MINISTRY OF HEALTH OF UKRAINE
BUKOVINIAN STATE MEDICAL UNIVERSITY
DEPARTMENT OF INTERNAL MEDICINE, CLINICAL PHARMACOLOGY AND OCCUPATIONAL DISEASES

EMERGENCY STATES IN INTERNAL MEDICINE

FOR INDEPENDENT WORK OF STUDENTS:

Educational and methodical manual.2nd Edition

(Edited by Prof. Khukhlina OS)

Chernivtsi 2025

UDC 616.1/.4-083.98(075.8)
X 98
ISBN 978-617-519-166-8
Emergency states in internal medicine for independent work of students: educational and methodical manual. 2nd Edition / Khukhlina O.S., Antoniv A.A., Kotsiubiychuk Z.Ya. / Edited by Khukhlina O.S.- Chernivtsi: BSMU, 2025. – 203 p.

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The textbook presents essential information on the most common emergency conditions encountered in internal medicine practice. It provides a structured overview of clinical manifestations, diagnostic features, and treatment approaches to urgent states. Special sections are devoted to the management of hypertensive crises, sudden cardiac arrest, acute left ventricular failure, respiratory insufficiency, various types of bleeding, and acute renal failure. Emphasis is placed on current clinical guidelines and evidence-based strategies for delivering timely and effective emergency care. This resource is intended for medical students, interns, and healthcare professionals involved in emergency and internal medicine.

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Recommended for publication by the Academic Council of the Bukovynian State Medical University of the Ministry of Health of Ukraine as a textbook for students of the HMEI III-IV level of accreditation (Protocol № _ from 24.04.2025)

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Topic 1. Preparation for practical training № 1 «Hypertensive crises: classification, diagnosis of complications, differentiated emergency care. Hypotension. Collapse. Sudden cardiac death»

Learning objective

The student must know:

- determination of arterial hypertension, hypertensive crises, arterial hypotension, collapse, sudden cardiac death
- clinical manifestations of hypertensive crisis, hypotension, collapse, sudden cardiac death
- criteria for diagnosing hypertensive crisis, hypotension, collapse, sudden cardiac death
- laboratory and instrumental manifestations of hypertensive crises, arterial hypotension, collapse, sudden cardiac death
- main manifestations, differential diagnosis of hypertensive crises, arterial hypotension, collapse, sudden cardiac death
- principles of emergency care for patients with uncomplicated and complicated hypertensive crises, hypotension, collapse, sudden cardiac death
- algorithm for providing emergency care

Be able:

- determine the state of emergency
- perform differential diagnosis with other emergencies
- assign appropriate emergency care

Master practical skills:

- pulse oximetry.
- electrocardiography in 12 standard leads.
- evaluation of sputum analysis
- evaluation of pleural fluid analysis

Theoretical material for independent student training.

A hypertensive crisis is characterized by a sudden and significant rise in arterial blood pressure, typically exceeding 30% above the patient's usual levels, which may result in clinical symptoms of target organ dysfunction or autonomic disturbances. This condition represents a critical emergency in internal medicine and requires immediate recognition and management.

The pathophysiological mechanisms are complex and primarily involve an imbalance between systemic and local hemodynamic regulation, affecting cerebral, coronary, renal, and peripheral circulation. Due to the human-specific nature of this pathology, experimental models remain approximate, and no single universally accepted development scheme exists. The central consequence of these circulatory disturbances is tissue and organ ischemia, which underscores the importance of early intervention and evidence-based therapeutic strategies.

The development of a hypertensive crisis (HC) is driven by a combination of pathogenetic factors that influence vascular tone and the regulation of arterial blood pressure. One of the key contributors is a genetic predisposition to vasospasm, which is often associated with impaired function of α-adrenergic and β-adrenergic receptors. These receptors play a crucial role in vascular relaxation and constriction; when their function is insufficient, it can lead to excessive vasoconstriction and elevated systemic vascular resistance.

Another important factor is the increased concentration of circulating vasoconstrictors, such as angiotensin II and norepinephrine, both of which contribute to sustained elevation of blood pressure by promoting vascular contraction and stimulating the sympathetic nervous system. In addition, a deficiency of endogenous vasodilatory substances—including kininogen, kinins, and prostacyclins—reduces the body's ability to counteract rising vascular tone, further exacerbating the hypertensive state. Damage to the vascular endothelium also plays a significant role, as it leads to decreased synthesis of nitric oxide and other vasodilators, weakening vascular relaxation and autoregulation.

These alterations compromise the delicate balance between vasoconstriction and vasodilation, predisposing patients to acute hypertensive events. Moreover, blood pressure regulation is influenced by both endogenous (internal) and exogenous (external) factors. Endogenous factors include neurohumoral, hormonal, and renal mechanisms, while exogenous factors encompass environmental stressors such as emotional stress, dietary habits, physical exertion, and exposure to extreme weather conditions. The interplay of these factors can overwhelm compensatory mechanisms and provoke a hypertensive crisis, especially in individuals with reduced adaptive capacity**.**

Exogenous factors:

• psycho-emotional stress;

• meteorological impact;

• increased salt and water intake;

• excessive insolation;

• intercurrent diseases;

• smoking;

• contraceptives.

Endogenous factors:

• secondary aldosteronism;

• excessive renin production due to decreased renal blood flow (especially pulse pressure);

• acute ischemia of the brain and heart;

• reflex effects from internal organs (prostate adenoma, nephroptosis, cholecystitis, pancreatitis);

• drug effects (sudden withdrawal of antihypertensive drugs);

• atherosclerosis of extracranial arteries with damage to the baroreflex apparatus;

• increased platelet aggregation and increased serotonin in the CNS;

• sleep apnea syndrome (episodes of asphyxia and alveolar hypoventilation during sleep);

• reduction of oxygen content in tissues and stimulation of chemoreceptors of arteries and veins;

• increase the activity of the sympathetic nervous system;

• increase in intracranial pressure.

The immediate causes of HA in patients with hypertension with reduced adaptive capacity of the CNS are:

a) dysfunction (hyperreactivity) of the diencephalic part of the brain, which causes:

• increased antidiuretic activity and adrenocorticotropic hormone (ACTH) levels in the blood;

• increased production of antidiuretic hormone;

• increased aldosterone levels;

• fluid retention and hypervolemia;

• increased vascular reactivity with spasms;

• irritation of baro- and volume-receptors;

• inhibition of antidiuretic hormone secretion.

b) high variability of blood pressure (day and night) due to atherosclerosis of extracranial arteries and dysfunction of the baroreflex apparatus.

Crisis classification of the working group of the Ukrainian Society of Cardiology (1999). Depending on the presence or absence of damage to target organs and the need for urgent reduction of AT, there are ***complicated and uncomplicated crises.***

Complicated HA - manifested by signs of acute or progressive damage to target organs, pose a direct threat to the patient's life, require immediate, within one hour, a decrease in AT. Treatment is carried out in the intensive care unit with the use of parenteral administration of antihypertensive drugs.

Complicated HA include: 1) myocardial infarction; 2) stroke; 3) acute stratifying aortic aneurysm; 4) acute left ventricular failure; 5) unstable angina; 6) arrhythmias (paroxysms of tachycardia, atrial fibrillation and flutter, high-grade ventricular arrhythmia); 7) transient ischemic attack; 8) eclampsia; 9) acute hypertensive encephalopathy; 10) bleeding (including nasal).

Uncomplicated HA is characterized by the absence of clinical signs of acute or progressive lesions of target organs. Such crises are accompanied by the appearance or

intensification of symptoms from the target organs (intense headache, pain in the heart, extrasystole) or from the autonomic nervous system (autonomic vascular disorders, tremors, frequent urination). Uncomplicated HA should also include an increase in CAT to 240 mm Hg. Art., or DBP up to 140 mm Hg. Art., regardless of the presence or absence of symptoms from the target organs; as well as a significant increase in pressure in the early postoperative period due to the risk of bleeding. These conditions require a reduction in blood pressure for several hours. Hospitalization is not mandatory. Treatment with oral antihypertensive drugs.

The most important issue in the problem of hypertensive crisis is the tactics of treatment. There is no consensus on this issue, as Ukrainian and foreign recommendations differ. Drugs such as dibazole, papaverine, nifedipine, and others are not used abroad to buy a hypertensive crisis. In our country, unfortunately, these drugs are one of the most common drugs in both prehospital and hospital treatment of hypertensive crisis.

Urgent measures should be aimed at:

- reduction of increased left ventricular function;
- elimination of peripheral vasoconstriction and hypervolemia;
- elimination of cerebral ischemia (especially in the convulsive variant);
- elimination of acute coronary or heart failure.

Complicated hypertensive crisis is a direct indication for hospitalization and rapid initiation of antihypertensive therapy, which uses the intravenous route of administration of drugs.

The rate of blood pressure in complicated HYPERTENSION CRISIS:

- within 30–120 min → decrease in blood pressure by 15–25%;
- for 2-6 hours → blood pressure level 160/100 - 150/90 mm Hg. st .;
- more → oral drugs.

A sharp decrease in blood pressure to normal values is contraindicated because it can lead to hyperperfusion, ischemia up to necrosis. In acute cerebrovascular accident, the

rate of blood pressure reduction should be slow, and the presence of aortic aneurysm stratification requires a rapid decrease in pressure by 25% within 5-10 minutes. Target systolic blood pressure in stratifying aortic aneurysm 110–100 mm Hg. Art.

The following is a list of drugs that the European and American Societies of Cardiologists recommend as drugs of choice in the treatment of complicated crises.

Treatment of hypertensive crisis, as well as hypertension, should be completely individual. In complicated hypertensive crises, therapy should depend on the lesion of target organs. As mentioned above, in this type of hypertensive crisis using intravenous drugs, the action of which begins within a few minutes.

Hypotension - a decrease in blood pressure of more than 20% of baseline / normal values or in absolute numbers - below 90 mm Hg. Art. systolic pressure or 60 mm Hg. Art. average blood pressure. The pressure drop can be acute or chronic.

Acute hypotension (collapse, shock) usually occurs in cardiac disorders, heavy blood loss, dehydration and quickly leads to hypoxia of the brain and internal organs. Thus, acute hypotension is always a complication of a disease or external influence, always has an obvious cause that must be taken into account in treatment.

Chronic hypotension is caused by completely different causes than acute. In people with low blood pressure, its regulation is usually disturbed, the real causes of which can be of different nature.

People with low blood pressure do not have as high a risk of heart attack and stroke as hypertensives, so standards and treatments for chronic hypotension are less well developed. The quality of life of hypotensives can be very low due to constant weakness, headaches, decreased activity and other symptoms.

There are the following types of hypotension:

- Acute hypotension
- Chronic hypotension
- Primary chronic arterial hypotension
- Secondary chronic arterial hypotension

Acute symptomatic hypotension (sharp drop in pressure). For example, very low blood pressure is often accompanied by acute myocardial infarction, pulmonary embolism, severe arrhythmias, intracardiac blockade, allergic reactions, blood loss, etc. WORLD. Urgent medical attention is required.

Physiological (chronic) hypotension is manifested in trained athletes and as a hereditary predisposition to low blood pressure, which does not exceed the norm.

Sudden cardiac death (SCD), or primary circulatory arrest, is the death in the presence of witnesses that occurs suddenly in ischemic heart disease (SCD) within 1 hour of the onset of the disease or in people who were completely healthy one day before. or in patients who were in satisfactory condition. RCC does not include death from myocardial infarction (MI), which occurred more than 1 hour after its onset, as well as death from shock and pulmonary edema, because the cause in these cases is not the disease, but these complications.

It should be understood that the 60-minute time interval belongs mainly to the duration of the most acute symptoms of the disease, which occur before circulatory arrest, and that the period from fatal arrhythmias (ventricular fibrillation (VF), asystole, electromechanical dissociation (EMD)) to loss of consciousness very short. According to the mechanism of development, RCC is often arrhythmic in ventricular tachycardia (VT).

Knowledge control:

1. Determination of arterial hypertensive crisis, collapse, sudden cardiac death.
2. Complicated and uncomplicated hypertensive crises, features of treatment tactics.
3. Possible complications of hypertensive crises.
4. Primary and secondary prevention of hypertensive crisis, collapse, sudden cardiac death.
5. Forecast and efficiency.
6. Arterial hypotension, features of treatment tactics.

7. Collapse: clinic, diagnosis, treatment.
8. Emergency care in case of sudden cardiac death

Test tasks:

1. BP is considered normal if:

A) SAT does not exceed 160 mm Hg. Art., DBP - 94 mm Hg. Art.

C) SAT does not exceed 159 mm Hg. Art., DBP - 94 mm Hg. Art.

C) SAT does not exceed 150 mm Hg. Art., DBP - from 95 to 100 mm Hg. Art.

E) SAT does not exceed 130 mm Hg. Art., DBP - 85 mm Hg. Art.

E) SAT does not exceed 139 mm Hg. Art., DBP - 89 mm Hg. Art.

2. Directly leads to an increase in blood pressure:

A) renin

B) angiotensinogen

C) angiotensin I

D) angiotensin II

3. The action of angiotensin II is due to:

A) Increasing the concentration of sodium ions in vascular smooth muscle cells

B) stimulation of aldosterone synthesis

C) release of vasopressin and ACTH

D) stimulation of norepinephrine release

E) all these factors

4. Between the level of elevated blood pressure and the severity of the hypertensive crisis:

A) the connection is direct

B) there is no clear connection

5. The diagnostic criterion for stage II hypertension is:

A) lower blood pressure in compliance with the regime of work and rest, diet

B) lowering blood pressure under the influence of antihypertensive drugs

C) left ventricular myocardial hypertrophy, hypertensive retinal vascular angiopathy

D) short-term increase in blood pressure

E) a steady increase in blood pressure

6. The diagnostic criterion for stage III hypertension is:

A) the presence of a history of myocardial infarction

B) lowering blood pressure under the influence of antihypertensive drugs

C) left ventricular myocardial hypertrophy

D) short-term increase in blood pressure

E) a steady increase in blood pressure

7. The level of blood pressure is determined by:

A) heart rate (minute volume)

B) peripheral resistance

C) both factors

D) there is no correct answer

8. With prolonged hypertension is formed:

A) heart failure

B) encephalopathy

C) cerebrovascular disorders

D) chronic renal failure

E) all of the above

9. The criterion for increasing the SAT I degree is:

A) 130-139 mm Hg. Art.

B) 140-159 mm Hg. Art.

C) 160-170 mm Hg. Art.

D) 180-190 mm Hg. Art.

E) 130-159 mm Hg. Art.

10. The criterion for increasing the first-degree DBP is:

A) 80-84 mm Hg. Art.

B) 85-89 mm Hg. Art.

C) 90-94 mm Hg. Art.

D) 95-99 mm Hg. Art.

E) 90-99 mm Hg. Art.

Topic 2. Preparation for practical training № 2 «Pulmonary edema»

Learning objective

The student must know:

- determination of pulmonary edema
- clinical manifestations of pulmonary edema
- criteria for diagnosing pulmonary edema
- laboratory and instrumental manifestations of pulmonary edema
- main manifestations, differential diagnosis of pulmonary edema
- principles of emergency care for patients with pulmonary edema
- algorithm for providing emergency care

Be able:

- determine the state of emergency
- perform differential diagnosis with other emergencies
- Assign appropriate emergency care

Master practical skills:

- pulse oximetry
- description of radiographs
- electrocardiography in 12 standard leads.
- evaluation of sputum analysis
- evaluation of pleural fluid analysis

Theoretical material for independent student training.

Pulmonary edema is a critical and potentially life-threatening clinical condition characterized by the accumulation of fluid in the alveolar spaces and interstitium of the lungs. This syndrome typically arises when fluid from the bloodstream escapes the pulmonary capillaries into the alveoli due to elevated hydrostatic pressure in the pulmonary veins and capillaries. One of the most common causes of this pressure increase is acute left ventricular failure, which leads to a backlog of blood in the

pulmonary circulation. In addition to hydrostatic mechanisms, pulmonary edema can also develop as a result of increased permeability of the alveolar-capillary membrane, often due to direct injury, inflammation, or systemic conditions such as sepsis or acute respiratory distress syndrome (ARDS). The presence of fluid in the alveoli impairs gas exchange, leading to severe hypoxemia, dyspnea, and respiratory distress. Prompt recognition and intervention are crucial, as untreated pulmonary edema may rapidly progress to respiratory failure and cardiac arrest.

Etiology and pathogenesis

With pulmonary edema, fluid (transudate) accumulates in the alveoli and bronchi with a small surface tension due to the protein contained in it, and therefore foams. It also permeates the interstitial lung tissue. The clinical picture of severe asthma develops. The causes of edema are various. Most often it is the result of stagnation in the small circulation. This leads to increased pressure in the pulmonary capillaries and increased transudation. There may be other reasons: increased permeability of small blood vessels, a pronounced tendency of lung tissue to bind water, decreased oncotic and osmotic blood pressure, impaired lymph outflow in the lung basin, expansion of the total filtration surface of the lungs. In severe diseases, these causes often interact with each other, and their effect is potentiated by an increase in total circulating blood volume, pronounced vegetative dystonia (predominance of sympathetic tone of the autonomic nervous system), persistent and severe hypoxia, electrolyte metabolism with accumulation of sodium ions in tissue.

Depending on the causes, cardiogenic (primarily due to cardiac causes) and non-cardiogenic (other mechanisms) pulmonary edema can be distinguished.

Alveolar pulmonary edema can develop very quickly, but it is usually preceded by a prolonged stage of interstitial edema. The diagnosis of alveolar pulmonary edema is confirmed by chest radiography. Mortality from alveolar pulmonary edema is about 50%.

According to the pathogenesis, there are two forms of pulmonary edema - with an increase in stroke volume, accelerated blood circulation, increased blood pressure in the large and small circulation (not observed in myocardial infarction) and with decreased stroke volume, low blood pressure, threatening decrease in venous return .

Pulmonary edema is a consequence of a sudden increase in hydrostatic pressure in the pulmonary artery, increased permeability of alveolar-capillary membranes with reduced myocardial contractility, the development of circulatory centralization syndrome with increased venous return.

According to the clinical course, there are instantaneous (death occurs in a few minutes), acute (lasting up to 1 hour), prolonged (lasting up to 2 days) and recurrent options. The latter has a wavy nature, is most common in myocardial infarction. Typical clinical signs are severe respiratory failure, coughing pink foamy sputum, orthopnoe, pale, cold-covered skin. Peripheral cyanosis is also observed. During auscultation, wet rales of various calibers over most of the lungs, tachycardia, protodiastolic gallop rhythm, and systolic murmur of relative mitral regurgitation are detected: BP may rise or fall sharply (shock). Chest radiography confirms the presence of wet lung syndrome. During the analysis of the gas composition of the blood reveal severe or moderate hypoxemia, hypercapnia, decreased pH of arterial blood (respiratory acidosis).

During the main treatment the patient is given a semi-sitting position in bed, venous tourniquets are placed on the extremities, foam is aspirated from the airways, oxygen inhalation with defoamers (alcohol, antifomsilane) is established, diuresis and the amount of foamy sputum and heart rate are controlled. respiration, blood pressure.

Medical treatment should be comprehensive and aimed at:

1) reduction of hydrostatic pressure in the vessels of the small circle of blood circulation and reduction of venous return to the right ventricle;
2) reduction of BCC and pulmonary dehydration;

3) reducing the permeability of alveolar-capillary membranes;
4) strengthening of contractile ability of a myocardium;
5) elimination of pain and acute disorders of heart rhythm and conduction;
6) fight against hypoxia and disorders of acid-base status and water-electrolyte metabolism;
7) elimination of bronchosia and improvement of alveolar ventilation. The reduction of hydrostatic pressure in the pulmonary vessels and the reduction of venous return to the heart is carried out by some drugs. In particular, they include narcotic analgesics and neuroleptics that have α-adrenoblocking properties - morphine hydrochloride, droperidol, fentanyl, haloperidol.

Morphine hydrochloride - ampoules of 1 ml of 1% solution. Gives an analgesic effect, depresses the respiratory center, reduces shortness of breath, stimulates the vagus nerve center with the development of bradycardia. Reduces fear of death, eliminates anxiety. Reduces systemic blood pressure and venous return to the heart. Apply intravenous slow administration of 1 ml of 1% morphine hydrochloride solution. In less urgent cases, the same dose is administered intramuscularly. Contraindications to the drug: severe airway obstruction, chronic pulmonary heart disease, pregnancy. It is better to administer narcotic analgesics intravenously at a dilution of 1:20 in isotonic sodium chloride solution - 2-3 ml every 30-60 minutes.

Promedol - ampoules of 1 ml of 1% or 2% solution. Enter in the same way as morphine hydrochloride; its effect is much weaker than that of morphine hydrochloride.

Fentanyl - ampoules of 2 ml and 10 ml of 0.005% solution. Gives a strong, fast, but short-term analgesic effect (lasting 15 - 30 minutes). Depresses the respiratory center, causes bradycardia (it is eliminated by atropine sulfate, although the latter should be used with caution in pulmonary edema). Inject 1 - 2 ml of 0.005% solution of fentanyl intravenously or intramuscularly in combination with neuroleptics - droperidol (2 - 4 ml of 0.25% solution) or haloperidol (1 - 2 ml of 0.5% solution) or use the combined

drug thalamolan (1 ml contains 2.5 mg of droperidol and 0.05 mg of fentanyl).

Droperidol - ampoules of 10 ml of 0.25% solution. It belongs to the group of neuroleptics. The action is fast, strong, but short-lived. Has anti-shock and antiemetic properties, lowers blood pressure, has an antiarrhythmic effect.

Ganglioblockers are used to dilate peripheral vessels and deposit blood in the periphery, resulting in reduced venous return of blood to the right ventricle. It is used at the raised or normal BP, is not used in case of arterial hypotension. Pentamine: 1 ml of 5% solution is diluted in 20 ml of isotonic sodium chloride solution and administered intravenously by titration, ie 2-3 ml of diluted drug every 2-3 minutes under constant control of blood pressure. After achieving the desired effect, the introduction of entamine is stopped.

Nitrates - nitroglycerin, perlinganite, isoket - increase the capacity of venous vessels, reduce venous pressure, reduce venous return to the heart. Nitrates directly relax vascular smooth muscle. Vasodilation occurs 2 minutes after the start of intravenous infusion (scheme of administration - see treatment of unstable angina).

ACE inhibitors provide vasodilation by inhibiting angiotensin P-induced vasoconstriction, inhibit aldosterone production, reduce left ventricular filling pressure, right atrial pressure, increase cardiac output with little effect on heart rate.
Captopril or enalapril or fosinolryl are commonly used. The effect of captopril begins 30 minutes after ingestion of 12.5 mg of the drug. After 4 - 6 hours the patient is given orally 25 mg every 6 - 8 hours. Enalapril is first administered orally at a dose of 2.5 mg, the maintenance dose is 10 - 20 mg per day. These drugs are of limited use for the treatment of emergencies due to the lack of injectable forms, they are used in further treatment.

Calcium antagonists from the group of dihydropirtsidines (nifedinine) in myocardial

infarction are contraindicated due to activation of the sympathetic-adrenal system with increased mortality.

Reduction of BCC and elimination of pulmonary dehydration is mainly carried out by diuretics. At high or normal blood pressure, strong loop diuretics are used - furosemide (Lasix), ethacrynic acid (uregit). their effect is due to the inhibition of reabsorption of № + and water in the Henle loop, reducing the volume of extracellular fluid, cardiac output, reducing the response to the pressor effects of angioteizin 11 and norepinephrine. Furosemide (Lasix) is administered intravenously in a dose of 20 - 60 - 120 mg. The clinical effect is observed in 3 - 5 minutes. Repeatedly administered as needed after 2 - 4 hours, Furosemide is contraindicated in cases of hypotension, hypovolemia, anemia, acute or chronic renal failure with a sharp decrease in glomerular filtration.

Plaits of the limb are applied to deposit part of the BCC on the periphery. With properly applied tourniquets, 600-800 ml of blood or more can be retained in each leg. After elimination of alveolar edema of the lungs, the tourniquets should be slowly loosened to avoid rapid entry into the bloodstream at the same time a significant amount of blood.

Bloodletting is the oldest but most reliable way to reduce BCC. Usually 400 -700 ml of venous blood are removed at the same time. But in myocardial infarction, this method is rarely used. This is due to the presence of powerful means for "bloodless bloodletting" (lasix, laughter).

Antihistamines and glucocorticosteroids are used to reduce the permeability of alveolar-capillary membranes. Diphenhydramine is administered in a dose of 10 - 20 mg intravenously (on a polarizing mixture) or intramuscularly.

Hydrocortisone at a dose of 150-300 mg is administered intravenously in 200 ml of isotonic sodium chloride solution, prednisolone at a dose of 60-120 mg is administered in 100 ml of isotonic sodium chloride solution or in 5% glucose solution intravenously.

In resistant cases with a very low emission fraction (<20%):

1. In order to enhance the contractile capacity of the myocardium with great caution should be prescribed cardiac glycosides (monitoring of the general condition, ECG, heart rate) and non-glycosidic inotropic drugs. Of the cardiac glycosides, strophanthin is preferred. Usually strophanthin is administered in a dose of 0.250-0.375 mg (0.5 - 0.75 ml of 0.05% solution) intravenously slowly over 5 minutes. It is better to enter this dose of the drug drip for 10 - 15 minutes. If necessary, you can additionally administer at intervals of 1 h at 0.1 -0.125 mg (0.2 - 0.25 ml of 0.05% solution) of the drug until the clinical effect (slowing of heart rate, reduction of shortness of breath). The total daily dose of the drug for 4 hours should not exceed 0.5 - 0.625 mg (1 - 1.25 ml of 0.05% solution). It should be remembered that in acute myocardial infarction tolerance to cardiac glycosides is reduced. The drug is not recommended for patients receiving cardiac glycosides, calcium salts, because it accelerates the development of dititalis intoxication with the occurrence of fatal ventricular fibrillation.
2. Dobutamine (dobutrex), which is available in 250 mg vials, can be used as a non-glycosidic inotropic agent. This amount is diluted in 250 ml of isotonic sodium chloride solution and administered intravenously at a rate of 0.5 - 20 μg (kg * min), starting at a rate of 1 drop per 1 min, gradually increasing the frequency of drops to 28 per 1 min (risk of tachycardia, arrhythmia , blood pressure fluctuations, increased myocardial ischemia).

Elimination of pain and acute cardiac arrhythmias and conduction is carried out individually, depending on the specific situation.

To combat hypoxia and disorders of the acid-base state and water-electrolyte balance, oxygen therapy or, better, the introduction of oxygenated perfluorone to eliminate severe hypoxemia, reduce the permeability of lung membranes. The best method of oxygen therapy is the inhalation of oxygen through tubes installed in the nasal passages to a depth of 7 - 10 cm, with the supply of oxygen through them in a volume of 8-10 liters per 1 minute. To ensure access of oxygen to the lungs, it is urgent to restore patency of the upper respiratory tract. To do this, perform aspiration of foam from the upper respiratory tract and trachea using mechanical, electrical or other aspirators.

Aspiration of foam and fluid from the trachea is sometimes possible only after tracheal intubation or tracheostomy. Aspiration of foam from the bronchi of medium caliber is impossible.

Cardiac asthma occurs due to blood stasis in the small circulation, most often at night, and is characterized by an attack of asthma. There is a lack of air, shortness of breath, palpitations, disturbed by a weak dry cough. The examination attracts the attention of a suffering face, orthopedic position with lowered legs; skin grayish-pale, covered with cold sweat, acrocyanosis, severe shortness of breath. The pulse of the patient is weak, often arrhythmic. The boundaries of the heart are often expanded to the left. At auscultation of heart tones are deaf, the rhythm of a gallop (ventricular diastolic gallop) is quite often listened or the III tone of heart connected with fast filling of ventricles appears. This low-frequency tone is heard at the apex of the heart and in the left axillaю; II tone over the pulmonary artery is amplified and bifurcated. Blood pressure gradually decreases. At auscultation in lungs hard breath is defined, dry, quite often damp rales are listened. On the ECG - a decrease in the amplitude of the teeth T, the interval S-T and changes characteristic of the underlying disease. On the radiograph of the lungs there is a blurring of the pulmonary pattern, decreased transparency of the basal lungs, dilation of the interparticle septa.

Toxic pulmonary edema is a pathological process that develops as a result of inhalation and the predominant effect on the lung tissue of toxic irritants with the development of massive sweating of protein-rich fluid in the interstitial tissue and alveoli. These are mainly gases or substances that easily turn into a gaseous state. Chemicals with a pronounced irritant effect on the respiratory system are also called poisons of suffocating action, because their effect is accompanied by impaired pulmonary gas exchange and oxygen deficiency.

There are several forms of toxic pulmonary edema.

1. Asphyxial form of toxic pulmonary edema is observed when exposed to high

concentrations of toxic substances, resulting in reflex spasm of the muscles of the larynx and vocal cords, narrowing of the glottis. The ***clinical picture*** is characterized by significantly difficult breathing, accompanied by noise and wheezing (stridor breathing), progressive cyanosis of the skin. Instant death due to asphyxia and respiratory arrest is possible. Under certain conditions, asphyxia can occur due to the very rapid development of toxic pulmonary edema.

It is this form and gave the group of toxic substances irritating somewhat conditional name - "suffocating".

2. A mild form of toxic pulmonary edema is often not diagnosed. This is the so-called dumb edema, which is detected only during X-ray examination, with clinical manifestations of pulmonary edema are almost absent.
3. Expanded or completed form of toxic pulmonary edema has in its development ***classically five successive stages (periods).***

1) ***The period of initial manifestations***, the period of irritation or reflex stage. At direct contact with toxic substance the phenomena of irritation of a mucous membrane of respiratory tracts and eyes arise. ***Clinical symptoms*** are characterized by dry cough, shortness of breath, sore throat, chest pain. There is rhinorrhea, tearing. With decreasing solubility of toxic substances, the manifestations of clinical symptoms of this period, which last 15-20 minutes, also decrease.

2) ***Latent (hidden) period***, the period of feigned well-being. It is characterized by the development of edema of the interstitial lung tissue.

Clinical manifestations are almost absent: lability of the pulse, mild shortness of breath and cyanosis, moderate manifestations of pulmonary emphysema. The duration of the period is on average 3-12 hours. With increasing solubility of the toxic substance, its duration decreases. Given this factor, it can range from 30 minutes to 24-36 hours. At X-ray inspection of bodies of a thorax strengthening and blurring of a vascular drawing is observed.

3) ***The beginning of edema, swelling***. During this period, there is a transition of fluid from the interstitial tissue into the lumen of the alveoli.

Clinically, there is a cough with serous-mucous sputum, increasing cyanosis, shortness

of breath, a feeling of tightness in the chest. There is a boxy shade of percussion tone and limited mobility of the pulmonary margin, on auscultation - fine-bubble wet rales, crepitation with a tendency to increase.

According to X-ray examination, the pulmonary pattern loses clarity, becomes blurred, the interlobular pleura is thickened. The roots of the lungs are dilated, have indistinct contours, disseminated small-spotted, not clearly delineated focal shadows appear in the lower and middle parts of the lungs.

From the peripheral blood there is a thickening with increasing viscosity, increased erythrocyte clotting rate (ESR), neutrophilic leukocytosis with a shift of the formula to the left, lymphopenia.

4) ***Completion of edema***. The alveoli and large bronchi are filled with fluid. The transition of the process to complete pulmonary edema often occurs very quickly and has a progressive course.

X-ray examination during this period reveals numerous small spotted shadows in the lower and middle parts of the lungs, due to the accumulation of fluid in the alveoli. Over time, the shadows gradually increase in size due to the merging of individual foci and form large spotted formations with blurred contours, resembling a cloudy sky or melting snow flakes. Eclipses alternate with areas of enlightenment caused by foci of bullous emphysema. The roots of the lungs are enlarged with blurred contours.

During this period, there are two phases of the pathological process: hypercapnic type of hypoxemia, or blue type of asphyxia, and hypocapnic type of hypoxemia, or gray type of asphyxia.

Hypercapnic type of hypoxemia, or blue type of asphyxia. Clinically, shortness of breath increases (respiratory rate is 50-60 beats / min), worse cough, accompanied by the release of bloody foamy sputum. Expressed cyanosis of the skin and mucous membranes from an excess of restored hemoglobin, wheezing, hyperthermia. A large number of wet rales of various calibers are heard over the entire surface of the lungs. Characteristic tachycardia, blood pressure with a tendency to increase.

At research of blood erythrocytosis, leukocytosis, hypercoagulation, increase in the content of hemoglobin, decrease in SHE is noted.

There is a deficiency of arterial blood oxygen saturation with a simultaneous increase in carbon dioxide. The content of carbon dioxide in the arterial blood reaches 80-85% (at a rate of 45-60%). There is a compensated gas acidosis. Blue asphyxia may turn gray.

Hypocapnic type of hypoxemia, or gray type of asphyxia. This is often the next phase of edema after blue asphyxia, but sometimes gray asphyxia occurs immediately after the third period, bypassing the blue asphyxia phase.

The patient is indifferent, the skin and visible mucous membranes are gray-gray. The face is covered with cold sweat, features are sharp, breathing is intermittent. The limbs are cold to the touch. There is a frequent pulse of small filling, lowering blood pressure. The development of collapse is possible.

The gas composition of the blood is characterized by a reduced content of oxygen and carbon dioxide.

If this condition does not end in death, it changes to the fifth period.

5) ***The period of reversal of edema***. There is an allocation and resorption of fluid from the alveoli. Toxic pulmonary edema, including all stages, averages 4-8 hours, but in some cases can last up to 24-36 hours. Gradually during the day the number of wheezes decreases, cough stops, cyanosis disappears. X-ray changes are subject to reverse development, hematological indicators are normalized. Complete recovery is observed within 4-6 days. Sometimes the reverse development can be "lightning fast". The manifestations of edema quickly disappear, the patient feels healthy.

4. The abortive form of toxic pulmonary edema has four periods of development except for the period of complete edema.

The prognosis for toxic pulmonary edema depends on the severity of the poisoning and the general condition of the body. Cases of mild severity end with complete recovery of the patient. In moderate and severe intoxication, the prognosis for complete recovery is questionable. Severe forms of pulmonary edema can lead to the death of the patient 24-48 hours after exposure to toxic irritants. In 85% of cases after chronic pulmonary edema develop chronic respiratory diseases.

Recovery of patients after toxic pulmonary edema may be delayed due to complications.

1. Pneumonia. In some cases, usually on the 3-5th day of the disease in the period of abatement of clinical manifestations of edema and improvement, the general condition of the patient deteriorates sharply. The body temperature rises to 38-39 oC, cough with mucus-purulent sputum intensifies, wet rales appear in the lungs. From the general analysis of blood leukocytosis, increase in SHE are noted. At carrying out radiography small infiltrative foci on type of focal pneumonia come to light. Pneumonia that develops after toxic pulmonary edema is severe and can cause death on the 8-9th day of illness.
2. Secondary pulmonary edema, which occurs at the end of the 2nd - in the middle of the 3rd week of the disease as a consequence of acute left ventricular failure.
3. Pneumosclerosis. In persons who have suffered toxic pulmonary edema, in the long term the development of diffuse and focal pneumosclerosis is possible.
4. Toxic encephalopathy with various clinical manifestations: irritability, anxiety, depressive-hypochondriac reactions, stupor, drowsiness, lethargy, memory and attention impairment.
5. Toxic hepatitis. It is characterized by hepatomegaly, changes in functional liver tests.

Diagnosis of toxic pulmonary edema is based on:

1. Data of professional anamnesis, which testify to the work of the victim with irritants.
2. Information on the emergency situation at work related to the release of irritating gases into the air in significant concentrations.
3. Anamnestic data on the presence of initial manifestations, the period of irritation or reflex stage in the victims during contact with irritants. Of particular importance is the simultaneous damage to the respiratory system, eyes, and sometimes the skin.
4. Data on the group nature of the disease of employees of one shop or station.
5. The presence of a certain frequency in the development of toxic pulmonary edema with a typical clinical picture. Some irritants also have their own characteristics, in addition to the above, which may be the subject of a separate publication.

6. Dynamics of radiological changes.
7. Carrying out differential diagnosis with other similar pathological processes.

Differential diagnosis of toxic pulmonary edema is performed when:

1. Acute infectious and inflammatory diseases of the respiratory system of non-professional origin. With toxic pulmonary edema, as a rule, less pronounced signs of infectious-inflammatory syndrome: less pronounced increase in body temperature, changes in peripheral blood.
2. Pulmonary edema of cardiogenic origin. Toxic pulmonary edema differs from cardiogenic in the absence of signs of cardiac pathology, which could be the cause of acute decompensation of cardiac activity.

Treatment of persons with toxic pulmonary edema has a number of general approaches and is differentiated depending on the phase of asphyxia at the time of completion of edema according to the clinical picture.

1. Removal of the victim from the affected area.
2. Replacement of contaminated clothing, treatment of skin with water or soap, rinsing the eyes with antiseptic or analgesic drops. Inhalation, rinsing of the mouth and nasal lavage with 2% sodium bicarbonate solution.
3. At defeat of a larynx the mode of silence is necessary. In case of severe laryngospasm, a tracheostomy should be performed immediately.
4. Persons who have been in contact with irritating gases as a result of an accident shall be hospitalized for 24 hours, despite their satisfactory general condition at the time of examination. Given the stages of development of toxic pulmonary edema, it should be borne in mind that the pathological process has a latent, latent period (a period of feigned well-being), after which toxic pulmonary edema develops.
5. Carrying out of the actions directed on decrease in permeability of vessels.
6. Distracting reflexes.
7. Oxygen therapy is performed to eliminate oxygen deficiency with different approaches depending on the phase of hypoxemia.

At the stage of blue hypoxemia, inhalations of oxygen or oxygen-air mixture (oxygen content - 50-60%) are used in a humidified and heated state in combination with substances that convert foam into liquid and improve ventilation in the lungs.

In gray asphyxia, a mixture of 60% oxygen and 5% carbon dioxide is inhaled with air or carbogen containing 95% oxygen and 5% carbon dioxide, primarily to saturate the blood with carbon dioxide, because the human respiratory center responds to the content of carbon dioxide in the blood. If in this case you start with inhalation of oxygen, the carbon dioxide content in the blood will drop sharply in contrast to oxygen, which, in turn, will lead to reflex respiratory arrest. After 5-10 minutes of inhalation of mixtures with carbon dioxide, switch to inhalation of oxygen or oxygen-air mixture.

8. Dehydration by diuretics.
9. Appointment of euphyllin as a drug that has a positive effect on various links in the pathogenesis of toxic pulmonary edema. Euphyllin has a bronchodilator and diuretic effect, improves cerebral and coronary circulation, reduces pressure in the pulmonary artery system.
10. Means that tonify the cardiovascular system.
11. Ganglioblockers and nitrates are used to relieve the small circulation.
12. Deposition of blood by applying tourniquets to the lower extremities or bloodletting with a volume of 250-350 ml. With gray asphyxia, bloodletting is contraindicated.
13. Correction of acid-base balance.
14. To stabilize hemodynamic disorders (tachycardia, acute left ventricular failure), the introduction of cardiac glycosides is indicated.
15. In case of respiratory arrest, respiratory analeptics should be administered.
16. After removal of the patient from the state of edema, prophylactic administration of antibiotics and sulfonamides is possible to prevent the development of infectious complications.

Examination of performance in toxic pulmonary edema depends on the severity of the process and residual changes.

In accordance with the Resolution of the Cabinet of Ministers of Ukraine dated 08.11.2000 № 1662 "On approval of the list of occupational diseases" section I of this

list highlights "Diseases arising under the influence of chemical factors", where paragraph 1 highlights acute chronic intoxications and their consequences for which are characterized by isolated or combined damage to organs and systems. It provides a section on respiratory diseases caused by chemicals, including primary raw materials, intermediates, by-products and end products.

If residual changes are observed after the transferred toxic pulmonary edema, they are included in this section.

Prevention of toxic pulmonary edema is reduced to the use of individual means of protection, sealing equipment and production processes, careful control over the concentration of toxic substances in the air of the working area. Effective ventilation and preliminary and periodic medical examinations are mandatory.

Knowledge control:

1. Determination of cardiogenic and noncardiogenic pulmonary edema .
2. The main mechanisms of development of cardiogenic and noncardiogenic pulmonary edema.
3. Possible complications of cardiogenic and noncardiogenic pulmonary edema.
4. Primary and secondary prevention of cardiogenic and noncardiogenic pulmonary edema.
5. Clinic, diagnosis and emergency care for pulmonary edema on the background of acute left ventricular and left atrial insufficiency (myocardial infarction).
6. Clinic, diagnosis and emergency care for pulmonary edema on the background of acute left ventricular and left atrial insufficiency (hypertensive crisis).
7. Clinic, diagnosis and emergency care for pulmonary edema on the background of acute left ventricular and left atrial insufficiency (mitral stenosis).
8. Features of toxic pulmonary edema.
9. Tactics of patient management with pulmonary edema.

Test tasks:

1. Duration of acute pulmonary edema:

A) Up to 12 hours

B) Up to 4 hours

C) Up to several days

2. Cardiogenic pulmonary edema is caused by:

A) Increased contractility of the left ventricle

B) Decreased pressure in the pulmonary arteries

C) Increased pressure in the pulmonary capillaries and severe left ventricular failure

D) Decrease in hydrostatic pressure in pulmonary capillaries

3. The most characteristic signs of left ventricular heart failure:

A) Severe swelling of the jugular veins, edema

B) Rapid increase in the size of the liver

C) Tachycardia, severe shortness of breath, pulmonary edema

4. Clinical sign that is not characteristic of pulmonary edema:

A) Cyanosis

B) Severe shortness of breath

C) Foamy sputum from the mouth

D) Insignificant number or absence of wheezing in the lungs

5. Specify a symptom that is not characteristic of an asthma attack:

A) prolonged exhalation

B) high blood pressure

C) small-bubble rales

D) percussion - box sound

E) edema of the extremities

6. At the patient with the formed mitral defect with advantage of insufficiency of the mitral valve the general weakness, the expressed short wind gradually appeared. Objectively: acrocyanosis, edema of the legs, wet rales in the lower lungs, dilation of the heart. What pathology is indicated by the appearance of these signs?

A) Chronic heart failure

B) Chronic vascular insufficiency

C) Acute heart failure

D) Pneumonia

E) Pericardial effusion

7. At the patient of 18 years three days ago the quantity of urine decreased, appeared shortness of breath when walking, the temperature rose to 38 ° C. Sit. On the neck swollen veins. Blood pressure - 90/60 mm Hg. Art. Respiratory rate (RRM) 24 / min, pulse - 116 / min, disappears on inspiration. The boundaries of the heart are significantly expanded. Heart sounds are barely audible. Liver +4 cm, swelling of the legs. Radiologically: expansion of the heart shadow. What is the most important cause of heart failure in a patient?

A) Paroxysmal cardiac arrhythmia

B) Muscle failure (myocarditis)

C) Excessive fluid retention in the body as a result of acute renal insufficiency

D) Diastolic dysfunction (hypodiastole)

E) Acute glomerulonephritis

8. In patients with chronic heart failure, attacks of cardiac asthma and Pulmonary edema often develops at night during sleep. What is it connected with?

A) Increased postload

B) Increasing preload

C) Influence of the parasympathetic nervous system

D) Shallow breathing

E) Nightmares

9. A 47-year-old patient suddenly began shortness of breath, which turned into shortness of breath, there was wheezing, foam from the mouth. Pulse 80 per 1 min, rhythmic, blood pressure - 150/100 mm Hg, in the lungs on both sides a lot of wet rales. History of coronary heart disease, hypertension, obstructive bronchitis.

Which drug will you use first when providing care?

A) Nitroglycerin

B) Morphine

C) Digoxin

D) Furosemide

E) Defoamer

10. A 58-year-old man was in the intensive care unit due to an acute myocardial infarction. Blood pressure was 150/100 mm Hg. st., heart rate - 100 / min. 3 days later he complained of an asthma attack. Objectively: blood pressure - 100/65 mm Hg. st., heart rate - 120 / min, CDR - 32 / min. In the lower parts of the lungs appeared wet rales, over the top began to listen to the rhythm of the gallop, systolic murmur. What is diagnosis?

A) Pulmonary artery thromboembolism

B) Acute pericarditis

C) Pulmonary edema

D) Myocardial rupture

E)Cardiogenic shock

Topic 3. Preparation for practical training № 3 «Acute arrhythmias and conduction»

Learning objective

The student must know:

- the definition of arrhythmias
- the criteria of normal sinus rhythm
- major etiological factors and triggers of rhythm and conduction disorders
- the mechanisms of rhythm and conduction disorders
- up-to-date classification of rhythm and conduction disorders
- the criteria for diagnosis of rhythm and conduction disorders
- the particular patterns of rhythm and conduction disorders
- the risk stratification of patients with rhythm and conduction disorders
- the value, prejudicial evidence and contraindications of different diagnostic tests for diagnosis of rhythm and conduction disorders
- etiological factors, pathogenesis, clinical patterns of different supraventricular arrhythmias (tachy-, bradycardias, atrial fibrillation, flutter, premature beats etc.)
- etiological factors, pathogenesis, clinical patterns of different ventricular arrhythmias (tachy-, bradycardias, premature beats etc.)
- risk factors and major causes of sudden cardiac death
- etiological factors, pathogenesis, clinical patterns of conduction disorders
- the clinical pharmacology of the basic drugs used in the treatment of rhythm and conduction disorders
- principles of non-pharmacological treatment of rhythm and conduction disorders

Be able:

- to determine the clinical pattern of rhythm and conduction disorder
- to collect complaints and the anamnesis according to the clinical pattern of rhythm and conduction disorder
- to make up the program of laboratory and instrumental tests for diagnosis of rhythm and conduction disorders

- to make up the program of differential diagnosis of rhythm and conduction disorders
- to formulate the clinical diagnosis according to the up-to-date classification of rhythm and conduction disorders
- to make up the program of differential treatment depending on the age and clinical pattern of rhythm and conduction disorders
- to determine the treatment tactics of district therapeutist during the medical observation of patient
- to make the decision apropos of disability examination

Master practical skills:

- to collect complaints and the anamnesis
- to make up the detailed clinical checkup of patient
- to interpret the results of laboratory and instrumental tests
- to make up the scheme of differential treatment of rhythm and conduction disorders.

Theoretical material for independent student training.

Cardiac arrhythmias result from abnormalities of impulse generation, conduction, or both. It is, however, difficult to establish with certainty an underlying mechanism for many clinical arrhythmias. The response of a tachycardia to pacing (initiation, termination, entrainment) is used in the clinical electrophysiology laboratory to make the diagnosis of reentry. There are even fewer specific tools available to diagnose non-reentrant arrhythmias. It is clear that molecular changes in the heart predispose to the development of abnormalities of cardiac rhythm. However, an exclusively molecular approach to understanding arrhythmia mechanisms is limited by failure to include cellular and network properties of the heart.

Arrhythmia Mechanisms

Electrophysiologic Property	Molecular Components	Mechanism	Prototypic Arrhythmias
Cellular			
Impulse Initiation			
Automaticity	If, ICa-L, ICa-T, IK, IK1	Suppression/acceleration of phase 4	Sinus bradycardia, sinus tachycardia
Triggered automaticity	Calcium overload, ITI	DADs	Digitalis toxicity, reperfusion VT
	ICa-L, IK, INa	EADs	Torsades des pointes, congenital and acquired
Excitation	INa	Suppression of phase 0	Ischemic VF
	IK-ATP	AP shortening, inexcitability	
	ICa-L	Suppression	AV block
Repolarization	INa, ICa-L, IK, IK1, Ca2+ homeostasis	AP prolongation, EADS, DADs	Polymorphic VT (HF, LVH)
	ICa-L, K channels, Ca2+ homeostasis	AP shortening	Atrial fibrillation
Multicellular			
Cellular coupling	Connexins (Cx43), INa, IK-ATP	Decreased coupling	Ischemic VT/VF
Tissue Structure	Extracellular matrix, collagen	Excitable gap and functional reentry	Monomorphic VT, atrial fibrillation

Note: DAD, delayed afterdepolarization; VT, ventricular tachyarrhythmia; IVR, idioventricular rhythm; EAD, early afterdepolarization; VF, ventricular fibrillation; AV, atrioventricular; HF, heart failure; AP, action potential.

Normal automaticity may be affected by a number other factors associated with heart disease. Hypokalemia and ischemia may reduce the activity of the Na+,K+-ATPase, thereby reducing the background repolarizing current and enhancing phase 4 diastolic depolarization. The end result would be an increase in the spontaneous firing rate of

pacemaking cells. Modest increases in extracellular potassium may render the maximum diastolic potential more positive, thereby also increasing the firing rate of pacemaking cells. A more significant increase in [K+]o, however, renders the heart inexcitable by depolarizing the membrane potential.

Abnormal automaticity may underlie atrial tachycardia, accelerated idioventricular rhythms, and ventricular tachycardia, particularly that associated with ischemia and reperfusion. It has also been suggested that injury currents at the borders of ischemic myocardium may depolarize adjacent non-ischemic tissue, predisposing to automatic ventricular tachycardia.

Triggered automaticity or activity refers to impulse initiation that is dependent on afterdepolarizations. Afterdepolarizations are membrane voltage oscillations that occur during (early afterdepolarizations, EAD) or following (delayed afterdepolarization, DADs) an action potential.

EAD-mediated triggered activity likely underlies initiation of the characteristic polymorphic ventricular tachycardia, torsades des pointes, seen in patients with congenital and acquired forms of the LQTS. Structural heart disease, such as cardiac hypertrophy and failure, may also delay ventricular repolarization (so-called electrical remodeling) and predispose to arrhythmias related to abnormalities of repolarization. The abnormalities of repolarization in hypertrophy and failure are often magnified by concomitant drug therapy or electrolyte disturbances.

The most common arrhythmia mechanism is reentry. Reentry is a property of networks of myocytes. Fundamentally, reentry is defined as circulation of an activation wave around an inexcitable obstacle. Thus, the requirements for reentry are two electrophysiologically dissimilar pathways for impulse propagation around an inexcitable region such that unidirectional block occurs in one of the pathways and a region of excitable tissue exists at the head of the propagating wavefront. Structural and electrophysiologic properties of the heart may contribute to the development of the

inexcitable obstacle and of unidirectional block. The complex geometry of muscle bundles in the heart and spatial heterogeneity of cellular coupling or other active membrane properties (i.e., ionic currents) appear to be critical.

A key feature in classifying reentrant arrhythmias, particularly for therapy, is the presence and size of an excitable gap. An excitable gap exists when the tachycardia circuit is longer than the tachycardia wavelength (λ= conduction velocity x refractory period, representing the size of the circuit that can sustain reentry), allowing appropriately timed stimuli to reset propagation in the circuit. Reentrant arrhythmias may exist in the heart in the absence of an excitable gap and with a tachycardia wavelength nearly the same size as the path length. In this case, the wavefront propagates through partially refractory tissue with no anatomic obstacle and no fully excitable gap; this is referred to as leading circle reentry, a form of functional reentry (reentry that depends on functional properties of the tissue). Unlike excitable gap reentry, there is no fixed anatomic circuit in leading circle reentry, and it may therefore not be possible to disrupt the tachycardia with pacing or destruction of a part of the circuit. Furthermore, the circuit in leading circle reentry tends to be less stable than that in excitable gap reentrant arrhythmias, with large variations in cycle length and predilection to termination.

Anatomically determined, excitable gap reentry can explain several clinically important tachycardias, such as AV reentry, atrial flutter, bundle branch reentry ventricular tachycardia, and ventricular tachycardia in scarred myocardium. Atrial flutter represents an example of a reentrant tachycardia with a large excitable gap not always due to an anatomic constraint but to functional block (reflecting the special properties of the crista terminalis discussed above). There is strong evidence to suggest that arrhythmias, such as atrial and ventricular fibrillation, are associated with more complex activation of the heart and are due to functional reentry.

Structural heart disease is associated with changes in conduction and refractoriness that increase the risk of reentrant arrhythmias. Chronically ischemic myocardium exhibits

a down-regulation of the gap junction channel protein (connexin 43) that carries intercellular ionic current. The border zones of infarcted and failing ventricular myocardium exhibit not only functional alterations of ionic currents but also remodeling of tissue and altered distribution of gap junctions. The changes in gap junction channel expression and distribution, in combination with macroscopic tissue alterations, support a role for slowed conduction in reentrant arrhythmias that complicate chronic coronary artery disease. Aged human atrial myocardium exhibits altered conduction, manifest as highly fractionated atrial electrograms, producing an ideal substrate for the reentry that may underlie the very common development of atrial fibrillation in the elderly.

APPROACH TO THE PATIENT: CARDIAC ARRHYTHMIA

The evaluation of patients with suspected cardiac arrhythmias is highly individualized; however, two key features, the history and ECG, are pivotal in directing the diagnostic workup and therapy. Patients with cardiac arrhythmias exhibit a wide spectrum of clinical presentations from asymptomatic ECG abnormalities to survival from cardiac arrest. In general, the more severe the presenting symptoms, the more aggressive are the evaluation and treatment. Loss of consciousness that is believed to be of cardiac origin typically mandates an exhaustive search for the etiology and often requires invasive, device-based therapy. The presence of structural heart disease and prior myocardial infarction dictates a change in the approach to the management of syncope or ventricular arrhythmias. The presence of a family history of serious ventricular arrhythmias or premature sudden death will influence the evaluation of presumed heritable arrhythmias.

The physical examination is focused on determining if there is cardiopulmonary disease that is associated with specific cardiac arrhythmias. The absence of significant cardiopulmonary disease often, but not always, suggests benignity of the rhythm disturbance. In contrast, palpitations, syncope, or near syncope in the setting of significant heart or lung disease has more ominous implications. In addition, the

physical examination may reveal the presence of a persistent arrhythmia such as atrial fibrillation.

The judicious use of noninvasive diagnostic tests is an important element in the evaluation of patients with arrhythmias, and there is none more important that the ECG, particularly if recorded at the time of symptoms. Uncommon but diagnostically important signatures of electrophysiologic disturbances may be unearthed on the resting ECG, such as delta waves in Wolff-Parkinson-White (WPW) syndrome, prolongation or shortening of the QT interval, right precordial ST-segment abnormalities in Brugada syndrome, and epsilon waves in arrhythmogenic right ventricular dysplasia. Variants of body surface ECG recording can provide important information about arrhythmia substrates and triggers. Holter monitoring and event recording, either continuous or intermittent, record the body surface ECG over longer periods of time, enhancing the possibility of observing the cardiac rhythm during symptoms. Implantable long-term monitors and commercial ambulatory ECG monitoring services exist that permit prolonged telemetric monitoring for both diagnosis and to assess the efficacy of therapy.

Long-term recordings permit the assessment of the time-varying behavior of the heart rhythm. Heart rate variability (HRV) and QT interval variability (QTV) provide noninvasive methods to assess autonomic nervous system influence on the heart. HRV arises because of subtle changes in sinus rate due to changes in sympathovagal input to the sinus node. Normal time domain, frequency domain, and geometric methods metrics have been established for HRV; a decrease in HRV and an increase in low-frequency power have been associated with increased sympathetic nervous system tone and increased mortality in patients after myocardial infarction. Signal-averaged electrocardiography (SAECG) uses signal-averaging techniques to amplify small potentials in the body surface ECG that are associated with slow conduction in the myocardium. The presence of these small potentials, referred to as late potentials because of their timing with respect to the QRS complex, and prolongation of the filtered (or averaged) QRS duration are indicative of slowed conduction in the ventricle and have been associated with an increased risk of ventricular arrhythmias after

myocardial infarction. Exercise electrocardiography is important in determining the presence of myocardial demand ischemia; more recently, analysis of the morphology of the QT interval with exercise has been used to assess the risk of serious ventricular arrhythmias. Microscopic alterations in the T wave (T wave alternans, TWA) at low heart rates identify patients at risk for ventricular arrhythmias. A number of other tests of the variability in the T-wave morphology or duration of the QT interval have been used to assess instability in repolarization of the ventricle and an increased risk of arrhythmias.

Head-up tilt (HUT) testing is a useful in the evaluation of some patients with syncope. The physiologic response to HUT is incompletely understood; however, redistribution of blood volume and increased ventricular contractility occur consistently. Exaggerated activation of a central reflex in response to HUT produces a stereotypic response of an initial increase in heart rate, then a drop in blood pressure followed by a reduction in heart rate characteristic of neurally mediated hypotension. Other responses to HUT may be observed in patients with orthostatic hypotension and autonomic insufficiency. HUT is most often used in patients with recurrent syncope, although it may be useful in patients with single syncopal episodes with associated injury, particularly in the absence of structural heart disease. In patients with structural heart disease, HUT may be indicated in those with syncope, in whom other causes (e.g., asystole, ventricular tachyarrhythmias) have been excluded. HUT has been suggested as a useful tool in the diagnosis and therapy of recurrent idiopathic vertigo, chronic fatigue syndrome, recurrent transient ischemic attacks, and repeated falls of unknown etiology in the elderly. Importantly, HUT is relatively contraindicated in the presence of severe coronary artery disease with proximal coronary stenoses, known severe cerebrovascular disease, severe mitral stenosis, and obstruction to left ventricular outflow (e.g., aortic stenosis). The method of HUT is variable, but the angle of tilt and the duration of upright posture are central to the diagnostic utility of the test. The use of pharmacologic provocation of orthostatic stress with isoproterenol, nitrates, adenosine, and edrophonium have been used to shorten the test and enhance specificity.

Electrophysiologic testing is central to the understanding and treatment of many cardiac arrhythmias. Indeed, most frequently electrophysiologic testing is interventional, providing both diagnosis and therapy. The components of the electrophysiologic test are baseline measurements of conduction under resting and stressed (rate or pharmacologic) conditions and maneuvers, both pacing and pharmacologic, to induce arrhythmias. A number of sophisticated electrical mapping and catheter-guidance techniques have been developed to facilitate catheter-based therapeutics in the electrophysiology laboratory.

Classification of rhythm and conduction disturbances (according to Ukrainian society of cardiology, 2008)

Abnormalities of impulse generation.

I49.8. Sinus tachycardia

Sinus bradycardia

Sinus arrhythmia

I49.5. Sinus arrest

I49.8. Slipped out beats and rhythms

- atrial (slow, accelerated)
- AV-nodal (slow, accelerated)
- ventricular (slow, accelerated)

I45.8. AV-dissociation.

I49.8. Supraventricular pacemaker migration.

Premature beats:

I49.1. Atrial.

I49.2. AV-nodal.

I49.3. Ventricular:

- solitary (less than 30 beats per hour)
- frequent (more than 30 beats per hour)
- allorhythmia
- polymorphic

- paired
- early (T-P)

I47.1. Tachycardias

- reciprocal (paroxysmal, chronic)
- ectopic (paroxysmal, chronic)

Supraventricular tachycardias:

- sino-atrial
- atrial
- AV-nodal (common, uncommon)
- with accessory pathways (orthodromic, antidromic)

Ventricular tachycardias:

I47.2. Unsteady (from 3 beats to 30 seconds): mono-, polymorphic

I47.2. Steady (more than 30 seconds): mono-, polymorphic

I47.0. Stable reciprocal: mono-, polymorphic

I48.0. Atrial fibrillation and flutter:

- new onset (bradysystolic, tachysystolic)
- recurrent
- paroxysmal – rhythm recovery in 48 h (bradysystolic, tachysystolic)
- persistent – necessity of intervention for rhythm recovery (bradysystolic, tachysystolic)
- stable - rhythm recovery is impossible or not appropriate (bradysystolic, tachysystolic)

I49.0. Ventriculal fibrillation/flutter.

Conduction disorders.

I45.5. Sino-auricular block

AV-block

I44.0. I degree

I44.1. II degree (I, II types)

I44.2. III degree

Intraventricular.

Bundle branch blocks.

I45.0. Right bundle branch block

I44.4. Left anterior bundle branch block

I44.5. Left posterior bundle branch block

- transient
- stable

I45.2. Left bundle branch block

Right and left anterior bundle branch block

Right and left posterior bundle branch block

I45.3. Blocks of three branches.

Combined disorders or impulse generation and conduction.

I49.4. Parasystole

- atrial
- AV-nodal
- ventricular

Diseases, syndromes and phenomena

I49.8. Idiopathic arrhythmias

Preexcitation syndromes (WPW, LGL)

Early ventricular repolarization syndrome

Long QT-syndrome (acquired, inherited)

I49.5. Sick sinus node syndrome

I46.9. Morgagni-Adams-Stokes syndrome

I49.8. Arrhythmogenic right ventricular dysplasia

I49.8. Brugada syndrome

I49.0. Frederick's syndrome

I46.1. Sudden cardiac death (arrhythmic)

- with recovery of cardiac activity (ventricular fibrillation, asystole, electromechanical dissociation)

- sudden cardiac death (irreversible) (ventricular fibrillation, asystole, electromechanical dissociation, cardiac arrest)

I46.0. With recovery of cardiac activity

I46.9. Cardiac arrest (irreversible).

THE TACHYARRHYTHMIAS: INTRODUCTION

Tachyarrhythmias typically refer to isolated premature complexes (depolarizations) or to nonsustained and sustained forms of tachycardia originating from myocardial foci or reentrant circuits. The standard definition of tachycardia is rhythm that produces a ventricular rate >100 beats/min. This definition has some limitations in that atrial rates can exceed 100 beats/min despite a slow ventricular rate. Furthermore, ventricular rates may exceed the baseline sinus rate and be <100 beats/min but still represent an important "tachycardia" response, such as is observed with accelerated ventricular rhythms.

Symptoms Due to Tachyarrhythmias

Tachyarrhythmias classically produce symptoms of palpitations or racing of the pulse. For premature beats, skipping of the pulse or a pause may be experienced, and patients may even sense slowing of the heart rate. A more dramatic irregularity of the pulse will be experienced with chaotic rapid rhythms or tachyarrhythmias that originate in the atrium and conduct variably to the ventricles. For very rapid tachyarrhythmias, hemodynamic compromise can occur, as can dizziness or syncope due to a decrease in cardiac output or breathlessness due to a marked increase in cardiac filling pressures. Occasionally, chest discomfort may be experienced that mimics symptoms of myocardial ischemia. The underlying cardiac condition typically dictates the severity of symptoms at any specific heart rate. Even patients with normal systolic left ventricular (LV) function may experience severe symptoms if diastolic compliance due to hypertrophy or valvular obstruction is present. Hemodynamic collapse with the development of ventricular fibrillation (VF) can lead to sudden cardiac death (SCD). SCD remains one of the principal causes of death in the adult population, thus

emphasizing the importance of appropriate tachyarrhythmia prevention as well as management.

Diagnostic Tests in Evaluating Tachyarrhythmias

In patients who present with non-life-threatening symptoms, such as palpitations or dizziness, electrocardiogram (ECG) confirmation of an arrhythmia with the development of recurrent symptoms is essential. A 24-h Holter monitor should be considered only for patients with daily symptoms. For intermittent symptoms that are of a prolonged duration, a patient-activated event monitor can be used to obtain the ECG information without the need for continuous ECG lead attachment and recordings. A patient-activated monitor with a continuously recorded memory loop ("loop recorder") can be used to document short-lived episodes and the onset of the arrhythmia. This is the preferred monitoring technique for symptomatic patients with less frequent arrhythmia events but it requires continuous ECG recording. Patients with infrequent, severe symptoms that cannot be identified by intermittent ECG monitoring may receive an implanted loop ECG monitor that provides more extended periods of monitoring and automatic arrhythmia detection.

In patients who present with more severe symptoms, such as syncope, outpatient monitoring may be insufficient. In patients with structural heart disease and syncope in whom there is suspicion of ventricular tachycardia (VT), hospitalization and diagnostic electrophysiologic testing are warranted, with strong consideration for an implantable cardioverter/defibrillator (ICD) device. The 12-lead ECG recorded in sinus rhythm should be carefully assessed in patients without structural heart disease for evidence of ST-segment elevation in leads V1 and V2 consistent with the Brugada syndrome, QT interval changes consistent with long or short QT syndromes, or a short PR interval and delta wave consistent with Wolff-Parkinson-White (WPW) syndrome. These ECG patterns identify an arrhythmogenic substrate that may cause intermittent life-threatening symptoms and warrant further evaluation and therapy. The individual syndromes are discussed in detail later in this chapter.

Monitoring for asymptomatic tachyarrhythmias is indicated in several specific situations. In patients with a suspected tachycardia-induced cardiomyopathy marked by chamber dilatation and depression in systolic function, the demonstration of arrhythmia control is essential. Monitoring for asymptomatic ventricular premature complexes (VPCs) and nonsustained VT can be helpful in stratifying the risk of SCD in patients with depressed LV function after myocardial infarction. Finally, in patients with asymptomatic atrial fibrillation (AF), anticoagulation treatment strategies depend on an accurate assessment of the presence of this arrhythmia. The duration of monitoring for asymptomatic arrhythmias may vary. The transition from 24-h Holter monitoring to more extended periods of monitoring with technology capable of automatic arrhythmia detection improves the reliability of the monitoring information used in decision-making.

A 12-lead ECG recording during the tachycardia can be an important diagnostic tool in identifying the mechanism and the origin of a tachycardia not afforded by one- or two-lead ECG recordings. A 12-lead ECG of the tachyarrhythmia should be recorded and incorporated as a permanent part of the medical record whenever possible. For patients whose arrhythmias are provoked by exercise, an exercise test may provide the opportunity to obtain 12-lead ECG recordings of the arrhythmia and may obviate the need for more extended periods of monitoring.

Many paroxysmal supraventricular tachyarrhythmias are not associated with a significant risk of structural heart disease, and an evaluation for the presence of ischemic heart disease and cardiac function is uncommonly required unless dictated by the severity or characteristics of the symptoms. However in patients with focal or macroreentrant atrial tachycardias (ATs), atrial flutter (AFL), or AF, an evaluation of cardiac chamber size and function and of valve function is warranted. In patients with VT, an echocardiographic assessment of LV and right ventricular (RV) size and function should be the norm. VT occurring in the setting of depressed LV function should raise the suspicion of advanced coronary artery disease. Polymorphic VT in the absence of QT prolongation should always raise the concern for a potentially unstable ischemic process that may need to be corrected to effect VT control.

Atrial Premature Complexes

APCs are the most common arrhythmia identified during extended ECG monitoring. The incidence of APCs frequently increases with age and with the presence of structural heart diseases. APCs typically are asymptomatic, although some patients experience palpitations or an irregularity of the pulse.

ECG Diagnosis of APCs

The ECG diagnosis of premature atrial complexes is based on the identification of a P wave that occurs prior to the anticipated sinus beat. The source of the APC appears to parallel the typical sites of origin for ATs. The orifices of the superior vena cava and pulmonary veins, the coronary sinus, the crista terminalis, mitral and tricuspid valve annuli, and left and right atrial appendages are common sites of origin of APCs. The P wave contour differs from that noted during sinus rhythm, although APCs from the right atrial appendage, superior vena cava (SVC), and superior aspect of the crista terminalis in the region of the sinus node may mimic the sinus P wave morphology. In response to an APC, the PR interval lengthens, although APCs that originate near the atrioventricular (AV) nodal region may actually have a shorter PR interval because the atrial conduction time to the junction is shortened. A very early APC may not conduct to the ventricle and can create a pulse irregularity that may be perceived as a pause or "dropped beat." If the APC conducts rapidly through the AV node, a partially recovered His-Purkinje system will be encountered and a QRS pattern consistent with a right or left bundle branch block may occur. This wide QRS pattern and the failure to recognize the preceding P wave may result in the misdiagnosis of VPCs. APCs characteristically reset the sinus node. The resulting sum of the pre- and post-APC RR interval is less than two sinus PP intervals.

Atrial Premature Complexes: Treatment

APCs uncommonly require intervention. For extremely symptomatic patients who do not respond to explanation and reassurance, an attempt can be made to suppress the

APCs with pharmacologic agents. The repetitive focus can even be targeted for catheter ablation. Beta blockers are typical first-line therapy, but they may exacerbate symptoms if AV block occurs with the APC and irregularity of the pulse consequently becomes more profound. The use of class IC antiarrhythmic agents may eliminate the APCs but should be avoided if structural heart disease is present.

Junctional Premature Complexes

Junctional premature complexes are extremely uncommon. The complexes originate from the AV node and His bundle region and may produce retrograde atrial activation with the P wave distorting the initial or terminal portions of the QRS complex producing pseudo Q or S waves in leads II, III, and aVF. Extrasystoles originating in the bundle of His that do not conduct to the ventricle and also block the atria can produce unexplained surface ECG PR prolongation that does not follow a typical Wenckebach periodicity, i.e., gradual PR prolongation culminating in atrial activity that fails to conduct to the ventricles. Intracardiac recordings can frequently identify a His depolarization, thus identifying the origin of the complex to the AV junction. Symptomatic patients may be typically treated with beta blockers or, if there is no structural heart disease, class IC antiarrhythmic agents.

SINUS TACHYCARDIA

Physiologic sinus tachycardia represents a normal or appropriate response to physiologic stress, such as occurs with exercise, anxiety, or fever. Pathologic conditions, such as thyrotoxicosis, anemia, or hypotension, may also produce sinus tachycardia. It is important to distinguish sinus tachycardia from other SVTs. Sinus tachycardia will produce a P wave contour consistent with its origin from the sinus node located in the superior-lateral and posterior aspect of the right atrium. The P wave is upright in leads II, III and aVF, and negative in lead aVR. The P wave morphology in lead V1 characteristically has a biphasic, positive/negative contour. Onset of sinus tachycardia is gradual, and in response to carotid sinus pressure there may be some modest and transient slowing but no abrupt termination. Importantly, the diagnosis

should not be based on the PR interval or the presence of a P wave before every QRS complex. The PR interval and the presence of 1:1 AV conduction properties are entirely determined by AV nodal and His-Purkinje conduction and, therefore, the PR interval can be dramatically prolonged while sinus tachycardia remains the mechanism of the atrial activity.

Physiologic Sinus Tachycardia: Treatment

Treatment of physiologic sinus tachycardia is directed at the underlying condition causing the tachycardia response. Uncommonly, beta blockers are used to minimize the tachycardia response if it is determined to be potentially harmful, as may occur in a patient with ischemic heart disease and rate-related anginal symptoms.

Inappropriate Sinus Tachycardia

Inappropriate sinus tachycardia represents an uncommon but important medical condition in which the heart rate increases either spontaneously or out of proportion to the degree of physiologic stress/exercise. Dizziness and even frank syncope can often accompany the sinus tachycardia and symptoms of palpitations. The syndrome can be quite disabling. Associated symptoms of chest pain, headaches, and gastrointestinal upset are common. In many patients, the syndrome occurs after a viral illness and may resolve spontaneously over the course of 3–12 months, suggesting a postviral dysautonomia.

Excluding the diagnosis of an automatic AT that originates in the region of the sinus node can be difficult and may require invasive electrophysiologic evaluation. Frequently, patients are misdiagnosed as having an anxiety disorder with physiologic sinus tachycardia.

Inappropriate Sinus Tachycardia: Treatment

For symptomatic patients, maintaining an increased state of hydration, salt loading, and careful titration of beta blockers to the maximum tolerated dose, administered in divided doses, frequently minimizes symptoms. For severely symptomatic patients

who are intolerant of or unresponsive to beta blockers, catheter ablation directed at modifying the sinus node may be effective. Because of the high recurrence rate after ablation and the frequent need for atrial pacing therapy, this intervention remains second-line treatment.

ATRIAL FIBRILLATION

AF is the most common sustained arrhythmia. It is marked by disorganized, rapid, and irregular atrial activation. The ventricular response to the rapid atrial activation is also irregular. In the untreated patient, the ventricular rate also tends to be rapid and is entirely dependent on the conduction properties of the AV junction. Although typically the rate will vary between 120 and 160 beats/min, in some patients it can be >200 beats/min. In other patients, because of heightened vagal tone or intrinsic AV nodal conduction properties, the ventricular response is <100 beats/min and occasionally even profoundly slow. The mechanism for AF initiation and maintenance, although still debated, appears to represent a complex interaction between drivers responsible for the initiation and the complex anatomic atrial substrate that promotes the maintenance of multiple wavelets of (micro)reentry. The drivers appears to originate predominantly from the atrialized musculature that enters the pulmonary veins and either represent focal abnormal automaticity or triggered firing that is somewhat modulated by autonomic influences. Sustained forms of microreentry as drivers have also been documented around the orifice of pulmonary veins; nonpulmonary vein drivers have also been demonstrated. The role these drivers play in maintaining the tachycardias may also be significant and may explain the success of pulmonary vein isolation procedures in eliminating more chronic or persistent forms of AF.

Although AF is common in the adult population, it is extremely unusual in children unless structural heart disease is present or there is another arrhythmia that precipitates the AF, such as paroxysmal SVT in patients with WPW syndrome. The incidence of AF increases with age such that >5% of the adult population over 70 will experience the arrhythmia. As many patients are asymptomatic with AF, it is anticipated that the

overall incidence, particularly that noted in the elderly, may be more than double previously reported rates. Occasionally AF appears to have a well-defined etiology, such as acute hyperthyroidism, an acute vagotonic episode, or acute alcohol intoxication. Acute AF is particularly common during the acute or early recovery phase of major vascular, abdominal, and thoracic surgery where autonomic fluxes and/or direct mechanical irritation potentiate the arrhythmia. AF may also be triggered by other supraventricular tachycardias (see "AV Nodal Tachycardias"), such as AV nodal reentrant tachycardia (AVNRT), and elimination of these arrhythmias may prevent AF recurrence.

AF has clinical importance related to (1) the loss of atrial contractility, (2) the inappropriate fast ventricular response, and (3) the loss of atrial appendage contractility and emptying leading to the risk of clot formation and subsequent thromboembolic events.

Symptoms from AF vary dramatically. Many patients are asymptomatic and have no apparent hemodynamic consequences to the development of AF. Other patients experience only minor palpitations or sense irregularity of their pulse. Many patients, however, experience severe palpitations. The hemodynamic effect in patients can be quite dramatic, depending on the need for normal atrial contractility and the ventricular response. Hypotension, pulmonary congestion, and anginal symptoms may be severe in some patients. In patients with the LV diastolic dysfunction that occurs with hypertension, hypertrophic cardiomyopathy, or obstructive aortic valvular disease, symptoms may be even more dramatic, especially if the ventricular rate does not permit adequate ventricular filling. Exercise intolerance and easy fatigability are the hallmarks of poor rate control with exertion. Occasionally, the only manifestation of AF is severe dizziness or syncope associated with the pause that occurs upon termination of AF before sinus rhythm resumes.

The ECG in AF is characterized by the lack of organized atrial activity and the irregularly irregular ventricular response. Occasionally, one needs to record from multiple ECG leads simultaneously to identify the chaotic continuous atrial activation. Lead V1 may frequently show the appearance of organized atrial activity that mimics AFL. This occurs because the crista terminalis serves as an effective anatomic barrier to electrical conduction, and the activation of the lateral right atrium may be represented by a more uniform activation wavefront that originates over the roof of the right atrium. ECG assessment of the PP interval (<200 ms) and the chaotic P wave morphology in the remaining ECG leads will confirm the presence of AF.

Evaluation of the patient with AF should include a search for reversible causes of the arrhythmia, such as hyperthyroidism or anemia. An echocardiogram should be performed to determine if there is structural heart disease. Persistent or labile hypertension should be identified and treated, and heart failure treatment should be optimized.

Treatment

Treatment for AF must take into account the clinical situation in which the arrhythmia is encountered, the chronicity of the AF, the status of the patient's level of anticoagulation, risk factors for stroke, the patient's symptoms, the hemodynamic impact of the AF, and the ventricular rate.

Acute Rate Control

In the absence of hemodynamic compromise that might warrant emergent cardioversion to terminate the AF, the initial goals of therapy are (1) to establish control of the ventricular rate, and (2) to address anticoagulation status and begin IV heparin treatment if the duration of AF is >12 h and risk factors for stroke with AF are present. Ventricular rate control for acute AF is best established with beta blockers and/or calcium channel blocking agents, verapamil or diltiazem. The route of administration and dose will be dictated by the ventricular rate and clinical status. Digoxin may add

to the rate-controlling benefit of the other agents but is uncommonly used as a stand-alone agent, especially in acute AF.

Anticoagulation is of particular importance in patients who have known risk factors for stroke associated with AF. Factors associated with the highest risk of stroke include a history of stroke, transient ischemic attack or systemic embolism, or the presence of rheumatic mitral stenosis. Other identified risk factors include age >65 years, history of congestive heart failure, diabetes mellitus, hypertension, LV dysfunction, and evidence of marked left atrial enlargement (>5.0 cm). Chronic anticoagulation with warfarin targeting an INR between 2.0 and 3.0 is recommended in patients with persistent or frequent and long-lived paroxysmal AF and risk factors. If patients have not been adequately anticoagulated and the AF is more than 24–48 h in duration, a transesophageal echocardiogram (TEE) can be performed to exclude the presence of a left atrial thrombus that might dislodge with the attempted restoration of sinus rhythm using either nonpharmacologic or pharmacologic therapy. Anticoagulation must be instituted coincident with the TEE and maintained for at least 1 month following restoration of sinus rhythm if the duration of AF has been prolonged or is unknown. Heparin is maintained routinely until the INR is 1.8 with the administration of warfarin after the TEE. For patients who do not warrant early cardioversion of AF, anticoagulation should be maintained for at least 3 weeks with the INR confirmed to be >1.8 on at least two separate occasions prior to attempts at cardioversion.

Termination of AF acutely may be warranted based on clinical parameters and/or hemodynamic status. Confirmation of appropriate anticoagulation status as described above must be documented unless symptoms and clinical status warrant emergent intervention. Direct current transthoracic cardioversion during short-acting anesthesia is a reliable way to terminate AF. Conversion rates using a 200-J biphasic shock delivered synchronously with the QRS complex typically are >90%. Pharmacologic therapy to terminate AF is less reliable. Oral and/or IV administration of amiodarone or procainamide have only modest success. The acute IV administration of ibutilide appears to be somewhat more effective and may be used in selected patients to facilitate termination with direct current (DC) cardioversion.

Commonly Used Antiarrhythmic Agents—Intravenous Dose Range/Primary Indication

Commonly Used Antiarrhythmic Agents—Intravenous Dose Range/Primary Indication				
Drug	Loading	Maintenance	Primary Indication	Classa
Adenosine	6–18 mg (rapid bolus)	N/A	Terminate reentrant SVT involving AV node	—
Amiodarone	15 mg/min for 10 min, 1 mg/min for 6 h	0.5–1 mg/min	AF, AFL, SVT, VT/VF	III
Digoxin	0.25 mg q2h until 1.0 mg total	0.125–0.25 mg/d	AF/AFL rate control	—
Diltiazem	0.25 mg/kg over 3–5 min (max 20 mg)	5–15 mg/h	SVT, AF/AFL rate control	IV
Esmolol	500 g/kg over 1 min	50 g/kg per min	AF/AFL rate control	II
Ibutilide	1 mg over 10 min if over 60 kg	N/A	Terminate AF/AFL	III
Lidocaine	1–3 mg/kg at 20–50 mg/min	1–4 mg/min	VT	IB
Metoprolol	5 mg over 3–5 min times 3 doses	1.25–5 mg q6h	SVT, AF rate control; exercise-induced VT; long QT	II
Procainamide	15 mg/kg over 60 min	1–4 mg/min	Convert/prevent AF/VT	IA
Quinidine	6–10 mg/kg at 0.3–0.5 mg/kg per min	N/A	Convert/prevent AF/VT	IA
Verapamil	5–10 mg over 3–5 min	2.5–10 mg/h	SVT, AF rate control	IV

Classification of antiarrhythmic drugs:

Class I—agents that primarily block inward sodium current;

Class IA agents also prolong action potential duration;

Class II—antisympathetic agents;

Class III—agents that primarily prolong action potential duration;

Class IV—calcium channel-blocking agents.

Note: SVT, supraventricular tachycardia; AV, atrioventricular; AF, atrial fibrillation; AFL, atrial flutter; VT, ventricular tachycardia; VF, ventricular fibrillation.

Commonly Used Antiarrhythmic Agents—Chronic Oral Dosing/Primary Indications

Commonly Used Antiarrhythmic Agents—Chronic Oral Dosing/Primary Indications					
Drug	Dosing Oral, mg, Maintenance	Half-Life, h	Primary Route(s) of Metabolism/Elimination	Most Common Indication	Classa
Acebutolol	200–400 mg q12h	6–7	Renal/hepatic	AF rate control/SVT	II
				Long QT/RVOT VT	
Amiodarone	100–400 qd	40–55 d	Hepatic	AF/VT prevention	III
Atenolol	25–100 mg/d	6–9	Renal	AF rate control/SVT	II
				Long QT/RVOT VT	
Digoxin	0.125–0.5 qd	38–48	Renal	AF rate control	—
Diltiazem	30–60 q6h	3–4.5	Hepatic	AF rate control/SVT	IV
Disopyramide	100–300 q6–8h	4–10	Renal 50%/hepatic	AF/SVT prevention	Ia
Dofetilide	0.125–0.5 q12h	10	Renal	AF prevention	III
Flecainide	50–200 q12h	7–22	Hepatic 75%/renal	AF/SVT/VT prevention	Ic
Metoprolol	25–100 q6h	3–8	Hepatic	AF rate control/SVT	II
				Long QT/RVOT	

				VT	
Mexiletine	150–300 q8–12h	10–14	Hepatic	VT prevention	Ib
Moricizine	100–400 q8h	3–13	Hepatic 60%/renal	AF prevention	Ic
Nadolol	40–240 mg/d	10–24	Renal	Same as metoprolol	II
Procainamide	250–500 q3–6h	3–5	Hepatic/renal	AF/SVT/VT prevention	Ia
Propafenone	150–300 q8h	2–8	Hepatic	AF/SVT/VT prevention	Ic
Quinidine	300–600 q6h	6–8	Hepatic 75%/renal	AF/SVT/VT prevention	Ia
Sotalol	80–160 q12h	12	Renal	AF/VT prevention	III
Verapamil	80–120 q6–8h	4.5–12	Hepatic/renal	AF rate control/RVOT VT	IV
				Idiopathic LV VT	

Pharmacologic therapy to maintain sinus rhythm can be instituted once sinus rhythm has been established or in anticipation of cardioversion to attempt to maintain sinus rhythm . A single episode of AF may not warrant any intervention or only a short course of beta blocker therapy. To prevent recurrent AF unresponsive to beta blockade, a trial of antiarrhythmic therapy may be warranted, particularly if the AF is associated with rapid rates and/or significant symptoms. The selection of antiarrhythmic agents should be dictated primarily by the presence or absence of coronary artery disease, depressed LV function not attributable to a reversible tachycardia-induced cardiomyopathy, and/or severe hypertension with evidence of marked LV hypertrophy. The presence of any significant structural heart disease typically narrows treatment to the use of sotalol, amiodarone, or dofetilide. Severely depressed LV function may preclude sotalol

therapy or require only low-dose therapy be considered. Owing to the risk of QT prolongation and polymorphic VT, sotalol and dofetilide need to be initiated in hospital in most cases.

In patients without evidence of structural heart disease or hypertensive heart disease without evidence of severe hypertrophy, the use of the class IC antiarrhythmic agents flecainide or propafenone appears to be well tolerated and does not have significant proarrhythmia risk. It is important to recognize that no drug is uniformly effective, and arrhythmia recurrence should be anticipated in over half the patients during long-term follow-up regardless of type and number of agents tried. It is also important to recognize that although the maintenance of sinus rhythm has been associated with improved long-term survival, the survival outcome of patients randomized to the pharmacologic maintenance of sinus rhythm was not superior to those treated with rate control and anticoagulation in the AFFIRM and RACE trials. The AFFIRM and RACE trials compared outcome with respect to survival and thromboembolic events in patients with AF and risk factors for stroke using the two treatment strategies. It is believed that the poor outcome related to pharmacologic therapy used to maintain sinus rhythm was primarily due to frequent inefficacy of such drug therapy and an increased incidence of asymptomatic AF. Many of the drugs used for rhythm control, including sotalol, amiodarone, propafenone, and flecainide, enhance slowing of AV nodal conduction. The absence of symptoms frequently leads to stopping anticoagulant therapy, and asymptomatic AF without anticoagulation increases stroke risk. Any consideration for stopping anticoagulation must, therefore, be accompanied by a prolonged period of ECG monitoring to document asymptomatic AF. It is also recommended that patients participate in monitoring by learning to take their pulse on a twice-daily basis and to reliably identify its regularity if discontinuing anticoagulant therapy is seriously contemplated.

It is clear that to reduce the risk of drug-induced complications when treating AF, a thorough understanding of the drug planned to be used is critical—its dosing, metabolism, and common side effects and important drug-drug interactions. When

using antiarrhythmic agents that slow atrial conduction, strong consideration should be given to adding a beta blocker or a calcium channel blocker (verapamil or diltiazem) to the treatment regimen. This should help to avoid a rapid ventricular response if AF is converted to "slow" AF with the drug therapy.

Common Nonarrhythmic Toxicity of Most Frequently Used Antiarrhythmic Agents	
Drug	Common Nonarrhythmic Toxicity
Amiodarone	Tremor, peripheral neuropathy, pulmonary inflammation, hypothyroidism and hyperthyroidism, photosensitivity
Adenosine	Cough, flushing
Digoxin	Anorexia, nausea, vomiting, visual changes
Disopyramide	Anticholinergic effects, decreased myocardial contractility
Dofetilide	Nausea
Flecainide	Dizziness, nausea, headache, decreased myocardial contractility
Ibutilide	Nausea
Lidocaine	Dizziness, confusion, delirium, seizures, coma
Mexiletine	Ataxia, tremor, gait disturbances, rash, nausea
Moricizine	Mood changes, tremor, loss of mental clarity, nausea,
Procainamide	Lupus erythematosus–like syndrome (more common in slow acetylators), anorexia, nausea, neutropenia
Propafenone	Taste disturbance, dyspepsia, nausea, vomiting
Quinidine	Diarrhea, nausea, vomiting, cinchonism, thrombocytopenia
Sotalol	Hypotension, bronchospasm

Proarrhythmic Manifestations of Most Frequently Used Antiarrhythmic Agents	
Drug	Common Proarrhythmic Toxicity
Amiodarone	Sinus bradycardia, AV block, increase in defibrillation threshold
	Rare: long QT and torsades des pointes, 1:1 ventricular conduction with atrial flutter

Adenosine	All arrhythmias potentiated by profound pauses, atrial fibrillation
Digoxin	High-grade AV block, fascicular tachycardia, accelerated junctional rhythm, atrial tachycardia
Disopyramide	Long QT and torsades des pointes, 1:1 ventricular response to atrial flutter; increased risk of some ventricular tachycardias in patients with structural heart disease
Dofetilide	Long QT and torsades des pointes
Flecainide	1:1 Ventricular response to atrial flutter; increased risk of some ventricular tachycardias in patients with structural heart disease; sinus bradycardia
Ibutilide	Long QT and torsades des pointes
Procainamide	Long QT and torsades des pointes, 1:1 ventricular response to atrial flutter; increased risk of some ventricular tachycardias in patients with structural heart disease
Propafenone	1:1 Ventricular response to atrial flutter; increased risk of some ventricular tachycardias in patients with structural heart disease; sinus bradycardia
Quinidine	Long QT and torsades des pointes, 1:1 ventricular response to atrial flutter; increased risk of some ventricular tachycardias in patients with structural heart disease
Sotalol	Long QT and torsades des pointes, sinus bradycardia

ATRIAL FLUTTER AND MACROREENTRANT ATRIAL TACHYCARDIAS

Macroreentrant arrhythmias involving the atrial myocardium are collectively referred to as AFL. The terms AFL and macroreentrant AT are frequently used interchangeably, with both denoting a nonfocal source of an atrial arrhythmia. The typical or most common AFL circuit rotates in a clockwise or counterclockwise direction in the right atrium around the tricuspid valve annulus. The posterior boundary of the right AFL circuit is defined by the crista terminalis, the Eustachian ridge, and the inferior and superior vena cavae. Counterclockwise right AFL represents ~80% of all AFL with superiorly directed activation of the interatrial septum, which produces the saw-toothed appearance of the P waves in ECG leads II, III, and aVF. Clockwise rotation of the same right atrial circuit produces predominantly positive P waves in leads II, III, and aVF. Macroreentrant left AFL may also develop, albeit much less commonly. This type of arrhythmia may be the sequelae of surgical or catheter-based ablation procedures that create large anatomic barriers or promote slowing of conduction in the left atrium,

especially around the mitral valve annulus. Atypical AFL or macroreentrant AT can also develop around incisions created during surgery for valvular or congenital heart disease or in and/or around large areas of atrial fibrosis.

Classic or typical right AFL has an atrial rate of 260–300 beats/min with a ventricular response that tends to be 2:1, or typically 130–150 beats/min. In the setting of severe atrial conduction disease and or antiarrhythmic drug therapy, the atrial rate can slow to <200 beats/min. In this setting, a 1:1 rapid ventricular response may occur, particularly with exertion, and produce adverse hemodynamic effects (Fig. 226-5). Atypical AFL or macroreentrant AT related to prior surgical incisions and atrial fibrosis demonstrates less predictability in terms of the atrial rate and is more likely to demonstrate slower rates that overlap with those identified with focal atrial tachycardias.

Because lead V1 is frequently monitored in a hospitalized patient, coarse AF may be misdiagnosed as AFL. This occurs because in both typical right AFL and coarse AF the crista terminalis in the right atrium may serve as an effective anatomic barrier. The free wall of the right atrium, whose electrical depolarization is best reflected on the body surface by lead V1, may demonstrate a uniform wavefront of atrial activation under both conditions. The timing of atrial activation is much more rapid in AF and always demonstrates variable atrial intervals with some intervals between defined P waves <200 ms. A review of the other ECG leads demonstrates the disorganized atrial depolarization that is characteristic of AF. Frequently, an individual patient may alternate between AF and AFL or, less commonly, may manifest AF in one atria and AFL in the other, making the distinction more difficult.

Atrial Flutter: Treatment

Because of the anticipated rapid regular ventricular rate associated with AFL and the failure to respond to pharmacologic therapy directed at slowing the ventricular rate, patients are frequently treated with DC cardioversion. The organized atrial flutter activity can frequently be terminated with low-energy external cardioversion of 50–100 J. The risk of thromboembolic events associated with typical AFL is high, and anticoagulation must be managed similarly to that described for patients with AF.

Asymptomatic patients with AFL may develop heart failure symptoms with tachycardia-induced severe LV dysfunction. In all patients, an effort should be made to control the ventricular rate pharmacologically or restore sinus rhythm. Rate control with calcium antagonists (diltiazem or verapamil), beta blockers, and/or digoxin may be difficult. Even higher grade AV slowing, such as a 4:1 AV response, may only be transient and is easily overcome with activity or emotional stress. Owing to the typically faster ventricular rate, AFL tends to be poorly tolerated in comparison to AF. In selected patients with high anesthestic risk, an attempt at pharmacologic cardioversion with procainamide, amiodarone, or ibultilide is appropriate. Antiarrhythmic drug therapy may also enhance the efficacy of direct current cardioversion and the maintenance of sinus rhythm after cardioversion. Recurrence rates of AFL with pharmacologic attempts at rhythm control exceed 80% by 1 year.

Patients who manifest recurrent AFL appear to be effectively treated with catheter ablative therapy. For typical right AFL, an isthmus ablation line from the tricuspid annulus to the opening of the inferior vena cava can permanently eliminate flutter, with an anticipated success rate of >90% in most experienced centers. In patients with macroreentrant atrial tachycardia or AFL involving prior surgical incisions or in areas of atrial fibrosis, detailed mapping of the arrhythmia circuit is required to design the best ablation strategy to interrupt the circuit. In selected patient with AF and typical right AFL, pharmacologic therapy may help to prevent the AF but not the AFL. In this type of patient, hybrid therapy with antiarrhythmic agents coupled with a right atrial isthmus ablation may produce AF and AFL control.

AV NODAL TACHYCARDIAS

AV Nodal Reentrant Tachycardia

AVNRT is the most common paroxysmal regular SVT. It is more commonly observed in women than men and is typically manifest in the second to fourth decades of life. In general, because AVNRT tends to occur in the absence of structural heart disease, it is usually well tolerated. In the presence of hypertension or other forms of structural heart disease that limit ventricular filing, hypotension or syncope may occur.

AVNRT develops because of the presence of two electrophysiologically distinct pathways for conduction in the complex syncytium of muscle fibers that make up the AV node. The fast pathway located in the more superior part of the node has a longer refractory period, while the pathway lower in the AV node region conducts more slowly but has a shorter refractory period. As a result of the inhomogeneities of conduction and refractoriness, a reentrant circuit can develop in response to premature stimulation. Although conduction occurs over both pathways during sinus rhythm, only the conduction over the fast pathway is manifest and, as a result, the PR interval is normal. APCs occurring at a critical coupling interval are blocked in the fast pathway because of the longer refractory period and are conducted slowly over the slow pathway. When sufficient conduction slowing occurs, the blocked fast pathway can recover excitability and atrial activation can occur over the fast pathway to complete the circuit. Repetitive activation down the slow and up the fast pathway results in typical AV nodal reentrant tachycardia.

ECG Findings in AVNRT

The APC initiating AVNRT is characteristically followed by a long PR interval consistent with conduction via the slow pathway. AVNRT is manifest typically as a narrow QRS complex tachycardia at rates that range from 120 to 250 beats/min. The QRS-P wave pattern associated with typical AVNRT is quite characteristic, with simultaneous activation of the atria and ventricles from the reentrant AV nodal circuit. The P wave will frequently be buried inside the QRS complex and either not be visible or will distort the initial or terminal portion of the QRS complex (Fig. 226-7). Because atrial activation originates in the region of the AV node, a negative deflection will be generated by retrograde atrial depolarization.

Occasionally, AVNRT occurs with activation in the reverse direction, conducting down the fast pathway and returning up the slow pathway. This form of AVNRT occurs much less commonly and produces a prolonged RP interval during the tachycardia with

a negative P wave in leads 2, 3, and aVF. This atypical form of AVNRT is more easily precipitated by ventricular stimulation.

Acute Treatment

Treatment is directed at altering conduction within the AV node. Vagal stimulation, such as occurs with the Valsalva maneuver or carotid sinus massage, can slow conduction in the AV node sufficiently to terminate AVNRT. In patients in whom physical maneuvers do not terminate the tachyarrhythmia, the administration of adenosine, 6–12 mg IV, frequently does so. Intravenous beta blockade or calcium channel therapy should be considered second-line agents. If hemodynamic compromise is present, R wave synchronous DC cardioversion using 100–200 J can terminate the tachyarrhythmia.

Prevention

Prevention may be achieved with drugs that slow conduction in the antegrade slow pathway, such as digitalis, beta blockers, or calcium channel blockers. In patients who have a history of exercise-precipitated AVNRT, the use of beta blockers frequently eliminates symptoms. In patients who do not respond to drug therapy directed at the antegrade slow pathway, treatment with class IA or IC agents directed at altering conduction of the fast pathway may be considered.

Catheter ablation, directed at elimination or modification of slow pathway conduction, is very effective in permanently eliminating AVNRT. Patients with recurrent AVNRT that produces significant symptoms or heart rates >200 beats/min and patients reluctant to take chronic drug therapy should be considered for ablative therapy. Catheter ablation can cure AV nodal reentry in >95% of patients. The risk of AV block requiring a permanent pacemaker is ~1% with the ablation procedure. This risk may be further minimized with the use of cryoablation techniques when the slow pathway is in close proximity to the compact AV node.

AV Junctional Tachycardias

These can also occur in the setting of enhanced normal automaticity, abnormal automaticity, or triggered activity. These tachycardias may or may not be associated with retrograde conduction to the atria, and the P waves may appear dissociated or produce intermittent conduction and early activation of the junction. These arrhythmias may occur as a manifestation of increased adrenergic tone or drug effect in patients with sinus node dysfunction or following surgical or catheter ablation. The arrhythmia may also be a manifestation of digoxin toxicity. The most common manifestation of digoxin intoxication is the sudden regularization of the response to AF. A junctional tachycardia due to digoxin toxicity typically does not manifest retrograde conduction. Sinus activity may appear dissociated or result in intermittent capture beats with a long PR interval. If the rate is >50 beats/min and <100 beats/min, the term accelerated junctional rhythm applies. Occasionally, automatic rhythms are mimicked by AVNRT that fails to conduct to the atrium. The triggering events associated with the onset of the tachycardia may provide a clue to the appropriate diagnosis. Initiation of the tachycardia without an atrial premature beat with a gradual acceleration in rate suggests an automatic focus.

Treatment

Treatment of automatic/triggered junctional tachycardias is directed at decreasing adrenergic stimulation and reversing digoxin toxicity, if present. Digoxin therapy can be withheld if toxicity is suspected, and the administration of digoxin-specific antibody fragments can rapidly reverse digoxin toxicity if the tachycardia is producing significant symptoms and rapid termination is indicated. Junctional tachycardia due to abnormal automaticity can be treated pharmacologically with beta blockers. A trial of class IA or IC drugs may also be attempted. For incessant automatic junctional tachycardia, focal catheter ablation can be performed but is associated with an increased risk of AV block.

Tachycardias Associated with Accessory AV Pathways

Tachycardias that involve accessory pathways (APs) between atria and ventricles commonly manifest a normal QRS complex with a short or long RP interval. They

must be considered in the differential diagnosis of other narrow-complex tachycardias. Importantly, most tachycardias associated with APs involve a large macroreentrant circuit that includes the ventricles (Fig. 226-7). Thus, identifying these arrhythmias as "supraventricular" is actually a misnomer, and they deserve separate consideration.

APs are typically capable of conducting rapidly both in an antegrade and retrograde direction. In the absence of an AP, the sinus impulse normally activates the ventricles via the AV node and His-Purkinje system, resulting in a PR interval of 120–200 ms. When an antegradely conducting AP is present, the sinus impulse bypasses the AV node and can rapidly activate the ventricles, resulting in ventricular preexcitation. The resulting PR interval is shorter than anticipated. In addition, because the initial ventricular activation is due to muscle-to-muscle conduction, as opposed to rapid spread of activation via the His-Purkinje system, the initial portion of the QRS complex is slurred, creating the characteristic "delta wave." The remaining portion of the QRS complex in sinus rhythm is created by a fusion of the ventricular activation wavefront originating from the Purkinje network and the continued spread of activation from the site of insertion of the AP. Evidence of ventricular preexcitation includes evidence in sinus rhythm of a short PR interval and a delta wave.

Treatment

Acute treatment of AP-mediated macroreentrant orthodromic tachycardias is similar to that for AV nodal reentry and is directed at altering conduction in the AV node. Vagal stimulation with the Valsalva maneuver and carotid sinus pressure may create sufficient AV nodal slowing to terminate the AVRT. Intravenous administration of adenosine, 6–12 mg, is first-line pharmacologic therapy; IV calcium channel blockers, verapamil or diltiazem, or beta blockers may also be effective. In patients who demonstrate manifest preexcitation and AF, therapy should be aimed at preventing a rapid ventricular response. In life-threatening situations, DC cardioversion should be used to terminate the AF. In non-life-threatening situations, procainamide at a dose of 15 mg/kg administered IV over 20–30 min will slow the ventricular response and may organize and terminate AF. Ibutilide can also be used to facilitate termination of AF.

During AF there may be rapid conduction over the AV node as well as the AP. Caution should be used in attempting to slow AV nodal conduction with the use of digoxin or verapamil; when administered IV, these drugs may actually result in an acute increase in rate over the AP, placing the patient at risk for development of VF. Digoxin appears to shorten the refractory period of the AP directly and thus increases the ventricular rate. Verapamil appears to shorten the refractory period indirectly by causing vasodilatation and a reflex increase in sympathetic tone.

Chronic oral administration of beta blockers and/or verapamil or diltiazem may be used to prevent recurrent supraventricular reentrant tachycardias associated with APs. In patients with evidence of AF and a rapid ventricular response and in those with recurrences of SVT on AV nodal blocking drugs, strong consideration should be given to the administration of either a class IA or IC antiarrhythmic drug, such as quinidine, flecainide, or propafenone, that slow conduction and increase refractoriness in the AP.

Patients with a history of recurrent symptomatic SVT episodes, incessant SVT, and heart rates >200 beats/min with SVT should be given strong consideration for undergoing catheter ablation. Patients who have demonstrated rapid antegrade conduction over their AP or the potential for rapid conduction should also be considered for catheter ablation. Catheter ablation therapy has been demonstrated to be successful in >95% of patients with documented WPW syndrome and appears effective regardless of age. The risk of catheter ablative therapy is low and is dictated primarily by the location of the AP. Ablation of para-Hisian APs is associated with a risk of heart block, and ablation in the left atrium is associated with a small but definite risk of thromboembolic phenomenon. These risks must be weighed against the potential serious complications associated with hemodynamic compromise, the risk of VF, and the severity of the patient's symptoms with AP-mediated tachycardias.

Patients who demonstrate evidence of ventricular preexcitation in the absence of any prior arrhythmia history deserve special consideration. The first arrhythmia

manifestation can be a rapid SVT or, albeit of low risk (<1%), of a life-threatening rapid response to AF. Patients who demonstrate intermittent preexcitation during ECG monitoring or an abrupt loss of AP conduction during exercise testing are at low risk of a life-threatening rapid response to AF. All other patients should be advised of their risks and therapeutic options in advance of a documented arrhythmia event.

VENTRICULAR PREMATURE COMPLEXES (VPCS)

The origin of premature beats in the ventricle at sites remote from the Purkinje network produces slow ventricular activation and a wide QRS complex that is typically >140 ms in duration. VPCs are common and increase with age and the presence of structural heart disease. VPCs can occur with a certain degree of periodicity that has become incorporated into the lexicon of electrocardiography. VPCs may occur in patterns of bigeminy, in which every sinus beat is followed by a VPC, or trigeminy, in which two sinus beats are followed by a VPC. VPCs may have different morphologies and are thus referred to as multiformed. Two successive VPCs are termed pairs or couplets. Three or more consecutive VPCs are termed VT when the rate is >100 beats/min. If the repetitive VPCs terminate spontaneously and are more than three beats in duration, the arrhythmia is referred to as nonsustained VT.

APCs with aberrant ventricular conduction may also create a wide and early QRS complex. The premature P wave can occasionally be difficult to discern when it falls on the preceding T wave, and other clues must be used to make the diagnosis. The QRS pattern for a VPC does not appear to follow a typical right or left bundle branch block pattern as the QRS morphology is associated with aberrant atrial conduction and can be quite bizarre. On occasion, VPCs can arise from the Purkinje network of the ventricles, in which case the QRS pattern mimics aberration. The 12-lead ECG recording of the VPC may be required to identify subtle morphologic clues regarding the QRS complex to confirm its ventricular origin. Most commonly, VPCs are associated with a "fully compensatory pause"; i.e., the duration between the last QRS before the PVC and the next QRS complex is equal to twice the sinus rate. The VPC

typically does not conduct to the atrium. If the VPC does conduct to the atrium, it may not be sufficiently early to reset the sinus node. As a result, sinus activity will occur and the antegrade wavefront from the sinus node may encounter some delay in the AV node or His-Purkinje system from the blocked VPC wavefront, or it may collide with the retrograde atrial wavefront. Sinus activity will continue undisturbed, resulting in a delay to the next QRS complex. Occasionally the VPC can occur early enough and conduct retrograde to the atrium to reset the sinus node; the pause that results will be less than compensatory. VPCs that fail to influence the oncoming sinus impulse are termed interpolated VPCs. A ventricular focus that fires repetitively at a fixed interval may produce variably coupled VPCs, depending on the sinus rate. This type of focus is referred to as a parasystolicfocus because its firing does not appear to be modulated by sinus activity and the conducted QRS complex. The ventricular ectopy will occur at a characteristic fixed integer or multiple of these intervals. The variability in coupling relative to the underlying QRS complex and a fixed interval between complexes of ventricular origin provide the diagnostic information necessary to identify a parasystolic focus.

Treatment

The threshold for treatment of VPCs is high, and the treatment is primarily directed at eliminating severe symptoms associated with palpitations. VPCs of sufficient frequency can cause a reversible cardiomyopathy. Depressed LV function in the setting of ventricular bigeminy and/or frequent nonsustained VT should raise the possibility of a cardiomyopathy that is reversible with control of the ventricular arrhythmia. In the absence of structural heart disease, VPCs do not appear to have prognostic significance. In patients with structural heart disease, frequent VPCs and runs of nonsustained VT have prognostic significance and may portend an increased risk of SCD. However, no study has documented that elimination of VPCs with antiarrhythmic drug therapy reduces the risk of arrhythmic death in patients with severe structural heart disease. In fact, drug therapies that slow myocardial conduction and/or enhance dispersion of

refractoriness can actually increase the risk of life-threatening arrhythmias (drug-induced QT prolongation and TDP) despite being effective at eliminating VPCs.

ACCELERATED IDIOVENTRICULAR RHYTHM (AIVR)

AIVR refers to a ventricular rhythm that is characterized by three or more complexes at a rate >40 beats/min and <120 beats/min. The arrhythmia mechanism causing AIVR is thought to be due to abnormal automaticity. By definition there is an overlap between AIVR and "slow" VT; both rhythms can manifest rates between 90 and 120 beats/min. Because AIVR tends to be a benign rhythm with different therapeutic implications, it is worthwhile to attempt to distinguish it from "slow" VT. AIVR has a characteristic gradual onset and offset and more variability in cycle length. It is typically a brief, self-limiting arrhythmia. AIVR can be seen in the absence of any structural heart disease, but it is frequently present in the setting of acute myocardial infarction, cocaine intoxication, acute myocarditis, digoxin intoxication, and postoperative cardiac surgery. Sustained forms of AIVR can exist, particularly in the setting of acute myocardial infarction and postoperatively. In the setting of sustained AIVR, hemodynamic compromise can occur because of the loss of AV synchrony. Patients with RV infarction associated with proximal right coronary artery occlusion are most susceptible to associated bradyarrhythmias and the hemodynamic consequences of AIVR. In these patients, acceleration of the atrial rate, either by the cautious administration of atropine or by atrial pacing, may be an important treatment consideration.

Ventricular Tachycardia

VT originates below the bundle of His at a rate >100 beats/min; most have rates >120 beats/min. Sustained VT at rates <120 beats/min and even <100 beats/min can be observed, particularly in association with the administration of antiarrhythmic agents that can slow the rate. Because of the overlap in rates with AIVR, the arrhythmia ECG characteristics and the clinical circumstance can sometimes be used to distinguish the

two forms of tachycardia. Slow sustained VT is less likely to show a marked warm-up in rate and the marked cycle-length oscillations seen with AIVR, and it is more likely to occur in the setting of chronic infarction or cardiomyopathy and less likely with acute infarction or myocarditis. Obviously, significant overlap may exist. Typically, slow VT will be initiated with programmed stimulation and is found to represent a large macroreentrant circuit in chronically diseased myocardium capable of supporting markedly slow conduction.

The QRS complex during VT may be uniform (monomorphic) or may vary from beat to beat (polymorphic). Polymorphic VT in patients who demonstrate a long QT interval during their baseline rhythm is typically referred to as TDP. The polymorphic VT associated with QT prolongation dramatically oscillates around the baseline on most of the monitored ECG leads, mimicking the "turning of the points" stitching pattern .

Monomorphic VT suggests a stable tachycardia focus in the absence of structural heart disease or a fixed anatomic substrate that can create the substrate for a stable reentrant VT circuit when structural disease is present. Monomorphic VT tends to be a reproducible and recurrent phenomenon and may be initiated with pacing and programmed ventricular stimulation. In contrast, polymorphic VT suggests a more dynamic and/or unstable process and, by its very nature, is less reproducible. Polymorphic VT may be produced by acute ischemia, myocarditis, or dynamic changes in the QT interval and enhanced dispersion of ventricular refractoriness. Polymorphic VTs are not reliably initiated with pacing or programmed stimulation.

A time duration of 30 s is frequently used to distinguish sustained from nonsustained VT. Hemodynamically unstable VT that requires termination before 30 s or VT that is terminated by therapy from an implantable defibrillator is also typically classified as sustained. Ventricular flutter appears as a sine wave on the ECG and has a rate of >250 beats/min. A rapid rate coupled with the sine wave nature of the arrhythmia makes it impossible to identify a discrete QRS morphology. When antiarrhythmic drugs are

being administered, a sine wave appearance of the QRS complex can be observed, even at rates of 200 beats/min. VF is characterized by completely disorganized ventricular activation on the surface ECG. Polymorphic ventricular arrhythmias, ventricular flutter, and VF always produce hemodynamic collapse if allowed to continue. The hemodynamic stability of a unimorphic VT depends on the presence and severity of the underlying structural heart disease, the location of the site of origin of the arrhythmia, and the heart rate.

It is important to distinguish monomorphic VT from SVT with aberrant ventricular conduction due to right or left bundle branch block.

Importantly, the sinus or baseline 12-lead ECG tracing can provide important clues that help establish the correct diagnosis of a wide complex tachycardia. The presence of an aberrant QRS pattern that matches exactly that of the wide complex rhythm strongly supports the diagnosis of SVT. A right or left bundle branch block QRS pattern that does not match the QRS and/or that is wider in duration than the QRS during the wide complex tachycardia supports the diagnosis of VT. Most patients with VT have structural heart disease and show evidence of a prior Q wave myocardial infarction during sinus rhythm. Important exceptions to this rule are discussed (see "Unique VT Syndromes"). Finally, the presence of a preexcited QRS pattern on the 12-lead ECG in sinus rhythm suggests that the wide complex rhythm represents an atrial arrhythmia, such as AFL or a focal AT, with rapid conduction over an AP or antidromic macroreentrant tachycardia. If the arrhythmia is irregular with changing QRS complexes, then the diagnosis of AF with ventricular preexcitation should be considered.

With the exception of some idiopathic outflow tract tachycardias, most VTs do not respond to vagal stimulation provoked by carotid sinus massage, the Valsalva maneuver, or adenosine administration. The IV administration of verapamil and/or adenosine is not recommended as a diagnostic test. Verapamil has been associated with hemodynamic collapse when administered to patients with structural heart disease and VT.

Patients with VT frequently demonstrate AV disassociation. Findings on physical examination of intermittent cannon a waves and variability of the first heart sound are consistent with AV dissociation. The presence of AV dissociation is characteristically marked by the presence of sinus capture or fusion beats. The presence of 1:1 ventriculo-atrial conduction does not preclude a diagnosis of VT.

Additional characteristics of the 12-lead ECG during the tachycardia that suggest VT include (1) the presence of a QRS duration >140 ms in the absence of drug therapy, (2) a superior and rightward QRS frontal plane axis, (3) a bizarre QRS complex that does not mimic the characteristic QRS pattern associated with left or right bundle branch block, and (4) slurring of the initial portion of the QRS.

Treatment

Sustained polymorphic VT, ventricular flutter, and VF all lead to immediate hemodynamic collapse. Emergency asynchronous defibrillation is therefore required, with at least 200-J monophasic or 100-J biphasic shock. The shock should be delivered asynchronously to avoid delays related to sensing of the QRS complex. If the arrhythmia persists, repeated shocks with the maximum energy output of the defibrillator are essential to optimize the chance of successful resuscitation. Intravenous lidocaine and/or amiodarone should be administered but should not delay repeated attempts at defibrillation.

For any monomorphic wide complex rhythm that results in hemodynamic compromise, a prompt R wave synchronous shock is required. Conscious sedation should be provided if the hemodynamic status permits. For patients with a well-tolerated wide complex tachycardia, the appropriate diagnosis should be established based on strict ECG criteria. Pharmacologic treatment to terminate monomorphic VT is not typically successful (<30%). Intravenous procainamide, lidocaine, or amiodarone can be utilized. If the arrhythmia persists, synchronous R wave cardioversion after the

administration of conscious sedation is appropriate. Selected patients with focal outflow tract tachycardias who demonstrate triggered or automatic VT may respond to IV beta blocker administration. Idiopathic LV septal VT appears to respond uniquely to IV verapamil administration.

VT in patients with structural heart disease is now almost always treated with the implantation of an ICD to manage anticipated VT recurrence. The ICD can provide rapid pacing and shock therapy to treat most VTs effectively.

Prevention of VT remains important, and >50% of patients with a history of VT and an ICD may need to be treated with adjunctive antiarrhythmic drug therapy to prevent VT recurrences or to manage atrial arrhythmias. Because of the presence of an ICD, there is more flexibility with respect to antiarrhythmic drug therapy selection. The use of sotalol or amiodarone represents first-line therapy for patients with a history of structural heart disease and life-threatening monomorphic or polymorphic VT not due to long QT syndrome. Importantly, sotalol has been associated with a decrease in the defibrillation threshold, which reflects the amount of energy necessary to terminate VF. Amiodarone may be better tolerated in patients with a more marginal hemodynamic status and systolic blood pressure. The risk of end organ toxicity from amiodarone must be weighed against the ease of use and general efficacy. Antiarrhythmic drug therapy with agents such as quinidine, procainamide, or propafenone, which might not normally be used in patients with structural heart disease because of the risk of proarrhythmia, may be considered in patients with an ICD and recurrent VT.

Catheter ablative therapy for VT in patients without structural heart disease results in cure rates >90%. In patients with structural heart disease, catheter ablation that includes a strategy for eliminating unmappable/rapid VT and one that incorporates endocardial as well as epicardial mapping and ablation should be employed. In most patients, catheter ablation can reduce or eliminate the requirement for toxic drug therapy and should be considered in any patient with recurrent VT. The utilization of ablative

therapy to reduce the incidence of ICD shocks for VT in patients who receive the ICD as part of primary prevention for VT is being actively investigated.

Management of VT Storm

Repeated VT episodes requiring external cardioversion/defibrillation or repeated appropriate ICD shock therapy is referred to as VT storm. While a definition of more than two episodes in 24 h is used, most patients with VT storm will experience many more episodes. In the extreme form of VT storm, the tachycardia becomes incessant and the baseline rhythm is unable to be restored for any extended period. In patients with recurrent polymorphic VT in the absence of the long QT interval, one should have a high suspicion of active ischemic disease or fulminant myocarditis. Intravenous lidocaine or amiodarone administration should be coupled with prompt assessment of the status of the coronary anatomy. Endomyocardial biopsy, if indicated by clinical circumstance, may be used to confirm the diagnosis of myocarditis, although the diagnostic yield is low. In patients who demonstrate QT prolongation and recurrent pause-dependent polymorphic VT (TDP), removal of an offending QT-prolonging drug, correction of potassium or magnesium deficiencies, and emergency pacing to prevent pauses should be considered. Intravenous beta blockade therapy should be considered for polymorphic VT storm. A targeted treatment strategy should be employed if the diagnosis of the polymorphic VT syndrome can be established. For example, quinidine or isoproterenol can be used in the treatment of Brugada's syndrome (see "Brugada Syndrome: Treatment"). Intraaortic balloon counterpulsation or acute coronary angioplasty may be needed to stop recurrent polymorphic VT precipitated by acute ischemia. In selected patients with a repeating VPC trigger for their polymorphic VT, the VPC can be targeted for ablation to prevent recurrent VT.

In patients with recurrent monomorphic VT, acute IV administration of lidocaine, procainamide, or amiodarone can prevent recurrences. The use of such therapy is empirical, and a clinical response is not certain. Procainamide and amiodarone are more likely to slow the tachycardia and make it hemodynamically tolerated.

Unfortunately, antiarrhythmic drugs, especially those that slow conduction (e.g., amiodarone, procainamide), can also facilitate recurrent VT or even result in incessant VT. VT catheter ablation can eliminate frequent recurrent or incessant VT and frequent ICD shocks. Such therapy should be deployed earlier in the course of arrhythmia events to prevent adverse consequences of recurrent VT episodes and adverse effects from antiarrhythmic drugs.

THE BRADYARRHYTHMIAS

Electrical activation of the heart normally originates in the sinoatrial (SA) node, the predominant pacemaker. Other subsidiary pacemakers in the atrioventricular (AV) node, specialized conducting system, and muscle may initiate electrical activation if the SA node is dysfunctional or suppressed. Typically subsidiary pacemakers discharge at a slower rate and, in the absence of an appropriate increase in stroke volume, may result in tissue hypoperfusion.

Spontaneous activation and contraction of the heart are the consequence of the specialized pacemaking tissue found within these anatomic locales. Action potentials in the heart are regionally heterogeneous. The action potentials in cells isolated from nodal tissue are distinct from those recorded from atrial and ventricular myocytes. The complement of ionic currents present in nodal cells results in a less negative resting membrane potential compared with atrial or ventricular myocytes. Electrical diastole in nodal cells is characterized by slow diastolic depolarization (phase 4), which generates an action potential as the membrane voltage reaches threshold. The action potential upstrokes (phase 0) are slow compared with atrial or ventricular myocytes, being mediated by calcium rather than sodium current. Cells with properties of SA and AV nodal tissue are electrically connected to the remainder of the myocardium by cells with an electrophysiologic phenotype between that of nodal cells and atrial or ventricular myocytes. Cells in the SA node exhibit the most rapid phase 4 depolarization and thus are the dominant pacemakers in the normal heart.

Bradycardia results from either a failure of impulse initiation or impulse conduction. Failure of impulse initiation may be caused by depressed automaticity resulting from a slowing or failure of phase 4 diastolic depolarization, which may result from disease or exposure to drugs. Prominently, the autonomic nervous system modulates the rate of phase 4 diastolic depolarization and, thus, the firing rate of both primary (SA node) and subsidiary pacemakers. Failure of conduction of an impulse from nodal tissue to atrial or ventricular myocardium may produce bradycardia as a result of exit block. Conditions that alter activation and connectivity of cells (e.g., fibrosis) in the heart may result in failure of impulse conduction.

SA node dysfunction and AV conduction block are the most common causes of pathologic bradycardia. SA node dysfunction may be difficult to distinguish from physiologic sinus bradycardia, particularly in the young. SA node dysfunction increases in frequency between the fifth and sixth decades of life and should be considered in patients with fatigue, exercise intolerance, or syncope and sinus bradycardia. Transient AV block is common in the young and likely the result of the high vagal tone found in up to 10% of young adults. Acquired and persistent failure of AV conduction is decidedly rare in healthy adult populations, with an estimated incidence of ~200/million population per year.

Permanent pacemaking is the only reliable therapy for symptomatic bradycardia in the absence of extrinsic and reversible etiologies such as increased vagal tone, hypoxia, hypothermia, and drugs.

Etiologies of SA Node Dysfunction	
Extrinsic	**Intrinsic**
Autonomic	Sick sinus syndrome (SSS)
Carotid sinus hypersensitivity	Coronary artery disease (chronic and acute MI)
Vasovagal (cardioinhibitory) stimulation	Inflammatory

Drugs	Pericarditis
Beta blockers	Myocarditis (including viral)
Calcium channel blockers	Rheumatic heart disease
Digoxin	Collagen vascular diseases
Antiarrhythmics (class I and III)	Lyme disease
Adenosine	Senile amyloidosis
Clonidine (other sympatholytics)	Congenital heart disease
Lithium carbonate	TGA/Mustard and Fontan repairs
Cimetidine	Iatrogenic
Amitriptyline	Radiation therapy
Phenothiazines	Post surgical
Narcotics (methadone)	Chest trauma
Pentamidine	Familial
Hypothyroidism	AD SSS, OMIM #163800 (15q24-25)
Sleep apnea	AR SSS, OMIM #608567 (3p21)
Hypoxia	SA node disease with myopia, OMIM 182190
Endotracheal suctioning (vagal maneuvers)	Kearns-Sayre syndrome, OMIM #530000
Hypothermia	Myotonic dystrophy
Increased intracranial pressure	Type 1, OMIM #160900 (19q13.2-13.3)
	Type 2, OMIM #602668 (3q13.3-q24)
	Friedreich's ataxia, OMIM #229300 (9q13, 9p23-p11)

Note: MI, myocardial infarction; TGA, transposition of the great arteries; AD, autosomal dominant; AR, autosomal recessive; OMIM, Online Mendelian Inheritance in Man (database).

SA NODE DISEASE

Structure and Physiology of the SA Node

The SA node is composed of a cluster of small fusiform cells located in the sulcus terminalis on the epicardial surface of the heart at the right atrial–superior vena caval junction, where they envelop the SA nodal artery. The SA node is structurally

heterogeneous, but the central prototypic nodal cells have fewer distinct myofibrils than the surrounding atrial myocardium, no intercalated disks visible on light microscopy, a poorly developed sarcoplasmic reticulum, and no T-tubules. Cells in the peripheral regions of the SA node are transitional in both structure and function. The SA nodal artery arises from the right coronary artery in 55–60% and left circumflex artery in 40–45% of persons. The SA node is richly innervated by sympathetic and parasympathetic nerves and ganglia.

Irregular and slow propagation of impulses from the SA node can be explained by the electrophysiology of nodal cells and the structure of the SA node itself. The action potentials of SA nodal cells are characterized by a relatively depolarized membrane potential of –40 to –60 mV, slow phase 0 upstroke, and relatively rapid phase 4 diastolic depolarization compared to the action potentials recorded in cardiac muscle cells. The relative absence of inward rectifier potassium current (IK1) accounts for the depolarized membrane potential; the slow upstroke of phase 0 is the result of the absence of available fast sodium current (INa) and is mediated by L-type calcium current (ICa-L); and phase 4 depolarization is the result of the aggregate activity of a number of ionic currents. Prominently, both L- and T-type (ICa-T) calcium currents, the pacemaker current (so-called funny current, or If) formed by the tetramerization of hyperpolarization-activated cyclic nucleotide-gated channels, and the electrogenic sodium-calcium exchanger provide depolarizing current that is antagonized by delayed rectifier (IKr) and acetylcholine-gated (IKACh) potassium currents. ICa-L, ICa-T, and If are modulated by -adrenergic stimulation and IKACh by vagal stimulation, explaining the exquisite sensitivity of diastolic depolarization to autonomic nervous system activity. The slow conduction within the SA node is explained by the absence of INa and poor electrical coupling of cells in the node, resulting from sizeable amounts of interstitial tissue and a low abundance of gap junctions. The poor coupling allows for graded electrophysiological properties within the node, with the peripheral transitional cells being silenced by electrotonic coupling to atrial myocardium.

Etiology of SA Nodal Disease

SA nodal dysfunction has been classified as intrinsic or extrinsic. The distinction is important because extrinsic dysfunction is often reversible and should generally be corrected before considering pacemaker therapy. The most common causes of extrinsic SA node dysfunction are drugs and autonomic nervous system influences that suppress automaticity and/or compromise conduction. Other extrinsic causes include hypothyroidism, sleep apnea, and conditions likely to occur in critically ill patients such as hypothermia, hypoxia, increased intracranial pressure (Cushing's response), and endotracheal suctioning via activation of the vagus nerve.

Intrinsic sinus node dysfunction is degenerative and often characterized pathologically by fibrous replacement of the SA node or its connections to the atrium. Acute and chronic coronary artery disease (CAD) may be associated with SA node dysfunction, although in the setting of acute myocardial infarction (MI; typically inferior), the abnormalities are transient. Inflammatory processes may alter SA node function, ultimately producing replacement fibrosis. Pericarditis, myocarditis, and rheumatic heart disease have been associated with SA nodal disease with sinus bradycardia, sinus arrest, and exit block. Carditis associated with systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and mixed connective tissue disorders (MCTDs) may also affect SA node structure and function. Senile amyloidosis is an infiltrative disorder in patients typically in their ninth decade of life; deposition of amyloid protein in the atrial myocardium can impair SA node function. Some SA node disease is iatrogenic and the result of surgical correction of congenital heart disease, particularly palliative repair of corrected transposition of the great arteries by the Mustard procedure.

Rare heritable forms of sinus node disease have been described, and several have been genetically characterized. Autosomal dominant sinus node dysfunction in conjunction with supraventricular tachycardia (i.e., tachycardia-bradycardia variant of sick-sinus syndrome, SSS) has been linked to mutations in the pacemaker current (If) subunit gene HCN4 on chromosome 15. An autosomal recessive form of SSS with the

prominent feature of atrial inexcitability and absence of P waves on the electrocardiogram (ECG) is caused by mutations in the cardiac sodium channel gene, SCN5A, on chromosome 3. SSS associated with myopia has been described but not genetically characterized. There are several neuromuscular diseases including Kearns-Sayre syndrome (ophthalmoplegia, pigmentary degeneration of the retina, and cardiomyopathy) and myotonic dystrophy that have a predilection for the conducting system and SA node.

SSS in both the young and the elderly is associated with an increase in fibrous tissue in the SA node. The onset of SSS may be hastened by coexisting disease, such as CAD, diabetes mellitus, hypertension, and valvular diseases and cardiomyopathies.

Clinical Features of SA Node Disease

SA node dysfunction may be completely asymptomatic and manifest as an ECG anomaly such as sinus bradycardia; sinus arrest and exit block; or alternating supraventricular tachycardia, usually atrial fibrillation, and bradycardia. Symptoms associated with SA node dysfunction, and in particular tachycardia-bradycardia syndrome, may be related to both bradycardia and tachycardia. For example, tachycardia may be associated with palpitations, angina pectoris, and heart failure; and bradycardia may be associated with hypotension syncope, presyncope, fatigue, and weakness. In the setting of SSS, overdrive suppression of the SA node may result in prolonged pauses and syncope upon termination of the tachycardia. In many cases, symptoms associated with SA node dysfunction are the result of concomitant cardiovascular disease. A significant minority of patients with SSS will develop signs and symptoms of heart failure that may be related to slow or fast heart rates.

One-third to one-half of patients with SA node dysfunction will develop supraventricular tachycardia, usually atrial fibrillation or atrial flutter. The incidence of chronic atrial fibrillation in patients with SA node dysfunction increases with advanced age, hypertension, diabetes mellitus, left ventricular dilation, valvular heart

disease, and ventricular pacing. Remarkably, some symptomatic patients may experience an improvement in symptoms with the development of atrial fibrillation, presumably from an increase in their average heart rate. Patients with the tachycardia-bradycardia variant of SSS, similar to patients with atrial fibrillation, are at risk for thromboembolism, and those at greatest risk, including patients 65 years, or patients with a prior history of stroke, valvular heart disease, left ventricular dysfunction, or atrial enlargement, should be treated with anticoagulants. Up to one-quarter of patients with SA node disease will have concurrent AV conduction disease; although only a minority will require specific therapy for high-grade AV block.

The natural history of SA node dysfunction is one of varying intensity of symptoms even in patients who present with syncope. Symptoms related to SA node dysfunction may be significant, but overall mortality is usually not compromised in the absence of other significant comorbid conditions. These features of the natural history need to be taken into account when considering therapy in these patients.

Electrocardiography of SA Node Disease

The electrocardiographic manifestations of SA node dysfunction include sinus bradycardia, sinus pauses, sinus arrest, sinus exit block, tachycardia (in SSS), and chronotropic incompetence. It is often difficult to distinguish pathologic from physiologic sinus bradycardia. By definition sinus bradycardia is a rhythm driven by the SA node with a rate of <60 beats/min; sinus bradycardia is very common and typically benign. Resting heart rates of <60 beats/min are very common in young healthy individuals and physically conditioned subjects. A sinus rate of <40 beats/min in the awake state in the absence of physical conditioning is generally considered abnormal. Sinus pauses and sinus arrest result from the failure of the SA node to discharge, producing a pause without P waves visible on the ECG. Sinus pauses of up to 3 s are common in the awake athlete, and pauses of this duration or longer may be observed in asymptomatic elderly subjects. Intermittent failure of conduction from the SA node produces sinus exit block. The severity of sinus exit block may vary in a

manner similar to that of AV block (see below). Prolongation of conduction from the sinus node will not be apparent on the ECG; second-degree SA block will produce intermittent conduction from the SA node and a regularly irregular atrial rhythm.

Type I second-degree SA block results from progressive prolongation of SA node conduction with intermittent failure of the impulses originating in the sinus node to conduct to the surrounding atrial tissue. Second-degree SA block appears on the ECG as an intermittent absence of P waves (Fig. 225-4). In type II second-degree SA block there is no change in the P-R interval before the pause. Complete or third-degree SA block results in no P waves on the ECG. Tachycardia-bradycardia syndrome is manifest as alternating sinus bradycardia and atrial tachyarrhythmias. Although atrial tachycardia, atrial flutter, and atrial fibrillation may be observed, the latter is the most common tachycardia. Chronotropic incompetence is the inability to increase the heart rate in response to exercise or other stress appropriately and is defined in greater detail below.

Diagnostic Testing

SA node dysfunction is most commonly a clinical or electrocardiographic diagnosis. Sinus bradycardia or pauses on the resting ECG are rarely sufficient to diagnose SA node disease, and longer-term recording and symptom correlation are generally required. Symptoms in the absence of sinus bradyarrhythmias may be sufficient to exclude a diagnosis of SA node dysfunction.

Electrocardiographic recording plays a central role in the diagnosis and management of SA node dysfunction. Despite the limitations of the resting ECG, longer-term recording employing Holter or event monitors may permit correlation of symptoms with the cardiac rhythm. Many contemporary event monitors may be automatically triggered to record the ECG when certain programmed heart rate criteria are met. Implantable ECG monitors permit long-term recording (12–18 months) in particularly challenging patients.

Failure to increase the heart rate with exercise is referred to as chronotropic incompetence. This is alternatively defined as a failure to reach 85% of predicted maximal heart rate at peak exercise, or failure to achieve a heart rate > 100 beats/min with exercise or a maximal heart rate with exercise less than two standard deviations below that of an age-matched control population. Exercise testing may be useful in discriminating chronotropic incompetence from resting bradycardia and may aid in the identification of the mechanism of exercise intolerance.

Autonomic nervous system testing is useful in diagnosing carotid sinus hypersensitivity; pauses >3 s are consistent with the diagnosis but may be present in asymptomatic elderly subjects. Determining the intrinsic heart rate (IHR) may distinguish SA node dysfunction from slow heart rates resulting from high vagal tone. The normal IHR after administration of 0.2 mg/kg propranolol and 0.04 mg/kg atropine is 117.2 – (0.53 x age) in beats/min; a low IHR is indicative of SA disease.
Electrophysiologic testing may play a role in the assessment of patients with presumed SA node dysfunction and in the evaluation of syncope, particularly in the setting of structural heart disease. In this circumstance, electrophysiologic testing is used to rule out more malignant etiologies of syncope such as ventricular tachyarrhythmias and AV conduction block. There are several ways to assess SA node function invasively. These include the sinus node recovery time (SNRT), defined as the longest pause after cessation of overdrive pacing of the right atrium near the SA node (normal: <1500 ms or, corrected for sinus cycle length, <550 ms); and the sinoatrial conduction time (SACT), defined as one-half the difference between the intrinsic sinus cycle length and a noncompensatory pause after a premature atrial stimulus (normal < 125 ms). The combination of an abnormal SNRT, an abnormal SACT, and a low IHR is a sensitive and specific indicator of intrinsic SA node disease.

Treatment

Since SA node dysfunction is not associated with increased mortality, the aim of therapy is alleviation of symptoms. Exclusion of extrinsic causes of SA node dysfunction and correlation of the cardiac rhythm with symptoms is an essential part of patient management. Pacemaker implantation is the primary therapeutic intervention in patients with symptomatic SA node dysfunction. Pharmacologic considerations are important in the evaluation and management of patients with SA nodal disease. A number of drugs modulate SA node function and are extrinsic causes of dysfunction (Table 225-1). Beta blockers and calcium channel blockers increase SNRT in patients with SA node dysfunction, and antiarrhythmic drugs with class I and III action may promote SA node exit block. In general such agents should be discontinued prior to making decisions regarding the need for permanent pacing in patients with SA node disease. Chronic pharmacologic therapy for sinus bradyarrhythmias is limited. Some pharmacologic agents may improve SA node function; digitalis, for example, has been shown to shorten SNRT in patients with SA node dysfunction. Isoproterenol or atropine administered IV may increase the sinus rate acutely. Theophylline has been used both acutely and chronically to increase heart rate but has liabilities when used in patients with tachycardia-bradycardia syndrome, increasing the frequency of supraventricular tachyarrhythmias; and in patients with structural heart disease, increasing the risk of potentially serious ventricular arrhythmias. At the current time, there is only a single randomized study of therapy for SA node dysfunction. In patients with resting heart rates <50 and >30 beats/min on a Holter monitor, patients who received dual-chamber pacemakers experienced significantly fewer syncopal episodes and had symptomatic improvement compared to patients randomized to theophylline or no treatment.

In certain circumstances, sinus bradycardia requires no specific treatment or only temporary rate support. Sinus bradycardia is common in patients with acute inferior or posterior MI and can be exacerbated by vagal activation induced by pain or the use of drugs such as morphine. Ischemia of the SA nodal artery probably occurs in acute

coronary syndromes more typically with involvement with the right coronary artery, and even with infarction, the effect on SA node function is most often transient.

Sinus bradycardia is a prominent feature of carotid sinus hypersensitivity and neurally mediated hypotension associated with vasovagal syncope that responds to pacemaker therapy. Carotid hypersensitivity with recurrent syncope or presyncope associated with a predominant cardioinhibitory component responds to pacemaker implantation. Several randomized trials have demonstrated that patients with drug-refractory vasovagal syncope have fewer recurrences and longer time to recurrence of symptoms with permanent pacing.

ATRIOVENTRICULAR CONDUCTION DISEASE

Structure and Physiology of the AV Node

The AV conduction axis is structurally complex, involving the atria and ventricles as well as the AV node. Unlike the SA node, the AV node is a subendocardial structure originating in the transitional zone, which is composed of aggregates of cells in the posterior-inferior right atrium. Superior, medial, and posterior transitional atrionodal bundles converge on the compact AV node. The compact AV node (~1 x 3 x 5 mm) is located at the apex of the triangle of Koch, which is defined by the coronary sinus ostium posteriorly, the septal tricuspid valve annulus anteriorly, and the tendon of Todaro superiorly. The compact AV node continues as the penetrating AV bundle where it immediately traverses the central fibrous body and is in close proximity to the aortic, mitral, and tricuspid valve annuli; thus, it is subject to injury in the setting of valvular heart disease or its surgical treatment. The penetrating AV bundle continues through the annulus fibrosis and emerges along the ventricular septum adjacent to the membranous septum as the bundle of His. The right bundle branch (RBB) emerges from the distal AV bundle in a band that traverses the right ventricle (moderator band). In contrast, the left bundle branch (LBB) is a broad subendocardial sheet of tissue on the septal left ventricle. The Purkinje fiber network emerges from the RBB and LBB

and extensively ramifies on the endocardial surfaces of the right and left ventricles, respectively.

The blood supply to the penetrating AV bundle is from the AV nodal artery and first septal perforator of the left anterior descending coronary artery. The bundle branches also have a dual blood supply from the septal perforators of the left anterior descending coronary artery and branches of the posterior descending coronary artery. The AV node is highly innervated with postganglionic sympathetic and parasympathetic nerves. The bundle of His and distal conducting system are minimally influenced by autonomic tone.

The cells that comprise the AV node complex are heterogeneous with a range of action potential profiles. In the transitional zones, the cells have an electrical phenotype between atrial myocytes and cells of the compact node. Atrionodal transitional connections may exhibit decremental conduction, defined as slowing of conduction with increasingly rapid rates of stimulation. Fast and slow AV nodal pathways have been described, but controversy remains as to whether these two types of pathway are anatomically distinct or represent functional heterogeneities in different regions of the AV nodal complex. Myocytes that comprise the compact node are depolarized (resting membrane potential ~ –60 mV); exhibit action potentials with low amplitudes, slow upstrokes of phase 0 (<10 V/s), and phase 4 diastolic depolarization; high-input resistance; and relative insensitivity to external [K+]. The action potential phenotype is explained by the complement of ionic currents expressed. AV nodal cells lack IK1 and INa; ICa-L is responsible for phase 0; and phase 4 depolarization reflects the composite activity of the depolarizing currents If, ICa-L, ICa-T, and INCX and the repolarizing currents IKr and IKACh. Electrical coupling between cells in the AV node is tenuous due to the relatively sparse expression of gap junction channels (predominantly connexin-40) and increased extracellular volume.

The His bundle and bundle branches are insulated from ventricular myocardium. The most rapid conduction in the heart is observed in these tissues. The action potentials exhibit very rapid upstrokes (phase 0), prolonged plateaus (phase 2), and modest automaticity (phase 4 depolarization). Gap junctions, composed largely of connexin-40, are abundant but bundles are poorly connected transversely to ventricular myocardium.

Etiology of AV Conduction Disease

Conduction block from the atrium to the ventricle can occur for a variety of reasons in a number of clinical situations, and AV conduction block may be classified in a number of ways. The etiologies may be functional or structural, in part analogous to extrinsic and intrinsic causes of SA nodal dysfunction. The block may be classified by its severity from first to third degree or complete AV block, or by the location of block within the AV conduction system. Most etiologies produce structural changes, typically fibrosis, in segments of the AV conduction axis that are generally permanent. Heightened vagal tone during sleep or in well-conditioned individuals can be associated with all grades of AV block. Carotid sinus hypersensitivity, vasovagal syncope, and cough and micturition syncope may be associated with SA node slowing and AV conduction block. Transient metabolic and endocrinologic disturbances as well as a number of pharmacologic agents may also produce reversible AV conduction block.

Etiologies of Atrioventricular Block	
Autonomic	
Carotid sinus hypersensitivity	Vasovagal
Metabolic/endocrine	
Hyperkalemia	Hypothyroidism
Hypermagnesemia	Adrenal insufficiency
Drug-related	

Beta blockers	Adenosine
Calcium channel blockers	Antiarrhythmics (class I & III)
Digitalis	Lithium
Infectious	
Endocarditis	Tuberculosis
Lyme disease	Diphtheria
Chagas disease	Toxoplasmosis
Syphilis	
Heritable/congenital	
Congenital heart disease	Facioscapulohumeral MD, OMIM #158900 (4q35)
Maternal SLE	
Kearns-Sayre syndrome, OMIM #530000	Emery-Dreifuss MD, OMIM #310300 (Xq28)
Myotonic dystrophy	Progressive familial heart block, OMIM #113900 (19q13.2-q13.3, 3p21)
Type 1, OMIM #160900 (19q13.2-13.3)	
Type 2, OMIM #602668 (3q13.3-q24)	
Inflammatory	
SLE	MCTD
Rheumatoid arthritis	Scleroderma
Infiltrative	
Amyloidosis	Hemochromatosis
Sarcoidosis	
Neoplastic/traumatic	
Lymphoma	Radiation
Mesothelioma	Catheter ablation
Melanoma	

Degenerative	
Lev disease	Lenègre disease
Coronary artery disease	
Acute MI	

Note: SLE, systemic lupus erythematosus; OMIM, Online Mendelian Inheritance in Man (database); MCTD, mixed connective tissue disease; MI, myocardial infarction.

Several infectious diseases have a predilection for the conducting system. Lyme disease may involve the heart in up to 50% of cases; 10% of patients with Lyme carditis develop AV conduction block, which is generally reversible but may require temporary pacing support. Chagas disease, common in Latin America, and syphilis may produce more persistent AV conduction disturbances. Some autoimmune and infiltrative diseases may produce AV conduction block including SLE, RA, MCTD, scleroderma, amyloidosis (primary and secondary), sarcoidosis, and hemochromatosis; rare malignancies may also impair AV conduction.

Idiopathic progressive fibrosis of the conduction system is one of the more common and degenerative causes of AV conduction block. Aging is associated with degenerative changes in the summit of the ventricular septum, central fibrous body, and aortic and mitral annuli and has been described as "sclerosis of the left cardiac skeleton." The process typically begins in the fourth decade of life and may be accelerated by atherosclerosis, hypertension with arteriosclerosis, and diabetes mellitus. Accelerated forms of progressive familial heart block have been identified in families with mutations in the cardiac sodium channel gene (SCN5A) and a second locus that has been mapped to chromosome 19.

AV conduction block has been associated with heritable neuromuscular diseases, including the nucleotide repeat disease myotonic dystrophy, the mitochondrial myopathy Kearns-Sayre syndrome, and several of the monogenic muscular dystrophies. Congenital AV block may be observed in complex congenital cardiac

anomalies, such as transposition of the great arteries, ostium primum atrial septal defects (ASD), ventricular septal defects (VSD), endocardial cushion defects, and some single ventricle defects. Congenital AV block in the setting of a structurally normal heart has been seen in children born to mothers with SLE. Iatrogenic AV block may occur during mitral or aortic valve surgery, rarely in the setting of thoracic radiation, and as a consequence catheter ablation. AV block is a decidedly rare complication of the surgical repair of VSDs or ASDs but may complicate Fontan or Mustard repairs of transposition of the great arteries.

CAD may produce transient or persistent AV block. In the setting of coronary spasm, ischemia, particularly in the right coronary artery distribution, may produce transient AV block. In acute MI, AV block transiently develops in 10–25% of patients; most commonly this is first- or second-degree AV block but complete heart block (CHB) may also occur. Second-degree and higher grade AV block tends to occur more often in inferior rather than anterior acute MI; however, the level of block in inferior MI tends to be in the AV node with more stable, narrow escape rhythms. In contrast, acute anterior MI is associated with block in the distal AV nodal complex, His bundle, or bundle branches and results in wide complex, unstable escape rhythms and a worse prognosis with high mortality.

Electrocardiography and Electrophysiology of AV Conduction Block

Atrioventricular conduction block is typically diagnosed electrocardiographically which characterizes the severity of the conduction disturbance and allows one to draw inferences about the location of block. AV conduction block manifests as slow conduction in its mildest forms and failure to conduct, either intermittent or persistently, in more severe varieties. First-degree AV block (PR interval > 200 ms) is a slowing of conduction through the AV junction. The site of delay is typically in the AV node but may be in the atria, AV node bundle of His, or His-Purkinje system; a wide QRS complex favors distal conduction and narrow QRS complex delay in the node proper or, less commonly, in the bundle of His. In second-degree AV block there

is an intermittent failure of electrical impulse conduction from atrium to ventricle. Second-degree AV block is subclassified as Mobitz type 1 or Wenckebach and Mobitz type 2. The periodic failure of conduction in Mobitz type 1 block is characterized by a progressively lengthening PR interval, shortening of the RR interval, and a pause that is less than two times the immediately preceding RR interval on the ECG. The ECG complex after the pause exhibits a shorter PR interval that that immediately preceding the pause. This ECG pattern most often arises because of decremental conduction of electrical impulses in the AV node.

It is important to distinguish type 1 from type 2 second-degree AV nodal block because the latter has more serious prognostic implications. Type 2 second-degree AV block is characterized by intermittent failure of conduction of the P wave without changes in the preceding PR or RR intervals. When AV block is 2:1 it may be difficult to distinguish type 1 from type 2 block. Type 2 second-degree AV block typically occurs in the distal or infra-His conduction system, is often associated with intraventricular conduction delays (e.g., bundle branch block), and is more likely to proceed to higher grades of AV block than is type 1 second-degree AV block. Second-degree AV block (particularly type 2) may be associated with a series of nonconducted P waves, referred to as paroxysmal AV block, and implies significant conduction system disease and an indication for permanent pacing. Complete failure of conduction from atrium to ventricle is referred to as complete or third-degree AV block. AV block that is intermediate between second and third degree is referred to as high-grade AV block, and, as with CHB, implies advanced AV conduction system disease. In both cases, block is most often distal to the AV node, and the duration of the QRS complex can be helpful in determining the level of block. In the absence of a preexisting bundle branch block, a wide QRS escape rhythm implies block in the distal His or bundle branches; in contrast, a narrow QRS rhythm implies block in the AV node or proximal His and an escape rhythm originating in the AV junction. Narrow QRS escape rhythms are typically faster and more stable than wide QRS escape rhythms and originate more proximally in the AV conduction system.

Diagnostic Testing

Diagnostic testing in the evaluation of AV block is aimed at determining the level of conduction block, particularly in asymptomatic patients, since the prognosis and therapy depend upon whether block is in or below the AV node. Vagal maneuvers, carotid sinus massage, exercise, and administration of drugs such as atropine or isoproterenol may be diagnostically informative. Owing to the differences in innervation of the AV node and infranodal conduction system, vagal stimulation and carotid sinus massage slow conduction in the AV node but have less of an effect on infranodal tissue and may even improve conduction due to a reduced rate of activation of distal tissues. Conversely, atropine, isoproterenol, and exercise improve conduction through the AV node and impair infranodal conduction. In patients with congenital CHB and a narrow QRS complex, exercise typically increases heart rate; by contrast, those with acquired CHB, particularly with wide QRS, do not respond to exercise with an increase in heart rate.

Additional diagnostic evaluation, including electrophysiologic testing, may be indicated in patients with syncope and suspected high-grade AV block. This is particularly relevant if noninvasive testing does not reveal the cause of syncope or if the patient has structural heart disease with ventricular tachyarrhythmias as a cause of symptoms. Electrophysiologic testing provides more precise information regarding the location of AV conduction block and permits studies of AV conduction under conditions of pharmacologic stress and exercise. Recording of the His bundle electrogram by a catheter positioned at the superior margin of the tricuspid valve annulus provides information about conduction at all levels of the AV conduction axis. A properly recorded His bundle electrogram reveals local atrial activity, the His electrogram, and local ventricular activation; when monitored simultaneously with recorded body surface electrocardiographic traces, intraatrial, AV nodal, and infranodal conduction times can be assessed.

The PA interval, the time from the earliest onset of the P wave on the surface ECG to the onset of the atrial deflection on the His bundle catheter, is an index of intraatrial conduction time and should be 50 ms. The time from the most rapid deflection of the atrial electrogram in the His bundle recording to the His electrogram (AH interval) represents conduction through the AV node and is normally <130 ms. Finally, the time from the His electrogram to the earliest onset of the QRS on the surface ECG (HV interval) represents the conduction time through the His-Purkinje system and is normally 55 ms. Rate stress produced by pacing can unveil abnormal AV conduction. Mobitz I second-degree AV block at short atrial paced cycle lengths is a normal response; however, when it occurs at atrial cycle lengths > 500 ms (<120 beats/min) in the absence of high vagal tone, it is abnormal. Typically type I second-degree AV block is associated with prolongation of the AH interval representing conduction slowing and block in the AV node. Block below the node with prolongation of the HV interval or a His bundle electrogram with no ventricular activation is abnormal unless it is elicited at fast pacing rates or short coupling intervals with extra stimulation.

First-degree AV block is classically intranodal and is associated with a prolonged AH interval. Often, AH prolongation is due to the effect of drugs (beta blockers, calcium channel blockers, digitalis), or increased vagal tone. Atropine can be used to reverse high vagal tone; however, if AH prolongation and AV block at long pacing cycle lengths persist, intrinsic AV node disease is likely. Mobitz type 1 second-degree AV block is usually intranodal and type 2 second-degree block is infranodal, frequently in the His-Purkinje system. It is often difficult to determine the type of second-degree AV block when 2:1 conduction is present; however, the finding of a His bundle electrogram after every atrial electrogram indicates that block is occurring in the distal conduction system.

Intracardiac recording at electrophysiologic study that reveals the presence of His-Purkinje conduction block is associated with an increased risk of progression to higher grades of block and is generally an indication for pacing. In the setting of bundle branch

block, the HV interval may reveal the condition of the unblocked bundle and the prognosis for developing more advanced AV conduction block. Prolongation of the HV interval in patients with asymptomatic bundle branch block is associated with an increased risk of developing higher-grade AV block. The risk increases with greater prolongation of the HV interval such that in patients with an HV interval > 100 ms, the annual incidence of complete AV block approaches 10%, indicating a need for pacing. In patients with acquired CHB, even if intermittent, there is little role for electrophysiologic testing, and pacemaker implantation is almost always indicated.

Atrioventricular Conduction Block: Treatment

Temporary or permanent artificial pacing is the most reliable treatment for patients with symptomatic AV conduction system disease. However, exclusion of reversible causes of AV block and the need for temporary heart rate support based on the hemodynamic condition of the patient are essential considerations in each patient. Correction of electrolyte derangements and ischemia, inhibition of excessive vagal tone, and withholding drugs with AV nodal blocking properties may increase the heart rate. Adjunctive pharmacologic treatment with atropine or isoproterenol may be useful if block is in the AV node. Since most pharmacologic treatment may take some time to initiate and become effective, temporary pacing may be necessary. The most expeditious technique is the use of transcutaneous pacing, where pacing patches are placed anteriorly over the cardiac apex (cathode) and posteriorly between the spine and scapula or above the right nipple (anode). Acutely, transcutaneous pacing is highly effective, but its duration is limited by patient discomfort and longer-term failure to capture the ventricle owing to changes in lead impedance. If a patient requires more than a few minutes of pacemaker support, transvenous temporary pacing should be instituted. Temporary pacing leads can be placed from the jugular or subclavian venous system and advanced to the right ventricle, permitting stable temporary pacing for many days, if necessary. In most circumstances, in the absence of prompt resolution, conduction block distal to the AV node requires permanent pacemaking.

Permanent Pacemakers

Nomenclature and Complications

The main therapeutic intervention in SA node dysfunction and AV conduction block is permanent pacing. Since the first implementation of permanent pacing in the 1950s, many advances in technology have resulted in miniaturization, increased longevity of pulse generators, improvement in leads, and increased functionality. In order to better understand pacemaker therapy of bradycardias, it is important to be familiar with fundamentals of pacemaking. Pacemaker modes and function are named using a five-letter code. The first letter indicates the chamber(s) that is paced (O, none; A, atrium; V, ventricle; D, dual; S, single), the second is the chamber(s) in which sensing occurs (O, none; A, atrium; V, ventricle; D, dual; S, single), the third is the response to a sensed event (O, none; I, inhibition; T, triggered; D, inhibition + triggered), the fourth letter refers to the programmability or rate response (R, rate responsive), and the fifth refers to the existence of antitachycardia functions if present (O, none; P, antitachycardia pacing; S, shock; D, pace + shock). Almost all modern pacemakers are multiprogrammable and have the capability for rate responsiveness using one of several rate sensors: activity or motion, minute ventilation, or QT interval. The most commonly programmed modes of implanted single- and dual-chamber pacemakers are VVIR and DDDR, respectively, although multiple modes can be programmed in modern pacemakers.

Although pacemakers are highly reliable, they are subject to a number of complications related to implantation and electronic function. In adults, permanent pacemakers are most commonly implanted with access to the heart by way of the subclavian–superior vena cava venous system. Rare, but possible, acute complications of transvenous pacemaker implantation include infection, hematoma, pneumothorax, cardiac perforation, diaphragmatic/phrenic nerve stimulation, and lead dislodgment. Limitations of chronic pacemaker therapy include infection, erosion, lead failure, and abnormalities resulting from inappropriate programming or interaction with the patient's native electrical cardiac function. Rotation of the pacemaker pulse generator

in its subcutaneous pocket, either intentionally or inadvertently, often referred to as "twiddler's syndrome," can wrap the leads around the generator and produce dislodgment with failure to sense or pace the heart. The small size and light weight of contemporary pacemakers makes this a rare complication.

A common problem is pacemaker syndrome; a constellation of signs and symptoms associated with any mode of pacing that does not maintain or restore AV synchrony. The symptoms include neck pulsation, fatigue, palpitations, cough, confusion, exertional dyspnea, dizziness, and syncope, and they may be associated with an elevation in jugular venous pressure, canon A waves, and stigmata of congestive heart failure, including edema, rales, and a third heart sound. Often, there is a substantial drop in blood pressure with ventricular pacing. The management of pacemaker syndrome involves changing the pacing mode to restore AV synchrony.

Pacemaker Therapy in SA Node Dysfunction

Pacing in SA nodal disease is indicated to alleviate symptoms of bradycardia. Consensus guidelines published by the AHA/ACC/HRS outline the indications for the use of pacemakers, and categorize them by class based on levels of evidence. Class I conditions are those for which there is evidence or consensus of opinion that therapy is useful and effective. In class II conditions there is conflicting evidence or a divergence of opinion about the efficacy of a procedure or treatment; in class IIa conditions the weight of evidence or opinion favors treatment, and in class IIb conditions, efficacy is less well established by the evidence or opinion of experts. In class III conditions, the evidence or weight of opinion indicates that the therapy is not efficacious or useful, and may be harmful.

Class I indications for pacing in SA node dysfunction include documented symptomatic bradycardia, sinus node dysfunction–associated long-term drug therapy for which there is no alternative, or symptomatic chronotropic incompetence. Class IIa indications include those outlined previously in which sinus node dysfunction is

suspected but not documented and for syncope of unexplained origin in the presence of major abnormalities of SA node dysfunction. Mildly symptomatic individuals with heart rates consistently <40 beats/min comprise a class IIb indication for pacing. Pacing is not indicated in patients with SA node dysfunction who do not have symptoms and in those in whom bradycardia is associated with the use of nonessential drugs.

Summary of Guidelines for Pacemaker Implantation in SA Node Dysfunction

Class I

1. SA node dysfunction with symptomatic bradycardia or sinus pauses
2. Symptomatic SA node dysfunction as a result of essential long-term drug therapy with no acceptable alternatives
3. Symptomatic chronotropic incompetence

Class IIa

1. SA node dysfunction with heart rates < 40 beats/min without a clear and consistent relationship between bradycardia and symptoms
2. SA node dysfunction with heart rates < 40 beats/min on an essential long-term drug therapy with no acceptable alternatives, without a clear and consistent relationship between bradycardia and symptoms
3. Syncope of unknown origin when major abnormalities of SA node dysfunction are discovered or provoked by electrophysiologic testing

Class IIb

1. Mildly symptomatic patients with waking chronic heart rates < 40 beats/min

Class III

1. SA node dysfunction in asymptomatic patients even those with heart rates < 40 beats/min
2. SA node dysfunction in which symptoms suggestive of bradycardia are not associated with a slow heart rate
3. SA node dysfunction with symptomatic bradycardia due to nonessential drug therapy

There is some controversy regarding the mode of pacing that should be employed in SA node disease. A number of randomized, single-blind trials of pacing mode have been performed. There are no trials that demonstrate an improvement in mortality with AV synchronous compared with single-chamber pacing in SA node disease. In some of these studies, the incidence of atrial fibrillation and thromboembolic events was reduced with AV synchronous pacing. In trials of patients with dual-chamber pacemakers designed to compare single-chamber with dual-chamber pacing by crossover design, the need for AV synchronous pacing due to pacemaker syndrome was common. Pacing modes that preserve AV synchrony appear to be associated with a reduction in the incidence of atrial fibrillation and improved quality of life. Because of the low but finite incidence of AV conduction disease, patients with SA node dysfunction will usually undergo dual-chamber pacemaker implantation.

Pacemaker Therapy in Carotid Sinus Hypersensitivity and Vasovagal Syncope

Carotid sinus hypersensitivity, if accompanied by a significant cardioinhibitory component, responds well to pacing. In this circumstance, pacing is only required intermittently and single-chamber ventricular pacing is often sufficient. The mechanism of vasovagal syncope is incompletely understood but appears to involve activation of cardiac mechanoreceptors with consequent activation of neural centers that mediate vagal activation and withdrawal of sympathetic nervous system tone. Several randomized clinical trials have been performed in patients with drug-refractory vasovagal syncope, with a reduction in the frequency and the time to recurrent syncope in patients who were paced compared to those who were not.

Pacemakers in AV Conduction Disease

There are no randomized trials that evaluate the efficacy of pacing in patients with AV block as there are no reliable therapeutic alternatives for AV block and untreated high-grade AV block is potentially lethal. The consensus guidelines for pacing in acquired AV conduction block in adults provide a general outline for situations in which pacing is indicated. Pacemaker implantation should be performed in any patient with

symptomatic bradycardia and irreversible second- or third-degree AV block, regardless of the cause or level of block in the conducting system. Symptoms may include those directly related to bradycardia and low cardiac output or to worsening heart failure, angina, or intolerance to an essential medication. Pacing in patients with asymptomatic AV block should be individualized; situations in which pacing should be considered are in those patients with acquired CHB, particularly in the setting of cardiac enlargement; left ventricular dysfunction; and waking heart rates of 40 beats/min. Patients who have asymptomatic second-degree AV block of either type should be considered for pacing if the block is demonstrated to be intra- or infraHis, or is associated with a wide QRS complex. Pacing may be indicated in asymptomatic patients under special circumstances; in patients with profound first-degree AV block and left ventricular dysfunction in whom a shorter AV interval produces hemodynamic improvement, and in the setting of milder forms of AV conduction delay (first-degree AV block, intraventricular conduction delay) in patients with neuromuscular diseases that have a predilection for the conduction system, such as myotonic dystrophy and other muscular dystrophies, and Kearns-Sayre syndrome.

Guideline Summary for Pacemaker Implantation in Acquired AV Block

Class I

1. Third-degree or high-grade AV block at any anatomic level associated with:
   a. Symptomatic bradycardia
   b. Essential drug therapy that produces symptomatic bradycardia
   c. Periods of asystole > 3 s or any escape rate < 40 beats/min while awake
   d. Postoperative AV block not expected to resolve
   e. Catheter ablation of the AV junction
   f. Neuromuscular diseases such as myotonic dystrophy, Kearns-Sayre syndrome, Erb dystrophy, and peroneal muscular atrophy, regardless of the presence of symptoms
2. Second-degree AV block with symptomatic bradycardia
3. Type II second-degree AV block with a wide QRS complex with or without symptoms

Class IIa

1. Asymptomatic third-degree AV block regardless of level
2. Asymptomatic type II second-degree AV block with a narrow QRS complex
3. Asymptomatic type II second-degree AV block with block within or below the His at electrophysiologic study
4. First- or second-degree AV block with symptoms similar to pacemaker syndrome

Class IIb

1. Marked first-degree AV block (PR interval > 300 ms) in patients with LV dysfunction in whom shortening the AV delay would improve hemodynamics
2. Neuromuscular diseases, such as myotonic dystrophy, Kearns-Sayre syndrome, Erb dystrophy, and peroneal muscular atrophy, with any degree of AV block regardless of the presence of symptoms

Class III

1. Asymptomatic first-degree AV block
2. Asymptomatic type I second-degree AV block at the AV node level
3. AV block that is expected to resolve or is unlikely to recur (Lyme disease, drug toxicity)

Pacemaker Therapy in Myocardial Infarction

Atrioventricular block in acute MI is often transient, particularly in inferior infarction. The circumstances under which pacing is indicated in acute MI are persistent second- or third-degree AV block, particularly if symptomatic, and transient second- or third-degree AV block associated with bundle branch block (Table 225-5). Pacing is generally not indicated in the setting of transient AV block in the absence of intraventricular conduction delays, or in the presence of fascicular block or first-degree AV block that develops in the setting of preexisting bundle branch block. Fascicular blocks that develop in acute MI in the absence of other forms of AV block also do not require pacing.

Guideline Summary for Pacemaker Implantation in AV Conduction Block in Acute Myocardial Infarction (AMI)

Class I

1. Persistent second-degree AV block in the His-Purkinje system with bilateral bundle branch block or third-degree block within or below the His after AMI
2. Transient advanced (second- or third-degree) infranodal AV block and associated bundle branch block. If the site of block is uncertain, an electrophysiologic study may be necessary
3. Persistent and symptomatic second- or third-degree AV block

Class IIb

1. Persistent second- or third-degree AV block at the AV node level

Class III

1. Transient AV block in the absence of intraventricular conduction defects
2. Transient AV block in the presence of isolated left anterior fascicular block
3. Acquired left anterior fascicular block in the absence of AV block
4. Persistent first-degree AV block in the presence of bundle branch block that is old or age-indeterminate

Indications for Pacemaker Implantation in Chronic Bifascicular and Trifascicular Block

Class I

1. Intermittent third-degree AV block
2. Type II second-degree AV block
3. Alternating bundle branch block

Class IIa

1. Syncope not demonstrated to be due to AV block when other likely causes (e.g., ventricular tachycardia) have been excluded
2. Incidental finding at electrophysiologic study of a markedly prolonged HV interval (>100 ms) in asymptomatic patients
3. Incidental finding at electrophysiologic study of pacing-induced infra-His block that is not physiologic

Class IIb

1. Neuromuscular diseases, such as myotonic dystrophy, Kearns-Sayre syndrome, Erb dystrophy, and peroneal muscular atrophy, with any degree of fascicular block regardless of the presence of symptoms, because there may be unpredictable progression of AV conduction disease

Class III

1. Fascicular block without AV block or symptoms
2. Fascicular block with first-degree AV block without symptoms

Distal forms of AV conduction block may require pacemaker implantation in certain clinical settings. In patients with bifascicular or trifascicular block and symptoms, particularly syncope that is not attributable to other causes, should undergo pacemaker implantation. Pacemaking is indicated in asymptomatic patients with bifascicular or trifascicular block who experience intermittent third-degree, type II second-degree AV block, or alternating bundle branch block. In patients with fascicular block who are undergoing electrophysiologic study, a markedly prolonged HV interval or block below the His at long cycle lengths may also constitute an indication for permanent pacing. In patients with fascicular block and the neuromuscular diseases previously described should also undergo pacemaker implantation.

Selection of Pacing Mode

In general, a pacing mode that maintains AV synchrony reduces complications of pacing such as pacemaker syndrome and pacemaker-mediated tachycardia. This is particularly true in younger patients, but the importance of dual-chamber pacing, especially in the elderly, is not well established. Several studies have failed to demonstrate a difference in mortality in older patients with AV block treated with a single- (VVI) compared to a dual- (DDD) chamber pacing mode. In some of these studies that randomized pacing mode, the risk of chronic atrial fibrillation and stroke risk decreased with physiologic pacing. In patients with sinus rhythm and AV block, the very modest increase in risk with dual-chamber pacemaker implantation appears to be justified to avoid the possible complications of single-chamber pacing.

Knowledge control:

1. What is the definition of arrhythmia?
2. What are he criteria of normal sinus rhythm?
3. The major etiological factors and triggers of rhythm and conduction disorders.
4. The mechanisms of rhythm and conduction disorders.
5. What is the up-to-date classification of rhythm and conduction disorders?
6. Point the criteria for diagnosis of rhythm and conduction disorders.
7. What particular patterns of rhythm and conduction disorders should be indexed?
8. Risk stratification of patients with rhythm and conduction disorders
9. The value, prejudicial evidence and contraindications of different diagnostic tests for diagnosis of rhythm and conduction disorders
10. Etiological factors, pathogenesis, clinical patterns of different supraventricular arrhythmias (tachy-, bradycardias, atrial fibrillation, flutter, premature beats etc.)
11. Etiological factors, pathogenesis, clinical patterns of different ventricular arrhythmias (tachy-, bradycardias, premature beats etc.)
12. Risk factors and major causes of sudden cardiac death
13. Etiological factors, pathogenesis, clinical patterns of conduction disorders
14. The clinical pharmacology of the basic drugs used in the treatment of rhythm and conduction disorders
15. Principles of non-pharmacological treatment of rhythm and conduction disorders.

Test tasks:

1. A 5-year-old child had an attack of palpitation with nausea, dizziness, generalized fatigue. On ECG: tachycardia with heartbeat rate of 220/min. Ventricle complexes are deformed and widened. P wave is absent. What medication is to be prescribed to provide first aid?

A. Isoptin

B. Seduxen

C. Lydocain

D. Novocainamides

E. Strophantin

2. A patient with ischemic heart disease and chronic heart failure develops sudden loss of consciousness. On exam: cyanosis, the widened pupils, peripheral pulse and blood pressure are not denned. On ECG: ventricular complexes are absent; instead of them there are waves of different shape and amplitude with irregular rhythm. What is the mechanism of this rhythm disorder development?

A. Disorder of neurohumoral regulatory systems

B. Accelerated diastolic depolarization, a disorder in electrolyte balance

C. Sick sinus syndrome

D. Multiple microreentry in the ventricles

E. Enhanced automatic activity of the ventricles

3. A patient with a history of coronary artery disease and atrial fibrillation develops sudden pain and weakness of the left leg. Examination reveals a cool, pale extremity with absent pulses below the groin and normal contralateral leg. What is the most likely diagnosis?

A. Arterial embolism

B. Acute thrombophlebitis

C. Cerebrovascular accident

D. Arterial thrombosis

E. Dissecting aortic aneurysm

4. A youth aged 17 complains of a sudden onset of palpitation 10 minutes ago. On examination, skin of the normal colour. Heart borders without changes, HR=Ps=200 bmp, regular rhythm. BP - 135/75 mm Hg. Heart sounds are intensified. On ECG: QRS = 0.09 sec. What measure is to be undertaken on the first stage of aid?

A. Cardioversion

B. Novocainamid I.V.

C. Vagal tests

D. Propranolol per os

E. No treatment

5. A 67 y.o. patient complains of palpitation, dizziness, noise in ears, feeling of shortage of air. Objectively: pale, damp skin. Vesicular respiration, respiratory rate — 22 per min, pulse — 200 bpm, AP—100/70 mm Hg. On ECG: heart rate — 200 bmp, ventricular complexes are widened, deformed, location of segments ST and of wave T is discordant. The wave P is not changed, superimposes QRST, natural conformity between P and QRS is not present. What kind of arrhythmia is present?

A. Paroxismal ventricular tachycardia
B. Atrial flutter
C. Atrial tachycardia
D. Sinus tachycardia
E. Ventricular extrasystole

6. A 70 y.o. patient complains of weakness, dizziness, short periods of loss of consciousness, pain in the region of heart. Objectively: HR- 40/min, sounds are rhytmic, the 1st sound is dull, occasionally very intensive. AP — 180/90 mm Hg. What is the most probable reason of hemodynamic disorders?

A. Sinus bradycardia
B. Complete block of the left branch of His bundle
C. I degree atrioventricular heart block
D. III degree atrioventricular heart block
E. Bradysystolic form of the atrial fibrillation

7. A 47-year-old man presents to the hospital complaining of palpitations. The patient reports that while cooking breakfast this morning, he felt his heart "racing in his chest" and was unable to catch his breath. He states that sitting down brought no relief. He called for an ambulance and he was brought to the emergency department. The man has no significant past medical history and takes no medications regularly, other than ranitidine for occasional heartburn. On examination, the patient is quite thin, but well

developed and in mild distress. His globes appear exophthalmic. His pulse is 140/min and irregularly irregular. There are no murmurs, and the lung examination is clear. A non-tender midline thyroid mass is palpable. Which of the following findings on his echocardiogram would suggest a diagnosis of long-standing atrial fibrillation?

A. Dilated left ventricle

B. Dilated right ventricle

C. Enlarged left atrium

D. Hypertrophied ventricular septum

E. Pericardial thickening

8. Which of the following is considered the most cost-effective screening method to identify young athletes (younger than 40 years) at risk for sudden cardiac death (SCD)?

A. Careful medical history and examination

B. Chest x-ray

C. Echocardiography

D. Exercise ECG

E. Resting ECG

9. A 21-year-old man is brought by his roommate to the emergency department because of abrupt onset of shortness of breath, mild chest pain, and a sensation of rapid heart beating. The patient says that in the past he had similar episodes, which resolved with the Valsalva maneuver or breath holding. This time, these measures were unsuccessful. He does not take anymedication and is otherwise in good health. An ECG documents supraventricular tachycardia with a pulse of 200/min. Under ECG monitoring, gentle massage over the right carotid sinus is attempted, but the attack does not cease. Which of the following is the most appropriate next step in treatment?

A. Further carotid sinus massage

B. IV lidocaine

C. IV procainamide

D. IV verapamil

E. Oral verapamil

10. A 61-year-old man is hospitalized after receiving an implantable cardiac defibrillator (ICD). The patient has a long history of coronary disease and sustained an anteri-or wall myocardial infarction 3 years ago. Two weeks ago, he had an episode of pulseless ventricular tachycardia and was successfully resuscitated. This episode led to the ICD placement. In addition to the ICD, the cardiologist also plans to initiate antiarrhythmic therapy with amiodarone. Which of the following is the most important side effect of this therapy?

A. Hypotension

B. Pulmonary fibrosis

C. Prolongation of the QT interval

D. Recurrent ventricular arrhythmia

E. Skin discoloration

11. A 23-year-old woman comes to the clinic because of palpitations for the past 18 hours. She has no medical history. Her only medication is an oral contraceptive pill. She describes a rash to sulfa-containing agents and denies tobacco, alcohol, or drug use. On examination, she is anxious appearing. Her temperature is 37.0 C (98.6 F), blood pressure is 102/67 mm Hg, pulse is 109/min, and respirations are 24/min. Her cardiac rhythm is irregular. No murmurs can be heard. Her lungs are clear to auscultation bilaterally. An electrocardiogram shows atrial fibrillation. The most appropriate next step in management is to order a

A. cardiac stress test

B. serum thyroid-stimulating hormone level

C. transesophageal echocardiogram

D. urine hCG level

E. ventilation-perfusion scan

12. A 52-year-old man comes to the emergency department complaining of crushing substernal chest pain and shortness of breath. As you are interviewing the patient, he

suddenly becomes unresponsive. The electrocardiographic findings are shown. You do not feel a pulse. You quickly stabilize his airway and begin chest compressions. A nurse beginsventilating the patient with an ambu-bag and face mask. The most appropriate next step in management is to

A. amiodarone load

B defibrillate at 200 J

C. intubate immediately

D. push adenosine

E. push epinephrine

13. A 23-year-old woman comes to the urgent care clinic for the evaluation of a "rapid heart beat." She describes two prior episodes of this heart rhythm. She has no prior medical history, and is on no medications. She denies any allergies to any medications. Her temperature is 37.2 C (99.0 F), blood pressure is 112/67 mm Hg, pulse is 131/min, and respirations are 25/min. Her cardiac rhythm is regular and her breath sounds are clear to auscultation bilaterally. An electrocardiogram shows a paroxysmal, supraventricular tachycardia (PSVT).

The most appropriate management at this time is

A. administration of intravenous heparin

B. administration of a loading dose of digoxin

C. carotid massage

D. immediate cardioversion

14. A 76-year-old woman from Portugal is admitted to the hospital because of a poor appetite and weight loss. She has a past medical history of hypertension, hyper-cholesterolemia, and a background of "strokes" in her family. While hospitalized she begins to experience feelings of palpitations and shortness of breath. An electrocardiogram shows atrial fibrillation, and when you compare this electrocardiogram with previous ones in her charts you note that this is her first episode of atrial fibrillation. Appropriate rate control is achieved with diltiazem.

Echocardiography reveals no cardiomegaly and a normal left atrial dimension. The therapy that would give this patient the highest likelihood of conversion from atrial fibrillation to sinus rhythm is

A. amiodarone

B. direct-current cardioversion

C. propafenone

D. quinidine

E. sotalol

15. The appropriate step is taken, however the attack does not cease. The most appropriate next step in management is to

A. administer adenosine, intravenously

B. administer lidocaine, intravenously

C. administer procainamide, intravenously

D. insert a permanent pacemaker

E. perform a direct-current cardioversion

16. A 70-year-old woman with a history of recurrent ventricular tachycardia comes to the office with joint and muscle pain, fatigue, and a rash of 4 weeks duration. She tells you that she takes several "heart pills." On reviewing her chart, you note that no new medications have been started in the previous 6 months. Your physical examination finds her to be in no acute distress but with some discomfort in the joints of her hands and feet and muscle tenderness. On her nose and cheeks there is a confluent erythema and edema. Laboratory studies indicate a low hemoglobin and hematocrit level with elevated reticulocyte count. The medication that is the most likely cause of her condition is

A. digoxin

B. disopyramide

C. minoxidil

D. procainamide

E. quinidine.

Topic 4. Preparation for practical training № 4 «Acute respiratory failure. Acute respiratory distress syndrome. Acute allergies»

Learning objective

The student must know:

- determination of acute respiratory failure, acute respiratory distress syndrome, acute allergies;
- clinical manifestations of acute respiratory failure, acute respiratory distress syndrome, acute allergies;
- criteria for diagnosing acute respiratory failure, acute respiratory distress syndrome, acute allergies;
- laboratory and instrumental manifestations of acute respiratory failure, acute respiratory distress syndrome, acute allergies;
- main manifestations, differential diagnosis of acute respiratory failure, acute respiratory distress syndrome, acute allergies;
- principles of emergency care for patients with acute respiratory failure, acute respiratory distress syndrome, acute allergies;
- algorithm for providing emergency care

Be able:

- determine the state of emergency
- perform differential diagnosis with other emergencies
- assign appropriate emergency care

Master practical skills:

- pulse oximetry.
- electrocardiography in 12 standard leads.

Theoretical material for independent student training.

Respiratory Failure includes any condition that affects breathing and ultimately results in failure of the lungs to function properly. The main tasks of the lungs and chest are to get oxygen into the bloodstream from air that is inhaled (breathed in) and, at the

same to time, to eliminate carbon dioxide (C02) from the bloodstream through air that is exhaled (breathed out). In respiratory failure, either the level of oxygen in the blood becomes dangerously low, and/or the level of C02 becomes dangerously high. Ministry of Health and Family Welfare has come out with the Standard Treatment Guidelines for Acute Respiratory Failure. Following are its major recommendations.

Case definition: Respiratory failure is defined as a failure of gas exchange manifestedeither as hypoxemia (PO2 <60mm Hg on room air) i.e. inadequate blood oxygenation or hypercapnia (PaCO2>45 mm Hg) i.e. excess of circulating carbon dioxide or frequently a combination of both types of gas exchange abnormalities. Practically/ clinically diagnosed as respiratory fatigue.

Differential Diagnosis/ Types :

Type 1

Type 1 respiratory failure is defined as hypoxemia without hypercapnia, and indeed the PaCO2 may be normal or low. The basic defect in type 1 respiratory failure is failure of oxygenation characterized by:

PaO2 low (< 60 mmHg (8.0 kPa) on room air

PaCO2 normal or low

This type of respiratory failure is caused by conditions that affect oxygenation such as:

• Parenchymal disease (V/Q mismatch)

• Diseases of vasculature and shunts: right-to-left shunt, pulmonary embolism

• Interstitial lung diseases: ARDS, pneumonia, emphysema.

Type 2

The basic defect in type 2 respiratory failure is characterized by:

PaO2 decreased

PaCO2 increased

Type 2 respiratory failure occurs as a result of alveolar hypoventilation and results in inability to effectively eliminate carbon dioxide. The commonest cause of type II respiratory failure is COPD.

Other causes are:

1. Impaired central nervous system drive to breathe

Drug over dose

Brain stem injury

Sleep disordered breathing

Hypothyroidism

2. Impaired strength with failure of neuromuscular function in the respiratory system Myasthenia Gravis

Guillian Barre Syndrome

Amyotrophic Lateral Sclerosis

Phrenic nerve injury

Respiratory muscle weakness secondary to myopathy,electrolyte imbalance, fatigue

3. Increased loads on the respiratory system

- Resistive-bronchospasm (Asthma, Emphysema, Chronic Obstructive Pulmonary Disease)
- Decreased lung compliance-Alveolar edema, Atelectasis, Auto peep
- Decreased chest wall compliance- Pneumothorax, Pleural effusion, Abdominal distension Increased minute ventilation requirement- pulmonary embolism by increase in dead space ventilation, sepsis and in any patient with type I respiratory failure with fatigue.

Type 3 and 4 occur in setting of perioperative period due to atelectasis and muscle hypoperfusion respectively.

Investigations:

Pulse oxymetric assessment of SpO2 to assess blood oxygen content / hypoxia.

Chest x-ray:Details regarding evidence of consolidation, pulmonary edema, COPD and various other pathology

Complete blood count, electrolytes

Electrocardiogram

ARDS

Acute respiratory distress syndrome (ARDS) is a form of acute-onset hypoxemic

respiratory failure caused by acute inflammatory edema of the lungs and not primarily due to left heart failure. Histologically, ARDS is characterized by diffuse alveolar damage (DAD) and extravasation of protein-rich edema with frequent evolution to pulmonary fibrosis.

Any pulmonary or extrapulmonary process that generates uncontrolled inflammation can lead to ARDS, including pneumonia, sepsis, aspiration of gastric contents, and trauma. ARDS requires invasive respiratory support in the majority of cases and is associated with a high mortality.

Mechanical ventilation affects the natural history of ARDS by promoting ventilator associated lung injury (VALI). Low tidal volume (TV) ventilation has been shown to decrease mortality.

Clinical features

- Acute onset of dyspnea and hypoxemia, not adequately responsive to oxygen therapy.
- Low lung compliance.
- Difficulty in excreting CO2.
- Need for higher PEEP.
- Pulmonary hypertension.
- Late evolution to pulmonary fibrosis.
- Prolonged mechanical ventilation.
- Protracted disability.

Key management points

Airway management: Most ARDS patients will require endotracheal intubation. Certain subpopulations of patients may respond to noninvasive ventilation (NIV). A recent study showed reduced mortality and no change in intubation rates in patients with non-hypercapnic, acute hypoxemic respiratory failure who received high-flow oxygen therapy, compared with NIV via facemask. Also, a study looking at NIV using

a helmet showed a significant reduction in intubation rates and mortality in patients with ARDS, compared with traditional facemask NIV.

Mechanical ventilation: Set small TV (<6.5 ml/kg) relative to PBW. This is usually accomplished in VC mode, but PC ventilation is probably equivalent providing tidal volumes are appropriate. Maintain inspiratory plateau pressures (Pplat) (Figure 2) lower than 30 cmH2O to prevent VALI. Maintain respiratory rate less than 30-35 breaths/min. Unless a major contraindication to hypercapnia or acidemia exists, normalization of arterial PCO2 is not a primary goal of ventilatory support. Arterial pH values as low as 7.2 may be tolerable by most patients. Use PEEP and FiO2 to obtain PaO2 between 55 and 80 mmHg (SpO2 88-95%). The use of full ventilatory support and muscle relaxation may be desirable in the early stages of moderate – severe ARDS to ensure constant small TV. However, early use of partial ventilatory support with close monitoring of TV's, particularly in mild-moderate disease may be preferred in patients who can tolerate it to minimize ventilator-induced diaphragm dysfunction (VIDD).

EMERGENCY MANAGEMENT

Secure the airway. Intubation is a high-risk procedure in these patients due to the risk of rapid deterioration of oxygenation and hemodynamics. An airway management expert should be present.

Prepare for resuscitation with fluids and vasopressors/inotropes if needed. Central vessel and arterial cannulation will be required in most cases.

Consider alveolar recruitment maneuvers immediately after intubation to restore acceptable oxygenation.

Start mechanical ventilation with AC. Set high initial FiO2 and a moderate to high (~10 cmH2O) level of PEEP for initial stabilization. Assess patient response and wean FiO2 quickly when possible to less than 0.7.

If FiO2 remains high despite elimination of respiratory effort, ↑ PEEP to enable reductions in FiO2.

DIAGNOSIS

Diagnostic criteria and tests

The previous American-European Consensus Conference (AECC) criteria defined acute lung injury (ALI) as a broader class of lung injury with ARDS as its higher-severity subcategory. ALI is no longer a diagnostic category under the current Berlin Definition of ARDS, which include the following clinical and radiological criteria:

Timing: Within 1 week of a known clinical insult or new or worsening respiratory symptoms.

Chest imaging: Bilateral opacities on CXR or chest computerized tomography (CT) not fully explained by effusions, lobar/lung collapse, or nodules.

Origin of edema: Respiratory failure not fully explained by cardiac failure or fluid overload (need objective assessment – such as echocardiography – to exclude hydrostatic edema if no risk factor present).

Oxygenation:

Mild: 200 mmHg < PaO2/FiO2 ≤ 300 mmHg with PEEP or CPAP ≥ 5 cmH2O

Moderate: 100 mmHg < PaO2/FiO2 ≤ 200 mmHg with PEEP ≥ 5 cmH2O

Severe: PaO2/FiO2 ≤ 100 mmHg with PEEP ≥ 5 cmH2O

Similar to the AECC criteria, the Berlin criteria have limitations that reduce their ability to identify patients with diffuse alveolar damage (DAD), the pathologic correlate of ARDS, as shown by autopsy studies. However, all the studies that provide the evidence for our best care practices in ARDS used the clinical definition to enroll patients. In addition, clinical criteria do not account for the etiology of the injury and they do not distinguish between the main phenotypes of direct versus indirect injury of the lungs. Although the Berlin criteria introduced a requirement for a minimum PEEP of 5 cmH2O, response to predefined PEEP and FiO2 and to recruitment maneuvers identify patients at a higher versus lower risk of death. For these reasons, clinical criteria for ARDS diagnosis select populations of patients who are exceedingly heterogenous in their outcomes and responses to treatment, which renders problematic informed enrollment into trials and individualized clinical decision making.

Normal lab values

Bilateral alveolar infiltrates on chest radiograph (Figure 3). Heterogeneous distribution of chest CT densities, which are mainly dorsally localized and coexist with normally or near-normally aerated lung regions (Figure 4). Low compliance of the respiratory system, measured with an inspiratory hold maneuver (Figure 2). Elevated alveolar dead space ratio (VD/VT).

ESTABLISHING THE DIAGNOSIS

The patient fulfills Berlin criteria and the PaO2/FiO2 ratio does not improve after simple interventions such as diuresis, alveolar recruitment maneuvers, or use of moderate PEEP for a limited period of time. The patient has a low respiratory system compliance.

Other possible diagnoses

Unrecognized cardiogenic pulmonary edema and fluid overload: The differentiation between hydrostatic pulmonary edema and ARDS can be difficult, since the hypoxemia and radiological appearance are similar in the two conditions. Although the Berlin criteria require left heart failure to be ruled out to diagnose ARDS, the two conditions often coexist. Pure hydrostatic pulmonary edema usually responds quickly to diuretics and other cardiac-specific therapies.

Atelectasis: Bilateral infiltrates and hypoxemia due to alveolar collapse can be confused with ARDS but usually respond dramatically to alveolar recruitment strategies. Bilateral radiological infiltrates caused by pneumonia or traumatic lung contusions in the absence of widespread pulmonary inflammation can be difficult to distinguish from ARDS, as the latter may be patchy. The clinical course, the response to mechanical ventilation and PEEP settings and the appearance on CT scan can help establish the diagnosis. However, these patient populations should be treated in an identical fashion with lung-protective ventilation.

Interstitial lung diseases such as idiopathic pulmonary fibrosis can present with acute clinical deterioration together with radiological (new-onset diffuse infiltrates) and physiological (hypoxemia, low lung compliance) signs that are similar to ARDS. The history of chronic illness and previous radiographs/pulmonary function tests may help in the diagnosis. Acute interstitial pneumonia (Hamman Rich) can present with subacute evolution of respiratory functional impairment and diffuse radiological infiltrates with no known predisposing factors to ARDS. When the differential diagnosis is uncertain, open lung biopsy should be considered prior to initiation of immunosuppressant therapy.

Acute eosinophilic pneumonia presents with bilateral infiltrates. The diagnosis is confirmed by abundance of eosinophils in the bronchoalveolar lavage. Occasionally, a radiological infiltrative pattern can be caused by malignancy.

Diffuse Alveolar hemorrhage due to vasculitic processes such as Goodpasture's syndrome and Wegener's granulomatosis presents with hypoxemia, diffuse radiological infiltrates and hemoptysis (although this symptom can be absent). The presence of acute anemia and hemorrhagic sputum by fiberoptic bronchoscopy and bronchoalveolar lavage usually confirm the diagnosis of alveolar hemorrhage. Serologic testing and lung and kidney biopsies are used to narrow the differential diagnosis.

Confirmatory tests

There are no specific confirmatory tests that can be performed for ARDS. However, in cases where no predisposing factors are evident (e.g. trauma, aspiration, sepsis), diagnostic testing should include fiberoptic bronchoscopy and bronchoalveolar lavage fluid sampling to rule out infection, alveolar hemorrhage, eosinophilia and cancer. Serologic testing for autoimmune diseases and viral infections should be obtained when appropriate. If the diagnosis remains uncertain after bronchoscopy, open lung

biopsy should be considered if clinical conditions allow, especially in cases where immunosuppressant therapy is contemplated.

Chest CT can help confirm the presence of bilateral ground-glass opacities suggestive of DAD. CT can give some indication of the amount of fibrosis, the presence of coexisting processes (i.e. pleural effusions, pulmonary abscess) and the extent of atelectasis.

Pulmonary artery catheterization is not required to confirm the diagnosis of ARDS. Heart failure can be ruled out by clinical assessment or by echocardiography.
Measuring respiratory mechanics helps identify low compliance as a cofactor in causing respiratory failure and is usually present; however, this is not required for diagnosis.

Specific Treatment

There is no specific therapy for ARDS, other than treatment of the precipitating causes. The treatment of ARDS is mainly supportive and is centered on evidence-based respiratory care, thoughtful management of hemodynamics and judicious administration of fluids or diuretics. The only approaches that have been shown to affect ARDS outcomes are the manipulation of ventilator settings with the goal of protecting the lungs from VALI and the use of prone positioning for extended duration in high severity patients.

Lung-protective strategies

When low-TV ventilation was compared to higher TV, the former resulted in lower mortality and better secondary outcomes. The strategy used in this study included setting TV to 6 ml/kg PBW, limiting Pplat to less than 30 cmH2O and using a nomogram to set PEEP and FiO2. This is currently considered the standard ventilatory management for ARDS. Although Pplat limitation to less than 30 cmH2O and TV limitation to 6 ml/kg IBW is recommended, there is no evidence that this constitutes a

safety limit.

Radiological evidence suggests overdistension and inflammatory activation at Pplat values between 25 and 30. Of note, if the plateau pressure is less than 30 cmH2O while receiving a high TV above 6 ml/kg IBW, the TV should still be reduced to approximately 6 ml/kg, as evidence suggests that the mortality benefit associated with low tidal volumes is independent of the compliance and Pplat.

The use of higher levels of PEEP (with or without recruitment maneuvers) to enhance alveolar opening and minimize atelectrauma has been advocated based on animal studies. In the two clinical trials that showed a benefit from this "open lung approach," high PEEP/low TV was tested against lower PEEP/high TV. However, in studies where only the effect of higher PEEP was tested in ARDS, the open lung approach did not result in improved survival.

At the same time, these studies showed that high PEEP was not unsafe. Furthermore, a recent meta-analysis using 2,299 patients from three studies detected a 10% relative mortality reduction (NNT 25) in those patients who met ARDS criteria at study entry and were randomized to high PEEP. This mortality reduction in the high PEEP group was associated with a smaller number of patients who needed rescue therapies for refractory hypoxemia, suggesting a benefit from high PEEP in a select ARDS subpopulation. Furthermore, the survival benefit of high PEEP was concentrated in the more severely ill patients who responded to this treatment with improvement in oxygenation. Since the radiological response to alveolar recruitment is variable among patients and is related to survival, CT studies – albeit a cumbersome approach – can have a role in identifying patients who are at high risk of death and who may benefit from high PEEP strategies.

Although the rationale for using a fixed small (6 ml/kg PBW) Tidal Volume in ARDS was based on the concept that the ARDS lung is essentially small ("baby lung"), a one

size fits all approach of using a tidal volume normalized to PBW doesn't account for the wide variability in the degree of lung aeration between patients. To account for these differences, it was recently proposed that since respiratory system compliance correlates with the volume of aerated lung, TV should be normalized to compliance to estimate the tidal lung "stress" in a given patient. The TV/compliance is equal to the Plateau Pressure – PEEP a.k.a. the driving pressure. Data to support this concept is accumulating. Recently, a complex statistical analysis (meta-analysis of individual patient data from over 3,500 subjects from ARDS trials) revealed that, in fact, mortality correlated best with the lowest driving pressure, and not the TV/PBW, Plateau Pressure, or PEEP level. Although this was a retrospective analysis, it makes sense physiologically and justifies future controlled trials targeting driving pressure minimization as a goal. To achieve this goal either TV or PEEP can be manipulated, however, all the patients enrolled in the driving pressure study had their driving pressure reduced by either a change in PEEP or through a TV reduction to 6 ml/kg PBW. Thus, until we have prospective data to inform this best, we advocate setting the TV to < 6.5 ml/kg PBW and then titrating PEEP upward to minimize the driving pressure to ≤ 14. Interestingly, this approach to PEEP titration is very similar to PEEP titration practices prevalent in the late 70's and 80's, which was driven by data published by Peter Suter in 1975 showing that PEEP titrated to the highest compliance (lowest DP) correlated best with oxygen delivery. Although O2 delivery was the wrong outcome variable he delineated this approach using sound physiologic principles.

Ventilatory management during the first 12 hours

Early ventilatory management after intubation should be focused on lung protection and characterization of pulmonary mechanics.

Set initial PEEP at 10 cmH2O and FiO2 of 1.0 and repeat blood gases to verify patient severity after intubation.

Maintain deep sedation and muscle relaxation: paralysis can be considered in the early stage to facilitate respiratory mechanics measurements and maximize lung protection in what is possibly the most crucial stage of the disease. Additionally, muscle relaxation

during the first 48 hours may have outcome benefits.

Identify potential for alveolar recruitment by performing recruitment maneuvers or trials at different PEEP levels. Recruitment response can be evaluated using changes in oxygenation, compliance and PaCO2 together with hemodynamic tolerance. The benefit of alveolar recruitment versus hemodynamic impairment at high PEEP should be critically weighed. Choose the lowest PEEP that allows FiO2 below 0.6 and Pplat below 30 cmH2O. If driving pressure remains > 14-16, titrate PEEP up and down to achieve a driving pressure goal of < 14.

Identify optimal tidal volume. Gradually reduce TV to 6 ml/kg PBW and reduce further if Pplat is above 30 cmH2O. Increase respiratory rate (RR) up to 35 (closely monitor for autoPEEP). Tolerate hypercapnia until pH is below 7.10-7.15. At that point consider chemical buffering. If RR = 35 with intolerable acidemia, consider decreasing PEEP and increasing TV to 8 ml/kg if Pplat is below 30.

Prone positioning: Patients may respond to this maneuver with dramatic improvement in gas exchange. Three previous clinical trials did not document a mortality benefit, however a more recent study that employed prone positioning for an extended period of time (> 16 hours) in patients with more severe ARDS (PaO2/FiO2 < 150 mmHg) showed a dramatic improvement in survival. Prone positioning should no longer be considered a rescue therapy and instead should be included in the initial management of moderate to severe ARDS unresponsive the aforementioned maneuvers.

Based on response to ventilator settings and severity of functional compromise, the use of adjunctive and non-conventional therapies should be considered early.

Respiratory mechanics should be intermittently assessed and at minimum compliance, plateau pressures, and driving pressure should be measured. While these ventilator goals should be achieved in all patients, for the individual patient the combination of

TV< 6.5 ml/kg PBW and PEEP that minimizes driving pressure and maximizes lung protection and recruitment should be identified along with the minimum acceptable FiO2.

Refractory cases

Refractory ARDS cases are those that present with critical hypoxemia that does not respond to standard respiratory care including prone positioning. The limits of acceptable PaO2 have not been established since most deaths from ARDS are not directly due to hypoxemia. However, patients with refractory hypoxemia tend to have a higher mortality. Depending on the institutional experience and clinicians' preferences, these patients can be treated with:

Super-recruitment maneuvers: They may improve oxygenation but they also can have hemodynamic effects and potentially worsen alveolar strain and VALI.

In severe, refractory cases, heavy sedation and paralysis can be used to decrease O2 consumption and, by thus increasing venous saturation, indirectly increase arterial oxygenation. Muscle paralysis also eliminates expiratory muscle activity (i.e. forced exhalation), which can counteract the effect of PEEP on lung volumes and decrease intra-abdominal pressure.

Inhaled nitric oxide or epoprostenol: It often has significant gas exchange benefits but also has no documented outcome effects and high costs. Inhaled prostacyclin is a relatively less expensive alternative that is more widely available and has comparable effects. Enhanced sitting position and/or reverse Trendelenburg can have beneficial effects on oxygenation by decreasing abdominal pressure and increasing FRC.

Advanced modes of ventilation that may have physiological appeal include airway pressure release ventilation (APRV) and Bi-Level ventilation. In spite of their physiological appeal and effectiveness in improving gas exchange and in preserving

diaphragm activity and strength, these ventilatory modes are not supported by clinical outcome data. They should be considered as rescue strategies in refractory hypoxemia until further studies are done. High frequency oscillatory ventilation (HFOV) has been shown to significantly increase mortality in moderate to severe ARDS and should be avoided.

ECLA: Although typically considered a rescue therapy, a recent study showed better outcomes in ARDS patients who were randomized to receive consideration for ECLA in a specialized medical center, as opposed to those who remained in their original location. However, the results of this study are clouded by the likely presence of a mixed effect of the treatment and of the transfer to the ECLA center. ECLA remains a rescue therapy pending results of ongoing clinical trials.

A higher number of patients can be considered refractory due to the inability to control respiratory acidosis within the boundaries of the lung-protective strategy. Buffer infusions can be considered to tolerate extreme acidemia. If its efficacy is confirmed in clinical trials, veno-venous ECLA can be considered as a means to remove CO2 while protecting the lungs from VALI with very low stretch ventilation.

Exogenous surfactant administration: Although its positive outcome effects have been documented in preterm newborns and in pediatric ARDS, multiple studies have failed to show outcome effects from surfactant therapy in adults.

Steroids: Preliminary studies showed beneficial effects of low- to medium-dose steroids in late-stage ARDS with no documented ongoing infection. However, a recent ARDSnet trial could not detect positive outcome effects in the general population.

Anaphylaxis

Anaphylaxis is an acute systemic reaction with symptoms of an immediate-type allergic reaction which can involve the whole organism and is potentially life-threatening.

The symptoms of anaphylactic reactions are caused by release of different mediators (e.g. histamine, prostaglandins, leukotrienes, tryptase, platelet-activating factor, cytokines, chemokines) from mast cells and basophil granulocytes, the individual significance of each of these is not assessed clearly in detail. However, there is a consensus that histamine plays a central role in anaphylactic reactions.

The pathomechanism of anaphylaxis usually represents an immunological reaction, most often an immunoglobulin E mediated allergy. However, specific antibodies of other classes can trigger similar complement-dependent symptoms through the formation of circulating immune complexes (immune complex anaphylaxis).

There are also a high number of anaphylactic reactions where no immunological sensitization is detectable; these reactions are called „pseudo-allergic reactions“ or recently „non-allergic anaphylaxis“. The mechanisms of this non-allergic anaphylaxis comprise G protein-induced, direct release of vasoactive mediators, direct activation of the complement system, interactions with the kallikrein-kinin system, interactions with arachidonic acid metabolism as well as psychoneurogenic reflex mechanisms. Knowledge on the pathophysiology of these reactions is much more limited than on allergic anaphylaxis.
In patients with increased basal serum tryptase and/or mastocytosis, anaphylaxis may be particularly severe.
Preceding intake of β-adrenoceptor antagonists and ACE inhibitors can lead to a deterioration of the anaphylactic symptoms. For β-adrenoceptor antagonists, blocking of the cardiostimulatory effect of adrenaline as well as its mast cell-stabilizing effect play a role, and, in the case of ACE inhibitors, reduced bradykinin clearence with resulting marked vasodilatation. Also the intake of nonsteroidal anti-inflammatory drugs (NSAIDs) can result in severe anaphylactic reactions due to increased leukotriene formation and facilitated absorption of ingested allergens.

CLINICAL SYMPTOMS

Anaphylactic reactions essentially manifest on the skin, in the respiratory tract, gastrointestinal tract, and cardiovascular system. The working group has discussed whether the guideline should be based on a severity classification, as the treatment of anaphylaxis is symptom-related. The majority voted for a severity classification. There are different severity classifications in the literature. Each severity classification has advantages and disadvantages. The majority of the group opted to modify the severity classification which is most frequently used in Germany at present. Anaphylaxis is classified by degrees of severity from I–IV, depending on the intensity of the clinical symptoms.

The symptoms of anaphylactic reactions usually begin acutely and may progress very quickly. Thus, symptoms can deteriorate within minutes resulting in death. The reaction may, however, also come to a spontaneous standstill at any stage and regress spontaneously. In a reaction of grade I severity, the further development and dynamics of the reaction are primarily not foreseeable. The symptoms may occur either simultaneously or sequentially. There may be primarily circulatory reactions without preceding cutaneous or respiratory signs. Occasionally there are protracted or biphasic courses with recurrent symptoms 6–24 hours after successful initial therapy. Apart from acute onset of symptoms and biphasic courses, delayed anaphylactic reactions may occur where symptoms only begin some hours after exposure. The most striking example of this particular dynamic has been documented for the allergen galactose-alpha-1,3-galactose in mammalian meat allergy and is probably based on delayed release or systemic availability of allergens or their binding sites.

At the beginning of an anaphylaxis, minor prodromal symptoms or signs can appear, like itching or burning of the palms and soles or in the genital area, a metallic taste, fearfulness, headache or disorientation. Young children cannot specifically express these feelings and they may present with symptoms such as restlessness or withdrawal behaviour even before the occurrence of objective signs.

In anaphylaxis most often the skin and mucous membranes are affected with pruritus, erythema (flush) as well as urticaria and angioedema (Quincke's edema). These may occur in areas of the skin having had no direct contact with the trigger (systemic spread).

In the upper respiratory tract, patients often describe burning, tingling or itching of the tongue or palate as early symptoms. In the oropharynx, swelling of uvula and tongue can be observed. Clinical signs are a muffled voice, dysphagia with salivation or inspiratory stridor. The possible consequences of laryngeal edema are airway obstruction with life-threatening hypoxia within a short time period.
In the lungs, in particular patients with asthma can develop bronchoconstriction and dyspnoea. Clinical signs are wheezing, prolonged expiration and increased respiratory rate. Bronchial obstruction is the leading symptom in life-threatening reactions especially in children and adolescents. The degree of asthma correlates directly with the severity of the anaphylactic reaction. Also to a variable extent vasoconstriction can occur, at times resulting in an extreme increase in pulmonary vascular resistance, respiratory arrest and the need for resuscitation. Pulmonary edema can also occur as a consequence of this permeability disturbance.

Gastrointestinal symptoms include crampy abdominal pain, nausea, vomiting and diarrhea. There may also be increased intestinal motility with meteorism, the urge to defecate and even involuntary defecation. Further abdominal symptoms consist of the urge to urinate, micturition as well as uterine cramps. In children, mild oral symptoms or perioral reddening with vomiting may be the only symptoms of food-induced anaphylaxis.

Because of vasodilatation and increased vascular permeability, fluid loss into the extravascular space occurs leading to hemoconcentration and hypovolemia, followed by arterial hypotension and tachycardia. Direct cardiac symptoms include arrhythmia,

bradycardia or myocardial infarction.

Central nervous system symptoms are restlessness, withdrawal behaviour, headache, seizures, impaired and loss of consciousness. In children, a change in behaviour is often observed, expressed by anxiety or sometimes aggression. Older children, adolescents and adults can experience “a sense of impending doom“.

In particular the causes of fatal anaphylaxis are airway obstruction and/or cardiovascular failure, either due to direct cardiac involvement or as a consequence of the microcirculatory dysfunction with shock; rare causes are disseminated intravascular coagulation or adrenaline overdose.

Knowledge control:

1. Determination of acute respiratory failure, acute respiratory distress syndrome.
2. Acute respiratory failure, acute respiratory distress syndrome, features of treatment tactics.
3. Possible complications of acute respiratory failure, acute respiratory distress syndrome.
4. Primary and secondary prevention of acute respiratory failure, acute respiratory distress syndrome.
5. Forecast and efficiency.
6. Acute allergie, features of treatment tactics.
7. Emergency care in case of acute allergie.

Test tasks:

1. After a contact with chemicals a plant worker has suddenly developed stridor, voice hoarseness, barking cough, progressing dyspnea. Objective examination reveals acrocyanosis. What is your provisional diagnosis?

A. Laryngeal edema
B. Laryngeal carcinoma
C. PATE

D. Pulmonary atelectasis
E. Pneumothorax

2. A patient with nosocomial pneumonia has signs of collapse. Which of the following pneumonia complication is the most likely to be accompanied with collapse?

A. Septic shock
B. Exudative pleuritis
C. Bronchial obstruction
D. Toxic hepatitis
E. Emphysema

3. A 38 y.o. woman is seriously ill. She complains of frequent paroxysms of expiratory dyspnea. The last paroxysm lasted over 12 hours and failed to respond to theophylline. The skin is palish gray, moist, RR of 26/min. On auscultation, breath sounds are absent over some areas. Your preliminary diagnosis?

A. Bronchial asthma, status asthmaticus
B. Chronic obstructive bronchitis
C. Atopic bronchial asthma, respiratory failure of the III degree
D. Bronchiectasis, respiratory failure of the II-III degree
E. Ischemic heart disease, pulmonary edema

4. Five days after a total hip joint replacement a 72 year old woman becomes acutely short of breath, diaphoretic and hypotensive. Both lung fields are clear to auscultation and percussion, but examination of the neck reveals mild jugular venous distension with prominent A waves. Heart sounds are normal. ECG shows sinus tachycardia with a new right bundle branch block and minor nonspecific ST − T wave changes. The most likely diagnosis is:

A. Pulmonary thromboembolism
B. Acute myocardial infarction
C. Aortic dissection

D. Pericarditis

E. Aspiration

5. A 52 year old male patient complains about attacks of asphyxia, pain in his left side during respiration. These manifestations turned up all of a sudden. It is known from his anamnesis that he had been treated for thrombophlebitis of the right leg for the last month. In the admission ward the patient suddenly lost consciousness, there was a sudden attack of asphyxia and pain in his left side. Objectively: heart rate - 102/min, respiratory rate - 28/min, AP- 90/70 mm Hg. Auscultation revealed diastolic shock above the pulmonary artery, gallop rhythm, small bubbling rales above the lungs under the scapula on the right, pleural friction rub. What examination method will be the most informative for a diagnosis?

A. Angiography of pulmonary vessels

B. Echocardioscopy

C. Study of external respiration function

D. ECG

E. Coagulogram

6. A 49-year-old patient complains of dyspnea, cough. There are no sputum discharges. He has repeatedly used salbutamol and intal but with no effect. Objectively: he is only able to sit while leaning on the table. Cyanosis of face, acrocyanosis are present. Breathing is shallow, laboured, in some parts it cannot be auscultated; there are diffuse rales, expiration is significantly prolonged. Heart sounds are muffled, tachycardia is present. Ps - 112/min., AP - 110/70 mmHg. Liver is located near the costal arch. There is no peripheral edema. What is your provisional diagnosis?

A. Status asthmaticus

B. Chronic obstructive bronchitis

C. Bronchial asthma, moderate gravity

D. Foreign object aspiration

E. Cardiac asthma

7. A 54-year-old drowned man was rescued from the water and delivered to the shore. Objectively: the man is unconscious, pale, breathing cannot be auscultated, pulse is thready. Resuscitation measures allowed to save the patient. What complications may develop in the near future?

A. Pulmonary edema
B. Respiratory arrest
C. Encephalopathy
D. Cardiac arrest
E. Bronchospasm

8. A 55-year-old male had been treated at the surgical department for acute lower-extremity thrombophlebitis. On the 7-th day of treatment he suddenly developed pain in the left part of chest, dyspnea and cough. Body temperaturewas36,1°C, respiratory rate - 36/min. The patient was also found to have diminished breath sounds without wheezing. Ps - 140/min, thready. AP - 70/50 mm Hg. The ECG shows Q-S syndrome. What is the most likely diagnosis?

A. Pulmonary embolism
B. Myocardial infarction
C. Cardiac asthma
D. Bronchial asthma
E. Pneumothorax

9. A 40-year-old woman has been hospitalized for attacks of asphyxia, cough with phlegm. She has a 4-year history of the disease. The first attack of asphyxia occurred during her stay in the countryside. Further attacks occurred while cleaning the room. After 3 days of inpatient treatment the patient's condition has significantly improved. What is the most likely etiological factor?

A. Household allergens
B. Pollen

C. Infectious
D. Chemicals
E. Psychogenic

10. A woman has developed sudden thoracic pain on the right with expectoration of pink sputum and body temperature rise up to 37,7°C on the 4th day after the surgery for cystoma of the right ovary. On lung examination: dullness of the lung sound on the lower right is observed. Isolated moist crackles can be auscultated in the same area. What complication is the most likely?

A. Pulmonary infarction
B. Pneumonia
C. Pulmonary abscess
D. Exudative pleurisy
E. Pneumothorax

Topic 5. Preparation for practical training №5 «Emergencies in gastroenterology»

Learning objective

The student must know:

- determination of gastrointestinal bleeding, bile colic, intestinal colic, hepatic encephalopathy, hepatic coma;
- clinical manifestations of gastrointestinal bleeding, bile colic, intestinal colic, hepatic encephalopathy, hepatic coma;
- criteria for diagnosing gastrointestinal bleeding, bile colic, intestinal colic, hepatic encephalopathy, hepatic coma;
- laboratory and instrumental manifestations of gastrointestinal bleeding, bile colic, intestinal colic, hepatic encephalopathy, hepatic coma;
- main manifestations, differential diagnosis of gastrointestinal bleeding, bile colic, intestinal colic, hepatic encephalopathy, hepatic coma;
- principles of emergency care for patients with gastrointestinal bleeding, bile colic, intestinal colic, hepatic encephalopathy, hepatic coma;
- algorithm for providing emergency care

Be able:

- determine the state of emergency

- perform differential diagnosis with other emergencies
- Assign appropriate emergency care

Master practical skills:

- pulse oximetry.
- electrocardiography in 12 standard leads.

Theoretical material for independent student training.

GASTROINTESTINAL BLEEDING

Gastrointestinal bleeding can fall into two broad categories: upper and lower sources of bleeding. The anatomic landmark that separates upper and lower bleeds is the ligament of treitz, also known as the suspensory ligament of the duodenum. This peritoneal structure suspends the duodenojejunal flexure from the retroperitoneum. Bleeding that originates above the ligament of treitz usually presents either as hematemesis or melena whereas bleeding that originates below most commonly presents as hematochezia. Hematemesis is the regurgitation of blood or blood mixed with stomach contents. Melena is dark, black, and tarry feces that typically has a strong characteristic odor caused by the digestive enzyme activity and intestinal bacteria on hemoglobin. Hematochezia is the passing of bright red blood via the rectum.

ETIOLOGY

Upper GI Bleeding

- Peptic ulcer disease (can be secondary to excess gastric acid, H. pylori infection, NSAID overuse, or physiologic stress)
- Esophagitis
- Gastritis and Duodenitis
- Varices
- Portal Hypertensive Gastropathy (PHG)
- Angiodysplasia

- Dieulafoy's lesion (bleeding dilated vessel that erodes through the gastrointestinal epithelium but has no primary ulceration; can any location along the GI tract
- Gastric Antral Valvular Ectasia (GAVE; also known as watermelon stomach)
- Mallory-Weiss tears
- Cameron lesions (bleeding ulcers occurring at the site of a hiatal hernia
- Aortoenteric fistulas
- Foreign body ingestion
- Post-surgical bleeds (post-anastomotic bleeding, post-polypectomy bleeding, post-sphincterotomy bleeding)
- Upper GI tumors
- Hemobilia (bleeding from the biliary tract)
- Hemosuccus pancreaticus (bleeding from the pancreatic duct)

<u>Lower GI Bleeding</u>

- Diverticulosis (colonic wall protrusion at the site of penetrating vessels; over time mucosa overlying the vessel can be injured and rupture leading to bleeding) [diverticulosis]
- Angiodysplasia
- Infectious Colitis
- Ischemic Colitis
- Inflammatory Bowel Disease
- Colon cancer
- Hemorrhoids
- Anal fissures
- Rectal varices
- Dieulafoy's lesion (more rarely found outside of the stomach, but can be found throughout GI tract)
- Radiation-induced damage following treatment of abdominal or pelvic cancers
- Post-surgical (post-polypectomy bleeding, post-biopsy bleeding)

History

- Question patient for potential clues regarding:
- Previous episodes of GI bleeding
- Past medical history relevant to potential bleeding sources (e.g., varices, portal hypertension, alcohol abuse, tobacco abuse, ulcers, H. pylori, diverticulitis, hemorrhoids, IBD)
- Comorbid conditions that could affect management
- Contributory or confounding medications (NSAIDs, anticoagulants, antiplatelet agents, bismuth, iron)
- Symptoms associated with bleeding (e.g., painless vs. painful, trouble swallowing, unintentional weight loss, preceding emesis or retching, change in bowel habits)

Physical

- Look for signs of hemodynamic instability:
  - Resting tachycardia — associated with the loss of less than 15% total blood volume
  - Orthostatic Hypotension — carries an association with the loss of approximately 15% total blood volume
  - Supine Hypotension — associated with the loss of approximately 40% total blood volume
- Abdominal pain may raise suspicion for perforation or ischemia.
- A rectal exam is important for the evaluation of:
  - Anal fissures
  - Hemorrhoids
  - Anorectal mass
  - Stool exam

Labs

- Complete blood count
- Hemoglobin/Hematocrit
- INR, PT, PTT
- Lactate
- Liver function tests

Diagnostic Studies

- Upper Endoscopy
  - Can be diagnostic and therapeutic
  - Allows visualization of the upper GI tract (typically including from the oral cavity up to the duodenum) and treatment with injection therapy, thermal coagulation, or hemostatic clips/bands
- Lower Endoscopy/Colonoscopy
  - Can be diagnostic and therapeutic
  - Allows visualization of the lower GI tract (including the colon and terminal ileum) and treatment with injection therapy, thermal coagulation, or hemostatic clips/bands
- Push Enteroscopy
  - Allows further visualization of the small bowel
- Deep Small Bowel Enteroscopy
  - Allows further visualization of the small bowel
- Nuclear Scintigraphy
  - Tagged RBC scan
  - Detects bleeding occurring at a rate of 0.1 to 0.5mL/min using technetium-99m (can only detect active bleeding
  - Can be helpful to localize angiographic and surgical interventions
- CT Angiography
  - Allows for identification of an actively bleeding vessel
- Standard Angiography
  - Allows for identification of a bleeding vessel and potential treatment via embolization or intra-arterial vasopressin
  - Requires the active bleeding be at a rate of 0.5 to 1.0mL/min to visualize site
- Meckel's scan
  - Nuclear medicine scan to look for ectopic gastric mucosa

Acute management of GI bleeding typically involves an assessment of the appropriate setting for treatment followed by resuscitation and supportive therapy while investigating the underlying cause and attempting to correct it.

Risk Stratification

Specific risk calculators attempt to help identify patients who would benefit from ICU level of care; most stratify based on mortality risk. The AIMS65 score and the Rockall Score calculate the mortality rate of upper GI bleeds. There are two separate Rockall scores; One is calculated before endoscopy and identifies pre-endoscopy mortality, whereas the second score is calculated post-endoscopy and calculates overall mortality and re-bleeding risks. The Oakland Score is a risk calculator that attempts to help calculate the probability of a safe discharge in lower GI bleeds.

Setting

- ICU
  - Patients with hemodynamic instability, continuous bleeding, or those with a significant risk of morbidity/mortality should undergo monitoring in an intensive care unit to facilitate more frequent observation of vital signs and more emergent therapeutic intervention.
- General Medical Ward
  - Most other patients can undergo monitoring on a general medical floor. However, they would likely benefit from continuous telemetry monitoring for earlier recognition of hemodynamic compromise
- Outpatient
  - Most patients with GI bleeding will require hospitalization. However, some young, healthy patients with self-limited and asymptomatic bleeding may be safely discharged and evaluated on an outpatient basis.

Treatments

- Nothing by mouth

- Provide supplemental oxygen if patient hypoxic (typically via nasal cannula, but patients with ongoing hematemesis or altered mental status may require intubation). Avoid NIPPV due to the risk of aspiration with ongoing vomiting.
- Adequate IV access - at least two large-bore peripheral IVs (18 gauge or larger) or a centrally placed cordis
- IV fluid resuscitation (with Normal Saline or Lactated Ringer's solution)
- Type and Cross
- Transfusions

o RBC transfusion

 Typically started if hemoglobin is < 7g/dL, including in patients with coronary heart disease

o Platelet transfusion

 started if platelet count < 50,000/microL

o Prothrombin complex concentrate

 Transfuse if INR > 2

- Medications

o PPIs

 Used empirically for upper GI bleeds and can be continued or discontinued upon identification of the bleeding source

o Prokinetic Agents

 Given to improve visualization at the time of endoscopy

o Vasoactive medications

 Somatostatin and its analog octreotide can be used to treat variceal bleeding by inhibiting vasodilatory hormone release

o Antibiotics

 Considered prophylactically in patients with cirrhosis to prevent translocation, especially from endoscopy

o Anticoagulant/antiplatelet agents

 Should be stopped if possible in acute bleeds

- Consider the reversal of agents on a case-by-case basis dependent on the severity of bleeding and risks of reversal

• Other

o Consider NGT lavage if necessary to remove fresh blood or clots to facilitate endoscopy

o Placement of a Blakemore or Minnesota tube should be considered in patients with hemodynamic instability/massive GI bleeds in the setting of known varices, which should be done only once the airway is secured. This procedure carries a significant complication risk (including arrhythmias, gastric or esophageal perforation) and should only be done by an experienced provider as a temporizing measure.

o Surgery should be consulted promptly in patients with massive bleeding or hemodynamic instability who have bleeding that is not amenable to any other treatment Few diagnoses mimic gi bleeding. Occasionally, hemoptysis may be confused for hematemesis or vice versa. Ingestion of bismuth-containing products or iron supplements may cause stools to appear melanic. Certain foods/dyes may turn emesis or stool red, purple, or maroon (such as beets).

BILIARY COLIC

Biliary colic is a steady or intermittent ache in the upper abdomen, usually under the right side of the rib cage. It happens when something blocks the normal flow of bile from the gallbladder. Bile is a liquid that helps to digest fats. Under normal circumstances, bile is made in the liver and stored in the gallbladder. When you eat a meal, bile passes from the gallbladder through the cystic duct and the common bile duct into the small intestine, where it mixes with partially digested food.

Gallstones are the most common reason for biliary colic. If a gallstone blocks either of these ducts, the normal flow of bile into the intestine is disrupted. The muscle cells in the bile duct contract vigorously to try to move the stone, causing the pain of biliary colic. A stricture of the bile duct or a tumor also can block bile flow and cause biliary colic.

SYMPTOMS

A person with biliary colic usually complains of an ache or a feeling of pressure in the upper abdomen. This pain can be in the center of the upper abdomen just below the breastbone, or in the upper right part of the abdomen near the gallbladder and liver. In some people, the abdominal pain spreads back toward the right shoulder blade. Many people also have nausea and vomiting.

Because symptoms of biliary colic usually are triggered by the digestive system's demand for bile, they are especially common after fatty meals. The symptoms also can occur when a person who has been fasting suddenly breaks the fast and eats a very large meal.

DIAGNOSIS

After you describe your symptoms, your doctor will perform a physical examination, paying particular attention to the upper right portion of your abdomen (the area of your liver and gallbladder). Ultrasound, the same painless procedure used to produce pictures of babies in the womb, can be used to produce pictures of your abdomen so your doctor can look for gallstones. Blood tests also may be done, especially if you have any fever or if your pain persists.

LABORATORY TEST

Certain blood tests can help in the initial evaluation of suspected cases:

Fbc and crp – assess for the presence of any inflammatory response, which will be raised in cholecystitis

Lfts – biliary colic and acute cholecystitis are likely to show a raised alp (indicating ductal occlusion), yet alt and bilirubin should remain within normal limits (unless a mirizzi syndrome, discussed below)

Amylase (or lipase) – to check for any evidence of pancreatitis

A urinalysis, including a pregnancy test if relevant, should be performed to exclude any renal or tubo-ovarian pathology.

IMAGING

A trans-abdominal ultrasound is one of the most sensitive modalities for visualising gallstone disease and is typically used first line to investigate suspected gallstone pathology.

Three specific areas are often visualised on us:

The presence of gallstones or sludge (the start of gallstone formation)

Gallbladder wall thickness (if thick walled, then inflammation is likely)

Bile duct dilatation (indicates a possible stone in the distal bile ducts)

If results from us scans are inconclusive, further imaging options are available. The gold standard investigation* for gallstones is magnetic resonance cholangiopancreatography (mrcp), largely replacing ercp for diagnostic purposes. Mrcp can show potential defects in the biliary tree caused by gallstone disease, with a sensitivity approaching 100%.

Patients with biliary colic should be prescribed analgesia (regular paracetamol +/- nsaids +/- opiates analgesia).

The patient should be advised about lifestyle factors that may help control symptoms (and help with future surgery), such as a low fat diet, weight loss, and increasing exercise.

Following first presentation of biliary colic, there is a high chance of symptom recurrence or the development of complications of gallstones, therefore an elective laparoscopic cholecystectomy is warranted and should be offered within 6 weeks of first presentation.

INTESTINAL COLIC

Intestinal colic is an intermittent, crampy abdominal pain that emanates from the increased gut peristalsis against an obstruction. This squeezing pain builds up and then eases off and usually comes in waves in an attempt to overcome the obstruction. The colicky abdominal pain increases in frequency and later becomes constant as peritonitis ensues. The visceral pain of intestinal colic is usually referred towards the midline rather than being localised as the gut has a midline origin of development. The visceral sensory fibres are carried by the sympathetic nerves on their way to the spinal cord. Thus foregut (lower oesophagus to mid-second part of duodenum) colicky pain is carried by the greater splanchnic nerve (T5-T9) and referred to the epigastrium; mid-gut (mid second part of duodenum to proximal two-thirds of transverse colon) colicky pain is carried by the lesser splanchnic nerve (T10-T11) and referred to the umbilicus while hindgut (beyond the distal third of transverse colon) colicky abdominal pain being carried by the least splanchnic nerve (T12) is referred to the suprapubic area. The other sources of pain are somatic (localized) from abdominal distension and peritoneal irritation when ischaemia or perforation supervenes. The consequences of bowel obstruction are progressive dehydration, electrolyte imbalance and systemic toxicity due to migration of toxins and bacteria translocation either through the intact but ischaemic bowel or through a perforation. Small bowel obstruction accounts for about 85% of cases of intestinal colic and the other 15% are due to large bowel obstruction.

The rare patient with a Richter‘s hernia in which only the antimesenteric portion of the small bowel is trapped without bowel obstruction may be undetected on physical examination, and, patients with partial obstruction can be considered at minimal risk of strangulation. Rarely small bowel obstruction can be caused by internal hernias related to mesenteric defects or recesses. A modern clinical example is the internal hernias that develop after a laparoscopic gastric bypass in which small mesenteric defects (transverse mesocolon, enteroenterostomy or behind the Roux limb can be created and there are fewer adhesions to tether small bowel loops and prevent them from herniating causing obstruction and potentially strangulation. In addition patients who have greater degrees of weight loss after laparoscopic Roux-en-Y gastric bypass

may be more prone to internal hernia because of loss of the protective space-occupying effect of mesenteric fat. Intestinal obstruction is a serious and costly medical condition indicating often emergency surgery. Small bowel obstruction constitutes 1.9% of all hospital and 3.5 % of all emergency treatment that has led to laparotomy in the United States. The overall mortality is approximately 10% and is greatest in patients with ischaemic bowel which may or may not have perforated prior to surgery. The most common causes of death are intra-abdominal sepsis, myocardial infarction and pulmonary embolism.

HEPATIC ENCEPHALOPATHY

Hepatic encephalopathy encompasses a spectrum or continuum of disease and, consequently, the symptoms and severity of the disorder can vary widely from one person to another. The severity of hepatic encephalopathy can range from mild, barely discernable symptoms to serious, life-threatening complications. Hepatic encephalopathy may develop slowly over time in individuals with chronic liver disease or may occur episodically, worsening and then improving only to recur. An episode of hepatic encephalopathy is often triggered by certain conditions such as infection, gastrointestinal bleeding, constipation, certain drugs, surgery or an alcohol binge. Episodes of hepatic encephalopathy can develop rapidly and without warning, often necessitating hospitalization.

It is important to note that affected individuals may not have all of the symptoms discussed below. Affected individuals should talk to their physician and medical team about their specific case, associated symptoms and overall prognosis. Many of the symptoms of hepatic encephalopathy are reversible when promptly identified and treated.

Hepatic encephalopathy is sometimes broken down into three subtypes: Type A, which is associated with acute liver failure; Type B, which is associated a portosystemic shunt (a shunt that bypasses the liver) with no existing liver disease present; and Type C,

which is associated with scarring and poor function of the liver (cirrhosis), which often occurs with chronic liver disease.

While the symptoms are similar among these different subtypes of hepatic encephalopathy, individuals with acute liver failure are more likely to have swelling (edema) in the brain and increased pressure within the skull (intracranial hypertension), which can potentially cause life-threatening complications.

Researchers now believe that as many as 70 percent of individuals with cirrhosis development symptoms of hepatic encephalopathy. Many individuals only develop mild symptoms, so-called minimal hepatic encephalopathy (MHE).

MHE may not be associated with any obvious or outwardly noticeable signs or symptoms. However, there may be subtle or minimal changes in memory, concentration, and intellectual function. Coordination may also be affected and some affected individuals may take longer to respond to situations (increased reaction time). These symptoms, although termed “subtle”, can still have significant consequences on daily life such as impairing a person’s ability to drive a car.

Hepatic encephalopathy can be associated with more severe symptoms including reduced alertness, shortened attention span, disruptions in sleep patterns, mild confusion, slowing of the ability to perform mental tasks and mood or personality changes. More noticeable changes in memory, concentration or intellectual function than occur in MHE may also be seen. When affected individuals have obvious, outward signs and symptoms, the disorder may be referred to as overt hepatic encephalopathy.

Eventually, affected individuals may develop lethargy, slurred speech, confusion, significant delays in performing mental tasks, and regression of skills requiring the coordination of mental and physical activities (psychomotor retardation). Affected individuals may also develop obvious personality changes including inappropriate

behavior or lack of restraint. Some individuals may slowly flap their hands up and down when attempting to hold their arms out, a condition known as asterixis.

In the most severe form of hepatic encephalopathy, affected individuals may develop marked confusion or disorientation, amnesia, greatly dulled or reduced consciousness (stupor) or loss of consciousness (coma). Additional severe and potentially life-threatening complications of cirrhosis include permanent nervous system damage, heart failure, kidney abnormalities including kidney failure, breathing (respiratory) abnormalities and blood poisoning (sepsis).

Causes

Hepatic encephalopathy occurs in individuals with liver disease when toxins that are normally cleared in the liver accumulate in the blood eventually traveling to and damaging the brain. The exact underlying mechanisms by which hepatic encephalopathy develops in individuals with liver disease are not fully understood.

Researchers believe that high blood pressure of the main vein of the liver (portal hypertension) results in blood bypassing the liver. Normally, blood travels through the portal vein and enters the liver where toxins are removed or filtered from the blood (detoxification). By bypassing the liver, unfiltered blood ends up circulating throughout the body eventually reaching the brain where certain toxics damage brain tissue.

Although the exact underlying process by which hepatic encephalopathy develops is unknown, high levels of substances produced by the digestive breakdown of proteins, such as ammonia, are believed to play a major role. Ammonia is elevated in individuals with acute and chronic liver disease and is known to affect the brain in other disorders such as Reye syndrome and certain metabolic disorders. Ammonia is normally converted to urea in the liver and cleared out of the body through the urine. Ammonia is highly toxic to the brain. Although ammonia is generally accepted to a play a role in

hepatic encephalopathy, some individuals with elevated ammonia levels do not develop symptoms, suggesting that additional factors play a role in the development of the disorder.

Additional factors that have been explored as potentially playing a role in the development of hepatic encephalopathy include manganese toxicity and impaired function of certain central nervous system cells called astrocytes, which play a role in regulating the blood-brain barrier and also help to detoxify certain chemicals including ammonia; dysfunction of the blood-brain barrier, which prevents dangerous substances from reaching the brain; amino acid imbalances; short chain fatty acids; infection; inflammation; and increased activity of GABA, an inhibitory neurotransmitter in the central nervous system. More research is necessary to determine the exact, underlying factors that ultimately cause the development of hepatic encephalopathy and its associated symptoms.

As briefly discussed above, in individuals with chronic liver disease, episodes of hepatic encephalopathy may be triggered by certain events or occurrences such as low levels of oxygen in the body, dehydration, constipation, gastrointestinal bleeding, an alcohol binge, infection, kidney abnormalities and the use of certain drugs especially those that act on the central nervous system such as tranquilizers and other sleep medications, antidepressants, and antipsychotics. In some cases, surgery can precipitate an episode of hepatic encephalopathy. Gastrointestinal bleeding is the most common precipitating event associated with hepatic encephalopathy, most likely because individuals with cirrhosis are at a greater risk of gastrointestinal bleeding than the general population.

Diagnosis

A diagnosis of hepatic encephalopathy may be suspected in some individuals with liver disease based upon identification of characteristic symptoms, a detailed patient history, a thorough clinical evaluation and a variety of specialized tests that are used to rule out

other conditions. Such tests may include a complete blood count, liver function tests, tests that evaluate serum ammonia levels, and an electroencephalogram, which is a test that measures the electrical activity of the brain, may be useful in detecting encephalopathy. Specialized imaging techniques such as magnetic resonance imaging (MRI) and computed tomography (CT) scans may be used to rule out other conditions affecting the brain such as tumors.

What every clinician should know

HE is a neuropsychiatric disorder of altered consciousness that consists of three types:

Type A: HE associated with acute hepatic failure

Type B: HE associated with portal-systemic bypass without intrinsic hepatocellular damage

Type C: HE associated with end-stage liver disease (ESLD) or cirrhosis with portal-systemic shunt

Clinical features

HE can range from minimal confusion to coma. The West Haven criteria for grading severity of HE are the most commonly used (Table).

Classification	Symptoms and physical findings
Minimal encephalopathy	Minimal changes in memory, evidence on psychometric testing, absence of detectable changes in personality and behavior
Grade I	Trivial lack of awareness, euphoria or anxiety, shortened attention span, impaired performance of addition or subtraction
Grade II	Lethargy or apathy, minimal disorientation for time or place, subtle personality change, inappropriate behavior, asterixis usually present

Grade III	Somnolence to semistupor, but responsive to verbal stimuli, confusion, gross disorientation, clonus, nystagmus, positive Babinski sign
Grade IV	Hepatic coma

Key management points

Because HE in patients with ESLD is usually triggered by precipitating factors such as infection, gastrointestinal bleeding, electrolyte abnormalities, and medication noncompliance, it is important to identify these factors and manage them accordingly. In addition to general supportive care, the following strategy should be taken when managing HE:

- Reduce ammonia production and absorption
- Increase ammonia excretion
- Target potential neurotransmitters, toxic substances
- Provide nutritional support

As mentioned above, HE in ESLD is not usually due to worsening liver disease; rather, it is a result of a precipitating factor.

Standard Therapies

Treatment

The specific therapies used to treat hepatic encephalopathy may vary depending upon numerous factors including whether there is a triggering event, the presence or absence of certain symptoms, the severity of the disorder and the severity of the underlying liver disease, an individual's age and general health and other factors. An episode of hepatic encephalopathy can be a medical emergency that requires an emergency room visit or hospitalization.

Initial therapies may be aimed at identifying and removing a triggering event such as infection, gastrointestinal bleeding, certain drugs or kidney dysfunction. Such therapies

may include medications to treat infections, medications or procedures to alleviate or control bleeding, stopping the use of medications that can trigger an episode and any appropriate therapy for kidney issues.

Additional treatment for individuals with hepatic encephalopathy is usually aimed at lowering the levels of ammonia and other toxins in the blood. Since such toxins originally arise in the gut, therapies are directed toward the gastrointestinal system. Such therapies may include, using synthetic sugars such as lactulose, which speeds up the passage of food through the gastrointestinal tract and inhibits the absorption of toxins by the intestines and antibiotics, which act on bacteria in the colon. Lactulose and antibiotics may be used in conjunction.

In 2010, the Food and Drug Administration (FDA) approved the use of rifaximin (Xifaxan®) to reduce the risk of overt hepatic encephalopathy in individuals 18 and older. Xifaxan reduces the risk of overt hepatic encephalopathy and reduces the number of hospitalizations due to hepatic encephalopathy. Xifaxan is thought to act on microorganisms found in the digestive tracts of humans (gut flora).

Knowledge control:

1. Determination of gastrointestinal bleeding, bile colic, intestinal colic.
2. Gastrointestinal bleeding, bile colic, intestinal colic, features of treatment tactics.
3. Possible complications of gastrointestinal bleeding, bile colic, intestinal colic.
4. Primary and secondary prevention of gastrointestinal bleeding, bile colic, intestinal colic.
5. Forecast and efficiency.
6. Hepatic encephalopathy, hepatic coma, features of treatment tactics.
7. Emergency care in case of hepatic encephalopathy, hepatic coma.

Test tasks:

1. A 20- year old woman with 3-4 months history of bloody diarrhea, stool examination

negative for an ova and parasites, stool culture negative for Clostridium, Campylobacter and Yersinia, normal bowel series edema, hyperemia and ulceration of rectum and sigmoid colon seen on sigmoidoscopic examination.

a.Ulcerative colitis

b.Granulomatous colitis

c.Gastroenteritis

d.Lactose intolerance

e.Carcinoid syndrome

2. Patient, 46 years old, complains of bloating, intermittent pain in the paraumbilical abdomen region, diarrhoea. The diagnosis of chronic enteritis. Diarrhoeal syndrome in this patient is characterized by all signs, except:

a.Accompanied by tenesmus

b.Frequency of 2-3 times a day

c.Yellow stool down

d.Accompanied by abdominal murmur

e.Feces in large quantity

3. The patient 42 years old complains of permanent pain in the epigastric area with irradiation in the back, nausea, vomiting, heartburn. Patients with peptic ulcer duodenum for 20 years. Objectively: reduced nutrition, tongue coated, moist. The abdomen is tense, painful when palpation in the pyloroduodenal zone. Positive Obraztsovs Symptom. Subfreshness Blood analysis: leukocytes 10.0 * 10 / l, ESR-24mm / h. Radiologically: in the bulb of the duodenum, a three-layer niche is connected 0.7 * 1.0 s. Gregersen's reaction (-). What complication takes place in this case?

a. Penetration

b. Perforation

c. Bleeding

d. Malignancy

e. Gatekeeper stenosis

4. At the woman of 28 years, transferred 1,5 years ago laporoskopicheskuju a cholecystectomy there were pains in right hypochondrium of former intensity. She noted an achalic chair, darkening of urine. Which method is most indicated to clarify the diagnosis?

a. Retrograde cholangiography

b. Liver scintigraphy

c. Esophagogastroduodenoscopy

d. Thermography of the trunk

e. Ultrasonography

5. At the age of 18, a patient has complaints about rheumatic abdominal pain, fluid feces up to 6 times / day with admixture of mucus and fresh blood. Ill ill during the year. Weight 10 kg. Abdominal: Abdomen is mild, painful along the colon, especially to the left. Sigmoid colon is spasmodic. In blood: er. - 3.2 * 10 <sup> 12 </ sup> / l, Nv - 92 g / l, leak. - 10.6 × 10 <sup> 9 </ sup> l, SHZE - 34 mm / year. Irygoscopy - the large intestine is narrowed, gaustri absent, contours are fuzzy, the symptom of the "tap water pipe". What is the most likely diagnosis?

a. Nonspecific ulcerative colitis

b. Chronic enterocolitis

c. Amoeba dysentery

d. Tuberculosis of the intestine

e. Crohn's disease

6. The patient 52 years old complains about bloody vomiting, heaviness in the right subfamily, lack of appetite, and weakness. Abuse of alcohol. Ob-de: reduced nutrition, icterity of sclera, skin, on the skin of the face - vascular "stars", ascites of the expansion of the veins of the anterior abdominal wall. The liver acts - 4 cm, the spleen - 3 cm under the edge arc. What is the probable cause of bleeding?

a. Cirrhosis

b. Erotic esophagitis
c. Melorie-Weiss syndrome
d. Thrombosis of the portal vein
e. Esophagus tumor

7. In a 40-year-old patient with acute viral hepatitis B on the 10th day of inpatient treatment, the general condition deteriorated sharply: "Nausea, re-vomiting, increased pain in the right hemorrhage, and jaundice of sclera and skin became evident. In blood leukocytosis, hyperbilirubinemia with predominance of indirect fraction. What complication has developed?

a. Liver encephalopathy
b. Intrahepatic cholestasis
c. Renal insufficiency
d. Exacerbation of cholecystitis
e. Obstructive jaundice

8. The patient T. 60 years complained in anamnesis for pain in the epigastric region and in the right hypochondrium, not associated with eating, skin itching, nosebleeds, bleeding of the gums, entered the resuscitation with hemorrhage from the esophagus. What is the most likely cause of bleeding?

a. Cirrhosis
b. Erotic esophagitis
c. Peptic ulcer
d. Achalasia of the esophagus
e. Esophageal cancer

9. A patient S. 51 years old, complains about vomiting with blood impurities. Abused alcohol. He has been ill for 40 years when jaundice first appeared. On examination: skin and visible mucous membranes, "vascular sprouts". Lowered Power. Abdomen enlarged in volume, umbilical vein, ascites. The edge of the liver is acute, painful, + 3

cm in, spleen + 2 cm .. An. blood: Hb - 80 g / l, leech. - 3 • • 10 <sup> 9 </ sup> r, thrombosis. - 85 • • 10 <sup> 9 </ sup> g. The cause of portal hypertension in a patient is:

a. Cirrhosis

b. Thrombosis of the spleen veins

c. Constrictive pericarditis

d. Badda-Kiri syndrome

e. Hemochromatosis

10. A 79-year-old woman comes to the emergency department because of a large amount of hematochezia. She was feeling well until 2 days ago, when she felt the sudden urge to defecate. She went to the bathroom and passed bright red blood without clots or stool but otherwise felt well. The patient has no history of gastrointestinal bleeding and takes no medications. Colonoscopy, performed 5 years ago for evaluation of constipation, showed extensive left-sided diverticulosis. On physical examination, supine blood pressure is 160/90 mm Hg and pulse rate is 80/min. Blood pressure remains the same on sitting, but her pulse rate increases to 110/min. Abdominal examination is normal. Digital rectal examination reveals bright red blood; no masses or stool is palpated. Hemoglobin is 11.0 g/dL (baseline hemoglobin was 13.4 g/dL 6 weeks ago). Coagulation parameters and platelet count are normal. The patient is given 1.5 L of normal saline, and the orthostatic changes resolve promptly. Which of the following is the next best step in her management?

a.Colonoscopy

b.Bleeding scan

c.Angiography

d.Immediate surgical consultation

e.Upper endoscopy

Topic 6. Preparation for practical training № 6 «DIC syndrome. Acute bleeding and blood loss»

Learning objective

The student must know:

- etiology and pathogenesis of different forms of disseminated intravascular coagulation (DIC) syndrome, bleeding, blood loss;

- the variants and main clinical syndromes of disseminated intravascular coagulation (DIC) syndrome, bleeding, blood loss;
- principles of diagnosis differential diagnosis, diagnostic possibilities of additional methods of investigation of disseminated intravascular coagulation (DIC) syndrome, bleeding, blood loss;
- principles of management, clinical pharmacology of the drugs used in treatment of disseminated intravascular coagulation (DIC) syndrome, bleeding, blood loss;
- principles of management of blood transfusion therapy

Be able:

- to collect patient's anamnesis (including professional, hemotransfussional, alergological);
- to examine a patient with haemoragic diathesis;
- to form plan of investigations of a patient with disseminated intravascular coagulation (DIC) syndrome, bleeding, blood loss;
- on the basis of laboratory criterias to prove prior diagnosis, to conduct differential diagnosis, to form clinical diagnosis taking into considerations demands of today's classification;
- to indicate adequate treatment of a patient with disseminated intravascular coagulation (DIC) syndrome, bleeding, blood loss accounting etiology, degree of weight and complications.

Master practical skills:

- pulse oximetry.
- electrocardiography in 12 standard leads.
- evaluation of sputum analysis
- evaluation of pleural fluid analysis

Theoretical material for independent student training.

During thrombotic thrombocytopenic purpura, there may be a condition that requires emergency care - ***DIC syndrome.***

Definition. The term DIC syndrome (thrombohemorrhagic syndrome) refers to a nonspecific pathological process based on massive blood clotting, which causes blockage of microcirculation by cell aggregates and loose masses of fibrin and is accompanied by thrombosis, hemorrhage, life-threatening acidosis and dystrophy.

Etiology. The etiology of DIC is diverse, as it is an intermediate link in the evolution of many pathological processes, including critical and terminal conditions. DIC - syndrome is accompanied by:

Classification. There are four stages in the development of DIC syndrome (ZS Barkagan, 1988). Activation of coagulation mechanisms leads to hypercoagulation (stage I). This stage is short-lived (especially in acute forms) and can quickly progress to the stage of hypocoagulation (III) as a result of platelet consumption, plasma coagulation factors, conversion of fibrinogen to PDF and RFMC due to activation of fibrinolysis. Between stages I and III there is a short period (minutes, hours) of false "normocoagulation" - transitional, stage II. This is followed by stage IV - the final, which is characterized by either compensation for hemostasis, or the development of irreversible changes and death.

Clinical picture. The clinic of DIC syndrome depends on the underlying disease and the course.

In the acute course, the most severe manifestations of DIC syndrome are hemocoagulation shock (collapse), which is based on the blockade of microcirculation in vital organs. Shock complicates the course of DIC syndrome in 15-20% of patients, while DIC syndrome almost always accompanies shock states of various etiologies. The most severely damaged organs are those with a developed microcirculatory network (lungs, kidneys, adrenal glands, gastrointestinal tract, liver, etc.). Syndromes develop: shock lung, acute renal failure, hepatorenal syndrome, acute erosions and ulcers of the gastric and intestinal mucosa, acute adrenal insufficiency, thrombotic and

hemorrhagic lesions of the brain and meninges. In subacute and chronic forms of DIC - the symptoms of the underlying disease come to the fore. Hemorrhages appear on the skin: small hemorrhages and ecchymoses are combined with hematomas. It is characteristic of all forms of DIC - renal involvement syndrome with manifestations of oliguria, moderate azotemia to cortical necrosis and uremia. Chronic forms can be latent. In malignant tumors, the clinical manifestations of the prolonged phase of hypercoagulation may be thrombosis and thrombophlebitis.

Classification of DIC syndrome

Forms in the course of Stages (phases) Pathogenetic variants

Acute (minutes, hours, days)

Subacute (days, weeks, months)

Chronic recurrent (months, years)

Latent

I. Hypercoagulation

II. Transient (normal coagulation)

III. Hypocoagulation

IV. Compensation for hemostasis disorders

Irreversible changes Infectious, infectious-septic, "obstetric model", hemolytic, immunocomplex, traumatic, "trypsin", neoplastic, etc.

Diagnostic criteria of DIC syndrome.

A. Clinical.

There are no specific clinical symptoms of DIC - syndrome, so in the early stages of the diagnosis is situational - rapid assessment of "DIC - danger".

1. The most common manifestations of the syndrome are bleeding - on average in 55-75% of patients: multiple hemorrhages of different localization. Characterized by a decrease in the size and density of blood clots. Early hemorrhages are more extensive and localized in the areas of tissue damage (in the area of the operating field, in the injection

sites, etc.), in the later stages are manifested by bleeding from the mucous membranes and deep hematomas (type III bleeding).

2. A combination of thrombosis and bleeding.

3. Acute onset of failure of two or more organs (acute respiratory, renal, hepatic, adrenal insufficiency) - multiorgan failure.

4. Prolonged shock with hemorrhages.

B. Laboratory.

1. Cellular markers:

1.1. Spontaneous platelet aggregation.

1.2. Thrombocytopenia (less than 150 · 109 / l).

1.3. The phenomenon of mechanical damage to erythrocytes (cell fragments - in a blood smear, in a solution of ficolverografin with a specific gravity of 1.077 more than 500 cells in 1 μl).

2. Plasma markers.

2.1. Hypercoagulation, hypocoagulation, complete blood clotting (Lee-White test).

2.2. Increase in the content of paracoagulation products (RFMC and PDF) in plasma and serum (positive: ethanol test (ET), protamine sulfate test (PST), staphylococcal adhesion test (TCC), orthophenanthroline test).

2.3. Decrease in the level of ATIII below 70%.

2.4. Decreased amount of prothrombin, fibrinogen.

In the comparative analysis of the results of paracoagulation tests it was found that the most informative for the diagnosis of DIC is the orthophenanthroline test. In contrast to ET and PST, it is more sensitive and allows you to quantify the plasma content of RFMC (the ability to establish the degree of thrombinemia and control the dynamics of DIC - syndrome, the effectiveness of therapy.

Differential diagnosis. The first phase of DIC syndrome should be differentiated from the hypercoagulable syndrome associated with the primary activation of platelet hemostasis in intoxications, infections, hyperthrombocytosis, vascular wall damage.

Clinically, the hypercoagulable syndrome is latent, not accompanied by multiple organ failure. Detected in a laboratory study by shortening the clotting time according to Lee-White. In contrast to the hypercoagulant phase of DIC, paracoagulation (ET) tests are negative, prothrombin time is shortened, fibrinogen levels are elevated, platelet counts are normal or increased, and Duke's bleeding time is normal.

Manifestations of bleeding are characteristic of parenchymal liver disease and are caused by impaired biosynthesis of procoagulants (proconvertin, prothrombin, antihemophilic globulin B, and in severe cases - factors V, XI, XIII and I.

In contrast to the phase of hypocoagulation of DIC syndrome, the intensity of hemorrhagic manifestations depends on hepatocyte dysfunction: (increased titers of ALT, AST bilirubin level), at the same time reduced plasma prothrombin albumin. At clinical research hepato- and splenomegaly is defined, at cirrhosis - a syndrome of portal hypertension. ET, orthophenanthraline tests are negative. PST in conditions of dysfibrinogenemia is less specific.

Treatment. The effectiveness of treatment of DIC syndrome depends on how early the etiotropic therapy of the pathological process that caused it, anti-shock measures, detoxification, combating target organ dysfunction and hypoxia. Given the high frequency of infectious-septic forms of postoperative and obstetric DIC syndromes, the addition of bacteremia to the initial "non-infectious forms" (up to 70%), a comprehensive therapy of DIC syndrome is recommended.

1. In stage I of DIC syndrome, transfusion therapy should begin with drugs that normalize rheological disorders caused by intravascular activation and aggregation of platelets and other blood cells (trental, dipyridamole, rheopolyglucin and other low molecular weight dextrans).
2. Early pre-jet injection of fresh-frozen donor plasma (FPS) as a source not only of blood pressure III and other components of the blood coagulation system, but also of protein C - a physiological anticoagulant that protects the body from pathogenic Escherichia

coli and bacterial endotoxin. (Nowadays, JSC III concentrates have been synthesized abroad).

FPS (average 6-12 mg / kg) with heparin (15000-20000 IU / day), effectively acts on the key mechanisms of development of DIC syndrome and is the basic method of treatment of DIC syndrome. The combination of SZP with simultaneous administration of heparin (heparin-cryoplasmic therapy) promotes rapid inhibition and rupture of intravascular coagulation. The rate of formation of the complex "antithrombin III-thrombin" increases almost 1000 times, which leads to rapid inactivation of thrombin (factor IIa). At the same time factors are neutralized: Xa, XIIa, IXa, XIa.

3. In the II and III stages of DIC - syndrome, with severe hypocoagulation and hemorrhage to inhibit excessive activation of fibrinolysis, it is advisable to use in addition to FPS large doses of trasilol (105 IU or more per day) or its analogues in combination with mini doses of heparin (2500 IU per day during the acute period (4-5 hours) The introduction of heparin is carried out under the control of hemostasis (not more than 500 IU / h).
4. Carrying out intensive (intravenous) antibiotic therapy (semi-synthetic penicillins, ristomycin, cephalosporins, etc.) at the first signs of infectious-septic process or symptoms of endotoxic shock. Prophylactic "sterilization" of the intestine (oral erythromycin).
5. At blood loss to 1000 ml, parameters of hemoglobin not less than 60 g / l, absence of threat of repeated bleeding from replacement transfusions of erythromass should be refused.
6. To remove microclots, cell aggregates, proteolysis products, activated leukocytes, etc. recommended therapeutic plasma - leukocyte apheresis with removal of the leukocyte layer (in infectious-septic, hemolytic, traumatic, burn DIC - syndromes).
7. At dominance at patients of massive thrombotic displays and heavy disturbances of function of bodies of ischemic character ("thromboembolic" form of DIC - a syndrome) replacement therapy of SZP is combined with intermittent administration of thrombolytic drugs. 400-600 SZP with 5000-10000 IU of heparin is injected pre-injected, followed by intravenous infusion of streptokinase (streptase, etc.) at a dose of

500000 IU. Further before each administration of thrombolytic drug cryoplasma and heparin (under the control of laboratory tests) are entered.

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symptoms of endotoxic shock. Prophylactic "sterilization" of the intestine (oral erythromycin).

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8. Absolutely contraindicated in all types of DIC - syndrome of pre-administration of fibrinogen and dry plasma drugs (increases the blockade of microcirculation, increases blood viscosity). The use of fibrinolysis inhibitors (aminocaproic acid) is also not recommended.

Course, complications, prognosis. Isolation of clinical forms of DIC - syndrome for course (acute, subacute, chronic) is to some extent conditional, as possible transitions of chronic latent form to acute, and acute - to subacute and chronic. The wave-like course with repeated change of phases of hyper- and hypocoagulation is usually associated either with insufficient effectiveness of treatment, or with secondary infection and transformation of non-infectious DIC - bacteremic syndrome, which often progresses instantly. The source of infection can be damaged tissues (operating field, uterine contents after childbirth), intestines, etc. Violation of hemostasis (thrombosis and hemorrhage) and hemodynamics (blockade of microcirculation by cellular aggregates and fibrin-monomer complexes) leads to dysfunction and dystrophy of vital organs, including skin with symmetrical necrosis and gangrene, thrombosis of

spinal arterines and spinal arthrosis. Causes of death - multiorgan failure, "shock lung", lesions of the central nervous system (encephalopathy, coma), cortical necrosis and uremia.

According to world statistics, mortality rates in DIC syndrome range from 30-76%, averaging about 50%.

Knowledge control:

1. The definitions of disseminated intravascular coagulation (DIC) syndrome, bleeding, blood loss
2. The etiology and pathogenesis of disseminated intravascular coagulation (DIC) syndrome, bleeding, blood loss.
3. Classification of disseminated intravascular coagulation (DIC) syndrome, bleeding, blood loss.
4. The main clinical syndromes of disseminated intravascular coagulation (DIC) syndrome, bleeding, blood loss.
5. Additional methods of investigation of disseminated intravascular coagulation (DIC) syndrome, bleeding, blood loss.
6. The differential diagnosis of disseminated intravascular coagulation (DIC) syndrome, bleeding, blood loss.
7. The management of disseminated intravascular coagulation (DIC) syndrome, bleeding, blood loss acounting etiology, degree of weight and complications.
8. The questions of prognosis, prevention.

Test tasks:

1. A 2-months-old child after preventive vaccination had a prolonged hemorrhage from the vaccination place and due to those an intramuscular hematoma. Duri ng examination of the child a considerable rise of prothrombin consumption and a significant prolongation of the activated partial thromboplastic time were found. What is the most probable diagnosis?

A. Hemophilia

B. Werlhof's disease

C. Henoch-Schoenlein disease

D. Hemorrhagic disease of the neonate

E. Inborn afibrinogenemia

2. A 16-year-old woman complains of the abdominal pain and purpuric spots on the skin. Laboratory investigations revealed normal platelet count with hematuria and proteinuria. What is the most probable diagnosis?

A. Henoch-Schoenlein purpura

B. Thrombotic thrombocytopenic purpura

C. Heavy metal poisoning

D. Hemolytic uremic syndrome

E. Subacute bacterial endocarditis

3. A neonate was born from the 1st gestation on term. The jaundice was revealed on the 2nd day of life, and then it became more acute. The adynamia, vomiting and hepatomegaly were observed. Indirect bilirubin level was 275/imol/L, direct bilirubin level - Sμ mol/L, Hb — 150 g/1. Mother's blood group - 0[I], Rh+, child's blood group-A[II], Rh+. What is the most probable diagnosis?

A. Hemolytic disease of the neonate [ABO incompatibility], icteric type

B. Physiological jaundice

C. Hepatitis

D. Hemolytic disease of the neonate [Rh -incompatibility]

E. Jaundice due to conjugation disorder

4. The child was born from the 5th pregnancy and 1st delivery. Mother's blood group — A[II] Rh-, neonate's -A[II] Rh+. The level of indirect bilirubin in umbilical blood was 58/μmol/L, hemoglobin - 40 g/L, RBC — 3,8* 1012/L. The level of indirect bilirubin in 2 hours was 82μmol/l. The hemolytic disease of the neonate [icteric-anemic type, Rh-incompatibility] was diagnosed. Choose the therapeutic tactics.

A. Replacement blood transfusion

B. Hormonal therapy

C. Symptomatic therapy

D. Plasma transfusion

E. Antibiotics

5. A 42-year-old man has died in a road accident after the hemorrhage on the site, due to acute hemorrhagic anemia. What minimum percent of all volume of blood could result in death at acute hemorrhage?

A. 25-30%

B. 15-20%

C. 10-14%

D. 35-50%

E. 6-9%

6. A 3-day-old newborn who has suffered asphyxia in labor presents with bleeding from umbiligal sore. Labo tests: hypocoagulation, thrombocytopenia, hypothrombinemia. What is the most likely cause of clinical and laboratory changes?

E. Disseminated intravascular coagulation (DIC)

A. Trauma of umbilical vessel

B. Thrombocytopenic purpura

C. Inborn angiopathy

D. Hemolytic disease of newborn

7. A neonate was born from the 1st gestation on term. The jaundice was revealed on the 2nd day of life, and then it became more acute. The adynamia, vomiting and hepatomegaly were observed. Indirect bilirubin level was 275 /itmol/L, direct bilirubin level - 5 mol/L, Hb -150 g/L. Mother's blood group - 0[I], Rh+, child's blood group-A[II], Rh+. What is the most probable diagnosis?

A. Hemolytic disease of the neonate [ABO incompatibility]

B. Jaundice due to conjugation disorder

C. Physiological jaundice

D. Hemolytic disease of the neonate [Rh -incompatibility]

E. Hepatitis

8. A man with liver cirrhosis complains of nasal bleedings, right subcostal pain, weakness, nausea. On physical examination: jaundice, hemorrhagic rash, enlarged liver span (of 14 cm), liver edge irregular. What is the cause of hemorrhagic syndrome in this patient?

A. Decreased liver production of focoagulants

B. Disseminated intravascular coagulation

C. Thrombocytopenia

D. K and C hypovitaminosis

E. Portal hypertension

9. A woman, aged 30, in the second childbirth there is a baby born with anaemicicteric form of the hemolytic disease. Blood group of the mother is A(II) Rh-, blood group of the new born is B(III) Rh+, blood group of the father is B(I1I) Rh+. What is the most probable cause of immune conflict?

A. Rhesus incompatibility

B. Antigen A conflict

C. Antigen AB conflict

D. Antigen ABO conflict

E. Antigen B conflict

10. A victim of a road accident suffered multiple fractures of extremities and pelvis bones. In medical history; haemophilia A. On examination: hematomes are forming on the injured areas. The patient's condition is aggravating. BP — 90/50 mm Hg. What is the most expedient combination of infusion medications for patient's treatment after administering polyglukine and saline?

A. Cryoprecipitate, packed red blood cells

B. Packed red blood cells, fresh frozen plasma

C. Packed red blood cells

D. Cryoprecipitate, glucose

E. Fresh frozen plasma, albumin

11. A 33 y.o. patient was admitted to the hospital with stopped recurrent peptic ulcer bleeding. On examination he is exhausted, pale. Hb — 77 g/L, Ht — 0,25. Due to anemia there were two attempts of blood transfution of identical blood group A(ll)Rh+. Both attempts were stopped because of anaphylactic reaction. What blood transfution environment is desirable in this case?

A. Washed erythrocytes

B. Erythrocyte emulsion

C. Erythrocyte mass (native)

D. Freshcitrated blood

E. Erythrocyte mass poor for leucocytes and thrombocytes

12. A girl, aged 13, consults the school doctor on account of moderate bloody discharge from the genital tracts, which appeared 2 days ago. Secondary sexual characters are developed. What is the most probable cause of bloody discharge?

A. Menarche

B. Endometrium cancer

C. Werlhof 's disease

D. Juvenile haemorrhage

E. Haemophilia

13. A 19 y.o. patient was admitted to the hospital with acute destructive appendicitis. He sufferes from hemophilia B-type. What antihemophilic medicine should be inclended in pre-and post-operative treatment plan?

A. Fresh frosen plasma

B. Fresh frosen blood

C. Dried plasma

D. Native plasma

E. Cryoprecipitate

14. A 18 y.o. woman complains of weakness, dizziness, loss of appetite, menorrhagia. There are petechiae on the skin of the upper extremities. Blood test: Hb — 105 g/L; RBC- 3,2*1012/L; coloured index- 0,95; thromb.- 20*109/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. Iron deficiency anemia

C. Marchiafava-Micheli's disease

D. Hemophilia

E. Hemorrhagic diathesis

15. Full term newborn has developed jaundice at 10 hours of age. Hemolytic disease of newborn due to Rh-incompatibility was diagnosed. 2 hours later the infant has indirect serum bilirubin level increasing up to 14 mmol/L. What is most appropriate for treatment of hyperbilirubinemia in this infant?

A. Exchange blood transfusion

B. Phenobarbital

C Intestinal sorbents

D. Infusion therapy

E.Phototherapy

Topic 7. Preparation for practical training № 7 «Acute renal failure. Renal colic»

Learning objective

The student must know:

- determination of acute renal failure, renal colic;
- clinical manifestations of acute renal failure, renal colic;
- criteria for diagnosing acute renal failure, renal colic;
- laboratory and instrumental manifestations of acute renal failure, renal colic;
- main manifestations, differential diagnosis of acute renal failure, renal colic;
- principles of emergency care for patients with acute renal failure, renal colic;
- algorithm for providing emergency care

Be able:

- determine the state of emergency
- perform differential diagnosis with other emergencies
- assign appropriate emergency care

Master practical skills:

- pulse oximetry.
- electrocardiography in 12 standard leads.
- Ultrasound examination of the pelvic organs

Theoretical material for independent student training.

The concept of Acute Renal Failure (ARF) has undergone significant re-examination in recent years. Traditionally, emphasis was given to the most severe acute reduction in kidney function, as manifested by severe azotaemia and often by oliguria or anuria. However, recent evidence suggests that even relatively mild injury or impairment of kidney function manifested by small changes in serum creatinine (sCr) and/or urine output (UO), is a predictor of serious clinical consequences.

Acute Kidney Injury (AKI) is the term that has recently replaced the term ARF. AKI is defined as an abrupt (within hours) decrease in kidney function, which encompasses both injury (structural damage) and impairment (loss of function). It is a syndrome that rarely has a sole and distinct pathophysiology. Many patients with AKI have a mixed aetiology where the presence of sepsis, ischaemia and nephrotoxicity often co-exist and complicate recognition and treatment. Furthermore the syndrome is quite common among patients without critical illness and it is essential that health care professionals, particularly those without specialisation in renal disorders, detect it easily.

Classification of AKI includes pre-renal AKI, acute post-renal obstructive nephropathy and intrinsic acute kidney diseases. Of these, only 'intrinsic' AKI represents true kidney disease, while pre-renal and post-renal AKI are the consequence of extra-renal diseases leading to the decreased glomerular filtration rate (GFR). If these pre- and/or post-renal conditions persist, they will eventually evolve to renal cellular damage and hence intrinsic renal disease.

The current diagnostic approach of AKI is based on an acute decrease of GFR, as reflected by an acute rise in sCr levels and/or a decline in UO over a given time interval. Recently several biomarkers have been proposed for the diagnosis of AKI and these are in various stages of development and validation. Nevertheless, it is not clear, if a single or multiple biomarker approach is necessary to diagnose the complicated and multifactorial aspects of AKI.

However, in addition to the analytical difficulties associated with each specific biomarker, there is also an issue concerning the appropriate reference point, and more specifically about using sCr as the standard, for the clinical evaluation of these biomarkers. It is known that sCr is insensitive to acute changes of renal function and levels can vary widely with age, gender, muscle mass, diet, medications and hydration status. Moreover it is not a direct marker of tubular damage, but rather a marker of GFR, and substantial increases in sCr can be observed in renal hypo-perfusion even

when the kidneys are structurally intact, resulting in pre-renal azotaemia. For these reasons sCr is considered an ‘imperfect gold standard’ for the diagnosis of AKI. Another issue with sCr is that in most clinical situations its true baseline value is not known, which makes the evaluation of patients very difficult. Moreover, given the phenotypic variability of AKI (different clinical phenotypes with distinct underlying pathophysiologies), it is not clear whether different approaches are necessary for diagnosis and monitoring of the clinical course and therapy.

In this review we will discuss the epidemiology and the definition of AKI. We will also discuss the clinical phenotypes, their pathophysiology and the link between AKI and remote organ dysfunction. Acute kidney failure occurs when your kidneys suddenly become unable to filter waste products from your blood. When your kidneys lose their filtering ability, dangerous levels of wastes may accumulate, and your blood's chemical makeup may get out of balance.

Acute kidney failure — also called acute renal failure or acute kidney injury — develops rapidly, usually in less than a few days. Acute kidney failure is most common in people who are already hospitalized, particularly in critically ill people who need intensive care.

Acute kidney failure can be fatal and requires intensive treatment. However, acute kidney failure may be reversible. If you're otherwise in good health, you may recover normal or nearly normal kidney function.

HISTORY

The first description of ARF, then termed ischuria renalis, was by William Heberden in 1802. At the beginning of the twentieth century, ARF, then named Acute Bright’s disease, was described in William Osler’s Textbook for Medicine (1909), to be “as a consequence of toxic agents, pregnancy, burns, trauma or operations on the kidneys”. During the First World War the syndrome was named war nephritis, and was reported in several publications. The syndrome was forgotten until the Second World War, when

Bywaters and Beall published their classical paper on crush syndrome. Acute tubular necrosis (ATN) was the term that was used to describe this clinical entity, because of histological evidence for patchy necrosis of renal tubules at autopsy. For many years in clinical practice, the terms ATN and ARF were used interchangeably. However, it is Homer W. Smith who is credited for the introduction of the term acute renal failure, in a chapter on Acute renal failure related to traumatic injuries in his 1951 textbook The kidney-structure and Function in Health and Disease. Until recently, a precise biochemical definition for ARF was missing. As a consequence there was no consensus on the diagnostic criteria, resulting in multiple different definitions. A 2002 survey revealed at least 35 definitions in the scientific literature.

TERMINOLOGY AND DEFINITIONS

The term Acute Kidney Injury (AKI) was used for the first time by William MacNider in 1918 in a situation of acute mercury poisoning, but became the preferred term in 2004 when ARF was redefined with the now widely accepted consensus criteria known as RIFLE (an acronym of the Risk-Injury-Failure-Loss-End stage kidney disease).

Principal tools to detect AKI were consecutive measurements of sCr, serum urea (sUr), urinalysis, and measurements of UO. Urine indices such as fractional excretion of sodium (FeNa) and urea (FeUr) were also used to differentiate transient from persistent AKI. Agreement in diagnostic criteria for AKI came later from multiple consensus groups. First was the Acute Dialysis Quality Initiative (ADQI) group. In 2002 they developed a system for diagnosis and classification of acute impairment of kidney function through a broad consensus of experts, resulting in the RIFLE criteria. The characteristics of this diagnostic system are summarised in Table 1. With this system three severity grades are defined (Risk, Injury and Failure) and two outcome classes (Loss and End-Stage Renal Disease (ESRD)). The severity criteria of AKI are defined on the basis of the changes in sCr or UO where the worst of each criterion is used. The outcome criteria are defined by the duration of impairment of kidney function.

The importance of RIFLE criteria is that they move beyond ARF. The term “acute kidney injury/impairment” has been proposed to encompass the “entire spectrum of the syndrome from minor changes in markers of renal function to requirement for renal replacement therapy (RRT)”. Therefore the concept of AKI, as defined by RIFLE, creates a new paradigm. AKI encompasses ATN and ARF as well as other, less severe conditions. It includes patients without actual damage to the kidney but with functional impairment relative to physiologic demand. Including such patients in the classification of AKI is conceptually attractive because these are precisely the patients that may benefit from early intervention. The RIFLE criteria have also been modified for use in the paediatric setting. Nevertheless the RIFLE definition is not free of ambiguities. Pickering et al showed that there was a mismatch between increases in sCr concentration and decreases in GFR (estimated with MDRD or Cockroft-Gault formulae) in the descriptions of Risk and Failure severity grades. A 1.5-fold increase in sCr corresponds to a one-third decrease (not 25%) in GFR and a three-fold increase corresponds to a two-third decrease in GFR (not 75%). If the GFR is not directly measured but estimated by a formula then results might be also different depending on the formula used. With the MDRD formula a 1.5-fold increase in sCr corresponds to a 37% decrease in GFR, and a three-fold increase in sCr to a 72% decrease in GFR.

In 2007, the Acute Kidney Injury Network (AKIN) group proposed a modified version of the RIFLE criteria, which aimed to improve the sensitivity of AKI diagnostic criteria. There were several changes: an absolute increase in sCr of at least 0.3 mg/dL (26.5 μmol/L) was added to stage 1; the GFR criterion was removed; patients starting RRT were classified as stage 3, irrespectively of sCr values; and outcome classes were removed. The characteristics of this system are summarised in.

Only one criterion (sCr or UO) has to be fulfilled in order to qualify for a stage. Time becomes more important for AKI diagnosis in the AKIN definition: changes between two sCr values within a 48-hour period are required, while one week was proposed by

the ADQI group in the original RIFLE criteria. Severity of AKI in AKIN is staged over the course of 7 days by the fold-change in sCr from baseline.

The latest classification of AKI proposed by the Acute Kidney Injury Working Group of KDIGO (Kidney Disease: Improving Global Outcomes), is based on the previous two classifications, and had the aim of unifying the definition of AKI. By the KDIGO definition, AKI is diagnosed by an absolute increase in sCr, at least 0.3 mg/dL (26.5 μmol/L) within 48 hours or by a 50% increase in sCr from baseline within 7 days, or a urine volume of less than 0.5 mL/kg/h for at least 6 hours (Table).

A patient's progress can be staged over the entire time frame encompassed by an episode of AKI. An increase in sCr up to 3 times from baseline, or a sCr of more than 4.0 mg/dL (354 μmol/L) or initiation of RRT, are all classified as stage 3. KDIGO removes the 0.5 mg/dL increase for sCr >4 mg/dL to diagnose stage 3. KDIGO explicitly states that a rolling baseline can be used over 48-hour and 7-day periods for diagnosis of AKI, while in RIFLE or AKIN it is not clear how this is handled. Changes were also made to severity stage 3 to enable incorporation of paediatric population into both definition and staging.

AKI definition and staging according to KDIGO criteria - modified from reference
AKI is defined as any of the following:

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1 Increase in sCr ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours; or
2 Increase in sCr ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
3 Urine volume <0.5 mL/kg/h for 6 hours.

AKI is staged for severity according to the following criteria

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Stage 1 1.5–1.9 times baseline OR ≥0.3 mg/dL (≥26.5 μmol/L) absolute increase in sCr Urine volume <0.5 mL/kg/h for 6–12 hours

Stage 2 sCr ≥2.0–2.9 times baseline sCr ≥3.0 times from baseline OR Urine volume <0.5 mL/kg/h for ≥12 hours

Stage 3 Increase in sCr to ≥4.0 mg/dL(≥353.6 μmol/L) OR Initiation of renal replacement therapy OR, In patients <18 years, decrease in eGFR to <35 mL/min per 1.73 m2 Urine volume <0.3 mL/kg/h for ≥24 hours OR Anuria for ≥12 hours

sCr=serum creatinine, eGFR= estimated glomerular filtration rate

SYMPTOMS

Signs and symptoms of acute kidney failure may include:

Decreased urine output, although occasionally urine output remains normal

Fluid retention, causing swelling in your legs, ankles or feet

Shortness of breath

Fatigue

Confusion

Nausea

Weakness

Irregular heartbeat

Chest pain or pressure

Seizures or coma in severe cases

Sometimes acute kidney failure causes no signs or symptoms and is detected through lab tests done for another reason.

CAUSES

Acute kidney failure can occur when:

You have a condition that slows blood flow to your kidneys

You experience direct damage to your kidneys

Your kidneys' urine drainage tubes (ureters) become blocked and wastes can't leave your body through your urine

IMPAIRED BLOOD FLOW TO THE KIDNEYS

Diseases and conditions that may slow blood flow to the kidneys and lead to kidney injury include:

Blood or fluid loss

Blood pressure medications

Heart attack

Heart disease

Infection

Liver failure

Use of aspirin, ibuprofen (Advil, Motrin IB, others), naproxen sodium (Aleve, others) or related drugs

Severe allergic reaction (anaphylaxis)

Severe burns

Severe dehydration

DAMAGE TO THE KIDNEYS

These diseases, conditions and agents may damage the kidneys and lead to acute kidney failure:

Blood clots in the veins and arteries in and around the kidneys

Cholesterol deposits that block blood flow in the kidneys

Glomerulonephritis (gloe-mer-u-loe-nuh-FRY-tis), inflammation of the tiny filters in the kidneys (glomeruli)

Hemolytic uremic syndrome, a condition that results from premature destruction of red blood cells

Infection, such as with the virus that causes coronavirus disease 2019 (COVID-19)

Lupus, an immune system disorder causing glomerulonephritis

Medications, such as certain chemotherapy drugs, antibiotics and dyes used during imaging tests

Scleroderma, a group of rare diseases affecting the skin and connective tissues

Thrombotic thrombocytopenic purpura, a rare blood disorder

Toxins, such as alcohol, heavy metals and cocaine

Muscle tissue breakdown (rhabdomyolysis) that leads to kidney damage caused by toxins from muscle tissue destruction

Breakdown of tumor cells (tumor lysis syndrome), which leads to the release of toxins that can cause kidney injury

URINE BLOCKAGE IN THE KIDNEYS

Diseases and conditions that block the passage of urine out of the body (urinary obstructions) and can lead to acute kidney injury include:

Bladder cancer

Blood clots in the urinary tract

Cervical cancer

Colon cancer

Enlarged prostate

Kidney stones

Nerve damage involving the nerves that control the bladder

Prostate cancer

RISK FACTORS

Acute kidney failure almost always occurs in connection with another medical condition or event. Conditions that can increase your risk of acute kidney failure include:

Being hospitalized, especially for a serious condition that requires intensive care

Advanced age

Blockages in the blood vessels in your arms or legs (peripheral artery disease)

Diabetes

High blood pressure

Heart failure

Kidney diseases

Liver diseases

Certain cancers and their treatments

COMPLICATIONS

Potential complications of acute kidney failure include:

Fluid buildup. Acute kidney failure may lead to a buildup of fluid in your lungs, which can cause shortness of breath.

Chest pain. If the lining that covers your heart (pericardium) becomes inflamed, you may experience chest pain.

Muscle weakness. When your body's fluids and electrolytes — your body's blood chemistry — are out of balance, muscle weakness can result.

Permanent kidney damage. Occasionally, acute kidney failure causes permanent loss of kidney function, or end-stage renal disease. People with end-stage renal disease require either permanent dialysis — a mechanical filtration process used to remove toxins and wastes from the body — or a kidney transplant to survive.

Death. Acute kidney failure can lead to loss of kidney function and, ultimately, death.

PREVENTION

Acute kidney failure is often difficult to predict or prevent. But you may reduce your risk by taking care of your kidneys. Try to:

Pay attention to labels when taking over-the-counter (OTC) pain medications. Follow the instructions for OTC pain medications, such as aspirin, acetaminophen (Tylenol, others), ibuprofen (Advil, Motrin IB, others) and naproxen sodium (Aleve, others). Taking too much of these medications may increase your risk of kidney injury. This is especially true if you have pre-existing kidney disease, diabetes or high blood pressure.

Work with your doctor to manage kidney and other chronic conditions. If you have kidney disease or another condition that increases your risk of acute kidney failure,

such as diabetes or high blood pressure, stay on track with treatment goals and follow your doctor's recommendations to manage your condition.

Make a healthy lifestyle a priority. Be active; eat a sensible, balanced diet; and drink alcohol only in moderation — if at all.

DIAGNOSIS

If your signs and symptoms suggest that you have acute kidney failure, your doctor may recommend certain tests and procedures to verify your diagnosis. These may include:

Urine output measurements. Measuring how much you urinate in 24 hours may help your doctor determine the cause of your kidney failure.

Urine tests. Analyzing a sample of your urine (urinalysis) may reveal abnormalities that suggest kidney failure.

Blood tests. A sample of your blood may reveal rapidly rising levels of urea and creatinine — two substances used to measure kidney function.

Imaging tests. Imaging tests such as ultrasound and computerized tomography may be used to help your doctor see your kidneys.

Removing a sample of kidney tissue for testing. In some situations, your doctor may recommend a kidney biopsy to remove a small sample of kidney tissue for lab testing. Your doctor inserts a needle through your skin and into your kidney to remove the sample.

TREATMENT

Treatment for acute kidney failure typically requires a hospital stay. Most people with acute kidney failure are already hospitalized. How long you'll stay in the hospital depends on the reason for your acute kidney failure and how quickly your kidneys recover.

In some cases, you may be able to recover at home.

Treating the underlying cause of your kidney injury

Treatment for acute kidney failure involves identifying the illness or injury that originally damaged your kidneys. Your treatment options depend on what's causing your kidney failure.

Treating complications until your kidneys recover

Your doctor will also work to prevent complications and allow your kidneys time to heal. Treatments that help prevent complications include:

Treatments to balance the amount of fluids in your blood. If your acute kidney failure is caused by a lack of fluids in your blood, your doctor may recommend intravenous (IV) fluids. In other cases, acute kidney failure may cause you to have too much fluid, leading to swelling in your arms and legs. In these cases, your doctor may recommend medications (diuretics) to cause your body to expel extra fluids.

Medications to control blood potassium. If your kidneys aren't properly filtering potassium from your blood, your doctor may prescribe calcium, glucose or sodium polystyrene sulfonate (Kionex) to prevent the accumulation of high levels of potassium in your blood. Too much potassium in the blood can cause dangerous irregular heartbeats (arrhythmias) and muscle weakness.

Medications to restore blood calcium levels. If the levels of calcium in your blood drop too low, your doctor may recommend an infusion of calcium.

Dialysis to remove toxins from your blood. If toxins build up in your blood, you may need temporary hemodialysis — often referred to simply as dialysis — to help remove toxins and excess fluids from your body while your kidneys heal. Dialysis may also help remove excess potassium from your body. During dialysis, a machine pumps blood out of your body through an artificial kidney (dialyzer) that filters out waste. The blood is then returned to your body.

Acute Renal Colic

ETIOLOGY

There are multiple predictors and risk factors for stone formation. The following are the most common:

Inadequate urinary volume. Patients with low urine volumes (usually less than 1 L per day) increase the concentration of solutes (indicated by urine with an osmolarity greater than 600 mOsm/kg) and promote urinary stasis, which can cause supersaturation of solutes and lead to stone formation.

Hypercalciuria. Most often, this is an idiopathic finding, although it can be secondary to increased intestinal absorption of calcium, increased circulating calcium, hypervitaminosis D, hyperparathyroidism, high protein load, or systemic acidosis. Hypercalciuria increases the saturation of calcium salts like oxalate and phosphate, causing the formation of crystals. Calcium containing stones form approximately 80% of all renal stones. Hypercalciuria is usually defined as urinary calcium of 250 mg or more per 24 hours.

Elevated urine levels of uric acid (uric acid stones account for 5% to 10% of all renal calculi), oxalate, sodium urate, or cystine. Often these can be secondary to a high protein diet, high oxalate diet, or a genetic defect causing increased excretion. Most pure uric acid stones are caused by high urinary total acid levels and not by elevated urinary uric acid.

Infection stones. These are caused by urea-splitting organisms (Proteus or Klebsiella spp but not Escherichia coli) that break down urea in the urine, increasing concentrations of ammonia and pH, which promote stone formation and growth. Also called struvite or triple phosphate (Magnesium, Ammonium, Calcium) stones.

Inadequate urinary citrate levels. Citrate is the urinary equivalent of serum bicarbonate. It increases urinary pH, but it also acts as a specific inhibitor of crystal aggregation and stone formation. Optimal levels are approximately 250 mg/L to 300 mg/L of urine.

HISTORY AND PHYSICAL

Patients with renal colic typically present with sudden onset of flank pain radiating laterally to the abdomen and/or to the groin. Patients often report a dull constant level of pain with colicky episodes of increased pain. The constant pain is often due to stretching of the renal capsule due to obstruction, whereas colicky pain can be caused by peristalsis of the genitourinary tract smooth muscle against the obstruction. Many patients report associated nausea or vomiting, and some may report gross hematuria. As the stone migrates distally and approaches the bladder, the patient may experience dysuria, urinary frequency, urgency, or difficulty in urination.

Patients experiencing renal colic may present in very severe pain. Classically, these patients are unable to find a comfortable position and are often writhing on or pacing around the examination table. The exam may reveal flank pain more commonly than abdominal pain, and the skin may be cool or diaphoretic. There is often a prior personal or family history history of stones.

EVALUATION

Diagnosis is made through a combination of history and physical exam, laboratory, and imaging studies. Urinalysis shows some degree of microscopic or gross hematuria in 85% of stone patients, but should also be evaluated for signs of infection (e.g., white blood cells, bacteria). Urinary pH greater than 7.5 may be suggestive of a urease producing bacterial infection, while pH less than 5.5 may indicate the presence of uric acid calculi.

Basic metabolic panel (BMP) should be obtained to assess for renal function, dehydration, acid-base status, and electrolyte balance. Serum calcium should be checked. Complete blood count (CBC) can be considered to evaluate for white blood cell count if there is a concern for infection. Mild elevation of WBCs is commonly secondary to white blood cell demargination.

Consider obtaining a parathyroid hormone (PTH) level if primary hyperparathyroidism is suspected as a cause of any hypercalcemia. If possible, urine should be strained to capture stones for analysis to help determine if there is a reversible or preventable cause of stone development. Further metabolic testing such as 24-hour urine collection for volume, pH, calcium, oxalate, uric acid, citrate, sodium, and potassium concentrations should be considered in high-risk first-time stone formers, pediatric patients or recurrent stone formers. It is highly recommended in kidney stone patients with solitary kidneys, renal failure, renal transplants, gastrointestinal (GI) bypass, and any patient with high or increased anesthesia risk.

Unenhanced (or helical) CT is the gold standard of initial diagnosis, with a sensitivity of 98%, specificity of 100%, and negative predictive value of 97%. This modality allows rapid identification of stone, provides information as to the location and size of the stone, and any associated hydroureter, hydronephrosis, or ureteral edema, and can give information regarding potential other etiologies of pain (e.g., abdominal aortic aneurysm, malignancy). In those patients with no previous history of nephrolithiasis, CT should be performed to guide management. CT scans may underestimate stone size in comparison with an intravenous pyelogram or abdominal x-ray.

However, CT scan does expose patients to a radiation burden, and it can be costly. In some patients with a history of renal colic that present with pain similar to previous episodes of renal colic, it may be sufficient to perform ultrasonography (US). However, US is less sensitive (60% to 76%) than CT for detecting calculi less than 5 mm, but can reliably detect hydronephrosis and evidence of obstruction (increased resistive index in the affected kidney). It is also the modality of choice for evaluating a pregnant patient with concern for renal colic. Studies have shown that using ultrasonography as a primary imaging modality does not lead to an increase in complications in comparison to CT. Ultrasound is also a good way to follow a patient known to have uric acid stones.

An abdominal x-ray (KUB) can identify many stones, but 10% to 20% of renal stones are radiolucent and provide little information regarding hydronephrosis, obstruction, or the kidneys. Additionally, bowel gas, the bony pelvis, and abdominal organs may obstruct visualization of a stone. The KUB is recommended in kidney stone cases when the CT scan is positive, and the exact location of the stone is known. This helps in clearly identifying those stones that can be tracted by follow-up KUB and those that might be amenable to lithotripsy.

Using both a KUB and the renal US is a reasonable alternative to a CT scan and far cheaper with less radiation exposure. Symptomatic stones are likely to produce hydronephrosis or obstruction (visible on ultrasound) or will be seen directly on the KUB or the ultrasound.

TREATMENT / MANAGEMENT

Treatment includes the following:

Immediate intervention with analgesia and antiemetics. NSAIDs and opiates are first-line therapies for analgesia. NSAIDs work in two ways in renal colic. First, NSAIDs decrease the production of arachidonic acid metabolites, which mediate pain receptors, alleviating pain caused by distension of the renal capsule. Additionally, they cause contraction of the efferent arterioles to the glomerulus, causing a reduction in glomerular filtration, and reducing hydrostatic pressure across the glomerulus. Because patients are frequently unable to tolerate oral medications, parenteral NSAIDs such as ketorolac (15 mg to 30 mg intravenously (IV) or intramuscularly (IM)) or diclofenac (37.5 mg IV) are most commonly used.

Successful use of intravenous lidocaine for renal colic has been reported. The protocol is to inject lidocaine 120 mg in 100 mL normal saline intravenously over 10 minutes for pain management. It has been quite effective for intractable renal colic unresponsive to standard therapy and typically starts to work in 3-5 minutes. No adverse events have been reported.

Opiate pain medication, such as morphine sulfate (0.1 mg/kg IV or IM) or hydromorphone (0.02 mg/kg IV or IM), can also be used effectively for analgesia, especially when other measures have failed. However, opiates are associated with respiratory depression and sedation, and there is a risk of dependence associated with prolonged opiate use.

Fluid hydration. Although there is no evidence to support that empiric fluid will help "flush out" a stone, many patients are dehydrated secondary to decreased oral intake or vomiting and can benefit from hydration.

Medical expulsive therapy. Alpha 1 adrenergic receptors exist in increasing concentration in the distal ureter. The use of alpha blockade medications (for example, tamsulosin or nifedipine) is theorized to facilitate stone passage by decreasing intra-ureteral pressure and dilating the distal ureter. However, data from randomized control trials are somewhat mixed as to whether these medications improved stone passage. The consensus opinion is they may be helpful in smaller stones in the lower or distal ureter. They are probably of little use in larger stones in the proximal ureter.

Definitive management of impacted stones. There are several invasive methods to improve stone passage. These include shock wave lithotripsy, in which high energy shock waves are used to fragment stones, ureteroscopy with either laser or electrohydraulic stone fragmentation, or in rare cases, open surgery. In the presence of infection, a double J stent or percutaneous nephrostomy may be used to help with urinary drainage of the affected renal unit and definitive stone therapy postponed until the patient is stable.

Behavior modification and preventative management. Increase fluid intake to optimize urine output with a goal of 2 L to 2.5 L of urine daily. Patients with calcium stones and high urine calcium concentrations should limit sodium intake and have a goal of moderate calcium intake of 1000 mg to 1200 mg dietary calcium daily. Those with

calcium stones and low urinary citrate or those with uric acid stones and high urinary uric acid should increase intake of fruits and vegetables and decrease non-dairy animal protein. They may benefit from potassium citrate supplementation. Uric Acid stone formers are usually best treated with potassium citrate (urinary alkalinizer) to a pH of 6.5. Hyperuricosuric calcium stone formers can benefit from allopurinol. Thiazide diuretics are indicated in those with high urinary calcium and recurrent calcium stones to reduce the amount of urinary calcium. Patients with hyperoxaluria should be encouraged to lower their oxalate intake (spinach, nuts, chocolate, green leafy vegetables).

Knowledge control:

1. Determination of acute renal failure.
2. Acute renal failure, features of treatment tactics.
3. Possible complications of acute renal failure.
4. Primary and secondary prevention of acute renal failure.
5. Forecast and efficiency.
6. Renal colic, features of treatment tactics.
7. Emergency care in case of renal colic.

Test tasks:

1. 39-year-old man complains of morning headaches, appetite loss, nausea, morning vomiting, periodic nasal hemorrhages. The patient had a case of acute glomerulonephritis at the age of 15. Examination revealed rise of arterial pressure up to 220/130 mm Hg, skin hemorrhages on his arms and legs, pallor of skin and mucous membranes. What biochemical parameter is the most important for making diagnosis in this case?

A. Blood creatinine

B. Blood bilirubin

C. Blood sodium

D. Uric acid

E. Fibrinogen

2. 2 weeks after recovering from tonsillitis a 17-year-old boy developed edemas of face and lower limbs. Objectively: the patient is in grave condition, BP -120/80 mm Hg. Urine is of dark brown colour. Oliguria is present. On urine analysis: specific gravity - 1,015, protein - 1,2 g/l, RBCs are leached and cover the whole vision field, granular casts -1-2 in the vision field, salts are represented by urates (large quantity). What is the most likely diagnosis?

A. Acute glomerulonephritis with nephritic syndrome
B. Acute glomerulonephritis with nephrotic syndrome
C. Acute glomerulonephritis with nephrotic syndrome, hematuria and hypertension
D. Acute glomerulonephritis with isolated urinary syndrome
E. Nephrolithiasis

3. A 23-year-old patient after intake of brake fluid has developed anuria that has been lasting for 5 days already. Creatinine level increased up to 0,769 mmol/l. What treatment tactics should be chosen in the given case?

A. Hemodialysis
B. Detoxification therapy
C. Antidotal therapy
D. Diuretics
E. Plasmapheresis

4. A 28-year-old woman has a 12-year hi- story of chronic glomerulonephritis with latent course. Over the past six months she has developed general weakness, loss of appetite, low work performance, nausea. The patient complains of headache, pain in the joints. On examination: anemia, blood urea - 34,5 mi-llimole/l, blood creatinine - 0,766 milli-mole/l, hyperkalemia. What complication has developed?

A. Chronic renal insufficiency
B. Acute renal insufficiency

C.Nephrotic syndrome

D. Renal amyloidosis

E. Pyelonephritis

5. A 29 y.o. woman is critically ill. The illness is presented by high fever, chills, sweating, aching pain in lumbar area, discomfort during urination and frequent voiding. Pasternatsky's sign is positive in both sides. On lab examination: WBC20 ∗ 109/L; on urine analysis: protein 0,6g/L, leukocyturia, bacteriuria. Your preliminary diagnosis.

A. Acute pyelonephritis

B. Exacerbation of chronic pyelonephritis

C. Acute glomerulonephritis

D. Acute cystitis

E. Nephrolithiasis

6. A 50 y.o. woman who suffers from chronic pyelonephritis was prescribed a combination of antibiotics for the period of exacerbation - gentamicin (80 mg 3 times a day) and biseptol (960 mg twice a day). What consequences may be caused by such a combination of antibiotics?

A. Acute renal insufficiency

B. Glomerulosclerosis

C. Chronic renal insufficiency

D. Antibiotic combination is optimal and absolutely safe

E. Acute suprarenal insufficiency

7. A patient complains about sudden onsets of paroxysmal pain in the right lumbar region. 2 hours after the onset the patient had hematuria. Plain radiograph of the lumbar region shows no pathological shadows. USI reveals pyelocaliectasis on the right, the left kidney is normal. What is the most likely diagnosis?

A. Renal colic

B. Acute appendicitis

C. Bowel volvulus

D. Torsion of the right ovary cyst

E. Right renal pelvis tumor

8. An 11-yearold girl was taken by an acute disease: she got pain in the lumbar region, nausea, vomiting, frequent urination, body temperature 39oC. Objectively: the abdomen is soft, painful on palpation in the lumbar region. Common urine analysis revealed considerable leukocyturia, bacteriuria. The urine contained colibacilli. What is the most likely diagnosis?

A. Acute pyelonephritis

B. Acute appendicitis

C. Chronic glomerulonephritis

D. Acute vulvovaginitis

E. Acute glomerulonephritis

9. A 30-year-old woman with a long history of chronic pyelonephritis complains about considerable weakness, sleepiness, decrease in diuresis down to 100 ml per day.AP-200/120mmHg.Inblood: creatinine - 0,62 millimole/l, hypoproteinemia, albumins - 32 g/l, potassium - 6,8 millimole/l, hypochromic anemia, increased ESR. What is the first step in the patient treatment tactics?

A. Haemodialysis

B. Antibacterial therapy

C. Enterosorption

D. Haemosorption

E. Blood transfusion

10. A patient with acute respiratory viral infection (3rd day of disease) complains of pain in lumbar region, nausea, dysuria, oliguria. Urinalysis - hematuria (100-200 RBC in eyeshot spot), specific gravity 1002. The blood creatinine level is 0,18 millimole/l,

potassium level - 6,4 millimole/l. Make the diagnosis:

A. Acute interstitial nephritis

B. Acute renal failure

C. Acute glomerulonephritis

D. Acute cystitis

E. Acute renal colic

Topic 8. Preparation for practical training № 8 «Final module control»

List of theoretical questions:

1. Hypertensive crises: definition, classification, emergency care.
2. Uncomplicated hypertensive crises: tactics of patient management, emergency care.
3. Complicated hypertensive crises: tactics of patient management, emergency care.
4. Tactics of management of the patient with the complicated hypertensive crisis depending on the available complication.
5. Collapse: clinic, diagnosis, medical care.
6. Sudden cardiac death, emergency care.
7. Pulmonary edema: the main options and mechanisms of development, emergency care.
8. Emergency care for cardiac asthma and pulmonary edema on the background of acute myocardial infarction.
9. Emergency care for pulmonary edema on the background of a hypertensive crisis.
10. Features of the patient with pulmonary edema on the background of mitral stenosis.
11. Toxic pulmonary edema. Features of patient management, emergency care.
12. Supraventricular arrhythmias: clinic, ECG diagnostics, emergency care.
13. Ventricular arrhythmias: clinic, ECG diagnostics, emergency care.
14. Blockades of the heart: clinic, ECG diagnostics, emergency care.
15. Morgan-Adams-Stokes attack: clinic, emergency care.
16. Severe exacerbation of bronchial asthma: clinic, diagnosis, emergency care.
17. Anaphylactic shock: options, course, clinic, diagnosis, emergency care.

18. Quincke's edema: clinic, diagnosis, emergency care.
19. Acute respiratory distress syndrome in adults: clinic, diagnosis, emergency care.
20. Clinic, diagnosis, emergency care for gastrointestinal bleeding.
21. Bile colic: clinic, diagnosis, emergency care.
22. Intestinal colic: clinic, diagnosis, emergency care.
23. Incessant vomiting: emergency care, correction of water-electrolyte balance.
24. Profuse diarrhea: the main directions of therapy, correction of water-electrolyte balance.
25. Severe exacerbation of NUC: clinic, diagnosis, treatment tactics.
26. Hepatic encephalopathy: criteria for diagnosis, clinical picture, main directions of therapy.
27. Hepatic coma: diagnosis, intensive care.
28. DIC syndrome: the main pathogenetic mechanisms of development, clinic, diagnosis, treatment.
29. General principles of treatment of acute bleeding.
30. The main mechanisms of development and stages of acute renal failure. Intensive care of ARF. Indications for in vitro treatment of ARF.

SITUATIONAL TASKS

1. A 52-year-old patient was diagnosed with grade 2 hypertension with sodium-dependent pathogenetic form. Which of these drugs should be prescribed either as monotherapy or in combination with other antihypertensive drugs?

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

2. A 68-year-old man suffers from hypertension of the second degree. Constantly taking ACE inhibitors (enalapril - 10 mg / day). About: pulse - 60 beats / min, deaf heart tones,

accent of the second tone over the aorta. Echocardiography: signs of left ventricular myocardial hypertrophy. Recently, the effectiveness of treatment has decreased. Blood pressure is not lower than 160/110 mm Hg. Which group of drugs should be added to enalapril?

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

3. A 6-year-old child was hospitalized in the pediatric ward with bronchopneumonia. Suffers on atopic dermatitis. After intramuscular administration of ampicillin appeared feeling of tightness in the chest, dizziness, sharp pallor, cyanosis, cold sweat, accelerated noisy breathing. Which of the following drugs should be administered in manipulative immediately?

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

4. A 77-year-old man is in the intensive care unit for the second day with a diagnosis of "coronary heart disease: anterolateral myocardial infarction with a Q wave", notes the appearance of a dry cough, an increase in shortness of breath, which increases in the supine position. Objectively: body temperature - 37.2 ° C, acrocyanosis, orthopnea. Above the lower lungs on both sides - wet rales, CDR - 28 / min. Heart tones are weakened, heart rate and pulse - 110 / min, blood pressure - 130/70 mm Hg. Art. In the blood: hemoglobin - 130 g / l, L - 7.4 × 109 / l, ESR - 24 mm / h. On the radiograph of the lungs - the strengthening of the vascular pattern on both sides. What is the most likely cause of deterioration of the patient's condition? What groups of drugs will you prescribe in this case?

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

5. A 47-year-old patient suddenly began shortness of breath, which turned into shortness of breath, there was wheezing, foam from the mouth. Pulse 80 per 1 min, rhythmic, blood pressure - 150/100 mm Hg, in the lungs on both sides a lot of wet rales. History of coronary heart disease, hypertension, obstructive bronchitis.

Which drug will you use first when providing care?

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

6. A neonate was born from the 1st gestation on term. The jaundice was revealed on the 2nd day of life, and then it became more acute. The adynamia, vomiting and hepatomegaly were observed. Indirect bilirubin level was 275/imol/L, direct bilirubin level - Sμ mol/L, Hb — 150 g/1. Mother's blood group - 0[I], Rh+, child's blood group-A[II], Rh+. What is the most probable diagnosis?

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

7.The child was born from the 5th pregnancy and 1st delivery. Mother's blood group — A[II] Rh-, neonate's -A[II] Rh+. The level of indirect bilirubin in umbilical blood was 58/μmol/L, hemoglobin - 40 g/L, RBC — 3,8* 1012/L. The level of indirect bilirubin in 2 hours was 82μmol/l. The hemolytic disease of the neonate [icteric-anemic type, Rh-incompatibility] was diagnosed. Choose the therapeutic tactics.

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

8. A 42-year-old man has died in a road accident after the hemorrhage on the site, due to acute hemorrhagic anemia. What minimum percent of all volume of blood could result in death at acute hemorrhage?

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

9. A 3-day-old newborn who has suffered asphyxia in labor presents with bleeding from umbiligal sore. Labo tests: hypocoagulation, thrombocytopenia, hypothrombinemia. What is the most likely cause of clinical and laboratory changes?

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

10. A neonate was born from the 1st gestation on term. The jaundice was revealed on the 2nd day of life, and then it became more acute. The adynamia, vomiting and hepatomegaly were observed. Indirect bilirubin level was 275 /itmol/L, direct bilirubin level - 5 mol/L, Hb -150 g/L. Mother's blood group - 0[I], Rh+, child's blood group-A[II], Rh+. What is the most probable diagnosis?

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

11. A man with liver cirrhosis complains of nasal bleedings, right subcostal pain, weakness, nausea. On physical examination: jaundice, hemorrhagic rash, enlarged liver span (of 14 cm), liver edge irregular.

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

12. A woman, aged 30, in the second childbirth there is a baby born with anaemicicteric form of the hemolytic disease. Blood group of the mother is A(II) Rh-, blood group of the new born is B(III) Rh+, blood group of the father is B(I1I) Rh+.

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

13. A victim of a road accident suffered multiple fractures of extremities and pelvis bones. In medical history; haemophilia A. On examination: hematomes are forming on the injured areas. The patient's condition is aggravating. BP — 90/50 mm Hg.

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

14. A 33 y.o. patient was admitted to the hospital with stopped recurrent peptic ulcer bleeding. On examination he is exhausted, pale. Hb — 77 g/L, Ht — 0,25. Due to anemia there were two attempts of blood transfution of identical blood group A(ll)Rh+. Both attempts were stopped because of anaphylactic reaction.

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

15. A girl, aged 13, consults the school doctor on account of moderate bloody discharge from the genital tracts, which appeared 2 days ago. Secondary sexual characters are developed.

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

16. A 19 y.o. patient was admitted to the hospital with acute destructive appendicitis. He sufferes from hemophilia B-type.

Make a diagnosis.

What additional examination methods do the patient need to perform?

Differential diagnosis.

Emergency care of the patient.

DRUGS WITH DOSES, WHICH ARE USED FOR THE CONDITIONS SPECIFIED IN THE TOPICS

- Adrenalin-Darnytsia solution for in. 1.8 mg/ml per 1 ml
- Amiodarone 200 mg tablets
- Amiodarone for in. solution. 150 mg/3 ml by 3 ml
- Aminocaproic acid solution for in.5% per 100 ml
- Atropine sulfate solution for in. 1 mg/ml by 1 ml

- Benzohexonium solution for in. 2.5% per 1 ml
- Caffeine-sodium benzoate tablets 200 mg
- Caffeine-sodium benzoate solution for in. 100 mg/ml in 1 ml
- Caffeine-sodium benzoate solution for in. 200 mg/ml in 1 ml
- Captopril tablets of 12.5 mg, 25 mg, 50 mg
- Clofelin tablets of 0.15 mg
- Cordiamine solution for in. 250 mg/ml by 2 ml
- Dobutamine solution for in. 250 mg/50 ml of 50 ml
- Dopamine concentrate for district for in. 40 mg/ml of 5 ml
- Doxazosin 4 mg tablets
- Dronedarone tablets 400 mg
- Drotaverin 40 mg tablets
- Drotaverin hydrochloride solution for in. 20 mg/ml by 2 ml
- Ebrantil capsules of 30 mg, 60 mg
- Ebrantil solution for in. 5 mg/ml (25 mg) by 5 ml
- Ebrantil solution for in. 5 mg/ml (50 mg) in 10 ml
- Enalapril tablets of 5 mg, 10 mg, 20 mg
- Enoxaparin sodium 300 for in. solution. 10,000 anti-Xa IU/ml in 3 ml
- Esmolol solution for in. 10 mg/ml by 10 ml
- Esmolol solution for in. 10 mg/ml in 50 ml
- Esomeprazole powder for district for in. and info 40 mg
- Etacysin tablets 50 mg
- Farmadipin drops or. 2% in 25 ml
- Ethamsylate 250 mg tablets
- Ethamsylate solution for in. 250 mg/2 ml of 2 ml
- Flecainide tablets of 50 mg, 100 mg
- Furosemide solution for in. 10 mg/ml by 2 ml
- Heparin solution for in. 5000 IU/ml for 5 ml
- Lidocaine solution d/in. 100 mg/ml by 2 ml

- Magnesium sulfate solution for in. 250 mg/ml in 5 ml
- Mesaton solution for in. 10 mg/ml in 1 ml
- Methyldopa tablets of 250 mg
- Metoprolol solution for in. 1 mg/ml for 5 ml
- Morphine hydrochloride solution for in. 1% for 1 ml
- Nifedipine tablets of 10 mg, 20 mg
- Nitroglycerin concentrate for district for in. 10 mg/ml by 2 ml
- Norepinephrine tartrate 2 mg/ml concentrate for district for in. 4 ml
- Norepinephrine tartrate 2 mg/ml concentrate for district for in. 8 ml
- Omeprazole powder for district for in. 40 mg
- Pantoprazole lyophilisate for the district for in. 40 mg
- Papaverine hydrochloride solution for in. 20 mg/ml by 2 ml
- Platyphyllin hydrotartrate solution for in. 2 mg/ml by 1 ml
- Promedol solution for in. 20 mg/ml in 1 ml
- Propafenon tablets, intravenously. region 150 mg
- Rabeprazole lyophilizate for the district for in. 20 mg per 10 ml
- Rifaximin tablets 200 mg
- Sodium bicarbonate solution for in. 4% per 100 ml, 200 ml
- Spazmalgon solution for in. 2 ml
- Spazmalgon solution for in. 5 ml
- Torasemide solution for in. 20 mg/4 ml by 4 ml
- Tranexamic acid 500 tablets of 500 mg
- Tranexamic acid solution for in. 50 mg/ml in 5 ml
- Tranexamic acid solution for in. 100 mg/ml by 5 ml
- Vikasol (vitamin K3) solution for in. 10 mg/ml in 1 ml

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