Ministry of Education and Science of Ukraine
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Academic and Research Medical Institute

5603 Methodological instructions

for practical classes
on the subject **«Internal medicine»**
(module 3 «Modern practice of internal medicine»,
module 4 «Emergecies in internal medicine clinic»
for the students of speciality *222 «Medicine»*

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Internal medicine department with respiratory medicine center ARMI

Module 3
MODERN PRACTICE OF INTERNAL MEDICINE

Topic 1. MANAGEMENT OF PATIENS WITH ARTERIAL HYPERTENSION

Time frame – 6 hours.

Professional motivation. Individuals with a systolic BP of 120 to 139 mm Hg or a diastolic BP of 80 to 89 mm Hg should be considered as prehypertensive and require health-promoting lifestyle modifications to prevent cardiovascular disease. The prevalence of hypertension increases with age and most individuals with hypertension are diagnosed with primary (essential) hypertension. Hypertension occurs in 10–20% of persons aged 25 to 45 years and 30–40% of persons aged 55 to 74 years. Although it is a "silent" disease, these patients usually have no specific symptoms, hypertension is posed as a major risk factor for coronary artery disease (heart attack), cerebrovascular disease (stroke), and renal disease (kidney failure). It is the second most common reason for office visits to physicians in the United States. Analysis of the Framingham study data suggested that individuals aged 40 to 69 years have an increasing risk of stroke or coronary artery disease mortality with every 20 mm Hg increment in systolic blood pressure. On the other hand, a recent Cochrane review revealed that aiming for blood pressure targets lower than 140/90 mm Hg is not beneficial, as it is not proven that this approach will reduce heart attack and stroke.

There are 2 categories of hypertension. Over 90% of all cases of high blood pressure are called *"essential hypertension"*, which has no specific identifiable cause but is due to the body inability to regulate the blood pressure within the normal range – SBP 120–140 mm Hg / DBP 60–85 mm Hg. Onset is usually between ages 30 and 50 years. Essential hypertension is treated with medication, diet, and fluid restriction and is not curable. *"Secondary hypertension"*, on the other hand, is high blood pressure that has an identifiable cause, occurs in a wide age range, is severe, and is abrupt in onset. Secondary hypertension is potentially curable because it is most commonly caused by *stenosis* of the renal arteries. Less often, secondary hypertension can be caused by tumours of the adrenal gland that secrete hormones acting to increase the blood pressure.

Place of carrying out: class-room, wards of the cardiology department, ward of the emergency, department of functional diagnostics.

Study objective: to be able to put provisional diagnosis and assign management.

Basic level:

1. Mechanism of blood pressure regulation.
2. To be able to collect complaints, case history, carry out objective examination. Methods of blood pressure measurement.
3. To interpret instrumental and laboratory data in patients with arterial hypertension.
4. To discover signs inherent to AH.
5. To interpret side effects of antihypertensive drugs. To use diet for AH correction.

Student has to know how to examine patients with cardiovascular disorders.

The main theoretical questions:

1. Definition of arterial hypertension. Essential AH. Secondary AH.
2. Epidemiology and classification of the arterial hypertension.
3. Rick factors for arterial hypertension.
4. Complications in arterial hypertension.
5. Observantional program of the persons with arterial hypertension.
6. Differential diagnosis of arterial hypertension: essential and secondary (renal, endocrine, hemodynamic, central, etc.).
7. General principles of antihypertensive therapy:
    a) recommendations on lifestyle modification;
    b) the general measures employed;
    c) risk factors for an adverse prognosis in hypertension.
8. Recommendations of the European Society of Hypertension for AH treatment.
9. Approach to drug therapy. Antihypertensive "step by step" therapy.

10. Antihypertensive drugs: diuretics, ß-adrenergic blocking agents, angiotensin-convetrting enzyme inhibitors, angiotensin receptor antagonists, calcium channel antagonists, α-adrenergic receptor blockers.

11. Drug combinations.

12.Treatment in AH adjusted to ethnicity, age, pregnancy, concomitant diseases and complications (renal disease, coronary artery disease, diabetes mellitus, obesity).

13. Risk stratification of cardiovascular complications and determination of prognosis.

Assignment for self-assessment

1. What laboratory tests are included to the hypertension management program?

2. At a routine company physical examination, an asymptomatic 46-year-old man is found to have a BP of 150/110 mm Hg, but no other abnormalities are present. What should be done next?

Answers:

1. Urine for protein, blood, and glucose; microscopic urinalysis; serum creatinine and/or blood urea nitrogen; total cholesterol.

2. Obtain repeated BP recording in your office and/or the patient's home or work site.

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Topic 2. MANAGEMENT OF PATIENS WITH SECONDARY ARTERIAL HYPERTENSION

Time frame – 6 hours.

Professional motivation. The most common cause of secondary hypertension is renal artery stenosis. The most common cause of narrowing is atherosclerosis. Blockage of the renal arteries causes the kidney to increase production of the hormone renin. Increased levels of renin in the body cause a cascade of events to occur that result in peripheral vasoconstriction and fluid retention, causing an increase in blood pressure. Overall, about two thirds of cases of renovascular hypertension are caused by atherosclerosis and one third by fibromuscular dysplasia. Atherosclerosis is more common among men > 50 and affects mainly the proximal one third of the renal artery. Fibromuscular dysplasia is more common among younger patients (usually women) and usually affects the distal two third of the main renal artery and the branches of the renal arteries. Rarer causes include emboli, trauma, inadvertent ligation during surgery, and extrinsic compression of the renal pedicle by tumours.

Renovascular hypertension is characterized by high cardiac output and high peripheral resistance.

Renovascular hypertension is usually asymptomatic. A systolic-diastolic bruit in the epigastrium, usually transmitted to one or both upper quadrants and sometimes to the back, is almost pathognomonic, but it is present in only about 50% of patients with fibromuscular dysplasia and is rare in patients with renal atherosclerosis.

Renovascular hypertension should be suspected if diastolic hypertension develops abruptly in a patient < 30 or > 50; if new or previously stable hypertension rapidly worsens within 6 mo; or if hypertension is initially very severe, associated with worsening renal function, or highly refractory to drug treatment.

Approximately 5% of patients with hypertension have specific causes. The case history, examination, and routine laboratory tests may identify such patients. Endocrine hypertension accounts for approx. 3% of the secondary forms of hypertension and is a term assigned to states in which hormonal derangements result in clinically significant hypertension. The most common causes of endocrine hypertension are excess production of mineralocorticoids (i.e., primary hyperaldosteronism – 0.3–1.5%), catecholamines (pheochromocytoma – 0.1–0.3%), thyroid hormone, and glucocorticoids (Cushing's syndrome). One important question in this regard is when to screen for secondary causes. The clinician should carefully screen for other cardinal signs and symptoms of Cushing's syndrome, hyper- or hypothyroidism, acromegaly, or pheochromocytoma. Hypertension in young patients and refractory hypertension (characterized by poorly controlled blood pressure on > 3 antihypertensive drugs) or those previously well controlled who become refractory to treatment should alert the physician to screen for secondary causes.

The importance of endocrine mediated hypertension resides in the fact that in most cases, the cause is clear and can be traced to the actions of a hormone, often produced in excess by a tumour such as an aldosteronoma in a patient with hypertension due to primary aldosteronism. More importantly, once the diagnosis is made, a disease-specific targeted antihypertensive therapy can be implemented, and in some cases, surgical intervention may result in complete cure, obviating the need for life-long antihypertensive treatment.

Pheochromocytomas are uncommon; they are probably found in less than 0.1% of all patients with hypertension and in approximately two individuals per million population. In about 50% of patients with pheochromocytoma, hypertension is sustained but the blood pressure shows marked fluctuations, with peak pressures during symptomatic paroxysms. In about one-third of cases, hypertension is truly intermittent. In some cases, hypertension is absent.

It now appears that up to 5–15% of patients in whom primary (essential) hypertension is diagnosed actually have primary hyperaldosteronism, with most having normal serum potassium levels.

Place of carrying out: class-room, wards of nephrology, endocrinology.

Study objective: to improve the skills in management of patients with arterial hypertension in endocrine and renal diseases.

Basic level:

1. Student should be able to collect complaints, case history, carry out objective examination of patients with arterial hypertension.
2. To interpret instrumental and laboratory data in patients with arterial hypertension.
3. Mechanism of action, pharmacology/pharmacokinetics, side effects of antihypertensive drugs.
4. Anatomy and physiology of suprarenal gland.
5. Pathogenesis of the main clinical symptoms in acromegaly.
6. Pathogenesis of the main clinical symptoms in hyperaldosteronism (Conn's syndrome).
7. Pathogenesis of the main clinical symptoms in Cushing's syndrome.
8. Pathogenesis of the main clinical symptoms in hypo- or hyperthyroidism.
9. To interpret clinical, laboratory, and instrumental data in endocrine hypertension.
10. To find out data inherent to endocrine hypertension.

Student has to know:

1. Diseases which are accompanied by secondary arterial hypertension.
2. How to make program for investigation when evaluating a patient with arterial hypertension.
3. How to differentiate diseases with arterial hypertension.

4. How to put presumptive diagnosis, to prescribe dietary, medical treatment for the patients with renal hypertension.

5. How to make program for investigation when evaluating a patient with suspected endocrine-related hypertension.

6. Differential diagnosis of endocrine hypertension (pheochromocytoma, acromegaly, Cushing's syndrome, diabetes mellitus).

The main theoretical questions:

1. Clinical, laboratory, and instrumental diagnostic methods for revealing renal hypertension.
2. Pathogenesis of renal hypertension.
3. Classification of renal hypertension.
4. Clinical manifestation of renal hypertension.
5. Complications in renal hypertension and their pathogenesis.
6. Management of patients with renal hypertension.
7. Diagnosis and treatment of AH in acromegaly, hyperaldosteronism, Cushing's syndrome, hypo- or hyperthyroidism, pheochromocytoma.
8. Clinical findings, diagnosis, and emergency care in Addison's crisis.
9. Clinical findings, diagnosis, and emergency care in pheochromocytoma crisis.
10. Evidence-based treatment of secondary arterial hypertension

Assignment for self-assessment

1. The triad headache, palpitations, and sweating in a hypertensive patient was found to have a sensitivity of 91% and specificity of 94% for:

a) pheochromocytoma;
b) hyperaldosteronism;
c) Cushing's syndrome;
d) acromegaly.

2. There are several mechanisms of blood pressure elevation in Cushing's syndrome with the exception of:

a) increased hepatic production of angiotensinogen and cardiac output by glucocorticoids;
b) reduced production of prostaglandins via inhibition of phospholipase A;
c) increased insulin resistance;
d) oversaturation of 11beta-HSD activity with increased mineralocorticoid effect through stimulation of the mineralocorticoid receptor;
e) increased peripheral resistance.

3. Screening studies for Cushing's syndrome include: a) measuring 24-h urinary free cortisol excretion on at least 2 occasions; b) performing 1 mg dexamethasone suppression test; c) checking a midnight salivary cortisol and diurnal rhythm of cortisol secretion; d) stress excersise test.

4. A 37-year-old women was admitted to the hospital with such symptoms: rounded "moon" feaces with a plethoric appearance; truncal obesity with prominent supraclavicular and dorsal cervical fat pads; the distal extremities and fingers are usually quite slender; muscle wasting and weakness are present. The skin is thin and atrophic, with poor wound healing and easy bruising. Purple striae appear on the abdomen. Blood pressure is 165/100 mm Hg. Menstrual irregularities and hypertrichosis.

What is your primary diagnosis? Management.

5. A 40-year-old man with paroxysmal hypertension was admitted to the hospital. Tachycardia attack, tachypnoea, flushing, cold and clammy skin, severe headache, palpitation, nausea, vomiting, visual disturbances, dyspnoea, paresthesias occurred. Paroxysmal attacks are provoked by palpation of the abdomen or after emotional trauma.

What is your primary diagnosis? Management.

6. The best screening tests for primary hyperaldosteronism involve determinations of: a) plasma aldosterone concentration (normal: 1–16 ng/dL) and plasma renin activity (normal: 1–2.5 ng/mL/h); b) calculation of the plasma aldosterone/renin ratio (normal: < 25); c) plasma prostaglandins concentration.

Answers:

1. a. 2. e. 3. a, b, c.

4. Cushing's syndrome. Adrenal inhibitors such as metyrapone, mitotane, and aminoglutethimide may be used to control severe metabolic disturbances resulting from hyperfunction of the adrenal cortex. Probably surgery.

5. Pheochromocytoma. Treatment includes surgical removal of the tumour. It is usually possible to delay surgery until the patient is in optimum physical condition by the use of combination of a- and b-adrenergic blocking agents.

6. a, b.

Assignment for self-assessment

1. The "gold standard" (the definitive test) in diagnosis of renal artery stenosis is:
   a) arteriography;
   b) duplex ultrasonography;
   c) radionuclide imaging.
2. Renovascular hypertension should be suspected if:
   a) diastolic hypertension develops abruptly in a patient < 30 or > 50;
   b) new or previously stable hypertension rapidly worsens within 6 months;
   c) hypertension is initially very severe, associated with worsening renal function;
   d) hypertension is highly refractory to drug treatment;
   f) all of the above signs are correct.
3. A class of drugs that cause vasodilation and are used to treat hypertension and heart failure:
   a) ACE inhibitors;
   b) glycosides;
   c) potassium and sodium channel blockers (amiodarone).
4. Adverse effect of all ACE inhibitors:
   a) retention of potassium;
   b) retention of sodium;
   c) hypokalaemia;
   d) retention of catecholamine.
5. ACE inhibitors should be used with caution in patients with:
   a) aortic valve stenosis or cardiac outflow obstruction;
   b) congestive heart failure;
   c) prevention of nephropathy in diabetes mellitus.
6. The most common cause of renal artery stenosis is:
   a) atherosclerosis;
   b) increased production of the hormone rennin;
   c) extrinsic compression of the renal pedicle by tumours.

Answers:

1. a. 2. f. 3. a. 4. a. 5. a. 6. a.

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Topic 3. MANAGEMENT OF PATIENS WITH CARDIALGIA.

Time frame – 6 hours.

Professional motivation. The prevalence of chest pain or chest discomfort varies in different parts of Europe. In a British study of 7735 men, angina pectoris or a history of possible acute myocardial infarction (AMI) was reported in 14% and a further 24% suffered from atypical chest pain. The underlying cause of chest pain varies depending on whether a patient is seen by a general practitioner, calls the dispatch centre, is treated by the ambulance crew or is seen at the emergency department. Not unexpectedly, chest pain of cardiac origin is less commonly seen by the general practitioner (20%), whereas musculoskeletal disorders are common. A summary of prospective studies in general practices in the Netherlands, in England, and in Iceland shown that most of the episodes were caused by musculoskeletal problems and only about 20% were of cardiac origin. Patients with chest pain without a somatic diagnosis often suffer from psychiatric problems such as anxiety, depression or alcohol abuse.

The ischaemic origin of calls about chest pain is much more frequent at dispatch centres. About 25% of all emergency calls to a dispatch centre are initiated because of chest pain. Among such patients, 40% are reported to have confirmed myocardial ischaemia or infarction, and 66% either confirmed or possible myocardial ischaemia or infarction as the cause of their pain. Patients with acute myocardial infarction who call for an ambulance are different from those who do not. They are older, more likely to be female and have a higher prevalence of previous cardiovascular disease and more severe symptoms. They develop more complications and present a higher risk of cardiac arrest and death. The number and proportion of hospital admissions for chest pain vary. Data from the U.S. showed that 20% of all nonsurgical admissions are for chest pain, in patients with chest pain 17% ultimately met the criteria for cardiac ischaemia and 8% had myocardial infarction. Overall, a similar proportion of men and women seek medical care due to non-ischaemic chest pain. In some subsets such as patients with chest pain due to psychiatric causes there might be an over-representation of women. Patients with non-ischaemic chest pain also have a lower prevalence of various risk indicators, such as a history of previous acute myocardial infarction, angina pectoris, hypertension, and diabetes. Smoking is more frequent in this patient population. There are different types of non-ischaemic causes of chest pain: reflux oesophagitis, oesophageal spasm, pulmonary embolism, spontaneous pneumothorax, aortic dissection, pericarditis, pleuritis, early herpes zoster, peptic ulcer, cholecystitis, pancreatitis.

IHD is the leading cause of mortality in the developed world; it is responsible for more than 20% of deaths. IHD is the leading cause of death in the United States for both sexes in both white and black populations. The prevalence of IHD increases with age and is higher in men than in women in every age group. The American Heart Association (AHA) conservatively estimates that more than 6 million persons in the United States experience angina. In addition to posing an increased risk of MI and premature death, chronic stable angina often limits affected persons' capacity for work and other activities, which, in turn, negatively affects their quality of life. The direct and indirect costs of hospitalization, diagnostic procedures, and revascularization related to angina are substantial. Of patients with angina who undergo a coronary revascularization procedure, 30% or more never return to work.

The major modifiable risk factors for IHD are dyslipidemias – in particular, elevated levels of low-density lipoprotein (LDL) cholesterol and low levels of high-density lipoprotein (HDL) cholesterol – as well as hypertension, diabetes mellitus, and cigarette smoking.

Place of carrying out: class-room, wards of the cardiology and rheumatology departments, department of functional diagnostics, X-ray department.

Study objective: to be able to determine extent of examinations to put final diagnosis and assign management.

Basic level:

1. To be able to collect complaints, case history, carry out objective examination.
2. To interpret instrumental (ECG, EchoCG, X-ray) and laboratory data in patients with chest pain.
3. To identify signs from anamnesis and objective data inherent to cardialgia of different origin.
4. To interpret side effects of antianginal agents. To use physiotherapeutic procedures and diet for correction of chest pain related to diseases of musculoskeletal system, oesophagus, abdominal cavity organs.

Student has to be able to:

1. Examine patients with cardiovasculal disorders.
2. Make an algorithm of investigations in patients with cardialgia.
3. Determine approaches to treatment in different aetiology of cardialgia.

The main theoretical questions:

1. Aetiology of cardialgia. The main pathogenetic mechanisms in cardialgia development.
2. Clinical signs of cardialgia depending on aetiology: in coronary diseases, in neurocirculatory dystonia, in pericarditis, myocarditis, valvular disorders, lung and pleural diseases, in oesophageal and abdominal organs pathology, in aortic aneurism.
3. An algorithm for the diagnosis of acute chest pain.
4. Management of patients with different aetiology of cardialgia.
5. The main drugs for treatment of functional disorders of cardiovascular system.
6. The main drugs for treatment of noncoronary myocardium diseases.

Assignment for self-assessment

1. A 44-year-old woman is presenting with prolonged stabbing chest pain on the left from sternum, dizziness, paresthesia, general sweating, sleeplessness. She's sick for a year. The examination reveals emotional lability, a regular heart rate with a systolic murmur above heart apex. Blood pressure is 120/80 mm Hg; pulse is 88 beats/min, regular, respiratory rate is 16 breaths/min. Her lungs are clear. The abdomen is soft without tenderness or distention. The liver spans 10 cm in the midclavicular line with a smooth edge. There is no peripheral oedema, pulse is intact. Her weight is 84 kg, height is 176 cm. She is afebrile. On ECG: sinus rhythm, negative T-waves in V1-V4 leads which disappear (T-waves become positive) after potassium or propranolol test. Suggested diagnosis is:

a) dishormonal cardiomyopathy;
b) IHD: stable angina, FCII;
c) infective myocarditis;
d) rheumocarditis.

2. A 28-year-old man is presenting with chest pain, palpitations, and dyspnoea after adenoviral infection. Examination revealed pale skin, acrocyanosis, a regular weakened heart beats, cardiac borders expanded to the left and to the right. Blood pressure is 90/60 mm Hg; pulse is 92 beats/min, respiratory rate is 20 breaths/min. His lungs are clear. The abdomen is soft without tenderness or distention. The liver spans 10 cm in the midclavicular line with a smooth edge. There is no peripheral oedema. On ECG: decreased voltage of R-waves, PQ 0.22 sec. Suggested diagnosis is:

a) viral myocarditis;
b) infective endocarditis;
c) rheumatic myocarditis;
d) exudative pericarditis;
e) dilated cardiomyopathy.

Answers: 1. a. 2 a.

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Topic 4. MANAGEMENT OF PATIENS WITH HEART RHYTHM DISORDERS

Time frame – 6 hours.

Professional motivation. Supraventricular arrhythmias are relatively common, often repetitive, occasionally persistent, and rarely life-threatening. The precipitants of supraventricular arrhythmias vary with age, gender, and associated comorbidity. While supraventricular arrhythmias are a frequent cause of emergency room and primary care physician visits, they are infrequently the primary reason for hospital admission.

The estimated prevalence of paroxysmal supraventricular tachycardia (PSVT) in a 3.5% sample of medical records in the Marshfield (Wisconsin, the USA.). Occurrence rates have been determined for various subtypes of supraventricular arrhythmia after acute myocardial infarction or coronary artery bypass graft surgery and in congestive heart failure (CHF) patients. The incidence rate of supraventricular arrhythmias among patients with CHF is 11.1%; paroxysms are more common in older patients, males, and those with longstanding CHF and radiographic evidence of cardiomegaly.

The only reported epidemiologic study of patients with atrial flutter involved a selected sample of individuals treated in the Marshfield Clinic in predominantly white, rural mid-Wisconsin. Over 75% of 58,820 residents and virtually all health events were included in this population database. In approximately 60% of cases, atrial flutter occurred for the first time associated with a specific precipitating event (i.e., major surgery, pneumonia, or acute myocardial infarction). In the remaining patients, atrial flutter was associated with chronic comorbid conditions (i.e., heart failure, hypertension, and chronic lung disease). Only 1.7% of cases had no structural cardiac disease or precipitating cause (lone atrial flutter). The overall incidence of atrial flutter was 0.088%; 58% of these patients also had AF. Atrial flutter alone was seen in 0.037%. The incidence of atrial flutter increased markedly with age, from 5 per 100000 of those more than 50 years old to 587 per 100 000 over age 80. Atrial flutter is 2.5 times more common in men.

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, occurring in 1–2% of the general population. AF confers a 5-fold risk of stroke, and one in five of all strokes is attributed to this arrhythmia. Ischaemic strokes in association with AF are often fatal, and those patients who survive are left more disabled by their stroke and more likely to suffer a recurrence than patients with other causes of stroke. In consequence, the risk of death from AF-related stroke is doubled and the cost of care is increased 1.5-fold. AF may long remain undiagnosed (silent AF), and many patients with AF will never present to hospital. Hence, the “true” prevalence of AF is probably closer to 2% of the population. The prevalence of AF increases with age, from < 0.5% at 40–50 years, to 5–15% at 80 years. Men are more often affected than women. The lifetime risk of developing AF is 25% in those who have reached the age of 40.

Apart from stroke, AF is associated with increased rates of death, heart failure and hospitalizations, degraded quality of life, reduced exercise capacity, and left ventricular (LV) dysfunction. Only antithrombotic therapy has been shown to reduce AF-related deaths. Stroke in AF is often severe and results in long-term disability or death. Approximately every fifth stroke is due to AF; furthermore, undiagnosed “silent AF” is a likely cause of some “cryptogenic” strokes. Paroxysmal AF carries the same stroke risk as permanent or persistent AF.

Hospitalizations due to AF account for one-third of all admissions for cardiac arrhythmias. Acute coronary syndrome (ACS), aggravation of heart failure, thromboembolic complications, and acute arrhythmia management are the main causes. Cognitive dysfunction, including vascular dementia, may be related to AF. Small observational studies suggest that asymptomatic embolic events may contribute to cognitive dysfunction in AF patients in the absence of an overt stroke.

Ventricular arrhythmias include premature ventricular contraction, ventricular tachycardia, and ventricular fibrillation. Both of last are life-threatening arrhythmias most commonly associated with heart attacks. The most serious arrhythmia is ventricular fibrillation, which is an uncontrolled, irregular beat. If cardiopulmonary resuscitation (CPR) can be started, or if electrical energy is used to "shock" the heart back to a normal rhythm, then the heart may not be too damaged. About 220,000 deaths from heart attacks each year are thought to be caused by ventricular fibrillation. People who have heart disease or a history of heart attack have the highest risk of ventricular fibrillation.

A less serious type of ventricular arrhythmia is a premature ventricular contraction (PVC). PVCs generally are not a cause for alarm and often do not need treatment. But if patient has heart disease or a history of ventricular tachycardia, PVCs can cause a more serious arrhythmia.

The incidence of ventricular tachycardia (VT) in the United States is not well quantified because of the clinical overlap of VT with ventricular fibrillation (VF). Examination of sudden death data provides a rough estimate of VT incidence. Most sudden cardiac deaths are caused by VT or VF, at an estimated rate of approximately 300,000 deaths per year in the United States, or about half of the estimated cardiac mortality in this country. A prospective surveillance study gave a sudden death incidence of 53 per 100,000, accounting for 5.6% of all mortality. This is only a rough estimate of VT incidence, because many patients have nonfatal VT and because arrhythmic sudden deaths may be associated with VF or bradycardia rather than with VT. VT is observed more frequently in men, because ischaemic heart disease is more prevalent among men. In patients with ischaemic cardiomyopathy and nonsustained VT, sudden death mortality rates approach 30% in 2 years.

Place of carrying out: class-room, wards of the cardiology, department of functional diagnostics.

Study objective: to be able to verify supraventricular, ventricular extrasystole and extrasystole from AV-node, to distinguish fibrillation from atrium and ventricles, preexictation syndrome on ECG.

Basic level:

1. To be able to collect complaints, case history, carry out objective examination.
2. To be able to register ECG. ECG classification of the rhythm disorders.
3. Electrophysiology of the heart.
4. To interpret instrumental and laboratory data in patients with arrhythmias.
5. To interpret side effects of antiarrhythmic drugs. Preventive measures against arrhythmia development.

Student has to know:

1. Diseases which are accompanied by arrhythmias.
2. How to make algorithm of investigations in arrhythmias.
3. How to differentiate arrhythmias by clinical signs.

The main theoretical questions:

1. ECG classification of rhythm disorders.
2. Sinus tachycardia, sinus bradycardia. Clinical signs, ECG signs, management.
3. Extrasystoles, clinical signs, ECG signs, management.
4. Supraventricular tachycardias. ECG signs.
5. Management in paroxysmal tachycardias.
6. Ventricular paroxysmal tachycardias. ECG signs.
7. Management in paroxysmal ventricular tachycardias.
8. Atrial fibrillation and flutter. ECG signs. Management.
9. ECG signs of the preexcitation syndromes.

10. Ventricular arrhythmias related to specific pathology (MI, cardiomyopathy, valvular heart diseases). Device therapy.

Assignment for self-assessment

1. 34-year-old patient with sudden onset of fatigue, and palpitation addressed to the doctor's office. On ECG: presence of frequent and regular P waves and QRS complexes. What rhythm disorder has occured and what drug will you select for treatment?

2. A 52-year-old man arrived to the emergency room with irregular tachycardia, ventricular rate of 250/min, blood pressure of 80/60 mm Hg, and prolonged QRS complexes. It is known he has the Wolff-Parkinson-White syndrome. What medicines should be used for immediate management?

3. Negative P waves were registered on ECG in the II and III standard leads, QRS complexes are not changed and go after P waves. Pacemaker is located in:

a) sinus node;
b) AV node;
c) ventricles;
d) inferior part of the atrium;
e) everything is wrong.

Answers:

1. Paroxysmal superventricular tachycardia; verapamil will terminate over 90% of paroxysmal superventricular tachycardia.

2. Wolff-Parkinson-White syndrome is potentially life-threatening when the anomalous atrioventricular connection has a short refractory period and is capable of rapid atrioventricular conduction. Very rapid ventricular rates can produce cardiovascular collapse or precipitate ventricular fibrillation. Atrial fibrillation should be terminated immediately with cardioversion.

3. d.

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Topic 5 MANAGEMENT OF PATIENS WITH HEART CONDUCTION DISORDERS

Time frame – 6 hours.

Professional motivation. The exact incidence of sinus node dysfunction (SND) is unknown. The syndrome occurs in approximately one in 600 cardiac patients older than 65 years. Symptoms of SND almost invariably progress over time. The most dramatic symptom in patients with SND is syncope. About 50% of patients with SND develop tachy-brady syndrome over a lifetime; such patients have higher risk of stroke and death. The survival of patients with SND appears to depend primarily on the severity of underlying cardiac disease and is not significantly changed by pacemaker therapy.

Men and women are affected in equal numbers. SND may occur at any age but is primarily a disease of the elderly, with the average age being about 68 years old. SND in young patients is often related to underlying heart diseases.

Sick sinus syndrome describes abnormalities caused by the malfunction of the heart's natural pacemaker (sinoatrial node) when symptoms such as dizziness or fainting (syncope) are present. Possible complications of sick sinus syndrome include inadequate or inefficient pumping of the heart, heart failure, exercise intolerance, and injuries sustained by fainting spells and falling. Complications may develop from surgery to implant pacemakers, including infection, reaction to

medications or anaesthesia, and pacemaker failure. Sick sinus syndrome progresses slowly. No treatment is necessary as long as the individual is not experiencing symptoms. Even with a permanent artificial pacemaker, the long-term prognosis is excellent.

AV blocks occur more frequently in people older than 70 years, especially in those who have structural heart disease. Approximately 5% of patients with heart disease have first-degree AV block, and about 2% have second-degree AV block.

The incidence of AV block increases with age. The incidence of third-degree AV block is highest in people older than 70 years (approximately 5–10% of patients with heart disease). A 60% female preponderance exists in congenital third-degree AV block. For acquired third-degree AV block, a 60% male preponderance exists. No racial proclivity exists in AV blocks.

First-degree AV block can be found in healthy adults. At 20 years of age, the PR interval may exceed 0.20 seconds in 0.5–2% of healthy people. At age 60 years, more than 5% of healthy individuals have PR intervals exceeding 0.20 seconds.

Advanced AV block (usually type II second-degree and third-degree) is usually anatomically infranodal and is seen in advanced His-Purkinje disease. One study examined the prevalence of His-Purkinje disease in the Framingham population. Here, QRS intervals of > 0.12 seconds were significantly associated with coronary heart disease, CHF, AV block, hypertension, left ventricular hypertrophy, and ventricular extrasystoles. QRS intervals > 0.12 seconds were rare before 50 to 60 years of age and were found in 11% of older men and 5% of older women. While intraventricular block does not inevitably lead to AV block, it frequently precedes the development of advanced AV block. Thus, this characterisation of a wide-QRS interval population is likely similar to that of the advanced AV block population.

Mobitz II second-degree AV block (Mobitz II) is rare in healthy individuals, whereas Mobitz I (Wenckebach) second-degree AV block is observed in 1–2% of healthy young people, especially during sleep.

Congenital third-degree AV block is rare, at 1 case per 20,000 births. This form of heart block, in the absence of major structural abnormalities, is associated with maternal antibodies to Ro (SS-A) and La (SS-B) and secondary to maternal lupus. It is most commonly diagnosed between 18 and 24 weeks' gestation and may be first, second, or third degree (complete). Mortality approaches approximately 20%; most surviving children require pacemakers.

Patients treated with permanent pacing to treat AV blocks have an excellent prognosis. Patients with advanced AV blocks who are not treated with permanent pacing remain at high risk of sudden cardiac death.

The Reykjavik Study, a long-term prospective cardiovascular survey, which included a representative population of 9135 men and 9627 women, 33–79 years old, revealed that Right bundle branch block (RBBB) was found in 126 men and 67 women. The prevalence increased with age, from 0% among men and women 30–39 years of age to 4.1% and 1.6% in men and women, respectively, who were 75–79 years old. In men younger than 60 years RBBB had a significant relationship with hypertension, elevated fasting blood glucose, and increased heart size. In men with RBBB regardless of age, an association was found with cardiomegaly, ischaemic heart disease, arrhythmias, and bradycardia (P<005). A higher mortality from heart disease was found in men with RBBB compared to the control population. RBBB in women younger than 60 years is often associated with hypertension.

Place of carrying out: class-room, wards of the cardiology, department of functional diagnostics.

Study objective: to be able to verify different types of blocks, management of patients.

Basic level:

1. Anatomy and physiology of the cardiac conduction system.
2. To be able to collect complaints, case history, carry out an objective examination.
3. To be able to register ECG.
4. To interpret instrumental and laboratory data in patients with blocks.
5. To interpret side effects of drugs which are used in blocks.

Student has to know:

1. Diseases which are accompanied by blocks.
2. How to make algorithm of investigations in blocks.
3. Indications for pacemaker implantation: single-chamber and dual-chamber pacemaker.

The main theoretical questions:

1. Sinoatrial blocks. Causes, ECG signs. Treatment.
2. Intraatrial blocks, ECG signs.
3. Atrioventricular block. ECG signs. Treatment.
4. Adams-Stokes attacks. Diagnosis. Emergency.
5. Bundle branch blocks. Causes. Diagnosis. Classification: right bundle branch block. Block of the left branch of the bundle of His. Anterior/posterior fascicle of the left branch of His bundle.
6. Sinus node dysfunction. The sick sinus syndrome. Causes, ECG signs, treatment.
7. External defibrillation and cardioversion. Temporary/permanent pacemakers.

Assignment for self-assessment

1. A 63-year-old woman was admitted to the coronary care unit with palpitation, weakness and after short period of loss of consciousness. She indicates on impairment of state for about 4 months. Her pulse is 52 per min, arrhythmical, no murmur sounds. On ECG: sinus and irregular rhythm, PQ interval – 0.2 sec, QRS complexes – 0.08, gradual increase R-R interval with subsequent PQRST dropout. What is the reason of such state?

a) sinoatrial block;
b) AV-block, type I;
c) block of 3 fascicles of His bundle;
d) AV-block, type II.

2. The ECG examination of the 32-year-old male shows the PR interval of conducted beats is normal but some P waves are not conducted. What type of block is it? What is the management of this disorder?

3. A type of AV block characterised by progressive lengthening of the PR interval until the P wave fails to conduct is:

a) second degree AV-block: Mobiz type II;
b) second degree AV block: Mobiz type I;
c) first degree AV block;
d) third degree block.

4. Rhythms required permanent pacing in patients with cardiac disorders include:

a) supraventricular tachycardia;
b) second-degree AV block: Mobiz type I;
c) complete heart block;
d) Wolf-Parkinson-White syndrome.

Answers:

1. a.
2. Mobitz type II second degree AV block. A permanent pacemaker is indicated.
3. b. 4. c.

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Topic 6. MANAGEMENT OF PATIENS WITH CHRONIC CORONARY SYNDROME

Time frame – 6 hours.

Professional motivation. Stable angina is the initial manifestation of ischaemic heart disease in approximately 50% of these patients. The prevalence of angina in community studies increases sharply with age in both sexes from 0.1–1% in women aged 45–54 to 10–15% in women aged 65–74 and from 2–5% in men aged 45–54 to 10–20% in men aged 65–74. Therefore, it can be estimated that in most European countries, 20,000–40,000 individuals of the population per million suffer from angina.

According to the Framingham Heart Study, the lifetime risk of developing coronary artery disease at the age of 40 is 49% in men and 32% in women while the risk at 75 years of age is 35% in men and 24% in women. During 26 years of follow-up in the Framingham Heart Study, 80% of women under 75 years of age presented with angina pectoris rather than myocardial infraction. In contrast, only 20% of men presented with angina pectoris as their first manifestation.

Patients with stable angina are at risk of ACS developing: unstable angina, non-ST-elevation MI or ST-elevation MI. Data from the Framingham Heart Study showed that for men and women with an initial clinical presentation of stable angina, the 2-year incidence rates of nonfatal MI and CHD death were 14.3 and 5.5% in men and 6.2 and 3.8% in women, respectively. More contemporary data regarding prognosis can be gleaned from clinical trials of antianginal therapy and/or revascularization, although these data are biased by the selected nature of the populations studied. From these, estimates for annual mortality rates range from 0.9–1.4% per annum, with an annual incidence of nonfatal MI between 0.5% (INVEST) and 2.6% (TIBET).

LV function is the strongest predictor of survival in patients with chronic stable coronary disease; the next most important factor is the distribution and severity of coronary stenosis. Left main (LM) disease, three-vessel disease, and the proximal involvement of the left anterior descending are common characteristics predicting a poor outcome and increase the risk of ischaemic events. Myocardial revascularization can reduce the risk of death in selected anatomical subgroups, reduce the number of ischaemic episodes (ACIP), and in some instances may improve the LV function in high-risk patients. However, disease progression and the occurrence of acute events may not necessarily be related to the severity of stenosis at coronary arteriography. In all patients, smaller lipid filled plaques are present in addition to those that cause severe stenoses.

The risk of acute events is related to the overall plaque burden and to plaque vulnerability. Although an area of great research interest, our capabilities to identify vulnerable plaque remain limited.

Place of carrying out: class-room, wards of cardiology and rheumatology departments, department of functional diagnostics.

Study objective: to be able to determine extent of examinations to put final diagnosis and assign management.

Basic level:

1. To know classification and rick factors of ischaemic heart disease.
2. To be able to collect complaints, case history, carry out objective examination.
4. To interpret instrumental (ECG, 24 hour ECG monitoring (ECG Holter monitor), EchoCG) and laboratory data in patients with chest pain.
5. To identify signs from anamnesis and objective data inherent to stable angina.
6. To interpret side effects of antianginal agents.

Student has to be able to:

1. Examine patients with cardiovascular disorders.
2. Make an algorithm of stable angina management.

The main theoretical questions:

1. Classification of angina pectoris (functional classes). Diagnostic criteria.
2. Stress and pharmacology testing, evidence for performing and interpretation.
3. Treatment and preventive measurements in stable angina.
4. Importance of ECG, 24 hour ECG monitoring and coronarography in painless form of ischaemia.

Assignment for self-assessment

1. A 53-year-old man complains of pressing chest pain on 100 m walking that lasts about 15 min. The examination reveals a regular heart rate with a reduced intensity S_1 and normal S_2. Blood pressure is 140/90 mm Hg; pulse is 90 beats/min, regular, respiratory rate is 20 breaths/min. His lungs are clear. The abdomen is soft without tenderness or distention. On ECG: sinus rhythm, high and sharp T waves in V2–V4 leads. During the last week pain appears at night and at rest, not stopped after taking 1 tab. of nitroglycerin. What disease can you think of?

a) progressive angina;
b) stable angina, FC4;
c) myocardial infarction;
d) vasospastic angina;
e) stable angina, FC3.

2. A 38-year-old man complains of angina attacks and dyspnoea on excersises. The patient suffers from obstructive form of hypertrophic cardiomyopathy. The examination reveals a regular heart rate. Blood pressure is 145/85 mm Hg; pulse is 80 beats/min. What medicine is contraindicated in this situation?

a) bisoprolol;
b) verapamil;
c) aspirin;
d) nitroglycerin.

3. What ECG sign is typical for myocardial ischaemia?

a) ST elevation less than 1 mm;
b) ST depression less than 1 mm;
c) ST depression more than 1 mm;
d) ST elevation more than 5 mm.

4. What test should be made in inefficiency of 24 hour ECG monitoring for revealing of painless form of ischaemia?

a) pharmacological test with propranolol;
b) pacemaker setting;
c) excersise test.

5. A 58-year-old man complains of dyspnoea on excersises and mild oedema on the legs. He has never complained of chest pain, never used nitrates and other medicines. There are no pathological changes of ST segment and T wave on ECG at rest; in excersise test there is ST segment depression more than 2 mm. What should be suspected?

a) painless form of myocardial ischaemia;
b) vasospastic angina;
c) lung pathology;
d) state of absolute health.

Answers: 1. a. 2. d. 3. c. 4. c. 5. a.

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Topic 7. MANAGEMENT OF PATIENTS WITH CARDIOMEGALY

Time frame – 6 hours.

Professional motivation. The term "cardiomegaly" most commonly refers to an enlarged heart seen on chest X-ray before other tests are performed to diagnose the specific condition causing cardiomegaly.

Hypertrophic cardiomyopathy (HCM) is a complex and relatively common genetic cardiac disorder (about 1:500 in the general adult population) that has been the subject of intense scrutiny and investigation for over 40 years. Hypertrophic cardiomyopathy affects men and women equally and occurs in many races and countries, although it appears to be under-diagnosed in women, minorities, and under-served populations. Hypertrophic cardiomyopathy is a particularly common cause of sudden cardiac death (SCD) in young people (including trained athletes) and may cause death and disability in patients of all ages, although it is also frequently compatible with normal longevity.

Dilated cardiomyopathy is much more common than the other major forms of cardiomyopathy (hypertrophic, restrictive, and arrhythmogenic right ventricular cardiomyopathy). The estimated prevalence of dilated cardiomyopathy is 1:2500. This condition is among the most common causes of heart failure. The incidence of dilated cardiomyopathy discovered at autopsy is estimated to be 4.5 cases per 100,000 population per year, whereas the clinical incidence is 2.45 cases per 100,000 population per year. Dilated cardiomyopathy may manifest clinically at a wide range of ages, but this condition most commonly occurs in the third or fourth decade of life. Dilated cardiomyopathy is associated with a survival rate of less than 50% at 10 years. Peripartum cardiomyopathy may be reversible in up to 50% of patients but often recurs with subsequent pregnancy.

There is a negative association in dilated cardiomyopathy between survival and frequent ventricular tachyarrhythmias that require antiarrhythmic treatment or automated implantable cardioverter-defibrillator (AICD) placement. During the clinical course of idiopathic dilated cardiomyopathy, a number of clinical and diagnostic measures may be monitored to predict prognosis. The most important and best predictors are the New York Heart Association heart failure functional class, the left ventricular ejection fraction, and the peak oxygen consumption.

Acute pericarditis is more common in adults (typically between 20 to 50 years old) and in men. Epidemiologic data on the incidence of acute pericarditis are lacking, likely because this condition is frequently inapparent clinically, despite its presence in numerous disorders and there are a large number of undiagnosed cases. A diagnosis of acute pericarditis may account for up to 5% of presentations to emergency departments for chest pain and up to 0.1% of hospital admissions. In addition, acute pericarditis comprises 1% of emergency room visits in patients with ST-segment elevation. In fact, the reported incidence of acute pericardial tamponade is approximately 2% of penetrating trauma; however, this condition is rarely seen in blunt chest trauma. Uremic pericarditis may occur in 6–10% of patients with advanced renal failure before initiation of dialysis. When patients with large effusions are examined, uraemia may account for up to 20% of cases in some series. The widespread availability of dialysis has reduced the incidence of uremic pericarditis. Malignant disease is the most common cause of pericardial effusion with tamponade in developed countries. However, tuberculosis should be considered in endemic areas.

Place of carrying out: class-room, wards of rheumatological or cardiology department.

Study objective: to improve the skills in determination of the doctors' tactics in cardiomegaly; to develop differential diagnosis of the cardiomegaly caused by myocarditis, pericarditis, and cardiomyopathy; to determine differential approaches to their treatment.

Basic level:

1. To be able to collect complaints, case history, carry out objective examination.
2. To interpret instrumental (ECG, EchoCG, X-ray) and laboratory data in patients with cardiomegaly.
3. To identify signs from anamnesis and objective data inherent to cardiomegaly of different origin.
4. To interpret side effects of agents which are used in cardiomegaly.

Student has to be able to:

1. Find out cardiomegaly using instrumental methods of examination.
2. Make an algorithm of investigations in patients with cardiomegaly.
3. Determine approaches to treatment in different aetiology of cardiomegaly.
4. Differentiate cardiomegaly of various origin.

The main theoretical questions:

1. Definition of the cardiomegaly syndrome.
2. The main causes of cardiomegaly.
3. Approaches for differential diagnosis of cardiomegaly causes.
4. Modern aspects of myocarditis aetiology and pathogenesis. Classification of myocarditis.
5. Criteria for diagnosis of myocarditis. Treatment of myocarditis.
6. Aetiology and pathogenesis of pericarditis. Classification of pericarditis.
7. Criteria for diagnosis and treatment of pericarditis.
8. Classification of cardiomyopathies.
9. Modern aspects of the dilated cardiomyopathy aetiology and pathogenesis.
10. Criteria for diagnosis and management of patients with dilated cardiomyopathy.
11. Modern aspects of hypertrophic cardiomyopathy aetiology and pathogenesis.
12. Classification and treatment of hypertrophic cardiomyopathy.
13. Modern aspects of the restrictive cardiomyopathy aetiology and pathogenesis.
14. Classification and treatment of the restrictive cardiomyopathy.
15. Clinical and ECG signs of arrhythmic and tromboembolic complications.

Assignment for self-assessment

1. What disorders is chronic constrictive pericarditis associated with?
2. What idiopathic cardiomyopathy is related to heredity?
   a) dilated;
   b) hypertrophic;
   c) restrictive;
   d) arrhythmogenic right ventricular dysplasia.
3. What idiopathic cardiomyopathy is accompanied by disturbances of diastolic cardiac function?
   a) dilated;
   b) hypertrophic;
   c) restrictive;
   d) arrhythmogenic right ventricular dysplasia;
   e) hypertrophic, restrictive.
4. What idiopathic cardiomyopathy is accompanied by disturbances of systolic cardiac function?
   a) dilated;
   b) hypertrophic;
   c) restrictive;
   d) arrhythmogenic right ventricular dysplasia.
5. What cause of metabolic cardiomyopathy is the most frequent?
   a) uraemia;
   b) podagra;
   c) electrolytes deficit;
   d) endocrine pathology.
6. A 58-year-old man complains of dyspnoea, weakness, intermission of pulse, oedema on the legs. The examination reveals enlargement of cardiac size in percussion. Blood pressure is 130/80 mm Hg; pulse is 90 beats/min, irregular, respiratory rate is 20 breaths/min. On ECG: tachysystolic variant of atrial fibrilation. On cardiac ultrasound: enlargement of cardiac chambers, EF is 36%. What disease does this patient have?
   a) dilated cardiomyopathy;
   b) hypertrophic cardiomyopathy;
   c) myocarditis;
   d) myocardiodystrophy.

Answers:

1. Rheumatoid arthritis and radiotherapy have been recognized for some years as occasional causes of constrictive pericarditis. Recently, cardiac surgery (usually coronary bypass surgery), including insertion of epicardial pacemaker, has also been associated with later development of constriction.

2. b. 3. e. 4. a. 5. d. 6. a.

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Topic 8. MANAGEMENT OF PATIENTS WITH HEART FAILURE

Time frame – 6 hours.

Professional motivation. The European Society of Cardiology represents countries with a population of > 900 million, and there are at least 15 million patients with HF in those 51 countries. The prevalence of asymptomatic ventricular dysfunction is similar, so that HF or asymptomatic ventricular dysfunction is evident in ~4% of the population. The prevalence of HF is between 2 and 3% and rises sharply at ~75 years of age, so the prevalence in 70- to 80-year-old people is between 10 and 20%. In younger age groups HF is more common in men because the most common cause, coronary heart disease, occurs in earlier decades. In the elderly, the prevalence is equal between the sexes. The overall prevalence of HF is increasing because of the aging of the population, the success in prolonging survival in patients suffering coronary events, and the success in postponing coronary events by effective prevention in those at high risk or those who have already survived a first event (secondary prevention). In some countries the age-adjusted mortality from HF is falling at least in part due to modern treatment.

The mean age of patients with HF in the community in developed countries is 75 years. HF with preserved ejection fraction is more common in the elderly, women, and those with hypertension or diabetes. HF is the cause of 5% of acute hospital admissions, is present in 10% of patients in hospital beds, and accounts for ~2% of national expenditure on health, mostly due to the cost of hospital admissions.

The impact on prognosis of specific treatments in individual patients with HF is often difficult to predict. Conditions associated with a poor prognosis in heart failure are advanced age, hypotension, NYHA functional class III–IV, wide QRS, marked elevation of BNP/NT pro-BNP, hyponatraemia, low LVEF, etc.

Place of carrying out: class-room, wards of cardiology department.

Study objective is to verify diagnosis of chronic heart failure, to determine management of patients with CHF.

Basic level:

1. To be able to collect complaints, case history, carry out objective examination.
2. To interpret instrumental and laboratory data in patients with HF.
3. To discover signs inherent in HF.
4. To interpret side effects of drugs which are used in HF.

Student has to know:

1. How to examine patients with cardiovascular disorders.
2. Causes of heart failure, functional classes.
3. Criteria for diagnosis of heart failure.
4. How to make program for investigation of patients with HF.

5. Clinical pharmacology of diuretics, vasodilators, beta-adrenergic receptor blocking agents, digitalis glycosides, angiotensin-converting enzyme inhibitors (ACE); drugs, which improve heart metabolism.

The main theoretical questions:

1. Heart failure classification. Clinical manifestation of heart failure.
2. Diagnostic tests in heart failure.
3. Primary and secondary prophylaxis of heart failure. Prognosis in heart failure.
4. Principles of heart failure management.
5. Therapeutic strategies in systolic and dyastolic dysfunction: vasodilators; ACE; angiotensin II receptor antagonists; nitrates; adrenergic receptor antagonists (alpha-adrenergic receptor antagonists; beta-adrenergic receptor antagonists), calcium channel blockers; digitalis glycosides; diuretics; inotropic agents; phosphodiesterase inhibitors. Indications, contrindications, side effects.
6. Treatment of diastolic heart failure.
7. Surgical treatment of patients with heart failure (intra-aortic balloon counterpulsation, heart transplantation, cardioplasty). Impact of cardiac resynchronization therapy.

Assignment for self-assessment

1. A 39-year-old woman complains of dyspnoea on exertion, chest pain, palpitation. She had previous rheumatic fever twenty years ago. She was treated with acute pharyngitis two weeks ago. Physical examination reveals a low-pitched, rough, and rasping pansystolic murmur, loudest at the base of the heart in the second right intercostal space, weak and regular pulse, HR is 88 beats/min, BP is 150/90 mm Hg. What diagnosis do you suspect? Prescribe the treatment.
2. Initial dose for enalapril in CHFis:
   a) 2.5 mg once a day;
   b) 15 mg bid;
   c) 5 mg bid;
   d) 10 mg bid.

Answers:

1. Chronic rheumatic cardiac disease. Aortic stenosis. Chronic heart failure II A. Carvedilol 12.5 mg/daily, lisinopril 2.5 mg/daily, nitrosorbid 10 mg every 8 hours, aspirin 100 mg daily, verospiron 25 mg daily, extencillin 2.4 mln units im once in 3weeks.
2. a.

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9. MANAGEMENT OF PATIENTS WITH HEART MURMURS

Time frame – 6 hours.

Professional motivation.

Valvular heart disease is the most serious complication of acute rheumatic fever and infectious endocarditis. Reduced prevalence of rheumatic fever and increased life span in industrialized countries have progressively changed the distribution of aetiologies. Degenerative MR is the most common aetiology in Europe, whereas ischaemic and functional MR are increasingly frequent. Rheumatic mitral stenosis in young population is now considered to be rare in developed countries with an incidence of less than 1 per 100,000 population and relates to the decline of rheumatic fever. A similar condition occasionally occurs in association with other diseases such as systemic

lupus or infective endocarditis. Consequently, we should remain vigilant and be aware of the presenting symptoms and signs of rheumatic fever and rheumatic heart disease. In asymptomatic patients with mitral stenosis, survival was good up to 10 years, progression being highly variable with sudden deterioration, precipitated by complications, such as atrial fibrillation or embolism, in half of the patients. Symptomatic patients have a poor prognosis.

Patients with acute aortic regurgitation (AR) have a poor prognosis without intervention owing to the significant increase in diastolic LV pressure, leading to poor haemodynamic tolerance. There is little information in the literature on the progression from mild to severe AR. Patients with severe AR and symptoms have a poor prognosis. In asymptomatic patients with severe AR and normal LV function, the number of events during follow-up is low: sudden death <0.2% per year; symptoms, LV impairment, or death, 4.3% per year. Age, end-systolic diameter or volume, and EF at rest are predictors of outcome.

Aortic stenosis (AS) has become the most frequent type of VHD in Europe and North America. It primarily presents as calcific AS in adults of advanced age (2–7% of the population >65 years). The second most frequent aetiology, which dominates in the younger age group, is congenital, whereas rheumatic AS has become rare. Calcific AS is a chronic progressive disease. During a long latent period, patients remain asymptomatic. However, duration of the asymptomatic phase varies widely among individuals. Sudden cardiac death is a frequent cause of death in symptomatic patients but appears to be rare in the asymptomatic (≤1% per year). Predictors of the progression of AS and, therefore, of poor outcome in asymptomatic patients have been identified. They are: 1) clinical (older age, presence of atherosclerotic risk factors); 2) echocardiography (valve calcification, peak aortic jet velocity, LVEF, haemodynamic progression, and increase in gradient with exercise); the combination of a markedly calcified valve with a rapid increase in velocity of ≥0.3 m/s within 1 year has been shown to identify a high-risk group of patients (~80% death or requirement of surgery within 2 years); 3) exercise testing: symptom development on exercise testing in physically active patients, particularly those younger than 70 years, predicts a very high likelihood of symptom development within 12 months.

Organic mitral regurgitation (MR) covers all aetiologies in which leaflet abnormality is the primary cause of the disease, in opposition to ischaemic and functional MR, in which MR is the consequence of LV disease.

Place of carrying out: class-room, wards of the cardiology department, wards of the emergency, department of functional diagnostics.

Study objective: to improve students' skills to make differential diagnosis of systolic and diastolic murmurs, to make diagnosis, to manage patients with valvular disorders.

Basic level:

1. Pathophysiology of systolic and diastolic murmurs.
2. To be able to collect complaints, case history, carry out objective examination.
3. To do percussion and auscultation of the patients for diagnosis of heart murmurs.
4. To interpret instrumental (ECG, EchoCG, X-ray) and laboratory data in patients with valvular disorders.

Student has to know:

1. Differential diagnosis of the systolic murmur in the acquired and congenital valvular diseases.
2. Differential diagnosis of the diastolic murmur in the acquired and congenital valvular diseases.
3. ECG- and Echo findings in the acquired and congenital valvular diseases.
4. X-ray examination in the acquired and congenital valvular diseases.
5. Indications for surgical treatment of the acquired and congenital valvular diseases.

The main theoretical questions:

1. Criteria for diagnosis of aortic stenosis, treatment.
2. Criteria for diagnosis of aortic regurgitation, treatment.
3. Criteria for diagnosis of mitral stenosis, stages of mitral stenosis and choice of treatment depending on stage.

4. Criteria for diagnosis of mitral regurgitation, stages of mitral regurgitation and choice of treatment depending on stage.

5. To make plan of investigations for patient with valvular diseases.

6. Indications for surgical intervention. Valve prosthesis: influence on haemodynamic, signs of dysfunction.

7. Management of pregnant women with valvular disorders.

Assignment for self-assessment

1. A 40-year-old woman presented with palpitation and dyspnoea which increases progressively during the past 3 years. There was chorea and arteritis in childhood. Physical examination: acrocyanosis, PS is 104, irregular, pulse deficit is 22 per minute, a severe systolic murmur and moderate presystolic are heard above heart apex with radiation, the I sound is reduced. On ECG: left ventricular hypertrophy, atrial fibrillation. What is the clinical diagnosis?

2. A 56-year-old man complains of fatigue, dyspnoea on exertion, and palpitations. He has had a murmur since childhood, frequent respiratory infections. Examination reveals intensified right-ventricle beat, a lift at the left sternal border, fixed splitting of S_2, systolic ejection murmur in the pulmonary area (II to IV). Chest X-ray shows right ventricular enlargement and prominent pulmonary arteries. ECG demonstrates atrial fibrillation with a right bundle-branch block. What is the most likely diagnosis?

3. What medicines must be used to decrease pulmonary hypertension?
   a) diuretics and nitrates;
   b) cardiac glycosides;
   c) anticoagulants;
   d) antiarrhythmic drugs;
   e) antibiotics.

4. At what stages of mitral stenosis surgical treatment isn't indicated?
   a) at the I stage;
   b) at the I–II stages;
   c) at the IV–V stages;
   d) at the V stage;
   e) at the I and V stage.

5. At what stages of mitral regurgitation surgical treatment isn't indicated?
   a) at recurrent systemic embolisms despite of anticoagulant treatment;
   b) at the I–II and V stages;
   c) at moderate heart failure with atrial fibrillation, decreased EF or dilated cardiac chambers;
   d) at significant CHF (FC III–IV);
   e) at the I and V stage.

6. What medicines are used for asymptomatic patients with aortic stenosis?
   a) diuretics;
   b) cardiac glycosides;
   c) anticoagulants;
   d) vasodilators;
   e) antibiotics (for prevention of infective endocarditis).

7. A 33-year-old male was seen in the clinic with one year history of worsening exertional dyspnoea and orthopnoea. He had no recollection of any previous symptoms of rheumatic fever. No other past medical illness of note apart from mild asthma.

On clinical examination, he was slim built with blood pressure of 120/80 and a regular pulse. No evidence of peripheral oedema was present. Jugular venous pressure was not raised. Cardiovascular examination revealed a loud first heart sound, opening snap and mid diastolic murmur with presystolic accentuation. Electrocardiograph demonstrated sinus rhythm with right bundle branch block along with evidence of left atrial enlargement.

Transthoracic and transoesophageal echocardiography confirmed severe rheumatic mitral stenosis with thickening and fusion of the commissures, mitral valve area of 0.7–0.9 cm^2, mild

mitral regurgitation and left atrial dilatation. There was also marked pulmonary hypertension with a systolic pulmonary artery pressure estimated to be 70 mm Hg.

The clinical and biochemical markers: RBC – $4.0*10^{12}$/l; Hb – 146 g/l; ESR – 4 mm/h; WBC – $6*10^{-9}$/l; eos. – 2%, stab neutr. – 4%, segmented neutrophils – 59%, lymphocytes – 11%, monocytes – 5%. Total serum protein – 65 g/l, serum urea – 6.7 mmol/l, creatinine – 90 μmol/l, bilirubin – 19 μmol/l, AST – 10 units, fasting plasma glucose – 4.8 mmol/l, rheumatoid factor – 1:32, uric acid – 0.25 mmol/l.

Urinalysis: RBC – 1 to 2 per high-power field, WBC – 3 to 2 per high-power field, specific gravity – 1028. Urinary protein excretion is 0.15 g/day.

Suggest management for such patient.

Answers:

1. Combined mitral valve disorder with predominance of regurgitation.

2. Atrial septal defect. The murmur heard in childhood is often considered "innocent", and symptoms do not appear until adulthood. A left-to-right shunt of blood between the atria causes right ventricular overload and increased pulmonary circulation. These result in the classic findings of a pulmonic systolic ejection murmur, late pulmonic valve closure with wide splitting of S2, and tricuspid flow murmur. Chest X-ray has signs of cardiomegaly and pulmonary overcirculation. Characteristic ECG changes are atrial fibrillation and an incomplete or complete right bundle-branch block.

3. a. 4. e. 5. b. 6. e.

4. Percutaneous balloon mitral valvuloplasty. Interesting feature to note in this case is the marked degree of pulmonary hypertension secondary to mitral stenosis, which is particularly uncommon in this age group, as it has been estimated that progression from mild to severe disabling symptoms usually takes up to 10 years.

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Topic 10. MANAGEMENT OF PATIENTS WITH CONNECTIVE TISSUE DISEASES

Time frame – 6 hours.

Professional motivation. CTD is a heterogeneous group of disorders that have complex aetiologies that presumably reflect interactions between several distinct genetic loci. The acquired connective tissue diseases display certain common clinical features, as inflammation in joints (polyarthralgia and arthritis), serous membranes (pleurisy, pericarditis), small blood vessels (vasculitis) and a high frequency of involvement of various internal organs rich in connective tissue. It is often difficult to diagnose CTD, especially when the patient has symptoms that can occur with a number of different autoimmune diseases. It can take years for some patients to finally receive a correct diagnosis. Systemic lupus erythematosus affect any age group - the peak age at onset around the 2nd to 4th decades, with 65% of patients presenting between the ages of 16 and 65 years. Scleroderma may occur at any age, but the symptoms most frequently begin in mid-life. The disease is about 4 times more common in women than men. The current prevalence is about 240

cases per million adults. Involvement of internal organs results in significant morbidity and mortality of patients with CTD. Because of the clinical complexity and heterogeneity, it is very challenging to treat this diseases.

Place of carrying out: class-room, wards of the rheumatologic department.

Study objective: to improve the skills in making a differential diagnosis of CTD, to determine a management strategy.

Basic level:

1. To be able to collect complaints, case history, carry out physical examination in patients with CTD.
2. To interpret instrumental and laboratory data in patients with CTD.

Student has to be able to:

1. Make an algorithm of investigations in patients with CTD.
2. Determine approaches to treatment considering different aetiopathogenetic factors of haemorrhagic syndrome.
3. Interpret laboratory and instrumental results after examination for CTD verification, do assessment of activity and degree of organs and systems disorders.

The main theoretical questions:

1. Differential diagnosis of skin lesions in connective tissue diseases.
2. Differential diagnosis of the pulmonary involvement in CTD.
3. Differential diagnosis of the renal involvement in CTD.
4. Differential diagnosis of the cardiovascular involvement in CTD.
5. Specific methods of research in systemic vasculitis.
6. Criteria for diagnosis of systemic vasculitis. Autoimmune markers. Changes on angiography.
7. Principles of differential diagnosis in systemic vasculitis.
8. Clinical manifestation of systemic lupus erythematosus, systemic sclerosis, dermatomyositis, Sjogren's syndrome, and antiphospholipid syndrome. Differential diagnosis of polyarteritis nodosa and Takayasu's disease.
9. Clinical manifestation of pulmonary-renal syndrome, evaluation and treatment of the critically ill patient.
10. Principles of systemic vasculitis management.
11. Evidence-based treatment of CTD. Biological therapy. Pulse therapy. Pregnancy planning. Conditions for vaccination.

Real-life situations to be solved:

1. A 18-year-old woman had respiratory viral disease a month before and was treated by analgin, paracetamol, biseptol. Pain and swelling of knee joints, haemorrhagic rash on the anterior surface of shins appeared. She withheld medicines but in 3 weeks subfebrile temperature appeared and she restarted taking paracetamol. She was complaining of pain and swelling of knee joints, haemorrhagic rash (purpura) over the crus, hips, rumps, high temperature (38.2 °C), headache. With suspicion on meningitis patient was admitted to the infectious department. In 2 days colicy pain in abdomen and bloody diarrhoea appeared.

Objectively: general state of the patient is serious, skin of the face is pale, multiple conjugating haemorrhagic rash. The temperature is 38.2. BP – 100/65 mm Hg, pulse is 104 beats per minute. Cardiac activity is rhythmic, weakening of the first sound, no murmurs, vesicular respiration in lungs, painful abdomen during palpation. The patient has difficulty motions, swelling knee and ankle joints.

Laboratory examinations: RBC – $2.0*10^{12}$/l; Hb – 76 g/l; ESR – 44 mm/h; WBC – $26*10^{9}$/l; eos. – 2%, stab neutr. – 14%, segmented neutrophils – 59%, lymphocytes – 11%, monocytes – 5%. Total serum protein – 65 g/l, serum urea – 6.7 mmol/l, creatinine – 90 μmol/l, bilirubin – 19 μmol/l, AST – 10units, fasting plasma glucose – 4.8 mmol/l, rheumatoid factor – 1:32, CRP – ++, uric acid – 0.25 mmol/l.

Urinalysis: RBC – 45 to 50 per high-power field, WBC – 3 to 4 per high-power field, specific gravity – 1028, red cell casts are detected. Urinary protein excretion is 2.5 g/day. Occult blood test

in stool was positive. Abdominal ultrasound is normal. What is the presumptive diagnosis? Suggest additional investigations. What is the treatment protocol? What is prognosis determined by?

2. A 58 year old white man presented with a six month history of arthralgia that affected his shoulders, hands, ankles and feet, associated with early morning stiffness and intermittent joint swelling. Two weeks before he had developed ulceration on his elbow and tongue. He also reported weight loss, fever with profuse sweating, haemoptysis, nasal stuffiness, and a six month history of intermittent deafness. On examination, he had an ulcer over his right elbow measuring 2 × 3 cm and two small ulcers over the left side of his tongue. The second, third, and fourth metacarpophalangeal joints of his right hand and his left ankle were swollen. Urinalysis showed a trace of protein and blood. What is your differential diagnosis? What investigations would you perform to establish the diagnosis?

3. A 28 year old man presented with a 2 week history of arthralgia that affected his hands and ankles, associated with intermittent joint swelling. A month before he had developed erythema on his face and ulceration on his tongue. He also reported weight loss, loss of vision, fever, nasal stuffiness, periodical epistaxis. On examination, he had pale skin, nasal crusting, small ulcers on his tongue. His ankles were swollen. There is dullness above the inferior lobe of the right lung, moist rales. Heart sounds are weak, systolic murmur above apex, pulse is 96/min, rythmical, BP – 190/110. From the history: 4 months ago patient finished the treatment with antibiotics (from 3 different groups) due to infective endocarditis.

Urinanalyse showed a trace of protein and blood, the 24 hour urinary protein was slightly raised at 0.55 g in 24 hours. Blood tests: RBC – $2.7*10^{-12}$/l; Hb – 80 g/l and raised inflammatory markers: ESR of 59 mm/h, C-reactive protein of 84 mg/l. On the entering day haemoptysis appeared. After additional investigations there was revealed shadowing at both lung bases (infiltrates) on the chest X-ray more marked on the right, immunological test showed a positive antineutrophil cytoplasmic antibody with a titre of 1:1280. Blood cultures were negative. Transthoracic echocardiography confirmed moderate mitral regurgitation without vegetations, left atrial dilatation. There was also mild pulmonary hypertension with a systolic pulmonary artery pressure estimated to be 30 mm Hg.

Further investigations - a high resolution computed tomogram of the thorax: the lungs had a patchy ground glass appearance. In 3 days oedema on the legs and the level of proteinuria increased to 1.4 g in 24 hours, RBC – $2,5*10^{-12}$/l; Hb – 78 g/l; ESR – 60 mm/h; WBC – $16*10^{-9}$/l; eos. – 2%, stab neutr. – 14%, segmented neutrophils – 59%, lymphocytes – 11%, monocytes – 8%. Total serum protein – 45 g/l, serum urea – 9.7 mmol/l, creatinine – 190 μmol/l, bilirubin – 19 μmol/l, AST=20 units. Suggest additional investigations. What is your diagnosis? What is the treatment protocol?

Answers to the self-assessment

1. Presumptive diagnosis: haemorrhagic vasculitis with skin affection, articular, renal and abdominal syndromes; complicated by gastrointestinal bleeding.

Additional investigations: ECG, bleeding time, clotting time, thrombocytes' count, FGDS, consultations of neurologist and ophthalmologist. Antineutrophil cytoplasmic antibody (ANCA) levels, biopsy of involved organ or tissue, such as skin, sinuses, lung, nerve, and kidney. The biopsy elucidates the pattern of blood vessel inflammation.

Corticosteroid therapy is initiated with prednisone in a dose of 0.5 to 1.5 mg/kg per day.

2. The differential diagnoses are systemic vasculitis with multisystem involvement; infections (HIV, hepatitis B or C); endocarditis; rheumatoid arthritis; and malignancy. Blood tests, immunological tests, skin ulcer biopsy and nasal biopsy, chest radiograph and computed tomography.

3. A diagnosis of Wegener's granulomatosis, a form of necrotising vasculitis, was made on the basis of clinical presentation, the presence of classical antineutrophil cytoplasmic antibody, which is 99% specific for the diagnosis of primary systemic vasculitis (about 90% of patients with active Wegener's granulomatosis are positive for this antigen). It is preferable to have tissue biopsies. Diagnosis is confirmed with a tissue biopsy at a site where disease is active. Nasopharyngeal biopsies are preferable because they are relatively non-invasive compared with a lung or kidney

biopsy, which are at times the only options. In admission we can suspect SLE, so additional investigations should be immunological.

Treatment depends on the extent of involvement. In cases of widespread systemic involvement, and especially if the lungs or kidneys are involved, steroids and immunosuppressive therapy are needed. Cyclophosphamide is typically used to induce remission, and other immunosuppressive agents are considered once the disease is under control. If a diagnosis is in doubt, treatment should not be delayed because Wegener's granulomatosis has a high mortality if left untreated. With the use of cytotoxic drugs 8 year survival is reported to be 80%. So remission can be induced with pulse-therapy (bolus i.v. methylprednisolone (10 mg/kg) initially 3 days and cyclophosphamide (15 mg/kg) on the 2nd day), and subsequently with oral high-dosage prednisolone (1 mg/kg daily) and continuous oral cyclophosphamide (2 mg/kg daily). Doses of cyclophosphamide should be reduced in those with renal impairment. The dose of oral prednisolone is rapidly reduced once remission has occurred. Cyclophosphamide is usually continued for 6–12 months in total. Antihypertensive medicines, antiagregants.

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Topic 11. MANAGEMENT OF PATIENS WITH ARTICULAR SYNDROME AND MYALGIAS

Time frame – 6 hours.

Professional motivation. Arthritis comprises more than 100 different rheumatic diseases and conditions, the most common of which is osteoarthritis. Other frequently occurring forms of arthritis include rheumatoid arthritis, lupus, fibromyalgia, and gout. Common symptoms include pain, aching, stiffness, and swelling in or around the joints. Some forms of arthritis, such as rheumatoid arthritis and lupus, can affect multiple organs and cause widespread symptoms. Although arthritis is more common among adults aged 65 years or older, people of all ages (including children) can be affected. Nearly two-thirds of people with arthritis are younger than age 65 years. Arthritis is more common among women (24.3%) than men (18.7%) in every age group, and it affects members of all racial and ethnic groups. Arthritis also is more common among adults who are obese than among those who are normal weight or underweight.

Among all U.S. adults of working age (18–64 years), 5.3% (6.9 million people) reported that they have arthritis that limits their work. A recent community study estimated that the lifetime risk of developing knee osteoarthritis serious enough to cause painful symptoms is 45%. Risk increases to 57% among people with a past knee injury. Lifetime risk for knee osteoarthritis goes up with increasing weight and rises to 60% among people who are obese.

Rheumatoid arthritis (RA) affects all ages, races, and social and ethnic groups. It is most likely to strike people 35–50 years of age, but it can occur in children, teenagers, and elderly people. Women are two to three times more likely to develop RA than men. The rate is about 2–3% in people who have a close relative with RA, such as a parent, brother or sister, or child. The disease can be controlled in most people. Early, aggressive therapy, soon after the initial diagnosis, is optimally targeted to stop or slow down inflammation in the joints can prevent or reduce symptoms, prevent or reduce joint destruction and deformity, and prevent or lessen disability and other complications. RA itself is not a fatal disease. However, it can be associated with many complications and treatment-related side effects that can contribute to premature death. Although RA most often affects the joints, it is a disease of the entire body. It can affect many organs and body systems besides the joints. Therefore, RA is referred to as a systemic disease.

The early use of the disease modifying antirheumatic drugs (DMARDs) and biologic response modifiers in RA has resulted in patients experiencing more profound relief of symptoms and less joint damage and less disability over time.

Axial spondyloarthritis (axSpA) is an inflammatory rheumatic disease with a diverse clinical presentation. Most types of SpA begin around the ages of 15–45. Men are more likely to get SpA. The term axSpA comprises the whole spectrum of patients with radiographic sacroiliitis (AS or radiographic axSpA) and without radiographic sacroiliitis (non-radiographic axSpA). Patients with axSpA frequently experience extraarticular manifestations requiring multidisciplinary management.

Up to 30% of people with psoriasis develop psoriatic arthritis. In most cases psoriasis will precede arthritis, sometimes by many years. When arthritis symptoms occur with psoriasis, it is called psoriatic arthritis (PsA). About 20% of people who develop PsA will eventually have spinal involvement, which is called "psoriatic spondylitis". The inflammation in the spine can lead to complete fusion – as in ankylosing spondylitis – or skip areas where, for example, only the lower back and neck are involved. Those with spinal involvement are most likely to test positive for the HLA-B27 genetic marker.

Place of carrying out: class-room, wards of the rheumatologic department.

Study objective: to improve the skills of differential diagnosis of arthritis in rheumatoid arthritis, osteoarthritis (OA), gout, SpA, arthritis in systemic lupus erythematosus (SLE), dermatomyositis (DM), systemic scleroderma (SSD).

Basic level:

1. To be able to collect complaints, case history, carry out physical examination in patients with arthritis.
2. To interpret instrumental and laboratory data in patients with arthritis, and sacroileitis.
3. To interpret side effects of agents which are used in rheumatology.

Student has to be able to:

1. Find out joint and spine injury using instrumental methods of examination.
2. Make an algorithm of investigations in patients with arthritis.
3. Determine approaches to treatment in different aetiology of arthritis.

The main theoretical questions:

1. Clinical and roentgenologic semiotics of the joint diseases.
2. Diagnostic criteria of RA. Common complications. Management.
3. Diagnostic criteria of ankylosing spondylitis. Management.
4. Diagnostic criteria of reactive arthritis. Management.
5. Diagnostic criteria of psoriatic arthritis. Management.
6. Diagnostic criteria of gout. Management.
7. EULAR treatment standards. Basic treatment of rheumatic diseases with joint manifestations. DMARDs in autoimmune inflammatory joint diseases.
8. Symptomatic treatment of the joints disorders.
9. Using of nonsteroidal anti-inflammatory drugs (NSAID), corticosteroids, immunosuppressive drugs, physiotherapy and sanatorium-resort therapy. Indications and method of arthrocentesis.
10. Differential diagnosis of arthritis and arthralgia in connective tissue diseases (systemic lupus erythematosus (SLE), systemic sclerosis (SS), dermatomyositis (DM) and polymyositis (PM)).
11. Differential diagnosis of myalgias in neurogenic myopathy; chronic inflammatory demyelinating polyneuropathy; disorders at the level of neuromuscular synapses; vessels disorders; action of toxic substances; primary inflammatory diseases of muscle tissue (idiopathic inflammatory myopathies); infectious myositis (viral myositis, toxoplasmosis, trichinosis, cysticercosis, echinococcosis); congenital metabolic disorders (metabolic myopathies: disorders of muscle glycogen and lipid metabolism); mitochondrial myopathies; endocrine diseases (acromegaly, Addison's disease, hypercorticism, hyperparathyroidism, hypothyroidism, thyrotoxicosis, diabetes mellitus). Management of patients.

Assignment for self-assessment

1. Pain and swelling of the right knee has developed in 24-year-old man, following enterocolitis

epidemic in building team. Arthritis is accompanied by the considerable limitation of the motion range, cutting pain in the eyes, pain in mouth mucous membrane during eating hot and strong food. Patient has severe synovitis of the right knee. Laboratory tests: an elevated erythrocyte sedimentation rate (ESR). Consultation of the ophtalmologist – acute conjunctivitis. Questions: A. What is the provisional diagnosis? B. What is an additional plan of examination? C. What pathological forms should you make differentiation between?

2. A 22-year-old man complains of low back pain and stiffness that is worse on arising and improves with exercise. On examination, he is found to have limited mobility of the sacroiliac joints and lumbar spine. X-ray examination shows bilateral sacroiliitis. A serum test for histocompatibility antigen HLA-B27 is positive. What diagnosis do you suspect? Prescribe the main groups of drugs.

Answers:

1. A. Reiter's syndrome, epidemic form. B. Consultation of urinologist, urethra cytologie examination for finding chlamydies, proteins and its fractions, X-ray examination of knees and sacroiliac joints, synovial fluid aspiration with analysis. C. Peripheric form of ankylosing spondilitis, Psoriatic arthropathy, gonococcal arthritis, and tuberculous arthritis.

2. Ankylosing spondilitis. Disease-modifying drugs, nonsteroidal anti-inflammatory drugs, if it is necessary – corticosteroids, treatment of the muscular spasm.

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Topic 12. MANAGEMENT OF PATIENTS WITH DEGENERATIVE DISEASES OF THE JOINTS

Time frame – 4 hours.

Professional motivation. Arthritis comprises more than 100 different rheumatic diseases and conditions, the most common of which is osteoarthritis (OA). Other frequently occurring forms of arthritis include rheumatoid arthritis, lupus, fibromyalgia, and gout. Common symptoms include pain, aching, stiffness, and swelling in or around the joints. Some forms of arthritis, such as rheumatoid arthritis and lupus, can affect multiple organs and cause widespread symptoms. Although arthritis is more common among adults aged 65 years or older, people of all ages (including children) can be affected. Nearly two-thirds of people with arthritis are younger than age 65 years. Arthritis is more common among women (24.3%) than men (18.7%) in every age group, and it affects members of all racial and ethnic groups. Arthritis also is more common among adults who are obese than among those who are normal weight or underweight.

Place of carrying out: class-room, wards of the rheumatologic department.

Study objective: to improve skills in differential diagnosis between degenerative diseases of the joints and arthritis of other origin.

Basic level:

1. To be able to collect complaints, case history, carry out physical examination in patients with arthritis.
2. To interpret instrumental and laboratory data in patients with arthritis, and sacroileitis.
3. To interpret side effects of agents which are used in rheumatology.

Student has to be able to:

1. Find out joint and spine injury using instrumental methods of examination.
2. Make an algorithm of investigations in patients with arthritis.
3. Determine approaches to treatment in different aetiology of arthritis.

The main theoretical questions:

1. Diagnostic criteria for OA. Management.
2. EULAR treatment standards. Basic treatment of rheumatic diseases with joint manifestations.
3. Use of nonsteroidal anti-inflammatory drugs (NSAID), corticosteroids. Indications and method of arthrocentesis.
4. Differential diagnosis between degenerative diseases of the joints and RA, SpA, gout.

Assignment for self-assessment

1. A 54-year-old woman complains of night pain in knees, starting pain, limitation of the motion range. General state became worse a week after cooling. She has been ill through 5 years. Polyarthralgias started when the menstruation stopped. She didn't take any treatment.

Objectively: General state is satisfactory. BP – 130/75 mm Hg, pulse – 78 beats per minute. Examination of cardiovascular and respiratory systems is not remarkable. Abdomen is soft, liver isn't palpated. Knees are deformed, skin and local temperature is normal, the movement of knees is limited by 15°. Blood analysis: L – $6.4 \cdot 10^9$/l, ESR – 11 mm/hour, CRP – 0.8 mg/l. X-ray examination of joint – unequal loss of joint space, osteophytes. What is the provisional diagnosis?
What non-pharmacologic treatment modalities should be recommended?
What medicine is preferable to relieve pain in case of history of hypertension and/or diabetes?

Answers: Oseoarthritis of the knee joints. It would be important to encourage patient to lose even a minimal amount of weight through improved diet and increased physical activity. Reducing periods of inactivity will help with his knee OA pain, as sustained periods of rest can worsen OA symptoms; therefore, promoting simple activity (e.g., every 20-30 minutes) may reduce OA pain and stiffness. Specific exercises that will target the OA in her knees can be done on her own at home.
In history of hypertension and diabetes, an NSAID should be avoided as first-line therapy. Alternatively, acetaminophen (< 3 grams per day) may be a safe and effective treatment option.

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Topic 13. MANAGEMENT OF PATIENTS WITH OSTEOPOROSIS

Time frame – 6 hours.

Professional motivation. One in three women and one in five men over the age of 50 will be affected by a broken bone due to osteoporosis. In the UK, the prevalence of femoral neck BMD T-Score ≤ -2.5, in those aged 50 years and older, is 6.8% in men and 21.8% in women. Up to 20-24% of patients die in the first year after a hip fracture. Hip fracture survivors experience loss independence, with 40% unable to walk independently and 60% requiring assistance a year later, 80% are restricted in other activities, such as driving and grocery shopping. 33% of hip fracture patients are totally dependent or in a nursing home in the year after a hip fracture. A fracture affects people physically and emotionally, reduces overall quality of life, often causing depression and isolation as people reduce social interaction or are no longer able to do the activities they used to do.

Place of carrying out: class-room, wards of the rheumatologic department.

Study objective: to improve the skills of differential diagnosis

Basic level:

1. To be able to collect complaints, case history, carry out physical examination in patients with arthritis.
2. To interpret instrumental and laboratory data in patients with arthritis, and sacroileitis.
3. To interpret side effects of agents which are used in rheumatology.

Student has to be able to:

1. Find out joint and spine injury using instrumental methods of examination.
2. Make an algorithm of investigations in patients with arthritis. FRAX assessment.
3. Determine approaches to treatment in different aetiology of osteoporosis/ fragility fractures.

The main theoretical questions:

1. Risk factors of osteoporosis.
2. Mechanisms of development.
3. Diagnostic of osteoporosis (dual-energy X-Ray absorptiometry, FRAX scale, laboratory methods). Densitometric criteria.
4. Differential diagnosis.
5. Evidence-based management of patient with osteoporosis. Pharmacological treatment, treatment monitoring (densitometry, biochemical markers). Prevention.

6. Management of patients with primary (postmenopausal) osteoporosis
7. Management of patients with secondary osteoporosis. Management of patients with osteoporosis in the case of multiple myeloma, rheumatoid arthritis and other rheumatic diseases, malabsorption syndrome, hypercorticism, hyperparathyroidism

Assignment for self-assessment. A 75-year-old woman presents to the emergency room with left wrist pain after a fall at home. She tripped and fell while preparing dinner. She heard a "snap" and felt immediate pain. Her medical history is remarkable for hypertension that is well controlled with diuretics and ACE-inhibitor, menopause at age 52. She has no history of smoking. Her weight is 84 kg, and her height is 172cm. Her examination is remarkable for normal vital signs; a swollen, deformed left distal forearm and wrist, with limited mobility because of pain; and good radial pulses and capillary refill in the left fingernail beds. An x-ray confirms a fracture of the left radial head. The doctor put a cast on the patient's hand. The blood test was normal except for low levels of Vitamin D. The patient was also asked to get a DEXA scan, which revealed a T score of -2.9. What risk factor for fracture is this woman likely to have? What are the causes of this condition? What can her physician offer her to prevent future fractures?

Answers: Risk factors are menopause and age. Doctor should advise Vitamin D (1,000 mg) and calcium tablets, bisphosphonates, raloxifene (selective estrogen receptor modulator), exercise daily and eat a healthy diet.

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Topic 14. MANAGEMENT OF PATIENT WITH PULMONARY HYPERTENSION

Time frame – 2 hours.

Professional motivation. Pulmonary hypertension (PH) is a pathophysiological disorder that may be associated with a variety of cardiovascular and respiratory diseases, and managing of which requires a multidisciplinary approach. A pulmonary hypertension prevalence is about 1% of the global population, which increases up to 10% in individuals aged more than 65 years. A left-sided heart failure, particularly heart failure with preserved ejection fraction, is becoming a leading cause of PH. The prognosis of PH is significantly worse in patients with advanced disease.

Place of carrying out: class-room, wards of pulmonology.

Study objective: to be able to determine extent of examinations, put final diagnosis, and assign management for patients with pulmonary hypertension.

Basic level:

1. Anatomy and physiology, endoscopic peculiarities of respiratory tract.
2. The main clinical syndromes in PH.
3. To make physical examination of patients with PH.

Student has to know:

1. Criteria for diagnosis and treatment in PH.
2. Interpretation of laboratory and instrumental investigations.
3. Classification of pulmonary hypertension.
4. Diagnostic algorithm for PH.

The main theoretical questions:

1. WHO group 1: Pulmonary arterial hypertension.
2. PH due to left-sided heart disease.
3. Group 3, pulmonary hypertension associated with lung diseases and/or hypoxia.
4. Group 4, pulmonary hypertension associated with chronic pulmonary artery obstruction.
5. Clinical features of PH.
6. Diagnostic meaning of instrumental methods of examination (ECG, X-Ray, echocardiography, examination of the function of external respiration, CT, catheterization of the right parts of the heart).

7. Indications and assessment of vasoreactivity test.
8. Differential diagnosis of diseases, accompanied by PH.
9. Complications.
10. Evidence-based treatment of PH.
11. Prognosis and working capacity.

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Topic 15. MANAGEMENT OF PATIENT WITH THE FEVER OF UNKNOWN ORIGIN

Time frame – 6 hours.

Professional motivation. Fever of undetermined origin (FUO) presents one of the most challenging and perplexing problems in clinical medicine. Such fevers may persist for weeks or months in the absence of characteristic clinical findings or clues.

The two major systemic infections to consider in the evaluation of FUO are tuberculosis (usually disseminated but sometimes confined predominantly to the liver and spleen) and infective endocarditis. Most FUO cases caused by miliary tuberculosis arise in elderly patients in which, dissemination has followed activation of quiescent foci. Often, in cases caused by miliary tuberculosis, the intermediate-strength (5 tuberculin units) purified protein derivative skin test is negative, and miliary pulmonary lesions are not present on the chest X-ray.

Infective endocarditis, usually subacute, is also an important diagnostic consideration. Most patients with subacute bacterial endocarditis have a heart murmur. Blood cultures would be expected to provide the diagnosis in a patient with subacute bacterial endocarditis, particularly because only 5% of patients with endocarditis have negative blood cultures. The leading cause of negative blood cultures in patients with endocarditis is the prior administration of antibiotics. Other causes of culture-negative endocarditis that should be considered in patients with FUO include infection with fastidious bacteria, chlamydial infection, and Q fever.

Viral infections are usually self-limited and do not produce fever that last longer than 3 weeks. Important exceptions to this generalization are Epstein-Barr virus (EBV) and cytomegalovirus (CMV) infections, which may occasionally present as FUO (often with some mononucleosis-like features) in otherwise healthy individuals. More frequently, CMV infection develops in patients who have received multiple blood transfusions or who have undergone organ transplantation; CMV is the cause of 50% of all febrile episodes in renal transplant recipients. Fever is extremely common in patients infected with HIV; typically, the diagnostic challenge is not in determining the source of fever but in deciding which of several potentially pyrogenic processes is most important. However, patients infected with HIV can also present with prolonged, diagnostically obscure fevers.

More common types of localized infection that present as FUO include hepatic abscess, subphrenic abscess, and subhepatic and pericholecystic abscess. Liver abscesses are often occult; the physician should look for a history that includes symptoms of biliary tract disease, recent blunt abdominal trauma, or travel, which might suggest the diagnosis of amebiasis. Localized infection in the urinary tract is an important consideration in a patient with FUO; perinephric abscess and renal carbuncle are best diagnosed by ultrasonography or CT. Many other localized infections occasionally present as FUO; occult dental infections are one such example and illustrate the need for thoroughness in the evaluation of patients with obscure fevers.

Lymphoma, particularly Hodgkin disease, is the most common neoplastic cause of obscure fever. Lymphoma may be difficult to diagnose when the principal site of involvement is the retroperitoneal nodes, but abdominal CT scans greatly facilitate this diagnosis; a skin biopsy may

help identify intravascular lymphoma as the cause of an FUO. The development of fever in a patient who has myeloma or chronic lymphocytic leukemia is usually caused by superimposed infection and not by the neoplastic process; in some patients, however, the febrile course appears to be caused by the malignancy itself.

Solid tumours can also be associated with fever; hypernephroma is the leading example. As many as 10% of patients with colorectal carcinoma present with fever; either extension of the tumour through the bowel wall, producing a paracolonic abscess, or necrosis and abscess formation in a polypoid intraluminal lesion may be the underlying mechanism. Metastatic cancer may be responsible for continuing fever; hepatic involvement is not necessary for fever to occur. Fevers caused by malignant disease often respond to therapy with NSAIDs; fevers caused by infections may be less likely to respond completely to these agents, but this distinction is not sufficient as a diagnostic test.

A variety of connective tissue disorders and vasculitis may produce prolonged fevers before the development of articular or other characteristic manifestations. In the elderly, polymyalgia rheumatica and the closely related disorder giant cell arteritis (temporal arteritis) are the most common connective tissue disorders presenting as FUO. As many as 15% of cases of giant cell arteritis present as FUO, and in some patients, the vasculitis itself remains occult. Granulomatous diseases of noninfectious origin (sarcoidosis) may be responsible for FUO.

In 10% to 15% of patients with FUO, a detailed workup fails to reveal the diagnosis. In about half these cases, the fever resolves spontaneously. Reevaluation of the patient some weeks or even months later may provide the diagnosis.

Place of carrying out: class-room, wards of cardiology, rheumatology and pulmonology departments.

Study objective: to improve students' skills to make diagnosis of fever of unknown origin.

Basic level:

1. To be able to collect complaints, case history, carry out objective examination.
2. To interpret instrumental (ECG, EchoCG, X-ray) and laboratory data in patients with fever of unknown origin.
3. Modern aspects of aetiology and pathogenesis of rheumatic fever. Classification of rheumatic fever.
4. Criteria for rheumatic fever, infective endocarditis.
5. Criteria for AIDS, SLE, tuberculosis (other granulomatous diseases), etc.

Student has to be able to:

1. To make an algorithm of investigations in patients with fever of unknown origin.
2. To determine approaches to treatment of fever of unknown origin.
3. To find out clinical and laboratory symptoms in patients with rheumatic fever, to unite them into syndromes.

The main theoretical questions:

1. Criteria for fever of unknown origin. Common etiologies of fever of unknown origin (infections, malignancies, autoimmune conditions, miscellaneous).
2. Diagnostic significance of blood cultures, serologic tests, functional blood tests, skin tests, radiologic examinations, biopsy specimens.
3. Differential diagnosis of rheumatic fever and myocarditis.
4. Differential diagnosis of rheumatic fever and infective endocarditis.
5. Differential diagnosis of rheumatic polyarthritis and rheumatoid arthritis.
6. Differential approaches to treatment.
7. Diagnostic criteria and management in sarcoidosis.
8. Aetiological and pathogenetic treatment of rheumatic fever.
9. Aetiological and pathogenetic treatment of infective endocarditis.
10. Indications to operative treatment of infective endocarditis.

Assignment for self-assessment

1. A 34-year-old man was admitted to the emergency room with the recent onset of fever (38–

39 °C), dyspnoea, palpitation. A high-pitched, diastolic murmur, heard best in the third intercostal space along the left sternal border. Infective endocarditis is suspected. What sign would be found on echocardiography?

2. Doctor didn't prescribe antipyretic for patient with flu proceeding from protecting influence of high temterature. What mechanism of protective influence in fever do you know?

a) direct negative influence of fever on infecting agent;
b) activation of erythrogenesis;
c) activation of lysozyme production;
d) activation of interferon production;
e) activation of antibody formation.

3. A 19 year old woman was admitted to the hospital with history of high grade swinging temperature up to 38.8 °C. She had had a sore throat, which lasted for a few days, accompanied by fever, rigors, and myalgia. Her general practitioner prescribed amoxicillin, and she subsequently developed a macular rash on her wrists, back, and legs associated with the fever spikes. The symptoms were persistent over three weeks, prompting referral to the department. She hadn't travelled to anywhere recently. She had no history of recreational drug use or sexual contact and she was not taking any regular medication.

On initial examination she was tachycardic (100 beats/min) and febrile (37.5 °C) with a BP of 108/68 mm Hg. Her oral cavity and cardiovascular, respiratory, abdominal, and nervous system examinations were normal. There was no lymphadenopathy. Her right knee was tender but she had no swollen joints.

Laboratory findings: RBC – $3.0*10^{12}$/l; Hb – 116 g/l; ESR – 28 mm/h; WBC – $14*10^{9}$/l; eos. – 2%, stab – 6%, neutrophils – 79%, lymphocytes – 15%, monocytes – 5%. Total protein – 73 g/l, albumin 46 g/l, urea – 6.7 mmol/l, creatinine – 90 μmol/l, bilirubin – 19 μmol/l, AlT = 64 IU/l, γ glutamyltransferase – 227 (normally 12–43) IU/l, alkaline phosphatase 127 (30–115) IU/l, CRP = 326 mg/l, normal antistreptolysin O titres, negative blood film for malarial parasites, negative results for mononucleosis spot test, IgM for Epstein-Barr virus, cytomegalovirus polymerase chain reaction, hepatitis B surface antigen, and serology for hepatitis C, chlamydia, autoantibody screen negative (RF, ANA, double stranded DNA, extractable nuclear antigen, antineutrophil cytoplasmic antibodies).

Chest radiography and abdominal ultrasonography showed no abnormality. Blood and throat was sent for culture. Throat swab culture, fungal blood cultures, serial bacterial blood cultures, and malarial films gave negative results. Transthoracic echocardiograms appeared normal. Three weeks after admission she continued to have spiking temperatures of up to 40 °C. She also described a simultaneous erythematous rash, which was not raised and was most pronounced on the dorsal aspect of her legs. She thought that the rash was similar to her previous rash but not as prominent. She later developed a 1 cm firm, mobile lymph node in the right anterior triangle of her neck. Fine needle aspiration gave negative results and she had a biopsy. The lymph node biopsy specimen was initially reported to be consistent with reactive inflammation.

What differential diagnoses would you consider? What further investigations should be carried out?

Answers:

1. Vegetations are recognized substantially more frequently in two-dimensional echocardiography – show valvular destruction and vegetations.

2. d.

3. The differential diagnoses after initial investigations include malignancy (particularly lymphoma), sarcoidosis, Still's disease, connective tissue disease, vasculitis, and infective causes including tuberculosis, fungal infection, endocarditis and HIV. She had no relevant risk factors for HIV, but sexual histories can be initially unreliable, particularly if taken in the presence of relatives. Computed tomography of the abdomen and pelvis, transoesophageal echocardiograms, HIV IgM antibody, polymerase chain reaction (for detecting HIV DNA) should be carried out.

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Topic 16. MANAGEMENT OF PATIENTS WITH STOMACH DYSPEPSIA

Time frame – 6 hours.

Professional motivation. Dyspepsia is extremely prevalent, affecting up to 80% of the population at some time, and very often no abnormality is discovered during investigation, especially in younger patients. Patients with “alarm” symptoms, those over 55 years old with new dyspepsia and younger patients unresponsive to empirical treatment require prompt investigation to exclude serious gastrointestinal disease.

Gastro-oesophageal reflux disease is the most common gastrointestinal diagnosis recorded during visits to outpatient clinics. In the United States, it is estimated that 14 to 20% of adults are affected. Several extra-oesophageal manifestations of the disease are well recognized, including laryngitis and cough. With respect to the oesophagus, the spectrum of injury includes oesophagitis, stricture, the development of columnar metaplasia in place of the normal squamous epithelium (Barrett’s oesophagus), and adenocarcinoma. The rising incidence of oesophageal adenocarcinoma is of particular concern, an epidemiologic trend strongly linked to the increasing incidence of this condition.

A consistent paradox in gastro-oesophageal reflux disease is the imperfect correspondence between symptoms attributed to the condition and endoscopic features of the disease. In a population-based endoscopy study in which 1000 northern Europeans were randomly sampled, the prevalence of Barrett’s oesophagus was 1.6%, and that of oesophagitis was 15.5%. However, only 40% of subjects who were found to have Barrett’s oesophagus and one third of those who were found to have oesophagitis reported having reflux symptoms. Conversely, two thirds of patients reporting reflux symptoms had no oesophagitis. Furthermore, although gastro-oesophageal reflux is the most common cause of heartburn, other disorders (e.g., achalasia and eosinophilic oesophagitis) may also cause or contribute to heartburn.

The prevalence of *H. pylori* infection in the general population rises steadily with age, and in the UK approximately 50% of those over the age of 50 years are infected. In many parts of the underdeveloped world infection is much more common and is often acquired in childhood. Up to 90% of the population are infected by adult life. The vast majority of colonised people remain healthy and asymptomatic and only a minority develop clinical disease. Around 90% of duodenal ulcer patients and 70% of gastric ulcer patients are infected with *H. pylori*; the remaining 30% of gastric ulcers are due to NSAIDs. Although the prevalence of peptic ulcer is decreasing in many Western communities, it still affects approximately 10% of all adults at some time in their lives. The male to female ratio for duodenal ulcer varies from 5:1 to 2:1, whilst that for gastric ulcer is 2:1 or less.

Place of carrying out: class-room, wards of gastroenterology.

Study objective: to be able to determine extent of examinations, put final diagnosis, and assign management for patients with stomach dyspepsia.

Basic level:

1. Anatomy and physiology, endoscopic peculiarities of alimentary tract.
2. The main clinical syndromes in the alimentary tract disorders.
3. To make physical examination of patients with disorders of gastrointestinal system.

Student has to know:

1. Criteria for diagnosis and treatment in gastro-oesophageal reflux disease (GERD).
2. Interpretation of laboratory and instrumental investigations (gastric and duodenal juice, X-ray examination of the gastrointestinal system). Barrett's oesophagus.
3. Rome IV diagnostic criteria for functional gastrointestinal disorders.
4. How to make an algorithm of investigations in patients with stomach dyspepsia.
5. Diagnostic and management possibilities of endoscopy with biopsy in gastroenterology.
6. *H. pylori*-associated gastritis. Peptic ulcer disease.

The main theoretical questions:

1. Criteria for functional dyspepsia.
2. "Alarm" symptoms of dyspepsia.
3. Differential programs of stomach dyspepsia treatment.
4. Factors associated with the development of gastro-oesophageal reflux disease. Features of hiatus hernia.
5. Criteria for diagnosis and treatment of GERD. Complications of GERD. Lifestyle modifications.
6. Indications for 24-hours pH-metry of oesophagus, evaluation of results.
7. Diagnostic tests for *H. pylori* infection.
8. Peptic ulcer disease: clinical signs, investigations, management (*H. pylori* eradication, the first-line and second-line therapy). Indications for surgery. Complications of peptic ulcer disease.

Assignment for self-assessment

1. Diagnostic criteria for autoimmune atrophic gastritis are all mentioned, except:
   a) achlorhydria induces G-cell (gastrin producing) hyperplasia, which leads to hypergastrinemia;
   b) pernicious anaemia may develop in longstanding cases;
   c) anti-parietal cell and anti-intrinsic factor antibodies;
   d) low prevalence of Helicobacter pylori;
   e) high prevalence of Helicobacter pylori.
2. A 58-year-old man complaints were as follows: inability to swallow any solids, due to this, the patient was on a liquid diet, reflux after eating food, weight loss. He reported a 2-month history of progressively worsening dysphagia with solids only and weight loss of 10 kg over a period of 3 months. He denied cough, regurgitation, hoarseness, palpitations, and dyspnoea. Past medical history was significant for hypertension for 5 years which had been treated with valsartan and hydrochlorothiazide. He denied any history of cardiovascular problems or arrhythmias. He quit smoking 7 years before and denied drinking alcohol. There was no other significant medical, family or social history. Physical examination revealed: pale skin and mucus with yellow hue, weight – 51 kg, height – 172 cm. He is afebrile. BP is 120/75 mm Hg; pulse is 100 beats/min, regular, respiratory rate is 18 breaths/min.

The thyroid gland is normal to palpation. Normal chest conformity. Peripheral lymph nodes are not enlarged. There is vesicular breathing at auscultation of lungs. Tactile fremitus is normal. The heart apex is nondisplaced. There is no gallop or murmur. The abdomen is soft without tenderness or distention. The liver spans 12 cm in the midclavicular line with a smooth edge. There is no oedema on the legs. Distal pulses are equal.

Blood testing: RBC – $2.8*10^{12}$/l; Hb – 86 g/l; ESR – 10 mm/h; WBC – $8*10^{9}$/l; eos. – 2%, stab – 6%, neutrophils – 69%, lymphocytes – 15%, monocytes – 5%. Total protein – 63 g/l, albumin 36 g/l, urea – 8.7 mmol/l, creatinine – 100 μmol/l, bilirubin – 19 μmol/l, fasting glucose – 3.8 mmol/l, cholesterol – 5 mmol/l, triglycerides – 1.8 mmol/l. Urine chemistry: normal.

Chest X-ray: no infiltrates. Oesophagography revealed an irregular stenosing lesion accompanied by low elevation with a major axis of 40 mm in the lower thoracic oesophagus.

What investigations have diagnostic meaning? What pathological process is more probable? What does blood test indicate on?

3. Broncho-oesophageal syndrome in GERD is caused by:
   a) regurgitation of stomach contents to the airways;
   b) overweight;

c) dysphagia;
d) oesophagus spasm.

Answers:

1. e.

2. Oesophageal endoscopy and biopsy with histopathological examination. Diagnosis of type 4 oesophageal cancer. (Oesophageal endoscopy showed a stenosing lesion, which bled easily, low elevation and irregular erosion in the lower thoracic oesophagus. A biopsy and histopathological examination revealed either highly or moderately differentiated squamous cell cancer). Myelotoxic anaemia.

3. a.

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Topic 17. MANAGEMENT OF PATIENTS WITH ABDOMINAL PAIN

Time frame – 6 hours.

Professional motivation. Up to 10% of all presentations to the emergency department are patients presenting with abdominal pain. The differential diagnosis is very broad and covers multiple specialties. Functional gastrointestinal disorders are extremely common. Irritable bowel syndrome (IBS) is a functional bowel disorder in which abdominal pain is associated with defecation or a change in bowel habit with features of disordered defecation and distension. Approximately 20% of the general population fulfil diagnostic criteria for IBS but only 10% of these consult their doctors because of gastrointestinal symptoms. Nevertheless, IBS is the most common cause of gastrointestinal referral and accounts for frequent absenteeism from work and impaired quality of life. Young women are most often affected. There is wide overlap with non-ulcer dyspepsia, chronic fatigue syndrome, dysmenorrhoea and urinary frequency.

In Western countries gallstones are common and occur in 7% of males and 15% of females aged 18–65 years, with an overall prevalence of 11%. In those under 40 years there is a 3:1 female preponderance, whereas in the elderly the sex ratio is about equal. Gallstones are common in North America, Europe and Australia, and are less frequent in India, the Far East and Africa. In developed countries the incidence of symptomatic gallstones appears to be increasing and they occur at an earlier age. Stones in the common bile duct (choledocholithiasis) occur in 10–15% of patients with gallstones. These stones account for more than 80% of common bile duct stones; they migrate from the gallbladder, and are similar in appearance and chemical composition to the stones found elsewhere. Primary bile duct stones may develop infrequently within the common bile duct many years after a cholecystectomy or represent the accumulation of biliary sludge consequent upon dysfunction of the sphincter of Oddi. In Far Eastern countries, where bile duct infection is common, primary common bile duct stones are thought to follow bacterial infection secondary to parasitic infections with *Clonorchis sinensis*, *Ascaris lumbricoides* or *Fasciola hepatica*. Common bile duct stones can cause partial or complete bile duct obstruction and may be complicated by cholangitis due to secondary bacterial infection, septicaemia, liver abscess, and biliary stricture.

Place of carrying out: class-room, wards of gastroenterology.

Stuydy objective is to improve students' skills in putting final diagnosis and assigning management of patients with abdominal pain.

Basic level:

1. To make physical examination of patients with disorders of gastrointestinal system.
2. The main syndromes and symptoms of the diseases of stomach and duodenum.
3. Mechanisms of the abdominal pain.
4. To evaluate data of the laboratory and instrumental investigations.

Student has to know:

1. Diseases which are accompanied by abdominal pain.
2. Criteria for diagnosis of gastritis.
3. Criteria for diagnosis of ulcer disease.
4. Treatment of gastritis and ulcer disease.
5. Complications of ulcer disease and its treatment.
6. Indications to the surgical treatment of ulcer disease.
7. Interpretation of laboratory and instrumental investigations (gastric and duodenal juice, X-ray examination of the gastrointestinal system).
8. How to make an algorithm of investigations in patients with abdominal pain.

The main theoretical questions:

1. Criteria for gastritis diagnosis.
2. Zollinger-Ellison syndrome.
3. Invasive and non-invasive methods for H. pylori diagnostics.
4. Criteria for diagnosis of the stomach tumours.
5. Peptic ulcer disease: indications for surgery. Complications of peptic ulcer disease and treatment.
6. Management of patients with gastritis, ulcer diseases.
7. Chronic pancreatitis: clinical features, investigations, complications, management.
8. Pancreatic carcinoma: clinical features, investigations, management.
9. Functional bowel disorders: criteria for irritable bowel syndrome. Management.
10. Ischaemic gut injury as a result of arterial occlusion: chronic mesenteric ischaemia.
11. Gallstones and choledocholithiasis: clinical features, investigations, complications, management.
12. Biliary motor disorder ("biliary dyskinesia").
13. Small bowel obstruction. Diverticular disease. Inflammatory bowel diseases.
14. Abdominal aortic aneurysm.
15. Gynecologic pathology.

Assignment for self-assessment

1. A 29 year old man was treated with the first line medicines for 10 days (according to Maastricht II consensus) due to ulcer disease. Now he continues treatment with omeprazol but 2 weeks ago persistant and rising pain appeared. He underwent appendectomy at the age of 22, which was uncomplicated. His father has a duodenum ulcer. On physical examination BP is 110/70 mm Hg, heart rate is 104 beats/min and respiratory rate is 18 breaths/min. He is afebrile. The chest is clear to auscultation and percussion. The heart is regular without extra sounds or murmurs. The abdomen is painful in epigastria, isn't tender when touched. The liver and spleen are not palpable. The liver spans 11 cm in the midclavicular line with a smooth edge.

Blood testing: RBC – $3.9*10^{12}$/l; Hb – 136 g/l; ESR – 8 mm/h; thrombocytes – $250*10^{9}$/l; WBC – $9*10^{9}$/l; eos. – 2%, neutrophils – 69%, lymphocytes – 32%, monocytes – 5%. Total protein – 63 g/l, albumins – 60%, globulins – 40% (α-globulins 10%, β-globulins 11%, γ-globulins 17%), urea – 6.7 mmol/l, creatinine – 70 μmol/l, bilirubin – 19 μmol/l, fasting glucose – 4.8 mmol/l, cholesterol – 4 mmol/l, AST – 37 U/L, ALT – 46 U/L, γ-GT – 57 U/L, sodium – 125 meq/L, prothrombin time – 80%, alkaline phosphatase – 46 U/L.

Chest radiographic findings, ECG are normal.

What complication caused impairment in patient's condition?

2. The main complaints in ulcerative colitis are: a) abdominal pain, frequent, small-volume fluid stools or constipation; b) heartburn, nausea; c) eructation; d) elevation of BP.

3. Signs of Crohn's disease are: a) fasting night pain in epigastria, relieving-pain vomiting; b) abdominal pain mostly in the morning, fluid stools with mucus; c) colicy abdominal pain that

relieve after defecation and passage of flatus; d) pain is often associated with diarrhoea which is watery and does not contain blood or

4. mucus, weight loss.

5. Signs of chronic cholecystitis complicated by cholangitis are: a) epigastric pain, vomiting; b) heartburn, hypersalivation; c) anorexia; d) diarrhoea; e) rigors, right-hypochondrium pain.

Answers:

1. Penetration.

2. a. 3. d. 4. e.

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Topic 18. MANAGEMENT OF PATIENTS WITH JAUNDICE

Time frame – 6 hours.

Professional motivation. Chronic hepatitis B affects about 300 million people around the world; infection is associated with cirrhosis and primary hepatocellular carcinoma. Chronic carrier rates of the virus following infection vary from 10–20% in Asia, Africa, the Middle East and the Pacific Islands, where most infections are acquired in infancy, to 2% in Europe and North America.

Prognosis varies depending on the cause of the hepatitis. The overall mortality of acute viral hepatitis is about 0.5% in otherwise well patients under 40 years of age, but mortality reaches about 3% in patients over 60 years and may be much higher in patients with other serious diseases, such as chronic liver disease, carcinoma or lymphoma. Prognosis in hepatitis B: full recovery occurs in 90–95% of adults following acute HBV infection. The remaining 5–10% develop a chronic infection which usually continues for life, although later recovery occurs occasionally. Infection passing from mother to child at birth leads to chronic infection in the child in 95% of cases and recovery is rare. Recovery from acute HBV infection occurs within 6 months and is characterised by the appearance of antibody to viral antigens. Persistence of HBeAg beyond this time indicates chronic infection. Combined HBV and HDV infection causes more aggressive disease. Most patients with chronic hepatitis B are asymptomatic and develop complications such as cirrhosis and hepatocellular carcinoma only after many years. Cirrhosis develops in 15–20% of patients with chronic HBV, over 5–20 years. This proportion is higher in those infected in childhood.

HCV caused over 90% of post-transfusion hepatitis before serological tests allowed the screening of blood donors, and accounted for the high incidence of chronic hepatitis in patients with haemophilia. Parenteral drug users continue to be at high risk of HCV infection. Chronic infection occurs in about 70–80% of patients and this is usually life-long. Most never suffer from acute illness. Chronic HCV usually remains asymptomatic for years and is not associated with an early increase in mortality. However, many patients eventually develop cirrhosis and some progress to hepatocellular carcinoma. Approximately 20% of chronically infected patients will develop cirrhosis after 20 years of infection, and around 50% after 30 years. Once cirrhosis is present, 2–5% per year will develop hepatocellular carcinoma.

Place of carrying out: class-room, wards of gastroenterology.

Study objective is to improve students' skills in differential diagnosis and treatment of patients with jaundice.

Basic level:

1. Bilirubin metabolism.
2. The main clinical syndromes in liver disorders.
3. To be able to collect complaints, case history, carry out objective examination of patients with liver disorders.
4. To interpret instrumental and laboratory data in patients with jaundice.

Student has to know:

1. How to put provisional and final diagnosis and assign management in jaundice.
2. Differential diagnosis in jaundice of different origin.

The main theoretical questions:

1. Jaundice causes. Examples of conditions with increased breakdown of red blood cells.
2. Congenital nonhaemolytic hyperbilirubinaemia. Criteria for diagnosis and treatment of Gilbert's syndrome.
3. Clinical and biochemical criteria for different types of jaundice.
4. Algorithm of investigations in patients with jaundice.
5. Hepatitis B, C, D: clinical features, investigations, complications.
6. Indications for interferon therapy in viral hepatitis. Criteria of effective therapy by interferons in hepatitis. Side effects of interferon therapy.
7. Autoimmune hepatitis: clinical features, investigations, complications, management.
8. Sclerosing cholangitis: clinical features, investigations, management.
9. Gallstones and choledocholithiasis: clinical features, investigations.

Assignment for self-assessment

1. A 32 year old man is noted to have fatigue at the end of a busy working week, yellow sclera. He underwent appendectomy at the age of 22, which was uncomplicated. Risk factors for chronic hepatitis are absent, except that he insufflated cocaine a few occasions during his college years.

On physical examination the patient looks generally well, except jaundice. Blood pressure is 132/92 mm Hg, heart rate is 84 beats/min, respiratory rate is 14 breaths/min. He is afebrile. The neck is supple without lymphadenopathy or thyromegaly. The chest is clear to auscultation and percussion with no gynecomastia or spider telangiectasias. The heart is regular without extra sounds or murmurs. The abdomen is soft without tenderness or distention. The left lobe of liver is not palpable nor is there splenomegaly. The liver spans 8 cm in the midclavicular line with a smooth edge. There is no abdominal collateral circulation, umbilical hernia, or bruit. There are no signs of ascites, other stigmata of chronic liver disease. The extremities show no clubbing, cyanosis, oedema, nor is there palmar erythema. Neurologic examination is within normal limits without asterixis. The skin has no stigmata of chronic liver disease.

Blood testing: RBC – $3.9*10^{12}$/l; Hb – 136 g/l; ESR – 8 mm/h; thrombocytes – $250*10^{9}$/l; WBC – $6*10^{9}$/l; eos. – 2%, neutrophils – 69%, lymphocytes – 32%, monocytes – 5%. Total protein – 63 g/l, albumins – 60%, globulins – 40% (α-globulins 10%, β-globulins 11%, γ-globulins 19%), urea – 6.7 mmol/l, creatinine – 70 μmol/l, bilirubin – 39 μmol/l, fasting glucose – 4.8 mmol/l, cholesterol – 6 mmol/l, AST – 87 U/L, ALT – 166U/L, γ-GT – 87 U/L, sodium – 105 meq/L, prothrombin time – 42.8%, alkaline phosphatase – 96 U/L, fibrinogen – 2 g/l.

Hepatitis serology: anti-HAV total – positive, anti-HAV IgM – negative, anti-HBc – positive, HBsAg – negative, anti-HBs – positive, anti-HCV – positive, HCV RNA – positive. Chest radiographic findings, ECG are normal. Abdominal ultrasound revealed a mildly echogenic liver with normal contour, portal vein diameter is 10 mm, spleen vein diameter is 5 mm. No gallstones are seen.

What is the most likely clinical diagnosis? What treatment does this patient need?

2. Mild jaundice, best seen by examining the sclerae in natural light, is usually detectable when serum bilirubin reaches: a) 25 μmol/l; b) 35 μmol/l; c) 60 μmol/l; d) 100 μmol/l.

3. Jaundice in pancreatic cancer differs from jaundice in gallstones by mentioned signs except: a) development without previous pain attack; b) fast increasing of bilirubin; c) positive Courvoisier-Terrier syndrome; d) persistant and intensive jaundice; e) appears in elder patients.

Answers:

1. The elevation of serum alanine aminotransferase indicates hepatocellular injury as opposed to cholestasis. Serologic testing reveals previous exposure to hepatitis A, hepatitis B, and hepatitis C. Hepatitis A infection does not become chronic. Hepatitis B serologic pattern is diagnostics of previous exposure, but not chronic infection. Hepatitis C antibody positivity with an exposure risk and elevation of aminotransferases makes the diagnosis of chronic HCV infection a near certainty.

The quantification of HCV RNA has become an important part of the therapy of patients chronically infected with HCV, although it is important to note that there is no correlation between viral load and disease severity. Liver biopsy is recommended before treatment to assess the grade and stage of disease and to exclude other forms of liver disease or complications (such as concurrent alcoholic liver disease, medication-induced liver injury, and iron overload).

The patient was noted to be viremic with HCV viral load of 650,000 IU/ml, genotype 1a. Liver biopsy revealed portal inflammatory cells with periportal hepatic fibrosis (grade 2 stage 2). After detailed discussion with the patient regarding the risks and benefits, administration of Sofosbuvir and velpatasvir are commenced in a two-drug fixed-dose combination containing 400 mg of sofosbuvir and 100 mg of velpatasvir in a single tablet. The recommended dose of the combination is 1 tablet taken orally once daily with or without food. The endpoint of HCV therapy is undetectable HCV RNA in serum or plasma by an assay with a lower limit of detection 12 weeks or 24 weeks after the end of treatment.

2. b. 3. b.

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Topic 19. MANAGEMENT OF PATIENTS WITH HEPATOMEGALY AND HEPATOLIENAL SYNDROME

Time frame – 6 hours.

Professional motivation. Hepatic cirrhosis can occur at any age and often causes prolonged morbidity. It frequently manifests itself in younger adults and is an important cause of premature death. Any condition leading to persistent or recurrent hepatocyte death may lead to hepatic cirrhosis, e.g., viral hepatitis and alcohol. Prolonged biliary damage or obstruction, as can occur in primary biliary cirrhosis, sclerosing cholangitis and post-surgical biliary strictures, will also result in cirrhosis. Persistent blockage of the venous return from the liver, e.g., veno-occlusive disease and Budd-Chiari syndrome, will eventually result in liver cirrhosis. Worldwide, the most common causes of cirrhosis are viral hepatitis and prolonged excessive alcohol consumption. The overall prognosis in cirrhosis is poor.

Many patients present with advanced disease and/or serious complications that carry a high mortality. Overall, only 25% of patients survive 5 years from diagnosis but, where liver function is good, 50% survive for 5 years and 25% for up to 10 years. The prognosis is more favourable where the underlying cause of the cirrhosis can be corrected, as in alcohol misuse, haemochromatosis and Wilson’s disease. Laboratory tests give only a rough guide to prognosis in individual patients.

Deteriorating liver function, as evidenced by jaundice, ascites or encephalopathy, indicates a poor prognosis unless a treatable cause such as infection is found. The course of cirrhosis is uncertain, as unforeseen complications such as variceal bleeding may lead to death unexpectedly.

Fatty liver is a common and generally benign condition. The majority of obese patients (60–90%) and up to 50% of type II diabetics have fatty liver. The outlook for most patients with steatosis is excellent, although a few deaths have been reported. In patients with alcoholic steatosis, the severity of the fatty change can predict the eventual progression to cirrhosis. Previously, the prognosis of patients with acute fatty liver of pregnancy was considered poor. However, milder forms of this condition are now more frequently recognised.

Place of carrying out: class-room, wards of the gastroenterology.

Study objective is to improve students' skills in putting final diagnosis and assigning management of patients with hepatomegaly.

Basic level:

1. Examination of the patients with hepatomegaly.
2. Evaluation of the laboratory and instrumental investigations data.
3. Classification of hepatitis and cirrhosis.

Student has to know:

1. Diseases for which hepatomegaly is inherent and how to put presumptive diagnosis.
2. Investigations in patients with suspected liver disease (the liver function tests, biochemical and coagulation tests, liver biopsy).
3. How to make differential diagnosis in hepatomegaly.
4. How to indicate the treatment for patients with hepatomegaly.

The main theoretical questions:

1. Definition and causes of hepatolienal syndrome.
2. Plan of investigations of hepatolienal syndrome.
3. Criteria for diagnosis of fatty liver.
4. Criteria for diagnosis of drugs-toxic hepatitis.
5. Classification of chronic hepatitis. Criteria for diagnosis of chronic autoimmune hepatitis.
6. Classification of cirrhosis. Criteria for diagnosis of liver cirrhosis.
7. Criteria for diagnosis of alcoholic cirrhosis.
8. Treatment of chronic hepatitis, and cirrhosis, their complications.

Assignment for self-assessment

1. Splenomegaly and ascitis are observed in: a) primary biliary cirrhosis; b) portal liver cirrhosis; c) Wilson's disease; d) portal hypertensive syndrome of different origin.

2. A 47 year old female patient was referred with a complaint of pruritus which developed 2 months before.

Medical history: she has ulcerative colitis (complaints of the bloody defecation with mucus for 6–7 times a day) and she uses mesalazine tablet with 3 g/day; the bloody diarrhoea with mucus had been regressed. A pruritus was begun about 2 months ago which become refractory and she was referred to the clinic. She did not have any connective tissue disease. She also did not have a story of drug use that will affect the hepatobiliary system except mesalazine. She is a non-smoker, non-alcoholic.

On the physical examination: she is fully conscious and oriented. Patient is of average build. Pulse is 72/minute regular, blood pressure is 130/90 mmHg, her skin and sclera's are in a mild icteric appearance, and the liver is exceeding the costa border about 2 cm. There was not any pathological finding on examination of the other systems.

Laboratory examinations: RBC – $3.5*10^{12}$/l; Hb – 116 g/l; ESR – 28 mm/h; thrombocytes – $250*10^{9}$/l; WBC – $6*10^{9}$/l; eos. – 2%, neutrophils – 69%, lymphocytes – 32%, monocytes – 5%. Total protein – 63 g/l, albumins – 60%, globulins – 40% (α-globulins 10%, β-globulins 11%, γ-globulins 19%), urea – 6.7 mmol/l, creatinine – 70 μmol/l, bilirubin – 39 μmol/l, fasting glucose – 4.8 mmol/l, cholesterol – 6 mmol/l, AST – 67 U/L (normal: 0–41 U/l), ALT – 106 U/L (normal: 0–40 U/L), γ-GT – 87 U/L, sodium – 105 meq/L, prothrombin time – 42.8%, alkaline phosphatase –

396 U/L (normal: 30–91 U/L), GGT–124 U/L (normal: 0–61 U/L), fibrinogen – 2 g/l. CRP – 2.08 mg/dL. Viral hepatitis panel is negative.

Immunological tests: anti-nuclear antibody (ANA), antismooth muscle antibody (ASMA), antiliver and antikidney microsome antibody (LKM), p-ANCA are negative. Antimitochondrial antibodies (AMA) are positive with a value >1/160 and anti-M2 antibody (AMA-M2) is also positive. Thyroid function tests are normal.

Abdominal ultrasonography: hepatomegaly. Magnetic resonance cholangiopancreatography: gallbladder, common bile duct and intrahepatic bile ducts were evaluated as normal.

Total colonoscopy: ulcerative colitis was detected in the descending colon, sigmoid colon and mild to moderate with rectal involvement.

Biopsy was taken from the sigmoid colon and rectum and crypts: cryptic micro abscesses and crypt distortion are observed. Liver biopsy: diffuse inflammation and the portal areas were infiltrated by the lymphocytes and histiocytes.

Upper gastrointestinal endoscopy revealed normal oesophageal mucosa and lumen, no oesophageal varices.

What is your clinical diagnosis? Management?

3. Bad prognostic signs in liver cirrhosis are:

a) increasing plasma bilirubin;

b) hypoalbuminemia or an albumin concentration < 30 g/l;

c) marked hyponatraemia (< 120 mmol/l not due to diuretic therapy);

d) prolonged prothrombin time;

e) all of the above signs are correct.

Answers:

1. d.

2. Primary biliary cirrhosis (PBC), stage 1. Ulcerative colitis.

Ursodeoxycholic acid is introduced as 15 mg/kg/day besides mesalazine therapy (on the follow-up conducted a month later, her complaint of pruritus was regressed and the outcome of liver function test reached normal ranges).

Ulcerative colitis is a disease which may have extraintestinal complications. Wide range variations of the liver diseases may be seen in the patients with ulcerative colitis. Hepatobiliary disease, primary sclerosing cholangitis is the most seen concomitant disease by 5% in the patients with ulcerative colitis. PBC is another autoimmune disease similar to primary sclerosing cholangitis characterized by itching, and hyperbilirubinemia. AMA is found in approximately 95% of the patients with a negative value of 5%. PBC generally affects the middle-aged females more than males. The prevalence of PBS in the patients with UC is 30 times higher than in the general population. The best test used in the differential diagnosis is AMA. AMA may be always positive in PBC, while it is always negative in primary sclerosing cholangitis.

3. e.

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Topic 20. MANAGEMENT OF PATIENTS WITH PORTAL HYPERTENSION

Time frame – 6 hours.

Professional motivation. Population-based prevalence data for portal hypertension are not available, but portal hypertension is a frequent manifestation of liver cirrhosis. Extrahepatic portal vein obstruction is frequently the cause of portal hypertension in childhood and adolescence, while cirrhosis causes 90% or more of portal hypertension in adults in Western countries. Schistosomiasis is the most common cause of portal hypertension worldwide but it is infrequent outside endemic areas. Variceal haemorrhage is the most common complication associated with portal hypertension. Almost 90% of patients with cirrhosis develop varices, and approximately 30% of varices bleed. The first episode of variceal haemorrhage is estimated to carry a mortality rate of 30–50%.

Place of carrying out: class-room, wards of the gastroenterology.

Study objective is to to be able to put final diagnosis in portal hypertensive syndrome and assign management.

Basic level:

1. Collateral circulation in portal hypertension.
2. To examine patients with liver diseases.
3. To determine symptoms, to group them into the syndromes, and to select the leading syndrome.
4. To evaluate data of the laboratory and instrumental investigations in portal hypertensive syndrome.

Student has to know:

1. Clinical signs in portal hypertension.
2. Investigational methods for the diagnosis of portal hypertension.
3. How to make differential diagnosis, clinical diagnosis due to modern classification.
4. How to indicate the treatment for patients with portal hypertensive syndrome.

The main theoretical questions:

1. Types of portal hypertension.
2. Methods for pressure evaluation in portal vein.
3. Differential diagnosis in portal hypertension.
4. Complications of portal hypertension.
5. Treatment of patients with portal hypertension. Pharmacological reduction of portal pressure.

Assignment for self-assessment

1. Methods of portal hypertension diagnostics are the mentioned besides: a) splenomanometry; b) hepatomanometry; c) splenoportography; d) oesophagography; e) FGDS.

2. What is the pressure in splenomanometry in moderate portal hypertension?

a) 200–300 mm; b) 120–150 mm; c) 350–500 mm; d) 50–80 mm.

3. Portal hypertension develops in: a) liver veins thrombosis; b) liver arteries thrombosis; c) splenic vein thrombosis; d) mesenteric arteries thrombosis; e) splenic infarction.

4. What advantages of endoscopic ligation of bleeding oesophageal varices do you know comparing to endoscopic sclerotherapy?

5. A 57-year-old man was admitted with a three day history of weakness, anorexia, unsteady gait. He reported smoking 1 pack per day and drinking alcohol for the past 10 years. Over the previous 6 months, the patient had been unemployed and reported increased alcohol consumption. On physical examination, the patient was noted to have marked ascites with a prominent fluid wave and bulging flanks, bilateral pitting oedema above the knees, pallor, spider teleangiectasia on the arms, palmer erythema, jaundice. His pulmonary and cardiovascular examinations were unremarkable. The abdomen is distended. The liver spans 17 cm in the midclavicular line with a smooth and dense edge. Blood pressure –130/80 mmHg, pulse rate – 69 beats/min. No endocrine changes.

Blood testing: RBC – $2.9*10^{12}$/l; Hb – 96 g/l; ESR – 8 mm/h; thrombocytes – $120*10^{9}$/l; WBC – $6*10^{9}$/l; eos. – 2%, neutrophils – 69%, lymphocytes – 32%, monocytes – 5%. Total protein – 50 g/l, albumins – 40%, globulins – 60% (α-globulins 10%, β-globulins 11%, γ-globulins 39%), urea – 6.7 mmol/l, creatinine – 70 μmol/l, bilirubin – 59 μmol/l, fasting glucose – 4.8 mmol/l, cholesterol – 6 mmol/l, AST – 107 U/L, ALT – 66 U/L, γ-GT – 97 U/L, sodium – 105 meq/L, prothrombin time – 42.8%, fibrinogen – 2 g/l. Chest radiographic findings, ECG are normal.

Abdominal ultrasound revealed a nodular liver surface, massive splenomegaly, portal vein diameter is 15 mm, moderate ascities. Upper gastrointestinal endoscopy showed grade III oesophageal varices and severe portal gastropathy.

What syndromes does this patient have? What additional diagnostic examinations are indicated?

What is the most likely clinical diagnosis?

Answers:

1. d. 2. a. 3. a.

4. Associated with lower complication rate, lower mortality rate, fewer number of treatments for varices eradication.

5. Portal hypertensive syndrome, hepatic encephalopathy, anaemic syndrome.

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Topic 21. MANAGEMENT OF PATIENTS WITH BRONCHOOBSTRUCTIVE SYNDROME

Time frame – 6 hours.

Professional motivation. According to WHO estimates, 65 million people have moderate to severe chronic obstructive pulmonary disease (COPD). Most of the information available on COPD prevalence, morbidity and mortality comes from high-income countries. At one time, COPD was more common in men, but because of increased tobacco use among women in high-income countries and the higher risk of exposure to indoor air pollution (such as biomass fuel used for cooking and heating) in low-income countries, the disease now affects men and women almost equally. People with COPD are at increased risk of developing heart disease, lung cancer. COPD is now one of the top three causes of death worldwide and 90% of these deaths occur in low- and middle-income countries.

According to WHO estimates, 235 million people suffer from asthma. There is evidence that its prevalence has increased considerably over the past 20 years, especially in children. Asthma is the most common chronic disease among children. Unfortunately the prevalence of asthma symptoms in children varies from 1 to more than 30 percent in different populations and is increasing in most countries, especially among young children. Fortunately asthma can be effectively treated and most patients can achieve good control of their disease. Asthma is not just a public health problem for high income countries: it occurs in all countries regardless of level of development.

Bronchiectasis shares many clinical features with chronic obstructive pulmonary disease (COPD), including inflamed and easily collapsible airways, obstruction to airflow, and frequent office visits and hospitalizations. The prevalence of bronchiectasis is unknown, due to the lack of standardised medical care and poor healthcare access in underdeveloped countries. The prevalence of bronchiectasis increases with age, bronchiectasis is more common in women. In the UK, incidence is estimated at 1.06 to 1.3 per 100,000 population. In general, it is estimated that the

incidence has decreased over the past several decades due to implementation of vaccination programmes and the development of more potent antibiotics. Infection is the most common cause of bronchiectasis in underdeveloped countries.

Factors that affect mortality in patients with moderate to severe bronchiectasis include advanced age, St George's Respiratory Questionnaire activity score, Pseudomonas aeruginosa infection, total lung capacity (TLC), and residual volume divided by TLC. Prognosis for people with bronchiectasis depends on how well infections and other complications are prevented or controlled. People with co-existing conditions, such as chronic bronchitis or emphysema, and people who have complications, such as pulmonary hypertension or cor pulmonale, tend to have a worse prognosis.

Study objective: to improve the practical skills in evaluation of the most important signs of ventilation abnormalities, to do the differentiation between lung diseases which accompany bronchial obstruction. To prescribe the treatment according to aetiology, peculiarities, and intensity of bronchial disorders and allergic status.

Basic level:

1. Examination of patient with lung disease.
2. Laboratory and instrumental data in patients with pathology of respiratory system.
3. Interpretation of sputum analysis, spirography, peakflowmetry, X-ray examination, chest tomography.
4. Symptoms and differential diagnosis of lung diseases.
5. Treatment of bronchial obstruction.

Student has to know:

1. Diagnostic algorithm in bronchoobstructive syndrome.
2. How to make clinical diagnosis.
3. Assessment of symptoms in COPD: Modified British Medical Research Council (mMRC) Questionnaire, COPD Assessment Test, The COPD Control Questionnaire
4. How to indicate differential programs of the treatment.
5. How to interpret side effects of corticosteroids, broncholytics (short- and long-acting).

The main theoretical questions:

1. Aetiology and pathogenesis of bronchial obstruction.
2. Clinical signs of syndromes: bronchial spasm (paroxysmal and steady), bronchial inflammation (diffuse and local), delay of sputum, obturation and compression of bronchus, trachea and bronchial narrowing, bronchial drainage disturbances, mucous hypersecretion, hypersensitivity of bronchus.
3. Classification and clinical signs in BA. Diagnostic significance of peakflowmetry.
4. Classification and clinical signs in COPD. Spirometry values.
5. Classification and clinical signs in bronchiectasis.
6. Differential diagnosis between BA, COPD, and bronchiectasis.
7. Management of patients with BA depending on levels of asthma control. Daily dosages for inhaled glucocorticosteroids. Indication for systemic steroid treatment.
8. Management of asthma exacerbation. Side effects of inhaled steroids.
9. Management of patients with COPD depending on severity. Indication for inhaled steroids.
10. Definition of bacterial exacerbation of COPD. Management.
11. Management of patients with bronchiectasis.

Assignment for self-assessment

1. Diagnostic criteria for COPD are:

a) FEV1<90% predicted, FEV1/FVC<80%; b) FEV1<80% predicted, FEV1/FVC<70%;

c) FEV1<70% predicted, FEV1/FVC<60%; d) FEV1<60% predicted, FEV1/FVC<50%;

2. A 21-years-old patient works at the pharmacy, complains of dry cough, recurrent attacks of dyspnoea for 2 months, on weekends symptoms decrease, t – 37.0 $^{\circ}$C. Current attack of dyspnoea was stopped by salbutamol. BP is 126/80 mm Hg, heart rate is 92 beats/minute and regular, respiratory rate is 18 breaths/minute. Examination reveals mildly oedematous nasal mucosa with no discharge. Cardiac examination shows regular rate and rhythm without murmur. On pulmonary

auscultation prolonged expiration and bilateral wheezing are heard over all parts of the lungs. X-ray shows no abnormalities. What is the presumptive diagnosis?

a) bronchial asthma;
b) COPD;
c) medicamentous disease;
d) spontaneous pneumothorax.

Answers:

1. b. 2. a.

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Topic 22. DIFFERENTIAL DIAGNOSIS AND MANAGEMENT OF PATIENTS WITH INFILTRATIVE PULMONARY OBSCURITY, PLEURAL EFFUSION

Time frame – 6 hours.

Professional motivation. Pulmonary infiltrates frequently develop in pneumonia, infiltrative tuberculosis, pulmonary infarction, lung cancer, acute eosinophilic pneumonia, Churg-Strauss syndrome.

The clinical approach to persistent pulmonary infiltrate requires evaluating several factors, including host factors (age, comorbidities, immunodeficiency), the severity of symptoms, and the possibility of a non-infectious aetiology. The history and clinical examination, augmented by laboratory evaluation and radiographic techniques, can narrow the differential diagnosis.

Heart failure is responsible for approximately one third of all pleural effusions and the leading cause of pleural effusion in the US is also CHF, with an estimated annual incidence of 500,000. Pneumonia is second with an incidence of 300,000. Approximately 40% of the hospitalised patients with pneumonia have an associated parapneumonic effusion. Malignancy is the third leading cause overall, with an estimated incidence of 200,000; however, it is the second most common cause of effusion in patients >50 years of age. Pulmonary embolus, viral disease, coronary artery bypass surgery, and cirrhosis are also common causes of effusion. Small pleural effusions are present in up to 40% of patients with pulmonary embolism. Of all patients with cirrhosis, 5% have an associated pleural effusion. TB is an important cause of pleural effusion in the developing world.The prognosis in pleural effusion varies in accordance with the condition’s underlying aetiology. Parapneumonic effusions, when recognized and treated promptly, typically resolve without significant sequelae. However, inappropriately treated parapneumonic effusions may lead to empyema, constrictive fibrosis, and sepsis. Development of malignant pleural effusion is associated with a very poor prognosis, with median survival of 4 months and mean survival of less than 1 year. The most common associated malignancy in men is lung cancer, and the most common associated malignancy in women is breast cancer. Effusions from cancers that are more responsive to chemotherapy, such as lymphoma or breast cancer, are more likely to be associated with prolonged survival, compared with those from lung cancer or mesothelioma.

Place of carrying out: class-room, wards of pulmonology, cardiology and rheumatology departments, X-ray department.

Study objective: to be able to determine extent of examinations to put final diagnosis and assign management.

Basic level:

1. Anatomy, physiology, and pathophysiology of respiratory system.
2. To be able to collect complaints, case history, carry out objective examination.
3. To interpret instrumental (X-ray, CT) and laboratory data in patients with pleural effusion.
4. To identify signs from objective data inherent to pleural effusion.
5. Aetiology, pathogenesis, classification, and diagnostic criteria for pneumonia.
6. Diagnostic criteria for tuberculosis, lung cancer, lung atelectasis and middle lobe syndrome.
7. X-ray examination of lungs.
8. Investigation of sputum: methodology of collection, interpretation of obtained data.
9. Pharmacodynamics, pharmacokinetics, indications and contraindications to antibacterial drugs administration. Principles of antibacterial therapy.

Student has to know:

1. Diagnostic algorithm in pulmonary infiltrates detection.
2. How to make clinical diagnosis.
3. How to establish differential programs of the treatment.
4. How to examine patients with pleural effusion.
5. How to make an algorithm of investigations in patients with pleural effusion.
6. How to determine approaches to treatment in different aetiology of pleural effusion

The main theoretical questions:

1. Differential diagnostics of pulmomycoses (systemic candidosis, histoplasmosis, coccidiomycosis, actinomycosis).
2. Differntial diagnosis in case of lung atelectasis and middle lobe syndrome.
3. Differential diagnostics of tuberculosis and pneumonia.
4. Differential diagnostics of lung cancer and pneumonia.
5. Differential diagnosis between pneumonia and pulmonary infarction.
6. Diagnostic criteria for eosinophilic pulmonary infiltration, sarcoidosis. Management.
7. Diagnostic algorithm in the most frequent pulmonary dissemination (disseminated (miliary) tuberculosis, pneumonia, pulmonary sarcoidosis, collagenoses).
8. Differential diagnosis of pleural effusion of different aetiology.
9. Infectious pleuritis, aceptic pleuritis: pathogenesis.
10. Techniques of pleural punction, indications, interpretation of obtained data of pleural effusion.

Real-life situation to be solved:

1. A 35 year old patient had sudden onset of fever, high temperature (40 $^{\circ}$C), headache, dry cough. He cought a cold during fishing. On examination: body temperature is 39.9 $^{\circ}$C, hyperemia of the cheeks, a light cyanosis of the lips, the skin is pale, humid, rapid, breathing is shallow – 32/min. On the 3rd day from the onset of disease the patient had haemoptysis. The expansion of the right lung is limited, there is dullness above the inferior lobe of the right lung, brochial breathing, moist rales on percusion. Heart sounds are weak, tachycardia – 96/min, rythmical, BP – 110/60. Other systems without any changes. Laboratory findings: RBC – $3.0*10^{12}$/l; Hb – 116 g/l; ESR – 28 mm/h; WBC – $16*10^{9}$/l; eos. – 2%, stab – 6%, neutrophils – 69%, lymphocytes – 15%, monocytes – 5%. Total protein – 73 g/l, albumin 46 g/l, urea – 6.7 mmol/l, creatinine – 90 μmol/l, bilirubin – 19 μmol/l, fasting glucose – 4.8 mmol/l, cholesterol – 5 mmol/l, triglycerides – 1.8 mmol/l. The X-ray findings: confluent opacities in inferior lobe.

What is the diagnosis? What complications of this disease do you know? What diseases should you make differentiation between? Treatment.

2. A 26 year old patient F. complains of moist cough. Two weeks ago there was dry cough and high temperature (38.2 $^{\circ}$C). On X-ray: infiltrate in the upper lobe (under the clavicular) of the left lung. After 10 days of antibioticotherapy X-ray investigation was performed: shadow of the upper left lobe resolved but oval infiltration with illegible edge of 2×2 cm appeared in the right lower lobe. In percution: clear pulmonary sound, on auscultation: vesicular breathing. Laboratory findings: RBC – $3.5*10^{12}$/l; Hb – 126 g/l; ESR – 18 mm/h; WBC – 10×10^{9}/l; eos. – 20%, stab –

2%, neutrophils – 69%, lymphocytes – 25%, monocytes – 5%. Total protein – 73 g/l, albumin 46 g/l, urea – 6.6 mmol/l, creatinine – 98 μmol/l, bilirubin – 19 μmol/l, fasting glucose – 4.8 mmol/l. Sputum analysis: no mycobacteria.

What is the possible diagnosis? What diseases should you make differentiation between? Additional investigations. Treatment?

Answers:

1. Pneumonia. Pulmonary failure, myocarditis, pleuritis. Tuberculosis, lung infarction. Antibiotics, broncholytics.

2. Eosinophilic infiltration. Pneumonia, tuberculosis. Chest CT. Corticosteroids.

Assignment for self-assessment

1. The most frequent causes of non-infectious pleuritis are:

a) diffuse connective tissue diseases;
b) chest trauma;
c) pulmonary infarction in pulmonary embolism;
d) malignancy;
e) acute pancreatitis, myocardial infarction;
f) all written above.

2. Specific gravity of transudate, protein content and leukocytes count in 1 mkl of transudate in laboratory investigation are:

a) <1005 g/l, <15g/l, <500;
b) <1010 g/l, <20g/l, <750;
c) <1015 g/l, <30g/l, <1000;
d) <1020 g/l, <35g/l, <1500;
e) <1025 g/l, <40g/l, <1500.

3. Patient F., 60 years old, with clinical symptoms of pleuritis was performed pleural punction. Obtained haemorrhagic fluid examination revealed a specific gravity of more than 1.030, protein – 3.5 g/dL; fluid LDH to serum LDH ratio 0.75; atypical cells.

What kind of fluid was obtained? What are the most frequent causes of exudative pleuritis?

1. A patient with low-grade fever and weight loss has poor excursion on the right side of the chest with decreased fremitus, flatness to percussion, and decreased breath sounds all on the right. The trachea is deviated to the left. The most likely diagnosis is:

a) pneumothorax;
b) pleural effusion;
c) consolidated pneumonia;
d) atelectasis.

Answers:

1. f. 2. c.

3. Exudative fluid. Tuberculosis, cancer, nonspecific inflammation.

4. b.

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Topic 23. ANAGEMENT OF PATIENTS WITH PNEUMONIA

Time frame – 6 hours.

Professional motivation. Community-acquired pneumonia (CAP) is a common and potentially serious illness. It is associated with considerable morbidity and mortality, particularly in elderly patients and those with significant comorbidities. The overall rate of CAP in adults is approximately 5.16 to 6.11 cases per 1000 persons per year; the rate of CAP increases with increasing age. There is seasonal variation, with more cases occurring during the winter months. The rates of pneumonia are higher for men than for women and for black persons compared with Caucasians. The aetiology of CAP varies by geographic region; however, Streptococcus pneumoniae is the most common cause of pneumonia worldwide.

Estimates of the incidence of community-acquired pneumonia range from 4 million to 5 million cases per year, with about 25% requiring hospitalization. Mortality is highest for CAP patients who require hospitalization, with a 30-day mortality rate of up to 23 percent in such patients. All-cause mortality in patients with CAP is as high as 28% within one year.

Hospital-acquired pneumonia (HAP) is the second most common nosocomial infection with an overall rate of 6.1 per 1000 discharges. It is estimated to occur in 250,000 persons per year, representing about 15% to 18% of all nosocomial infections. By comparison, the infection rate for nosocomial urinary tract infection, the most common hospital-acquired infection, is 11 per 1000 discharges. The incidence of HAP varies depending on the hospital environment.

The incidence of HAP is greater among patients in the ICU. Generally, approximately 30% of HAP occurs in critical care settings.

The incidence of ventilator-associated pneumonia (VAP) from the National Nosocomial Infections Surveillance (NNIS) data is 7.6 cases per 1000 ventilator-days. The risk for VAP peaks at day 5 of mechanical ventilation. NNIS data showed that the incidence of VAP was highest for trauma ICUs (15.2 per 1000 ventilator-days). The overall prevalence of VAP was 9.3%.

HAP has been shown to have the highest mortality rate of all nosocomial infections. In one study, the crude case-fatality rate was 30%, rising to 33% in cases attributable to an initial episode of HAP. In a Canadian study of non-ICU HAP, overall mortality rate was 20%, with a direct attributable mortality of 14%. The mortality rate from HAP varied from 7% in patients on general wards to as high as 62% in patients in bone marrow transplant units.

Death from bacteremic HAP occurred in 20% of patients within one week of their first positive blood culture, and *Pseudomonas aeruginosa* bacteremia was associated with the highest mortality rate (45%). The mortality rate in this study was similar for both the ICU (22.2%) and non-ICU patients (17.6%).

The mortality rate for VAP ranges from 24% to 50%, and can reach as high as 76% in specific settings or when lung infection is caused by high-risk pathogens. The attributable mortality of VAP in a Canadian study showed an increase in risk of death (absolute risk increase: 5.8%).

Study objective: to verify diagnosis of community-aquired pneumonia (CAP), HAP; to determine management of patients with pneumonia.

Basic level:

1. Anatomy, physiology, and pathophysiology of respiratory system.
2. To be able to collect complaints, case history, carry out objective examination.
3. To interpret instrumental and laboratory data in patients with CAP.
4. To interpret side effects of antibacterial drugs. Indications and contraindications.

Student has to know:

1. How to put provisional and final diagnosis and assign management in CAP, HAP.
2. How to differentiate CAP with TB, cancer.

The main theoretical questions:

1. Classification of pneumonia.
2. Symptoms, laboratory and instrumental data in CAP.
3. Signs of severe pneumonia.
4. Complications of pneumonia.

5. Management of pregnant women with pneumonia.
6. Antibiotics: groups, indications depending on aetiology of pneumonia.
7. Definition of HAP. Microbial aetiology. Ventilator-associated pneumonia.
8. Risk factors for HAP or VAP.
9. Clinical manifestations of HAP and VAP. Diagnostic approaches. Diagnostic algorithms.
10. Antibiotic treatment in case of HAP.
11. Major points and recommendations for prevention and risk reduction of HAP and VAP.
12. Pneumonia in immunocompromised patients: symptoms, laboratory and instrumental data. Management.

Real-life situation to be solved:

1. A 50 year old man presented with a 3 days history of fever and a productive cough. There was dyspnoea and patient addressed his complaints to a doctor. He doesn't smoke. There was no history of past surgical procedures, any drug or environmental allergies.

Objectively: he has a temperature of 37.6 °C, respiratiory rate is 20 breaths/min; heart rate of 96, regular; blood pressure of 135/80. He has bronchial breath sounds at the right lung base, impairment of the percussion note and intensified tactile fremitus. The heart is regular without extra sounds or murmurs. The abdomen is soft without tenderness or distention. The liver spans 10 cm in the midclavicular line with a smooth edge. The extremities show no oedema.

Laboratory examinations: RBC – $4.2*10^{12}$/l; Hb – 140 g/l; ESR – 22 mm/h; WBC – $11*10^{9}$/l; eosinophils – 1%, stab neutrophils – 5%, segmented neutrophils – 79%, lymphocytes – 11%, monocytes – 5%. Total serum protein – 65 g/l, serum urea – 5.7 mmol/l, creatinine – 110 μmol/l, bilirubin – 18 μmol/l, fasting plasma glucose – 5.3 mmol/l. Chest X-ray shows a right lobe infiltrate (homogeneous opacity).

What is your differential diagnosis? What is your final diagnosis? How would you treat this patient? How can you estimate the adequacy of therapy?

2. Patient M, 46 years old, complains of dry cough, dyspnoea after physical exertion during 3 month. On chest X-ray: diffuse lung fibrosis and bilateral mediastinal adenopathy. Differential diagnosis? What examinations are necessary?

3. Patient A, 35 year old man presented with a 5 days history of fever, muscular pain and dry cough. Sore throat and running nose started 2 weeks ago. He used amoxicillin 2 g/day but there was no effect. There was no history of past surgical procedures, any drug or environmental allergies.

Objectively: he has a temperature of 37.6 °C, respirations 20 breaths/min; heart rate of 96, regular; BP is 135/80. He has harsh breathing above lungs, percussion and tactile fremitus is normal. The heart is regular without extra sounds or murmurs. The abdomen is soft without tenderness or distention. The liver spans 12 cm in the midclavicular line with a smooth edge. The extremities show no oedema.

Laboratory examinations: RBC – $4.2*10^{12}$/l; Hb – 140 g/l; ESR – 24 mm/h; WBC– $8*10^{9}$/l; eosinophils – 1%, stab neutrophils – 5%, segmented neutrophils – 79%, lymphocytes – 19%, monocytes – 5%. Total serum protein – 65 g/l, serum urea – 5.7 mmol/l, creatinine – 110 μmol/l, bilirubin – 18 μmol/l, fasting plasma glucose – 5.3 mmol/l. Chest X-ray shows low-intensity homogeneous opacities in inferior lobe of right lung.

What is your presumptive diagnosis? How would you treat this patient?

Answers:

1. TB, lung cancer. CAP. Antibiotics, expectorants, bronchodilatators, oxygenotherapy. In 72 hours we have to check effectiveness of treatment using clinical signs, laboratory criteria.

2. Sarcoidosis, limphoma, mediastinal or lung cancer, lymphogranulomathosis. CT, sputum smear and microorganisms sensitivity, biopsy.

3. Mycoplasma pneumonia. Macrolides.

Real-life situation to be solved:

A 50 year old man complains of 4 days history of fever, dry cough, dyspnoea. 5 days ago patient admitted to the surgical department due to acute pancreatitis. He smokes. There was no history of past surgical procedures, any drug or environmental allergies.

Objectively: he has a temperature of 37.6 °C, respiratiory rate is 24 breaths/min; heart rate of 96, regular; blood pressure of 135/80. He has bronchial breath sounds at the right lung base, crepitation, impairment of the percussion note and intensified tactile fremitus. The heart is regular without extra sounds or murmurs. The abdomen is soft without tenderness or distention. The liver spans 10 cm in the midclavicular line with a smooth edge. The extremities show no oedema.

Laboratory examinations: RBC – $4.2*10^{12}$/l; Hb – 140 g/l; ESR – 22 mm/h; WBC– $11*10^{9}$/l; eosinophils – 1%, stab neutrophils – 5%, segmented neutrophils – 79%, lymphocytes – 11%, monocytes – 5%. Total serum protein – 65 g/l, serum urea – 5.7 mmol/l, creatinine – 110 μmol/l, bilirubin – 18 μmol/l, fasting plasma glucose – 5.3 mmol/l. Chest X-ray shows a right lobe infiltrate (homogeneous opacity).

What is your clinical diagnosis? How would you treat this patient? What aetiology of pneumonia is more probable?

Answer: hospital-acquired (nosocomial) pneumonia. Patient belongs to group 1 (according to treatment algorithm for HAP). Empirical treatment with iv/oral antibiotic (monotherapy) for 7–8 days, broncholytics. Staphylococci, gram-negative bacilli, *P. aeruginosa*.

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Topic 24. MANAGEMENT OF PATIENTS WITH CHRONIC COMPLICATIONS IN TYPE II DIABETES MELLITUS (DM)

Time frame – 6 hours.

Professional motivation. International Diabetes Federation (IDF) predicts that the number of people with diabetes will rise from 194 million today to more than 333 million by 2025 .Type 1 and type 2 diabetes are chronic, life-long conditions that require careful monitoring and control. Without proper management they can lead to very high blood sugar levels which can result in long-term damage to various organs and tissues: affects the heart and blood vessels and may cause fatal complications such as coronary heart disease (leading to heart attack) and stroke. Cardiovascular disease is the major cause of death in people with diabetes, accounting in most populations for 50% or more of all diabetes fatalities, and much disability. Diabetic nephropathy can result in total kidney failure and the need for dialysis or kidney transplant. Diabetes is an increasingly important cause of renal failure, and indeed has now become the single most common cause of end stage renal disease, i.e., that which requires either dialysis or kidney transplantation. Diabetic neuropathy can ultimately lead to ulceration and amputation of the toes, feet and lower limbs. Loss of feeling is a particular risk because it can allow foot injuries to escape notice and treatment, leading to major infections and amputation. Diabetic retinopathy is characterised by damage of the retina of the eye which can lead to vision loss.

Type 2 diabetes accounts for at least 90% of all cases of diabetes. The diagnosis of type 2 diabetes usually occurs after the age of 40 but can occur earlier, especially in populations with high diabetes prevalence. Type 2 diabetes can remain undetected for many years and the diagnosis is often made from associated complications or incidentally through an abnormal blood or urine glucose test.

Good diabetes control means keeping your blood sugar levels as close to normal as possible. This can be achieved by a combination of the following: physical activity, body weight, healthy eating, avoid tobacco; monitoring for complications (includes regular foot and eye checks, controlling blood pressure and blood glucose, and assessing risks for cardiovascular and kidney

disease). At present, type 1 diabetes cannot be prevented. The environmental triggers that are thought to generate the process that results in the destruction of the body's insulin-producing cells are still under investigation. Type 2 diabetes, however, can be prevented in many cases by maintaining a healthy weight and being physically active. IDF recommends that all people at high risk of developing type 2 diabetes be identified through opportunistic self-screening. People at high risk can be easily identified through a simple questionnaire to assess risk factors such as age, waist circumference, family history, cardiovascular history and gestational history. Once identified, people at high risk of diabetes should have their plasma glucose levels measured by a health professional to detect Impaired Fasting Glucose or Impaired Glucose Tolerance, both of which indicate an increased risk of type 2 diabetes. Prevention efforts should target those at risk in order to delay or avoid the onset of type 2 diabetes.

Study objective: to improve the skills of clinical examination of patients with diabetes mellitus, to establish the clinical diagnosis of type 2 DM and its complications.

Basic level:

1. Regulation of glucose level in blood. Pathophysiology of hyperglycemia.
2. To be able to collect complaints, case history, carry out physical examination in patients with type 2 DM.
3. To interpret clinical, laboratory and instrumental data in chronic complications of type 2 DM.
4. To find out data inherent to chronic complications in type 2 DM.
5. To interpret side effects of oral glucose-lowering drugs, insulinotherapy.

Student has to know:

1. Risk factors that have been associated with type 2 diabetes.
2. Criteria for diagnosis of DM. The oral glucose tolerance test: indications, normal response, impaired glucose tolerance, diabetes.
3. Treatment (lifestyle interventions, oral glucose-lowering drugs, insulinotherapy).
4. What are the chronic complications of diabetes?

The main theoretical questions:

1. Diabetes mellitus: classification, aetiology, pathogenesis.
2. Laboratory findings in diabetes mellitus patients. Diagnostic significance of glycated haemoglobin (HbA_1) measurement, C-peptide, ketonuria.
3. Diagnostic criteria of insulin dependant and insulin independent diabetes mellitus.
4. Classification and diagnostic criteria of diabetic nephropathy. Treatment.
5. Classification and diagnostic criteria of diabetic micro- and macroangiopathy.
6. Classification and diagnostic criteria of diabetic retinopathy.
7. Diabetic foot: diagnostic criteria and treatment.
8. What does good diabetes control mean? Self-monitoring of blood glucose.
9. Primary prevention for development of type 2 DM.
10. Treatment of insulin-dependant diabetes mellitus. Complications in insulinotherapy.

Assignment for self-assessment:

1. The Somogyi effect is:
   a) episode of nighttime hypoglycemia resulting in high blood sugar levels;
   b) period of high blood sugar in the morning (7–9 a.m.);
   c) night hyperglycemia related to deficit of prolong insulin;
   d) resistance to insulin.

2. A 26-year-old man presents with headache, weakness, facial and crus oedema. His current medication includes insulin 34 units/daily. He has a history of diabetes for the past 6 years.

The examination reveals oedematous face, legs, pale skin, heart rate is regular, 100/min. Blood pressure is 180/100 mm Hg; respiratory rate is 20 breaths/min. His lungs are clear. The abdomen is soft without tenderness or distention. The liver spans 10 cm in the midclavicular line with a smooth edge. His weight is 58 kg, height is 176 cm. He is afebrile.

Blood testing: RBC – $3.4*10^{12}$/l; Hb – 104 g/l; ESR – 10 mm/h; WBC – $7.2*10^{9}$/l. Total protein – 63 g/l, urea – 6.2 mmol/l, creatinine – 98 μmol/l, bilirubin – 19 μmol/l, glucose profile –

12–7.8–10 mmol/l, cholesterol – 5 mmol/l, triglycerides – 1.5 mmol/l. Haemoglobin A_1c – 7.9%. Urine chemistry: protein 2.5 g/l.

Chest X-ray: no infiltrates.

What complication has been developed in this patient?

a) diabetic nephropathy;
b) kidney amyloidosis;
c) chronic pyelonephritis;
d) nephrotic syndrome;
e) glomerulonephritis.

What are the main directions in treatment?

3. A 60-year-old man presented with dry mouth, paresthesia of the crus, dyspnoea on exertion that is accompanied by chest pain. Pain with radiation to neck or chest tightness lasts about 15 min. A rest or taking a pill under the tongue makes the symptoms go away. The patient suffered from anterior wall MI 10 months ago. His current medications include ramipril 5 mg twice a day, aspirin 100 mg, metformin 500 mg bid. His social history is positive for occasional alcohol and negative for smoking. He has a history of hypertension and diabetes for the past 4 years.

The examination reveals a regular heart rate with a reduced intensity S_1 and normal S_2. Blood pressure is 160/90 mm Hg; pulse is 82 beats/min, regular, respiratory rate is 20 breaths/min. His lungs are clear. The abdomen is soft without tenderness or distention. The liver spans 10 cm in the midclavicular line with a smooth edge. There is no peripheral oedema and the pulses are intact. His weight is 88 kg, height is 176 cm.

Blood testing: RBC – $4.4*10^{12}$/l; Hb – 134 g/l; ESR – 10 mm/h; WBC – $7.2*10^{9}$/l; eos. – 1%, stab neutr. – 4%, segmented neutrophils – 59%, lymphocytes – 15%, monocytes – 5%. Total protein – 63 g/l, urea – 6.2 mmol/l, creatinine – 98 μmol/l, bilirubin – 19 μmol/l, fasting glucose – 7.8 mmol/l, cholesterol – 7 mmol/l, triglycerides – 2.5 mmol/l. Haemoglobin A_1c – 7.9%. Potassum 5.0 μmol/l, GFR – 80 ml/min. Urine chemistry: protein 1.5 g/l. Chest X-ray: no infiltrates, mild cardiomegaly.

What can be done to slow diabetes complications?

Answers:

1. a. 2. a, treatment: compensation of diabetes mellitus, angioprotectors use, ACE-inhibitor, insulinotherapy in adequate dose.

3. Intensive control of elevated levels of blood sugar in patients with type 1 or type 2 diabetes decreases the complications of nephropathy, neuropathy, retinopathy, and may reduce the occurrence and severity of large blood vessel diseases. Aggressive control with intensive therapy means achieving fasting glucose levels between 70–120 mg/dl; glucose levels of less than 160 mg/dl after meals; and a near normal haemoglobin A1 levels.

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Topic 25. MANAGEMENT OF PATIENTS WITH METABOLIC SYNDROME

Time frame – 6 hours.

Professional motivation. Many people are unaware that they have metabolic syndrome (MS), even though the American Heart Association estimates that approximately 20–30% of the

population in industrialized countries have metabolic syndrome – between 58 and 73 million men and women. Metabolic syndrome is present in about 5% of people with normal body weight, 22% of those who are overweight and 60% of those considered obese. Adults who continue to gain five or more pounds per year raise their risk of developing metabolic syndrome by up to 45%. Metabolic syndrome increases the risk of type 2 diabetes (the common type of diabetes) anywhere from 9–30 times over the normal population. As to the risk of heart disease, studies vary, but the metabolic syndrome appears to increase the risk 2–4 times that of the normal population. Adult population with metabolic syndrome twice as likely to die from and three times as likely to have a heart attack or stroke compared with people without the syndrome.

Metabolic syndrome is associated with fat accumulation in the liver (fatty liver), resulting in inflammation. The kidneys can also be affected, as there is an association with microalbuminuria – the leaking of protein into the urine, a subtle but clear indication of kidney damage. Other problems associated with metabolic syndrome include obstructive sleep apnoea, polycystic ovary syndrome, increased risk of dementia with aging, and cognitive decline in the elderly.

Study objective: to be able to find out criteria of metabolic syndrome and determine management.

Basic level:

1. Measuring weight in relation to height: body mass index (BMI).
2. Criteria for the MS.

Student has to know:

1. The new International Diabetes Federation (IDF) definition of metabolic syndrome.
2. What is the pathogenesis of MS?
3. How is central obesity measured?
4. How to interpret clinical, laboratory, and instrumental data in patients with MS.

The main theoretical questions:

1. How is metabolic syndrome defined?
2. What diagnostic tests should be done to diagnose MS? Indications, methodology and interpretation of glucose-tolerant test.
3. How is metabolic syndrome treated?
4. How can cardiovascular risk be prevented and treated?

Assignment for self-assessment:

1. Metabolic syndrome is diagnosed if a person has central obesity and any 2 of the following are mentioned except (according to the new IDF definition):

a) raised fasting plasma glucose ≥ 100 mg/dL (5.6 mmol/L) or previously diagnosed type 2 diabetes;

b) serum triglycerides 150 mg/dl (1.7 mmol/L) or above;

c) HDL cholesterol 40 mg/dl (1.03 mmol/L) or lower in men and 50 mg/dl (1.29 mmol/L) or lower in women;

d) systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg or treatment of previously diagnosed hypertension; e) raised creatinine level ≥ 115.6 μmol/L.

2. Central obesity defined as:

a) a waist circumference over 94 cm in men and over 80 cm in women;

b) a waist circumference over 84 cm in men and over 70 cm in women;

c) a waist circumference over 104 cm in men and over 100 cm in women.

3. A 56-year-old man had ST-elevated MI. He has no history of diabetes. The examination reveals that heart rate is regular, 90/min. Blood pressure is 150/90 mm Hg; respiratory rate is 16 breaths/min. His lungs are clear. The abdomen is soft without tenderness or distention. His weight is 58 kg, height is 176 cm.

Blood testing: RBC – $3.4*10^{12}$/l; Hb – 134 g/l; ESR – 10 mm/h; WBC – $7.2*10^{9}$/l. Total protein – 63 g/l, urea – 6.2 mmol/l, creatinine – 98 μmol/l, bilirubin – 19 μmol/l, fasting glucose – 4.8 mmol/l, cholesterol – 5 mmol/l, triglycerides – 1.5 mmol/l, uric acid – 233 μmol/l. Chest X-ray: no infiltrates.

Determine the grade of obesity. What risk factor should be removed in secondary prevention?

a) hyperglycemia; b) hyperuricemia; c) hypercholesterolemia; d) obesity; e) hypertension.

Answers: 1. e. 2. a. 3. grade I, d.

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Topic 26. MANAGEMENT OF PATIENTS WITH GOITRE

Time frame – 6 hours.

Professional motivation. Patients with goitre may be asymptomatic, or may present with compressive symptoms such as cough or dysphagia. Goitre may also present with symptoms due to associated hypothyroidism or hyperthyroidism. The prevalence of goitre, diffuse and nodular, is dependent on the status of iodine intake of the population. Diffuse goitre is most commonly caused by iodine deficiency and is termed 'endemic goitre' when it affects >5% of the population in a given geographic area.

Study objective: to be able to find out criteria of metabolic syndrome and determine management.

Basic level:

1. To be able to collect complaints, case history, carry out objective examination of patients with thyroid gland diseases.
2. To interpret instrumental and laboratory data in patients with thyroid gland diseases.
3. Methods of assessment of the functional condition of the thyroid gland and additional examination in the case of presence of nodules in the thyroid glands.

Student has to know:

1. The interpretation of the diagnosis of hypothyroidism, thyrotoxicosis.
2. Red flag symptoms to look out for.
3. Indications for tests for thyroid dysfunction.

The main theoretical questions:

1. Differential diagnosis of Graves' disease and functional autonomy of the thyroid gland.
2. Differential diagnosis of thyroiditis with acute and subacute clinical course.
3. Chronic thyroiditis. The interpretation of the diagnosis of autoimmune thyroiditis.
4. Nodular forms of goiter. Monitoring of patients with thyroid nodules.
5. Pathomorphological classification of thyroid tumors
6. Differentiated treatment of patients with Goiter. Medical, surgical treatment of toxic goiter, use of 131-iodine for therapeutic aim.

Assignment for self-assessment:

1. A 70-year-old female with a history of hypertension and coronary artery disease, presented with complaints of weight loss, palpitations, headaches and heat intolerance. Physical examination revealed 4 cm thyroid nodule in the left lobe on palpation. Her blood pressure was 140/85 mmHg, and resting pulse was 102/min with sinus rhythm. Her TSH suppressed 0.22 uIU/mL (reference range: 0.40–4.00 uIU/mL) while free thyroxine 2.4 ng/dL (0.8–1.9 ng/dL) and free triiodothyronine 4.4 pg/mL (1.5–4.1 pg/mL) elevated. The radioiodine uptake scan showed the abnormal focus of hot uptake in the left lobe and suppression in the remaining thyroid tissue.

Questions: What is the scan suggestive for?

What test should be performed to rule out any remote possibility of thyroid cancer?

If the cytology report is suggestive of thyroid carcinoma, what treatment should be given to the patient?

Cytologist described finding as a solitary tumor of 3.0 cm in diameter, follicular variant of papillary thyroid carcinoma. No other cancerous tissue found in the remaining thyroid gland. Due to the small size of the tumor no ablative radioiodine therapy performed. What treatment should be administered after surgery?

Answers:

1. The scan data is suggestive of a hyperfunctioning toxic thyroid nodule. The patient had symptoms of hyperthyroidism. A fine needle aspiration needs to be performed. In case of thyroid carcinoma, the patient has to be underwent total thyroidectomy (the presence of a follicular variant of papillary carcinoma of thyroid associated with hyperfunctioning thyroid nodule is rare). To prevent hypothyroidism and stop TSH stimulation, lifelong thyroid hormone replacement therapy with levothyroxine should be prescribed. Serum TSH and serum thyroglobulin must be checked regularly. A radioactive iodine whole-body scan should be performed to detect metastatic spread.

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Topic 27. MANAGEMENT OF PATIENTS WITH URINE SEDIMENT CHANGES

Time frame – 6 hours.

Professional motivation. Proteinuria is a common finding in adults in primary care practice. Proteinuria is defined as urinary protein excretion of greater than 150 mg per day. An algorithmic approach can be used to differentiate benign causes of proteinuria from rarer, more serious disorders. Benign causes include fever, intense activity or exercise, dehydration, emotional stress, and acute illness. More serious causes include glomerulonephritis and multiple myeloma. Alkaline, dilute or concentrated urine; gross haematuria; and the presence of mucus, semen or white blood cells can cause a dipstick urinalysis to be falsely positive for protein. Of the three pathophysiologic mechanisms (glomerular, tubular, and overflow) that produce proteinuria, glomerular malfunction is the most common and usually corresponds to the urinary protein excretion of more than 2 g per 24 hours.

When a quantitative measurement of urinary protein is needed, most physicians prefer a 24-hour urine specimen. However, the urine protein-to-creatinine ratio performed on a random specimen has many advantages over the 24-hour collection, primarily convenience and possibly accuracy. Most patients evaluated for proteinuria have a benign cause. Proteinuria on initial dipstick urinalysis testing is found in as much as 17% of selected populations. Although a wide variety of conditions, ranging from benign to lethal, can cause proteinuria, fewer than 2 percent of patients whose urine dipstick test is positive for protein have serious and treatable urinary tract disorders.

Place of carrying out: class-room, wards of nephrology.

Study objective is to improve students' skills in the diagnosis of urine sediment changes and different forms of renal disorders, the management of patients with urine sediment.

Basic level:

1. Aetiology, pathogenesis of renal disorders with urine sediment changes.
2. Clinical, laboratory methods of nephritic syndromes diagnosis (estimation of urine sediment changes).

Student has to know:

1. How to make physical examination of patients with renal disease.
2. How to interpret results of the physical, laboratory and instrumental data with following differential diagnosis.
3. Who is at risk for proteinuria?
4. Peculiarities of the urine sediment changes in different forms of the renal disorders.

5. How to make program for investigation when evaluating a patient with suspected renal disorder.

The main theoretical questions:

1. Peculiarities of the urine sediment changes in acute and chronic glomerulonephritis, pyelonephritis, tuberculosis, amyloidosis, renal tumour, nephropathy of different origin.
2. What diseases are accompanied by macrohaematuria, isolated haematuria?
3. What diseases are accompanied by proteinuria, leukocyturia?
4. Involvement of the kidneys in the connective tissue diseases: Rheumatoid arthritis. Systemic lupus erythematosus. Systemic sclerosis. Sjogren's syndrome. Polyarteritis nodosa.
5. How is proteinuria (haematuria) treated?

Assignment for self-assessment

1. A female college student complains of dysuria and pollakiuria, nausea, vomiting, fever. Urinalysis reveals 28 to 30 WBCs per high-power field and numerous gram-negative bacteria. What diagnosis do you suspect?
2. Nephritic syndrome is characterized by the mentioned signs except:
    a) proteinuria less than 3.5 g/24-hours;
    b) erythrocyturia (more than 2000/ml in Nechiporenko test);
    c) leukocyturia (more than 4000/ml in Nechiporenko test);
    d) erythrocyturia (more than 3000/ml in Nechiporenko test);
    e) casts.
3. A 24-year-old farmer has had acute tonsillitis. In 2 weeks he noticed facial oedema on waking, elevated temperature of 37.7 °C, weakness. BP is 130/75mm. Urinalysis reveals: specific gravity – 1026, protein – 1.66 g/l, 28 to 30 RBCs per high-power field and numerous casts. What diagnosis do you suspect?
    a) acute glomerulonephritis, nephrotic syndrome;
    b) acute glomerulonephritis, isolated urinary syndrome;
    c) chronic glomerulonephritis, exacerbation;
    d) acute pyelonephritis;
    e) chronic pyelonephritis, exacerbation.
4. A 44-year-old man is referred to you for evaluation and treatment of recurrent renal colic and passage of renal stones. What kind of examination will you choose?
5. A 30-year-old man complains of headache, high BP, oedema on different parts of the body. He has been sick for 7 years. BP is elevating for the past 4 years. He is noted on heamaturia periodically. Physical examination reveals tachycardia 96/min, BP is 190/130mm Hg. Heart sounds are weak, rhythmical, accentuated S_2 above aorta. Blood testing: RBC – $3.4*10^{12}$/l; Hb – 114 g/l; ESR – 10 mm/h; WBC – $7.2*10^{9}$/l; eos. – 1%, stab neutr. – 4%, segmented neutrophils – 69%, lymphocytes – 19%, monocytes – 5%. Total protein – 63 g/l, urea – 6.2 mmol/l, creatinine – 198 μmol/l, bilirubin – 19 μmol/l, fasting glucose – 4.8 mmol/l, cholesterol – 7 mmol/l, triglycerides – 2.5 mmol/l. GFR 80 ml/min. Urinalysis reveals: specific gravity is 1015, protein – 2.6 g/l, 12 to 14 RBCs per high-power field, 4–6 WBCs per high-power field and numerous casts. Urine chemistry: protein – 3.5 g/l. What is the most likely diagnosis?
    a) chronic glomerulonephritis;
    b) kidney amyloidosis;
    c) kidney stones;
    d) chronic pyelonephritis.
6. Effectiveness of diuretics in chronic heart failure can be decreased in therapy by:
    a) diclofenac;
    b) ibuprofen;
    c) prednisolon;
    d) everything is right.
7. What diuretic has ototoxic action?
    a) verospiron;

b) hypothiazide;
c) furosemide;
d) triamteren.

8. A 40-year-old man was admitted at the nephrological department with diagnosis – chronic glomerulonephritis, nephrotic syndrome, hypertensive stage. Objectively: oedema on different parts of the body, pleural effusion and ascites. What pathogenic treatment should be prescribed in the first place?

a) antibiotics;
b) antiaggregants;
c) prednisolon;
d) antisensitizer;
e) diuretics.

Answers:

1. Acute pyelonephritis.
2. d. 3. b.
4. Intravenous pyelography.
5. b. 6. d. 7. c. 8. c.

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Topic 28. MANAGEMENT OF NEPHROTIC SYNDROME

Time frame – 6 hours.

Professional motivation. Nephrotic syndrome is caused by different disorders that damage the kidneys. This damage leads to the release of too much protein in the urine. These include kidney diseases such as minimal-change nephropathy, focal glomerulosclerosis, and membranous nephropathy. Nephrotic syndrome can also result from systemic diseases that affect other organs in addition to the kidneys, such as diabetes, amyloidosis, and lupus erythematosus.

Nephrotic syndrome may affect adults and children of both sexes and of any race. It may occur in typical form, or in association with nephritic syndrome. About 2 in every 10,000 people experience nephrotic syndrome. Nephrotic syndrome prevalence is difficult to establish in adults because the condition is usually a result of an underlying disease.

The main complications of nephrotic syndrome are hypovolaemia, infection (due to leakage of immunoglobulins, encapsulated bacteria such as *Haemophilus influenzae* and *Streptococcus pneumoniae* can cause infection) and thrombosis (due to leak of anti-thrombin 3, which helps prevent thrombosis. This often occurs in the renal veins.

Treatment for nephrotic syndrome and its complications appear to have reduced the morbidity and mortality once associated with the syndrome. From the therapeutic perspective, nephrotic syndrome may be classified as steroid sensitive, steroid resistant, steroid dependent, or frequently relapsing. Currently, the prognosis for patients with primary nephrotic syndrome depends on its cause. Poor patient response to steroid therapy may predict a poor outcome. Only approximately 20% of patients with focal glomerulosclerosis undergo remission of proteinuria; an additional 10% improve but remain proteinuric. Many patients experience frequent relapses, become steroid-dependent, or become steroid-resistant. End-stage renal disease develops in 25–30% of patients with focal segmental glomerulosclerosis by 5 years and in 30–40% of these patients by 10 years.

Nephritic syndrome is a collection of signs associated with disorders affecting the kidneys, more specifically glomerular disorders. It is characterized by having small pores in the podocytes of the glomerulus, large enough to permit proteins and red blood cells to pass into the urine. By contrast, nephrotic syndrome is characterized by only proteins (proteinuria) moving into the urine. Both nephritic syndrome and nephrotic syndrome result in hypoalbuminemia. The outlook depends on the disease that is causing nephritis. When the condition improves, symptoms of fluid retention (such as swelling and cough) and high blood pressure may go away in 1 or 2 weeks. However, urine tests may take months to return to normal. Although it is unusual for the disease to return, at least one-third of adults whose disease does return will develop end-stage kidney disease and may need dialysis or kidney transplant.

Place of carrying out: class-room, wards of the nephrology.

Study objective is to assign patients' management with nephrotic syndrome.

Basic level:

1. Student should be able to collect complaints, case history, carry out objective examination of patients with nephrotic syndrome.
2. To interpret instrumental and laboratory data in patients with nephrotic syndrome.
3. Mechanism of action, pharmacology/pharmacokinetics, side effects of glucocorticoids.
4. Mechanism of action, pharmacology/pharmacokinetics, side effects of anticoagulants.
5. Mechanism of action, pharmacology/pharmacokinetics, side effects of antiaggregants.

Student has to know:

1. Diseases which are accompanied by nephrotic syndrome.
2. Diseases which are accompanied by oedema.
3. How to make program for investigation when evaluating a patient with nephrotic syndrome, oedema.
4. Algorithm to differentiate diseases with nephrotic syndrome, oedema.
5. How to put presumptive diagnosis, to prescribe treatment in nephrotic syndrome.

The main theoretical questions:

1. Aetiology and mechanisms of oedema.
2. Clinical, laboratory, and instrumental diagnostic methods for revealing nephrotic syndrome.
3. Pathogenesis of the nephrotic proteinuria, hypoalbuminemia, hyperlipidemia.
4. Classification of the nephrotic syndrome.
5. Clinical manifestation of nephrotic syndrome and pathogenesis of nephrotic oedema.
6. Diagnostic algorithm in oedematous syndrome
7. Complications in nephrotic syndrome and their pathogenesis.
8. Management of patients with nephrotic syndrome.
9. Treatment of immune-inflammatory renal diseases (glomerulonephritis). Diuretics. Gluco-corticoids. Immunosuppressive therapy. Heparin therapy. Platelet aggregation inhibitors. Angiotensin-converting enzyme inhibitors.
10. Preventive and sanatorium-resort therapy in the renal disorders.

Assignment for self-assessment

1. A 49-year-old man has been ill with chronic osteomyelitis for 10 years after crus fracture. Nephrotic syndrome appeared 3 years ago. He died of uraemia. During dissection: dense and white kidneys, with scars in the cortical layer, greasy glitter on cross-section. What pathology had developed?

a) chronic glomerulonephritis;
b) primary amyloidosis;
c) secondary amyloidosis;
d) chronic pyelonephritis.

2. A 46-year-old woman was admitted to the nephrological department with oedema on crus, face, high BP (160/100 mm Hg). Urine chemistry: protein 3.8 g/l. What is the most appropriate pathogenic treatment for this patient?

a) antibiotics;
b) corticosteroids;

c) diuretics;
d) Ca-channel blockers;
e) NSAID.

Answers: 1. c. 2. b.

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Topic 29. MANAGEMENT OF PATIENTS WITH CHRONIC KIDNEY DISEASE

Time frame – 6 hours.

Professional motivation. Patients with chronic kidney disease stages 1–3 are generally asymptomatic; clinically manifestations typically appear in stages 4–5. Early diagnosis and treatment of the underlying cause and/or institution of secondary preventive measures is imperative in patients with chronic kidney disease. These may delay, or possibly halt, progression.

The social and economic consequences of chronic renal failure (CRF) are considerable. In the UK 85–95 new patients per million of the adult population are accepted for long-term dialysis treatment each year; the availability of dialysis and transplantation has transformed the outlook for such patients. The incidence of CRF is much higher in some other countries due to differences in regional and racial incidences of disease as well as because of differences in medical practice.

Dialysis and transplantation can be considered as highly effective forms of treatment, with a 5-year survival of approximately 80% for home haemodialysis, 80% following renal transplantation, 60% for hospital haemodialysis and 50% for continuous ambulatory peritoneal dialysis.

Place of carrying out: class-room, wards of nephrology.

Study objective is to improve students' skills in CRF diagnosis using clinical, laboratory, and instrumental signs and to determine management.

Basic level:

1. Pathogenesis of leading clinical syndromes of CRF.
2. To be able to collect complaints, case history, carry out objective examination of patients with CRF.
3. To interpret instrumental and laboratory data in patients with CRF.

Student has to know:

1. The definition of «chronic kidney disease»
2. How to discover signs inherent to CRF.
3. How to determine the stage of the CRF.
4. How to make program for investigation of patients with CRF.
5. Management of patients with CRF.

The main theoretical questions:

1. Aetiology and pathophysiology of CRF.
2. Classification of CRF. Stages of chronic kidney disease.
3. Peculiarities of clinical manifestations of CRF due to diseases. Potassium and calcium disorders. Haematological abnormalities.

4. Evidence-based treatment of hypertensive syndrome, anemias, infectious complications, calcium metabolism disturbances, and osteodystrophy.

5. Renal replacement therapy in CRF. Indications to haemodialysis, continuous ambulatory peritoneal dialysis, and transplantation. Immunosuppressive treatment after transplantation. Contraindications to haemodialysis. Complications.

6. Renal involvement in systemic disorders (diabetes mellitus, systemic vasculitis, SLE).

7. Adult polycystic kidney disease.

Assignment for self-assessment

1. A 50-year-old man with end-stage of CRF due to chronic glomerulonephritis is maintained on long-term haemodialysis three times each week. He has came to the dialysis unit with a 4.5 kg weight gain since his last dialysis 2 days ago. He is moderately short of breath and his blood pressure is 195/125 mm Hg. What is the most appropriate management of his hypertension at this point?

2. Pulmonary haemorrhage has appeared in patient with progressive nephritis and CRF. What is the most likely diagnosis?

a) SLE with renal involvement;
b) bronchiectasis;
c) pulmonary oedema;
d) pulmonary infarction;
e) Goodpasture's syndrome.

3. Indications to haemodialysis in CRF:

a) glomerular filtration < 5 ml/min.;
b) stable decrease of daily urine less than 700 ml;
c) hypercreatinaemia up to 1100–1300 μmol;
d) symptoms of pericarditis, encephalopathy, neuropathy;
e) all mentioned above.

4. The earliest symptom of CRF is:

a) high blood presure;
b) hypostenuria;
c) oedema;
d) polyuria;
e) anaemia.

Answers:

1. Hypertension in the end-stage of renal failure is usually related to an increase in extracellular fluid volume. The best management is the expeditious removal of fluid by ultrafiltration dialysis. Such treatment usually results in normalization of the blood pressure and relief of circulatory congestion.

2. e. 3. e. 4. a.

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Topic 30. MANAGEMENT OF PATIENTS WITH ANEMIA

Time frame – 6 hours.

Professional motivation. Anemia affects one-fourth of the world's population, and iron deficiency is the predominant cause. Iron deficiency anaemia is a major cause of morbidity and burden of other diseases worldwide. In many cases iron deficiency related with poor dietary intake

and malabsorption of dietary iron, as well as a number of significant gastrointestinal pathologies. Anaemia prior to scheduled major surgery is an independent risk factor for postoperative major morbidity and mortality. Major surgery should therefore be delayed until anaemia is corrected. a two-centre English study conducted in 2017 found 46% of women had anaemia at the booking or 28-week checks. Adequate iron supplementation during pregnancy prevents complications associated with severe anemia.

Place of carrying out: class-room, wards of haematology department.

Study objective is to improve students' skill to do clinical examination of the patients with anaemia, to find out clinical and laboratory manifestations, to specify treatment.

Basic level:

1. Main causes of microcytic anaemias.
2. Main causes of iron deficiency.
3. The common causes of macrocytic anaemia, normocytic anemia.
4. Examination of patients with anaemia.
5. To determine symptoms of anaemia.

Student has to know:

1. Clinical signs in anaemia.
2. Investigational methods for the diagnosis of anaemia.
3. How to specify treatment for patients with anaemia.

The main theoretical questions:

1. Assessing iron stores.
2. Diagnostic and differential diagnostic criteria of iron deficiency and chronic inflammatory anemia
3. Management of patients with microcytic anemias.
4. Diagnostic and differential diagnostic criteria of B12 deficiency and folic acid deficiency anemia
5. Management of patients with macrocytic anemias.
6. Management of anaemia in pregnancy.

7. Management of patients with anemia caused by hematopoetic disorders. Evidence-based treatment standards. Non-pharmacological and pharmacological treatment. Indications for blood transfusion. Primary and secondary prevention.

8. Management of patients with hemolytic anemias. Diagnostic criteria and evidence-based management of patients with acquired hemolytic anemias.

Assignment for self-assessment

1. How would you diagnose aplastic anemia?
   a. Blood smear
   b. Complete blood count
   c. Spleen biopsy
   d. Bone marrow biopsy

2. Medical examination of a 43 y.o. man revealed objectively pailness of skin and mucous membranes, smoothness of lingual papillas, transverse striation of nails, fissures in the mouth corners, tachycardia. Hemoglobin content amounts 90 g/l; there are anisocytosis, poikilocytosis. The most probable causative agent of this condition is deficiency of the following mi-croelement:
   a. Iron
   b. Copper
   c. Zinc
   d. Magnesium

3. A 50 year old patient has been admitted to the clinics with atrophic gastritis. Blood count: erythrocytes - 3, 8 • 10^{12}/l, Hb - 68 g/l, c.i. - 1, macroanisocytosis, poikilocytosis. There is megaloblastic type of haemopoesis. A number of leukocytes, reticulocytes and thrombocytes is lreduced. Which pathology is suspected?
   a. B12-deficiency anemia
   b. Irondeficiency anemia
   c. Hemolytic anemia
   d. Post-hemorrhagic anemia

Answers: 1.d 2.a 3. a

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Topic 31. MANAGEMENT OF PATIENT WITH LEUKEMOID REACTION AND LEUKEMIA

Time frame – 6 hours.

Professional motivation. There are several types of leukemia based on whether the leukemia is acute or chronic, and whether it starts in myeloid cells or lymphoid cells. Knowing the specific type of leukemia helps doctors predict patient's prognosis and select the best treatment.

Acute lymphocytic (or lymphoblastic) leukemia is more common in children. Acute myeloid leukemia (or acute myelocytic, acute myelogenous, acute granulocytic, acute non-lymphocytic leukemia) represents around 40% of all leukaemias, most common in people over the age of 50. Chronic lymphocytic leukemia (CLL) mainly affects older adults and accounts for about 30% of all leukemias. Chronic myeloid leukemia (CML) occurs mostly in adults, rarely it occurs in children, accounts for 15% of adult leukemias. The stage of chronic disease is determined by the "phase" as chronic, accelerated, and blastic phase (or blast crisis).

The majority of patients with CML are diagnosed in chronic phase. Patients are diagnosed with accelerated phase disease if the percentage of blasts increases to 15-29% in the blood or bone marrow, greater than 20% basophils develop in the blood, platelets either become severely elevated or low, or a clonal abnormality develops in addition to the Philadelphia chromosome. The most advanced stage of disease is blast crisis which is defined by an increase in bone marrow or peripheral blood blasts to at least 30%. Untreated, patients with chronic phase CML will progress to accelerated phase in 3-5 years. Patients diagnosed with accelerated phase have a median survival of 4 to 6 months without treatment. Survival is further limited if blast crisis occurs with a median survival among untreated patients of 2 to 4 months.

Place of carrying out: class-room, wards of haematology department.

Study objective is to improve students' skill to do clinical examination of the patients with leukemia, to find out clinical and laboratory manifestations, to specify the treatment.

Basic level:

1. Examination of patients with leukemia.
2. Knowledge of symptoms of leukemia.

Student has to know:

1. Clinical signs in leukemia.
2. Tests and procedures for patients with leukemia: complete blood count, blood clotting tests (PT, PTT, fibrinogen), bone marrow aspirate, bone marrow trephine biopsy, immunophenotyping by flow cytometry, screening for gene mutations, cytogenetic methods.
3. Treatment algorithm for patients with different types of leukemia.

The main theoretical questions:

1. The differential diagnosis of leukemia and leukemoid reaction. Principles of differentiated treatment.
2. Diagnostic criteria and evidence-based management of patients with ALL, AML.
3. Evidence-based management of patients with CML, CLL.
4. Bone marrow transplantation.
5. Complications on the background of treatment of hematological diseases. Supportive therapy.
6. Management of patient with tumor lysis syndrome, anemia caused by chemotherapy, with febrile neutropenia, hyperuricaemia.

7. Management of a patient with dyspeptic disorders on the background of chemotherapy.
8. Primary and secondary prevention.

Assignment for self-assessment

1. A man, aged 68, complains of tiredness, sweating, enlargement of cervical, submaxillary and axillary lymph nodes. Blood test: WBC- 35 * 10^9/L, lymphocytes - 60%, Botkin and Gumprecht bodies, level of haemoglobin and quantity of thrombocytes is normal. Myelogram showed 40% of lymphocytes. What is the most probable diagnosis?

a. Chronic myelolocytic leukemia
b. Chronic lymphocytic leukemia
c. Hodgkin lymphoma
d. Acute leukemia

2. A 27 y.o. patient has been having for almost a year fatigue, hyperhidrosis, heaviness in the left hypochondrium, especially after meals. Objectively: spleen and liver enlargement. In blood: erythrocytes - 3,2 • 10^{12}/l, Hb - 100 g/l, leukocutes 100 • 10^9/l, basophils - 7%, eosinophils - 5%, myelocytes - 15%, juveniles - 16%, stab neutrophils - 10%, segmentonuclear leukocytes - 45%, lymphocytes - 2%, monocytes - 0%, reticulocytes - 0,3%, thrombocytes - 400 • 10^9/l, ESR- 25 mm/h. What is the most probable diagnosis?

a. Chronic myelolocytic leukemia
b. Chronic lymphocytic leukemia
c. Acute leukemia
d. Erythremia

3. A 54 year old woman complains of increasing fatigue and easy bruising of 3 weeks' duration. Physical findings included pale, scattered ecchymoses and petechiae and mild hepatosplenomegaly. Blood count: RBC- 2, 5 • 10^{12}/l; Hb – 73 g/l; Ht - 20%; PLT- 23 • 10^9/l; and WBC-162 • 10^9/l with 82% blasts, that contained Auric rods; peroxidase stain was positive. What is the most probable diagnosis?

a. Acute leukemia
b. Chronic leukemia
c. Thrombocytopenia
d. Hemolytic anemia

Answers:

1.b 2.a 3. a

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Topic 32. MANAGEMENT OF PATIENTS WITH POLYCYTHEMIA

Time frame – 4 hours.

Professional motivation. Polycythemia vera (PV) is one of several "myeloproliferative neoplasms", almost all patients have a mutation of the JAK2 (Janus kinase 2) gene. The prevalence of PV is approximately 22 cases per 100,000 people. The average age at which PV is diagnosed is 60 to 65 years. Thrombotic events are the major cause of morbidity and mortality in PV, and their prevention is the main objective of treatment. About one-third of patients present with a thrombotic event and younger patients have an increased risk of early death from cardiovascular disease over the general population, accounting for 45% of all deaths in PV. Arterial thrombosis involving large arteries and peripheral vascular disease are more common than venous thromboembolism. Patients are also at a particularly high risk of bleeding into skin, mucous membranes and gastrointestinal tract.

Place of carrying out: class-room, wards of haematology department.

Study objective is to improve students' skill to do clinical examination of the patients with polycythemia, to find out clinical and laboratory manifestations, to specify treatment.

Basic level:

1. Examination of patients with polycythemia.
2. To determine symptoms of polycythemia.

Student has to know:

1. Clinical signs in polycythemia.
2. Investigational methods for the diagnosis of polycythemia. *JAK2* V617F mutational analysis. Bone marrow histology. Erythropoietin level.
3. Treatment algorithm for patients with polycythemia.

The main theoretical questions:

1. Diagnostic criteria in polycythemia vera.
2. Differential diagnosis between polycythemia vera and secondary polycythemia.
3. Differential diagnosis between polycythemia vera and chronic myelocytic leukemia, essential thrombocythemia, osteomyelofibrosis.
4. Evidence-based treatment of polycythemia vera. Indications to phlebotomy. Cytoreductive therapy.
5. Management of specific situations in polycythemia: thrombosis
6. Prognosis (survival and risk of transformation to myelofibrosis and acute myeloid leukemia).

Assignment for self-assessment

1. A 52 y.o. woman complains of weakness, painful itching after washing and bathing, sensation of heaviness in the head. On examination: hyperemia of skin of face, neck, extremities. AP-180/100 mm Hg. Speeln is 4 cm below the rib arch edge. What is the most probable diagnosis?

a. Polycythemia vera
b. Essential hypertension
c. Dermatomyositis
d. Allergic dermatitis
e. Systemic sclerodermia

Answers: 1.a

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Topic 33. MANAGEMENT OF PATIENT WITH HEMORRHAGIC SYNDROME

Time frame – 6 hours.

Professional motivation. Haemorrhagic syndrome can be caused by different pathogenetic mechanisms. The first group deals with the diseases related to changes in the number and functions of thrombocytes (thrombocytopenia and thrombocytopathy). The second group comprises diseases the bleeding of which is caused by blood coagulation disorders as a result of a hereditary or acquired deficiency of procoagulants or increased content of anticoagulants (haemophilia, dysprothrombinemia, hypo- and afibrinogenemia). The third group comprises diseases the bleeding of which is caused by damage to the vascular wall (Schonlein-Henoch disease, Rendu-Osler disease). Knowledge of pathogenesis of a certain disease allows us to select the only correct way of patient management. Many disorders can cause diffuse alveolar haemorrhage but autoimmune disorders are the most common (e.g., systemic vasculitides, Goodpasture's syndrome, antiphospholipid antibody syndrome); apart from autoimmune disorders they include pulmonary

infections (e.g., invasive aspergillosis, hantavirus infection), toxic exposures (e.g., trimellitic anhydride, isocyanates, crack cocaine, certain pesticides), drug reactions (e.g., propylthiouracil, amiodarone, methotrexate, montelukast, infliximab), cardiac disorders (e.g., mitral stenosis), idiopathic pulmonary haemosiderosis.

Pulmonary-renal syndrome is defined as the combination of diffuse alveolar haemorrhage (DAH) and glomerulonephritis. Haemoptysis is the most common clinical manifestation of DAH. However, 30–35% of patients may have DAH without evidence of haemoptysis. Breathlessness, cough and low-grade fever may also be present. In about 50% of cases of DAH, patients suffer from acute respiratory failure requiring mechanical ventilation. The most common renal manifestation of pulmonary-renal syndrome is haematuria, proteinuria and active urinary sediment. If left untreated, patients can progress to end-stage renal failure, requiring haemodialysis.

Several types of immunologic injury as well as other nonimmunologic mechanisms such as antiglomerular basement membrane (anti-GBM) antibodies, antineutrophil cytoplasm antibodies (ANCA), immunocomplexes and thrombotic microangiopathy are involved in the syndrome's pathogenesis. The underlying pulmonary lesion in the majority of cases of pulmonary-renal syndrome is small-vessel vasculitis, characterized by a destructive inflammatory process that involves arterioles, venules and alveolar capillaries (necrotic pulmonary capillaritis). The term "Goodpasture's syndrome" is used for the clinical entity of DAH and rapidly progressive glomerulonephritis associated with anti-GBM antibodies. Goodpasture's syndrome is extremely rare (one case per 1,000,000 population per year) and affects Caucasians of every age but mostly those at the age of 20-30 years and 50-60 years, with a slight predominance of males. This syndrome is responsible for about 20% of acute renal failure cases due to rapidly progressive glomerulonephritis. Circulating ANCA autoantibodies are detected in the majority of patients presenting with pulmonary-renal syndrome leading the differential diagnosis to three major systemic vasculitides syndromes: Wegener's granulomatosis, microscopic polyangiitis and Churg–Strauss syndrome. Wegener's disease is characterized by the triad of systemic necrotizing vasculitis, necrotizing granulomatous inflammation of the upper and lower respiratory tract, and necrotizing glomerulonephritis. The incidence of the disease is estimated in range 5.2–12.9/million with a male-to-female ratio of 1:1. The disease usually involves Caucasians (80–97%) with a mean age at the time of diagnosis of 40–55 years, although persons of every age may be affected. The lungs are involved in 90% of cases. Microscopic polyangiitis is a systemic small-vessel vasculitis manifested by pauci-immune necrotizing glomerulonephritis (80–100% of patients), pulmonary capillaritis (10–30%), skin lesions and arthralgias.

Churg-Strauss syndrome (CSS) presents with an initial asthma/sinusitis phase, followed by eosinophilia and vasculitis. In CSS, renal involvement is milder compared with Wegener's disease, Goodpasture's syndrome and microscopic polyangitis. The incidence of CSS is difficult to determine, but limited published data suggest that in the general population the incidence is on the order of 1 to 3 cases/millions persons per year. The disease is associated with peripheral eosinophilia as well as eosinophilic infiltration of tissues. Perinuclear ANCA is reported to be positive in up to 70% of cases.

Pulmonary-renal syndrome in ANCA-negative systemic vasculitis is very rare and has been described only occasionally in Behçet's disease, Henoch-Schönlein purpura, IgA nephropathy, and mixed cryoglobulinaemia. In Henoch-Schönlein purpura, acute capillaritis and DAH involve deposition of IgA immune-complexes along the pulmonary alveoli.

Place of carrying out: class-room, wards of haematology and rheumatology departments.

Study objective is to improve students' skill to do clinical examination of the patients with hemorrhagic syndrome, to find out clinical and laboratory manifestations, to specify treatment.

Basic level:

1. Examination of patients with hemorrhagic syndrome.
2. To determine symptoms of hemorrhagic syndrome.

Student has to know:

1. Clinical signs in hemorrhagic syndrome.

2. Investigational methods for the diagnosis of hemorrhagic syndrome.
3. Treatment algorithm for patients with hemorrhagic syndrome.

The main theoretical questions:

1. Differential diagnosis of hemorrhagic syndrome. Development of plan of examination, instrumental and laboratory methods of examination (clinical blood test, autoimmune markers, coagulogram, blood culture).
2. Evidence-based management of patients according to the cause.
3. Management of patients with coagulopathies (congenital - hemophilia A and B, Willebrand's disease, and acquired hemophilia).
4. Hemorrhagic diathesis caused by vascular wall damage.
5. Management of patients with hemorrhagic telangiectasia, hemorrhagic vasculitis such as immune-complex vasculitis (Henoch-Schonlein purpura), ANCA-associated vasculitis.
6. Management of a patient disorders of platelets and vascular stasis.
7. Differential diagnosis of thrombocytopenia in CTD, allergic reactions, leukemias and hypoplastic anemia, disseminated intravascular coagulation (DIC) syndrome, sepsis, HIV.
8. Management of patients, updated treatment standards.
9. Hemorrhagic diathesis caused by the impaired coagulation and platelet stasis. Diagnostic criteria and management of a patient with DIC syndrome.

Assignment for self-assessment

1. A 43-year-old male patient undergoing treatment for peptic ulcer complains of weakness, dizziness, coffee-ground vomiting, melena. After administration of haemostatics the patient's condition has not improved, fresh blood has shown up in the vomit, skin bruises of different sizes have appeared. In blood: thrombocytes - $50*10^9$/l, Lee-White clotting time - 35 minutes, APTT - 80 seconds. In this case it is most rational to administer the following preparation:
   a. Fresh frozen plasma
   b. Heparin
   c. Fibrinogen
   d. Vikasol
2. An 18 y.o. girl complains of weakness, dizziness, loss of appetite, menorrhagia. There are many-coloured petechiae on the skin of the upper extremities. Blood test: Hb - 105 g/l; RBC- $3,2*10^{12}$/L; C.I.- 0,95; PLT.- $20*10^9$/L. The sedimentation time according to Lee White is 5'; hemorrhagia duration according to Duke is 8', "pinch and tourniquet" test is positive. What is the most probable diagnosis?
   a. Idiopathic thrombocytopenic purpura
   b. Hemophilia
   c. Hemorrhagic diathesis
   d. Iron deficiency anemia
3. A 18 y.o. boy suddenly felt pain in his right knee, it became edematic. The day before he took part in a cross-country race. Family anamnesis has no data about hemophilia and bleeding sickness. Objectively: body temperature is 37,5°C. The knee is painful, hot to the touch, edematic with local tissue tension over it. Blood count: Hb - 123 g/L, leukocytes - $5,6*10^9$/L, thrombocytes - $354*10^9$/L, prothrombin time - 12 seconds (normally 10-15 seconds), partly activated thromboplastin time - 72 seconds (normally 35-45 seconds). Hemorrhage time is normal, VIII:C factor is 5% of norm. What is the most probable diagnosis?
   a. Hemophilia A
   b. Hemophilia B
   c. Schoenlein-Henoch disease
   d. Vitamin K deficiency

Answers:

1.a 2.b 3.c

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Topic 34. MANAGEMENT OF PATIENTS WITH THROMBOCYTOPENIC PURPURA

Time frame – 2 hours.

Professional motivation. The incidence of thrombotic thrombocytopenic purpura is about 4–6 per million people per year. Idiopathic thrombotic thrombocytopenic purpura occurs more often in women and African-American people, while the secondary forms do not show this distribution. Pregnant women and women in the postpartum period accounted for a notable portion (12–31%) of the cases in some studies; thrombotic thrombocytopenic purpura affects approximately 1 in 25,000 pregnancies.

The mortality rate is approximately 95% for untreated cases, but the prognosis is reasonably favourable (80–90% survival) for patients with idiopathic thrombotic thrombocytopenic purpura diagnosed and treated early with plasmapheresis.

Place of carrying out: class-room, wards of the haematology departments.

Study objective is to improve students' skill to do clinical examination of the patients with thrombotic thrombocytopenic purpura, to find out clinical and laboratory manifestations, to indicate the treatment.

Basic level:

1. Examination of patients with thrombocytopenic purpura.
2. To determine symptoms of thrombocytopenic purpura.

Student has to know:

1. Clinical signs in thrombocytopenic purpura.
2. Investigational methods for the diagnosis of thrombocytopenic purpura.
3. How to indicate the treatment for patients with thrombocytopenic purpura.

The main theoretical questions:

1. Causes and pathogenesis of thrombocytopenic purpura.
2. Diagnostic criteria for thrombocytopenic purpura.
3. Management of patients with thrombocytopenic purpura.

Assignment for self-assessment

A 44-year-old woman has complications on skin haemorrhages which appear spontaneously, menorrhagia, general weakness, dizziness. She has suffered from these diseases since childhood.

On examination, she was normotensive (BP 120/90). She has pale skin, haemorrhages on the anterior surface of the trunk, and internal surface of the extremities. Lymph nodes of the neck are enlarged. Her lungs are clear. Cardiac examination shows regular rate and rhythm without murmur. The abdomen is soft without tenderness or distention. The liver spans 9 cm in the midclavicular line with a smooth edge. Spleen is palpable. Kidneys are not palpable. Pasternatsky's sign is positive in both sides. Blood testing: RBC – 1.9×10^{-12}/l; Hb – 86 g/l; ESR – 16 mm/h; WBC – $8*10^{-9}$/l; eos. – 2%, neutrophils – 69%, lymphocytes – 15%, monocytes – 5%, platelets 20,000/μL of large size, with otherwise normal morphology. Total protein – 73 g/l, urea – 6.7 mmol/l, creatinine – 80 μmol/l, bilirubin – 11.8 μmol/l, fasting glucose – 5.0 mmol/L. Urinalysis: RBC – 1–3, WBC – 1–2, specific gravity – 1012, protein 0.03 g/L. Chest radiographic findings, ECG are normal. Ultrasound shows splenomegaly.

Questions: what is the most likely clinical diagnosis? What additional diagnostic studies are indicated? What is differential diagnosis? What treatment does this patient need?

Answer: thrombocytopenic purpura. Myelogram. Haemoblastosis, B12-deficit, haemolytic, aplastic anaemia, haemorrhagic vasculitis, autoimmune thrombocytopenia due to SLE. Glucocorticosteroids, cytostatics, splenectomy.

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Topic 35. MANAGEMENT OF PATIENT WITH LYMPHADENOPATHY

Time frame – 4 hours.

Professional motivation. Lymphadenopathy can be localized or diffuse. About 75% of most lymphadenopathies are localized, and about 50% of those occur in the head and neck regions. Generalized lymphadenopathy, which involves two or more non-contiguous regions, is reported to occur in 25% of lymphadenopathies. A thorough history and physical exam are one of the most important steps in determining the underlying cause of lymphadenopathy.

There are several potential causes of lymphadenopathy: infectious, autoimmune, malignant, and lymphoproliferative. There is a wide range of infectious etiologies, including bacterial, fungal, viral, mycobacterial, spirochetal, and protozoal organisms. Autoimmune disorders include sarcoidosis, amyloidosis, systemic lupus erythematosus, rheumatoid arthritis, eosinophilic granulomatosis with polyangiitis and others. Malignant diseases like lymphoma, leukemia, metastatic cancer, and head and neck cancers are also common causes of lymphadenopathy. Lymphoproliferative disorders such as hemophagocytic lymphohistiocytosis can also manifest with the enlargement of lymph nodes. A Dutch study revealed that 10% of patients with unclear lymphadenopathy were referred for a biopsy, and only 1.1% were found to be related to malignancy.

Place of carrying out: class-room, wards of haematology department.

Study objective is to improve students' skill to do clinical examination of the patients with lymphadenopathy, to find out clinical and laboratory manifestations, to determine the treatment.

Basic level:

1. History and examination of patients with lymphadenopathy.
2. Infectious causes of lymphadenopathy. Haematological and non-haematological neoplastic causes.

Student has to know:

1. Investigational methods in case of lymphadenopathy.
2. Diagnostic criteria for non-Hodgkin and Hodgkin lymphoma, sarcoidosis, dermatomyositis, Still disease, chronic lymphocytic leukemia.
3. Treatment algorithm for patients with lymphadenopathy.

The main theoretical questions:

1. The main causes of lymphadenopathy.
2. Differential diagnosis of Hodgkin's and non-Hodgkin's lymphoma, lymph node enlargement in the case of other diseases (tuberculosis, sarcoidosis, metastasis of malignant tumors, SLE, etc.).
3. Evidence-based treatment: non-pharmacological and pharmacological treatment.
4. Differential diagnosis in bilateral hilar lymphadenopathy.
5. Primary and secondary prevention.

Assignment for self-assessment

1. A 33 year old woman presented to the clinic because she had had an intermittent fever, dry cough, a 4kg weight loss for the past 4 months. Her past medical history and physical exam is unremarkable and her vitals are within normal range. Lab studies had shown AST of 106 U/L, and alkaline phosphatase of 205 U/L. A chest X-ray reveals hilar adenopathy but is otherwise unremarkable. What diseases should be differentiated?

Answers:

Tuberculosis, lymphoma, sarcoidosis

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Module 4
EMERGENCIES IN INTERNAL MEDICINE CLINIC

Topic 1. CURATION OF THE PATIENT WITH HYPERTENSIVE EMERGENCY

Time frame – 6 hours.

Professional motivation. 60 million US inhabitants suffer from hypertension. The vast majority of these patients have essential hypertension. Moreover, a large number of affected individuals are unaware of their hypertension. Three quarters of those affected do not have their BP well controlled. Fewer than 1% of these patients will develop one or multiple episodes of hypertensive crises. The incidence of hypertensive crises is higher among African Americans and the elderly. The majority of patients presenting with hypertensive crises have previously received a diagnosis of hypertension, and many have been prescribed antihypertensive therapy with inadequate BP control. The incidence of postoperative hypertensive crises varies depending on the population examined, being reported in 4 to 35% of patients shortly after the surgical procedure.

Place of carrying out: class-room, wards of the cardiology and rheumatology departments, department of functional diagnostics.

Study objective is to improve students' skills to do clinical examination of the patients with acute coronary syndrome or stroke, to find out clinical and laboratory manifestations, to group them into syndromes, to make the diagnosis, and provide treatment.

Basic level: examination of patients with hypertension.

Student has to know:

1. Definition of the hypertensive emergencies.
2. Variants of the hypertensive emergencies.
3. How to provide the emergency to the patients with hypertensive crises and determine future tactics of management.

The main theoretical questions:

1. Criteria for hypertensive emergency.
2. Classification of hypertensive emergencies.
3. Clinical manifestations in hypertensive emergencies.
4. Evidence-based algorithm of emergency care. Differential treatment depending on clinical manifestations: timeline and target BP, 1st line of treatment.
5. Antihypertensive drugs used in hypertensive emergencies: doses, side effects.
6. Treatment of hypertensive emergencies in special situations: acute aortic dissection, acute pulmonary oedema, acute myocardial ischaemia, acute renal failure.

Assignment for self-assessment

A 58-year-old woman presented to the emergency department complaining of worsening occipital headache and confusion. She reported numbness and weakness involving the right side of her body as well as blurry vision over the past 12 hours. Her past medical history: hypertension, bilateral renal artery stenosis, hyperlipidemia.

On arrival, her blood pressure was 200/130 mm Hg. On physical examination, she was confused. Papilloedema was seen on fundoscopic examination. She had mild motor weakness in the right upper extremity. Laboratory examinations revealed the following: serum creatinine was 2.5 mg/dL (baseline creatinine – 1.5 mg/dL). Electrocardiogram revealed left ventricular hypertrophy by voltage criteria and nonspecific ST-T wave abnormalities in the lateral leads. Computed tomography scan of the head without contrast revealed diffuse bilateral white matter changes consistent with hypertensive encephalopathy. Suggest emergency tactic.

Answer: hospitalization to the intensive care unit, intravenous nitroprusside. Blood pressure control and neurologic symptoms control.

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Topic 2. CURATION OF THE PATIENTS WITH ACUTE CORONARY SYNDROME AND MYOCARDIAL INFARCTION

Time frame – 6 hours.

Professional motivation. Patients with chest pain represent a very substantial proportion of all acute medical hospitalizations in Europe. Distinguishing patients with acute coronary syndromes (ACS) within the very large proportion with suspected cardiac pain are a diagnostic challenge, especially in individuals without clear symptoms or electrocardiographic features. Despite modern treatment, the rates of death, MI, and readmission of patients with ACS remain high.

Registry data consistently show that non-ST-elevation acute coronary syndrome (NSTE-ACS) is more frequent than ST-elevation acute coronary syndrome (STE-ACS). The annual incidence is ~3 per 1000 inhabitants, but varies between countries. Hospital mortality is higher in patients with STEMI than among those with NSTE-ACS (7% vs. 3–5%, respectively), but at 6 months the mortality rates are very similar in both conditions (12% and 13%, respectively). Long-term follow-up showed that death rates were higher among patients with NSTE-ACS than with STE-ACS, with a twofold difference at 4 years. This difference in mid- and long-term evolution may be due to different patient profiles, since NSTE-ACS patients tend to be older, with more comorbidities, especially diabetes and renal failure. Many deaths occur in the very first hours after STEMI due to ventricular fibrillation. The implementation of an organization to cope with out-of-hospital cardiac arrest is pivotal to provide prompt cardiopulmonary resuscitation, early defibrillation if needed, and effective advanced cardiac life support.

Place of carrying out: class-room, wards of the cardiology and rheumatology departments, department of functional diagnostics.

Study objective is to improve students' skills to do clinical examination of the patients with acute coronary syndrome, to find out clinical and laboratory manifestations, to make the diagnosis, and provide treatment.

Basic level:

1. Definition of the acute coronary syndrome.
2. Examination of patients with acute coronary syndrome.
3. Electrocardiographic detection of myocardial infarction.
4. Biomarker evaluation in myocardial infarction.

Student has to know:

1. Variants of clinical course of the myocardial infarction.
2. Interpretation of laboratory methods of examination for myocardial infarction.
3. Differential programs of the treatment of the acute coronary syndrome.
4. Differential treatment for the following complications of the myocardial infarction (cardiac insufficiency (collapse, pulmonary oedema, cardiogenic shock), pericarditis (epistenocardiac, Dresler's syndrome), mechanical causes of heart failure (myocardial rupture, ventricular septal defect due to perforation of the ventricular septum, mitral regurgitation, acute aneurysm, cardiac tamponade), thromboembolism, reinfarction, recurrent chest discomfort, arrhythmias, clinical death).
5. Anti-ischaemic agents (b-blockers, nitrates, calcium channel blockers, other antianginal drugs like ivabradine), antiplatelet agents, anticoagulants.

The main theoretical questions:

1. Definition of acute coronary syndrome.
2. Pathogenesis of acute coronary syndrome.
3. Non-ST-elevation acute coronary syndrome.
4. Criteria for the diagnosis and differential diagnosis of unstable angina.
5. Differential diagnosis of mimic non-ST-elevation acute coronary syndrome: cardiac and noncardiac conditions that can mimic non-ST-elevation acute coronary syndrome.
6. Non-invasive imaging techniques (echocardiography, cardiac magnetic resonance imaging) and invasive imaging techniques (coronary angiography).
7. Long-term management: secondary prevention of myocardial infarction.
8. Evidence-based emergency care in the pre-hospital and hospital stages in patients with ST-segment elevation myocardial infarction and non-ST segment elevation myocardial infarction, with unstable angina (restoring coronary flow and myocardial tissue reperfusion: percutaneous coronary interventions, fibrinolytic therapy, antithrombotic treatment).
9. Doses, side effects, and contraindications to fibrinolytic therapy.
10. Heart failure: Killip's classification, clinical features, treatment.
11. Cardiogenic shock: clinical features, treatment.
12. Mechanical complications: cardiac rupture and mitral regurgitation.
13. Arrhythmias and conduction disturbances in the acute phase. Management.
14. Management of specific types of infarction: right ventricular infarction, myocardial infarction in diabetic patients, patients with renal dysfunction.
15. Long-term medical treatment after STEMI.
16. Differential diagnosis of the myocardial infarction.
17. Indications for percutaneous coronary interventions, contraindications, possible complications. Coronary artery bypass surgery.

Assignment for self-assessment

1. For several months a 49-year-old physician has had recurrent episodes of severe retrosternal chest pressure; these episodes occur four to five mornings a week and last 15 to 20 minutes. Despite therapy with large dosages of a calcium channel blocking agent these episodes are proceeding. Three months ago a coronary arteriogram showed no fixed obstructions in the coronary arteries, but spasm of the midportion of the right coronary artery occurred during the study and was associated with pain and ST-segment elevation. What is the most appropriate next step?

2. In appearing of acute epigastrical pain or retrosternal burning in middle-aged men investigations should be started from:

a) oesophagogastroscopy;
b) roentgenoscopy of gastrointestinal tract;
c) ECG.

3. A 58-year-old man complains of pressing retrosternal pain with radiation to scapula which goes away in 30 min after taking nitroglycerin under the tongue. Such pain appears 1–2 times per month in the morning. The examination reveals a regular heart rate. Blood pressure is 145/85 mm Hg; pulse is 80 beats/min. In Holter monitoring during attack of pain ST elevation on 5 mm was revealed in V2–V5. On the next day ST was on isoline. What pathology does the patient have?

a) stable angina, FC4;
b) myocardial infarction;
c) acute coronary insufficiency;
d) unstable angina.

4. A 50-year-old man complains of attacks of pressing retrosternal pain up to 3 events successively which appear at early in the morning (about 4–5 a.m.) and go away in 5 min after taking a nitroglycerin under the tongue. The patient is tolerant to physical activity during the daytime. The examination reveals a regular heart rate, normal heart borders. Blood pressure is 120/80 mm Hg; pulse is 76 beats/min. On ECG during attack of pain ST 3 mm elevation was revealed in the I, II, aVL, V4–

V6; after attack ECG was normalized. In stress test (exercise test) there were no changes on ECG. What pathology does the patient have?

a) stable angina;
b) vasospastic angina;
c) angina at rest;
d) unstable angina.

Answers:

1. Many reports indicate that nitrates are effective in treatment of patients with coronary arteries spasm, and nitrates should be used in conjunction with calcium-channel blocking agents (calcium antagonist). If the patient described to be symptomatic despite of the usage of adequate dosages of nitrates and calcium antagonist, it would be appropriate to consider either adding the second calcium antagonist that may have a different mechanism of action, or switching to a different calcium antagonist.

2. c. 3. d. 4. b.

Assignment for self-assessment

1. A 65-year-old male patient on aspirin, nitrates and bisoprolol, being followed for chronic stable angina, presents to the hospital with a history of 2 to 3 episodes of more severe and long-lasting pressing chest pain each day over the past 3 days. His ECG and cardiac enzymes are normal. What is the most likely diagnosis?

a) myocardial infarction;
b) unstable angina;
c) stomach ulcer;
d) stable angina.

The best course of action of the following is to:

a) admit the patient and begin intravenous digoxin;
b) admit the patient and begin intravenous heparin;
c) admit the patient and give thrombolytic therapy;
d) admit the patient for observation with no change in medication;
e) discharge the patient from the hospital with increases in nitrates and bisoprolol.

2. A 61-year-old man is admitted to the coronary care unit with crushing chest pain and ST elevation in leads II, III, and aVF with reciprocal ST depression in the lateral leads. He is agitated, pale, and diaphoretic. Peripheral pulse is weak, and systolic BP is 90 mm Hg. Neck veins are distended, Kussmaul's sign is present, but no murmur. What is the most likely cause of hypotension?

3. You are examining a patient with the main complaint of relatively sudden onset of shortness of breath and weakness but no chest pain. ECG shows nonspecific ST-T changes. You would be particularly attuned to the possibility of painless, or silent, myocardial infarction in the:

a) advanced coronary artery disease patient with unstable angina on multiple medications;
b) elderly diabetic;
c) premenopausal female;
d) inferior MI patient;
e) MI patient with PVCs.

Answers:

1. b), b).

2. Right ventricular infarction.

3. b), the classic presentation of acute myocardial infarction involves heavy substernal chest pain or pressure. However, 15 to 20% of infarctions may be painless, with the greatest incidence in diabetics and the elderly. Dyspnoea or weakness may initially predominate in these patients. Other presentations include altered mental status, the appearance of an arrhythmia or hypotension. Diabetics are likely to have abnormal or absent pain response to myocardial ischaemia due to generalized autonomic nervous system dysfunction. The other choices have no specific link to greater likelihood of silent MI.

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Topic 3. CURATION OF THE PATIENT WITH MYOCARDIAL INFARCTION COMPLICATIONS

Time frame – 6 hours.

Professional motivation. ACS is the most frequent cause of acute new-onset heart failure. In-hospital mortality is especially high in patients with evidence of cardiogenic shock (from 40 to 60%). In contrast, patients with acute hypertensive heart failure have low in-hospital mortality, with patients usually discharged alive and frequently asymptomatic. Registries indicate that almost half of the patients hospitalized with acute heart failure are rehospitalized at least once within 12 months. Estimates of the combined outcome of death or rehospitalizations within 60 days of admission vary from 30 to 50%.

Patients who have suffered from cardiorespiratory arrest who present with asystole as the initial rhythm have a poor prognosis. Survival from cardiorespiratory arrest for patients who present with ventricular fibrillation or pulseless ventricular tachycardia can approach 45–50%. The key intervention in improving survival is timely defibrillation.

Place of carrying out: class-room, wards of the cardiology and rheumatology departments.

Study objective is to improve students' skill to distinguish clinical symptoms of acute heart failure, to determine management strategy of emergency medicine and resuscitation.

Basic level:

1. To be able to collect complaints, case history, carry out objective examination of the patients with acute heart failure.
2. To interpret instrumental (ECG, EchoCG, X-ray) and laboratory data in patients with acute heart failure.

Student has to know:

1. Criteria for diagnosis of acute heart failure.
2. Management of acute heart failure.

The main theoretical questions:

1. Definition of acute left ventricular failure.
2. Clinical classification of acute heart failure.
3. Causes of acute left ventricular failure.
4. The interpretation of the results of laboratory and instrumental examination during cardiogenic shock.
5. Evidence-based standards of emergency care of cardiogenic shock in pre-hospital and hospital stages.
6. Indications and dosing of i.v.vasodilators in acute heart failure.
7. Inotropic agents: indications for inotropic therapy. Dosing of positive inotropic agents in acute heart failure.
8. Sudden cardiac arrest: symptoms and emergency treatment. Prevention.
9. Emergency care of heart rhythm and conduction disorders.
10. The role of electropulse therapy. Indications and principles of cardiac pacing (temporary, permanent).

Assignment for self-assessment

At the grocery store you see an elderly lady slump to the floor. Coming to her to aid, your first step in adult basic life support (cardiopulmonary resuscitation) should be the following:

a) check for a carotid pulse;
b) assess breathing;
c) establish an airway;

d) determine responsiveness;

e) determine chest compression.

Answers: d, one cannot automatically assume initially that an individual has had a cardiac or respiratory arrest. Therefore, first determine responsiveness by tapping or gently shaking the victim and shouting, "Are you ok?" Then shout or phone for help, then position the victim and yourself. Follow this with the ABCDs (establishing the Airway, assessing Breathing, assessing Circulation, and managing any need for Defibrillation).

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Topic 4. CURATION OF THE PATIENT WITH PAROXYSMAL HEART RHYTHM AND CONDUCTION DISORDES

Time frame – 6 hours.

Professional motivation. The estimated prevalence of paroxysmal supraventricular tachycardia (SVT) is in a 3.5% sample of medical records in the Marshfield (Wisconsin, the USA). Occurrence rates have been determined after acute myocardial infarction or coronary artery bypass graft surgery and in congestive heart failure (CHF) patients. The incidence rate of supraventricular arrhythmias among patients with CHF is 11.1%; paroxysms are more common in older patients, males, and those with longstanding CHF and radiographic evidence of cardiomegaly. In approximately 60% of cases, atrial flutter occurred for the first time associated with a specific precipitating event (i.e., major surgery, pneumonia, or acute myocardial infarction). In the remaining patients, atrial flutter is associated with chronic comorbid conditions (i.e., heart failure, hypertension, and chronic lung disease). Only 1.7% of cases has no structural cardiac disease or precipitating cause (lone atrial flutter). The overall incidence of atrial flutter is 0.088%; 58% of these patients also had AF. Atrial flutter alone was seen in 0.037%. The incidence of atrial flutter increased markedly with age, from 5 per 100000 of those more than 50 years old to 587 per 100 000 over age 80. Atrial flutter is 2.5 times more common in men.

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, occurring in 1–2% of the general population. Over 6 million Europeans suffer from this arrhythmia, and its prevalence is estimated to at least double in the next 50 years as the population ages. AF confers a 5-fold risk of stroke, and one in five of all strokes is attributed to this arrhythmia. Ischaemic strokes in association with AF are often fatal, and those patients who survive are left more disabled by their stroke and more likely to suffer a recurrence than patients with other causes of stroke. In consequence, the risk of death from AF-related stroke is doubled and the cost of care is increased 1.5-fold. AF may long remain undiagnosed (silent AF), and many patients with AF will never present to hospital. Hence, the "true" prevalence of AF is probably closer to 2% of the population. The prevalence of AF increases with age, from <0.5% at 40–50 years, to 5–15% at 80 years. Men are more often affected than women. The lifetime risk of developing AF is ~25% in those who have reached the age of 40. The prevalence and incidence of AF in non-Caucasian populations is less well studied. The incidence of AF appears to be increasing (13% in the past two decades).

AF is associated with increased rates of death, stroke and other thromboembolic events, heart failure and hospitalizations, degraded quality of life, reduced exercise capacity, and left ventricular (LV) dysfunction. Death rates are doubled by AF, independently of other known predictors of mortality. Only antithrombotic therapy has been shown to reduce AF-related deaths. Stroke in AF is often severe and results in long-term disability or death. Approximately every fifth stroke is due to AF; further-more, undiagnosed "silent AF" is a likely cause of some "cryptogenic" strokes. Paroxysmal AF carries the same stroke risk as permanent or persistent AF.

Hospitalizations due to AF account for one-third of all admissions for cardiac arrhythmias. Acute coronary syndrome (ACS), aggravation of heart failure, thromboembolic complications, and acute arrhythmia management are the main causes. Left ventricular (LV) function is often impaired by the irregular, fast ventricular rate and by loss of atrial contractile function and increased end-diastolic LV filling pressure. Both rate control and maintenance of sinus rhythm can improve LV function in AF patients.

Ventricular arrhythmias include premature ventricular contraction, ventricular tachycardia and ventricular fibrillation. Both of last are life-threatening arrhythmias most commonly associated with heart attacks. The most serious arrhythmia is ventricular fibrillation, which is an uncontrolled, irregular beat. If cardiopulmonary resuscitation (CPR) can be started, or if electrical energy is used to "shock" the heart back to a normal rhythm, then the heart may not be too damaged. About 220,000 deaths from heart attacks each year are thought to be caused by ventricular fibrillation. People who have heart disease or a history of heart attack have the highest risk of ventricular fibrillation.

A less serious type of ventricular arrhythmia is a premature ventricular contraction (PVC). PVCs generally are not a cause for alarm and often do not need treatment. But if patient have heart disease or a history of ventricular tachycardia, PVCs can cause a more serious arrhythmia.

The incidence of ventricular tachycardia (VT) in the United States is not well quantified because of the clinical overlap of VT with ventricular fibrillation (VF). Examination of sudden death data provides a rough estimate of VT incidence. Most sudden cardiac deaths are caused by VT or VF, at an estimated rate of approximately 300,000 deaths per year in the United States, or about half of the estimated cardiac mortality in this country. A prospective surveillance study gave a sudden death incidence of 53 per 100,000, accounting for 5.6% of all mortality. This is only a rough estimate of VT incidence, because many patients have nonfatal VT and because arrhythmic sudden deaths may be associated with VF or bradycardia rather than with VT.

The clinical manifestations of bradycardia can vary widely from insidious symptoms to episodes of frank syncope. Bradycardia can be broadly classified into 2 general categories: sinus node dysfunction (SND) and atrioventricular block (AV). The exact incidence of SND is unknown. The syndrome occurs in approximately one in 600 cardiac patients older than 65 years. Symptoms of SND almost invariably progress over time. The most dramatic symptom in patients with SND is syncope. About 50% of patients with SND develop tachy-brady syndrome over a lifetime; such patients have higher risk of stroke and death. The survival of patients with SND appears to depend primarily on the severity of underlying cardiac disease and is not significantly changed by pacemaker therapy. However, incidence of sudden death owing directly to SND is extremely low.

Possible complications of sick sinus syndrome include inadequate or inefficient pumping of the heart, heart failure, exercise intolerance, and injuries sustained by fainting spells and falling. Complications may develop from surgery to implant pacemakers, including infection, reaction to medications or anesthesia, and pacemaker failure. Sick sinus syndrome progresses slowly. No treatment is necessary as long as the individual is not experiencing symptoms. Even with a permanent artificial pacemaker, the long-term prognosis is excellent.

AV blocks occur more frequently in people older than 70 years, especially in those who have structural heart disease. Approximately 5% of patients with heart disease have first-degree AV block, and about 2% have second-degree AV block.

One study examined 24-hour Holter monitors in 625 asymptomatic, heart-disease-free people, aged 15 to 83 years. Transient type I second-degree AV block was seen in 14 (2.2%) patients, more frequently in patients with resting heart rates of <60 bpm. First-degree AV block has been associated with about a 2-fold increase in the probability of atrial fibrillation, a 3-fold increase in the probability of pacemaker implantation, and an increase in all-cause mortality.

First-degree AV block can be found in healthy adults. At 20 years of age, the PR interval may exceed 0.20 seconds in 0.5–2% of healthy people. At age 60 years, more than 5% of healthy individuals have PR intervals exceeding 0.20 seconds.

Advanced AV block (type II second-degree and third-degree) is usually anatomically infranodal and is seen in advanced His-Purkinje disease. One study examined the prevalence of His-Purkinje disease

in the Framingham population: QRS intervals of >0.12 seconds were significantly associated with coronary heart disease, CHF, AV block, hypertension, left ventricular hypertrophy, and ventricular extrasystoles. QRS intervals >0.12 seconds were rare before 50 to 60 years of age and were found in 11% of older men and 5% of older women. While intraventricular block does not inevitably lead to AV block, it frequently precedes the development of advanced AV block. Thus, this characterisation of a wide-QRS interval population is likely similar to that of the advanced AV block population.

Mobitz II second-degree AV block is rare in healthy individuals, whereas Mobitz I (Wenckebach) second-degree AV block is observed in 1–2% of healthy young people, especially during sleep.

Patients treated with permanent pacing to treat AV blocks have an excellent prognosis. Patients with advanced AV blocks who are not treated with permanent pacing remain at high risk of sudden cardiac death. Although AV block generally is not associated with major morbidity, progressive degrees of AV block carry increasing morbidity and mortality.

Place of carrying out: class-room, wards of the cardiology and rheumatology departments, department of functional diagnostics.

Study objective is to improve students' skill to do clinical examination of the patients with tachyarrhythmias and bradycardia, indicate the treatment.

Basic level:

1. Clinical and ECG signs of extrasystoles, paroxysmal tachycardias, fibrillation, disturbances in conduction.
2. Examination of patients with tachyarrhythmias and bradycardia.
3. Drugs and doses for pharmacological conversion of (recent-onset) atrial fibrillation.

Student has to know:

1. Anti-arrhythmic medications: adenosine, amiodaron, calcium channel blockers: verapamil and diltiazem, lidocaine, sotalol, procainamide. Side effects, doses.
2. Management algorithm in bradycardia.
3. Management algorithm in tachyarrhythmias.

The main theoretical questions:

1. Classification of tachyarrhythmias.
2. The diagnostic of paroxysmal heart rhythm disorders.
3. Regular narrow-complex tachycardia: ECG signs, therapeutic choice.
4. Wide-complex tachycardia: ECG signs, therapeutic choice.
5. Irregular tachycardias: atrial fibrillation and flutter. ECG signs, therapeutic choice.
6. Pharmacological cardioversion of recent-onset atrial fibrillation. Choice of rate and rhythm control strategies.
7. Management of patients with preexcited tachycardias (associated with or mediated by an accessory pathway).
8. Ventricular tachycardia, ventricular fibrillation: ECG signs, emergency.
9. Electrical defibrillation or synchronized cardioversion: indications, initial dose for cardioversion of atrial fibrillation, atrial flutter and other SVTs.
10. Radiofrequency catheter ablation.
11. Evaluation and management of patients with bradycardia and cardiac conduction delay.
12. Sick sinus syndrome, AV-blocks: ECG signs.
13. Acute medical management of bradycardia attributable to SND or AV block.

Assignment for self-assessment

1. What medicines may accelerate arrhythmia via accessory pathway:
   a) digoxin, verapamil;
   b) amiodarone, heparin;
   c) amiodarone, sotalol.
2. In treatment with warfarin we have to check:
   a) INR (target 2–3);
   b) bleeding time (target up to 5 min);

c) clotting time (target up to 6 min);
d) INR (target 1–2);
e) bleeding time (target up to 10 min).

3. The first-line drug for acute symptomatic bradycardia:
   a) hydrocortisone;
   b) dextrose;
   c) atropine;
   d) amiodarone.
4. The recommended atropine dose for symptomatic bradycardia is:
   a) 0.5 mg IV every 3 to 5 minutes to a maximum total dose of 3 mg;
   b) 1.5 mg IV every 3 to 5 minutes to a maximum total dose of 5 mg;
   c) 2.5 mg IV every 3 to 5 minutes to a maximum total dose of 5 mg;
   d) 5 mg IV every 3 to 5 minutes to a maximum total dose of 10 mg.
5. Synchronized cardioversion is recommended to treat the following states, except:
   a) unstable SVT due to reentry;
   b) unstable atrial fibrillation;
   c) unstable atrial flutter;
   d) unstable monomorphic (regular) VT;
   e) unstable angina.

Answers:

1. a. 2. a. 3. c. 4. a. 5. e.

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Topic 5. CURATION OF THE PATIENT WITH ACUTE THROMBOSIS

Time frame – 2 hours.

Professional motivation. Acute venous and arterial thrombosis accounts for the most common causes of death in developed countries. This mortality depends on location and acuity of thrombosis, with myocardial infarction and cerebrovascular accident or stroke accounting for the highest proportion of thrombosis-associated death in the United States. In certain clinical circumstances, patients can be at increased risk of thrombosis and bleeding simultaneously (e.g., disseminated intravascular coagulopathy-DIC, or in patients with underlying malignancy who develop a coagulopathy). In venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), the annual incidence is 1 per 100000 in children, 1 per 10000 in reproductive age, 1 per 1000 in later middle age, and 1 per 100 in elderly. The incidence is increased in patients with cancer compared to those without cancer. About 20 to 50% of deep vein thrombosis patients develop a post-thrombotic syndrome, up to 9% of patients with a history of pulmonary embolism develop the pulmonary hypertension.

Acute thromboembolic occlusion of the superior mesenteric artery (SMA) is a condition with a serious prognosis. Acute mesenteric ischaemia (AMI) is an uncommon occurrence and represents 0.1% of hospital admissions. Despite considerable advances in medical diagnosis and treatments over the past 4 decades, mesenteric vascular occlusion still has a poor prognosis, with an in-hospital mortality rate of 59 to 93%. The high rate of mortality can be explained by the nonspecific signs and symptoms that characterize AMI.

Place of carrying out: class-room, pulmonology, orthopedic, rheumatology wards.

Study objective is to be able to identify symptoms of thrombosis and assign management.

Basic level:

1. Pathophysiology of thrombosis (factors that increases risk of thrombosis - venous stasis, endothelial injury, hypercoagulability).
2. Coagulation pathway. Anticoagulant mechanisms for prevention inadvertent activation of the clotting process.
3. Examination of patients with signs of thrombosis.
4. To evaluate data of the laboratory investigations in thrombosis.

Student has to know:

1. Clinical signs in venous thromboembolism.
2. How to evaluate data of the laboratory investigations in acute thrombosis.
3. Investigational methods for the diagnosis of DVT.
4. Pharmacological management, endovascular treatment.
5. Caprini risk assessment score

The main theoretical questions:

1. Etiologic factors associated with venous or arterial thromboses.
2. Diagnostic criteria of mesenteric vascular thrombosis, deep vein thrombosis, thrombosis of the superior vena cava. Modified Wells' criteria.
3. Upper-extremity deep venous thrombosis (2 forms of upper-extremity DVT are effort-induced thrombosis (Paget-von Schrötter's syndrome) and secondary thrombosis).
4. Approaches for confirming the diagnosis of DVT (Wells' score for probability of DVT, venous ultrasonography, venography, magnetic resonance imaging, biomarkers).
5. Acute thromboembolic occlusion of the superior mesenteric artery.
6. The management of patients with mesenteric vascular thrombosis, deep vein thrombosis, superior vena cava thrombosis.
7. Budd-Chiari syndrome.
8. The first aid in venous thromboembolism.
9. Complications of anticoagulant therapy.
10. Management in patients with active malignancy.
11. DVT prophylaxis: mechanical and pharmacological methods of prophylaxis.
12. DVT and PE risk is high in patients undergoing major orthopedic surgeries.
13. DVT prophylaxis in pregnancy.

Assignment for self-assessment

1. A 65-year-old man was presented to emergency room with asymmetric lower leg pain after an intense workout. He was known to have a history of hypertension, chronic kidney disease, and gout. On examination, warm and red skin, tenderness along the right calf. He denied long distance travel, immobilization, surgery, smoking, or prior malignancy. His vitals signs were unremarkable. A lower extremity venous ultrasound examination was performed and revealed a clot in his right peroneal and posterior tibial veins. What risk factors for development of this state do you know? Management.

Answer: Standard risk factors for DVT are immobilization, pregnancy, recent surgery (particularly orthopedic), malignancy, older age, smoking, coagulation deficits or hypercoagulable states, connective tissue disorders. Screening for malignancy is indicated. Intravenous anticoagulant heparin is commenced as patient experiences renal insufficiency, bridged to warfarin for three months. Heparin 80 IU/kg bolus, maintenance dose -18 IU/kg/h. An APTT ratio of 1.5 e 2.5 should be reached within 24 hours of starting treatment.

2. A 22-year-old woman was admitted to the hospital with complaints of abdominal "bloating". She had been in excellent health until 4 weeks earlier, when she started taking estradiol tablets. 4 days later, she began to have bloating and discontinued the medication; an ultrasonographic examination of the abdomen was normal, vaginal examination 3 months earlier had been normal. Her menses were normal; her last menstrual period had occurred 23 days before admission. She took no medications. She did not smoke. The family history included renal-vein thrombosis in her father and deep venous thrombosis in a paternal aunt.

There was no recent history of anorexia, nausea, vomiting, chills, fever, lymphadenopathy, back or bone pain, arthralgia, pruritus, menstrual changes, abdominal trauma, risk factors for infection with the human immunodeficiency virus.

On examination, there was abdominal distention, ascites and palpable liver edge 2 cm below the right costal margin.

Haematologic laboratory tests: complete blood count is normal. Test for fibrin-split products was positive (titre 60 μg/ml (normal value <10). The conjugated bilirubin concentration 9 μmol/l, total bilirubin – 26 μmol/l, γ-GT – 59 U/l (normal range – 7 to 33), urea – 6 mol/l, creatinine – 90 μmol/l, glucose – 4.8 mol/l, total protein – 68 g/l, albumin – 60%, globulin – 40%, aspartate aminotransferase – 38 units, alanine aminotransferase – 42 units, anticardiolipin IgG and IgM antibodies are normal, slightly prolonged prothrombin time, slightly prolonged activated partial-thromboplastin time, fibrinogen – 5 g/l. CT scan of the abdomen confirmed the presence of ascites; the liver and spleen were enlarged. Abdominal paracentesis yielded 3 liters of ascitic fluid that contained 50 white cells/mm^3, all of which were lymphocytes; the total protein concentration was 3.9 g/dl. Microscopical examination of the fluid revealed no microorganisms, and cytologic examination showed no malignant-tumour cells. One day later, the patient had increasing abdominal pain and low-grade fever.

On the second hospital day, the temperature was 38 °C, the pulse- 112, the respirations - 18, the blood pressure - 110/70 mm Hg. Physical examination revealed abdominal distention; diffuse tenderness, which was most marked in the right upper quadrant; palpable liver edge – 3 cm below the costal margin. There was + peripheral oedema. No signs of deep venous thrombosis were detected. No prominent venous pattern was observed in the abdominal wall, and the spleen was not felt.

An ECG revealed no abnormalities. Radiographs of the chest revealed a right pleural effusion and a probable left pleural effusion. Ultrasonographic examination of the abdomen showed ascites and heterogeneous echogenicity of the liver texture with areas of increased echogenicity. The portal, superior mesenteric, and splenic veins were patent, with hepatopetal flow. The hepatic artery was patent, and the middle and left hepatic veins were small but patent. Cardiac ultrasonographic study showed a moderate pericardial effusion, without evidence of cardiac constriction. Hepatic venographic examination revealed a stenotic middle hepatic vein with intraluminal filling defects consistent with nonocclusive thrombi; the hepatic-vein tributaries were obliterated. The mean hepatic-vein wedge pressure was 38 mm Hg; the right free hepatic-vein pressure was 15/6 mm Hg, with a mean pressure of 9 mm Hg. The portal vein was not opacified during wedged injection of the hepatic vein.

On the eighth hospital day, an ultrasonographic examination of the portal vein showed that it was widely patent, with normal hepatopetal flow. The hepatic artery appeared normal, with normal Doppler-signal characteristics.

What is the clinical diagnosis? What is the mechanism of ascites formation? What diseases should be differentiated in this patient if she has pleural effusions? What factors are responsible for hepatic-vein thrombosis? What additional investigations should be suggested? Treatment.

Answers: the clinical course of this woman's illness with the rapid development of liver disease over a period of a few weeks is typical of the Budd-Chiari syndrome, but occasionally the symptoms extend over a period of months to years. Selective hepatic venographic findings indicate on the Budd-Chiari syndrome – thrombosis of the hepatic venous circulation. The results of liver-function tests are usually not markedly abnormal, as was the case in this patient.

The high mean hepatic wedge pressure indicated the presence of portal hypertension, which resulted from increased resistance to hepatic blood flow. Portal hypertension leads to the extravasation of fluid from plasma into the peritoneal cavity. Another factor contributing to the formation of ascites is the weeping of hepatic lymph from the surface of the liver as a result of the obstruction of hepatic sinusoids and lymphatics. The differential diagnosis of pleural effusions includes SLE, cancer and infectious diseases, but the normal sedimentation rate makes these diagnoses untenable in this case. Since this woman had one site of thrombosis in the hepatic veins, it is tempting to postulate that the pleural effusions resulted from pulmonary emboli with infarction. The absence of respiratory tract symptoms and pleuritic chest pain, however, makes it more likely that the effusions were due to the

hepatic dysfunction. The factors responsible for hepatic-vein thrombosis are divided into 2 groups. The first group includes acquired diseases (polycythemia vera, paroxysmal nocturnal haemoglobinuria, neoplasms), those involving predisposing factors (such as the postoperative or postpartum state or use of oral contraceptives), and acquired abnormalities (such as the lupus anticoagulant or antiphospholipid syndrome). Two haematologic diseases that account for approximately 20% of cases of the Budd-Chiari syndrome are polycythemia vera and paroxysmal nocturnal haemoglobinuria. Neoplasms (hepatocellular carcinoma, renal-cell carcinoma, adrenal carcinoma), infections (amebic abscesses) account for about 10% of the cases. Among the predisposing factors, use of oral contraceptives and pregnancy are associated with about 20% of the cases, and trauma with 2%. The second group of patients includes those with hereditary or biologic defects that confer a predisposition to thrombosis.

The absence of a high titre of anticardiolipin antibodies is evidence against the diagnosis of the antiphospholipid syndrome. With a base-line prolongation of the prothrombin and partial-thromboplastin times due to liver disease or vitamin K deficiency in this patient, it would be very difficult to interpret the results of the clotting assays that are used to detect the presence of a lupus anticoagulant. The moderate elevation in the level of fibrin-split products probably resulted from endogenous fibrinolysis of hepatic-vein thrombi rather than from a process such as disseminated intravascular coagulation.

Congenital deficiencies of antithrombin III, protein C, protein S are associated with an increased risk of venous thrombosis and have been reported in patients with the Budd-Chiari syndrome. These deficiencies are usually inherited as autosomal dominant disorders. In rare cases, hereditary abnormalities in fibrinogen are also associated with a thrombotic diathesis. The diagnostic yield of a laboratory evaluation is increased somewhat if the patient has the first thrombotic episode at a young age, recurrent thromboembolic events, and family history of thrombosis.

Test for factor V Leiden can be performed by amplifying a DNA fragment containing the factor V mutation site by the polymerase chain reaction in peripheral-blood mononuclear cells. Use of oral contraceptives and pregnancy, including the postpartum state, are important triggers for thrombotic events in patients with resistance to activated protein C or other hereditary thrombotic disorders. The risk of venous thrombosis among those who use oral contraceptives and have resistance to activated protein C increases by about 35 times. We can think of Budd-Chiari syndrome, with a hereditary defect conferring a predisposition to thrombosis.

The aim of additional investigations is to identify a hypercoagulable state: total and free protein S levels, antithrombin III, resistance to activated protein C, a PCR test to detect the factor V Leiden mutation; values for protein C.

The patient should be treated with warfarin. If the patient is not treated, fibrosis and portal hypertension develop rapidly.

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Topic 6. CURATION OF THE PATIENT WITH PULMONARY EMBOLISM. TREATMENT STRATEGY IN SUDDEN CARDIAC DEATH

Time frame – 6 hours.

Professional motivation. Pulmonary embolism (PE) is a common complication of hospitalization and contributes to 5 to 10% of deaths in hospitalized patients, making it one of the leading causes of preventable hospital deaths. Despite it being an enormous health problem, the true incidence of pulmonary embolism is uncertain.

The diagnosis of venous thrombi and pulmonary emboli can be difficult and requires specialized imaging techniques that are not available in all hospitals or healthcare settings.

In the United States, the estimated incidence of diagnosed PE is 71 to 117 per 100,000 person-years, but the true incidence is likely to be much more than this rate because studies show that for every case of diagnosed, nonfatal PE, there are 2.5 cases of fatal pulmonary embolism diagnosed only after death. Other studies have estimated that more than one million people in the United States are affected by pulmonary embolism per year, with 100,000 to 200,000 of these events being fatal.

Over half of all diagnosed cases of PE in the United States occur in patients in hospitals or nursing homes. One recent report estimated that more than 12 million patients (31% of patients discharged from hospitals in the United States) are at risk of pulmonary embolism.

PE has earned the reputation of a silent killer because less than half of patients who die of PE were diagnosed with the problem prior to death. PE occurs in approximately 10% of patients with acute DVT. Most patients (up to 75%) are asymptomatic.

Place of carrying out: class-room, wards of the pulmonology.

Study objective is to be able to identify symptoms of pulmonary embolism and assign management.

Basic level:

1. Examination of patients with PE.
2. To determine symptoms of PE.
3. To evaluate data of the laboratory investigations of PE.

Student has to know:

1. Clinical signs in PE.
2. Investigational methods for the diagnosis of PE.
3. Markers of right ventricular dysfunction.

The main theoretical questions:

1. Risk factors for pulmonary embolism.
2. What are the symptoms of PE?
3. Standards of evidence-based emergency diagnostic in PE.
4. Evidence-based treatment of PE in pre-hospital and hospital stages.
5. Clot elimination by means of embolectomy or dissolution by IV thrombolytic therapy.
6. Anticoagulation: unfractionated heparin, low molecular weight heparin, long-term anticoagulation by warfarin. Dosage, complication of warfarin/heparin treatment, duration of treatment.
7. Follow-up management of the patients.
8. Standards of emergency diagnostic and treatment of sudden cardiac death in pre-hospital and hospital stages. Technique of resuscitation measures. Defibrillation.

Assignment for self-assessment

A 35-year-old woman was hospitalized for premature labor at 37 weeks of gestation. Fetal distress was identified, and an emergency cesarean section resulted in the delivery of a healthy baby. Two days later, the mother reported “crampy” pain in her right leg and was prescribed pain medications. Four days after delivery, she developed sudden shortness of breath and rapid heart rate. What is your presumptive diagnosis? What risk factors for development of this state do you know? What investigations should be performed? Management.

Answer: pulmonary embolism is suspected. Intravenous anticoagulant heparin is indicated. Additional investigations: computed tomography scan with a contrast dye injected into the vein to outline the pulmonary arteries, a lower extremity ultrasound. This patient's risk factors for pulmonary thromboembolism include immobility, the high levels of estrogens associated with pregnancy, and the tissue injury associated with surgery. Anticoagulant treatment should be administered for at least 3 months after delivery.

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Topic 7. CURATION OF THE PATIENT WITH EMERGENCIES IN RHEUMATOLOGY

Time frame – 4 hours.

Professional motivation. There are certain conditions that need to be diagnosed quickly: systemic vasculitis, patients who present with renal involvement, pulmonary-renal involvement (if they have alveolar hemorrhages and renal involvement), patients who have got cerebral vasculitis. The most common rheumatological emergency seen in the emergency department is acute monoarthritis. Vasculitis in RA, SLE can occur in both small- and medium-sized vessels. Medium vessel rheumatoid vasculitis may cause organ infarction and necrosis. Systemic rheumatoid vasculitis has a poor prognosis without immune-suppressive therapy. Corticosteroids are the mainstay of treatment for most inflammatory rheumatological conditions. At high doses, they provide rapid control of inflammatory disease.

Place of carrying out: class-room, wards of pulmonology and rheumatology departments.

Study objective is to be able to identify symptoms of antiphospholipid syndrome, central nervous system vasculitis and assign management.

Basic level:

1. Examination of patients with antiphospholipid syndrome, central nervous system vasculitis.
2. To determine symptoms of antiphospholipid syndrome, central nervous system vasculitis.
3. To evaluate data of laboratory investigations.

Student has to know:

1. Clinical signs in rheumatic diseases with manifestations of central and peripheral nervous system vasculitis: systemic lupus erythematous, scleroderma, rheumatoid arthritis, Sjögren syndrome, systemic necrotizing vasculitis (polyarteritis nodosa, Churg-Strauss syndrome, microscopic polyangitis, Kawasaki disease), systemic granulomatous vasculitis (Wegener's granulomatosis).
2. Investigational methods for the diagnosis.

The main theoretical questions:

1. Catastrophic antiphospholipid syndrome (cAPS).
2. Central nervous system vasculitis.
3. Kidney-lung syndrome.
4. Scleroderma renal crisis.
5. Dermatopolymyositis
6. Standards of evidence-based emergency diagnostic.
7. Evidence-based treatment in pre-hospital and hospital stages. Pulse therapy with corticosteroids and cytostatics in patients with connective tissue diseases and systemic vasculitis.
8. Indications and methods of extracorporeal blood purification.
9. Indications and methods of intravenous immunoglobulins injection

Assignment for self-assessment

A 38 year old man presented with a 2week history of arthralgia that affected his hands and ankles, associated with intermittent joint swelling. Month before he had developed erythema on his face and ulceration on his tongue. He also reported weight loss, loss of vision, fevers, nasal stuffiness, periodically epistaxis. On examination, he had pale skin, nasal crusting, small ulcers on his tongue. His ankles were swollen. There are clear pulmonary sounds. Heart sounds are weak, systolic murmur above apex, pulse 96/min, rhythmical, BP – 190/110. From the history: 4 months ago patient finished the treatment with antibiotics (from 3 different groups) due to infective endocarditis.

Urinanalyse showed a trace of protein and blood, the 24 hour urinary protein was slightly raised at 0.55 g in 24 hours. Blood tests: RBC – $2,7*10^{12}$/l; Hb – 80 g/l, ESR = 59 mm/h, C-reactive protein = 84 mg/l. On the entering day haemoptysis appeared. Chest X-ray: shadowing at both lung (infiltrates) more marked on the right, with cavitation. Immunological test: antibodies to double stranded-DNA showed a negative titre of 1:12. Blood cultures were negative. Transthoracic echocardiography confirmed moderate mitral regurgitation without vegetations, left atrial dilatation, systolic pulmonary artery pressure = 30 mmHg.

A high resolution computed tomogram of the thorax: lungs had a patchy ground glass appearance, bilateral, well-defined pulmonary nodules. Cavitations are with irregular walls.

In 3 days oedema on the legs and the level of proteinuria increased to 1,4 g in 24 hours, RBC – $2,5*10^{12}$/l; Hb – 78 g/l; ESR – 60 mm/h; WBC – $16*10^{9}$/l; eos. – 2%, stab neutr. – 14%, segmented neutrophils – 59%, lymphocytes – 11%, monocytes – 8%. Total serum protein – 45g\l, serum urea – 9,7 mmol/l, creatinine – 190 μmol/l, bilirubin – 19 μmol/l, AST=20units.

What is the differential diagnosis and what is the most likely diagnosis? What is the treatment protocol?

Answer: Small-vessel vasculitis, tuberculosis. ANCA test? Viral screening (hepatitis B,C, HIV), the most likely diagnosis – Wegener granulomatosis, severe course with organ-threatening manifestations. Pulse therapy - IV methylprednisolone 500–1,000 mg/day for 3–5 days, cyclophosphamide iv dose depends on eGFR, lasting 6 months

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Topic 8. CURATION OF THE PATIENT WITH ACUTE BACK PAIN

Time frame – 2 hours.

Professional motivation. The prevalence of low back pain increases markedly with age, and many of the disorders are affected by lifestyle factors, such as obesity and certain types of physical activity. Although the economic and public health effects of back disorders and especially low back pain are enormous, epidemiologic research into the problem is in a formative stage, especially compared with cardiovascular conditions and cancer. As a result of the increasing number of older people throughout the world, the burden on the individual and society as a whole is expected to increase dramatically. While not a disease, back pain is a major cause of disability, especially in areas where compensation systems take it into cognizance. Approximately 90% cases of back pain have no identifiable cause and are designated as nonspecific. A variety of diagnostic labels have been used by health care professionals.

Over a lifetime 80% of people have lower back pain, with 26% of American adults reporting pain of at least one day in duration every three months. 41% of adults aged between 26 and 44 years reported having back pain in the previous 6 months. Most people with acute lower back pain recover completely over a few weeks regardless of treatment. 60% of people recover after seven weeks, regardless of the treatments they receive. Consistent with these statistics, a recent study found that almost 30% of patients did not recover from the presenting episode of low back pain within a year. For

those patients whose low back pain continues on to chronicity, it is rarely self limiting, as fewer than 10% of those patients whose low back pain becomes chronic report no pain five years later.

Place of carrying out: class-room, wards of the rheumatologic department.

Study objective: to improve the skills of differential diagnosis of states which are accompanied by low back pain, to determine management of such patients.

Basic level:

1. To be able to collect complaints, case history, carry out physical examination in patients with low back pain.
2. To interpret instrumental and laboratory data in patients with low back pain.

Student has to know:

1. How to find out joint and spine injury using instrumental methods of examination.
2. What diseases are accompanied by low back pain.
3. How to make an algorithm of investigations in patients with low back pain.
4. How to determine approaches to treatment in different aetiology of low back pain.

The main theoretical questions:

1. Diagnostic criteria of ankylosing spondylitis. Management.
2. Diagnostic criteria of reactive arthritis, Reiter's disease. Management.
3. Diagnostic criteria of psoriatic arthritis. Management.
4. Diagnostic criteria of gout. Pathogenic management.
5. Symptomatic treatment of the disorders of the joints.
6. Use of nonsteroidal anti-inflammatory drugs (NSAID), corticosteroids, muscle relaxants in treatment of dorsalgia, side effects and advantages. Physiotherapy and sanatorium-resort therapy.
7. Diagnostic differences between pain in inflammatory and degenerative joint diseases.
8. Differential diagnostic of acute back pain in diseases of the heart, aorta, respiratory system, gastrointestinal tract, kidneys, urinary tract (kidney stones).
9. Updated diagnostic and evidence-based treatment standards.

Assignment for self-assessment

1. Radiographic data in degenerative joint disease of the spine:
   a) vertebral sclerosis;
   b) osteophytes;
   c) decrease of intervertebral space height;
   d) lumbar lordosis straightening;
   e) everything listed above.

2. A 22-year-old man complains of low back pain and stiffness that is worse on arising and improves with exercise. On examination, he is found to have limited mobility of the sacroiliac joints and lumbar spine. X-ray examination shows bilateral sacroilitis. A serum test for histocompatibility antigen HLA-B27 is positive.

What diagnosis do you suspect? Prescribe the main groups of drugs.

Answers:

1. e.

2. Ankylosing spondilitis. Disease-modifying drugs, nonsteroidal anti-inflammatory drugs, if it is necessary – corticosteroids, treatment of the muscular spasm.

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Topic 9. CURATION OF THE PATIENT WITH SEVERE EXACERBATION OF BRONCHIAL ASTHMA, ACUTE ALLERGIC REACTIONS

Time frame – 6 hours.

Professional motivation. Inadequate control of asthma leads to much morbidity and poor quality of life. Complications as pneumonia, pneumothorax, pneumomediastinum, respiratory failure and arrest, death are mostly related to acute exacerbations. A common feature of death of asthma is that the patient and/or the medical staff have underestimated the severity of the attack.

The American College of Allergy, Asthma and Immunology Epidemiology of Anaphylaxis Working group summarised the findings from a number of important international epidemiological studies and concluded that the overall frequency of episodes of anaphylaxis using current data lies between 30 and 950 cases per 100,000 persons per year.

The same group provided data indicating a lifetime prevalence of between 50 and 2000 episodes per 100,000 persons or 0.05–2.0%. More recent UK primary care data concur, indicating a lifetime age-standardised prevalence of a recorded diagnosis of anaphylaxis of 75.5 per 100,000 in 2005.13 Calculations based on these data indicate that approximately 1 in 1,333 of the English population have experienced anaphylaxis at some point in their lives.

The overall prognosis of anaphylaxis is good, with a case fatality ratio of less than 1% reported in most population-based studies. Risk of death is, however, increased in those with preexisting asthma, particularly if asthma is poorly controlled or in those asthmatics who fail to use, or delay treatment with, adrenaline. There are approximately 20 anaphylaxis deaths reported each year in the UK, although this may be a substantial under-estimate.

Place of carrying out: class-room, wards of the pulmonology.

Study objective is to be able to identify severe asthma attack and assign the first aid and management; is to be able to identify signs of anaphylaxis and assign management.

Basic level:

1. Aetiology and pathogenesis of bronchial obstruction.
2. Interpretation of sputum analysis, spirography, peakflowmetry, X-ray examination, chest tomography.
3. Pathophysiology of anaphylactic reactions.
4. To examine patients with allergic reactions.
5. To determine symptoms of anaphylaxis.

Student has to know:

1. Clinical signs of severe asthma attack.
2. Clinical signs of anaphylaxis, Quincke’s oedema.
3. Investigational methods for the diagnosis of severe asthma attack.
4. How to make differential diagnosis, clinical diagnosis.
5. How to provide treatment for patients with severe asthma attack, anaphylaxis.

The main theoretical questions:

1. What causes a severe asthma attack?
2. What are the symptoms of a severe asthma attack?
3. Assessment of asthma exacerbation severity.
4. How is a severe asthma attack diagnosed?
5. How is a severe asthma attack treated?
6. Self-management of asthma exacerbation and evaluation of response to therapy. Evidence-based treatment of asthma exacerbations in general practice and the emergency department.
7. Definition of anaphylaxis. Triggers for anaphylactic reactions.
8. Criteria for anaphylaxis.
9. General principles of allergic diseases therapy.
10. Emergency treatment of patients with anaphylaxis.
11. The diagnostic and treatment of generalized urticaria and Quincke's edema.

Assignment for self-assessment

A 27-year-old woman had been experiencing severe asthma since she was a teenager. Her symptoms had worsened over the previous three days, after she'd caught a cold. Now she was using salbutamol every hour with no relief. She delayed calling her primary doctor's office in the hope that her symptoms would get better.

She frequently suffered from cough, wheezing and chest tightness. She awakened with nighttime symptoms two to three times per week. She was using high dose inhaled steroids daily to decrease airway inflammation and also using inhaled salbutamol. She had a history of multiple hospitalizations for asthma, including one admission to the intensive care unit two years earlier. At that time, she had required mechanical ventilation for several days.

The patient was markedly short of breath and could only speak in short sentences. She had a fever of 37 degrees, was breathing rapidly, and her heart rate was 150/minute. She was no longer wheezing and doctor could barely hear any breath sounds at all. Her lips were a little blue. Oxygen saturation is only 84%.

What treatment should be given? Who is at risk for the development of status asthmaticus? Can status asthmaticus be prevented?

Answer:

Nebulized albuterol (salbutamol) administered by face mask, oxygen by nasal cannula and high doses of intravenous steroids.

Although patients with mild asthma will occasionally have episodes of status, this dangerous condition occurs mostly in patients with very severe disease and in those who have had previous severe attacks. The best way to decrease the possibility of having a severe asthma attack is to take the medications regularly as prescribed.

Assignment for self-assessment

A 60-year-old female with acute pancreatitis was given 50 mg of ranitidine as a slow intravenous bolus for epigastric discomfort. She had myocardial infarction in the past. She was allergic to metronidazole. She had no family history of drug allergies. Few minutes after the injection, the patient complained of itching at the injection site that spread to involve the entire upper limb. She also complained of swelling of her tongue and difficulty in breathing. Within minutes her level of consciousness deteriorated and she became comatose. The initial examination revealed the following features: a grossly oedematous face, neck and extremities, a grossly swollen tongue, congested conjunctiva, cyanosis, diffuse rhonchi over both lung fields. Suggest treatment for this patient.

Answer:

Immediate administration of intramuscular adrenaline, intravenous hydrocortisone and high flow oxygen. Commence cardiopulmonary resuscitation in case of cardiorespiratory arrest.

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Topic 10. CURATION OF THE PATIENT WITH EMERGENCIES IN DIABETES MELLITUS

Time frame – 6 hours.

Professional motivation. Hypoglycemia is a common side effect of insulin therapy in diabetes, particularly in people with type 1 diabetes. Mild (self-treated) episodes occur frequently

(1–2 episodes/week), while severe hypoglycemia, defined as any episode requiring external help, affects up to 30% of people with type 1 diabetes annually (1–5), with an incidence ranging from 1.0 to 1.6 episodes per patient per year in unselected northern European populations. In contrast, the rate of severe hypoglycemia in people with type 2 diabetes treated with insulin is reported to be low, but these have been recorded in people with a short duration of insulin therapy.

Prolonged hypoglycemia may result in serious neurologic complications and death.

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are two of the most serious acute complications of diabetes. These hyperglycemic emergencies continue to be important causes of morbidity and mortality among patients with diabetes in spite of major advances in the understanding of their pathogenesis and more uniform agreement about their diagnosis and treatment. The annual incidence rate for DKA estimated from population-based studies ranges from 4.6 to 8 episodes per 1,000 patients with diabetes, and in more recent epidemiological studies in the U.S., it was estimated that hospitalizations for DKA during the past two decades are increasing. Currently, DKA appears in 4–9% of all hospital discharge summaries among patients with diabetes. It is estimated that the rate of hospital admissions due to HHS is lower than the rate due to DKA and accounts for <1% of all primary diabetic admissions. Mortality rates, which are <5% in DKA and 15% in HHS, increase substantially with aging and the presence of concomitant life-threatening illness. It is important to note that up to 20% of patients may present in the emergency room with either DKA or HHS without a previous diagnosis of diabetes. In the African-American population, DKA has been increasingly noted in newly diagnosed obese type 2 diabetic patients. Therefore, the concept that the presence of DKA in type 2 diabetes is a rare occurrence is incorrect.

Place of carrying out: class-room, wards of the endocrinology.

Study objective is to be able to identify symptoms of hypoglycemia, DKA, HHS and assign management.

Basic level:

1. Examination of patients with diabetes.
2. To determine symptoms of hypoglycemia.
3. To evaluate data of the laboratory investigations of hypoglycemia.
4. Pathogenesis of DKA: carbohydrate metabolism, lipid and ketone metabolism, water and electrolyte metabolism.
5. Examination of patients with DKA (case history and physical examination).

Student has to know:

1. Clinical signs of hypoglycemia. Clinical signs of hyperglycemia
2. Investigational methods for the diagnosis of hypoglycemia, hyperglycemia.
3. How to provide treatment for patients with hypoglycemia, DKA, HHS.

The main theoretical questions:

1. What causes hypoglycemia?
2. What are the symptoms of hypoglycemia?
3. Health and lifestyle management to prevent hypoglycemia.
4. Differential approach to the first aid in hypoglycemia.
5. Clinical signs of diabetic ketoacidosis (the triad of DKA). Diagnostic criteria for DKA, HHS.
6. Management of patient with hyperglycemic hyperosmolar non-ketoacidosis coma. Diagnostic criteria and evidence-based management in ketoacidosis coma. Monitoring of the patients.
7. Diagnostic criteria and management of patients with lactic acidemic coma.

Assignment for self-assessment

1. The hypoglycemia protocol says to start treatment when the fasting blood glucose is less than:
   a) 70 mg/dl regardless symptoms or not;
   b) 80 mg/dl regardless symptoms or not;
   c) 90 mg/dl regardless symptoms or not.

2. A 26 year old man with a history of type I diabetes is admitted to the emergency because he is sleepy and desoriented. His fasting blood glucose is 44 mg/dl. Doctor tried to give a cup of juice but the patient is not swallowing well. What should be done?

3. A 20 year old man with a history of type I diabetes is admitted with pyrexia, drowsiness, and fast deep breathing. You suspect DKA. What is the initial treatment priority?

a) IV drip of 5% dextrose solution;
b) IV drip of 0.9% saline;
c) 10 units of subcutaneous short-acting insulin;
d) insulin via infusion pump;
e) potassium supplementation.

Answers:

1. a.

2. Glucagon im, check fasting blood glucose in 20 minutes.

3. b, patient with DKA tend to be significantly dehydrated due to osmotic diuresis and reduced fluid intake. In adults this is usually at least 3.5 litres. A treatment plan in DKA would be: check blood gas, capillary glucose; give IV drip of 0.9% saline 15–30 ml/kg/h for first 2 hours then at reduced rate; 10 units of subcutaneous short acting insulin followed by infusion at a rate of 2–6 units/h; monitor potassium and capillary blood glucose.

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Topic 11. CURATION OF THE PATIENT WITH SYNCOPE

Time frame – 2 hours.

Professional motivation. Syncope is a common condition. It affects 3% of population, accounting for around 5% of acute medical admissions and 3% of emergency department visits. Syncope is more common as we get older and affects up to 6% of people over age 75.

Place of carrying out: class-room, wards of neurology or cardiology department.

Study objective is to improve students' skills in differential diagnosis and treatment of syncope.

Basic level of knowledge and skills:

1. Mechanisms of syncope.
2. Examination of patients who experienced syncope.

Student has to know:

1. Criteria of syncope associated with heart rhythm and conduction disorders.
2. Criteria of syncope associated with cardiovascular diseases.
3. Criteria of syncope associated with orthostatic hypotension, neurogenic syncope.
4. Instrumental methods for verification of syncope.

The main theoretical questions:

1. Differential diagnosis in case of syncope.
2. Treatment of reflex syncope, orthostatic hypotension.
3. Treatment of arrhythmogenic syncope.
4. The place of pacing, catheter ablation, antiarrhythmic therapy with implantable cardioverter-defibrillator.
5. The essence of performing maneuvers to prevent syncope (horizontal position, techniques with physical pressure, cough suppression, sneezing, tilt-training).

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Topic 12. CURATION OF THE PATIENT WITH ACUTE ADRENAL INSUFFICIENCY, THYROTOXIC CRISIS, MYXEDEMA COMA

Time frame – 4 hours.

Professional motivation. Adrenal insufficiency (AI) is an often-unrecognised endocrine disorder, which can lead to adrenal crisis and death if not identified and treated. One in every 6–12 patients with AI will have an adrenal crisis within the next year, while one in 200 patients will die from such a crisis. One more life-threatening condition is thyroid storm. With a mortality rate estimated at 10%, it demands a rapid diagnosis and emergency treatment. Myxedema coma is a rare life-threatening clinical condition - with an incidence rate of 0.22 per million per year - in patients with longstanding severe untreated hypothyroidism, in whom adaptive mechanisms fail to maintain homeostasis.

Place of carrying out: class-room, wards of emergency, endocrine or cardiology department.

Study objective is to improve students' skills in differential diagnosis and treatment of syncope.

Basic level of knowledge and skills:

1. Mechanisms of syncope.
2. Examination of patients who experienced syncope.

Student has to know:

1. Criteria for acute adrenal insufficiency.
2. Criteria for thyrotoxic crisis.
3. Criteria for myxedema coma.
4. Instrumental methods for verification of syncope.

The main theoretical questions:

1. Diagnostic criteria and evidence-based management of patients with acute adrenal insufficiency.
2. Peculiarities of clinical manifestations of Waterhouse-Friderichsen Syndrome.
3. Diagnostic criteria and evidence-based management of patients with thyrotoxic crisis.
4. Diagnostic criteria and management of patients with severe hypothyroidism (myxedema coma)

Assignment for self-assessment

A 31-year-old woman is brought to the emergency department with altered mental status. Examination reveals dry and darken skin on her face, neck, on the backs of her hands. Skin turgor testing reveals no tenting. Her temperature is 35.5^0C, the pulse is 100 per min, respirations are 20 per min, and blood pressure is 60/35 mm Hg. Findings on cardiac and pulmonary auscultation are normal. The abdomen is soft, tender in the epigastric region; spleen and liver are not enlarged. Diarrhea occured twice a day. She has no remarkable medical history. Her relatives state that she had been complaining of fatigue, headache, unintentional 8 kg weight loss for the past year. She began to experience worsening symptoms a few days ago with psychologic stress.

Laboratory studies show: hemoglobin – 118 g/L, erythrocytes – $3.2*10^{12}$/L, leukocytes – $9.2*10^9$/L, segmented neutrophils – 55%, eosinophils – 5%, basophils – 1 %, lymphocytes – 30%, monocytes – 9%, platelet count – $240*10^9$/L, glucose – 3,8 mmol/l, sodium – 128 mmol/l, potassium – 6 mmol/l (Na:K ratio = 21; normal 30), chloride – 110 mmol/l, HCO_3 – 20 mmol/l, urea – 8 mmol/l, creatinine – 80 μmol/l. *ECG findings:* flattened P waves, peaked T waves. *Chest X-ray:* no abnormalities. *CT scan of the abdomen:* spots of calcinations in the adrenal glands.

Questions: Identify patient's preliminary emergency condition. Define treatment strategy.

Answers:

Diagnosis: adrenal crisis. 100 mg hydrocortisone by iv injection, followed by 200 mg hydrocortisone/24 h continuous iv infusion in glucose 5%/24 h, y followed by 50 mg every 6 h im.

Resuscitation with 500 ml fluid bolus of sodium chloride 0.9% over 15 minutes and then replacement of any electrolyte deficits, careful monitoring of electrolytes and fluid balance. Cardiac monitoring (if necessary transfer to the intensive care unit for monitoring

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Topic 13. CURATION OF THE PATIENT WITH ACUTE ABDOMINAL PAIN

Time frame – 4 hours.

Professional motivation. Acute pain in abdominal part is the symptom of dangerous state. Therefore well-timed diagnosis and correct choice of medical tactics is necessary for emergency care. Acute abdominal pain accounts for approximately 50% of all urgent admissions to general surgical units. Cancer is a more common cause of acute pain in those over 70 years than in those under 50 years. Older people with vague abdominal symptoms should therefore be carefully assessed and serious pathology should be excluded.

Acute pancreatitis accounts for 3% of all cases of abdominal pain admitted to hospital. It affects 2–28 per 100,000 of the population and may be increasing in incidence. Despite recent advances in management, the mortality has remained unchanged at 10–15%. About 80% of all cases are mild with a mortality less than 5%; 98% of deaths occur in 20% of severe cases. One-third occur within the first week, usually from multi-organ failure. After this time the majority of deaths result from sepsis, especially that complicating infected necrosis.

In ischaemic gut injury the key steps in treatment are resuscitation, correction of cardiac disease, and intravenous antibiotic therapy, followed by laparotomy. If this is done early enough, embolectomy and vascular reconstruction may salvage some small bowel. In these rare cases a “second look” laparotomy is undertaken 24 hours later and further necrotic bowel resected. The results of therapy are dependent upon early intervention; patients treated at a late stage have a 75% mortality rate. Survivors often have nutritional failure from short bowel syndrome and require intensive nutritional support, sometimes including home parenteral nutrition.

Place of carrying out: class-room, wards of the gastroenterology.

Study objective is to improve students’ skills in differential diagnosis and treatment of acute abdominal pain.

Basic level of knowledge and skills:

1. Mechanisms of pain originating in case of abdominal organs diseases.
2. Procedure of examination of the patients with an acute abdominal pain.

Student has to know:

1. Clinical signs of the bowel diseases.
2. Investigational methods used in case of acute abdominal pain.
3. Mechanisms of action of the drugs which are used in the treatment of acute abdominal pain.
4. How to evaluate data of the laboratory and instrumental investigations.
5. Diagnostic algorithm in acute abdominal pain.

The main theoretical questions:

1. Diagnostic criteria for acute pancreatitis. Complications, management.
2. Criteria for diagnosis of acute small bowel ischaemia.
3. Criteria for diagnosis of peptic ulcer disease. Complications of peptic ulcer disease and its treatment.
4. Criteria for diagnosis of gallstones and choledocholithiasis; complications, management.
5. Criteria for diagnosis of aortic aneurism.

6. Criteria for diagnosis of ureteric colic.
7. Definition of medical tactics at an acute abdominal pain.

Assignment for self-assessment

A 42-year-old man was admitted to the hospital due to the presence of acute pain in the epigastric region without any irradiation. The pain is intermittent, can be decreased after meal or a glass of milk; the patient feels the most severe pain at night and in the early morning. The patient has also nausea and sometimes vomiting after which may feel better. The patient is also constipated. This pain started 1 week ago after the stressful situation. The patient didn't have such a pain before. During this period of time the patient didn't go to the doctor, he took aAlmagel without the effect. His father suffers from gastritis, his grandmother died from stomach cancer.

Complete blood count: Hb – 110 g/l, er. – 3.2×10^9/l, leuc. – 8.4×10^{12}/l, ESR – 11mm/hour; biochemical analysis: protein – 62 g/l, alb. – 60%, glob. – 40%, creatini – 76 μmol/l, urea – 6.2 mmol/l, ALT – 21 U/l, AST – 18 U/l.

Gastroscopy: redness of the stomach mucosa, ulcer 0.5×0.6 cm in the diameter in the anterior wall of the duodenum bulb.

Make the diagnosis; name the main aetiology factor. Name other laboratory and instrumental findings to confirm the diagnosis. Which complications may have the patient? Name treatment strategy.

Answers:

1. Peptic ulcer disease; H. pylory infection.
2. Invasive or noninvasive tests for the detecting of H. pylory; pH-monitoring; coprologycal investigation.
3. Bleeding, perforation, penetration, gastric outlet obstruction.
4. Anti H. pylory therapy (triple or quadriple), PPI after this therapy.

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Topic 14. CURATION OF THE PATIENTS WITH ACUTE KIDNEY INJURY

Time frame – 6 hours.

Professional motivation. Acute renal injury (AKI) can present in all medical settings but is predominantly acquired in hospitals. The condition develops in 5% of all hospitalized patients, and approximately 0.5% of hospitalized patients require dialysis.

AKI occurs in approximately 19% of patients with moderate sepsis, 23% – with severe sepsis, and 51% – with septic shock when blood cultures are positive.

Over the past 40 years, the survival rate for acute renal failure has not improved, primarily because affected patients are now older and have more comorbid conditions. Infection accounts for 75% of deaths in patients with AKI, and cardiorespiratory complications are the second most common cause of death. Depending on the severity of renal failure, the mortality rate can range from 7% to as high as 80%. The combination of AKI and sepsis is associated with a 70% mortality, as compared with a 45% mortality among patients with AKI alone.

Place of carrying out: class-room, wards of the nephrology department and hemodyalisis.

Study objective: to improve the skills in the diagnosis of AKI, to determine management for patients.

Basic level:

1. To be able to collect complaints, case history, carry out physical examination in patients with AKI.
2. To interpret instrumental and laboratory data in patients with AKI.

Student has to know:

1. Causes and clinical signs of AKI.
2. Biochemical abnormalities, changes in fluid and electrolyte balance of AKI.
3. Mechanisms of the development of the pulmonary oedema, anaemia.
4. Emergency resuscitation in hyperkalaemia, hypovolemia, pulmonary oedema.

The main theoretical questions:

1. Causes and pathogenesis of AKI.
2. Diagnostic criteria of AKI.
3. Blood and urine studies to distinguish prerenal from intrinsic AKI.
4. Evidence-based management of patients depending on the underlying cause of the AKI.
5. Control of blood pressure in acute renal failure due to accelerated hypertension.
6. Prognosis for patients with AKI.

Assignment for self-assessment

1. What is the cause of AKI classified as "postrenal"?
   a) failure on the basis of inadequate perfusion;
   b) failure on the basis of parenchymal pathology;
   c) failure secondary to obstruction;
   d) everything listed above.

2. A 50-year-old man is hospitalized for acute myocardial infarction. He has decreased cardiac output with hypotension requiring multiple pressor agents. His urine output drops over the next 3 days. His serum urea nitrogen increases to 59 mg/dL, with creatinine of 2.9 mg/dL. Urinalysis reveals no protein or glucose, a trace blood, and numerous hyaline casts. What is the name of this condition? What is the cause? Management.

Answers:

1. c.

2. Prerenal factors (severe hypotension, low cardiac output – cardiogenic shock due to MI) was initial factors of AKI. This patient has oliguria-anuria stage now. Our management must be start from elimination of aetiologic factors (shock), correction of blood pressure. Cessation of any diuresis stimulation, limitation water intake.

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Електронне навчальне видання

Методичні вказівки

до практичних занять
із дисципліни **«Внутрішня медицина»**
(модуль 3 «Сучасна практика внутрішньої медицини»,
модуль 4 «Невідкладані стани в клініці внутрішньої медицини»)
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