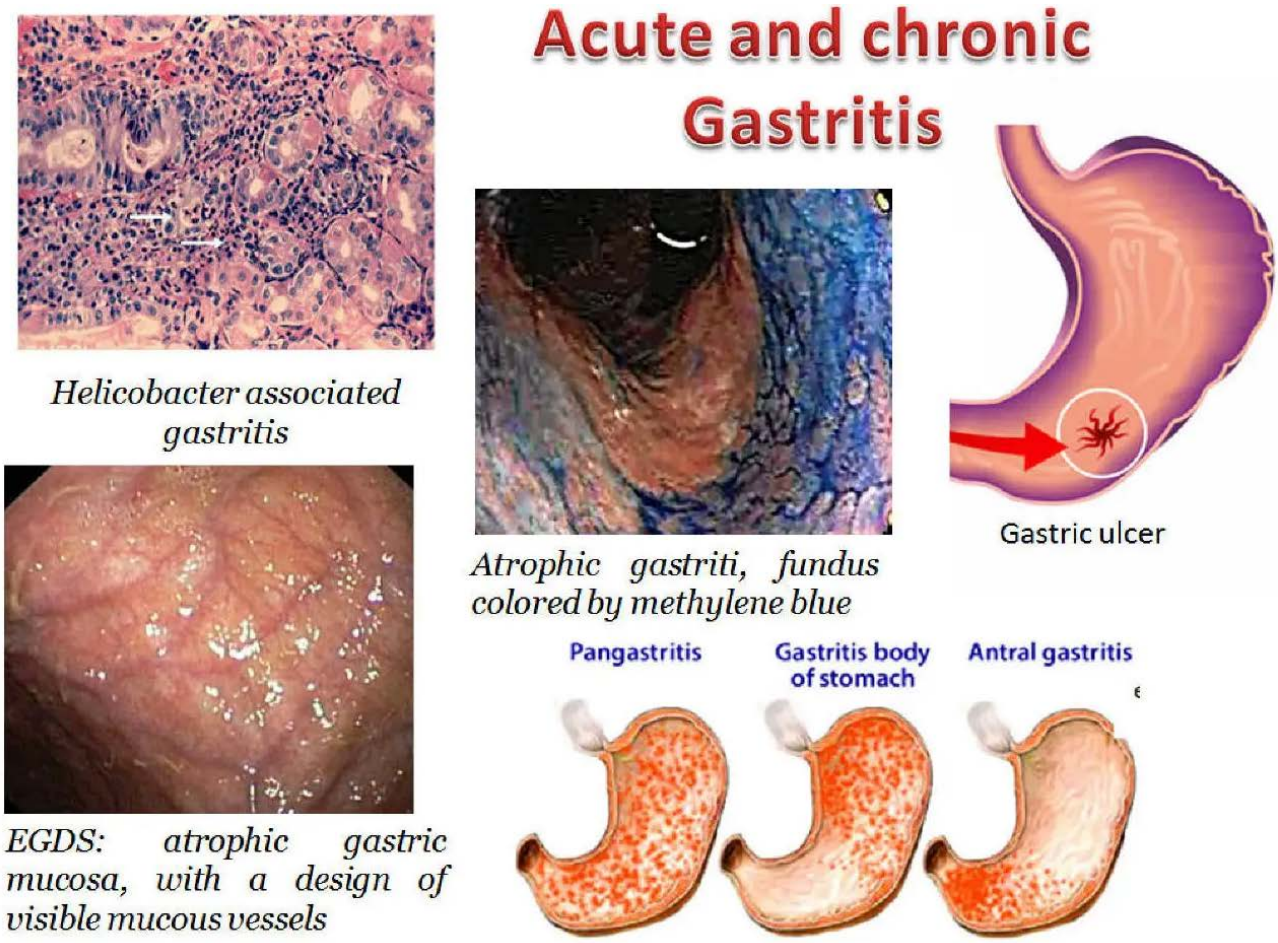

Image 25. Symptoms of Acute and Chronic gastritis

This image was downloaded from website https://www.gastroepato.it/en_gastriti.htm

Objective examination

General patient's condition is usually from satisfactory to moderate grave. The consciousness is clear, the posture active. The color of the skin and visible mucosa has corporeal color.

The data of inspection, palpation, percussion and auscultation of respiratory and cardiovascular systems are without peculiarities.

Palpation of the epigastrium is in most cases painless or may be distinguish moderate pain in epigastrium and umbilical regions.

Additional methods of examination

Gastric secretory function. The acid secretion may remain normal or it may decrease. Free hydrochloric acid may be absent from the gastric juice (achlorhydria).

Roentgenography is but of little use in the diagnosis of chronic gastritis.

Gastroscopy can give valuable diagnostic information, especially if it is combined with sighting biopsy.

Biopsy is important for the study of patients with chronic gastritis.

Detecting of Helicobacter pylori.

PEPTIC ULCER DISEASE (Gastric and Duodenal Ulcer)

Peptic ulcer is a general chronic and relapsing disease characterized by seasonal exacerbations with ulceration of the stomach wall or the duodenum. Approximately 10% of all adults have peptic ulcer at some time in their lives. Duodenal ulcer is more common 4 times than gastric ulcer. The male to female ratio for duodenal ulcer varies from 4:1 or 2:1. Gastric ulcer is more common in the older (over 50 year), and duodenal ulcer in those from 30-60 year. Duodenal ulcer is more common in male at age 30-55 years. 90-95% of duodenal ulcers occur in the first portion of duodenum. More than 90% of gastric ulcers occur in the lesser curvature.

Etiology

- associated with Helicobacter pylori;
- influence of drugs;
- results of pathological hypersecretion;
- mixed etiology.

Many ulcers are caused by a bacterium called Helicobacter pylori (H. pylori). Around 90% of duodenal ulcer patients and 70% of gastric ulcer patients are infected with H. pylori. Peptic ulcers frequently also can be caused by daily use of pain relievers called non-steroidal anti-inflammatory drugs (NSAIDs). The remaining 30% of gastric ulcers are due NSAIDs.

Having a close relative with peptic ulcer disease also increases your risk, as does smoking and alcohol use.

Pathogenesis

An ulcer forms when there is an imbalance between aggressive factors and defense factors. Aggressive factors: H. pylori infection, NSAIDs, acid and pepsin, smoking, alcohol and other factors. Defense factors: gastric mucosa, gastroprotective prostaglandins, mucus layer on epithelial cells, bicarbonate secreted by epithelial cells and adequate blood supply of gastric mucosa.

Clinical features

The leading symptom of peptic ulcer is abdominal pain. In peptic ulcer the pain is localized in epigastric region, may radiate to the back and is of variable quality: gnawing, burning, boring, or hunger like. The pain is intermittent, last from a few minutes to many hours, be worse when your stomach is empty. Food, antacids or other antisecretory drugs often bring relief. The seasonal character of pain is very typical of peptic ulcer disease.

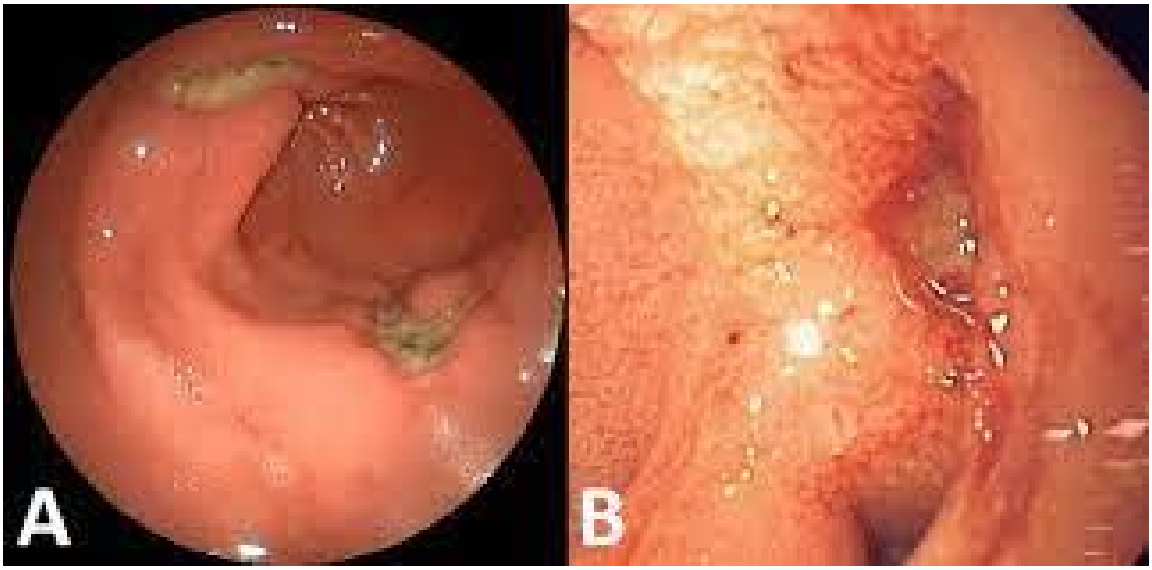

Image 26. Features of peptic ulcers on OGD (A) peptic ulcer located in the gastric antrum (B) haemorrhaging gastric ulcer

This image was downloaded from website https://teachmesurgery.com

In patients with peptic ulcer the main complaints are abdominal pain and displays of dyspeptic syndrome. Heartburn, vomiting, belching, regurgitation, and salivation are frequent symptoms. Vomiting relieves pain of gastric ulcer and some patients force themselves to vomit after eating to relieve symptoms. Heartburn is a specific burning sensation behind the sternum, associated with regurgitation of gastric contens into the inferior portion of lie esophagus. The mechanism of heartburn is associated with motor dysfunction of the esophagus (in addition to the acid fact of the gastric contents, which was formerly believed to be decisive). Appetite is often increased. The intestinal symptoms of peptic ulcer disease are constipations, which are closely connected with the character of nutrition and bed-rest during exacerbations, and are mainly connected with reflex dyskinesia of the intestine.

Objective examination

General patient's condition is usually from moderate grave to extremely grave. The consciousness is clear, the posture usually active or may be forced in cause of complications development. *The color of the skin* and visible mucosa has corporeal color. With disease progression and prolonged duration may occurs pale color and loss of weight. The tongue is usually clean. The data of inspection, palpation, percussion and auscultation of respiratory and cardiovascular systems are without peculiarities.

In superficial tentative oriental palpation and percussion of the abdomen may be distinguish pain in epigastrium and umbilical regions with local muscular resistance.

Additional methods of examination

Endoscopy (fibroesophagogastroduodenoscopia) is the procedure of choice for diagnosis of peptic ulcer. Endoscopy with biopsy and the subsequent morphological research of a bioptates - confirms presence of ulcer defect and specifies of its localization, depth, the form, the sizes, condition of the bottom and edges of the ulcer.

Barium meal (or X-ray examination). A direct proof of peptic ulcer is a niche, which is found in 75-80 per cent of patients. The ulcer is usually located on the lesser curvature. In duodenal ulcer, the can be found inside the bulb or outside it (extrabulbar ulcer). Barium meal is less commonly used now. Endoscopy should be done if it shows gastric ulcer to rule out malignancy.

Gastric secretory function. The main method of study of gastric secretion is pH-measure (intragastral pH-metria). Normal basal pH in body stomach is 1.6-2.2. There is pH more than 2.2 – hyperacidity. There is pH less than 1.6 – hypoacidity. If the ulcer is found in the stomach, hydrochloric acid, pepsin, mucoprotein and albumin fractions of the gastric juice vary within normal limits. In duodenal ulcer all these indices significance exceed normal values.

Determining of Helicobacter pylori. *Blood test or Serological test* - determine antibodies of H. pylori in blood. *Breath test*. You drink a solution that contains a radioactive carbon atom. If H. pylori is in your body, it will break down the solution and release the carbon. Your bloodstream carries the carbon to your lungs, where it's exhaled and can be detected in your breath. *Stool test* **–** determine antigen of H. pylori in feaces. H. pylori can be detected *histologically* on biopsy of gastric mucosa.

Rapid urease activity test. Culture. Biopsies obtained can be cultured on special medium.

Clinical blood analysis. May be determining of the signs of ferric deficiency anemia at chronic or acute bleeding.

Examination of faeces. Latent haemorrihage is almost always revealed on examination of faeces during exacerbation of peptic ulcer.

Complications

Haemorrhage. This is the most frequent complication. It may be manifested by haematemesis (blood vomiting) and tarry faeces (melaena). Among other causes of gastric haemorrhagel peptic ulcer is accounted for 15-25 per cent of patients. The patient general condition depends on the length and intensity of bleeding.

Perforation. Free perforation into peritonial cavity occurs in approximately 2-3% of patients. Signs of perforation are a sudden stabbing pain, the reflex collapse, acute abdomen, and progressive peritonitis (unless a timely surgical aid is given to the patient). The pain is felt beneath the xiphoid process or in the right hypochondrium. The abdominal wall is tense. The patient assumes a forced posture on his back; the tongue is dry and coated. The pulse is retarded.

Penetration. Extension of the ulcer crater beyond the gastric or duodenal wall into contiguous structure e.g. pancreas especially if ulcer is in posterior wall of duodenum. Less commonly ulcer may penetrate into liver, biliary tract or colon.

Stenosis or pyloric obstruction. Ulcers heal to leave scars. If the ulcer was in the pylorus, the cicatricial tissue may narrow the lumen and interfere with free passage of he gastric contents into the duodenum. First the narrowing is compensated for by hypertrophy of the gastric muscles, but later the stomach becomes distended, food stays inside it for a longer period. Patient presents with abdominal bloating, nausea, vomiting and weight loss. Patients complain of permanent pain, eructation with rotten egg wind, and profuse morning vomiting with food that was ingested several days ago. Constipation is alternated with diarrhea. In the presence pyloric stenosis peristaltic and antiperistaltic movements of the epigastrium can be seen.

TOPIC 9
PANCREATITIS. CHOLECYSTITIS. GALLSTONES DISEASE DENTAL ASPECTS

CHRONIC PANCREATITIS

Chronic pancreatitis is commonly defined as a continuing, chronic, inflammatory process of the pancreas, characterized by irreversible morphologic changes. This chronic inflammation can lead to chronic abdominal pain and/or impairment of endocrine and exocrine function of the pancreas. By definition, chronic pancreatitis is a completely different process from acute pancreatitis. In acute pancreatitis, the patient presents with acute and severe abdominal pain, nausea, and vomiting. The pancreas is acutely inflamed (neutrophils and edema), and the serum levels of pancreatic enzymes (amylase and lipase) are elevated. Full recovery is observed in most patients with acute pancreatitis, whereas in chronic pancreatitis, the primary process is a chronic, irreversible inflammation (monocyte and lymphocyte) that leads to fibrosis with calcification.

Etiology

Causes of chronic pancreatitis („TIGAR-O‟:)

Toxic-metabolic

- Alcohol
- Tobacco
- Hypercalcaemia
- Chronic renal failure

Idiopathic

- Tropical
- Early/late onset types

Genetic

- Hereditary pancreatitis (cationic trypsinogen mutation)
- Isolated or as part of multi-organ problem

Recurrent and severe acute pancreatitis

- Post-necrotic
- Recurrent acute pancreatitis

Obstructive

- Ductal adenocarcinoma

 Autoimmun

- Intraductal papillary mucinous neoplasia
- Pancreas divisum
- Sphincter of Oddi stenosis

Chronic pancreatitis occurs most often in patients with alcoholism (45–80% of all cases). The risk of chronic pancreatitis increases with the duration and amount of alcohol consumed, but pancreatitis develops in only 5–10% of heavy drinkers. Tobacco smoking is a risk factor for idiopathic chronic pancreatitis and has been reported to accelerate progression of alcoholic chronic pancreatitis. About 2% of patients with hyperparathyroidism develop pancreatitis. In tropical Africa and Asia, tropical pancreatitis, related in part to malnutrition, is the most common cause of chronic pancreatitis. A stricture, stone, or tumor obstructing the pancreas can lead to obstructive chronic pancreatitis. Autoimmune pancreatitis is associated with hypergammaglobulinemia (IgG4 in particular) and often with autoantibodies and other autoimmune diseases and is responsive to corticosteroids. Between 10% and 30% of cases of chronic pancreatitis are idiopathic, with either early onset (median age 23) or late onset (median age 62). Genetic factors may predispose to chronic pancreatitis in some of these cases and include mutations of the cystic fibrosis transmembrane conductance regulator (CFTR) gene, the pancreatic secretory trypsin inhibitory gene (PSTI, serine protease inhibitor, SPINK1), and possibly the gene for uridine 5-diphosphate glucuronosyltransferase.

Pathophysiology

The cause of chronic pancreatitis usually is metabolic in nature. The proposed pathologic mechanisms of chronic pancreatitis are as follows:

• Intraductal plugging and obstruction - Eg, ethanol (ETOH) abuse, stones, tumors

• Direct toxins and toxic metabolites - These act on the pancreatic acinar cell to stimulate the release of cytokines, which stimulate the stellate cell to produce collagen and to establish fibrosis; cytokines also act to stimulate inflammation by neutrophils, macrophages, and lymphocytes (eg, ETOH, tropical sprue)

• Oxidative stress - Eg, idiopathic pancreatitis

• Necrosis-fibrosis - Recurrent acute pancreatitis that heals with fibrosis

• Ischemia - From obstruction and fibrosis; important in exacerbating or perpetuating disease rather than in initiating disease

• Autoimmune disorders - Chronic pancreatitis has been found in association with other

autoimmune diseases, such as Sjögren syndrome, primary biliary cirrhosis, and renal tubular
acidosis.

• Secondary forms of autoimmune chronic pancreatitis are associated with primary biliary cirrhosis, primary sclerosing cholangitis, and Sjögren syndrome.

• While alcohol greatly influences the understanding of its pathophysiology because it is the most common etiology (60-70%), approximately 20-30% of cases are idiopathic and 10% of cases are due to rare diseases.

Whatever the etiology of chronic pancreatitis, pancreatic fibrogenesis appears to be a typical response to injury. This involves a complex interplay of growth factors, cytokines, and chemokines, leading to deposition of extracellular matrix and fibroblast proliferation. In pancreatic injury, local expression and release of transforming growth factor beta (TGF-beta) stimulates the growth of cells of mesenchymal origin and enhances the synthesis of extracellular matrix proteins, such as collagens, fibronectin, and proteoglycans.

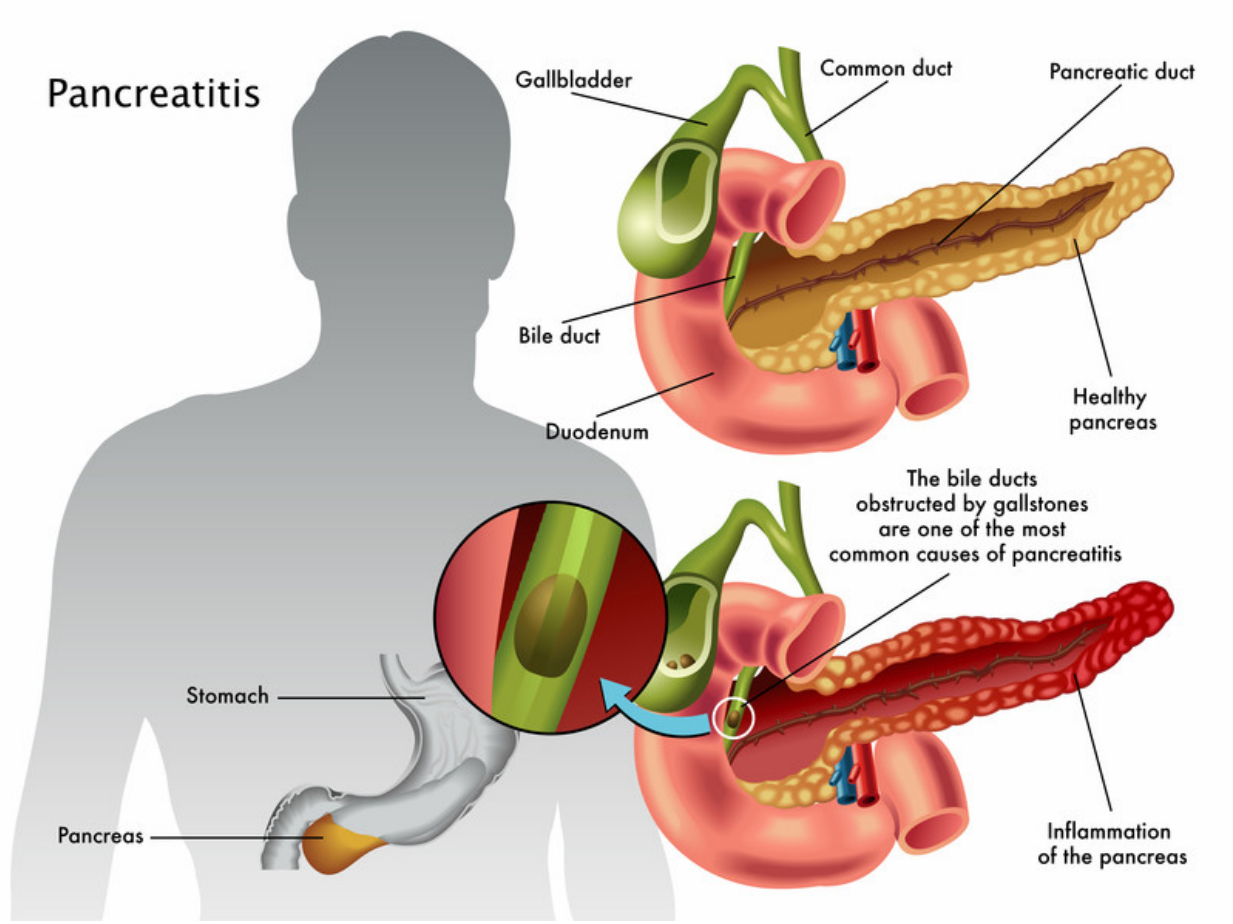

Image 27. Chronic pancreatitis

This image was downloaded from website https://www.health.harvard.edu

Clinical features

Clinically, the patient experiences intermittent attacks of severe pain, often in the idabdomen or left upper abdomen and occasionally radiating in a bandlike fashion or localized to the midback. The pain may occur either after meals or independently of meals, but it is not fleeting or transient and tends to last at least several hours. Unfortunately, patients often are symptomatic for years before the diagnosis is established; the average time from the onset of symptoms until a diagnosis of chronic pancreatitis is 5 years. The delay in diagnosis is even longer in people without alcoholism, in whom the average time is 7 years from onset of symptoms to diagnosis. The natural history of pain in chronic pancreatitis is highly variable. Most patients experience intermittent attacks of pain at unpredictable intervals, while a minority of patients experience chronic pain. In alcohol-induced disease, eventual cessation of alcohol intake may reduce the severity of pain.

Pain is due to a combination of increased pressure within the pancreatic ducts and direct involvement of pancreatic and peripancreatic nerves by the inflammatory process. Pain may be relieved by leaning forward. Weight loss is common and results from a combination of anorexia, avoidance of food because of postprandial pain, malabsorbtion and/or diabetes. Steatorrhea occurs when more than 90% of the exocrine tissue had been destroyed; protein malabsorption only develops in the most advanced cases.

In most instances, the standard physical examination does not help to establish a diagnosis of chronic pancreatitis; however, a few points are noteworthy. During an attack, patients may assume a characteristic position in an attempt to relieve their abdominal pain (eg, lying on the left side, flexing the spine and drawing the knees up toward the chest). Occasionally, a tender fullness or mass may be palpated in the epigastrium, suggesting the presence of a pseudocyst or an inflammatory mass in the abdomen. Patients with advanced disease (ie, patients with steatorrhea) exhibit decreased subcutaneous fat, temporal wasting, sunken supraclavicular fossa, and other physical signs of malnutrition.

Diagnosis

Tests to establish the diagnosis

- Ultrasound CT (may show atrophy, calcification or ductal dilatation)
- Abdominal X-ray (may show calcification)
- Magnetic Resonance Cholangiopancreatography (MRCP)
- Endoscopic ultrasound

Tests of pancreatic function

- Collection of pure pancreatic juice after secretin injection (gold standard but invasive and
- seldom used)
- Fecal pancreatic elastase

Tests of anatomy prior to surgery

- MRCP

Blood tests

Serum amylase and lipase levels may be slightly elevated in chronic pancreatitis; high levels are found only during acute attacks of pancreatitis. In the later stages of chronic pancreatitis, atrophy of the pancreatic parenchyma can result in normal serum enzyme levels because of significant fibrosis of the pancreas, resulting in decreased concentrations of these enzymes within the pancreas. While low concentrations of serum trypsin are relatively specific for advanced chronic pancreatitis, they are not sensitive enough to be helpful in most patients with mild to moderate disease. Laboratory studies to identify causative factors of chronic pancreatitis include serum calcium and triglyceride levels. When common etiologies are not found, research protocols are available to test for genetic mutations in cationic trypsinogen and CFTR.

Fecal tests

Because maldigestion and malabsorption do not occur until more than 90% of the pancreas has been destroyed, steatorrhea is a manifestation of advanced chronic pancreatitis. Neither qualitative nor quantitative fecal fat analysis can detect early disease.

Assays of fecal chymotrypsin and human pancreatic elastase-1 have the same limitations but are useful in confirming advanced chronic pancreatitis with exocrine insufficiency. These tests allow to determine or to rule out pancreatic exocrine insufficiency and its degree. The study of elastase-1 in stool allows to determine pancreatic insufficiency of moderate and severe cases is 95-100%.

Pancreatic Function Tests

Direct tests

These tests are the most sensitive and can be used to detect chronic pancreatitis at its earliest stage; however, they are somewhat invasive, labor intensive, and expensive.

- Determination in duodenal aspirates
- Determination in pancreatic juice

Indirect tests

Noninvasive tests of pancreatic function have been developed for detecting chronic pancreatitis. In principle, these tests work via oral administration of a complex substance that is hydrolyzed by a
specific pancreatic enzyme to release a marker substance. The intestine absorbs the marker, which then is measured in the serum or urine. These tests are capable of detecting moderate to severe chronic pancreatitis. The presence of renal, intestinal, and liver disease may interfere with the accuracy of these tests.

Respiratory pancreatic tests

^{13}C-triglyceride breath test - determines pancreatic lipase activity in the lumen of the intestine and can differentiate pancreatic steatorrhea from enteric steatorrhea.

Protein breath test with ^{13}C-marked egg white - reduced in case of CP - lack of trypsin.

Amylase (^{13}C-corn-starch) breath test – allows to detect deficiency of pancreatic amylase in duodenum (normal – in the end of 4th hour - 10-30%).

Neither currently is freely available.

Imaging

Plain films show calcifications due to pancreaticolithiasis in 30% of affected patients. CT may show calcifications not seen on plain films as well as ductal dilatation and heterogeneity or atrophy of the gland. Occasionally, the findings raise suspicion of pancreatic cancer (“tumefactive chronic pancreatitis”). Endoscopic retrograde cholangiopancreatography (ERCP) is the most sensitive imaging study for chronic pancreatitis and may show dilated ducts, intraductal stones, strictures, or pseudocyst, but the results may be normal in patients with so-called minimal change pancreatitis. MRCP (including secretin-enhanced MRCP) and endoscopic ultrasonography (with pancreatic tissue sampling) are less invasive alternatives to ERCP.

CHRONIC CHOLECYSTITIS

Cholecystitis is the inflammatory gallbladder. The incidence of the disease is rather high; women are mostly affected. Inflammatory response can be evoked by three factors: mechanical inflammation; chemical inflammation and bacterial inflammation. The disease can be provoked by gall stones, dyskinesia of the bile ducts, anatomical properties of the gall bladder and bile ducts, ptosis of the internal organs, pregnancy, inactive mode of life, rare meals, etc. Chronic cholecystitis may develop after acute cholecystitis but in most cases it develops gradually as an independent disease.

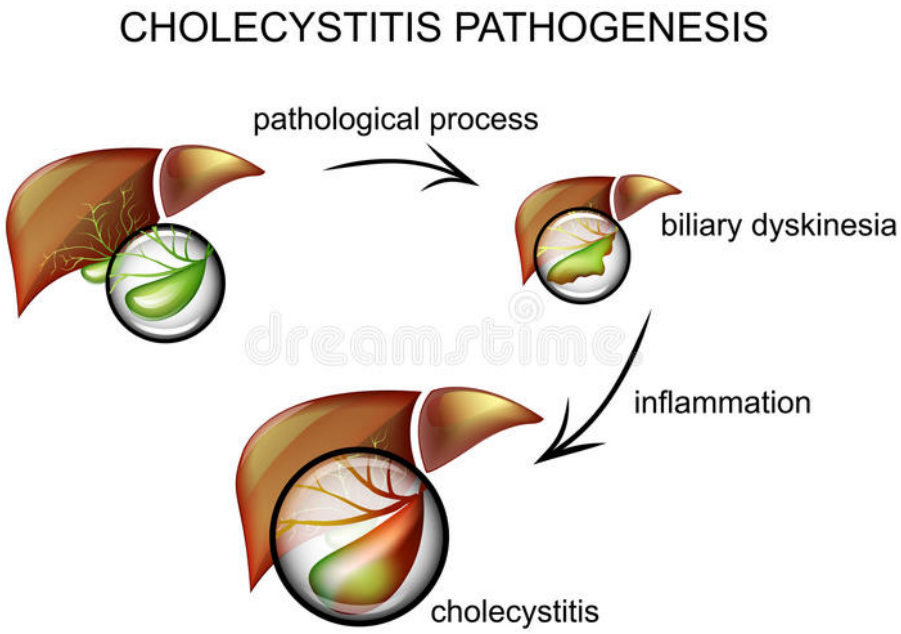

Image 28. Cholecystitis pathogenesis

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Clinical features

The patient complains of dull boring pain in the right hypochondrium which usually develops 1-3 hours after taking abundant specially fat and roasted food. The pain radiates upward to the region of the right shoulder, neck and the scapula. If cholecystitis concurs with cholelithiasis, sharp pain may arise (like in biliary colic).

Dyspeptic signs the also present: bitter and metallic taste in the mouth, eructation, nausea, abdominal flatulence, and alternation of diarrhoea with

constipation. The disease is sometimes not attended by pain except that the patient feels heaviness in the epigastrium or right hypochondrium, and dyspepsia develops.

Objective examination

The temperature is often subfebrile. *Surface palpation of the abdomen* reveals sensitivity and sometimes tenderness in the region of gall-bladder projection. The Mussy's, Ortner's, Murphy's, and Vasilenko's symptoms are positive. The gall bladder is impalpable.

- *Vasilenko's symptom* (sharp pain in the region of the gall bladder when it is tapped over at the height of inspiration);

- *Murphy's symptom* (sharp pain in the right hypochondrium when the examiner's nandifpifess the gall bladder at the height of inspiration);

- *Ortner's symptom* (pain during tapping over the right costal arch by the edge of the hand). If inflammation extends onto the peritoneum overlying the gall bladder;

- *Shchetkin-Blumberg's* symptom is positive. In this case, in the presence of gangrenous cholecystitis (gangrene of the gall bladder) and possible perforation of the gall-bladder wall, a dangerous sign appears;

- In moderate tension of the abdominal muscles it is sometimes possible (especially in purulent cholecystitis) to palpate an enlarged and very tender gall bladder. The liver does not usually increase, but its tender edge can sometimes be palpated;

- *The Mussy's* symptom (tenderness at the point of the phrenicus nerve, between the heads of the sternocleidomastoid muscle) can often be positive.

Additional methods of examination

Clinical blood analyses. The blood changes (during exacerbation) are characterized by moderate leucocytosis and mildly increased ESR.

Signs of inflammation (mucus, leucocytes, desquamated epithelium) on be found in B bile. If inflammation involves bile ducts (cholangitis), C the contains the same signs of inflammation. The vesical reflex (B bile) is sometimes impossible to obtain even by repeated probing. This indicates disordered contractility of the gall bladder which is typical of chronic cholecystitis. Bacteriological studies of B bile reveal the character of microbial flora. Polarographic study of bile can reveal signs of inflammation.

Cholecystography shows changes in the configuration of the gall bladder and the absence of its distinct contours. This indicates upset concenting capacity of the

gall-bladder mucosa. After taking a stimulating cal the gall bladder contracts insufficiently.

GALLSTONES DISEASE

Cholelithiasis is the medical term for gallstone disease. Cholelithiasis involves the presence of gallstones, which are concretions that form in the biliary tract, usually in the gallbladder. Choledocholithiasis refers to the presence of 1 or more gallstones in the common bile duct (CBD). Gallstones develop insidiously, and they may remain asymptomatic for decades. Migration of a gallstone into the opening of the cystic duct may block the outflow of bile during gallbladder contraction. The resulting increase in gallbladder wall tension produces a characteristic type of pain (biliary colic). Cystic duct obstruction, if it persists for more than a few hours, may lead to acute gallbladder inflammation (acute cholecystitis).

Choledocholithiasis refers to the presence of one or more gallstones in the common bile duct. Usually, this occurs when a gallstone passes from the gallbladder into the common bile duct.

Pathophysiology

Gallstone formation occurs because certain substances in bile are present in concentrations that approach the limits of their solubility. When bile is concentrated in the gallbladder, it can become supersaturated with these substances, which then precipitate from the solution as microscopic crystals. The crystals are trapped in gallbladder mucus, producing gallbladder sludge. Over time, the crystals grow, aggregate, and fuse to form macroscopic stones. Occlusion of the ducts by sludge and/or stones produces the complications of gallstone disease. The 2 main substances involved in gallstone formation are cholesterol and calcium bilirubinate.

Cholesterol gallstones

More than 80% of gallstones contain cholesterol as their major component. Liver cells secrete cholesterol into bile along with phospholipid (lecithin) in the form of small spherical membranous bubbles, termed unilamellar vesicles. Liver cells also secrete bile salts, which are powerful detergents required for the digestion and absorption of dietary fats. Bile salts in bile dissolve the unilamellar vesicles to form soluble aggregates called mixed micelles. This happens mainly in the gallbladder, where bile is concentrated by reabsorption of electrolytes and water.

Compared with vesicles (which can hold up to 1 molecule of cholesterol for every molecule of lecithin), mixed micelles have a lower carrying capacity for cholesterol (about 1 molecule of cholesterol for every 3 molecules of lecithin). If bile contains a relatively high proportion of cholesterol to begin with, then as bile is concentrated, progressive dissolution of vesicles may lead to a state in which the cholesterol-carrying capacity of the micelles and residual vesicles is exceeded. At this point, bile is supersaturated with cholesterol, and cholesterol monohydrate crystals may form.

Thus, the main factors that determine whether cholesterol gallstones will form are (1) the amount of cholesterol secreted by liver cells, relative to lecithin and bile salts, and (2) the degree of concentration and extent of stasis of bile in the gallbladder.

Calcium, bilirubin, and pigment gallstones

Bilirubin, a yellow pigment derived from the breakdown of heme, is actively secreted into bile by liver cells. Most of the bilirubin in bile is in the form of glucuronide conjugates, which are water soluble and stable, but a small proportion consists of unconjugated bilirubin. Unconjugated bilirubin, like fatty acids, phosphate, carbonate, and other anions, tends to form insoluble precipitates with calcium. Calcium enters bile passively along with other electrolytes.

In situations of high heme turnover, such as chronic hemolysis or cirrhosis, unconjugated bilirubin may be present in bile at higher than normal concentrations. Calcium bilirubinate may then crystallize from the solution and eventually form stones. Over time, various oxidations cause the bilirubin precipitates to take on a jet-black color, and stones formed in this manner are termed black pigment gallstones. Black pigment stones represent 10-20% of gallstones.

Bile is normally sterile, but in some unusual circumstances (eg, above a biliary stricture), it may become colonized with bacteria. The bacteria hydrolyze conjugated bilirubin, and the resulting increase in unconjugated bilirubin may lead to precipitation of calcium bilirubinate crystals. Bacteria also hydrolyze lecithin to release fatty acids, which also may bind calcium and precipitate from the solution. The resulting concretions have a claylike consistency and are termed brown pigment stones. Unlike cholesterol or black pigment gallstones, which form almost exclusively in the gallbladder, brown pigment gallstones often form de novo in the bile ducts. Brown pigment gallstones are unusual in the United States but are

fairly common in some parts of Southeast Asia, possibly related to liver fluke infestation.

Mixed gallstones

Cholesterol gallstones may become colonized with bacteria and can elicit gallbladder mucosal inflammation. Lytic enzymes from the bacteria and leukocytes hydrolyze bilirubin conjugates and fatty acids. As a result, over time, cholesterol stones may accumulate a substantial proportion of calcium bilirubinate and other calcium salts, producing mixed gallstones. Large stones may develop a surface rim of calcium resembling an eggshell that may be visible on plain x-ray films.

Etiology

Cholesterol gallstones, black pigment gallstones, and brown pigment gallstones have different pathogeneses and different risk factors.

Cholesterol gallstones

Cholesterol gallstones are associated with female sex, European or Native American ancestry, and increasing age. Other risk factors include the following:

- Obesity
- Pregnancy
- Gallbladder stasis
- Drugs
- Heredity

Black and brown pigment gallstones

Black pigment gallstones occur disproportionately in individuals with high heme turnover. Disorders of hemolysis associated with pigment gallstones include sickle cell anemia, hereditary spherocytosis, and beta-thalassemia. About half of all cirrhotic patients have pigment gallstones. Prerequisites for the formation of brown pigment gallstones include intraductal stasis and chronic colonization of bile with bacteria. In rice-growing regions of East Asia, infestation with biliary flukes may produce biliary strictures and predispose to formation of brown pigment stones throughout intrahepatic and extrahepatic bile ducts.

Crohn disease, ileal resection, or other diseases of the ileum decrease bile salt reabsorption and increase the risk of gallstone formation. Other illnesses or states that predispose to gallstone formation include burns, use of total parenteral nutrition, paralysis, ICU care, and major trauma. This is due, in general, to decreased enteral stimulation of the gallbladder with resultant biliary stasis and stone formation.

Clinical features

Gallstone disease may be thought of as having the following 4 stages:

- The lithogenic state, in which conditions favor gallstone formation
- Asymptomatic gallstones
- Symptomatic gallstones, characterized by episodes of biliary colic
- Complicated cholelithiasis

Symptoms and complications of gallstone disease result from effects occurring within the gallbladder or from stones that escape the gallbladder to lodge in the common bile duct.

Asymptomatic gallstones

Gallstones may be present in the gallbladder for decades without causing symptoms or complications. In patients with asymptomatic gallstones discovered incidentally, the likelihood of developing symptoms or complications is 1-2% per year. In most cases, asymptomatic gallstones do
not require any treatment.

Biliary colic

Pain termed biliary colic occurs when gallstones or sludge fortuitously impact in the cystic duct during a gallbladder contraction, increasing gallbladder wall tension. In most cases, the pain resolves over 30 to 90 minutes as the gallbladder relaxes and the obstruction is relieved.

Episodes of biliary colic are sporadic and unpredictable. The patient localizes the pain to the epigastrium or right upper quadrant and may describe radiation to the right scapular tip (Collins sign). The pain begins postprandially (usually within an hour after a fatty meal), is often described as intense and dull, and may last from 1-5 hours. From onset, the pain increases steadily over about 10 to 20 minutes and then gradually wanes when the gallbladder stops contracting and the stone falls back into the gallbladder. The pain is constant in nature and is not relieved by emesis, antacids, defecation, flatus, or positional changes. It may be accompanied by diaphoresis, nausea, and vomiting.

Other symptoms, often associated with cholelithiasis, include indigestion, dyspepsia, belching, bloating, and fat intolerance. However, these are very nonspecific and occur in similar frequencies in individuals with and without gallstones; cholecystectomy has not been shown to improve these symptoms.

Distinguishing uncomplicated biliary colic from acute cholecystitis or other complications is important. Key findings that may be noted include the following:

• Uncomplicated biliary colic – Pain that is poorly localized and visceral; an essentially benign abdominal examination without rebound or guarding; absence of fever

• Acute cholecystitis – Well-localized pain in the right upper quadrant, usually with rebound
and guarding; positive Murphy sign (nonspecific); frequent presence of fever; absence of peritoneal
signs; frequent presence of tachycardia and diaphoresis; in severe cases, absent or hypoactive bowel
sounds.

The presence of fever, persistent tachycardia, hypotension, or jaundice necessitates a search for complications, which may include the following:

- Cholecystitis
- Cholangitis
- Pancreatitis
- Other systemic causes

Diagnosis

Asymptomatic gallstones are often found incidentally on plain radiographs, abdominal sonograms, or CT scan for workup of other processes. Plain radiographs have little role in the diagnosis of gallstones or gallbladder disease. Cholesterol and pigment stones are radiopaque and visible on radiographs in only 10-30% of instances, depending on their extent of calcification.

Patients with uncomplicated cholelithiasis or simple biliary colic typically have normal laboratory test results; laboratory studies are generally not necessary unless complications are suspected.

Blood tests, when indicated, may include the following:

- Complete blood count (CBC) with differential
- Liver function panel
- Amylase
- Lipase

Acute cholecystitis is associated with polymorphonuclear leukocytosis. However, up to one third of the patients with cholecystitis may not manifest

leukocytosis. In severe cases, mild elevations of liver enzymes may be caused by inflammatory injury of the adjacent liver.

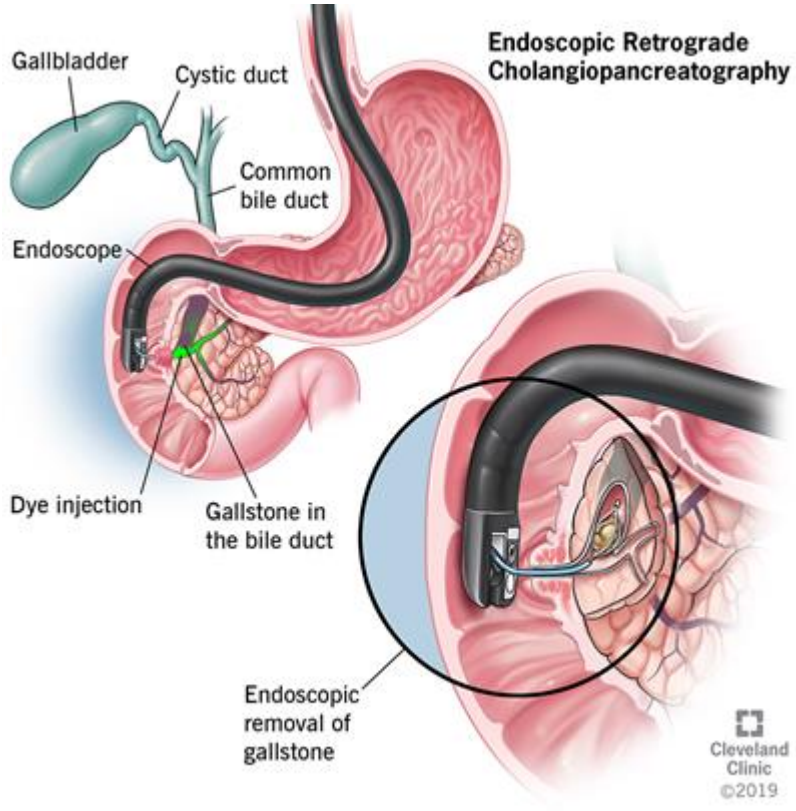

Image 29. Endoscopic retrograde cholangiopancreatography (ERCP) can diagnose and sometimes treat gallstones

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

Choledocholithiasis with acute common bile duct (CBD) obstruction initially produces an acute increase in the level of liver transaminases (alanine and aspartate aminotransferases), followed within hours by a rising serum bilirubin level. The higher the bilirubin level, the greater the predictive value for CBD obstruction. CBD stones are present in approximately 60% of patients with serum bilirubin levels greater than 3 mg/dL.

If obstruction persists, a progressive decline in the level of transaminases with rising alkaline phosphatase and bilirubin levels may be noted over several days. Prothrombin time may be elevated in patients with prolonged CBD obstruction, secondary to depletion of vitamin K (the absorption of which is bile-dependent). Concurrent obstruction of the pancreatic duct by a stone in the ampulla of Vater may be accompanied by increases in serum lipase and amylase levels.

Imaging modalities that may be useful include the following:

• Abdominal radiography (upright and supine) – Used primarily to exclude other causes of abdominal pain (eg, intestinal obstruction). Black pigment or mixed gallstones may contain sufficient calcium to appear radiopaque on plain films. The finding of air in the bile ducts on plain films may indicate development of a choledochoenteric fistula or ascending cholangitis with gas-forming organisms. Calcification in the gallbladder wall (the so-called porcelain gallbladder) is indicative of severe chronic cholecystitis. The main role of plain films in evaluating patients with

suspected gallstone disease is to exclude other causes of acute abdominal pain, such as intestinal obstruction, visceral perforation, renal stones, or chronic calcific pancreatitis.

• Ultrasonography – The procedure of choice in suspected gallbladder or biliary disease. It is the most sensitive, specific, noninvasive, and inexpensive test for the detection of gallstones. It is highly sensitive and specific for gallstones greater than 2 mm. It is less so for microlithiasis or biliary sludge. Ultrasonography is very useful for diagnosing uncomplicated acute cholecystitis. The sonographic features of acute cholecystitis include gallbladder wall thickening (>5 mm), pericholecystic fluid, gallbladder distention (>5 cm), and a sonographic Murphy sign. The presence of multiple criteria increases its diagnostic accuracy.

• Endoscopic ultrasonography (EUS) – An accurate and relatively noninvasive means of identifying stones in the distal CBD

• Laparoscopic ultrasonography – Promising as a potential method for bile duct imaging during laparoscopic cholecystectomy

• Computed tomography (CT) – More expensive and less sensitive than ultrasonography for

detecting gallbladder stones, but superior for demonstrating stones in the distal CBD

• Magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography

(MRCP) – Usually reserved for cases in which choledocholithiasis is suspected

• Scintigraphy – Highly accurate for the diagnosis of cystic duct obstruction

• Endoscopic retrograde cholangiopancreatography (ERCP) is usually performed in conjunction with endoscopic retrograde sphincterotomy and gallstone extraction.

• Percutaneous transhepatic cholangiography (PTC).

TOPIC 10
CHRONIC HEPATITIS. CIRRHOSIS
DENTAL ASPECTS

Definition and modern classifications of chronic hepatitis and hepatic cirrhosis. Main causes of hepatitis and cirrhosis. The mechanisms of affection of liver in viral hepatitis. Main complaints and clinical features of the patients with chronic hepatitis and cirrhosis of liver. Hepatic histology and biochemical tests for hepatocellular damage. Child-Pugh classification and index of histological activity. Portal hypertension, liver failure and hepatorenal failure. Main complications of hepatic cirrhosis.

CHRONIC HEPATITIS

Chronic hepatitis represents a series of liver disorders of varying causes and severity in which hepatic inflammation and necrosis continue for at least 6 months. Milder forms are nonprogressive or only slowly progressive, while more severe forms may be associated with scarring and architectural reorganization, which, when advanced, lead ultimately to cirrhosis. Finally, clinical and laboratory features of chronic hepatitis are observed occasionally in patients with such hereditary/metabolic disorders as Wilson's disease (copper overload), α1 antitrypsin deficiency, and nonalcoholic fatty liver disease and even occasionally in patients with alcoholic liver injury. Although all types of chronic hepatitis share certain clinical, laboratory, and histopathologic features, chronic viral and chronic autoimmune hepatitis are sufficiently distinct to merit separate discussions.

Classification

Chronic hepatitis includes chronic viral hepatitis, drug-induced chronic hepatitis, and autoimmune chronic hepatitis. In many cases, clinical and laboratory features are insufficient to allow assignment into one of these three categories; these "idiopathic" cases are also believed to represent autoimmune chronic hepatitis.

Common to all forms of chronic hepatitis are histopathologic distinctions based on localization and extent of liver injury. These vary from the milder forms, labeled chronic persistent hepatitis and chronic lobular hepatitis, to the more severe form, formerly called chronic active hepatitis. When first defined, these designations were believed to have prognostic implications, which were not corroborated by subsequent observations. Categorization of chronic hepatitis based primarily on histopathologic features has been replaced by a more informative classification based on a combination of clinical, serologic, and histologic variables. Classification of chronic

hepatitis is based on its cause; its histologic activity, or grade; and its degree of progression, or stage. Thus, neither clinical features alone nor histologic features—requiring liver biopsy—alone are sufficient to characterize and distinguish among the several categories of chronic hepatitis.

I. *According to causes*:

- chronic hepatitis B;
- chronic hepatitis C;
- chronic hepatitis D;
- chronic hepatitis other viral;
- autoimmune hepatitis, including several subcategories, I and II and III, based on serologic distinctions;
- dug-associated chronic hepatitis;
- toxic (including alcohol);
- metabolic;
- cyptogenic chronic hepatitis.

Non-alcoholic liver disease is also known as “non-alcocholic steatohepatitis” can be related to chronic hepatitis. In 40-70 per cent of cases chronic hepatitis develops as an outcome of on acute epidemic or serum hepatitis.

II. Classification by grade or by stage:

0 - no fibrosis;

1 – mild fibrosis;

2 – moderate fibrosis;

3 – severe fibrosis, including bridging fibrosis;

4 – cirrhosis.

III. *Classification by according to the index of histologic activity on Knodell in points*:

a) periportal hepatocytis necrosis, including the bridge-like - 0-10 points;

b) intrasegmental focal necrosis and hepatocytis dystrophy - 0-4 points;

c) inflammatory infiltrate in portal tracts - 0-4 points;

d) fibrosis - 0-4 points.

The index of histologic activity from 1 up to 6 points testifies to presence of the "minimal" chronic hepatitis, 7-12 points - the "moderate", 13-18 points - a "grave" chronic hepatitis.

IV. *Classification by function of the liver on Child-Pugh*:

Class A (stage compensation);

Class B (stage subcompensation);

Class C (stage decompensation).

Etiology and pathogenesis

HBV is not a cytopathic virus. Rather, liver injury in chronic hepatitis B is a consequence of the local immune response at the immune elimination phase. In particular, liver injury is related to cytotoxic T cells that recognize and kill infected hepatocytes that express HBV antigens at their surface and to the local production of cytokines. Chronic inflammation triggers fibrogenesis through the activation of hepatic stellate cells. The hepatitis B X protein may also directly activate fibrogenesis. As a result, many patients with chronic hepatitis B have progressive fibrosis, which may evolve into cirrhosis.

Chronic HCV infection is responsible for necroinflammatory lesions of varying severity, sometimes associated with steatosis, which is the accumulation of triglycerides in hepatocytes. HCV is not a cytopathic virus. Liver injury in chronic hepatitis C is related to the action of immune effectors that recognize and kill infected hepatocytes that express HCV antigens at their surface. Chronic inflammation triggers fibrogenesis through the activation of hepatic stellate cells. Fibrosis progresses at nonlinear rates that are generally faster in older patients, in males, and in the presence of chronic alcohol intake, viral coinfections, or immunosuppression. The severity of chronic hepatitis is independent of the HCV RNA level and of the HCV genotype. This chronic inflammation and progression of fibrosis predispose patients to cirrhosis and hepatocellular carcinoma.

Chronic hepatitis D is generally severe, with more than 80% of patients developing cirrhosis.

Autoimmune hepatitis is believed to be caused by autoimmune reactions against normal hepatocytes in genetically predisposed persons or persons exposed to unidentified triggers of an autoimmune process against liver antigens. Associations are seen with the human leukocyte antigen (HLA) class I B8 and class II DR3 and DR52a loci. In Asians, autoimmune hepatitis is associated with HLA DR4.

Toxic hepatitis. The liver is central to the metabolism of exogenous substances. Most drugs and xenobiotics cross the intestinal brush border because they are lipophilic. Biotransformation is the process by which lipophilic therapeutic agents are rendered more hydrophilic by the liver, resulting in drug excretion in urine or bile. In most instances, biotransformation changes a nonpolar to a polar compound through several steps. Foremost are oxidative pathways (e.g., hydroxylation) mediated by the cytochromes (CYPs) P-450. The next step is typically esterification to form sulfates

and glucuronides, a process that results in the addition of highly polar groups to the hydroxyl group. These two enzymatic steps are referred to as phase I (CYP oxidation) and phase II (esterification). Other important metabolic pathways involve glutathione-S-transferase, acetylating enzymes, and alcohol dehydrogenase, but the principal metabolic pathways for most pharmacologic agents involve CYPs and subsequent esterification. The exact details of the pathogenesis of liver injury are unclear for most drugs. Although most liver injury involves direct hepatocyte necrosis or apoptosis (hepatocellular injury), some drugs injure primarily the bile ducts or canaliculi and cause cholestasis without significant damage to hepatocytes. Other drugs affect sinusoidal cells or present a particular pattern of liver injury affecting multiple cell types (mixed type). Another approach to drug reactions emphasizes the histologic changes involved and the cell type.

Table 14

REACTION TYPE	IMPLICATED DRUGS OR TOXINS
Autoimmune (attack on cell surface markers)	Lovastatin, methyldopa, nitrofurantoin
Cholestatic (attack on bile ducts)	Anabolic steroids, carbamazepine, chlorpromazine, estrogen, erythromycin
Fibrosis (activation of stellate cells leads to fibrosis)	Methotrexate, vitamin A excess
Granulomatous (macrophage stimulation)	Allopurinol, diltiazem, nitrofurantoin, quinidine, sulfa drugs
Hepatocellular (damage to smooth endoplasmic reticulum and immune cell surface)	Acetaminophen, Amanita poisoning, diclofenac, isoniazid, lovastatin, nefazodone, trazodone, venlafaxine
Immunoallergic (cytotoxic cell attack on surface determinants)	Halothane, phenytoin, sulfamethoxazole
Mixed (see above)	Amoxicillin-clavulanate, carbamazepine, cyclosporine, herbs, methimazole
Oncogenic (hepatic adenoma formation)	Oral contraceptives, androgenic agents
Steatohepatitis (mitochondrial dysfunction: β-oxidation and respiratory chain)	Amiodarone, perhexiline maleate, tamoxifen
Vascular collapse (ischemic damage)	Cocaine, ecstasy, nicotinic acid
Veno-occlusive disease (endotheliitis of sinusoidal endothelial cells)	Busulfan, cytoxan

Steatosis in the liver can be present in a microvesicular or macrovesicular pattern. Macrovesicular steatosis, the most common form, is characterized histologically by a single vacuole of fat filling up the hepatocyte and displacing the nucleus to the cell's periphery. Macrovesicular steatosis is typically caused by alcohol, diabetes, or obesity. Sometimes drugs such as corticosteroids or methotrexate may cause these hepatic changes. Amiodarone has been associated with a picture resembling alcoholic hepatitis, occasionally with progression to cirrhosis. The pathophysiology involves accumulation of phospholipids in the liver, eyes, thyroid, and skin. Treatment is primarily withdrawal of the drug and observation, although the half-life of amiodarone is prolonged.

In microvesicular steatosis, hepatocytes contain numerous small fat vesicles that do not displace the nucleus. These lesions are associated with disruption of mitochondrial DNA, resulting in anaerobic metabolism that leads to lactic acidosis in the most severe cases. Macrovesicular and microvesicular lesions may be observed concomitantly in some patients, and microvesicular lesions are more often associated with a poor prognosis. Hepatocellular necrosis may also be present. Acute fatty liver of pregnancy and Reye's syndrome are two examples of severe liver diseases caused by microvesicular steatosis.

Nonalcoholic fatty liver disease NAFLD is seen most commonly in obese, diabetic, and hyperlipidemic nonalcoholic patients. Not all obese patients have fatty liver disease, but NASH occurs in about 3 to 5% of the overweight and obese population, and liver fibrosis is increased in up to 40% of these individuals. Most patients with hepatic steatosis have stable, nonprogressive disease, but NASH can progress to cirrhosis. Many patients who were previously described as having cryptogenic cirrhosis are now thought to have NASH, especially because catabolic cirrhosis reduces macrovesicular steatosis, so late biopsy may show just a bland cirrhosis. Histologically, NAFLD resembles alcoholic liver disease, but it occurs in individuals without significant alcohol consumption. Average alcohol consumption greater than two drinks per day in men and greater than one drink per day in women generally is not consistent with a diagnosis of NAFLD. In addition, the definition of NAFLD excludes patients with a history of exposure to steatogenic medications such as amiodarone, methotrexate, and tamoxifen. NAFLD encompasses a spectrum of abnormal liver histology, ranging from simple steatosis to nonalcoholic steatohepatitis (NASH) and cirrhosis. In simple steatosis, liver histology reveals macrovesicular steatosis without ballooning degeneration of hepatocytes or liver fibrosis. NASH,

which is a more advanced form of NAFLD, is histologically characterized by macrovesicular steatosis, ballooning degeneration of the hepatocytes, and sinusoidal fibrosis.

The major risk factors for NAFLD include obesity, type 2 diabetes mellitus, metabolic syndrome, and dyslipidemia. Other comorbidities associated with NAFLD include polycystic ovary syndrome, hypothyroidism, hypopituitarism, and sleep apnea. Two fundamental defects in NAFLD are insulin resistance/hyperinsulinemia and excessive levels of nonesterified fatty liver within the hepatocytes. An excessive influx of nonesterified fatty acids into the hepatocytes results in macrovesicular steatosis, which is predominantly centrilobular in location. Additionally, patients with NAFLD have increased de novo intrahepatic lipogenesis. Although patients with NAFLD robustly esterify free fatty acids in neutral triglycerides, free fatty acids within the hepatocytes are considered the primary mediators of cell injury (lipotoxicity). In the background of hepatic steatosis, factors that promote cell injury, inflammation, and fibrosis include oxidative stress, endoplasmic reticulum stress, apoptosis, adipocytokines, and stellate cell activation. The sources of oxidative stress include mitochondria and microsomes. Adipocytokines that play an important role in the pathogenesis of NAFLD include adiponectin and TNF-α. It is unclear why some patients with NAFLD exhibit NASH, whereas other patients with a comparable risk factor profile have only simple steatosis. There is a consistent and significant relationship of PNPLA3 genetic polymorphisms with the severity of steatosis and other histologic features of NAFLD. However, the genetic factors that play a role in NASH and NAFLD have not been fully elucidated.

Alcoholic fatty liver disease will develop in nearly 90% of individuals who consume alcohol heavily (on average, >6 drinks per day), and some individuals develop the more severe conditions of alcoholic hepatitis and alcoholic cirrhosis. The mechanisms underlying alcoholic liver injury can be broadly categorized into those caused by the effects of alcohol directly on hepatocytes and those caused by the effects mediated by Kupffer cells. The hepatocyte mechanisms include the altered redox state induced by alcohol and aldehyde dehydrogenase reactions, the oxidative stress and lipid peroxidation caused by the induction of CYP2E1 enzymes and the mitochondrial electron transfer system, and the effects of alcohol on the nuclear transcription factors (AMP kinase and SREBP-1c), protein adduct formation, and altered methionine and folate metabolism with resulting endoplasmic reticulum stress. Chronic alcohol consumption increases gut permeability, and the resulting portal

endotoxemia activates Kupffer cells. Activated Kupffer cells release a number of proinflammatory mediators, including tumor necrosis factor-α (TNF-α), transforming growth factor-β1 (TGF-β1), interleukins 1, 6, 8, and 10, and platelet-derived growth factor (PDGF). TNF-α has plethora of biologic effects and causes hepatocyte apoptosis, whereas TGF-β1 and PDGF play important roles in stellate cell activation, collagen production, and hepatic fibrosis. Among the known risk factors for developing alcoholic liver disease, the amount of alcohol consumed is the single most important. For unclear reasons, only 30 to 35% of individuals with heavy and long-term drinking develop alcoholic hepatitis, and less than 20% develop cirrhosis. Women are at higher risk; for example, the risk of alcoholic cirrhosis increases after 10 years of alcohol consumption at quantities of more than 60 to 80 g/ day in men, whereas in women, it can develop at quantities of only more than 20 g/day. Moreover, the peak incidence of alcoholic liver disease in women is approximately a decade earlier than in men. The type of alcoholic beverage consumed may not be as critical, but “spirits” and beer may be more hepatotoxic than wine. African-American and Hispanic ethnic groups may be predisposed to more significant alcoholic liver injury. Both obesity and protein-calorie malnutrition, in which micronutrients and antioxidant capacity are diminished, also are important predispositions. Polymorphisms in genes associated with alcohol metabolism (alcohol and aldehyde dehydrogenases and cytochrome P-450 enzymes) and dysregulated cytokine production (e.g., TNF-α) may also influence genetic susceptibility. In patients with other forms of chronic liver disease (e.g., viral hepatitis B or C), concomitant alcohol consumption significantly aggravates liver injury.

Pathological anatomy

Among diffuse inflammatory affections of the liver benign (non-active, persisting), active and cholestatic chronic hepatitis are distinguished. Non-active hepatitis is characterized by inflammation in the periportal zones, preservation of the lobular structure, and sometimes by moderate dystrophic changes in the hepatocytes. The inflammatory and cicatricial processes are more distinct in the liver affected by active hepatitis. Inflammatory infiltration extends from the periportal zones inside the liver. Hepatocytes are extensively necrotized and have dystrophic changes; fibrosis is found in the liver.

Clinical features

Chronic hepatitis are characterized by dyspeptic symptoms; jaundice; moderate enlargement and induration of the liver; enlargement of the spleen; dysfunction of the liver as determined by laboratory tests and radiohepatography.

But the clinical picture and also the course of each clinico-morphological form of hepatitis have their special features. Chronic benign hepatitis is characterized by obliterated clinical picture. The patients complain of heaviness or dull pain in the right hypochondrium, decreased appetite, bitter taste in the mouth, nausea and eructation. Jaundice is usually absent or it is moderate. Objective studies reveal a mildly enlarged liver with a smooth surface and a moderately firm edge, which is slightly tender to palpation. Enlargement of the spleen is not marked.

Chronic active hepatitis is characterized by complaints and objective symptoms: weakness, loss of weight, fever, pain in the right hypochondrium, loss of appetite, nausea, regurgitation, meteorism, skin itching, jaundice, and frequent nasal bleeding. The liver is enlarged, firm, with a sharp edge. The spleen is enlarged.

The clinical *symptoms of chronic viral and autoimmune hepatitis* are typically nonspecific, and many patients have no symptoms. Fatigue, sleep disorders, and right upper quadrant pain may be present. Often the diagnosis is made when liver test abnormalities are identified by blood testing during a routine health evaluation or assessment for an unrelated problem or at the time of voluntary blood donation. More advanced symptoms include poor appetite, nausea, weight loss, muscle weakness, itching, dark urine, and jaundice. Patients can progress to full-blown cirrhosis, with its typical clinical manifestations. If cirrhosis is present, weakness, weight loss, abdominal swelling, edema, bruisability, gastrointestinal bleeding, and hepatic encephalopathy with mental confusion may arise. Other findings may include spider angiomas, palmar erythema, ascites, edema, and skin excoriations.

Patients with *alcoholic liver disease* may have signs and symptoms from underlying alcoholism as well as those caused by liver disease. Stigmata of chronic alcoholism include palmar erythema, spider nevi, bilateral gynecomastia, testicular atrophy, bilateral parotid enlargement, and Dupuytren’s contractures. The clinical features of liver disease will depend on the stage of alcoholic liver disease, that is, whether a patient has alcoholic fatty liver or more advanced liver disease such as alcoholic hepatitis and cirrhosis. Patients with alcoholic fatty liver disease are generally asymptomatic, but some patients may have anorexia, fatigue, right upper quadrant discomfort, and tender hepatomegaly.

Patients with alcoholic fatty liver typically do not have jaundice, ascites, or splenomegaly. Patients with alcoholic hepatitis may have a more dramatic presentation with severe malaise, fatigue, anorexia, fever, evidence of protein-calorie malnutrition, and features of decompensated liver disease, including jaundice, coagulopathy, ascites, and encephalopathy. Physical examination invariably shows at least some features of chronic alcoholism, and jaundice, ascites, and splenomegaly are common.

NAFLD is often asymptomatic but may rarely also cause fatigue and right upper quadrant pain. Physical examination may reveal hepatomegaly, palmar erythema, and spider nevi. If liver disease is advanced, the features of liver failure, such as ascites, encephalopathy, and abdominal collateral vessels, are present.

Additional methods of examination

Clinical blood analyses. Laboratory tests often reveal anaemia, leucopenia, thrombocytopenia (a sign of hypersplenism), and increased erythrocyte sedimentation rate.

Biochemical blood analysis: they show hyperbilirubinaemia, hyperproteinaemia, hypergamma-globulinaemia, positive protein-sedimentation tests, increased activity of transaminase and alkaline phosphotase; decreased activity of cholinesterase; the prothrombin index is sharply decreased; excretion of bromsulphthalein is delayed.

Chronic viral and autoimmune hepatitis. Levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are usually two to five times the upper limit of normal. The ALT level is generally higher than the AST level, but both can be normal in mild or inactive disease or 10 to 25 times the upper limit of normal during acute exacerbations. Biologic tests can establish the specific diagnosis. Alkaline phosphatase and γ-glutamyl transpeptidase levels are usually minimally elevated unless cirrhosis is present. Serum bilirubin and albumin levels and the prothrombin time are normal unless the disease is severe or advanced. Serum immunoglobulin levels are mildly elevated or normal in chronic viral hepatitis but may be very elevated in autoimmune hepatitis. Results that suggest the presence of advanced fibrosis are a platelet count below 160,000, AST levels higher than ALT levels, elevation in serum bilirubin, decrease in serum albumin, prolongation of the prothrombin time, elevation in α-fetoprotein levels, and presence of rheumatoid factor or high globulin levels.

Alcoholic liver disease. These patients may also have biochemical evidence of alcoholism and alcoholic liver disease with macrocytosis as well as elevated levels of

aspartate aminotransferase (AST) and γ-glutamyl transpeptidase (GGT). Liver biochemistries are abnormal with an elevated AST and ratio of AST to alanine transferase (ALT), alkaline phosphatase, GGT, and total bilirubin, but decreased levels of serum albumin. The AST rarely exceeds 300 IU/L. Serum electrolyte abnormalities including hypokalemia, hypomagnesemia, hypocalcemia, and hypophosphatemia are frequent. An AST/ALT ratio of more than 2 is typical in alcoholic liver disease, and ALT values greater than 150 to 200 IU/L are very rare in alcoholic liver disease.

NAFLD is generally suspected when aminotransferase levels are asymptomatically elevated in an individual with metabolic risk factors (obesity and diabetes) or when liver imaging (ultrasound, CT, or MRI) obtained for another reason shows fatty infiltration. The diagnosis of NAFLD requires that there is no history of previous or ongoing significant alcohol consumption, no exposure to steatogenic medications, and no evidence of other causes of liver disease, such as viral hepatitis B or C. Elevated levels of aminotransferases, although common, are not required for the diagnosis of NAFLD. In contrast to alcoholic liver disease, ALT levels are higher than AST levels, but they rarely exceed 250 IU/L. In general, AST and ALT levels do not have diagnostic or prognostic significance.

Table 15

Markers of viral hepatits

	Antigen(s)	**Antibodies**	**Remarks**
HCV	C100-3 C33c C22-3 NS5	Anti-HCV	Bloodborne agent, formerly labeled non-A, non-B hepatitis. *Acute diagnosis:* anti-HCV (C33c, C22-3, NS5), HCV RNA. *Chronic diagnosis*: anti-HCV (C100-3, C33c, C223, NS5) and HCV RNA; cytoplasmic location in hepatocytes.
HBV	HBsAg HBcAg HBeAg HBcAg HBeAg HBsAg	Anti-HBs Anti-HBc Anti-HBe Anti-HBc Anti-HBe Anti-HBs	Bloodborne virus; carrier state. *Acute diagnosis:* HBsAg, IgM anti-HBc *Chronic diagnosis*: IgG anti-HBc, HBsAg *Markers of replication:* HBeAg, HBV DNA Liver, lymphocytes, other organs Nucleocapsid contains DNA and DNA polymerase; present in hepatocyte nucleus; HBcAg does not circulate;
HDV	HBsAg	Anti-HBs	Defective RNA virus, requires helper function of

	HDAg	Anti-HDV	HBV (hepadnaviruses); HDV antigen (HDAg) present in hepatocyte nucleus *Diagnosis:* anti-HDV, HDV RNA; HBV/HDV co-infection—IgM anti-HBc and anti-HDV; HDV superinfection—IgG anti-HBc and anti-HDV

Hepatic ultrasound can determine the texture and size of the liver and spleen, exclude hepatic masses, and assess the gallbladder, intrahepatic bile ducts, and portal venous flow. Computed tomography and magnetic resonance imaging of the liver are helpful if a mass or other abnormality is found by ultrasound. Hepatic elastography can assess liver stiffness as a marker of fibrosis.

Puncture biopsy of the liver and (for special indications) laparoscopy establish the special histological and macroscopic changes in the liver characteristic of these forms. Chronic cholestatic hepatitis is mainly characterized by the cholestatic increased activity of alkaline phosphatase in the blood, and high cholesterol of blood. Persistent subfebrile temperature and regular increase erythrocyte sedimentation rate are also not infrequent.

Table 16

Liver test patterns in hepatobiliary disorders

Type of Disorder	Bilirubin	Aminotransferases	Alkaline Phosphatase	Albumin	Prothrombin Time
Hemolysis/Gilbert's syndrome	Normal to 86 μmol/L (5 mg/dL) 85% due to indirect fractions No bilirubinuria	Normal	Normal	Normal	Normal
Acute hepatocellular necrosis (viral and drug hepatitis, hepatotoxins, acute heart failure)	Both fractions may be elevated Peak usually follows aminotransferases Bilirubinuria	Elevated, often >500 IU, ALT > AST	Normal to <3× normal elevation	Normal	Usually normal. If >5× above control and not corrected by parenteral vitamin K, suggests poor prognosis

Chronic hepatocellular disorders	Both fractions may be elevated Bilirubinuria	Elevated, but usually <300 IU	Normal to <3× normal elevation	Often decreased	Often prolonged Fails to correct with parenteral vitamin K
Alcoholic hepatitis, cirrhosis	Both fractions may be elevated Bilirubinuria	AST:ALT >2 suggests alcoholic hepatitis or cirrhosis	Normal to <3× normal elevation	Often decreased	Often prolonged Fails to correct with parenteral vitamin K
Intra- and extrahepatic cholestasis	Both fractions may be elevated	Normal to moderate elevation	Elevated, often >4× normal elevation	Normal, unless chronic	Normal If prolonged, will correct with parenteral vitamin K
Obstructive jaundice	Bilirubinuria	Rarely >500 IU		Normal	Normal
Infiltrative diseases (tumor, granulomata); partial bile duct obstruction	Usually normal	Normal to slight elevation	Elevated, often >4× normal elevation Fractionate, or confirm liver origin with 5'-nucleotidase or γ glutamyl transpeptidase		

CIRRHOSIS OF THE LIVER

Cirrhosis of the liver is a chronic progressive disease characterized by diffuse affection of liver's parenchyma and stroma with quantity reduction of functioning cells, their nodular regeneration and excessive development of connective tissue that leads to cytoarchitectonic reorganization of the liver and development of hepatic insufficiency.

Classification

Liver cirrhosis can be classified according to etiology (see etiological factors below).

Although cirrhosis is histologically an “all or nothing” diagnosis, clinically it can be classified by its status as compensated or decompensated. Decompensated cirrhosis is defined by the presence of ascites, variceal bleeding, encephalopathy, or jaundice, which are complications that result from the main consequences of cirrhosis: portal hypertension and liver insufficiency.

When all the causes have been investigated and excluded, cirrhosis is considered “cryptogenic”.

According to morphological features: micronodular (nodules 1-3 mm), macronodular (nodules >3mm), mixed, septal.

There are two most commonly used scoring systems in cirrhosis: Child-Pugh (range, 5-15) and model of end-stage liver disease (MELD) score (range, 6-40).

MELD score: [0.957 × LN (creatinine in mg/dL) + 0.378 × LN (bilirubin in mg/dL) + 1.12 × LN (INR) + 0.643] × 10. Where LN is natural logarithm.

Child-Pugh classification: Child A - score of 5-6; Child B - score of 7-9; Child C - score of 10-15 (table 3).

Table 17

Child-Pugh classification

Parameters	**Points Ascribed**		
	1	**2**	**3**
Ascites	None	Grade 1-2 (or easy to treat)	Grade 3-4 (or refractory)
Hepatic encephalopathy	None	Grade 1-2 (or induced by a precipitant)	Grade 3-4 (or spontaneous)
Bilirubin (mg/dL) (μmol/L)	<2 <34	2-3 34–51	>3 >51
Albumin (g/dL) (g/L)	>3.5 >35	2.8-3.5 30–35	<2.8 <30
Prothrombin time (seconds> control) or INR (international normalized ratio)	<4 <1.7	4-6 1.7-2.3	>6 >2.3

Etiology

Cirrhosis of the liver is a polyetiological disease. It may develop due to postviral hepatitis: hepatitis B, C and D; alcohol; drugs (isoniazid, methotrexate and other); toxic factor; biliary obstruction: primary and secondary biliary cirrhosis; genetically caused disorders of a metabolism: deficiency of alpha-1-antitripsini; Konovalov-Wilson's disease; cardiac failure; cryptogenic.

Clinical features

The two main consequences of cirrhosis are portal hypertension, with the accompanying hyperdynamic circulatory state, and liver insufficiency.

The development of varices and ascites is a direct consequence of portal hypertension and the hyperdynamic circulatory state, whereas jaundice occurs as a result of an inability of the liver to excrete bilirubin (i.e., liver insufficiency).

Encephalopathy is the result of both portal hypertension and liver insufficiency.

Ascites, in turn, can become complicated by infection, which is called spontaneous bacterial peritonitis, and by functional renal failure, which is called hepatorenal syndrome.

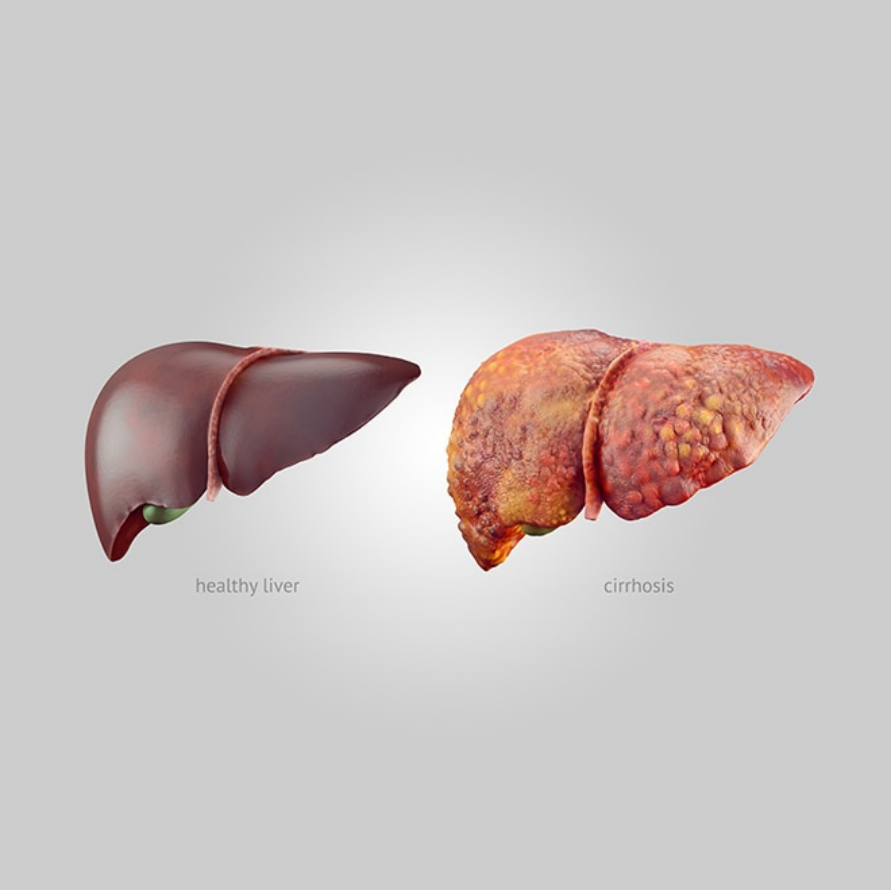

Image 30. Cirrhosis of the liver

This image was downloaded from website https://www.niddk.nih.gov

They are defined by a stage of process and presence of complications - from full absence of symptoms up to common clinical picture of hepatic coma. The sharp painful syndrome is not specific. More often, the patients have complaints on the feeling of weight and dull pains in right hypochondria and epigastria, that amplifying after taking food and physical activity. The patients also suffering from the dyspeptic symptoms that connected with disorders of digestion, general intoxication and accompanying pathologies of a gastro-intestinal tract: the swelling of a stomach, less often - a nausea, vomiting, a heartburn, bitterness in a mouth, infringements of a stool. Also can be present the general complaints - weakness, fatigue, decrease in working capacity, weight reduction, rise in temperature (asteno-vegetative syndrome); yellowness of the skin and visible mucosa, skin itch, hemorrhages, nasal and uteri bleedings (coagulopathy syndrome).

The liver cirrhosis allocates the following clinical syndromes:

- the syndrome of portal hypertension (includes edematous-ascitic syndrome);
- the syndrome of hepato-cellular insufficiency;
- hepatic encephalopathy;
- hepatolienal syndrome.

Portal Hypertension and the Hyperdynamic Circulatory State. In cirrhosis, portal hypertension results from both an increase in resistance to portal flow and an increase in portal venous inflow. The initial mechanism is increased sinusoidal vascular resistance secondary to deposition of fibrous tissue and subsequent compression by regenerative nodules (fixed component) and active vasoconstriction (functional component), which is amenable to the action of vasodilators such as nitroprusside and is caused by a deficiency in intrahepatic nitric oxide (NO), as well as enhanced activity of vasoconstrictors. Early in the portal hypertensive process, the spleen grows and sequesters platelets and other formed blood cells, thereby leading to hypersplenism.

As collaterals develop, an increase in portal blood inflow maintains the portal hypertensive state as a result of splanchnic vasodilation, which in turn is secondary to increased production of NO. Thus, the paradox in portal hypertension is that a deficiency of NO in the intrahepatic vasculature leads to vasoconstriction and increased resistance, whereas overproduction of NO in the extrahepatic circulation leads to vasodilation and increased flow.

Varices and Variceal Hemorrhage. The complication of cirrhosis that results most directly from portal hypertension is the development of portal-systemic

collaterals, the most relevant of which are those that form through dilation of the coronary and gastric veins and constitute gastroesophageal varices. The initial formation of esophageal collaterals depends on a threshold portal pressure, clinically established by a hepatic venous pressure gradient of 10 to 12 mm Hg, below which varices do not develop. Development of a hyperdynamic circulatory state leads to further dilation and growth of varices and eventually to their rupture and variceal hemorrhage, one of the most dreaded complications of portal hypertension.

Ascites and Hepatorenal Syndrome. Ascites in cirrhosis is secondary to sinusoidal hypertension and retention of sodium. Cirrhosis leads to sinusoidal hypertension by blocking hepatic venous outflow both anatomically by fibrosis and regenerative nodules and functionally by increased postsinusoidal vascular tone. Similar to the formation of esophageal varices, a threshold hepatic venous pressure gradient of 12 mm Hg is needed for the formation of ascites. In addition, retention of sodium replenishes the intravascular volume and allows the continuous formation of ascites.

Spontaneous Bacterial Peritonitis. Spontaneous bacterial peritonitis, an infection of ascitic fluid, occurs in the absence of perforation of a hollow viscus or an intra-abdominal inflammatory focus such as an abscess, acute pancreatitis, or cholecystitis. Bacterial translocation, or the migration of bacteria from the intestinal lumen to mesenteric lymph nodes and other extraintestinal sites, is the main mechanism implicated in spontaneous bacterial peritonitis. Impaired local and systemic immune defenses are a major element in promoting bacterial translocation and, together with shunting of blood away from the hepatic Kupffer cells through portosystemic collaterals, allow a transient bacteremia to become more prolonged, thereby colonizing ascitic fluid. Spontaneous bacterial peritonitis occurs in patients with reduced ascites defense mechanisms, such as a low complement level in ascitic fluid. Another factor that promotes bacterial translocation in cirrhosis is bacterial overgrowth attributed to a decrease in small bowel motility and intestinal transit time.

Jaundice. Jaundice in cirrhosis is a reflection of the inability of the liver to excrete bilirubin and is therefore the result of liver insufficiency. However, in cholestatic diseases leading to cirrhosis (e.g., primary biliary cirrhosis, primary sclerosing cholangitis, vanishing bile duct syndrome), jaundice is more likely due to biliary damage than liver insufficiency. Other indicators of liver insufficiency, such as the prothrombin time or the presence of encephalopathy, help determine the most likely contributor to hyperbilirubinemia.

Encephalopathy. Ammonia, a toxin normally removed by the liver, plays a key role in the pathogenesis of hepatic encephalopathy. In cirrhosis, ammonia accumulates in the systemic circulation because of shunting of blood through portosystemic collaterals and decreased liver metabolism (i.e., liver insufficiency).

Objective examination

General patient's condition is from satisfactory to extremely grave. May observed deranged consciousness with hepatic coma develops at final stage of diseases.

In general inspection may detect jaundice, expansion of the veins on the forward abdomen wall, palmary erythema, red lustrous lips, scarlet (lacquered) tongue, spider nevi or telangiectasia, Dupuitrens' contracture, hynecomastia at men, traces of scratches on all body, xanthomatous plaques on the skin (observed in patients with biliary cirrhosis of the liver. Inspection of the abdominal skin can relation or the veins that can be seen through the thinned skin of the abdominal wall (caput medusae). Collateral venous system can be seen on the chest as well. There can be an expressed loss of weight of a body down to cachexia, enlargement of abdomen in sizes, edematous ascitic syndrome even anasarca.

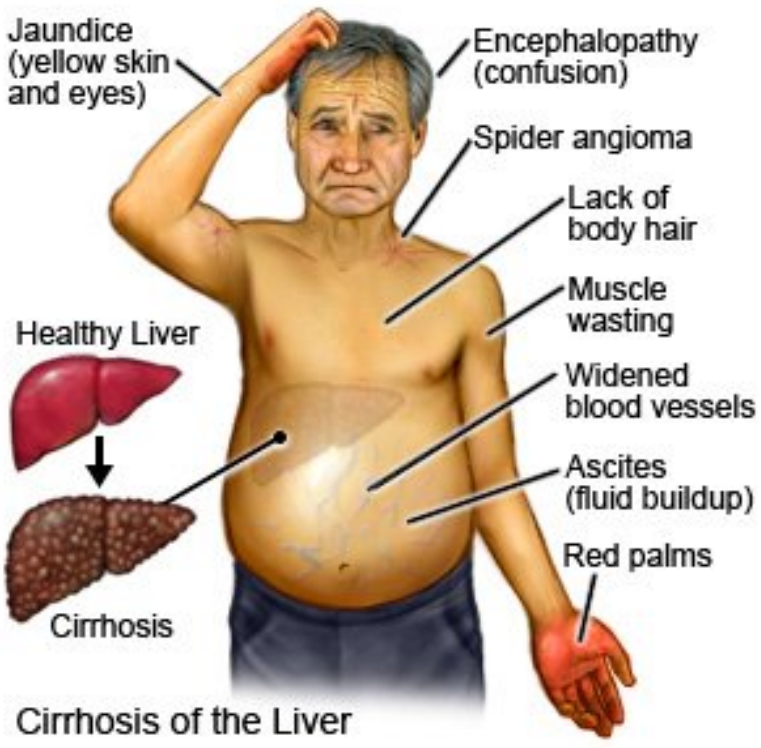

Image 31. Symptoms of Cirrhosis of the liver

This image was downloaded from website https://www.drugs.com/cg/cirrhosis

In superficial tentative oriental palpation of the abdomen may be detect moderate pain in right and left hypochondrias, muscular resistance and positive fluctuation symptoms.

In percussion of the liver according M. G. Kurlov and palpation of the liver and spleen may be detecting enlargement of the liver and spleen sizes with increase of their density and rough surface. However, in patients with significant amount of the fluid in abdominal cavity the enlarged lower liver border and spleen are not accessible for palpation.

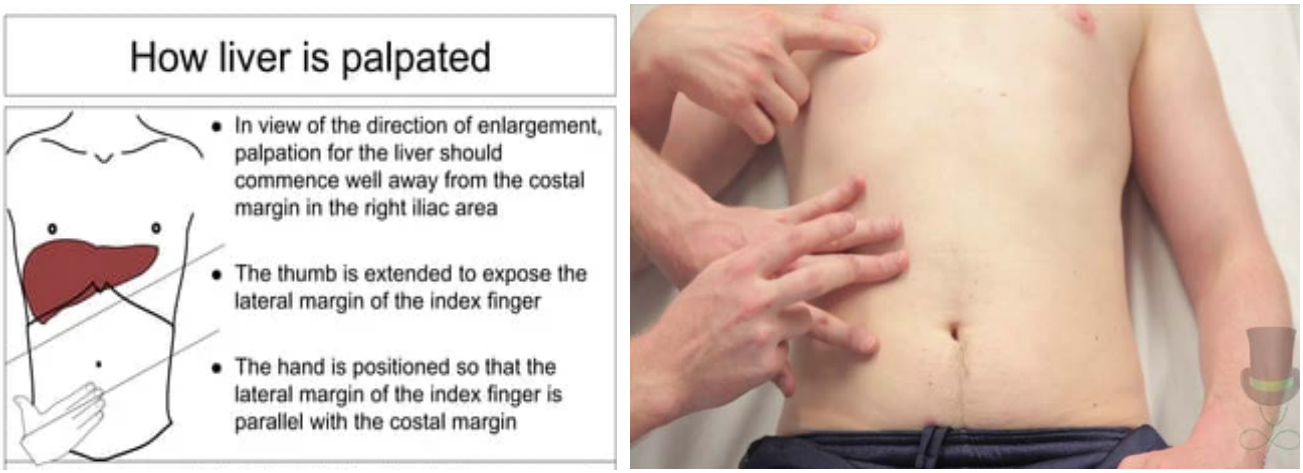

Image 32. Palpation of the liver
This image was downloaded from website https://www.slideshare.net

Complications: encephalopathy, hepatic insufficiency, portal hypertension, hepatorenal syndrome, bacterial peritonitis, bleeding from varicous expanded veins.

Additional methods of examination

Clinical blood analyses. An active cirrhotic process is characterized by anaemia, leucopenia, thrombocytopenia, and increased ESR. Anaemia can be due to hypersplenism and gastro-intestinal haemorrhage, and often increased haemolysis, which is accompanied by reticulocytosis of the peripheral blood.

Biochemical blood analysis. The blood serum bilirubin content considerable only in the final stage of the disease. At the same time, the affection of the excretory motion of the cirrhotic liver can be assessed by the presence of the conjugated fraction of bilirubin (bound bilirubin). Its content increases in normal and increased total bilirubin. The blood serum bilirubin content varies in biliary cirrhosis of the liver, mostly at the expense of bound bilirubin.

- Affection of liver cells is manifested by characteristic changes in the protein indices: decreased concentration of serum albumins and hypergammaglobulinaemia which in turn decreases the albumin-globulin coefficient.

- The blood level of lipids and cholesterol also increases considerably in the presence of biliary cirrhosis. A sensitive index of liver dysfunction is the decreased activity of cholinesterase.

- Transaminase activity increases in exacerbation of liver cirrhosis. Activity of alkaline phosphatase also increases in biliary cirrhosis.

- The decreased prothrombin content (which is synthesized by the liver cells), increased antithrombin coagulative activity and decreased total coagulative activity of plasma are important in the aetiology of haemorrhagic diathesis in liver cirrhosis.

- Detection of α-phetoprotein is required for screening on malignant transformation of cirrhosis. Research of the ceruloplasmin maintenance - etiologic factor establishment (Konovalov-Wilson's disease).

Ultrasound examination (ultrasonography) - revealing of hepatomegalia, spleenomegalia and infringement of hepatic structure.

Varicose veins of the esophagus are revealed by X-rays or by upper *gastrointestinal endoscopy*.

Rectoromanoscopia – detection of varicous dilated veins of rectal textures.

Instrumental non-obligatory methods (under indications): hepatoscyntigraphia; computed tomography and magnetic resonance imaging.

LIST OF FINAL CONTROL QUESTIONS

1. What etiology of COPD, Asthma?
2. What are the main causes of dyspnea?
3. Differential diagnosis of dyspnea.
4. Diagnostic capabilities of spirography.
5. Diagnostic capabilities of X-ray examination of respiratory organs.
6. Classification of arterial hypertension.
7. Clinical symptoms of hypertension.
8. Clinical symptoms of target organ damage in hypertension.
9. Prevention of hypertension.
10. What are the clinical features of different chronic heart failure grade?
11. What are the main types of chronic heart failure?
12. Differential diagnosis of chest pain.
13. Point the substance provisions of modern clinical classification of CAD.
14. Name the typical clinical symptoms of stable angina.
15. Work out a plan of laboratory and instrumental inspection of patient on CAD.
16. What are the signs and symptoms of valvular heart disease?
17. Modern classification of systemic vasculitis.
18. What is the definition of hematemesis, melena and hematochezia?
19. Differential diagnosis of enterorrhagia and melena.
20. Specify complications of peptic ulcer.
21. Define etiology of chronic pancreatitis.
22. Name the typical clinical displays of chronic pancreatitis.
23. Work out a plan of laboratory and instrumental inspection of patient on chronic disease of gall-bladder.
24. Differential diagnosis of jaundice.
25. What are the laboratory characteristics of chronic hepatitis and its stages?
26. Diagnostic criteria of chronic hepatitis according to etiology.
27. Diagnostic criteria of liver cirrhosis.
28. What lifestyle modifications should be recommended for patients with liver cirrhosis?
29. Dental considerations in patients with respiratory problems.

30. Dental considerations in patients with arterial hypertension.
31. Dental considerations in patients with CAD.
32. Dental considerations in patients with peptic ulcer.
33. Dental considerations in patients with chronic hepatitis and liver cirrhosis.
34. Dental considerations in patients with chronic disease of gall-bladder and pancreas.
35. Dental considerations in patients with systemic vasculitis.

TASKS FOR FINAL CONTROL

TOPIC 1

1. Most important component of the COPD pathophysiology is:

A. Mucus hypersecretion and dysfunction of the ciliated epithelium.

B. Restriction of air flow in the bronchi and excessive pulmonary edema.

C. Disruption of gas exchange.

D. Pulmonary hypertension.

E. Pulmonary heart

2. In the study of the external breathing function the most important in COPD are:

A. Volume of forced expiration in the first second (FEV1).

B. Forced Vital Lung Capacity (FVC).

B. The ratio of FEV1 / FVC

D. All of the above.

E. The most important indicator is not named

3. The COPD diagnostic criterion is a decrease in indicators, starting with:

A. FEV1 <90% of the appropriate in combination with FEV1 / FVC < 80%.

B. FEV1 < 80% of the corresponding in combination with FEV1 / FVC < 70%.

C. FEV1 < 70% of the proper in combination with FEV1 / FVC< 60%.

D. FEV1 < 60% of the due in combination with FEV1 / FVC < 50%.

E. FEV1 < 50% of the due in combination with FEV1 / FVC < 40%.

4. Short-acting bronchodilators, inhaled β2 -agonists include, except:

A. Salbutamol.

B. Terbutalin.

B. Fenoterol.

G. Salmeterol.

5. Inhalation corticosteroids do not include:

A. Beclamethasone.

B. Budesonide.

C. Prednisone.

D. Fluticasone.

6. Bronchodilators do not include:

A. β2 -agonist.

B. β2 - blockers

C. Cholinolytics

D. Theophylline.

E. Euphylline.

7. Patient 55 years, after appendectomy for 2 days complains of progressive shortness of breath
and cough with purulent sputum. Such symptoms are noted in the autumn and spring. Smokes
for 25 years. Temperature - 37.1°C. In the lungs - breathing is weakened with

single dry wheezing. In the blood: L - $10x10^9$ / l. X-ray: increased lung airiness, increased pulmonary pattern. Bronchoscopy: hyperemia of the mucous membrane with the presence of purulent-mucous character secretions. What is the previous diagnosis?

A. Bronchial asthma
B. Chronic bronchitis
C. Bronchoectatic disease
D. Pulmonary artery branches embolism E. Pneumonia

8. A 39-year-old truck driver complains of shortness of breath, a cough with a small amount of
mucous sputum, mostly in the morning. Has been suffering from COPD for a long time, sinusitis. Smokes, consumes alcohol occasionally. Objectively: temperature - 36.5°C, BH - 24 / min, pulse - 90 / min, blood pressure - 120/80 mm Hg. Art. At auscultation breathing is hard, a moderate amount of dry wheezing. FEV1 - 68% of due value. What preventive measures are appropriate in the first place?

A. Rational employment
B. Refusing to drink alcohol
C. Remediation of chronic infection foci
D. Smoking cessation
E. Moving to another climate zone

9. A 60-year-old man complains of shortness of breath, exacerbated by exertion, cough with a
small amount of mucous-purulent sputum mostly in the morning. COPD in anamnesis. Objectively: temperature - 36.0° C, RR - 22 / min, HR - 84 / min, BP - 110/70 mm Hg. Art. Skin is moist, diffuse cyanosis. At auscultation, the breath is stiff, scattered wheezing. FEV - 62% of due value; pharmacological test with salbutamol - increase of 5%. What is the most likely mechanism of bronchial obstruction development in the patient?

A. Hypercrynia
B. Inflammatory edema
C. Bronchospasm
D. Diffuse-sclerotic changes
E. Mucostasis

10. A 60-year-old man complains of shortness of breath, which is exacerbated by exercise. Smokers for about 30 years. Objectively: temperature - 36.5° C, RR - 22 / min, HR - 88 / min, BP - 130/85 mm Hg; barrel chest, band box sound over the entire surface of the pulmonary fields, weakened vesicular breathing. Which anamnesis disease most likely led to pathological changes?

A. COPD
B. Bronchiectatic disease
C. Pulmonary tuberculosis
D. Pneumonia
E. Tumor of the bronchus

Answers

1	2	3	4	5	6	7	8	9	10
B	D	B	D	B	B	B	D	D	A

TOPIC 2

1. Patient of 32 y. visited the doctor. It was found that 4 days ago he caught a cold: there was a tickle in the throat, fatigue. The next morning there was a dry cough, increased body temperature to 38,2˚S, lost appetite. Objectively:lower the right scapuladullness percussion sounds,moist fine bubbling sonorous rales were listened. What diagnosis is most likely?

A. Asthma
B. Non-hospital right-sided pneumonia
C. Acute bronchitis
D. Lung Cancer
E. Gangrene

2. The patient of 18 years complains of increased body temperature to 39˚C, pain in the right side of the chest, dry coughing after hypothermia. Objectively: the skin is moist,pale;BP - 110/70 mm Hg, HR - 96 / min, RR - 27 / min.Dullness percussion soundsbelow the left shoulder blade angle, a weakened vesicular breathing with moist fine bubbling rales, crackles were auscultated. What is the diagnosis?

A. Community-acquired lobar left-sided pneumonia
B. Aspiration right-sided pneumonia
C. Immunodeficiency right-sided pneumonia
D. Nosocomial (hospital) pneumonia
E. Left lungabscess

3. The patient of 29 years is treated an outpatient with acute respiratory viral infection (ARVI),
than the body temperature increased to 39 ° C, cough with "rusty sputum", breathlessness,faint
developed. During the X-ray study infiltration in the lower lobe of the right lung was revealed.
What is the complication developed in ARVI patient?

A. Acute bronchitis
B. Exudative pleurisy
C. Spontaneous pneumothorax
D. Pneumonia
E. Pulmonary atelectasis

4. The patient complains of a temperature to 38,9˚C, cough, stabbing chest pain, more at the left. On examination, the left half of the chest is lagging in breathing act. Auscultation – lower the left
shoulder blade angle bronchial breathing,moist fine bubblingrales

were auscultated. CBC: RBC - 4.12×10^{12} / L, WBC - $10,2 \times 10^{9}$ / L, ESR - 28 mm / hr. What is the diagnosis?

A. Left-sided lobar pneumonia
B. The left-sided pleural effusion
C. Lung Cancer
D. Left-sided infarct - pneumonia
E. Pulmonary tuberculosis

5. Patient K. of 25 years complains of cough with a minor amount of muco-purulent sputum, shortness of breath, increased body T to 38,5˚C, weakness. Felt ill 7 days ago after supercool exposure. Objectively: lungs examination - dullness percussion soundlower theright shoulder blade angle and right axillary area; weakened vesicular breathing, moist fine bubbling sonorousrales. What is the previous diagnosis of the patient?

A. ARVI
B. Acute bronchitis
C. Right-sided pneumothorax
D. Pleural effusion
E. Community-acquired pneumonia

6. The male patient of 26 years was acutely illafter a fishing trip. The disease associates with hypothermia, it all began with a headache, weakness. Then the fever and dry cough came. Objectively: consciousness is retained, facial flushing, RR - 19 per minute. The lung percussion: a dull sound lower the rightscapulaangle, auscultation - crepitus, moist fine bubblingrales. BP - 110/70 mm Hg, HR - 78 per minute, body temperature is 38,7˚C. CBC: WBC. - 10×10^{9} / L, ESR -17 mm / h. Lungs X-ray: the homogeneous infiltrative blackout in the lower lobe of the right lung. Which of the following diagnoses is the most likely?

A. Community-acquired right-sided lobar pneumonia, clinical groupI, RF I st.
B. Community-acquired right-sided lobar pneumonia, clinical group II, Nam I st.
C. Community-acquired C. sided lobar pneumonia, clinical groupIII, RF I st
D. Community-acquired right-sided lobar pneumonia, clinical groupIV, RF I st.
E. Community-acquired sided lobar pneumonia, clinical groupV, RF I st.

7. A man of 56 years, acutely ill. The complaints of fever, cough with muco-purulent sputum. From history we know that he is sick with asthma for 20 years. Objectively: body temperature is 38,7˚C,consciousness is retained, facial flushing, RR- 21 per minute. The lung percussion: a dull sound lower the rightscapula angle, auscultation - crepitus, moist fine bubblingrales. BP - 110/70

mm Hg, HR - 78 per minute. CBC: RBC - 4.12×10 12 / L, WBC - 11× 10 9 / L, ESR - 24 mm / h. Lungs X-ray: the homogeneous infiltrative blackout in the lower lobe of the right lung.The most
likely diagnoses:

A. Community-acquiredright-sided lobar pneumonia, clinical group III, RF Ist.
B. Community-acquired right-sided lobar pneumonia, clinical group I, RF Ist.
C. Community-acquired right-sided lobar pneumonia, clinical group II, RF Ist.
D. Community-acquired right-sided lobar pneumonia, clinical group IV, RF Ist.
E. Bronchial asthma, persistent course, moderate severity, RF Ist.

8. The male patient of 26 years was acutely illafter a fishing trip. The disease associates with hypothermia, it all began with a headache, weakness. Then the fever and cough with "rusty" sputum came. Objectively: consciousness is retained, facial flushing, RR - 36 per minute. The lung percussion: a dull sound lower the right scapula angle, auscultation - crepitus, moist fine bubbling rales. BP - 100/70 mm Hg, HR - 98 per minute, body temperature is 38,7˚C. CBC: WBC. - 14× 10 9 / L, ESR -24 mm / h. Lungs X-ray: the homogeneous infiltrative blackout in the lower lobe of the right lung. Which of the following diagnoses is the most likely?

A. Community-acquired right-sided lobar pneumonia, III clinical group, RF II stage.
B. Community-acquired right-sided lobar pneumonia, II clinical group, RF II stage.
C. Community-acquired sided lobar pneumonia, I clinical group, RF II stage.
D. Community-acquired right-sided lobar pneumonia, IV clinical group, RF II stage.
E. Community-acquired sided lobar pneumonia, V clinical group, RF II stage.

9. The male patient of 26 years was acutely ill after a fishing trip. The disease associates with hypothermia, it all began with a headache, weakness. Then the fever and cough with "rusty" sputum came. Objectively: consciousness is retained, facial flushing, RR - 36 per minute. The lung percussion: a dull sound at right side of the chest, auscultation - crepitus, moist fine bubbling rales. BP - 90/70 mm Hg, HR - 110 per minute, body temperature is 38,7˚C. CBC: WBC. - 14× 10^9 / L, ESR -24 mm / h. Lungs X-ray: the homogeneous infiltrative entire blackout in the right lung. Which of the following diagnoses is the most likely?

A. Community-acquired pneumonia, right-total, the V clinical group, RF II stage.
B. Community-acquired pneumonia, right-total, II clinical group, RF II stage.
C. Community-acquired pneumonia, right-total, and clinical group, RF II stage.
D. Community-acquired pneumonia, right-total, IV of clinical group, RF II stage.
E. Community-acquired pneumonia, right-total, IV clinical group, RF II stage.

10. The male patient of 26 years was acutely ill after a fishing trip. The disease associates with hypothermia, it all began with a headache, weakness. Then the fever and dry cough came. Objectively: consciousness is retained, facial flushing, RR - 19 per minute. The lung percussion: a dull sound lower the right scapula angle, auscultation - crepitus, moist fine bubbling rales. BP - 110/70 mm Hg, HR - 78 per minute, body temperature is 38,7˚C. CBC: WBC. - 10×10^9 / L, ESR -17 mm / h. Lungs X-ray: the homogeneous infiltrative blackout in the lower lobe of the right lung. Community-acquired right-sided lobar pneumonia, I clinical group, RF I st was diagnosed. What
is the management tactics?

A. The treatment at the intensive care unit (ICU)
B. Treatment in a therapeutic hospital
C. Ambulatory treatment
D. Treatment in a surgical department
E. Treatment in a pulmonary hospital

Answers

1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
B	A	D	A	E	A	C	A	E	C

TOPIC 3

1. A 41-year-old woman comes to the physician's office complaining of fatigue, muscle weakness, cramping, headaches, polydipsia, and polyuria. She has been treated for hypertension for 6 years, and her doctors have told her that she has renal problems. Beta-blockers, calcium channel blockers, and diuretics have been used to control her hypertension. There is a family history of renal disease and hypertension. Her blood pressure is

240/140 mm Hg and her pulse is 85/min. The remainder of her examination is normaI. A routine chemical panel shows hypokalemia, hypernatremia, and metabolic alkalosis. Pathologic examination of this patient would most likely reveal which of the following findings?

A. Adrenal adenoma
B. Adrenal carcinoma
C. Bilateral nodular hyperplasia
D. Multiple adrenal adenomas
E. Unilateral nodular adrenal hyperplasia

2. A 34-year-old man undergoing a routine physical examination is found to have a blood pressure of 165/105 mm Hg. The measurement is repeated 40 minutes later, and is 162/103 mm Hg. The physician asks the patient to return the next week and the week following, and each time repeats the evaluation yielding the following results: 170/102, 168/107, 175/108, 167/102 mm Hg. This patient's blood pressure should be classified as which of the following?

A. Optimal
B. Normal
C. High-normal
D. Stage 1 (mild) hypertension
E. Stage 2 (moderate) hypertension
F. Stage 3 (severe) hypertension

3. A 35-year-old man has hypertension, which has been difficult to control with medication. Periodically, he experiences periods when he develops intense symptoms including racing heart, lightheadedness, flushing, diaphoresis, clammy skin, headache, and a sense of impending doom. He has gone to the emergency department of a local hospital several times during these episodes, but by the time he is seen several hours later, the symptoms have long passed, and nothing can be found on physical examination or serum chemistry studies.
The patient's physician orders a 24-hour urine to be collected, which is found to contain significantly elevated levels of vanillylmandelic acid. This compound is a degradation product of which of the following?

A. Acetylcholine
B. Cholesterol
C. Epinephrine
D. Serotonin
E. Testosterone

4. Patients with hypertension would be most likely to have which of the following findings on renal biopsy?

A. Crescent formation
B. Hyaline arteriosclerosis
C. KimmelstieI-Wilson nodules

D. Papillary necrosis
E. Subepithelial electron-dense humps

5. All of the following statements are true about the management of hypertensive emergencies EXCEPT:

A. Mean arterial pressure (MAP) should be reduced by 20% to 25% over the first 2 to 3 hours in a patient with hypertensive encephalopathy.
B. Myocardial ischemia in a patient with a blood pressure (BP) of 174/110 mm Hg is considered a hypertensive emergency.
C. An asymptomatic patient with a BP of 170/116 mm Hg requires immediate pressure reduction prior to discharge.
D. The presence of proteinuria, hematuria, and casts in the urine of a patient with severe hypertension suggests a hypertensive emergency.
E. Papilledema distinguishes malignant hypertension from accelerated hypertension

6. All of the following pairs of antihypertensive agents and side-effects/complications are correctly matched EXCEPT:

A. Nitroglycerin: methemoglobinemia
B. Nicardipine: local phlebitis
C. Fenoldopam: fluid retention
D. Phentolamine: tachycardia, flushing, headache
E. Trimethaphan: paresis of bowel and bladder

7. A 18-year-old man presents to the emergency department following complaints of lower extrem extremity weakness. BP recordings reveal systolic and diastolic pressures that are lower in the legs than in the arms. A chest radiograph demonstrates rib notching and a figure-three silhouette of the aorta. The most likely cause of these findings is:

A. Aortic dissection
B. Incorrect cuff size when measuring lower extremity pressures
C. Renal stenosis
D. Coarctation of the aorta
E. Tetralogy of Fallot

8. A 48-year-old man presents with a 2-day history of worsening morning occipital headaches and blurring of vision in his right eye. He has a BP of 220/130 mm Hg and a heart rate of 78 bpm. On funduscopic examination, the physiologic cup of the optic disc in the right eye is

obscured. Flameshaped hemorrhages are noted. The remainder of the physical examination is normal. Laboratory findings include hematuria (2+) and a serum creatinine level of 2.1 mg/dL. Optimal management of this patient would be:

A. Gradual reduction of diastolic BP to 100 mm Hg over 2 days

B. Reduction of diastolic BP to 90 mm Hg over 2 to 3 hours

C. Reduction of MAP to 120 mm Hg over 2 to 3 hours

D. Reduction of MAP to 120 mm Hg over 6 to 12 hours

E. Measurement of intracranial pressure prior to lowering the BP

9. A 19-year-old woman presents to her doctor's office for an annual physical examination. She has been previously healthy and is currently doing well without complaints. She is a non-smoker and has no significant past medical history or family history. Her temperature is 36.9 °C (98.5 °F), blood pressure is 160/90 mm Hg (confirmed in all extremities), pulse is 84/min, and respirations are 16/min. Her pulses are symmetric and equal, her cardiac and pulmonary examinations are unremarkable, and there is an abdominal bruit with a systolic and diastolic component. Serum chemistry reveals: Sodium – 145 mEq/L, potassium – 3.1 mEq/L, chloride – 102 mEq/L, bicarbonate – 28 mEq/L, bIood urea nitrogen – 14 mg/dL, creatinine - 1.0 mg/dL, gIucose – 80 mg/dL. Which of the following is the most likely cause of her elevated blood pressure?

A. Coarctation of the aorta

B. Cushing syndrome

C. Pheochromocytoma

D. Renovascular hypertension

E. Thyrotoxicosis

10. A 70-year-old man feels trembling of all body, pulsation in the head, periodic syncope. The left border of heart is on the left front axillary line, diastolic noise in the Botkin-Erb’s point. BP is 150/20 mm Hg. What disease is most likely in the patient?

A. Thyrotoxic heart

B. Hypertrophic cardiomyopathy

C. Insufficiency of aortic valves

D. Arterial hypertension

E. Mitral orifice stenosis

Answers

1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
A	E	C	B	C	C	D	C	D	C

TOPIC 4

1. A 78-years-old previously healthy man is admitted to the ER with complaints of angina, dyspnea, and near syncope. Electrocardiogram is normal, and a loud systolic murmur is heard in the second right intercostal space with radiation to the carotids. Give your presumable diagnosis:

A. Myocardial infarction
B. Pericarditis
C. Mitral regurgitation
D. Aortic stenosis
E. Aortic insufficiency

2. What is the main cause of atherosclerotic lesions?

A. Hypercholesterolemia, dyslipoproteinemia
B. Infection
C. Trauma
D. Rheumatism, endocarditis
E. Myocardial infarction

3. Which factor is the leader in the development of atherosclerosis?

A.. Smoking
B. Diabetes.
C. Suprarenalism.
D. Frequent hypothermia.
E. Dyslipoproteinemia.

4. A 4-years-old boy is evaluated for a systolic murmur upon auscultation of the chest. Chest radiograph demonstrates cardiomegaly and rib notching. Physical examination reveals diminished femoral pulses. A 40 mm differential exists between upper and lower extremity blood pressures. Give your presumable diagnosis:

A. Patent ductus arteriosis
B. Coarctation of aorta
C. Atrial septal defect
D. Bilateral common femoral artery stenosis
E. Aortic stenosis

5. What are the contrast agents used for angiography?

A. Triyodtrast, verografin.
B. Methylene blue.
C. Barium sulfate.
D. Alprostan.
E. Vasoprostan.

6. All of the following lesions BUT ONE have a right-to-left shunt in the presence of normal pulmonary vascular resistance:

A. Tetralogy of Fallot
B. Ventricular septal defect
C. Tricuspid atresia
D. Pulmonic stenosis and atrial septal defect
E. Complete atrioventricular canal

7. A l-week-old severely cyanotic infant is most likely to have:

A. Aortic stenosis or partial anomalous pulmonary venous drainage with atrial septal defect

B. Coronary arteriovenous fistula or pulmonary stenosis

C. Transposition of the great vessels, tetralogy of Fallot, or truncus arteriosus

8. Tetralogy of Fallot includes all BUT ONE of the following lesions:

A. Ventricular septal defect

B. Pulmonic stenosis

C. Hypoplastic left ventricle

D. Overriding aorta

E. Right ventricular hypertrophy

9. What is the morphological basis of atherosclerotic lesions?

A. The accumulation of lipids in the intima

B. Thrombosis

C. Inflammatory process

D. Embolism

E. Aneurysm

10. What is the most common cause of a heart attack and stroke?

A. Patchy deposits (called plaques) that form in the lining of the artery wall

B. Plaques growing into the opening (lumen) of the artery, gradually causing it to narrow

C. Plaques that split open (rupture) and expose the plaque material within to the bloodstream, causing blood clots to form

D. Thickening of arteriole walls, causing arteriosclerosis

Answers

1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
D	A	E	B	A	B	C	C	A	C

TOPIC 5

1. A 58 y.o. man complained of severe inspiratory dyspnea and expectoration of frothy and bloodtinged sputum. He has been suffering from essential hypertension and ischemic heart disease. On examination: acrocyanosis, "bubbling" breathing, Ps- 30/min, BP-230/130mm Hg, bilateral rales. Choose medicines for treatment.

A. Morphine, furosemide, nitroprusside sodium

B. Theophylline, prednisolon

C. Albuterol, atropine, papaverine

D. Strophanthine, potassium chloride, plathyphylline

E. Cordiamine, isoproterenol

2. A patient has got a sudden attack of severe substernal pain at night. On examination: confusion, pallor of the skin, acrocyanosis, cold sweat, BP-

80/50 mm Hg, Ps- 120/min, irregular and weak pulse. What condition are these symptoms typical for?

A. Acute left-side heart failure
B. Cardiogenic shock
C. Acute right-side heart failure
D. Radicular syndrome
E. Acute vascular insufficiency

3. A 62 year old patient complains of rest dyspnea, heart pains. 3 years ago he had myocardial infarction. Physical examination: orthopnea, acrocyanosis, swollen cervical veins. Ps - 92, total heart enlargement, the liver is enlarged by 7 cm, shin edema. What is the stage of chronic heart failure (CHF)?

A. CHF- 0
B. CHF- 1
C. CHF- 2 A
D. CHF- 2 B
E. CHF- 3

4. The patient with aquired heart failure has diastolic pressure of 0 mm Hg. What heart failure does the child have?

A. Mitral stenosis
B. Aortal insufficiency
C. Aortal stenosis
D. Mitral insufficiency
E. Rheumatism

5. A 63-year-old male patient with persistent atrialfibrillation complains of moderate dyspnea. Objectively: peripheral edemata are absent, vesicular breathing is present, heart rate - 72/min, AP- 140/90mmHg.What combi-nation of drugs will be most effective for the secondary prevention of heart failure?

A. Diuretics, beta-blockers
B. Beta-blockers, cardiac glycosides
C. Cardiac glycosides, diuretics
D. Cardiac glycosides, ACE inhibitors
E. Beta-blockers, ACE inhibitors

6. A 57-year-old male patient had an attack of retrosternal pain that lasted more than 1,5 hours. Objectively: the patient is inert,adynamic, has pale skin, cold extremities, poor volume pulse, heart rate - 120/min, AP- 70/40 mm Hg. ECG shows ST elevation in II, III, aVF leads. What condition are these changes typical for?

A. Perforated gastric ulcer
B. Arrhythmogenic shock
C. Cardiogenic shock
D. Acute pericarditis
E. Acute pancreatitis

7. A 57-year-old man complains of shortness of breath, swelling on shanks, irregularity in cardiac work, pain in the left chest half with irradiation to the left scapula.Treatment is uineffective. On physical exam: heart’s sounds are dimini-shed, soft

systolic murmur on the apex. Ps - 100/min, arrhythmical, BP - 115/75 mm Hg. The liver is +2 cm, painful. Roentgenoscopy: enlargement of heart shadow to all sides, pulsation is weak. Electrocardiogram (ECG): leftventricled extrasystolia, decreased voltage. What method of investigation is necessary to do to determine the diagnosis?

A. Veloergometria
B. Echocardiography
C. X-ray kymography
D. ECG in the dynamics
E. Coronarography

8. A 64 y.o. patient has developed of squeering substernal pain which had appeared 2 hours ago and irradiated to the left shoulder, marked weakness. On examination: pale skin, cold sweat. Pulse- 108 bpm, AP- 70/50 mm Hg, heart sound are deaf, vesicular breathing, soft abdomen, painless, varicouse vein on the left shin, ECG: synus rhythm, heart rate is 100 bmp, ST-segment is sharply elevated in II, III aVF leads. What is the most likely disorder?

A. Cardiogenic shock
B. Cardiac asthma
C. Pulmonary artery thromboembolia
D. Disquamative aortic aneurizm
E. Cardiac tamponade

9. A 60-year-old patient complains about asphyxia, palpitation, rapid fatiguability. He has 8 year history of essential hypertension. Objectively: the left cardiac border is 2 cm deviated to the left from the medioclavicular line, heart sounds are rhythmic and weak; there is diastolic shock above aorta. AP- 170/100 mm Hg. Liver - +2 cm; shin pastosity is present. ECG shows deviation of cardiac axis to the left, left ventricle hypertrophy. Ejection fraction - 63%. What type of heart failure is observed?

A. It’s a norm
B. Systolic
C. Combined
D. Diastolic
E. Unspecified

10. A 23-year-old patient with hypertrophic cardiomyopathy complains of dyspnea on minimal exertion. EhoCG reveals asymmetric left ventricular hypertrophy, signs of pulmonary hypertension, dilatation of the left atrium. EF is 64%. The revealed alterations are indicative of:

A. Systolic heart failure
B. Diastolic heart failure
C. Primary pulmonary hypertension
D. Primary arterial hypertension
E. Symptomatic arterial hypertension

Answers

1	2	3	4	5	6	7	8	9	10
A	B	D	B	E	C	B	A	D	B

TOPIC 6

1. A 40 y.o. patient of rheumatic heart disease complains of anorexia, weakness and loss of weigth, breathless and swelling of feet. On examination: t-39^{0}C, pulse is 100/min. As ucultation: diastolic murmur in the mitral area. Petechical lesion a round clavicle; spleen was palpable, tooth extraction one month ago.

A. Subacute bacteria endocarditis
B. Recurrence of rheumatic fever
C. Thrombocytopenia purpure
D. Mitral stenosis
E. Aortic stenosis

2. A female rheumatic patient experiences diastolic thoracic wall tremor (diastolic thrill), accentuated S1 at apex, there is diastolic murmur with presystolic intensification, opening snap, S2 accent at pulmonary artery. What rind of heart disorder is observed?

A. Pulmonary artery stenosis
B. Aortic valve insufficiency
C. Mitral stenosis
D. Mitral valve insufficiency
E. Opened arterial duct

3. A patient, aged 49, complains of fever of 37,5oC, heart pain, dyspnea. S1 is clapping;S2 is accentuated in the aortic area; opening snap, presystolic murmur can be auscultated. What is the most efficient examination for valvular disorder assessment?

A. Echocardiography+Doppler-Echocardiography
B. Phonocardiography
C. Ballistocardiogram
D. Chest X-ray
E. ECG

4. A 42 year old woman complains of dyspnea, edema of the legs and tachycardia during minor physical exertion. Heart borders are displaced to the left and S1 is accentuated, there is diastolic murmur on apex. The liver is enlarged by 5 cm. What is the cause of heart failure?

A. Tricuspid regurgitation
B. Mitral regurgitation
C. Tricuspid stenosis
D. Mitral stenosis
E. Aortic stenosis

5. A 33-year-old man with a history of rheumatic fever complains of fever up

to 38 − 39oC, abdominal pain, dyspnea, tachycardia. Heart borders are displaced to the left by 2 cm, systolic and diastolic murmurs above aorta, BP of 160/30 mm Hg. Petechial rash occurs after measurement of blood pressure. Liver is enlarged by 3 cm, spleen is palpable. Urine is brown-yellow. What is the most likely diagnosis?

A. Rheumatic fever
B. Infectious endocarditis
C. Acute hepatitis
D. Acute nephritis
E. Aortic regurgitation

6. Examination of a 35-year-old patient with rheumatism revealed that the right heart border was 1 cm displaced outwards from the right parasternal line, the upper border was on the level with inferior margin of the 1st rib, the left border was 1 cm in from the left midclavicular line. Auscultation revealed atrial fibrillation, loud apical first sound, diastolic shock above the pulmonary artery. Echocardiocopy revealed abnormal pattern of the mitral valvemotion. What heart disease is characterized by these symptoms?

A. Mitral stenosis
B. Mitral valve prolapse
C. Mitral valve insufficiency
D. Aortic stenosis
E. Tricuspid valve insufficiency

7. Six months ago, a 5-year-old child was operated for CHD. For the last 3 weeks he has complained of fever, heart pain, aching muscles and bones. Examination results: "whitecoffee"skin colour, auscultation revealed systolic murmur in the region of heart along with a noise in the III-IV intercostal space. Examinati-on offingertips revealed Janeway lesions. What is your provisional diagnosis?

A. Nonrheumatic carditis
B. Sepsis
C. Infectious endocarditis
D. Acute rheumatic fever
E. Typhoid fever

8. A 67-year-old male complains of dyspnea on exertion, attacks of retrosternal pain, dizziness. He has no history of rheumatism. Objectively: pale skin, acrocyanosis. There are rales in the lower parts of lungs. There is systolic thri-ll in the II intercostal space on the right, coarse systolic murmur conducted to the vessels of neck. AP-130/90 mm Hg, heart rate - 90/min, regular rhythm. The liver extends 5 cm under the edge of costal arch, shin edemata are present. Specify the assumed valvular defect:

A. Tricuspid regurgitation
B. Pulmonary artery stenosis
C. Mitral insufficiency
D. Ventricular septal defect
E. Aortic stenosis

9. A 17 y.o. patient complains of acute pain in the knee joint and t0– 380C. He was ill with angina 3 weeks ago.

Objectively: deformation and swelling of the knee joints with skin hyperemia. Small movement causes an acute pain in the joints. Which diagnose is the most correct?

A. Systemic lupus eritematodes
B. Rheumatic fever, polyarthritis
C. Reactive polyarthritis
D. Infectious-allergic polyarthritis
E. Rheumarthritis

10. A 18 y.o. male patient complains of pain in knee and ankle joints, temperature elevation to 39, 50C.He had a respiratory disease 1,5 week ago. On examination: temperature- 38, 50C, swollen knee and ankle joints, pulse- 106 bpm, rhythmic, AP- 90/60 mm Hg, heart borders without changes, sounds are weakened, soft systolic apical murmur. What indicator is connected with possible etiology of the process?

A. Rheumatic factor
B. 1-antitrypsine
C. Creatinkinase
D. Antistreptolysine-0
E. Seromucoid

Answers

1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
A	C	A	D	B	A	C	E	D	D

TOPIC 7

1. A 31 y.o. patient has been suffering from systemic scleroderma for 14 years. She has been treated in hospital many times. She complains of occasional dull pain in the heart region, palpitation, dyspnea, headache, eye-lid edemata, weight loss and deformation of extremities joints. What organ affection worsens the disease prognosis?

A. Gastrointestinal tract
B. Heart
C. Lungs
D. Kidneys
E. Skin and joints

2. A 41 y.o. woman complains of weakness, fatigue, fever up to 380C, rash on the face skin, pain in the wrists and the elbows. On physical examination: erythematous rash on the cheeks with "butterfly"look, the wrists and elbow joints are involved symmetrically, swollen, sensitive, friction rub over the lungs, the heart sounds are weak, regular, HR88/min, BP- 160/95 mm Hg. Hematology shows anemia, leucopenia, lymphopenia; on urinalysis: proteinuria, leukocyturia, casts. What

is the main mechanism of disease development?

A. Production of antibodies to double stranded DNA

B. Production of myocytes antibodies

C. Production of antibodies to endothelial cells

D. Production of myosin antibodies

E. Production of antimitochondrial antibodies

3. A 32 year old patient complains about pain in small joints of her hands, paresthesia at the tips of fingers, weakness, difficult diglutition. She has been suffering from this for 13 years. Objectively: face amimia, shortening of nail bones, skin indurations in the area of shoulder girdle are present. Roentgenological examination of lungs revealed basal pneumosclerosis. Fibrogastroscopy revealed esophagus constriction in its cardial part. Blood count: leukocytes - 9, 8 · 109/l, ESR – 22 mm/h, γ-globulin - 22%. What is the most probable diagnosis?

A. Systemic lupus erythematosus

B. Systemic scleroderma

C. Rheumatoid arthritis

D. Dermatomyositis

E. Myxedema

4. A 13 year old girl was admitted to the cardiological department because of pain in the muscles and joints. Examination of her face revealed an edematic erythema in form of butterfly in the region of nose bridge and cheeks. What is the most probable diagnosis?

A. Periarteritis nodosa

B. Rheumatism

C. Dermatomyositis

D. Rheumatoid arthritis

E. Systemic lupus erythematosus

5. A 30-year-old patient presented with body temperature rise up to 38, 5oC, pain in the small articulations of hands; face edemata and erythema. In blood: RBCs - 2, 6 · 1012/l; Hb- 98 г/л; WBCs - 2 · 109/l; ESR - 58 mm/h. In the urine: protein - 3,1 g/l; RBCs - 10-15 in the vision field. What disease can be suspected in this case?

A. Systemic lupus erythematosus

B. Sepsis

C. Systemic scleroderma

D. Periarteritis nodosa

E. Acute glomerulonephritis

6. A 58-year-old patient complains about sensation of numbness, sudden paleness of II-IV fingers, muscle rigidness, intermittent pulse. The patient presents also with

polyarthralgia, dysphagia, constipations. The patient's face is masklike, solid edema of hands is present. The heart is enlarged; auscultation revealed dry rales in lungs. In blood: ESR - 20 mm/h, crude protein - 85/l, γ- globulines - 25%. What is the most likely diagnosis?

A. Rheumatoid arthritis
B. Dermatomyositis
C. Systemic scleroderma
D. Systemic lupus erythematosus
E. Raynaud's disease

7. A 32-year-old patient has a 3-year history of asthma attacks, that can be hardly stopped with berotec. Over a few last months he has experienced pain in the joints and sensitivity disorder of legs and feet skin. Ps - 80/min, AP - 210/100 mm Hg. In blood: eosinophilia at the rate of 15%. What disease can be suspected in this case?

A. Dermatomyositis
B. Systemic lupus erythematosus
C. Systemic scleroderma
D. Periarteritis nodosa
E. Wegener's disease

8. A 58-year-old patient complains about sensation of numbness, sudden paleness of II-IV fingers, muscle rigidness, intermittent pulse. The patient presents also with polyarthralgia, dysphagia, constipations. The patient's face is masklike, solid edema of hands is present. The heart is enlarged; auscultation revealed dry rales in lungs. In blood: ESR - 20 mm/h, crude protein - 85/l, γ- globulines - 25%. What is the most likely diagnosis?

A. Dermatomyositis
B. Systemic scleroderma
C. Rheumatoid arthritis
D. Systemic lupus erythematosus
E. Raynaud's disease

9. A 28-year-old female patient with a six-year history of Raynaud's syndrome has recently developed pain in the small joints of hands, difficult movement of food down the esophagus. What kind of disease can you think of in this case?

A. Systemic scleroderma
B. Periarteritis nodosa
C. Rheumatoid arthritis
D. Systemic lupus erythematosus
E. Pseudotrichiniasis

10. After a holiday in the Crimea, a 36-yearold female patient presents with severe pain in the elbow joints, dyspnea and weakness. The body temperature is of 37, 6oC, the skin is pale, there is erythema of cheeks and

nose, lower lip ulceration. Visual inspection reveals no changes in the joints, the right elbow movement is limited. There is murmur and pleural friction in the lungs below the right angle of the scapula. Cardiac sounds are muffled, there is tachycardia, gallop rhythm, Ps- 114/min. AP- 100/60. What is the most likely diagnosis?

A. Rheumatoid arthritis
B. Rheumatic heart disease
C. SLE
D. Infectious allergic myocarditis
E. Dry pleurisy

Answers

1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
D	A	B	E	A	C	D	B	A	C

TOPIC 8

1. Etiology of chronic gastritis type A:

A. H. pylori
B. NSAIDs
C. autoimmune
D. chemical damage
E. all answers are correct

2. H2-blockers include:

A. Famotidine
B. Itoprid
C. Pantoprazole
D. Clarithromycine
E. L-Carnitine

3. Prokinetics include:

A. Famotidine
B. Itopride
C. Pantoprazole
D. Clarithromycine
E. L-Carnitine

4. IPP include:

A. Famotidine
B. Itoprid
C. Pantoprazole
D. Clarithromycine
E. L-Carnitine

5. The most common etiological factor of peptic ulcer disease:

A. long-term NSAIDs intake
B. duodenogastral reflux
C. H. pylori infection
D. stress
E. smoking

6. The 48 years old patient complains of periodic pain in epigastrium, without irradiation, heartburn, which amplify after meals, migraine and sleeplessness.

After reception of 20 mg of rabeprazole during first two days these symptoms disappeared. For what disease this clinical picture is typical?

A. Type A chronic gastritis
B. Duodenal ulcer
C. Functional dyspepsia
D. Chronic pancreatitis
E. Chronic hepatitis

7. Patient P., 35 years old, complains of pressing epigastric pain in 1 hour after eating, heartburn, sour belch. He is considered to be ill during last 2 years. A pain in pyloroduodenal area presents upon the abdominal palpation. Upper endoscopy found an antral gastritis. What is the preliminary diagnosis?

A. Chronic gastritis
B. Duodenal ulcer
C. Functional dyspepsia
D. Chronic pancreatitis
E. Chronic hepatitis

8. A 33 y.o. male patient was admitted to a hospital. A patient is pale, at an attempt to stand up he complains of strong dizziness. There was vomiting like coffee-grounds approximately hour ago. BP- 90/60 mm Hg., pulse- 120 b/min. In anamnesis, a patient has suffered from ulcer of the stomach, painless form during 4 years. An ulcer was exposed at gastrofibroscopy. Your diagnosis:

A. Ulcer of duodenum, complicated with bleeding
B. Ulcer of stomach, complicated with bleeding
C. Erosive gastritis
D. Acute pleurisy
E. Acute myocardial infarction, abdominal

9. A 27 y.o. man complains of pain in epigastrium which is relieved by food intake. EGDF shows antral erosive gastritis, biopsy of antral mucous presents Helicobacter Pylori. What can be diagnosed in this case?

A. Rigid antral gastritis
B. Gastritis of A type
C. Reflux - gastritis
D. Menetrier’s disease
E. Gastritis of type B

10. A 35 y.o. woman consulted a doctor about occasional pains in paraumbilical and iliac region that reduce after defecation or passage of gases. Defecation takes place up to 6 times a day, stool is not solid, with some mucus in it. Appetite is normal, she has not put off weight. First such symptoms appeared 1,5 year ago, but colonoscopy data reveals no organic changes. Objectively: abdomen is soft, a little bit painful in the left iliac region. Blood and urine are normal. What is the preliminary diagnosis?

A. Irritable bowels syndrome
B. Celiac disease

C. Crohn's disease
D. Pseudomembranous colitis
E. Dispancreatism

Answers

1	2	3	4	5	6	7	8	9	10
C	A	B	B	C	C	A	B	E	A

TOPIC 9

1. Patient complains on nausea, pain in right hypochondrium, diarrhea, and frequent abdominal distension. In anamnesis: systematic alcohol consumption. Objective data: subnutrition, tongue covered with white film, belly is soft, sensitive to palpation in paraumbilical area. Liver and spleen are not enlarged. Feces analysis: steatorrhea, creatorhhea. What diagnosis of the listed below is the most probable one?

A. Chronic hepatitis
B. Helminthiasis
C. Chronic recurrent alcoholic pancreatitis
D. Chronic enterocolitis
E. Chronic cholecystitis

2. Patient complains on the pain in the epigastrium and left subcostal area; repeated vomiting which doesn‟t bring relief, abdominal distention, diarrhea, weight loss. Objective data: tongue is wet, covered with white film near the root. During profound belly palpation an insufficient painfulness is found in epigastrium and Mayo-Robson‟s point. What disease should you think of in the first turn?

A. Ulcer
B. Chronic atrophic gastritis
C. Chronic pancreatitis
D. Chronic cholecystitis
E. Chronic enteritis

3. A female patient has been suffering from chronic pancreatitis during previous 5 years. She complains on frequent watery excrements, loss of 12 kg during 2 months. What syndrome does the patient have?

A. Astheno-neurotic
B. Malabsorption
C. Dyspeptic
D. Pain
E. Epigastric

4. A woman, 32 years old, complains on the pain in the left hypochondrium emerging in 2 hours after meal, nausea, abdominal distention, tendency to diarrhea. Objective data: subicteric sclera,

painful belly during palpation in Gubergrits-Skulsky‟s point. The level of which enzymes should be determined?

A. Amylase
B. Lactate dehydrogenase
C. Creatine phosphokinase
D. Gammaglutamattranspeptidase
E. Aspartaaminotransferase

5. A patient complains on the pain in the upper right area of belly emerging in an hours after meal and irradiating to lumbus on the right side. During belly palpation there is painfulness in Chauffard‟s zone. What part of pancreas is damaged in this patient?

A. Head of pancreas
B. Body of pancreas
C. Tail of pancreas
D. Total pancreas damage
E. Focal damage

6. A patient with chronic pancreatitis has an increased level of blood serum glucose. What pancreatic function disorder does the patient have?

A. Exocrine
B. Endocrine
C. Absorption disorder
D. Acid-forming
E. Pepsinogenous

7. What hormones stimulate pancreatic activity?

A. Cholecystokinin-pancreozymin
B. Insulin
C. Thyrotropic
D. Counterinsular
E. Adrenalin

8. Which type of pancreatic juice secretion is the most typical for chronic pancreatitis?

A. Hyposecretory
B. Ductular
C. Upper obturative
D. Lower obturative
E. Hypersecretory

9. Which changes are typical for endocrine pancreatic insufficiency?

A. Jaundice
B. Nausea, vomiting
C. Hypoglycemic state, pancreatic diabetes development
D. Dyspeptic
E. Vitamin deficiency

10. Which clinic syndrome is associated with exocrine pancreatic disorder?

A. Pain
B. Maldigestion
C. Allergic
D. Epigastric
E. Right reactive vegetative

Answers

1	2	3	4	5	6	7	8	9	10
C	C	B	A	A	B	A	A	C	B

TOPIC 10

1. A 24-year-old female patient complains of pain in the right hypochondrium that is getting worse after taking meals; nausea, fever up to37,7oC, icteric skin, pain in the large joints. These presentations have been observed for 8 months. Objectively: hepatosplenomegaly. Blood test results: ESR- 47 mm/h, total bilirubin - 86,1 mmol/l, direct bilirubin - 42,3 mmol/l. Total protein - 62 g/l, albumins - 40%, globulins - 60%, gamma globulins - 38%. Viral hepatitis markers were not detected. The antibodies to smooth muscle cells are present. On ultrasound the portal vein diameter was of 1 cm. What is the most likely diagnosis?

A. Primary biliary cirrhosis
B. Autoimmune hepatitis
C. Gilbert's syndrome
D. Cholangiogenic hepatitis
E. Hemachromatosis

2. A 40 y. o. patient was admitted to the gasteroenterology department with skin itching, jaundice, discomfort in the right subcostal area, generalized weakness. On examination: skin is jaundice, traces of scratches, liver is +5 cm, spleen is 6x8 cm. In blood: alkaline phosphatase - 2,0 mmol/(hour*L), general bilirubin - 60 mkmol/L, cholesterol - 8,0 mmol/L. What is the leading syndrome in the patient?

A. Cytolytic
B. Cholestatic
C. Mesenchymal inflammatory
D. Asthenic
E. Liver-cells insufficiency

3. 23 years old patient has complaints on pain in the right subcostal area, periodic bitter belch, nausea, appetite loss. From the anamnesis: appendectomy had been conducted three years ago. In 2 months icterus appeared and patient was treated in infectious hospital. At the examination liver is enlarged on 2 cm. In blood: general bilirubin - 76 mkmol/l, direct bilirubin - 14,9 mkmol/, ALT - 1,35. What disease are you thinking of?

A. Cirrhosis of liver
B. Chronic cholangitis
C. Chronic cholecystitis
D. Benign Gilber`s icterus
E. Chronic hepatitis B

4. Patient K., 24 years old, complains of pain in the right subcostum and

joints, icteric skin, weight loss - 10 kg for a year, temperature 38°C. A disease began after childbirth half a year ago. Objectively: icteric skin and scleras, there are xanthomas on eyelids. Liver +4 cm, dense, painful, edge is sharp. Spleen +2 cm. Blood tests: AST - 2,8, ALT - 3,4, general bilirubin - 97,6, free - 54,6, HbsAg was not determined. Name the basic mechanism of pathogenesis:

A. Viral infection
B. Toxic damage of hepatocytes
C. Fatty dystrophy of liver
D. Violation of bile outflow
E. Autoimmune

5. 20 years old patient was diagnosed chronic viral hepatitis in gastroenterologic unit. What group of preparations can be included to the base therapy?

A. Hepatoprotector
B. Antibacterial
C. Anabolic steroid hormones
D. Vitamins
E. Glucocorticoids and cytostatic

6. Patient, 28 years old, has been contacting with toxic chemicals for 6 years. His complaints are headache, incresed fatigue, heavy feeling in the right subcostum, decreased appetite, icterus. Objectively: skin and scleras are subicteric. Abdomen is bloated, liver +5 cm, surface is even. In blood: Hb - 110 g/l, L - 8,1x109/l, blood sedimentation - 30 mm/h, general bilirubin - 65 mkmol/l, sugar - 6,3 mmol/l. What diagnosis is the most credible?

A. Hemochromatosis
B. Chronic toxic hepatitis
C. Chronic pancreatitis
D. Viral hepatitis
E. Benign hyperbilirubinemia

7. Woman, 37 years old, saw her doctor owing to the exacerbation of chronic hepatitis. Increased indirect bilirubin, AST, ALT levels and decreased protein and prothrombin levels were found in blood. What pathological process can stipulate these changes?

A. Cholestasis
B. Cytolysis
C. Portal hypertension
D. Hypersplenism
E. Violation of hemostasis

8. 39 years old patient complains of icterus, skin itching, nausea, pain in the right subcostum, especially after rich, fried food, increased body temperature in the evening, general weakness, hemorrhage of gums. He is ill for nearly two years. Skin and scleras are icteric, there are scratch tracks on the

skin and xanthelasmas on eyelids. Liver is increased on 4 cm. In the analyses there are hyperbilirubinemia at the expense of conjugated bilirubin, hypercholesterinemia, increased activity of alkaline phosphatase. What is the most reliable diagnosis?

A. Chronic cholestatic hepatitis
B. Chronic cholecystitis
C. Hemolytic anemia
D. Cholecystolithiasis
E. Cancer of pancreas head

9. The 28 y.o. woman applied to doctor because of limited loss of the hair. In the anamnesis - she had frequent headache indisposition, arthromyalgia, fever, irregular casual sexual life, drug user. RW is negative. What examination must be done first?

A. Examination for HIV
B. Examination for neuropathology
C. Examination for gonorrhea
D. Examination for fungi
E. Examination for trichomoniasis

10. 47 y.o. patient complains of intensive skin itching, jaundice, bone pain. The skin is hyperpigmentated. There are multiple xanthelasma palpebrae. The liver is +6 cm enlarged, solid with acute edge. The blood analysis revealed total bilirubin - 160 mkmol/L, direct - 110 mkmol/L, AST- 2,1 mmol/L, ALT- 1,8 mmol/L, alkaline phosphotase - 4,6 mmol/L, cholesterol9,2 mmol/L, antimitochondrial antibodies M2 in a high titer. What is the probable diagnosis?

A. Acute viral hepatitis B
B. Primary liver cancer
C. Chronic viral hepatitis B
D. Primary biliary liver cirrhosis
E. Alcoholic liver cirrhosis

Answers

1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
B	B	E	E	A	B	B	A	A	D

RECOMMENDED LITERATURE

Basic

1. Internal Medicine: in 2 books. Book 1. Diseases of the Cardiovascular and Respiratory Systems: textbook / N.M. Seredyuk, I.P. Vakaliuk, R.I. Yatsyshyn et al. Kyiv, Medicine., 2019. – 664 + 48 colored tabs (science editor: prof. Skrypnyk I.M.).

2. Internal medicine : Part 2 : textbook for English-speaking students of higher medical schools / edited by Professor M.A. Stanislavchuk and Professor V.K.Sierkova. – Vinnytsya : Nova Knyha, 2019. –360 p.

3. Pocket Guide to Global Strategy Initiative for Asthma, GINA, 2019 Review / Clinical Immunology. Allergology. Infectology. 2019. – No. 7 (120). – P.39-50.

4. Current Medical Diagnosis & Treatment (58 th edition). Authors: Maxine A. Papadakis, Stephen J. McPhee, Michael W. Rabow. Published by McGraw-Hill Education, 2018; 1904 pages.

5. Davidson's Principles and practice of medicine (23 rd edition). Editors: Stuart Ralston, Ian Penman, Mark Strachan, Richard Hobson. Published by Elsevier, 2018; 1440 pages.

6. Harrison's principles of internal medicine (20 th edition). Editors: J. Larry Jameson, Anthony S. Fauci, Dennis L. Kasper, Stephen L. Hauser, Dan L. Longo, Joseph Loscalzo. Published by McGraw-Hill Education, 2018; 2 volumes, 4100 pages.

7. The Merck Manual of Diagnosis and Therapy (20 th dition). Author: Robert S. Porter. Published by Merck Research Laboratories, 2018; 3530 pages.

Additional

8. Bates' Guide to Physical Examination and History Taking /Ed. Lynn S. Bickley, Peter G. zilagyi. – Wolters Kluwer, 2017. – 1066 p.

9. Kumar & Clark's Clinical Medicine, 8th edition / Edited by Parveen Kumar, Michael Clark. – Saunders Ltd. – 2012. – 1304 p. Clark. – Saunders Ltd. – 2012. – 1304 p.

10. Goldman's Cecil Medicine, 24th edition / Edited by Lee Goldman, Andrew I. Schafer. – Saunders Ltd. – 2011. – 2672 p.

11. Kaplan Medical USMLE Step 2 Clinical Knowledge Qbook, 5th edition/Edited by Kaplan inc. – Kaplan Publishing. – 2011. - 540 p.