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MODULE 1
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THEME 9
RHEUMATIC FEVER IN CHILDREN

Practical policies for students

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ЗМІСТОВИЙ МОДУЛЬ 4
ТЕМА 9
РЕВМАТИЧНА ЛИХОМАНКА У ДІТЕЙ

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Acute rheumatic fever (disease of Sokol'skyi-Buyot) due to international classification of diseases is a systemic inflammatory disease of connective tissue with predominant affection of cardiovascular system, which develops after acute infection provoked by β -hemolytic streptococcus of group A in predisposed persons, mainly, children and adolescents of 7–15 years old.

Term “rheumatism” was used in our country for determination of a disease for a long time.

Last years due to introduction of standardized approaches to diseases' classification this term was substituted with terms “acute rheumatic fever” and “chronic rheumatic heart disease” that corresponds to nomenclature of International diseases' classification of 10th revision (ICD-10) – rubrics 100–102 and 105–109 accordingly.

Rheumatic polyarthritis is known since Hippocratic, Halen and ancient Chinese medicine times (V century BC). Chorea was described in XVII century (Boillon, Sydenham), connection between rheumatic polyarthritis and heart's affection was established in XVII-XIX centuries (Volkovskiy F., 1818; Piteairu, 1788), and J. B. Bouillaul (1835–1840) and G. I. Sokol'skyi described formation of heart's malformation with rheumatic fever. Pathogenetic meaning of scarlet fever in anamnesis, low social-economic levels of life, overcrowding, bad nutrition was proposed by S. P. Botkin in 60y.y of XIX century. In XX century K. A. L. Ashoff (1904) described morphological marker of rheumocarditis – granulema, studying of formation mechanisms of which helped to understand specifics of heart's and other organs' affection (V. T. Talalrv, 1929; M. A. Skvortsov, 1937; A. I. Strukov, 1954) in rheumatic fever. A. R. Kisel (1940) marked out 5 diagnostic criteria of rheumatic fever, which he called “absolute”: nodules, annular erythema, chorea, migrating polyarthritis, and carditis, which were adopted all over the world as “great” or “major” criteria of rheumatic fever after publication of F. D. Jones (1944). The last period of development of rheumatic doctrine is connected with recognition of β -hemolytic streptococcus of group A role (N. D. Strazhesko, 1935; A. F. Coburn, 1931) and organization of struggle with this disease, where A. I. Nesterov was a pioneer.

Epidemiology

Acute rheumatic fever (ARF) is registered in all climate-geographical zones. By generalized WHO data (1989) morbidity with ARF in economically developed countries started to decrease at the beginning of XX century, most markedly during last 30 years (period of intensive antibiotics introduction and prevention of ARF as well).

Nowadays approximately 15,6 mln of people around the world suffer from ARF, almost 2,4 mln among them – children aged from 5 up to 14 years. More than 500 000 cases are newly registered annually. More than 350 000 persons die due to consequences of ARF. More than 4 000 kids suffer from chronic

rheumatic heart diseases. Morbidity with ARF among children in industrially developed countries is 1–5/100 000 per year (0,001–0,005%), in developing countries – is 100 times greater. This index in Ukraine remains rather high – 5,8/1000.

Outbreaks of disease, which took place during last decades in USA and other world countries, testify to actuality of ARF problem. Primary morbidity with ARF in Ukraine during last years increased from 0,5 up to 0,8/1000.

Foreign authors consider outbreaks of rheumatic fever as a consequence of various factors, including:

- dramatic increase of streptococcal infection;
- relaxation of alertness to consequences of streptococcus of group A virulent strains circulation;
- absence of theoretical approaches to prediction of post-streptococcal diseases, ARF in particular;
- insufficient knowledge by physicians of ARF acute stage's clinical symptoms due to its rareness during last decades.

Conducted analysis has shown that role of social factors in formation of ultimate ARF outbreaks is minimal as since representatives of middle society stratum fell ill predominantly.

Increase of morbidity with ARF proves postulate of J. Rotta that rheumatic fever won't disappear until streptococcus of group A circulates, and our population can't be redeemed from it during several following decades.

Etiology and pathogenesis

Connection between infection of upper respiratory tract provoked by β -hemolytic streptococcus of group A and consequent development of ARF is legibly established. Outstanding academician N.D. Strazhesko was the first who suggested and proved streptococcal hypothesis of rheumatic fever in 1935y: «Rheumatism – it's sepsis in hyperergic organism. Increased immunologic reactivity plays a big role. If streptococcal infection plays the main role in development of acute rheumatism, at chronic sequel – it's enhancement of antibodies' synthesis against cardiac membranes (myocardium and endocardium) that leads not only to affection of the heart but serves as prerequisite of development of complications».

This microorganism occupying mucous membranes of nasopharynx begins to product tremendous quantity of enzymes, damaging tissues. After incubation period (2–4 days) generalized answer of macroorganism appears by way of fever, deterioration of health, headaches, development of pharyngitis and angina.

Postulate of J. Rotta: Rheumatism won't disappear until β -hemolytic streptococcus of group A is circulating.

Studying of peculiarities of this microorganism revealed that development of ARF after upper respiratory tract infection is connected only

with virulent strains relating to several A-streptococcus serotypes, which contain special M-protein being a part of streptococcal wall, suppressing its phagocytosis and having typical genetic structure. Nowadays several rheumatogenic strains of A-streptococcus are isolated – M-5, M-6, M-18, M-24, and more than 90 variety of M-protein are identified.

Streptococci can secrete a wide spectrum of somatic and extracellular substances having toxic and antigenic properties. Streptolysins O and S, streptokynase, hyaluronidase, proteins, desoxyribonuclease B and others relate to them. These substances can damage various cells and tissues of an organism by virtue of it they play pathogenetic role.

Revealing in overwhelming majority of patients with ARF different anti-streptococcal antibodies – ASL-O, ASH, ASK, anti-DNAse B in high titers confirm indirectly the meaning of streptococcal infection.

But action of only streptococcus itself is not enough for development of the disease. Individual hyperimmune organism's reaction at streptococcal antigens is necessary for its development that is called forth genetically. Founder of pediatric school A. A. Kisel' at the beginning of last century pointed to the role of family predisposition at beginnings of rheumatic fever. Fact of ARF development in 0,3-3 % of children having streptococcal infection testifies to it.

Blood groups and dermatoglyphics were studied among genetic markers. It was established that persons with group A (II), B (III) and "non-secretors" AB and H are seen more often.

Redistribution of pattern phenomena on the fingers is the general rule.

Great importance in complicated pathogenesis of rheumatic fever is attached to immune inflammation and immunopathologic processes as well, in which streptococcal antigens and anti-streptococcal antibodies take the most active part.

Hypothesis of "antigen mimicry" between fragments of group A streptococci and antigens of human myocardium, as well as conception about similarity between polysaccharide component of wall membrane of streptococcus and glycoprotein of human cardiac valves won the recognition. This similarity of antigen composition creates possibility of lingering streptococcal persistence in an organism because condition of "partial immunologic tolerance" can appear. On another hand, it stipulates principal possibility of anti-streptococcal antibodies' influence not only upon pathogen itself but upon myocardium also.

The role of circulating anti-cardiac antibodies and immune complexes in the pathogenesis of the disease is discussed.

The series of investigations was given up to examination of cellular immunity disorders that cleared up changes of quantitative correlation of T- and B-lymphocytes and their functional activity. Trustworthy positive increase of

B-, T-lymphocytes and T-helper inductor (CD4) cells, decrease of T-suppressors (CD8) was revealed that testifies to immunoregulator deficiency at ARF.

Nowadays the new directions in examination of pathogenesis of post-streptococcal diseases, including ARF, are elaborated, and it is clear that aspects of this not simple problem are far from final resolution. Thus, according to vivid statement of Inman (1985) “one of the ironies of ARF consists in a situation that it will disappear earlier that it will be understood”.

Pathomorphological picture

It is ascertained that ARF is a complicated cascade of changes at which various as for intensity and significance inflammatory and proliferative processes take place. Systemic dysorganization of connective tissue in combination with specific proliferative and non-specific exudative-proliferative reactions as well as with affection of microcirculatory vessels lay in the basis of tissue disorders.

There are 4 stages (phases) of pathologic process' development at ARF: mucous swelling, fibrinoid disorders, proliferative reactions and phase of sclerosis.

Non-specific inflammatory reaction develops at the stage of mucous swelling. Possibility of reverse development of pathologic process at this stage is principally important.

Fibrinoid disorders are irreversible changes of connective tissue disorganization.

Proliferative stage shows formation of rheumatic granuloma (Ashoff-Talalaeв granuloma, by names of authors who described it). Rheumatic granuloma consists of large, irregular-shaped basophilic cells of histiocytic origin, giant polynuclear cells of myogenic origin with eosinophilic cytoplasm and lymphoid, plasmatic and mast cells. Mostly often they are localized on perivascular connective tissue or in myocardial interstitium (predominantly in left ventricle), papillary muscles, septum and endocardium, rarely – in external vascular membrane. Cycle of formation and scarring of granuloma takes 3–4 months on average.

Formation of required heart malformations is the outcome of the processes mentioned above. Mitral valve is affected most frequently, aortal and tricuspid – more rarely.

Nowadays granuloma is revealed significantly more rarely, that is connected obviously with changes of clinical and morphologic aspect of ARF, so called “pathomorphism” of the disease.

Disorders of microcirculatory vessels, which are found in all organs, concern to non-specific but important ones for ARF pathogenesis.

Serous membranes are involved into process constantly, especially at high activity of the process. Disorganization of connective tissue, exudative inflammation, and vasculitis are present in joints as well. Reversibility of the process not only in the phase of mucous swelling but in early stages of fibrinoid one – is the peculiarity of rheumatic affection of joints.

Involvement of cerebral vessels lies in the basis of CNS affection. Disorders of corpus striatum cells, sub-thalamic nuclei of cerebral and cerebellar cortex are pathologic substrate of chorea.

Affection of skin and subcutaneous tissue becomes apparent with vasculitis, endotheliosis and focal inflammatory reaction.

Classification and nomenclature of rheumatic fever

In 1964 A. I. Nesterov proposed classification of rheumatism, which was confirmed at special symposium of All-Union anti-rheumatic Committee and used up today (table 1).

Classification is composed with taking into account of following factors:

1. Phase of the disease (active, non-active) with specification of degree of pathologic process' activity;
2. Clinico-anatomic characteristics of affection of the heart and other organs;
3. Character of disease's course;
4. Condition of blood circulation.

Clinical-anatomic characteristics of heart affection in active phase implied primary rheumatic carditis, recurrent rheumatic carditis on the background of cardiac malformation, and rheumatism without obvious cardiac disorders. Among affections of other organs and systems in active phase polyarthritis, serositis, vasculitis, chorea, skin affections etc. can be found. It's necessary to take into account that in children chorea and polyarthritis may be present without involvement of the heart in pathologic process (rheumatism without obvious cardiac disorders).

Non-active phase of the disease involves consequences and residual manifestations of cardiac (cardiosclerosis, heart malformation) and extra-cardiac affections.

Degree of pathologic process' activity is based on characteristics of clinical, functional and laboratory indices.

At I activity's degree clinical and instrumental manifestations of rheumatism are slightly revealed, and laboratory indices are changes a little bit.

At II degree temperature is moderately increased or normal; signs of rheumatic carditis, polyarthralgia or chorea are mild or moderate. Indices of inflammatory activity are also changed moderately: leukocytosis up to $10 \times 10^9/l$, ESR 20–30 mm/h, CRP + - ++ (or more than 6 U), α_2 -globulins 11–13%, γ -globulins 22–25%, seromuroid more than 6 U, DFA – 0.25–0.3 U, sialic acids more than 0.400 U, ASL-O and ASK – 1.5–2 times more than norm.

At III degree all clinical manifestations are brightly expressed, and laboratory indices are significantly changed: leukocytosis 10 – $12 \times 10^9/l$, ESR more than 40 mm/h, CRP +++ - ++++ (or twice more than norm), α_2 -globulins more than 13–14%, γ -globulins more than 25%, seromuroid more than 6–10 U,

DFA – 0.25–0.5 U, sialic acids more than 0.500 U, ASL-O and ASK – 3–5 times more than norm.

Table 1 – Work classification and nomenclature of rheumatic fever

Phase and degree of rheumatism activity	Clinical-anatomic characteristics of affection		Character of the course	Blood flow insufficiency
	of the heart	of other organs and systems		
Active: degree of activity I, II, III	Primary rheumocarditis without valvular affection. Secondary rheumocarditis with valvular affection (which one). Rheumatism without obvious disorders of the heart	Polyarthritis, serositis (pleuritis, peritonitis, abdominal syndrome). Chorea, encephalitis, meningoen-cephalitis, cerebral vasculitis, nervous psychic disorders. Vasculitis, nephritis, hepatitis, pneumonia, skin affections, iritis, iridocyclitis, thyroididitis	Acute Subacute Lingering Permanently recurrent Latent	I ₀ I _I I _{IIA} I _{IIB} I _{III}
Non-active	Rheumatic myocardio-sclerosis. Heart disease (which one)	Consequen-ses and recurrent manifestations of extra-cardiac affections		

Definition of character of the course is based upon comparison of acuity of the onset and duration of the primary rheumatic fever’s course or its relapse.

At acute course the onset is rapid, with quick increase of all symptoms and quick effect of anti-inflammatory therapy as well, cycle of disease’s development doesn’t exceed 2–3 months. At subacute course the onset may be acute but back development of symptoms in dynamics of the disease is delayed, relapse of rheumatic fever may be seen that promotes the ending of attack not earlier than in 4–6 months. At lingering course development of clinical manifestations is gradual; their expressiveness doesn’t exceed the II degree of activity. Moderate rheumocarditis with slight dynamics of clinico-instrumental indices has the main significance. Disposition to torpid course is seen. Relapsed course is typical for recurrent rheumatic fever, when undulating course is stipulated by presence of relapses changing with incomplete remissions. At latent course, usually primary-chronic, diagnosis of the disease is established retrospectively, on the basis of formed cardiac malformation.

Insufficiency of blood flow provides separation of 5 stages (by N. D. Strazhesko and V. H. Vasilenko).

Regarding prognosis the circumstance that every following attack repeats the previous one by its clinical manifestations, degree of activity and character of the course has great significance.

During last 25–30 years clinical picture of ARF underwent marked changes. Severe forms of rheumocarditis are seen more rarely, there is tendency to mono-syndrome form of the disease, prevalence of moderate degree of activity of pathologic process. Frequency of valvular malformation and repeated attacks is decreased. Disease became more favorable with convalescence of majority of children. Continuously recurrent variant of ARF nowadays practically is not seen. It stipulated necessity of revision of existing classification, and in 2003 year Association of Russia Rheumatologists (ARR) proposed new classification (table 2). Clinical syndromes characterizing main and additional criteria of ARF, outcome of the disease and degree of insufficiency of blood flow were laid in its basis.

Table 2 – Classification of rheumatic fever (ARR, 2003)

Clinical variants	Clinical manifestations		Outcome	Stage of blood flow insufficiency	
	main	additional		CSV*	NYHA **
Acute rheumatic fever	Carditis	Fever	Recovery	0	0
	Arthritis	Arthralgia	Chronic rheumatic heart disease:	I	I
Repeated rheumatic fever	Chorea	Abdominal syndrome	without cardiac malformations***	IIA	II
	Annular erythema	Serosites	with cardiac malformations****	IIB	III
	Rheumatic nodules			III	IV

Footnotes:

* – by classification of N.D.Strazhesko and V.H.Vasilenko

** – functional class by NYHA

***– post-inflammatory regional fibrosis of valves without regurgitation, which is specified with echocardiography, is possible

****– at presence of first revealed cardiac malformation it'd necessary, if possible, to exclude other causes of its appearance (infectious endocarditis, primary phospholipids syndrome, valvular calcinosis of degenerative origin etc.

Clinical picture

Acute rheumatic fever appears more often in school and adolescent age, significantly more rare in pre-school age, in children of first 3 years of life practically is not seen. Girls fall ill a little bit more frequently than boys.

ARF is characterized with variety of clinical manifestations and variability of courses. Presence of distinct exudative component of inflammation is the main distinguishing feature of ARF in children.

Outstanding scientist-pediatrician A.A.Kisel (1939) gave brilliant description of main manifestation of ARF calling them absolute symptom-complex of disease. Polyarthritis, cardiac affection, chorea, annular erythema and rheumatic nodules have to do with them.

First attack of ARF as a rule starts acutely with rise of temperature up to febrile and signs of intoxication. Practically in all cases it's possible to find out disease of upper respiratory tract 2–3 weeks before. Polyarthritis or polyarthralgia develop simultaneously with rising of temperature.

Rheumatic polyarthritis. Joint syndrome is seen in 2/3 of children who fell ill with rheumatic fever for the first time and about in 1/2 of patients with repeated attack of the disease. Transient olygoarthritis, more rarely monoarthritis, are predominant forms of affection nowadays. Acute onset, fever, joints pains, swelling, limitation of movements, increase of temperature and redness of skin above joints are the main symptoms of rheumatic polyarthritis. Rheumatic arthritis is remarkable for involvement of big and medium joints in pathologic process, mostly often of knee and ankle ones, symmetric affection, migration, quick back development of pathologic process (especially on the background of anti-inflammatory therapy). In some cases atypical manifestations of joint syndrome are possible: affection of small joints of hands and feet, asymptomatic sacroileitis of I-II degree, more often in young males. In 10–15% of cases arthralgia appears which, in contrast to arthritis, is not accompanied by limitation of movements, pains on palpation and other symptoms of inflammation. In steady symmetric arthritis of big joints, insufficient answer for NSAID therapy and absence of clinical-instrumental signs of carditis it's necessary to think about post-streptococcal reactive arthritis.

BUT! They say: «Rheumatism licks the joints and bites the heart».

Rheumatic carditis. Affection of the heart – rheumocarditis – is fundamental in clinical picture of the disease that determines its course and prognosis. It is seen in 70-85 % of children who fell ill for the first time and somewhat more frequently at recurrent course. All heart membranes (myocardium, endocardium, pericardium) can be affected. In connection with difficulties of differentiation of separate membranes' affection the term “rheumocarditis” received wide propagation in clinical practice.

Children can complain of pains or unpleasant feelings in cardiac region, dyspnea at loading, heart beatings. Disorders of frequency of heart contractions in the form of tachycardia (30–40%) or bradycardia (20–30%) is an early symptom of rheumocarditis. Enlargement of cardiac borders predominantly to the left, which can be revealed in 80–85% of patients, muffling of cardiac tones

and appearance of murmurs (additional tones – III, IV – are auscultated in 40–75% of children) are typical clinical signs.

Appearance of systolic murmur is one of the most constant signs of rheumocarditis. It has different localization, intensity, duration, timbre and conductivity depending on predominant affection of myocardium or endocardium. Thus, at myocarditis the murmur usually is weak or moderate, is heard better in V point, more rarely – at pulmonary artery, is not conducted beyond the bounds of cardiac region.

At ECG dysfunction of sinus-atrium node in the form of tachy-, bradycardia or sinus arrhythmia is registered rather frequently. Disorders of rhythm are revealed a little bit rarely: migration of pace maker, interference with dissociation, extrasystole. Retardation of atrio-ventricular conductivity may be seen as well as disorders of bioelectrical processes in ventricular myocardium, changes of T-wave, displacement of ST segment, prolongation of electric systole (Fig. 1).

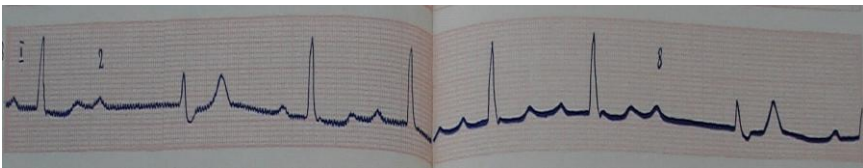


Fig. 1

Signs of decrease of contractile function and myocardial tone, enlargement of cardiac borders are revealed at X-ray in great majority of children with rheumatic carditis.

Valvulitis accompanied by myo- and/or pericarditis is considered to be main criteria of rheumocarditis nowadays. At valvulitis with affection of mitral valve systolic murmur acquires blowing nuance, is long-drawn. It is heard in a zone of projection of mitral valve; conducts beyond the cardiac borders; has variable intensity, optimally auscultated in a position of a patient on the left side holding his breath at the height of expiration and is a consequence of mitral regurgitation.

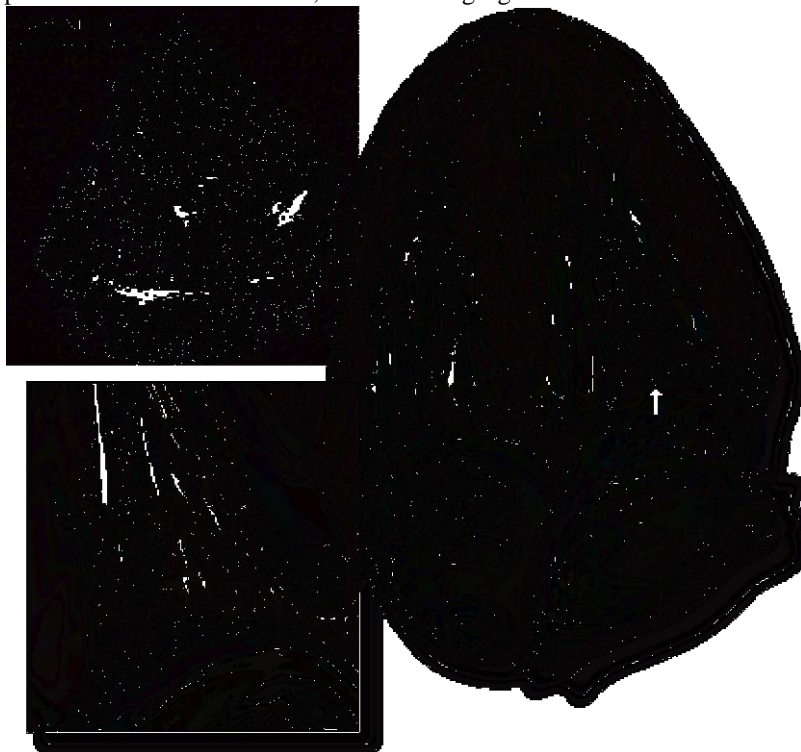
Revealing of “pouring” diastolic murmur optimally auscultated along left sternum border after deep expiration at inclination of a patient forward testifies to affection of aortic valve.

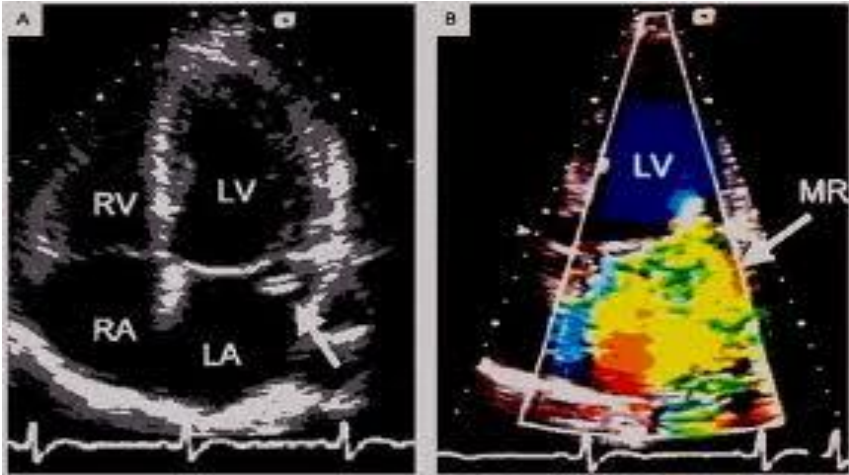
It’s necessary to underline that isolated affection of aortic valve without murmur of mitral regurgitation is not typical for acute rheumatic carditis but doesn’t exclude presence of the latter. At absence of valvulitis it’s necessary to interpret rheumatic origin of myopericarditis very carefully!

Involvement of pericardium in pathologic process at the first attack is revealed rarely. Signs of pericarditis are seen at acute hyperergic course of the disease and are combined with marked disorders of other cardiac membranes (pancarditis) and involvement other serous membranes in pathologic process (pleural, peritoneum).

As for insufficiency of blood flow – it is seen rarely in the modern course of primary rheumocarditis; usually it is I-II degree of HI.

Ultrasound examination of the heart helps a lot in diagnostics of rheumocarditis. At myocarditis enlargement of cavities are present, more frequently – of the left ventricle, hypertrophy and swelling of myocardium, decrease of indices of contractile and pump function of left ventricle. At valvulitis of mitral valve regional clavate thickening of front mitral fold, hypokinesia of back mitral fold, and mitral regurgitation can be revealed.





Affection of aortic valve manifests with basal protodiastolic murmur, typical for aortic regurgitation which begins immediately after II tone. As for character – high frequent, blowing, diminishing. It's auscultated best of all along left edge of sternum after deep inspiration at forward inclination of body.

Ultrasound examination at aortic valve's valvulitis allows revealing diastolic fibrillation of mitral folds with small amplitude in 50% of children. In some patients thickening of echo signal from aortic valve folds and aortic regurgitation may be present. These signs are objective criteria of rheumatic endocarditis diagnostics.



Value of ultrasound diagnostics of pericarditis is very high as since it permits to reveal even small quantity of liquid in pericardium cavity as well as inflammatory changes of its folds: thickening, presence of fibrin files.



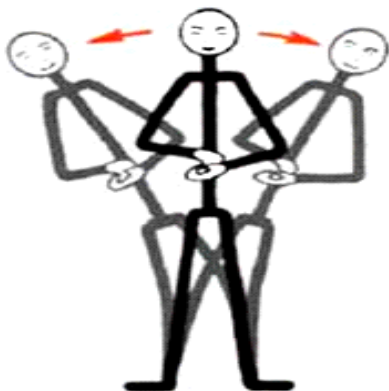
Predominance of moderate and slight activity of the process is modern peculiarity of its course. Percent of acquired heart disease formation after primary rheumocarditis decreased 2.5 times and consists nowadays 20–25%. Direct dependence between severity of the rheumocarditis and frequency of acquired heart disease appearance. Mitral insufficiency predominates in the structure of rheumatic heart disease, insufficiency of aortal valve, mitral-aortal disease and mitral stenosis are formed more rarely. In 7–10% of cases prolapse of mitral valve after primary rheumocarditis can be seen.

Slower rate of appearance (in comparison with previous decades), mild degree and steady compensation during years are peculiarities of acquired heart disease nowadays.

Increase of cases of heart disease formation is a peculiarity of recurrent rheumocarditis, especially in adolescents.

Chorea. It's typical manifestation of ARFin 16–18% of cases, predominantly in girls of 6–16 years old. It's accompanied, as a rule, by rheumocarditis or polyarthritits, rarely can be isolated. Duration of clinical manifestations is from 2 to 6 months.

Disease begins gradually with appearance of unstable mood, asthenia, whining, and irritability. Hyperkinesia, incoordination of movements, and decrease of muscular tone join more lately.



a



b



Hyperkinesia becomes apparent by forced movements of different muscular groups and is accompanied by disorders of handwriting, indistinct speech, and awkwardness of movements. It's difficult for a child to carry a spoon to the mouth, to eat and drink without assistance. Hyperkinesia is intensified at agitation and disappears in sleep. Accomplishment of coordination tests causes troubles. Positive symptom of "flabby shoulders" is present frequently (at raising arms by shoulders from behind the head is plunged between the latter). Retraction of epigastric region at inspiration (paradoxical respiration), retardation of back bending of shanks at checking up knee reflex (Gordon's symptom) can be revealed as well. In some patients muscular hypotonia may be so marked that they are totally paralyzed ("paralytic form", "soft chorea"). On the background of adequate therapy chorea manifestations usually disappear in 1–2 months. Nowadays manifestations of chorea are not so acute, "choreic storm" and "paralytic form" practically are not seen.

Modernly in foreign literature abbreviation PANDAS (**P**ediatric **A**utoimmune **N**europsychiatric **D**isorder associated with **A**. **S**treptococcal infection) is used as the synonym of chorea.

Diagnostic criteria of PANDAS are the following (S. Swedo et al., 1998):

- obsessive-compulsive disorders (fixed thoughts + obsessive actions) in combination with tics or without them;
- pre-pubertal age (less than 12 years);
- acute onset and attack-like course;
- proved connection with streptococcal infection of pharynx (positive culture from throat or increase of anti-streptococcal antibodies titer);
- neurologic disorders (hypermotility, chorea-like hyperkinesia).

Isolated chorea (without affection of the heart) as a rule doesn't give increase of acute phase indices and titers of anti-streptococcal antibodies. Long-term catamnestic supervision of children who were ill with chorea allow to certify that in 5–10% of cases rheumatic heart diseases at absence of clinically clear exacerbation of a process can be revealed in 7–8 years. Some researches consider that these children have sub-clinical signs of carditis consequences of which can be revealed lately.

Annular erythema (annular rash) is seen in 7–10% of children at the height of rheumatic attack. Clinically it manifests with pink annular rash, usually isn't accompanied by subjective feelings, isn't raised above skin, and disappears at press. Predominantly it is localized on the trunk, above joints, more rarely on extremities. Usually it disappears very quickly.

Diagnostic value of annular erythema nowadays is varied because it appears rather often at other infectious-allergic diseases and conditions.



Rheumatic nodules. Recently they are seen very rarely, predominantly in children with recurrent rheumocarditis. These are roundish, dense, varying in size from several millimeters up to 1–2 centimeters painless substances. Their predominant localization – at places of tendon's attaching, above osseous projections, in the region of knee, elbow, metacarpophalangeal articulations, and occipital bone. Cycle of back development is 1–2 months in average, without residual signs.

Affection of inner organs. At modern course of rheumatic fever inner organs are affected rarely. It manifests predominantly as abdominal syndrome in 5–7% of patients, as a rule in debut of the disease. Abdominal pain may be different as its severity and localization, with quick back development of symptoms on the background of anti-rheumatic therapy. Affection of lungs (rheumatic pneumonia, pulmonary vasculitis, pleurisy) and other organs which is seen in severe course of the first attack and recurrent rheumocarditis nowadays is revealed very rarely.

Laboratory investigations. Leucocytosis, increase of ESR and indices of acute phase (seromuroid, C-reactive protein, glycoproteids etc.), dysproteinemia with decrease of albumins and increase of globulins, especially α -2-globulins are present in great majority of children with rheumatic fever.

Proceeding from leading role of streptococcus in development of rheumatic fever and considering the diseases as clinico-immunologic problem, great importance is attached to shifts of immunologic indices in its early

diagnostics. Frequency of revealing of streptococcal antigen in blood serum at early stages of primary rheumocarditis is 60–75%, increase of ASL-O titers – in 75–80%, antistreptohyaluronidase (ASH) – in 80–90% of patients. Revealing of anti-cardial antibodies, which have marked cross activity with streptococcus of group A, is a reflection of autoimmune processes. In 1/3 of children circulating antibodies to connective tissue antigens, namely to structural glycoproteids and soluble fraction of main substance of connective tissue, are revealed in early stage of the disease.

Examination of humoral indices of immunity testifies to increase of all classes of immunoglobulins (A, M, and G). Circulating immune complexes are revealed as well.

Laboratory indices, as a rule, have direct connection with degree of activity of rheumatic process.

Diagnosics

Diagnostic criteria elaborated by Kisel A. A. (1940) and Jones T. D. (1944) were modified and supplied by Nedsterov A. I. (1963, 1966, 1973) and afterwards – by American Cardiology Association; in our country they are called “criteria of Kisel-Jones-Nesterov”.

Diagnostic criteria of Kisel-Jones-Nesterov:

Major manifestations:

1. Carditis
2. Polyarthritits
3. Chorea
4. Subcutaneous nodules
5. Annular erythema
6. Rheumatic anamnesis (connection with existed nasopharyngeal (streptococcal) infection, presence of ill with rheumatic fever in a family)
7. Proof ex juvantibus – improvement of disease’s course under influence of 3–5 days of anti-rheumatic treatment

Minor manifestations:

A. General:

1. Fever
2. Adynamia, tiredness, weakness
3. Pallor of skin
4. Sweating
5. Nasal bleedings
6. Abdominal sundrome

B. Special (mainly laboratory indices):

1. Leucocytosis (of neutrophil origin)
2. Dysproteinemia
 - a) increase of ESR

- b) hyperfibrinogenemia
- c) appearance of C-reactive protein
- d) increase of α -2 and γ -globulins
- e) increase of serum mucoproteids, glycoproteids

3. Pathologic serologic indices: streptococcal antigen in blood, increased titers of ASL-O, ASK, ASG.

4. Increased permeability of capillaries.

Particular difficulties arise at recognition of early manifestations of the disease that explains rather high percent of diagnostic errors. Summarizing achievements of theoretical and practical rheumatology A. I. Nesterov proposed early diagnostic criteria of rheumatic fever united into three main syndromes: clinico-epidemiologic, clinico-immunologic, and cardiovascular.

Clinico-epidemiologic syndrome includes streptococcal infection on the threshold of first symptoms of the disease legibly revealed in anamnesis as well as “streptococcal” environment in immediate proximity to the patient (in private life, at school, at works).

Clinico-immunologic syndrome summarizes clinical and laboratory indices. Groundless weakness and retardation of capacity of work after rhynopharyngeal infection, quick fatigability after physical load, unusual for a patient sweatiness, sub-febrile temperature, arthralgia, heart beatings relate to clinical indices. Laboratory ones reflects increase of common immunologic and inflammatory activity.

Cardiovascular syndrome is based upon summarizing of subjective and objective parameters, which are determined on clinical and instrumental examination of a patient proving presence of carditis and/or extra-cardial localization of rheumatic process.

American Rheumatology Association reviewed criteria of rheumatism in 1982. WHO research group (1989) recommends to use these criteria for verification of ORL diagnosis.

Table 3 – International criteria for diagnosing of acute rheumatic fever

Major criteria	Minor criteria	Data supporting previous A-streptococcal infection
Carditis Polyarthritits Chorea Annular erythema Subcutaneous rheumatic nodules	Clinical: – arthralgia – fever Laboratory: Increased reactants of acute phase – ESR, C-reactive protein Prolongation of PR interval at ECG	Positive A-streptococcal culture isolated from throat or positive test of quick definition of A-streptococcal antigen Increase or increasing titers of anti-streptococcal antibodies

Presence of two major or one major and two minor criteria testify to high probability of acute rheumatic fever if data about previous streptococcal infection provoked by streptococcus A are proved.

Differential diagnosis.

Variability of clinical manifestations at ARF often leads to incorrect interpretation of separate symptoms and, as a consequence, to diagnostic errors. Mostly often such conditions as functional cardiopathy, non-rheumatic carditis, some congenital heart diseases, syndrome of mitral valve prolapse, and infectious endocarditis may be interpreted by mistake as signs of rheumacarditis.

In contrast to rheumocarditis signs of laboratory activity are not present at functional cardiopathies, and clinical symptoms develop on the background of vegetative crises in children with foci of chronic infection at absence of objective signs of cardiac pathology. Echo-C has a decisive meaning for exclusion of rheumocarditis. Eco-CG, as a rule, doesn't reveal whatever disorders at functional cardiopathies or helps to diagnose various small structural heart anomalies (mitral valve prolapse, anomalous chords in heart's cavities, changes of great vessels' diameter etc.).

Rather close connection with viral infection is typical for non-rheumatic carditis. In such case children have complaints of cardiac character, disorders of rhythm appear (mainly – extrasystoles), laboratory signs are of minimal activity. Reverse dynamics of clinical and laboratory indices are rather slow.

At differential diagnostics of rheumocarditis it's necessary to exclude such threatening disease as infectious endocarditis. Danger consists in affection of healthy cardiac valves (primary form) or it develops as a complication of rheumatic heart disease (secondary form). At primary infectious endocarditis isolated affection of aortal valve with quick development of valvular regurgitation is seen significantly more often. At development of infectious endocarditis of mitral valve symptoms of congestive insufficiency in lesser circulation appear that is stipulated by gross destroy of valvular structure and overload of left cardiac parts. As a rule infectious endocarditis develops on the background of purulent infections or infected traumas as well as at carrying out various medical manipulations which are accompanied by bacteriemia. In clinical picture of infectious endocarditis irregular fever, frequently with chills and profuse sweating, thromboembolies of various localization (kidneys, spleen, brain etc.) prevail. Reaction at prescription of only anti-inflammatory therapy is absent, but good dynamics at use of adequate antibacterial therapy is seen. Eco-CG is of considerable help for specification of diagnosis; it can reveal vegetations on valves and chords, perforations or ruptures of valvular petals, chords, and myocardial abscesses.

The diagnosis of rheumatic polyarthritis is necessary to differentiate with a big group of diseases having articular syndrome: reactive arthritis,

juvenile rheumatoid arthritis, systemic lupus erythematosus, Lyme disease etc. Attentive analysis of anamnestic data, clinical peculiarities of the disease, and correct interpretation of laboratory parameters will allow a physician to orient and differentiate these conditions.

Evaluation of articular disorders after streptococcal infections is of great difficulty. Post-streptococcal arthritis develops after rather short latent period and persists during longer period than arthritis at typical acute rheumatic fever, at that it reacts insufficiently at anti-inflammatory therapy only. According to American Cardiology Association recommendations it's necessary to consider patients with post-streptococcal arthritis, nominally satisfying criteria of Kisel-Jones (if other genesis of arthritis is excluded) to be patients with ARF.

A functional tic is the most frequent source of errors at identification of chorea. Hyperkynesia at systemic lupus erythematosus, thyrotoxicosis, brain's tumors, anti-phospholipid syndrome are also included in the differential diagnosis.

Annular erythema can be seen at other diseases as well (toxico-allergic form of chronic tonsillitis, tuberculosis, allergic conditions); it's necessary to think of them also.

Acquired heart disease (chronic rheumatic heart's disease)

Frequency of acquired heart diseases is decreased as a result of using of common prophylactic methods. But even at modern stage in some children heart's disease is formed after rheumatic fever that requires corresponding treatment and rehabilitation.

Insufficiency of left atrio-ventricular valve is seen most frequently (62%), rarely – combined mitral malformation (17%), even more rarely - isolated insufficiency of aortal valves (5%), isolated stenosis of left atrio-ventricular orifice (3%) and stenosis of aortal orifice (3%). Some children have combined affection of two valves – mitral and aortal, left and right atrio-ventricular and combined affections (valvular insufficiency and stenosis of the orifice).

Insufficiency of left atrio-ventricular valve (mitral insufficiency) appears in cases when its folds are not closed completely during ventricular's systole. Back blood flow (regurgitation) from left ventricle to left atrium takes place through remaining hole that is accompanied by appearance of murmur. At that quantity of blood in left atrium is increased and pressure is increased also. Gradually hypertrophy of left ventricle's myocardium and dilatation of left atrium cavity increase.

Clinics. Already in active phase of primary rheumocarditis marked systolic murmur with blowing timbre may appear above apex and in IV intercostal space, that testifies to affection of mitral valve. If intensity of the murmur increases after ceasing of the rheumatic process it's possible to think about formation of mitral valve insufficiency, nevertheless this diagnosis becomes truthful only ion 12 months after the onset of the disease.

Patients with 1–2 degree of mitral insufficiency don't complain for a long time, with 3-4th degree – complain of dyspnea at physical load. Symptoms of heart insufficiency increase in clinical picture.

On palpation apex beat is intensified and displaced to the left and downwards. Heart's borders are displaced to the left. Degree of displacement depends upon expression of malformation and hypertrophy of left ventricle. Vascular pulsation may be seen in epigastric region. On auscultation weakening of I tone above apex may be revealed that is connected with incomplete closing of mitral valve folds. Blowing systolic murmur which has sometimes musical inflexion and occupies substantial part of systole is merging with I tone. At development of dystrophic processes in cardiac muscle the murmur is decreased markedly and may disappear that is unfavorable prognostic sign. Its epicenter is localized above apex, rarely – in IV intercostal space at left border of sternum, conducted to left axillary region, on the base of the heart, xiphoid process, and under angle of left scapula. Increase of pressure in left atrium and vessels of lesser circulation is accompanied by accent of II tone above pulmonary artery. Pulse and BP in a period of compensation are normal.

Data of instrumental examination.

At ECG the following data are typical:

- changes of P wave (prolongation, flattening, splitting) in I, II, aVL, V₁₋₂ leads that testifies to hypertrophy of left ventricle – P “mitrale”. At development of severe dystrophic processes in left atrium's muscle P wave becomes isoelectric;

- signs of ventricular hypertrophy appear at marked mitral insufficiency;
- increase of inner deviation time in V₅₋₆ leads;
- deviation of electric cardiac axis to the left;
- signs of systolic overloading and hypertrophy of left and right ventricles;
- disorders of rhythm and conductivity at late stage.

At X-ray the heart is increased in diameter, waist is smoothed, arch of pulmonary artery and left atrium is protruded.

At echocardiography:

- dilatation and hypertrophy of left ventricle
- dilatation of left atrium
- increase of amplitude and velocity of movements of front mitral valve's petal
- non complete closing of mitral valve's petals during systole
- mitral regurgitation with signs of flow's turbulence

The course and outcome.

At insignificant degree of regurgitation the malformation may have prolonged compensation period, duration of life is from 20 up to 40 years and more. At big defect the prognosis becomes clouded due to insufficiency of

mitral valve of III-IV degree, recurrence of rheumatic process. Decompensation of right ventricle type occurs, which is yielded to treatment only until irreversible changes in myocardium appear.

Treatment.

Treatment includes treatment and secondary prevention of main disease, treatment of heart insufficiency; III-IV degree of malformation is an indication for surgical treatment.

Stenosis of left atrio-ventricular orifice (mitral stenosis) in “pure” condition is seen rarely. More often it develops parallel with mitral insufficiency but more slowly, due to it mitral insufficiency is revealed earlier. Practically always this malformation is provoked by rheumatic fever. Stenosis of mitral orifice is formed due to affection of tendon ring by rheumatic process, scar changes in commissure region between base of petals and their accretion. Chords are affected also; sclerotic process is spread on wall endocardium of left atrium as well.

Mechanism of hemodynamics disorders is the following: during diastole blood from the left atrium comes in left ventricle through narrowed orifice with difficulties, that is accompanied by soft diastolic murmur increasing to the I tone. This murmur is auscultated best of all at the apex, when a child is lying on the left side. Pressure in the left atrium is increasing that leads to its dilatation and hypertrophy, increase of pressure in vessels of the lesser circulation, appearance of the II tone’s accent above pulmonary artery. Gradually dystrophic and proliferative processes in the vessels and intercellular tissue develop; permeability of vessels’ walls increases that leads to edema around capillaries, disorders of gaseous exchange, development of chronic hypoxia and respiratory insufficiency.

Less amount of blood comes to the left ventricle, its volume decreases, and due to it “flopping” I tone appears. Because of increase of pressure in lesser circulation load upon right ventricle increases, its hypertrophy and dilatation appear, that is accompanied by symptoms of cardiac insufficiency of right ventricular type (edema, liver’s enlargement).

Mitral stenosis in children may have asymptomatic course for rather long period of time. At its progression dyspnea, heart beatings, pains in cardiac region, signs of congestion in lesser circulation, possibly hemoptysis appear. Pallor and cyanosis with violet tint of lips and nails, mucous membranes, scanty redness in cheeks (“doll’s redness” – “facies mitralis”) are typical. Apex beat is decreased, on palpation pre-systolic vibration (“cat’s purr”) and pulsation in epigastrium may be determined. Heart’s borders may be not changed.

Instrumental data.

At X-ray typical cardiac configuration with smoothed waist and protruded arch of left atrium may be revealed. In more late stage cardiac shadow is enlarged because of right ventricle, congestive signs in lungs develop.

At ECG:

- signs of hypertrophy and overloading of right ventricle, left and right atria, typical mitral wave P, low and split in leads I, II, aVL, aVF, two-phase in chest leads;

- high wave R in leads III, V₁- V₂, aVR;
- deep wave S in leads I- V₅₋₆;
- incomplete blockade of His bundle's right branch.

At EchoCG:

- decreased rate of diastolic cover of anterior mitral valve's fold
- unilateral movement of mitral valve's folds
- thickening of folds
- reduction of amplitude of front fold's opening
- reduction of degree of folds divergence and square of atrio-ventricular

orifice

- increase of left atrium cavity
- hypertrophy of right ventricle
- turbulent increased diastolic transmitral blood flow, increase of through-valvular pressure gradient.

The course and outcome.

Mitral stenosis is one of the most unfavorable malformations. Decomensation of right-ventricular type occurs quickly.

Treatment.

Mitral commissurotomy is the unique radical method of treatment which is indicated at marked degree of stenosis.

Mitral disease – it is a combination of mitral valve's insufficiency with mitral stenosis, degree of disease's expression may vary. Clinical symptoms and instrumental data combine signs of both malformations with predominance of one of them.

Insufficiency of aortic valve.

1.5–3 years are necessary for development of organic insufficiency of aortic valve. It appears at affection of semilunar valve's folds, due to it they become thicker and deformed, their closure is disturbed. During diastole an orifice between semilunar folds is left through which blood from aorta immediately after end of systole returns to left ventricle that is accompanied by appearance of clear diastolic murmur after II tone. Volumetric overloading of left ventricle appears. During systole left ventricle ejects except usual blood volume some additional quantity, stroke volume rises, maximal blood pressure increases, minimal – decreases. Due to constant overloading hypertrophy of myocardium and dilation of left ventricle cavity appears.

Clinical picture of aortic insufficiency depends upon size of defect. Small defect doesn't provoke marked disorders of hemodynamics and slightly manifests. If defects are marked dyspnea at physical exertion, palpitations, pain in cardiac region, weakness, and fatigue appear. Skin is pale, cardiac hump may

appear, capillary pulse, pulsation of neck's vessels ("carotids dance"). Apex beat is resistant, moved to the left and downwards. Cardiac borders are enlarged to the left. I tone on the apex is weakened, II tone on the aorta is weakened also, long pouring diastolic murmur after II tone is heard. Murmur is heard better at inclined position, its epicenter is localized along left border of sternum in 3-4 intercostal space. In some patients short pre-systolic murmur of Flint may be heard, that is connected with relative narrowing of mitral orifice. Typical peculiarities of pulse: quick, frequent and galloping (pulsus celer, altus, freguens et saliens). Blood pressure is changed. Maximal pressure remains normal for a long time or increases moderately, minimal pressure decreases to low figures and afterwards – to 0. Pulse-pressure is increased markedly. Double tone of Traube and Djuruazyje may be heard during auscultation of arteries on extremities that is stipulated by alternate blood flow in vessels (ahead during systole, and back during diastole).

Instrumental data.

At ECG:

- deviation of electric axis to the left
- signs of left ventricle overloading (high R in leads I and V₄₋₆, deep S in leads III-V_{1,3}).

At EchoCG:

- non-closure of aortic valve folds in diastole
- high-frequency fine-amplitude oscillations of front fold of mitral valve
- left ventricle dilation
- moderate hypertrophy of left ventricle's myocardium and inter-ventricular septum
- increased stroke volume and fraction of ejection
- diastolic flow of regurgitation in ejective tract and cavity of left ventricle.

Course and outcome.

Compensation of aortic insufficiency is put into effect due to powerful muscular layer of left ventricle; because of it patients feel themselves well for a long time. Decompensation develops late at exhaustion of left ventricle's reserves. At first left ventricle's insufficiency appears, afterwards – right ventricle's one. Appeared decompensation is almost incurable.

Operation – implantation of artificial valve – is indicated at progress of the disease.

Stenosis of aortic orifice.

In "pure" state it occurs very rarely, more often it is combined with aortic valve insufficiency. Narrowing of aortic orifice occurs due to scar changes, deformation and union of semilunar folds of aortic valve. During systole blood from left ventricle flows through narrowed aortic orifice that provokes appearance of systolic murmur. Muscles of left ventricle experience overloading, due to it their hypertrophy appears that promotes compensation of

malformation. Aorta receives insufficient blood volume, pressure in it decreases, as a result coronary flow is disturbed and stenocardia appears.

Clinical manifestations depend upon degree of stenosis. If it is mild complaints and clinical manifestations are absent. If it is marked patients complain of weakness, dyspnea, palpitation, increased fatigue, cardiac pains, dizziness, syncope. Apex beat is displaced to the left and downwards, it is powerful, elevated, systolic vibration is present. Heart borders are enlarged to the left due to hypertrophy of left ventricle. I tone above apex is muffled, rough prolonged systolic murmur with epicenter in the second intercostal space at the left and right side is typical; it is conducted to the neck vessels, to scapula region and to the apex, II tone above aorta may be muffled. Pulse is rare, of small amplitude, slowly elevates and narrows (pulsus rarus, parvus et tardus).

Instrumental data.

At ECG:

- signs of left ventricle hypertrophy (wave R in V_{5-6} is increased, there is discordance of wave T, deep wave S in V_{1-2} , deep complex QRS of rS type).

At X-ray:

- enlargement of the heart to the left
- left forth arch is rounded, elevated and elongated
- waist is underlined.

At EchoCG:

- degree of divergence of aortic valve folds is decreased
- folds are thickened and fibrously changed, there are numerous parallel echo-signals in upper part of aorta
- marked hypertrophy of left ventricle's posterior wall and inter-ventricular septum is present
- rate of the diastolic closure of mitral valve's front fold is decreased
- turbulence and high rate of aortic flow, increase of pressure gradient at the level of narrowing is seen.

Prognosis.

Life duration from the moment of heart insufficiency appearance usually doesn't exceed 2–3 years. Sudden death ensues in 5–24% cases of mitral stenosis.

At marked degree of stenosis surgical treatment is indicated.

Combined aortic malformation.

Symptoms of stenosis or insufficiency may predominate in clinical manifestations and instrumental data. At first insufficiency of left type appears, afterwards insufficiency of right type joins. Developed decompensation is resistant to treatment.

Acquired rheumatic malformations of tricuspid and pulmonary artery valves occur very rarely.

Rheumatic fever treatment

Not only suppression of rheumatic process' activity, but prevention of the heart's malformations, that is, practical recovery of a patient, are the main tasks of the therapy.

Native scientists formulated the main links of complex therapy of rheumatic fever:

- 1) hospital treatment
- 2) after-care in local rheumatologic sanatorium
- 3) dispensary observation in cardio-rheumatologic polyclinic's consulting room.

In acute stage of the disease bed rest is prescribed, its duration depends upon activity of pathologic process and degree of cardiac affection. In a case of quick decrease of process' activity and mild cardiac affection bed rest lasts about one month, it can last 6 and more weeks. Therapeutic physical training begins from 2–3 week.

Most frequently patients aren't in need of special diet. If hormonal therapy is used, products containing a lot of potassium are included. In presence of heart insufficiency intake of liquids and salt is limited.

In etiotropic therapy penicillin and its analogues are preferred. They are used during 10–14 days in dose 50 000–100 000 U/kg/day. Afterwards drugs of this group with prolonged action are prescribed (benzatin benzylpenicillin – retarpen – 600 000 U if body weight is less than 27 kg, and 1 200 000U if body weight is more than 27 kg i.m. once in 3–4 weeks). In case of penicillin 100 000 mg/kg/day). In case of β -lactamic antibiotics intolerance macrolids are advisable (spiramycin 3 000 000 U/day orally twice a day during 10 days; azitromycin 10 mg/kg on the first day, afterwards 5 mg/kg during 2–5 days; roxitromycin 5 mg/kg/day orally twice a day during 10 days; clarithromycin 15 mg/kg/day orally twice a day during 10 days). But intake of these drugs is limited due to increased resistance of streptococci to macrolids, moreover, erythromycin's use (40 mg/kg/day orally tree times a day) provokes side effects on gastro-intestinal tract. Lincosamines (lincomycin 30 mg/kg/day i.m. three times a day during 10 days, clindamycin 20 mg/kg/day i.m. three times a day during 10 days) are prescribed only if intolerance both of β -lactams, and macrolides is present.

Use of tetracycline, sulfonamides, cotrimoxazole, and chloramphenicole in treatment of A-streptococcal infection of the throat nowadays is not defensible because of high frequency of resistance and, hence, low efficacy of treatment.

Prescription of anti-inflammatory drugs is one of the most important components of therapy. Modern doctor has powerful arsenal of anti-rheumatic drugs which are prescribed from the first days of the disease.

Beginning from the 50th years of XX century up nowadays rheumatologists rather widely use glucocorticosteroids which have anti-inflammatory, immunodepressive, antitoxic, membrane-stabilizing, and desensibilizing

effects. Their prescription is rational in children suffering from rheumatic fever with moderate and severe carditis, with maximal or moderate degree of process' activity, with acute and – more rarely – subacute course of the disease. In minimal degree of activity and flabby course of the disease hormonal drugs have not marked therapeutic action. In such cases use of non-steroid anti-inflammatory drugs (NSAID) are advisable.

Initial daily doses of hormones vary depending upon condition's severity, cardiac lesions and child's age. Prednisolon is prescribed in dose from 0.7 up to 1 mg/kg/day until therapeutic effect is received with following decrease of a dose (2.5 mg every 5–7 days) under control of clinical and laboratory data. Its withdrawal is possible not earlier than in 1.5–2 months from the beginning of the therapy. Other glucocorticoid drugs (dexametazon, triamcinolon) have no advantages in comparison with prednisolon.

It's necessary to remember about side effects of prednisolon – transitory BP increase, obesity, hypertrichosis, disorders of menstrual cycle, skin changes (dryness, acne, pigmentation etc.), disorders of central nervous system and gastro-intestinal tract function.

Prescription of non-steroid anti-inflammatory drugs is integral part of therapy. Their wide use is due to anti-inflammatory, analgetic, antipyretic effects. Suppression of prostaglandin-synthetase (cyclooxygenase) is the main mechanism of their action due to which formation of important inflammatory mediators – prostaglandins – from arachidonoc acid is decreased; as a result exudation is diminished. They suppress formation of cyclic endoperoxides, products of lipids oxidation, stabilize cellular and sub-cellular membranes.

Among great quantity of NSAID diclophenac sodium (synonyms – orthophen, voltaren, revodin) and indometacin are drugs of choice, their daily dose is 2–3 mg/kg. Course of treatment is 1–2 months.

In a case of mild carditis, rheumatic arthritis without carditis and recurrent attacks of rheumatic fever on the background of chronic rheumatic heart disease the treatment can be limited with NSAID without hormones. NSAID are used also for prolonged treatment after decrease of rheumatic process' activity and withdraw of prednisolone.

In therapy of lingered forms of rheumatic fever and rheumocarditis with valves affection derivates of aminoquinolin (rezochin, delagil, plaquenil in dose 5–10 mg/kg/day over a long period of time) are used widely.

At development of congestive cardiac insufficiency cardiac glycosides (digoxin), diuretics (furosemide, veroshpiron), adrenoblockers (propranolol, atenolol, corvitol), cardioprotectors, inhibitors of ACE (but not simultaneously with NSAIDs) are used.

Intake of haloperidol (0.5–1.0 mg/kg/day with increase of the dose by 0.5mg every 3 days if necessary, but not more than 5mg/day), valproate sodium (15–30mg/kg/day), i.v. injection of immunoglobulins, vitamins of group B, phenobarbital is recommended for treatment of rheumatic chorea.

Recently used acetylsalicylic acid (aspirin) is not used in therapy of children and adolescents nowadays due to probable severe side effects.

In severe cases with pancarditis and polyserositis pulse-therapy with methylprednisolone can be used.

Vitamins, potassium, cardiotropic drugs (riboxin, mildronate, carnitin, cocarboxylase etc.) are prescribed at the same time.

Treatment of streptococcal infection foci is one of the important therapy components. Conservative treatment of chronic tonsillitis brings desirable result not always. In decompensated forms tonsillectomy is necessary in 2–2.5 months after the beginning of the disease.

Patient is treated at a hospital approximately 1.5–2 months; afterwards he is transferred to local sanatorium. This second stage is managed for final disappearance of rheumatic process' activity and restoration of cardio-vascular system's functional ability with the help of therapeutic and prophylactic measures.

Dispensary supervision is the third stage which includes regular examination, prescription of sanitary measures, hardening procedures, treatment of chronic infectious foci, secondary prophylaxis. A child who suffered from acute rheumatic fever, regardless of its form, is observed constantly up to adolescence (health group III).

Timely started adequate therapy with following stage treatment and prophylactic measures promote not only suppression of rheumatic fever in great majority of patients with rheumocarditis (80–85%) but avert heart malformation, that is – practical convalescence or complete rehabilitation of a child.

Prophylaxis

Preventive program includes primary and secondary prophylaxis.

Primary prophylaxis has 2 aspects: general measures and struggle with streptococcal infection. It includes:

1. Measures of increasing of natural immunity and adaptation mechanisms. There are measures providing correct physical development of a child: hardening from first months of life, proper enriched diet, maximal use of fresh air, physical culture, struggle with overcrowding in house, schools and kindergartens, sanitary-hygienic measures decreasing possibility of streptococcal infection.

2. Energetic struggle with streptococcal infection. Acute streptococcal diseases must be treated with antibiotics during 10 days. Preference is shown for drugs of penicillin group; amoxicillin (25 mg/kg/day) is an optimal drug nowadays. Alternative scheme of nasopharyngeal A-streptococcal infection is elaborated: 5-days parenteral treatment with benzyl-penicillin with following single injection of benzatine benzyl-penicillin. Use of macrolids, cephalosporins, lincosamines etc. is possible if intolerance of β -lactamic antibiotics is present.

Working out of anti-streptococcal immunization and anti-streptococcal vaccine is discussed.

Secondary prophylaxis is directed at prevention of relapses and disease progress in children who suffered from rheumatic fever. It provides for regular injections of prolonged action penicillin. All-the-year-round bicillin prophylaxis with its monthly injection is considered to be an optimal regimen. It is prescribed for everybody who suffered from ARF during 5 subsequent years after disease. Such prophylaxis is carried out up to 18 years for patients with formed heart disease, and maybe even longer – for term of life.

Secondary prophylaxis is realized by regular injections of penicillins of prolonged actions – bicillin-5 or benzathine benzylpenicillin (retarpen) in following doses:

- 600 000 U, if body weight is less than 27 kg

- 1 200 000 U if body weight is more than 27 kg i.m. once in 3-4 weeks

At allergy for penicillins secondary prophylaxis is carried out with courses of macrolides – 20 days of every month.

Duration of secondary prophylaxis:

- at ARF without rheumocarditis and chorea – up to 21 years, but not less than 5 years;

- at rheumatic attack with rheumocarditis and valvulitis but without formation of acquired heart disease – up to 25 years, but not less than 10 years;

- at presence of formed acquired heart disease – up to 40 years old;

- for patients with valvular defect and for those who underwent surgical correction of heart disease WHO experts recommend to carry out secondary prophylaxis all life long.

If patient who suffered from ARF falls ill with angina, exacerbation of chronic tonsillitis, pharyngitis, recurrent acute respiratory infections or undergoes operative treatment (e.g., tooth extraction) he is prescribed 10 days antibiotic treatment in therapeutic doses in spite of received prophylaxis – so called current prophylaxis.

List of abbreviations

BP – blood pressure

AS – antistreptohyaluronidase

ASK – antistreptokynase

ASL-O – antistreptolysin O

NSAID – non-steroid anti-inflammatory drugs

ARF – acute rheumatic fever

PMV – prolapse of mitral valve

SGA – streptococcus of group A

EchoCG – echo-cardiography

Control questions

1. Teenager of 14 years old who suffered from rheumatic fever addressed district doctor. What method of secondary prophylaxis must be chosen?
 - A) Year round with retarpen in a dose of 600 000 U
 - B) Year round with retarpen in a dose of 600 000 U
 - C) Year round with bicillin-1 in a dose of 1 200 000 U
 - D) Seasonal with bicillin-1 in a dose of 600 000 U
 - E) Seasonal with NSAIDs
2. Rheumatic nodules are characterized with all signs, EXCEPT:
 - A) Small, dense, rounded formation
 - B) Markedly painful formations
 - C) Are localized in fascia, aponeurosis
 - D) Are localized on extensor surfaces of joints
 - E) As a rule completely disappear in 1-2 months
3. Which acquired heart disease appears most frequently after acute rheumatic fever?
 - A) Insufficiency of mitral valve
 - B) Stenosis of mitral valve
 - C) Insufficiency of aortic valve
 - D) Stenosis of aortic orifice
 - E) Insufficiency of tricuspid valve
4. Severity of rheumatic carditis course is defined by:
 - A) High fever
 - B) Increase of blood pressure
 - C) Enlargement of cardiac size
 - D) Irradiation of cardiac pains under the scapula, left shoulder
 - E) Enhancement of I tone on the apex
5. Ring-shaped erythematous rash on the skin of lower extremities, articular pains and elevated temperature up to 38⁰C appeared in a child of 10 years old who suffered from ARI 2 weeks ago. Joints were edematic, hot on palpation, volume of movements was limited. In several days local changes in knee joints disappeared, but similar changes in left elbow joint appeared. What disease is most probable in a child?
 - A) Metabolic arthritis
 - B) Juvenile rheumatoid arthritis
 - C) Acute rheumatic fever
 - D) Gouty arthritis
 - E) Traumatic arthritis
6. Distinctive feature of rheumatic polyarthritis is:
 - A) Involvement of big and medium joints in the process, more often knee and talocrural, radiocarpal and elbow
 - B) Asymmetry of affection
 - C) Presence of deformations
 - D) Slow backward development of the process
 - E) Stability of affection of the same joints

7. Anxiety, decrease of appetite, hacking, pastouseness and acrocyanosis appeared in a child of 4 months with atopic dermatitis in 7 days after vaccination. Auscultation: rough respiration, disseminated fine and moderate moist rales. Heart borders are enlarged to the left, tones are muffled, CR – 150/min, soft systolic murmur on the apex. Liver +4 cm, spleen +2 cm below ribs arch. Blood test is normal. What diagnosis is most probable?

- A) *Disease of Tolochinov-Rogeanu*
- B) *Acute rheumatic fever*
- C) *Postvaccinal myocarditis*
- D) *Pneumonia*
- E) *Hypertrophic cardiomyopathy*

8. A child of 10 years old was admitted to a hospital with diagnosis: acute rheumatic fever, carditis (endomyopericarditis), polyarthritis, CI IIB. Treatment: penicillin, voltaren, vitamin C. Blood test: leucocytosis $18 \times 10^9/l$, ESR 38 mm/h, glycoproteids 0,800U, CRP ++++. Prescription of what drug is pathogenetically grounded?

- A) *Paracetamol*
- B) *Prednisolon*
- C) *Riboxin*
- D) *Second antibiotic*
- E) *Delagil*

9. Systolic murmur at rheumatic valvulitis:

- A) *Depends upon change of body position and phase of respiration*
- B) *Isn't conducted to left axillary region*
- C) *Is connected with I tone*
- D) *Is connected with II tone*
- E) *It is short, rough by character*

10. A child of 12 years old complains of pains in right knee joint. Objectively: skin above joint is hyperemic, joint is edematic, painful on palpation, local temperature is elevated, and volume of movements is limited. Heart borders are enlarges to the left, tachycardia, I tone on the apex is muffled, systolic murmur on the apex. May diagnosis of acute rheumatic fever considered to be proved?

- A) *No, because 3 "big" diagnostic criteria are necessary*
- B) *No, because 3 "big" and 1 "small" diagnostic criteria are necessary*
- C) *Yes, because 2 "big" diagnostic criteria are revealed in a child*
- D) *No, because 2 "big" and 2 "small" diagnostic criteria are necessary*

11. Which acquired heart disease appears most frequently after acute rheumatic fever?

- A) *Insufficiency of mitral valve*
- B) *Stenosis of mitral valve*
- C) *Insufficiency of aortic valve*
- D) *Stenosis of aortic orifice*
- E) *Insufficiency of tricuspid valve*

12. A child of 8 years old with high degree of activity of rheumatic process stays at hospital and receives voltaren and prednisolon during a month. A child began to complain of abdominal pains. What examination is it necessary to perform for diagnostics of GIT bleeding?

- A) *Reaction of Gregersen (analysis of feces for occult blood)*
- B) *X-ray with barium*
- C) *Fibrogastroscopy*
- D) *Rectoromanoscopy*
- E) *Ultrasound examination*

13. A child of 7 years old was admitted to a hospital with diagnosis: acute rheumatic fever. In 7 days blowing systolic murmur heard in all positions, intensified after physical load and conducted beyond the borders of the heart accompanied decreasing of sonority of I tone on the apex. Which valve affection is it possible to think of?

- A) *Aortic*
- B) *Mitral*
- C) *Tricuspid*
- D) *Valve of pulmonary artery*

14. Duration of secondary prophylaxis at rheumatic attack with rheumocarditis and valvulitis but without formation of acquired heart disease is:

- A) *Up to 25 years, but not less than 3 years*
- B) *Up to 25 years, but not less than 5 years*
- C) *Up to 25 years, but not less than 7 years*
- D) *Up to 25 years, but not less than 9 years*
- E) *Up to 25 years, but not less than 10 years*

15. Streptococcal angina was diagnosed in a child of 7 years old. Pediatrician prescribed i.m. injection of penicillin 4 times a day. Penicillin test appeared to be positive. What group of antibiotics is preferable for treatment of this disease?

- A) *Tetracyclin*
- B) *Fluoroquinolones*
- C) *Cefalosporin*
- D) *Aminoglycosides*
- E) *Macrolides*

16. Parents of 11-years old child complain of his inattention, irritability, jerks of facial muscles, inaccurate food intake, changes of handwriting. These complaints appeared 10 days ago. 2 weeks before a child suffered from angina. Affection of the heart is not revealed. What diagnosis is most probable?

- A) *Epilepsy*
- B) *Chorea*
- C) *Encephalopathy*
- D) *Neurosis*
- E) *Cerebral spastic infantile paralysis*

17. It's typical for annular erythema:

- A) *Bright-red ring-like rash*
- B) *Rash isn't accompanied by itch*
- C) *Rash disappears in 1 month*
- D) *Appearance of rash on the face is typical*
- E) *Rash is of vesicular character, affects palms and feet*

18. What is duration of formation and scarring of Ashoff-Talalaev's granuloma?

- A) *7–14 days*
- B) *1–2 months*
- C) *3–4 months*
- D) *5–6 months*
- E) *1–2 years*

19. A child of 12 years old complains of pain in knee joints, difficulties at walking, elevated temperature up to 38⁰C, tiredness, dyspnea and heart beatings at physical load. From anamnesis it's known that that a child suffered from angina 2 weeks ago. Objectively: both knee joints are enlarged, skin above them is hyperemic, hot on palpation, volume of movements is limited. Respiratory system is normal. Heart borders are 1cm enlarged to the left, CR –

100/min, 1st tone at the apex is muffled, systolic murmur of blowing character at the apex, BP – 105/60 mm Hg. Liver is under ribs arch, spleen is impalpable. What is preliminary diagnosis?

- A) *Reactive arthritis*
- B) *Juvenile rheumatoid arthritis*
- C) *Acute rheumatic fever*
- D) *Non-rheumatic carditis*
- E) *Cardiomyopathy*

20. A child was admitted to a hospital with suspicion of acute rheumatic fever. What examination is it necessary to perform for confirmation of streptococcal etiology of the disease?

- A) *Blood test*
- B) *ECG*
- C) *Glycoproteids*
- D) *Titer of anti-streptolysin O*
- E) *CRP*

21. For rheumatic chorea it's typical everything, EXCEPT:

- A) *Distal hyperkinesia (bilateral jerking of muscles of the trunk and extremities which are enhanced at excitement and disappear during sleep)*
- B) *Ataxia (lurch, instability in Romberg's position, disorders of handwriting)*
- C) *Muscular hypertonia*
- D) *Signs of vegetative dysfunction (hyperhidrosis, red dermographism)*
- E) *Psychic disorders (tearfulness, depressed mood)*

22. Main criteria of acute rheumatic fever are all EXCEPT:

- A) *Fever*
- B) *Annular erythema*
- C) *Subcutaneous nodules*
- D) *Chorea*
- E) *Carditis*

23. The most typical clinical sign for rheumatic arthritis is:

- A) *Morning joint stiffness*
- B) *Affection of small joints*
- C) *Shifting character of affection*
- D) *Steady deformations of joints*
- E) *All above mentioned*

24. Duration of secondary prophylaxis at presence of formed acquired heart disease is:

- A) *Up to 20 years old*
- B) *Up to 25 years old*
- C) *Up to 30 years old*
- D) *Up to 35 years old*
- E) *Up to 40 years old*

25. Duration of secondary prophylaxis for patients with valvular acquired heart disease and for those who underwent surgical correction of acquired heart disease:

- A) *All life long*
- B) *During 25 years*
- C) *During 20 years*
- D) *During 10 years*
- E) *During 5 years*

26. Duration of secondary prophylaxis at ARF without rheumocarditis and chorea is:

- A) *Up to 16 years old, but not less than 5 years*
- B) *Up to 186 years old, but not less than 5 years*
- C) *Up to 19 years old, but not less than 5 years*
- D) *Up to 20 years old, but not less than 5 years*
- E) *Up to 21 years old, but not less than 5 years*

List of references

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Навчальне видання

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ТЕМА 9
РЕВМАТИЧНА ЛИХОМАНКА
У ДІТЕЙ

*Методичні вказівки
для студентів*

Упорядники Одинець Юрій Васильович
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MODULE 1
SUBSTANTIAL MODULE 4

THEME 9
RHEUMATIC FEVER IN CHILDREN

Practical policies for students