DANYLO HALYTSKYI LVIV NATIONAL MEDICAL UNIVERSITY

PEDIATRIC INFECTIOUS DISEASES DEPARTMENT

GUIDELINES

TO PRACTICAL TRAINING OF PROFILE COURSES OF CHOICE

“Surgery”

FOR 6TH YEAR STUDENTS OF THE MEDICAL FACULTY

SPECIALTY

"GENERAL MEDICINE"

TOPIC:

"Differential diagnosis and emergencies in viral hepatitis (VH) in children. Acute liver failure in VH in children. HIV infection and AIDS in children"

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Guidelines on the course of Pediatric Infectious Diseases

for students of the 6th year of General Medicine Faculty

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Guidelines to lesson for students of the 6th year from pediatric infectious diseases profile cours of choice "Surgery" specialty "General medicine"

« Differential diagnosis and emergencies in viral hepatitis (VH) in children. Acute liver failure in VH in children. HIV infection and AIDS in children»

I.

Aim: to know diagnostic criteria of viral hepatitis to perform differential diagnostics of them.

Professional motivation: Viral hepatitis is the most widespread infectious diseases of child's age. The most common hepatitis viruses is type A. The hepatitis A virus (HAV) is the commonest cause of viral hepatitis, responsible for up to 40% of cases worldwide. It is spread by contaminated food. Vaccines is available against hepatitis A.

Hepatitis B, or serum hepatitis, is a highly contagious disease spread by blood products or in body fluids. It often culminates in liver failure, and is also associated with liver cancer, although only 10% of those infected suffer chronic liver damage. Hepatitis C is mostly seen in people in need frequent transfusions, 75% of infected with hepatitis C will go on to develop chronic liver infections. Vaccines are available against hepatitis B.

Basic level

1. To know how to ask about complaints, history of the disease and life in children with hepatitis [propedeutic pediatrics, children infectious diseases].
2. To perform clinical examination of the child with hepatitis [propedeutic pediatrics, children infectious diseases].
3. To diagnose viral hepatitis after clinical, laboratory and instrumental examination of the child [infectious diseases, propedeutic pediatrics, microbiology, and pathophysiology].
4. To give etiological, pathogenetical and symptomatical treatment [pharmacology, children infectious diseases].

II. Primary aims of the study

A student should know:

1. Etiology and properties of causing factors of illness
2. Epidemiology (source of infection, ways of transmission, age-old receptivity and morbidity).
3. Pathogenesis of disease, pathomorphologic changes in the staggered organs.
4. Classification of the illness.
5. Clinical symptoms of pre-icteric, icteric and postichteric period of viral hepatitis
6. Methods of laboratory research.
7. Treatment of viral hepatitis
8. Consequences and complications of viral hepatitis
9. Measures of prophylaxis of viral hepatitis

A student should be able:

1. To follow the basic rules of work near a bed sick with viral hepatitis.
2. To take anamnesis with the estimation of epidemiology information
3. To examine a patient and reveal the basic clinical signs of illness.
4. To represent information of anamnesis and objective inspection in a hospital chart and formulate the preliminary diagnosis.
5. To write the plan of examination.
6. To write a clinical diagnosis (form of disease, type, severity, course of disease).
7. To prescribe treatment taking into account age, severity of illness.
8. To write out a prescription.
9. To organize disease measures in the hearth of infection (to find out the source of infection, fill an urgent report in SES, to set a quarantine, to define the circle of contact persons, conduct them bacteriological inspection).

10. To write epicrisis with the estimation of flow of illness, results of inspection, efficiency of treatment, prognosis, by recommendations for a subsequent supervision or treatment depending on the form of viral hepatitis.

III. Educational aims of the study

- forming the deontology presentations, skills of conduct with the patients
- to develop deontology presentations, be able to carry out deontology approach to the patient
- to develop the presentations of influence of ecological and socio-economic factors on the state of health
- to develop sense of responsibility for a timeliness and loyalty of professional actions
- to lay hands on ability to set psychological contact with a patient and his family

IV. Subject's integration

Table 1

Subjects	***To Know***	***To Know How***
Human Anatomy	*The main anatomic characteristics of GIT and liver*	
Physiology	*Function of GIT, and liver*	*To explain a variety of clinical signs and laboratory abnormalities*
Pathological Physiology	*Pathogenesis of disease*	*To explain the main symptoms and signs appearance, causes of failure of inadequate therapy*
Pathological	*Pathology*	*To explain the pathogenesis of*

Anatomy		*complications and causes of death*
Microbiology	*Etiology (classification, morphologic characteristic of the pathogen, methods of revealing and identification)*	*To reveal the causative agent*
Pharmacology	*The main solutions for detoxication and pathogenic treatment. Regimens of treatment. Treatment of complicated disease. Significance of supportive care*	*To administer treatment of GIT. To write the scheme of treatment of severe disease.*
Histology	*Histological changes typical for disease*	*Explanation of clinical signs appearance*
Propedeutics of Pediatric Diseases	*History of disease. Patient's examination.*	*To gather information about patient's history and chief complaints, to distinguish those, most important for diagnosis. To examine the patient, to reveal the main symptoms and signs of disease. To distinguish the set of diagnostic features of disease. To argue the diagnosis.*
Pediatric Diseases	*Syndrome of toxicosis*	*To differentiate with other disorders of GIT*
Neurology	*Diarrhea, vomiting, toxicosis, altered consciousness*	*Differential diagnosis with neurological disorders*
Clinical	*Immunologic changes as a part*	*To explain confirmative*

immunology and allergology	*of pathogenesis and host defenses*	*serologic tests*
Epidemiology	*The ways of transmission, main sources of infection*	*Epidemiological history*
Themes integration		
Escherichiosis, salmonellosis, shigellosis, non-viral hepatitis	*To know peculiarities of manifestations, laboratory diagnosis, treatment*	*To differentiate viral hepatitis with other infectious diseases with similar symptoms*

V. The contents of a theme

Viral Hepatitis A

Viral hepatitis A (VHA) is an acute cyclical disease with a short-time, often insignificant, manifestation of intoxication, having a benign prognosis.

Etiology: its infectious is the hepatitis A virus (HAV) which is an RNA containing spherical RNA containing particle having the size of 27–32 nm. It was discovered by S. Feinstone in 1973. It taxonomically belongs to the *Picornaviridae* family, the *Hepatovirus genus*. There are 7 genotypes identifited, the first 4 are isolated from humans and the latter 3 — from infected monkeys. All 7 genotypes have the same HAa-antigen and cause cross protective immunity.

HAa is found in feces of a patient (fecal antigen) that testifies for active replication of virus in hepatocytes. In blood serum the anti-HAV antibodies are found, at first the M-class, and later in the disease the G-class which testify to the presence of protective immunity.

The virus is characterized by stability in the environment, prolonged preservation time in food, water and other objects of environment.

Epidemiology. The infectious source is a sick human. Very dangerous

are the latent, inapparent and anicteric forms of the disease which present the major part of morbidity in hepatitis A. Significant danger is presented by attenuated, inapparent and anicteric forms of which present a majority of cases in VHA morbidity the fact that virus excretion starts long before the first clinical manifestations and the highest concentration is observed in preicteric period. After the appearance of jaundice the viral level in feces is significantly decreased and the time of the HAVa excretion does not exceed 6–7 days of icteric period. Thus the, effectiveness of hospitalization as a measure of patient isolation is very low. VHA is a typical intestinal infection. Children susceptibility to it is much higher than in other patients they form 70–80 % of all cases of VHA. The highest morbidity is registered in autumn and winter. There are outbreaks noted in children institutions. Immunity after recovery is steadfast, but in case of repeated infection one cannot exclude infection by other hepatotrophic viruses. Children of the first year of life are rarely ill with VHA. The HAV carriage has not been established.

Pathogenesis. VHA is called an auto-restricted infection that is caused by high viral immunogenicity. The rapid intensive immune response blocks viral replication and restricts its spreading on to the non-infected hepatocytes. HAV enters the intestine where it is particularly inactivated by enzymes. From here it spreads via blood to hepatocytes and penetrates into them. Owing to the interaction of the virus with biological macromolecules metabolic disorders appear in the membrane and other component parts of hepatocytes. A higher quantity of free radicals activates the peroxidation of lipids in the cell membranes. This leads to destruction of membrane structure, and excretion of enzymes from hepatocytes. A cytolytic syndrome with necrosis and necrobiosis of hepatocytes occurs.

The final effect of the proteolytic ferments is degeneration of hepatocytes and release of protein-complexes which become autoantigen. These autoantigens together with HAag stimulate T- and B-systems of immunity and

the process is accompanied with the production of antiviral antibodies, increase of T-lymphocyte functional activity with the antihepatic antibody formation. However the autoimmune aggression in VHA is not completely realized and that explains the practical absence of VHA severe forms. The anti-HAV antibodies are virusneutralising one and happen to be already effective in low titres.

Pathologic anatomy. Morphologic alteration in VHA (by means of needle biopsy data) are connected with the disease period. In prodromal period there is an activation of the stellate (Kupffer) cells reproduction, mononunclear infiltration along the portal tracts and alteration of hepatocytes (mitosis, dystrophic changes). In the period of maximal clinical manifestations ballon dystrophy and dilfuse necrosis of hepatocytes is observed, but in the necrotic zone we can see lymphohistiocytic infiltration, general infiltration along the portal tracts with parenchymal hepatic lesions (architectural changes in its structure). Simultaneously with dystrophy and necrobiosis there is regeneration and cellular infiltration reduction. Morphologic alteration ends in the 6–8 week of disease, but sometimes it lasts for 4–5 months.

The functional state of liver is completely regenerated, but residual hepatic fibrosis is possible. There are no cases of chronic hepatitis development.

Clinical features. The incubative period is 10–15 days (in average 5–30 days), it has no clinical manifestation. At the end of the incubative period there is a higher activity of cellular enzymes (ALT, AST) registered. The HAV is detected in the last third part of the incubative period, leading to epidemiologic danger.

Prodromal period (preicteric) of the disease begins acutely, the body temperature rises up to 38°–39 °C, there is intoxication, weakness, headache, nausea, vomiting, asthenia. Sometimes, there is a dull, acute or paroxysmal abdominal pain (“acute abdomen”), a feeling of heaviness in the right hypochondrium, mild catarrhal signs (rhinitis, hyperemia of fauces). Children

are capricions, have insomnia. There may be dyspeptic disturbances (constipation, or diarrhea). Intoxication disappears in 1–2 days, but anorexia and nausea stay on. On physical examination liver enlargement, algestheia and pain can berevealed. At the end of the preicteric period dark urine and discolored excrements (acholia), and also icteric scleras,can be found, as well as icteric mucouse membrane of the oral cavity. According to the laboratory findings this this is the period when enzumes (ALT, AST), thymol test increase, as well as bilirubin level, lypoprotein, and dysproteinemia. Using of the clinical pharacteristic we can discern dyspeptic, astheno-vegetative, catarrhal and mixed variants of the prodromal period. In 2–5 % of patients jaundice appears “in a day” without any complaint on their side. The general duration of the preicteric period of the VHA is 3–5 days (but it may continue 7 days or be shortened to 1–2 days).

The icteric period frequently appears on the 3rd–5th day of the disease. After the appearance of icteric scleras and mucous membranes there is a rapid rise in the icterus of skin of the face, limbs, trunk. Jaundice increases for — 2–3 days and lasts for 1–12 days. The significant sign is that jaundice is not accompanied by aggravation, but just the opposite by an improvement of the general patient condition. Appetite is recovered, dyspepsia decreases (there is less nausea and vomiting). There is disappeared the rigor and “rheumatic pain” in bones. The general condition improves is from the first to 2–3rd day after the jaundice appears. During the icteric period the subjective common state of patients is satisfactory.

Intensity of jaundice is often expressed moderately. The bilirubin lever exceeds the norm not more than 4–5 times. The first 2–4 days the jaundice may increase, but then it decreases quickly. Resumption of bile secretion begins with clear urine and appearance initially “variegated” and then stably darker feces. The general duration of the icteric period often does not exceed 1.5–2 weeks. Opposite to the quick positive dynamics of the patient general condition,

hepatomegalia is retained during the whole icteric period and sometime it is enhanced.

During palpation the liver border is smooth, somewhat painful (pains appear owing to the hepatic capsule extension). Frequently there is an enlarging of the lien (spleen). In the icteric the general clinical manifestations as asthenization, hypotension, bradycardia, weak cardiac tones, systolic murmur prevail.

In blood examinations there is leukopenia, lymphocytosis and eosinophilia, while ESR is normal. During the icteric period there are severe biochemical disorders demonstrating functional activity of the liver: the hyperbilirubinemia (a higher associated fraction), higher activity of the hepaticocellular enzymes, high thymol test findings, higher concentration of lipoproteins and dysproteinemia.

The third disease period (reparative, convalescence, postichteric) is characterized with the absence of complaints, the patient feels better, but in some cases the enlargement of the liver is retained and the liver functional activity is gradually improving. Fatigability, hypomnesia, asthenovegetative disorders can remain. Convalescence duration is 2–3 months.

The main criteria of VHA severity as well, as other types of viral hepatitis, is the intoxication manifestation, its presence and degree of manifestation. In the VHA mild disease forms prevail i. e. they are anicteric or icteric ones. The averagely manifested form is observed in less that one-third of all patients, and the severe one in 0.1–0.3 %. In the light form the general intoxication is not significant, jaundice is not intensive, liver may be enlarged up to 3 cm and be dense. The bilirubin level is not higher than 85 mcmole/L (the unassociated till 25 mcmole/L), thymol test is moderately higher, the hepato-cellular enzime activity exceeds normal concentration 5–10 times.

The averagely-severe form is characterized by moderate intoxication, temperature rises up to 38°–39 °C, after the jaundice begins weakness, anorexia

and sometimes nausea continue. Jaundice is sufficentily intensive, its duration is 2–6 weeks, liver is enlarged by 4–5 cm, spleen is also enlarged. The level of total bilirubin in blood serum is 86–200 mcmole/L (unassociated fraction is to 50 mcmole/L). There is a higher activity of the hepato-cellular ferments, thymol test indices are higher, but prothrombin index may decrease (to 70–60 %).

The severe form of the VHA is rare. The intoxication is considerable with CNS affection: high temperature, adynamia, weakness, anorexia, recurrent vomiting, sometimes excitement, insomnia, headache. There an allergic or hemorrhagic rash. The symptoms are rapidly augmenting. Jaundice becomes very expressive, the feces are acholic, urine is dark. There is oliguria. Liver is considerably increased and dense. The jaundice progressing leads to severe intoxication: mental confusion, recurrent vomiting, nasal bleeding, bradycardia. Bilirubin level in blood serum is over 170–200 mcmole/L (unassociated is over 50 mcmole/L). The prothrombin index is lower than 40 %, enzyme level is very high. Hypoalbuminuria is progressing and G-globulin level is rising.

Cholestatic syndrom occurs rarely, it has insignificant intoxication, prolonged hyperbilirubinemia accompanied with mildly higher activity of ALT and a high concentration of alkaline phosphatase.

Clinic form without jaundice are leaded to an atypical ones-they are the anicteric, latent and subclinic forms.

The clinical forms having no jaundice manifesctations are classifiecied as atypical forms and they are subdivided into anicteric, attenuated and subclinical forms. The anicteric form has no icteric skin and scleras. There is a short-time temperature rise, hyporexia, nausea, weakness, abdominal pain, liver enlargement. The color of urine and feces may change. There is a higher activity of ferments (ALT, AST) and thymol test in blood serum. The bilirubin level is normal. The duration of changes is 3–7 days.

The attenuated form is characterized with the subfebrile temperature, transitory short-time jaundice (2–3 days), dark urine and acholic feces. The attenuated form is termed as “rudimentary” one being a variant of the mild type.

The subclinical (inapparent) form has no clinical manifestations, but there is higher activity of enzymes (ALT, AST) and IgM and I antibodies in blood serum are found. The inapparent forms occur more frequently within the VHA outbreak of the and often are not clinically diagnosed, hence leading to the epidemic process continuation.

The course of the VHA may be acute (up to 3 months) and protracted (from 3 to 6 months). During the protracted form the normalizing clinical and biochemical disorders are retained, they are manifested by insignificant jaundice, enlarged and dense liver, stable but moderately high level of the hepato-cellular enzymatic activity. The protrected forms may lead to acute situations: an increase in of jaundice, enlargement of liver, aggravation of the fermental state of the liver. However, VHA has a favorable outcome, that is complete convalescence. Sometimes residual signs, are possible including hepatomegaly (residual fibrosis of the lever) alongside complete normalizing of its functional state, lesion of the bile ducts (dyskynesia).

VHA Diagnosis in typical cases does not evoke difficulties.

The basic criteria for the primary VHA diagnosis are:

1. Contact with a VHA patient during 35 days before illness.

2. Seasonal morbidity with a peak in spring and autumn. The patients are usually children, adolescents or young men.

3. The acute onset with manifested temperature rise and intoxication.

4. Enlargement of the liver is often accompanied by enlarged spleen.

5. Short predicteric period (4–6 days), mainly with dyspeptic disorders in general.

6. The general patient condition improvement with jaundice appearance.

7. Mild intoxication and short-time jaundice.

8. Rare development of severel forms.

9. Absence of chronization process.

10. AST level increase frequently strongly manifested. Positive thymol test since the first days of disease.

11. Anti HAV (IgM) antibodies in blood during the initial period as well as HAV-RNA; HAag in feces.

Differential diagnosis is the most complicated thing in the preicteric period. It is exactly, in this period that we have more diagnostic errors. More often doctors make a usually diagnosis of ARVI during that period. But in VHA, the catarrhal signs are not significant (hyperemia of the mucous membrane in the nasopharynx, mild tussiculation). But in ARVI there is no enlargement, density and painfulness of the liver on palpation. On the other hand, dyspeptic disorders typical for the preicteric period of VHA, as a rule, are absent in ARVI. In the preicteric period of VHA, doctors often mistakes VHA for acute enteric infections.

At the same time, in VHA the dyspeptic signs differ from the acute enteric infections. The VHA manifestation has no inflammatory process in the gastrointestinal tract, but appears as a result of generalized inflectional-toxic lesion of the gastrointestinal system.

In the abdominal variant of the VHA prodromal period there may be acute surgical diseases of abdominal cavity (appendicitis and others) prognosed. However, in VHA even in spite of the severe abdominal pain, muscular defence, the abdominal irritation signs are absent. The pain is mostly localized in the right subcostal region. An important differential diagnostic means is a common blood count which testifies for the absence of inflammatory reaction.

In the icteric period doctors have to differentiate this state with the suprahepatic jaundice (hemolytic jaundice) which of appears owing to an intensive hemolysis of erythrocytes with free bilirubin formation. When making differential diagnosis you should take into account a case and life history

(anemia, intoxication, hemorrhages). Estimating the leading complaints and objective examination findings one should pay attention to vertigo, sweating pale skin and mucous membranes, citric tint of jaundice, absence of acholic feces and dark urine. In case of suprahepatic jaundice there is no preicteric period. Laboratory examination shows a higher bilirubin fraction biochemical factor of liver function are not changed, there is a drop in erythrocyte count and a lower level of hemoglobin. Hepatic jaundice also leads to a higher bilirubin fraction, because of normal hepatic and ferments activity (the Gilbert-Rotor's and Dubin-Johnson syndromes). Different variants of hepatitis in infectious diseases (yersiniosis, inflectiousl mononucleosis, herpetic infection, salmonellosis) develop on the background of the main disease with its typical clinical syndromes.

The general attention is paid to the making a differential diagnosis of VHA a compared with other hepatocellular jaundices of other etiology (B, C, D, E). The most decisive differential diagnostic significance have the indications of specific HAV markers (anti-HAV-IgM) in blood.

Treatment. The main, in VHA treatment is a basic therapy. It is a complex of measures directed at creation of favorable conditions for hepatic function. Patient have to keep bed (for 2–3 weeks independent of their general condition and severity of the disease; the mild form must have a milder-bed regimen, but the severe forms have to kept in bed strictly). Improvement patient condition, better appetite, decrease in intoxication, normal colour of urine and feces are basc indications for a more lenient regime.

During diet prescription the doctor should take into account the decreases functional activity of patient's liver. In case of the full value food components one should take into account physiological requirements and energetic loses of the body as a whole. Proteins, fats and carbohydrates should corresponds to the patients age. The patient must exclude meat extractive dishes (bed-broths), fried meat and fish, smoked and salty food products, tinned foods, cocoa, chocolate.

The patient may eat fresh and boiled or fish or meat (lean chicken, veal, beef, rabbit. meat) with exception of pork, mutton, goose and duck meat. Milk products — sour milk, cream, sour cream, butter should also be excluded from the diet. The bats in the daily diet must be oil in 60–70 % of instances. Carbohydrates food are — gruels, potatoes, vegetable soups, honey, stewed or boilend fruit, starch jelly, juices, fresh fruits are allowed while yellow, red and orange vegetables and fruits like carrot and tomato juice, oranges, tangerines, pumpkin which has a lot of carotene should be taken out of the diet. The carotene surplus may enhance jaundice and affect the body. According to Pevzner' diets, in the first and second disease period diet № 5A, is prescribed while in the third period diet № 5. It is necessary to make sure that the patient drinks a sufficient quantity of fluid (1–2 liters per day). The fluids could be alkaline mineral waters, or tea, sweet — brier decoction. Meals must be frequent (4–5 times a day, but in small portions). It is expedient to prescribe vitamins complexes. After acholic feces stop cholagogue drugs ("Alochol", "Cholenzyme", "Herbal" decoctions of cholagogue phytotherapy) are used.

Patients with a mild course and most children patient with average course of the disease should keep bed, diet and vitamintherapy. In case of a severe course intravenous dropper infusion should be administered using with Neohemodesum, Rheopolyglucinum, 10 % solution of glucose for detoxication. Protracted illness needs a prescription of Essentiale, Legalon, Carsil for improvement of the patient condition.

Patients may be discharged from the hospital on the 21st day from jaundice appearance if intoxication, icterus, enlargened liver bilirubin and fermental activity levels in blood are absent.

The convalescents must go through prophylactic medical follow up examination during a 6 month's period (after 1, 3 and 6 months). During the 1st month after discharge from the hospital the convalescents are recommended to a physical regime with lower load (to have a bed rest for 1–2 hours in the day

time). Meals are the same as in the acute period. During the first 6 months physical exercises should be performed in special groups of physical exercise therapy. If necessary, rehabilitation is indicated in specialized departments at hospitals or regional special sanatoriums.

Prophylaxys. The patients are admtted into the infectious departments (with compulsory current disinfection regime). After it is necessary to conduct final disinfection in the place of residence of the patient with the use of sanitary-epidemiologic station measures. All contacts must found and supervised observed by medical professionals for 35 days. In all children's institutions a quarantine of 36 days should be kept from the first disease case. The teaching of hygienic every-day habits to children is important.

Viral Hepatitis B

VHB refers to the parenteral hepatitis group. In the past it was called serum VH. The VHB can be an acute or chronic hepatic disease which is characterized with a slow development, and prolonged course. It often has severe and malignant (fulminant) forms.

Etiology. The first data about the infectious agent were obtained in 1565. Aproleen was found in the Australian aborigines blood of was extracted the protein which was named as an Australian one. A connection it was discovered between this protein and the posttransfusion hepatitis agent. In 1979 D. Dane was the first to describe in his immuno-electronomicroscopic examinations the complete virion of B hepatitis virus, which was named a Dane particle. The virus has the dimensions of 42–52 nM, contains DNA and consists of three antigens: "Australian" HbsAg, nuclear (HbcAg) and the infectivity antigen (HbeAg). The receptors of polymerized albumen on the surface of virus have an certain importance these receptors determine its hepatotropism. Viral DNA exist, in free and integrated into cellular genome forms. That explains the possibility of development of both an acute and chronic infectious process.

VHB is determined to an individual hepatovirus family. It is very resistant, and stable to boiling in water during 30 minutes, to ether and formol. Its antigens and homologic antibodies are specific serologic markers of this infection. There are eight known subtypes of VHB, each of them has a specific geographic spreading.

Epidemiology.

The source of the VHB are patients with acute and chronic hepatits, as well as the so called healthy carriers of the HbsAg (antigen). In the VHB acute forms the patients infectivity appers from the moment of infection in the incubation and prodromal periods and it continues until complete sanation of the body in the convalescent period. In chronic forms the duration of epidemiological dangerous period is not limited. The virus is contained in blood, and also in different body fluids (saliva, urine, sperm, vaginal secretion, etc). For the HBV appearance it is enough to inoculate a very small volume of blood (0.0005 ml). The infection spreads due to the infected blood transfusion, as well as due to other factors which lead to skin and mucous membrane injuries with have contaminated instruments. There is a possibility of transplacental route of the VHB infection which occurs in placenta injury is not over 10 %. Most of the newborns are infected by perinatal way. The possibility of the VHB infection from the HbeAg-positive mothers is 50 %. The fecal-oral and contact transmission routes are limited.

Children of the first year of life (86 %) suffer from VHB more often. After three years the morbity is considerably decreased (because of reduced quantity of parenteral manipulations). VHB is equally frequently registered the year round. After the disease is over a stable immunity is formed and recurrent disease should be viewed as acute stage of chronic hepatitis, or infection by an other virus (A, C, E).

Pathogenesis.

Infectious agent parenterally penetrates the body and with the blood flow spreads further into the liver. In hepatocytes the viral DNA is released, penetrates inside the nucleus of hepatocytes and inserts into the cellular genome. Viral antigens are coded and their reproduction begins in large quantities. The Dane particles are blocked on the hepatocyte membranes favours clone formation of immunocompetent lymphocytes and is accompanied with the appearance of antiviral antibodies and increase in functional activity of the T-subpopulation lymphocytes (the natural killers). Sensibilized killers attack the infected hepatocytes and cause their cytolysis. Thus the body is freed from VHB by destroying infected hepatocytes. The developing autoimmune processes are adequate to the form and type of disease course. The disease course depends both on the infection dose and infectivity of the virus, as well as on the character of genetically determined immune response of the body.

The acute form of VHB develops in patients with adequate immune reaction. Functional activity of T-lymphocytes and macrophages is disordered insignificantly. The activity of the K-cells in the antibody-dependent K-cellular cytotoxic is considerably increased reaction in the acute period. Thus, optimal conditions formed for effective elimination of infected hepatocytes. Some increase in correlation coefficient of T-helpers as T-suppressors provides sufficient production of antiviral antibodies and allows to excrete the viral particles. In such cases the processes of peroxidation, lysosomal hydrolase activity are minimally expressed; the destructive effect of lysosomal hydrolases is inhibited by antioxidant systems and proteolysis inhibitors. Structural organization of the cell is preserved. Clinically such cases have a to tendency have a cyclic course with a favorable outcome.

In the malignant (fulminant) form there are significant disturbances in the patient immune state that is characterized with acute disorders in macrophageal immunity, reduction in the overall number of T-lymphocytes and in their functional activity, decrease of the T-suppressor percentage and relative

increase in the number of T-helpers. This allows formation for the viral antibody hyperproduction, K-cellular cytolysis increasing and irreversible destructive processes in the liver. Excessive accumulation of the toxic hydroperoxides and lysosomal enzyme activation accompanied by a significant reduction of proteolysis inhibitor synthesis, leads to hepatic parenchyma autolysis, protein disorganization, release of autoantigens and autoantibodies formation.

Such autoimmune reactions as these, intensify destruction in the liver. Thus, in fulminant desease, the liver becomes a “victim” of immune and autoimmune reactions.

Chronic hepatitis develops with significant changes, that is with lower numbers and activity of T-lymphocytes, macrophages, which favours viral persistence with a lower cytolysis level.

Pathomorphologic alterations are discovered in different tissues (parenchyma, connective tissue, reticuloendothelium, bile ducts). These are insignificant dystrophic necrotic alterations of hepatic cells or a massive necrosis of the hepatic parenchime.

The acute cyclic from gives dystrophic inflammatory and proliferative alterations in lobal center (with VHA located over the peripheral region).

The massive necrosis of liver is a necrotic degeneration of almost all hepatocytes. Regeneration is not significant (it manifests mainly in regeneration of paraportal hepatocytes), with the growth of connective tissue and disorder in hepatic cytoarchitectonics. There is also phlebitis of hepatic veins, edema of the bile bladder walls, degeneration of kidneys, myocardium, pancreatic necrosis, hemorrhages in internal organs, toxic encephalopathy.

Clinical features.

Incubation period of the VHB lasts 6–26 weeks (10–16 weeks in average). The disease progresses in stages there appears weakness, malaise, patients easily get tired, their workability is low, there is loss of appetite the

temperature rises. Often, these signs are weakly manifested and the disease beginning is manifested with dark urine and jaundice. From the first days some patients have nausea, recurrent vomiting, frequent dyspeptic symptoms. In the first-year of life children the prodromal period is shortened to 5–7 days, sometimes to 1–2 days. When jaundice appears intoxication is not reduced (as in VHA), but quite the reverse it remains or gets increased. More frequently the patient complain of nausea, vomiting, high temperature, heaviness and pain in the epigastric part and in the right subcostal region. Jaundice gradually heaviness during 5–6 days (sometimes 2 weeks) from the light-yellow to canary yellow and intensively-yellow colours. The intensity of icterus does not always correspond to the severity of disease, especially in the first-year-old babies, when jaundice is less intensive than in the older children with similar bilirubin level. The general duration of icterus in VHB is 3–4 weeks (sometimes to 6–8 weeks). Often, there is a dermal pruritus (cholestatic disease variant). In the VHB different rash on skin can be observed, such as urticarial, popular like in measles and scarlet fever. However the most frequent rash manifests itself as popular dermatitis) the Gianotti-Croti syndrome). Rash is symmetrically located on limbs, buttocks and trunk as red papules with the size of 2 mm. In several days there is desquamation. Simultaneously with jaundice development, the liver is enlarged, protruding 1–2 or 7–8 cm from the costal border. Its border is smooth, and dense on palpation. An enlargement of the spleen is observed in 40–50 % of cases. During the peak period of disease there is also a general depression of the nervous system (insomnia, flaccidity, emotional lability). On the side of the cardiovascular system, there is bradycardia, hypotension, ECG-disorders (enlarging of the QRS-complex, T-wave depression). There are acholic feces with a lower level of stercobilin. Common blood count shows some erythrocytosis and leukocytosis, in prodromal period they are changed to anemia and leukopenia with lumphocytosis during the icteric period. In blood serum there is a higher activity of the hepato-cellular enzymes (ALT, AST,

LDH and its isoenzymes), associated bilirubin fraction level owing to its excretion disturbance by hepatocytes and free fraction in severe forms with massive necrosis (conjugation disorder). Duration of hyperbilirubinemia is about 3–4 weeks. There are biliary pigments and urobilin in urine. In blood serum the reducing of protein level is accompanied with dysproteinmia (thymol and, mercury bichloryde, sublimate tests etc.), lower prothrombin index and fibrinogen level.

Classification of the VHB is similar to that of VHA, however in VHB average severe forms occur more frequently, especially in the first-year-of life of children. The prodromal (preicteric) period is shortened to 2–3 days. Children have emotional lability, nausea, vomiting, sometimes diarrhea, weakness, mild catarrhal alterations, often a fever to 38°–40 °C.

The icteric phase manifests itself with an intensive jaundice, hepatolienal syndrome (lasting to 30 days), hemorrhages and complications development due to the concomitants bacterial infection.

The most severe degree of the VHB, especially in infants younger than 12 months, is the malignant form, hepatodystrophy (acute yellow hepatic atrophy, toxic hepatic dystrophy), which appears in cases of diffuse massive hepatic necrosis. Incubative period is shortened to 2–3 days, the onset is acute, temperature raises to 39°–40 °C, apathy, adynamia followed by excitement (often a motor one). There are typical dyspeptic changes: regurgitation, vomiting, diarrhea. Prodromal period is shortened to several days, sometimes there is no prodromal period and the disease begins from icterus. From the jaundice period the child’s general condition is quickly aggravated: severe intoxication, hemorrhagic syndrome, “saffron” color of skin, tachycardia, dull cardiac sounds, extrasystoles, adynamia, limb tremor, higher tendonal reflexes, psychomotor excitement, crying, depression with disorientation, hallucinations, delirium. In the day time these patients are drowsy, but at night they have insomnia. The recurrent vomiting is a typical sign of fulminant form, coffee-

ground vomit testifies for the hemorrhagic syndrome. Nasal bleedings, dermal and mucosal hemorrhages, hemorrhages around the injection places are possible (coagulopathy syndrome). The specific feature is a decreasing liver, at first its lower border, which becomes acute and painful on palpation. Liver size reduction reflects dynamic development of the hepatic parenchymal necrosis: decreased size, tympanis sound about the hepatic border, but in the severest cases the hepatic dullness absolutely disappears. Hepatic size reducing is accompanied with an increase of intoxication; mental disorder, excitement, dermal hemorrhages, ecchymosis, nasal bleedings, general edema, black vomit, meningeal signs, convulsions. This is a precoma stage. As the time goes an excitement is changed with depression, delirium, hallucination, convulsions, mydriasis, “raw liver” smell — from the month, anuria, deep sleep. This is a coma stage. In laboratory findings there is anemia, neutrophilic leukocytosis, thrombopenia, higher ESR levels (owing to the free fraction). Bilirubin level gains high levers the following important tests are bilirubin-protein and bilirubin-enzymal dissociation (a higher bilirubin level and lowering of prothrombin, fibrinogen and other protein-complexes, as well as an activity o hepato-cellular enzymes). In the acute degeneration case there may be a lethal outcome in 1–2 days (in spite of all medical treatment).

In 80–86 % of patients the disease course may be acute with complete normalization of clinic syndromes and recovery of hepatic functional state.

The protracted course is encountered in 10 % of children patients. This pathologic process is over in 6 months after its beginning (undulating, unremitting and persistent). The tests reveal a prolonged circulation of HBsAg and HBeAg in blood. There is a possibility of a chronic variant (in 3–5 % of cases) with the process duration over 6 months. Chronization sighs are a hepatolienal syndrome, jaundice, vascular “stars”, red palms (“hepatic palms”), nasal hemorrhages, petechial rash; in blood — findings there are higher levels

of ALT, AST, immunoglobulin, associated bilirubin, positive thymol test and lower prothrombin index. Chronic hepatitis may develop into cirrhosis.

The congenital VHB. There is a possiblility of a transplacental transmission of VHB from mother to child in the third trimester of pregnancy if the mother being ill or carrier of HB virus with high concentration of HBsAg and HBeAg. Congenital manifested hepatitis develops: there is no prodromal period; icterus appears from the first days of life; progressive jaundice, hepatic enlargement up to 4–5 cm; enlarged spleen, dark urine, hemorrhagic syndromes, weakness, biochemic changes of typical for acute hepatitis. The disease course is severe and can have a lethal outcome. Sometime the illness is manifested with HBs and HBe antigenemia accompanied with clinical features of hepatolienal syndrome and some hyperfermentemia.

Often, the baby gets infected during delivery. Clinical signs of hepatitis manifest themselves on the 2nd–3rd month of life, disease course is sever with a malignant form of development.

Diagnosis of the VHB is based on clinical features: gradual development with growing of intoxication, icterus, hepatosplenomegalia, hyperbilirubinemia (generally-owing to the associated fraction), stable increase of hepatocellular enzyme level, presence of parenteral procedures in life history, also as a result of specific examination: HBV-markers and antibodies against the general viral antigens. HbsAg is discovered long before its first clinical signs (before the 3rd–5th week of illness). With HbsAg in an acute period the HbeAg-antibodies are discovered and, late the HbsAg-antibodies (in the third month).

Differential diagnosis of VHB is conducted so as to differ it from VHA. The differential features are sick children older than 1 year, the incubation period not over 45 days, the onset is acute, jaundice period is short, VHB does not develop chronic forms one-year-olds sick with HBV have bile duct tracts atresia, the following signs: icterus appears on 2nd–4th week and later, it progressively increases, liver is gradually enlarged, common condition is not

aggravated in the first 1–2 months, the associated bilirubin fraction prevails in blood, hepatocellular fermental activity is normal. Toxic, toxoplasmal, cytomegaloviral, listeriosic hepatitis types have no prodromal period, they have presence of other symptoms (premature birth, hypotrophy, nervous system affection, etc.), lower activity of hepatocellulr enzymes. Carotene icterus has following signs: normal color of scleras, the more intensive jaundice on palms of the hands and feet, ears around the mouth and nose. General condition is not poor and hepatic functional tests are normal.

Treatment.

All patients with VHB must be hospitalized for adminestering complex therapy. Bed rest is prescribed till complete recovery. Diet similar to the one in VHA. But in severe forms having intoxication fasting days are introduced; one should have per day: sugar 5–10 g/kg, fruit up 50 g/kg, fluid to 500–1500 ml. Medication therapy: interferon is a more prospective treatment: reaferon and other recombinant gene engineering interferons are prescribed over 2.500.000–5.000.000 IV per day (three times per week) In fulminant forms, comatous patient, etc. the patients in come in the 1st year of life (especially if there is an unfavorable personal case history) predmizone is administered in doses of prednisolonum from 1 to 5 mg/kg body weight per day (4–6 times) during 7–10 days. If there is a malignant form, such patients should be hospitalized into the intensive care department. For 3–7 days protein food is forbidden. The energetic requirements are provided by carbohydrates use to (5–10 % glucose solution with a dropper), the plasma, albumen, rheopolyglucinum, 5–10 % solution of glucose to 100–150 ml/kg body weight per day are introduced i. v. by dropper method according to the age and diuresis.

Glucocorticoids (prednizone) are introduced 5–10 mg/kg body weight per day intravenously or intramuscularly every 3–4 hours without a break at night. The inhibitors of proteolysis — Trasylol, Gordox are obligatorily used in a doze

of 100.000–250.000 units per day, or Contrikal to 50.000 Un, cocarboxilase, AT hosphatas, ascorbic acid, Vicasol, Heparin (DIC-syndrome), 4 % solution of sodium hydrocarbonate (metabolic acidosis). In case of bacterial complication antibiotics are prescribed. To prevent absorption of toxic metabolites of the intestinal microflora gastric lavage bat and high irrigative enemas are used. Substitutive hemotransfusion, plasmapheresis, hemodialysis, hyperbaric oxigenation can be perferms. During treatment you should also examine of kidneys (with the use of diuretics), in mental excitement seduxen is prescribed or oxybutyrte of sodium. In case of necessity cardiac, vascular and other symptomatic drugs are prescribed, the edematica-ascitic syndrome is corrected. Hypoxia correction using intensive therapy measures has success in those patients. Successful trestment of such pftietn is closely connected with the quality of treatment and care.

The patients are discharged when they get their clinical recovery (satisfactory general condition, absence of icterus, decrease of liver) and normal functional tests (normal bilirubin level, lowering of transferase activity in blood serum, — it may be higher than normal but only two-three times!) on the 30–40th day of illness.

Prophylactic medical examination after — 1, 3, 6, 9 and 12 months. Children are freed of inoculations during 1 year, they do exercises in a special groups. It is possible to treat patients at health resorts and sanatoriums (for children having only residual signs of hepatitis).

Prophylaxis

1. Obligatory examination of donors for HBsAg detection.

2. Prohibition of hemotransfusions and blood preparations use which haven’t been marked for HBsAg.

3. Use of disposable instruments.

4. Educating of children in the sanitary culture level.

In centres of VHB a current and final disinfection is performed. Children, who were bort of mothers with acute and chronic hepatitis-B or carriers of the HBsAg, must be followed up after 2, 3, 6 and 12 months after their discharge from the hospital (clinical examination and laboratory testing for of transminase activity and markers in blood are done after and 6 months). For specific prophylaxis an immunoglobuhn with high anti-HBV antibodies titres are used for children who were born from mothers suffering of the VHB or the HBsAg — carriers. Active vaccination against hepatitis is conducted with rerombinant vaccine in 1, 2, 7 months for newborns with mothers — HBsAg-carriers.

Viral hepatitis C

Viral hepatitis C is an infectious disease, which is transmitted parenterally, and characterized by not severe course and frequent development of chronic forms with following transformation into hepatocirrhosis and hepatocarcinoma.

Etiology.

The disease is caused by hepatitis C virus (HCV), which contains RNA. Peculiarity of HCV is heterogeneity of its genome. This fact makes very difficult serologic diagnosis and elaboration of the vaccine.

Epidemiology.

The source of infection is an infected patient with acute or chronic form of viral hepatitis C. HCV may be transmitted from the mother to the fetus through the placenta. Susceptibility to the infection is general.

Pathogenesis.

Pathogenesis of viral hepatitis C is not discovered. Pathological changes in liver are like ones in other viral hepatitis.

Clinical features.

The incubation period of viral hepatitis C is approximately from 6 to 8 weeks. Preicteric phase is short. Its duration is 5–7 days in average. Clinical

manifestations of preicteric and icteric phase are like ones in mild form of viral hepatitis B. Biochemical changes are typical for all viral hepatitis. Thymol test is abnormally high. Fulminant forms do not occur. In spite of favorable course of the acute period of the disease, forming of chronic hepatitis C occurs in 20–50 % of the patients.

Diagnosis. Etiologic diagnosis is made due to laboratory tests. In acute phase of the disease the antibodies of IgM class and presence of RNA HCV in the patient's serum have a diagnostic importance. The tests for the total antibodies (anti-HCV) to the virus antigens become positive in 10–30 weeks from the onset of the disease. Pointed diagnostic method has most spreading in practical medicine.

Treatment is prescribed by general rules of treatment of viral hepatitis. The early therapy by high doses of recombinant leukocyte interferons (IFN-L) should be administrated because the chronic process may result (3 million units of IFN-L three times weekly for 6–12 months).

Prophylaxis is based on rejecting blood and blood preparations, containing HCV. The most spread method for that is determining anti-HCV and serum alanin aminotransferase (ALT) levels in donors. If even one of the tests is positive, blood or blood preparations will be rejected. Definition of RNA HCV in serum by PCR is a more reliable diagnostic method.

VI. Planning of the lesson

Table 2

	The main stages of the lesson, contents	**The methods of control**	**Methodical equipment**	**Time in % from total time of the lesson**
10-20 %				
1	Organizational			

	stage			
2	Purposes of the lesson		Relevance of the Theme. Tutorial goals of a lesson	2-5 min
3	Control of basic knowledge and skills	Control questions	The list of control questions	15-25 min
	1.Etiology, epidemiology, classification of disease	Test-control (first grade)	Tests of the first level	
	2. Manifestations in connection with pathogenesis	Methods of the second grade: Individual questioning in oral and written form. Standard task solution. Second grade test-control	Questions Clinical cases (tests of the second grade) Theory tasks for writing answers. Second grade tests	
	3. Treatment	Methods of the third grade: 1. Solution of complicated tasks. 2.Third grade test-control	Third grade questions and tasks Third grade tests	
	4. Prevention			
70-80 %				
1	Formation of	Method of formation:	Patients with studied	120-140

	professional skills	practical training	disease and similar diseases, patients' histories, medical cases.	min
	To master the skills of: a) Diagnosis b) Laboratory confirmation c) Treatment	Examination of the patients, distinguishing of the set of important signs and symptoms. Composing of a plan of laboratory confirmation. Administration of the treatment depending on the form and severity of disease.	Laboratory data of the patients, antibacterial drugs and drugs for supportive care	
	Independent work with patients	Examination of the patients with Measles, Scarlet fever and other infectious diseases with similar manifestations (differential diagnostics).	Patients, patient's histories, medical cases.	
	Differential diagnostics	Practical training	Drawing schemes of pathogenesis and clinical course of disease; making up a differential	

			diagnostics table and list of prescriptions for intensive care.	
10 %				
1	Teacher's control, recommendations, the task for the next lesson			10-15 min

Students' self-study program.

1. Objectives for students' self-studies.

You should prepare for the practical class using the available textbook and lectures. Special attention should be paid to the following:

Diagnostic markers for hepatitis B, C, D

Hepatitis B

Table 3

HBsAg	Acute hepatitis – in incubation period Chronic hepatitis – tell us that virus is in blood
Anti-HBs	Recovery after acute hepatitis, say us about acute hepatitis in a past; evaluation of the vaccine's effectiveness
HBcAg	tell us that virus present in a blood
Anti-HBc IgM	Typical for acute hepatitis; chronic hepatitis – tell us about activity of the process

Anti-HBc IgG	Typical for chronic hepatitis
HBeAg	Marker of replication, tell us about high risk of chronic process
Anti-HBe	Transforming replication phase into integration phase
DNA HBV	Replication phase

Hepatitis C

Table 4

HCV Ag	Acute hepatitis
Anti-HCV IgM	Acute or chronic hepatitis
Anti-HCV IgG	Screening for chronic hepatitis C
RNA HBV	Replication phase

Hepatitis D

Table 5

Co-infection – association with acute hepatitis B (positive lab. markers)	
HDVAg	Acute hepatitis usually 1-2 weeks
Anti-HDV IgM	Acute infection process (high concentration
RNA HDV	Replication phase

Superinfection - association with chronic hepatitis B (positive lab. markers)	
HDVAg	Short-term circulation
Anti-HDV IgM	Typical for acute phase
Anti-HBc IgG	Infection in a past
RNA HDV	Replication phase

Differential diagnostic acute hepatitis

Table 6

Crateria	**Hepatitis A**	**Hepatitis B**	**Hepatitis C**	**Hepatitis D**	**Hepatitis E**
Family	Picornaviridae	Hepadnaviridae	Flaviviridae	Subvirus, satelite	Hepeviridae
Genus	Hepatovirus	Orthohepadnavirus	Hepacivirus	Deltavirus	Hepevirus
Genome consist	RNA	DNA	RNA	RNA	RNA
Source of infection	Sick person at the beginning of dis.	Sick person with acute or chronic forms, carriers	Sick person with acute or chronic forms	Sick person with acute or chronic forms	Sick person at the beginning of dis.
Way of transmiss	Fecal-oral,	Parenteral	Parenteral	Parenteral	Fecal-

ion	artificial				oral
Season	Fall, winter	No	No	No	Fall, winter
Incubation period	7-50 days (usually 14-30)	30-180 days (usually 60-90)	21-140 days (usually 30-50)	Superinfection -21-50 days; Co-infections - 40-200 days	15-40 daus (usually 30-40 days)
Age	Children and young person	All age, esp. babys uder 1 y.o, older than 40	All age, esp. older than 40	All age, esp. babys uder 1 y.o, older than 40	No information
Typical prodromal; period	Dyspeptic, flu-like syndrome	Astenovegetative syndrome, arthralgia	Astenovegetative syndrome, arthralgia		Dyspeptic, flu-like syndrome
Severity	Mild and moderate	All forms	Mostly mild	Severe hepatitis B	Mild, moderate, severe forms typical for

					pregnant
Fulminant form	No	0,1-0,2%	No	No	Pregnant
Cholestasis form	Not typical, but in 3-5% of pregnant women it possible	Present	Not typical	Not typical	Pregnant
Hemolysis	-	-	-	-	Pregnant
Liver failure	-	-	-	-	Typical
Chronic disease	Not typical	5-10%	40-70%	Superinfection – 80-90% Co-infection – 5-10%	Not typical
Vaccination	Present	Present	No	Against hepatitis B	No

Main markers of viral hepatitis in a blood

Table 7

Marker	Hepatitis A	Acute hepatitis B	Chronic hepatitis B		Hepatitis D		Hepatitis C		Hepatitis E
			Replication	Integration	Co-infection	Superinfectio	Acute	Chronic	
Anti-HAV IgM	+								
HBsAg		+	+	+	+	+			
HBcAg		+	+	+/-	+	+			
HBeAg		+	+	-	+/-	+/-			
Anti-HBs		-	-	-	-	+/-			
AntiHBc-IgM		+	-/+	-	+	-			
AntiHBc-IgG		-	+	+	+	+			
Anti HBe		-	-	+	-	+/-			

HBV DNA		+	+	-/+	+	+			
HDV Ag					+/-	-/+			
AntiHDV-IgM					+	+/-			
AntiHDV-IgG					-	+			
HDV RNA					+	+			
HCV cor Ag							+	+	
AntiHCV-IgM							+	+/-	
AntiHCV-IgG							-/+	+	
HCV RNA							+	+	
Anti HEV									+

Tasks and assignments for self-assessment

1. A 6-year-old boy has been diagnosed as having mild form of viral hepatitis A. What is the most important in treatment?

A. Regimen and diet

B. Hepatoprotectors

C. Antiviral medications

D. Corucosteroides

E. Infusion therapy

2. 4-year-old child. Complaints are fever T- 39ºC, abdominal pains, vomiting. The 5th day: dark urine, skin and mucous are jaundiced. Tongue is covered with white coating. Liver is enlarged + 3,5 cm. Faeces are pale. Bilirubin 127 (mk/mol/L), direct - 86, indirect - 41. ALT - 1,8 mmol/L/h, prothrombine index – 78 %. What's the primary diagnosis.

A. **Viral hepatitis***

B. Obstructive jaundice

C. Toxic hepatitis

D. Haemolytic anaemia Minkovski-Shoffar

E. Leptospyrosis

3. 5 -year-old child. Complaints: T - 38,7º C, vomiting, abdominal pain. 3rd day of the disease: malaise, skin and mucosa are without pathology. Tongue has white coating. Pharynx is clear. Abdomen is soft. Liver is enlarged + 2,5 cm. Faeces and urine are with normal colour. Child got in touch with person sick with viral hepatitis A and Scarlet fever 2 weeks ago. What examination do you prefer to found out the right diagnosis?

A. **Blood on aminotranspherases**

B. Smear from pharynx on haemolytic streptococcus

C. Urine analysis on bile pigments and urobilin

D. Blood on paired serums

E. Blood on bilirubin and fractions

4. At the eldest group of the kinder garden in Kyev was a case of viral hepatitis A. 16 children didn't have hepatitis A before. What do you prefer to use to prevent the viral hepatitis?

A. **Immunoglobulin***

B. Vaccination

C. Interferon

D. Remantadin

5. Should the patient with mild form of hepatitis A be hospitalized?

A. Yes

B. No

6. A 3-month-old baby has been admitted with a low-grade fever, motor anxiety, anorexia, jaundice, hepatosplenomegaly, dark urine, discolored stool occurs. The baby had blood transfusion 2 month ago. What is the most probable diagnosis?

A. Viral hepatits B

B. Hemolytic anemia

C. Viral hepatitis A

D. Atresia of biliferous tructs

E. Conjugation jaundice

7. 2-year-old. Complaints: malaise, appetite loss. 5^{th} day – dark urine, pale stool. 6^{th} - jaundice of skin and sclera, T - 37,4º C, repeated vomiting. Liver enlarged + 7 cm, lien +2,5 cm. Heart sounds are muted, bradycardia. Child not active. Sleeping disturbances. Bilirubin - 220 mmol/L, direct - 176. Prothrombine - 60%. ALT - 6,4 IU. Found HBS Ag. In age 1,5

years child have had pneumonia, have got treatment in the hospital. What is the primary diagnosis:

A. **Viral hepatitis B***

B. Haemolytic anaemia

C. Viral hepatitis A

D. Toxic hepatitis

E. Obstructive jaundice

8. 4-year-old child. Complaints are fever T- 39ºC, abdominal pains, vomiting. The 5th day: dark urine, skin and mucous are jaundiced. Tongue is covered with white coating. Liver is enlarged + 3,5 cm. Faeces are pale. Bilirubin 127 (mk/mol/L), direct - 86, indirect - 41. ALT - 1,8 mmol/L/h, prothrombine index – 78 %. What's the primary diagnosis.

A**. Viral hepatitis**

B. Obstructive jaundice

C. Toxic hepatitis

D. Haemolytic anaemia Minkovski-Shoffar

E. Leptospyrosis

9. 10-month old child on the 5^{th} day of the disease have got vomiting, denied meals, became anxious, doesn't recognize parent, have got seizures, haemorrhagic rash, the jaundice appeared, the liver size became smaller, liver is soft on palpation. T- 37,5 - 39,9°C. What caused the worsening?

A. **Liver coma***

B. Encephalitis

C. Meningitis

D. Spasmophilia

E. Acute intestinal infection

10.The possible ways of transmission of viral hepatitis B?

a. Fecal-oral

b. Transmissive

c. Air-borne

d. Parenteral

e. Water

f. **mother to child transmission**

Tasks

Case 1

Girl 2 years old acutely developed mental confusion, emotional instability, restlessness, bleeding manifestation, vomiting, progressive jaundice and reduced size of liver on the 5th day after the onset of clinical manifestation of jaundice due to viral hepatitis. Level of total bilirubin 277 mmol, including direct fraction 194 mmol/L; indirect fraction 83 μmol/L; level of ALT 4 μmol/L; prothrombin index 48%, protein level in blood 45 g/L, albumin 55%.

What happened with this patient? What is the main aim of treatment? Interpret the laboratory tests results. Which outcome might be expected?

Case 2

A 10 year old child presents with malaise, weakness, discomfort in the right subcostal area. Examination showed hardening and increase of the liver size (3-4 cm below the right rib arch). Color of skin and sclera is not changed. Urine is yellow, feces are brown colour. Level of total bilirubin – 22mmol/L, ALT 4.6 μmo/L. One month ago cases of viral hepatitis A were registered in the child's class.

Which clinical form of hepatitis A should be diagnosed? How to confirm diagnosis? Why colour of urine and feces is normal?

Case 3

Examination of 11 year old boy showed no clinical signs and the following blood test results: anti HAV IgM - high level, ALT 3.4 μmol/L. WBC 5,600 x 10^9 with 6% B, 27% PMN, 64% LC, 3% M, ESR 8 mm/hr.

Your diagnosis? Which clinical form of disease is present? Which color of feces and urine is suspected in the patient and why?

Case 4

A 10-year old patient on 3rd day of disease is complaining of temperature increase to 39 C, sore throat during swallowing, hard breathing through a nose. On examination: face slightly edematous, markedly enlarged neck lymph nodes, increase in size of the liver and spleen (3 and 2 cm below the rib arches respectively). The pharynx is hyperemic. The glands are swollen and covered by a white coating.

What is the preliminary diagnosis? Which changes of WBC and differential are characteristic for this disease? What is the probable causative agent of this disease?

Main markers of viral hepatitis in a blood

Marker	Hepatitis A	Acute hepatitis B	Chronic hepatitis B		Hepatitis D		Hepatitis C		Hepatitis E
			Replication phase	Integration phase	Co-infection	Superinfection	Acute	Chronic	
Anti-HAV IgM									

HBsAg									
HBcAg									
HBeAg									
Anti-HBs									
AntiHBc-IgM									
AntiHBc-IgG									
Anti HBe									
HBV DNA									
HDV Ag									
AntiHDV-IgM									
AntiHDV-IgG									
HDV RNA									
HCV cor Ag									
AntiHCV-IgM									

AntiHCV -IgG									
HCV RNA									
Anti HEV									

Student's practical activities:

I. Curation of patients with acute gastrointestinal infections at the children infectious department.

1. Ask complaints, anamnesis and life history.
2. Examine the patients; find clinical features of acute infection, liver failure
3. Prescribe laboratory investigations to prove the diagnose.

II. To perform the diagnosis:

1. Make previous diagnose due to complaints, disease history, epidemiological anamnesis, clinical objective features.
2. Make complete diagnose due to previous diagnose, laboratory dates, differential diagnosis.

III Provide the treatment (diet, medicine) depending on patient's age, severity of the disease.

IV Prescribe measures in the focus of infection, prevention of the disease.

V Clinical analyzing of the case.

Students must know:

1. Etiology, pathogenesis of liver failure
2. Classification of intoxication with dehydration.
3. Diagnostic criterions of different types of liver failure.
4. Differential diagnosis of hepatitis viral and other etiology, jaundice, liver failure.

5. Prehospital and hospital treatment of intoxication with dehydration, prognosis and prophylaxis.

Student should be able to

1. Find diagnostic clinical criterions liver failure during examination of patients.
2. To perform differential diagnosis among diseases which have the same clinical features.
3. To perform prehospital and hospital treatment of children in case of hepatitis and liver failure
4. To prescribe measures in the focus of infection.

I

Aim: to know diagnostic criterions of HIV/AIDS in children, how to examine a patient with this disease, and prove the diagnosis, differentiate, give the individual treatment and prevention.

Professional motivation:

As of 2018, of the estimated nearly 38 million people worldwide living with HIV, approximately 1.7 million are children under 15 years of age. Since 2010, new HIV infections among children have declined by 41%, but only half (54%) of all children living with HIV are getting treatment and 100,000 children died of AIDS-related illnesses in 2018. About 500 children are newly infected with HIV every day**.**

More than 90 percent of HIV infections in children result from mother-to-child-transmission, where the virus is passed from a mother living with HIV to her baby during pregnancy, childbirth, or breastfeeding. The risk of this form of transmission increases in direct relation to the severity of the mother's HIV infection.

Basic level

5. To know how to ask complaints, history of the disease and life in children [propedeutic pediatrics].
6. To perform clinical examination of the child [propedeutic pediatrics]To know microbiology, pathophysiology, pathomorphology and clinical features of HIV/AIDS [Microbiology, pathophysiology, and pathomorphology, Pediatric infectious diseases].
7. To diagnose HIV/AIDS after clinical, laboratory and instrumental examination of sick

person [infection diseases, propedeutic pediatrics, microbiology, and pathophysiology].

8. To give etiological, pathogenetical and symptomatical treatment of HIV/AIDS [pharmacology].
9. To prevent diseases that may be complicated by HIV/AIDS.

II. Primary aims of the study

A student should know:

- Etiology and epidemiology of a AIDS/HIV infection; TORCH- infection in children
- Pathogenesis and pathological anatomy;
- Classification of a AIDS/HIV infection;
- The clinical characteristic of different kinds of a AIDS/HIV infection; TORCH- infection in children
- Laboratory methods of examination at AIDS/HIV infection; TORCH- infection in children
- Complications, which are observed at a AIDS/HIV infection; TORCH- infection in children
- Differential diagnostics of a AIDS/HIV infection; TORCH- infection in children
- Medical tactics;
- Preventive and antiepidemic measures in the locus.

A student should be able:

• to question a patient in order for obtaining of information on disease history and epidemiologic anamnesis;

• to perform clinical examination of a patient;

• to formulate and to substantiate the diagnosis of AIDS/HIV infection; TORCH- infection

• to prepare a plan of additional patient examination;

• to evaluate results of laboratory examination;

• to make differential diagnosis to distinguish between similar diseases;

• to prescribe adequate pathogen and etiotropic treatment.of AIDS/HIV infection; TORCH-infection

III. Educational aims of the study

- to conduct clinical examination of a AIDS/HIV infection patient and other acute intestinal diseases;
- to formulate and substantiate a clinical diagnosis;
- to prepare a plan of paraclinic patient examination;
- to take samples of material for virologic and other quick analysis methods examination;
- to evaluate results of paraclinic patient examination;
- to organize hospitalization and treatment of a AIDS/HIV infection patient; TORCH-infection
- to plan and organize prophylactic measures against AIDS/HIV infection ; TORCH- infection

IV. Interdisciplinary integration

Table 1

Subjects	***To Know***	***To Know How***
1	***2***	***3***
Human Anatomy	The main anatomic characteristics of system target systems.	
Physiology	*Functions of the respiratory, nervous and immune systems*	*To explain a variety of clinical signs and laboratory abnormalities*
Pathological Physiology	*Pathogenesis of disease*	*To explain the main symptoms and manifestations appearance, causes of relapses, failure of inadequate therapy*
Pathological Anatomy	*Pathology*	*To explain the pathogenesis of complications and causes of death*
Microbiology	Etiology (classification, morphologic characteristic of the pathogen, methods of revealing and identification)	To culture the organism
Pharmacology	*The main antiviral and antibacterial agents. Regimens of treatment. Treatment of complicated influenza. Supportive care*	*To write the scheme of treatment of severe HIV/AIDS.*

Histology	*Histological changes in different clinical forms of influenza*	*Explanation of appearance of clinical signs*

Continuing ***Table 1***

1	***2***	**3**
Propedeutics of Internal Diseases	*History of disease. Examination of a patient.*	*To gather information about patient's history and chief complaints, to distinguish the ones, most important for diagnosis of HIV/AIDS. To examine the patient, to reveal the main symptoms and signs of disease. To distinguish the set of diagnostic features of HIV/AIDS. To argue the diagnosis.*
Surgery	Chest pain, cough, respiratory failure	*Differential diagnostics of surgical disorders, diagnostics of complications*
Internal Diseases	Chest pain, cough, respiratory insufficiency	*To differentiate with other disorders of respiratory system*
Neurology	*Severe headache, vomiting, meningeal signs, delirium, altered*	*Differential diagnostics of encephalitis, meningitis, stroke*

	consciousness	
Clinical immunology and allergology	*Immunologic changes as a part of pathogenesis and host defenses*	*To explain confirmative serologic tests*
Epidemiology	*The routes of transmission, main sources of infection*	*Epidemiological history*
Themes integration		
Encephalitis, meningitis, common cold, ARVI, diphtheria, tonsillitis, intestinal infection.	To know peculiarities of manifestations, laboratory diagnostics, treatment	To differentiate HIV/AIDS from other infectious diseases with similar symptoms

V. The contents of the theme

Secondary immunodeficiency syndrom is caused by a virus and characterized by severe immune deficiency resulting in opportunistic infections, malignancies, and neurologic lesion in individuals without prior history of immulogic abnormality.

Etiology. The cause is a retrovirus that has been termed the human T-lymphotrophic virus Type III (HTLV-III), lymphadenopathy-associated virus (LAV), and the AIDS-associated retrovirus (ARV) by different laboratories. More recently, it has also been referred to as the human immunodeficiency virus (HIV), the term that will be used here.

Retroviruses are very small viruses composed of a single strong of RNA, the intermediate nucleic acid in the production of proteins. Normally, the flow genetic information starts with a piece of DNA, which makes a piece of RNA, which in turn codes for, protein. Everything flows in that direction.

Retroviruses contain an enzyme called reverse transcriptase that can convert viral RNA in the cytoplasm into DNA, which may replicate from extrachromosomal sites or move into the cell nucleus where it becomes part of the host cell DNA. These integrated viral genes are duplicated with normal cellular genes, and all progeny of the originally infected cell will contain the viral genes. Expression of the viral genes for some retroviruses may be oncogenic, converting the cell into a cancer, or may have other pathologic effects which may alter normal cell function or produce cell death. Retroviruses have been known to cause malignant and nonmalignant diseases, and the same virus may cause different diseases in different animals; e.g., bovine leukemia virus causes a B cell lymphoma in cows, a T cell lymphoma in sheep, and an immunodeficiency disorder similar to AIDS in rabbits.

There are 3 groups of retroviruses that affect humans, and all have a remarkable affinity for lymphocytes, particularly for T4 lymphocytes. HIV preferentially infects the major subset of T-cells, defined phenotypically as T4 and functionally as "inducer/helper" cells, which are then depleted, resulting in a reduced ratio of T4 helper (Th) to T8 suppressor (Ts) cells. However, the virus also is capable of infecting some nonlymphoid cells, such as macrophages and nervous tissue cells, and presumably remains present for life.

Epidemiology. The major transmission routes of human immunodifficiency virus are sexual contact, parenteral exposure to blood and blood products and perinatal transmission. Early in the AIDS epidemic, epidemiological studies establish that receptive rectal intercourse was the predominant mode of HIV-1 acquisition by homosexual man. Other practices that could traumatize the rectal mucosa appeared to increase further the infection risk for the receptive partner. Insertive rectal sex could also place a men at risk for HIV-1 infection, although the insertive partner would be at lower risk than the receptive partner.

On a world-wide basis sex between man and women apparently is the most common mode of acquiring HIV-1 infection heterosexual transmission accounts for the vast majority of cases. In other country where AIDS cases attributed to heterosexual transmission, although still a small percentage of the total number of reported cases comprise the most rapidly growing category. Therefore an understanding of the rate at which HIV-1 is transmitted between heterosexual couples and of the factors that may impede or enhance heterosexual transmission is important in slowing the worldwide HIV-1 epidemic.

In the country, where HIV-1 infection is more common in men than women, studies of female-to-male transmission of HIV-1 infection are both fewer and smaller than studies of male-to-female transmission. Available date suggest female-to-male transmission may be less efficient than male-to-female transmission.

Overall these American and European studies suggest that heterosuxual transmission from HIV-infected persons to their regular sex partner is relatively-inefficient, especially female-to-male transmission. Furthermore, the risk of heterosexual transmission is not related simply to the number of episodes of sex with HIV-infected person because some people have remained uninfected after hundreds of such contacts whereas others have become infected after a single episode of intercourse.

Infectivity may be higher during early infection before the development of antibodies to HIV-1, also genital ulcer diseases and inflammation of the genital tract lead to increased susceptibility to HIV infection.

Perinatal or vertical transmission. Mother-to-infant transmission of HIV apparently is relatively efficient; without treatment approximately one in the Sour infants born to seropositive

mothers is infected. With one rapid spread of infection to women of reproductive age perinatal transmission is now a major consequence of HIV epidemic. The precise rate of perinatal transmission in a given setting has been difficult to define because of problems in the infant and the difficulties in maintaining long-term follow-up. Uninfected children born to seropositive mothers may retain passively aquired maternal antibody for 6 to 18 months.

The timing mechanisms, and risk factors for perinatal transmission might occur and guiding the development of effective interventions. These factors include maternal stage of disease maternal antibody response to infection, viral titer, variations in viral genotype and phenotype, and obstetric factors such as preterm birth, mode of delivery, and maternal or placental coinfection. Perinatal HIV transmission can occur both in utero or at birth. Several lines of evidence support the occurrence of human placenta tissue express CD4 receptors and are suseptible to HIV infection. Virus has been isolated from amniotic fluid and has been identified in fetal abortus tissue by culture, PCR and in situ hybridization. However, other investigators have not found HIV in fetal tissue and it is difficult to exclude contamination of these tissues by maternal blood. Clinically, the fact that subsets of infected infants have detectable virus at birth immunologic abnormalities in the neonatal period and rapid progression to AIDS in the first Sour months of life suggest in the utero transmission. The proportion of infants actually infected in utero and the time during gestation when this is most likely to occur, however, are not known.

Intraportum transmission, analogous to the vertical transmission of hepatitis B, likely occurs through direct contact with maternal blood secretions as the infant is delivered through the birth canal. HIV has been isolated from cervical secretions. Also the virus might be able to pass directly through maternal-fetal

transfusions, particularly during placental separation at birth. The fact that many infected children are born without detectable virus or immunologic abnormalities supports the likelihood that delivery represents a high risk for HIV transmission. Interestingly there has not been strong evidence that that delivery by caesarean section is protective. However, a recent report based on an international twin registry suggests that being the first of two twins delivered and vaginal delivery are risk factors for infection in twin births. This hypothesis and its relevance for singleton births warrant further study. Although it has not been shown that intrapartum fetal

scalp monitoring facilitates transmission, avoiding invasive of the fetus whenever possible, seem prudent.

Postpartum perinatal transmission of HIV through breast-feeding has been reported. Free virus has been found in the cellfree fraction of breast milk and might directly penetrate the infant's gastrointestinal mucosa. However, data from several cohort studies suggest that the additional risk of postpartum transmission is low in pregnant mother already infected with HIV. These finding may result from low viral titers in breast milk of previously infected women, concomitant IgA antibody or some other factor.

Extensive laboratory research and epidemiological studies indicate that HIV is not transmitted by shaking hands, hugging, kissing, contacting bodily secretion such as sweat, mucus (as in sneezing or coughing) or salive. Nor is HIV transmitted by food, swimming at a pools, drinking at a water fountain and also bloodsucking mosquitoes or other arthropods.

Pathogenesis. Following infection across a genital surface, involving infection of CD-4 bearing cells in the mucosa or submucosa, the virus presumably migrates to a regional lymph node, where viral replications occurs. A number of rounds of viral replication than occur within the bounds of the regional lymph node as no detectable virus or immune respons occurs for up to 42 days post infection. When the quantity of infected cells exceeds a threshold,viremia occurs,and the symptoms of an acute non-specific viral illness with tende adenopathy, sore troath, diffuse macular rush, arthralgia and fever. Following the acute viremia, when up to 10^7 viral particles/mL plasma can be found, a primary immune response develops with antibodies to viral proteins and a cytotoxic T-cells response, which limit viral replication and clear viral particles from the plasma. The reduction the viral load in plasma is not matched by a clearance of provirus in peripheral blood mononuclear cells, and cellular viremia continues in the face persistent and sustained cellular and humoral immune response for the duration of the infection. Even while plasma viral load is suppressed by the immune response, CD-4 T-lymphocyte number foil in linear manner over time. The most plausible explanation for the pathogenesis of AIDS over time is the sustained less CD-4 cells by ongoing HIV viral replication in nature peripheral blood T-cells and by a slight failure of production of match peripheral destruction of HIV CD-4 cells. However, recent controversy over the pathogenic mechanisms and homestasis

of T-cells has revealed that simple viral cytopathic effect on CD-4 cells may be overly simplistic model.

During the course of HIV infection, CD-4 cells continue to decline in peripheral blood and plasma viral load slowly rises. Over a definite period CD-4 cells number declines from 800 to 200 mL; at this level, the probability of the cellular immune system containing latent or environmental infections such as *P. carinii* falls and clinical opportunist infection becomes* increasingly possible. As the viral 1 retrovirus load rises. HIV isolates with altered co-receptor usage appear which can use the CXCR-4 chemocine receptor rather than CCR-5; these isolates are more cytopathic in vitro, and may lead to wider tissue distribution of HIV in later disease, AIDS is therefore, the clinical condition of an immune system which is sufficiently compromised by HIV infection that there is an inability to protect against the growth of low grade pathogenes or viral indeced tumors.

The fact that this virus, after infection of the host, besides destroyed strong immune system also can spread to many body tissues. The ultimate outcode of the infection depends on the host's immune reaction to the virus either through suppression of HIV replicationor through killing of the infected cell. In some individuals an active immune system has prevented development of the disease for years. The factors important in maintaining this immune response are not yet know and merit close attention. The immune deficiency produced by HIV infection makes patients suseptible to infection by a variety of organisms, including viryses, bacteria, fungi and parasites that are of low pathogenecity in the normal individual and of variable prevalence in different part of the world. In some individuals the immune system appears to make enhancing antibodies to HIV and this phenomenon occurs particularly with progression of disease. It is related to change to antibodies made and in some cases to modifications in the virus so that is more sensitive to enhancing antibodies. Moreover, the immune system can hyperreact, with production of antibodies that might also hasten the development of disease. Clearly changes in the virus and the immune response of the host play important roles in the ultimate steps leading to AIDS.

Anatomic pathology. Forty to sixty percent of AIDS patients develop neurologic dysfunction and up to 90 % have neuropathologic changes at autopsy. HIV itself can cause brain disease manifested as meningoencephalitis, mild cognitive dysfunction, or frank dementia. It is

felt that the pathogenesis of this neurologic damage is related to the presence of infected tissue macrophages that may release viral proteins or cytokines that result in brain dysfunction, inflammation, and tissue destruction. In this regard, studies of brain tissue from AIDS patients have shown that the predominant cell type infected with HIV is the monocyte/macrophages (M/M).

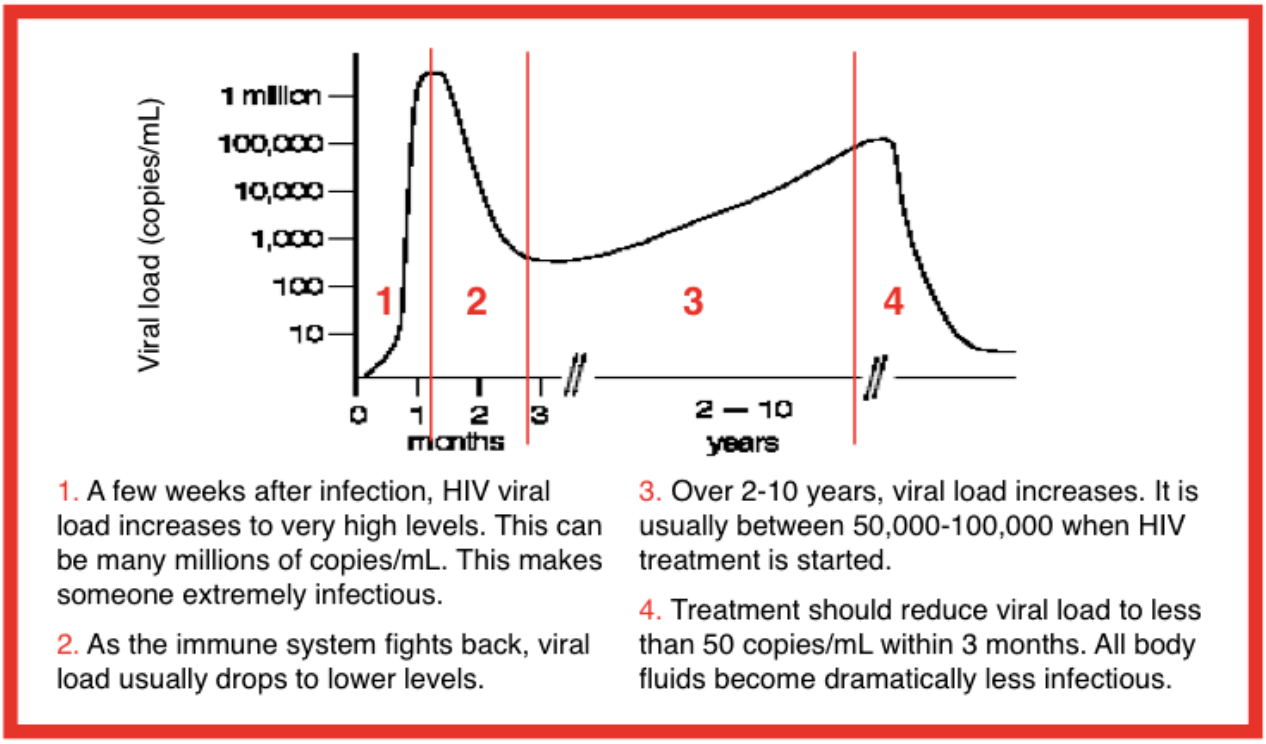
Infected M/M may release factors resulting in reactive glial cell growth, and, because glial cells have been shown to be infectable with HIV in vitro, infected brain M/M may provide a source of infectious HIV to these glial cells. The HIV envelope protein can inhibit neuronal growth in vitro; this may be due to competition between neuroleukin and gpl20 for binding to the neuroleukin receptor, because there is partial sequence homology between these two proteins. It is possible, but not yet demonstrated, that infected M/M in the brain may release large quantities of gpl20 resulting in the inhibition of neuronal growth.

A wide variety of hematologic abnormalities occur in HIV-infected individuals including pancytopenia and myelodysplasia. Although the etiology of these multiple abnormalities has not been completely delineated, it has been shown that the CD34+ bone marrow myeloid progenitor cell can be infected with HIV in vitro with the resultant production of large amounts of predominantly intracellular virus and minimal cytopathic effects. More recently, CD34+ cells isolated from the bone marrow of some infected individuals have been shown to be infected with HIV. Whether these precursor cells produce large amounts of virus in the bone marrow in vivo and the potential contribution of these cells to the hematologic abnormalities observed are currently unknown. Infected macrophages within the bone marrow have been reported to produce factors, presumably cytokines, which appear to suppress hema-topoiesis through their effects on the CD34 + precursor cell. Whether bone marrow macrophages are an important reservoir of HIV has not been definitively determined.

Finally, cells of the monocytic lineage that populate other organs are susceptible to infection with HIV and may contribute to pathogenesis of disease at these sites. Specifically, lung alveolar macrophages, Kopffer cells of the liver, and peritoneal macrophages are infectable in vitro with HIV, and alveolar macrophages from HIV-infected individuals are clearly infected in vivo. It is

currently unknown whether these cells contribute to tissue-specific disease, such as the diffuse pulmonary fibrosis that occurs frequently in pediatric AIDS patients.

Fig. 1. Clinical manifestations.



The symptoms vary depending on the age of the child. The following are the most common symptoms of HIV infection. However, each infant, child, or adolescent may experience symptoms differently. Symptoms may include:

- **Infants.** HIV status may be difficult to determine in the first year of like, so repeated tests may be done. Symptoms may include:

- **Failure to thrive.** Delayed physical and developmental growth as evidenced by poor weight gain and bone growth.
- **Swollen abdomen.** This is due to swelling of the liver and spleen.
- **Swollen lymph nodes**
- **Intermittent diarrhea.** Diarrhea that may come and go.
- **Pneumonia**
- **Oral thrush.** A fungal infection in the mouth that is characterized by white patches on the cheeks and tongue. These lesions may be painful to the infant.

- **Children.** Symptoms seen in children older than 1 year of age can be divided into three different categories, from mild to severe. They may include the above symptoms, but may also include the following:

Mild	Moderate	Severe
Swollen lymph nodes	Pneumonitis--swelling and inflammation of lung tissue	Two serious bacterial infections in a two-year period (meningitis, blood infection, or pneumonia)
Swelling of the parotid gland (salivary glands located in front of the ear)	Oral thrush that lasts for more than two months	A yeast infection that occurs in the digestive track or lungs
Constant or recurring sinus infections	Constant or recurring diarrhea	Encephalopathy--an inflammation of the brain
Constant or recurring ear infections	A fever that persists for more than one month	Tumors or malignant lesions
Dermatitis--an itchy, rash on the skin	Hepatitis--an inflammation of the liver that is often caused by an infection	Pneumocystis jiroveci pneumonia (the type of pneumonia most commonly seen with HIV)
Abdominal swelling from increased liver and spleen size	Complicated chickenpox	
	Kidney disease	

- **Adolescents.** Symptoms of HIV in teens may be the same as in children, and may also be more similar to the symptoms commonly seen in adults with HIV. Some teens and adults may develop a flu-like illness within a month or two after exposure to the HIV virus, although, many people do not develop any symptoms at all when they first become infected. In addition, the symptoms that do appear, which usually disappear within a week to a month, are often mistaken for those of another viral infection. Symptoms may include:

- Fever
- Headache
- Malaise (not feeling well)
- Enlarged lymph nodes

Persistent or severe symptoms may not surface for 10 years or more, after HIV infection first enters the body in teens and adults. This "asymptomatic" period of the infection is highly variable from person to person. But, during the asymptomatic period, HIV is actively infecting and killing cells of the immune system. Its most obvious effect is a decline in the blood levels of CD4+ cells (also called T4 cells)--the immune system's key infection fighters. The virus initially disables or destroys these cells without causing symptoms.

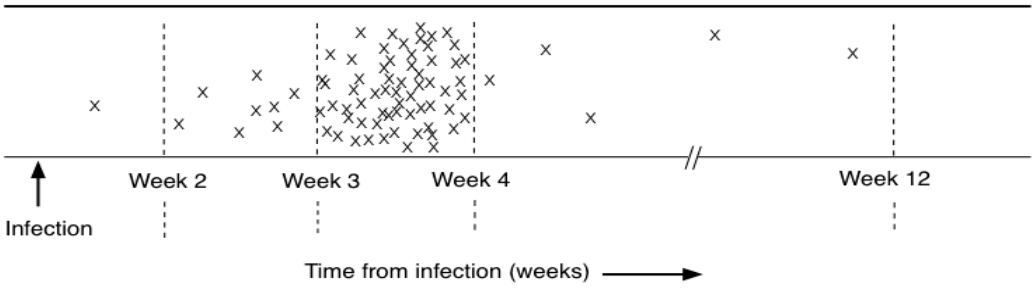
An HIV-infected child is usually diagnosed with AIDS when the immune system becomes severely damaged or other types of infections occur. As the immune system deteriorates, complications begin to develop. The following are some common complications, or symptoms, of the onset of AIDS. However, each child may experience symptoms differently. Symptoms may include:

- Lymph nodes that remain enlarged for more than three months
- Lack of energy
- Weight loss
- Frequent fevers and sweats
- Persistent or frequent yeast infections (oral or vaginal)
- Persistent skin rashes or flaky skin
- Pelvic inflammatory disease that does not respond to treatment
- Short-term memory loss
- Severe or unusual infections (opportunistic infections)

Some people develop frequent and severe herpes infections that cause mouth, genital, or anal sores, or a reactivation of chickenpox known as shingles.

The symptoms of an HIV infection may resemble other medical conditions. Always consult your child's doctor for a diagnosis.

Diagnosis. Fig. 2. Time to develop antibodies: 95% people do this by week 4 and more than 99.9% by week 12



Each 'x' represents the time when a different person develops HIV antibodies. Testing is only useful when the majority of infections would be detected. Testing after 2 or 3 weeks is not very useful.

Fig. 3. Timeline for HIV infection, immune responses and window period for tests

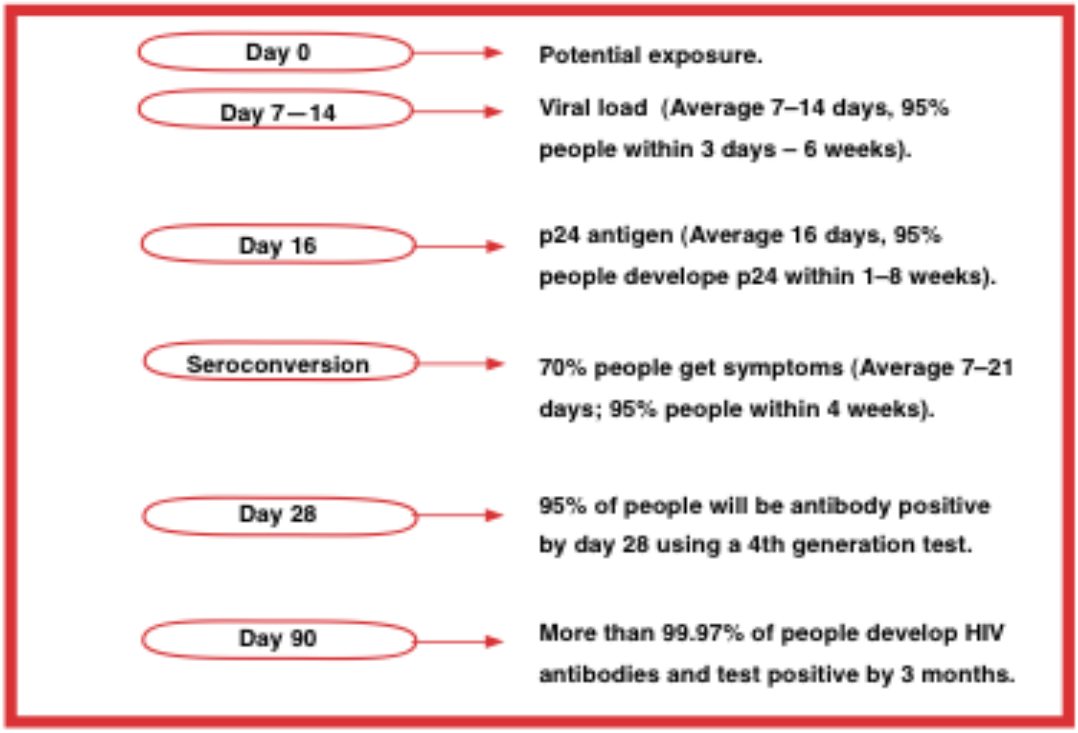


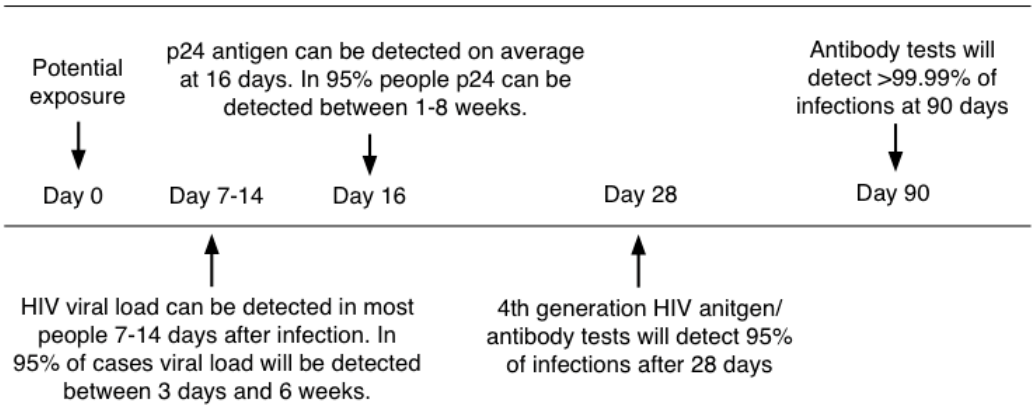
Figure 2 shows the range of times that people can take to respond to HIV infection.

- The earliest marker is HIV viral load. This is in the first weeks after infection (usually from 1 to 6 weeks after exposure). A high viral load is related to seroconversion symptoms.
- The first HIV protein (antigen) that can be measured is p24 (from 1 to 8 weeks after exposure).
- Viral load and p24 tests are not accurate for diagnosing early HIV if the results are negative.
- An HIV antibody response can be detected as early as two weeks in a few people and in more than 99.9% of people by 12 weeks. An antibody test at 4 weeks will detect 95% of infections.
- Antibody testing at 4 weeks can give you a good indication of your HIV status, but you need a test at 12 weeks after the exposure to be considered HIV negative.

Fig. 4. Different types of HIV test

Type of test	What the test look for?		
	RNA/ DNA *	Anti-gen	Anti-body
PCR/viral load	●		
p24 only test (Ag)		●	
4th generation antigen/antibody (Ag/Ab) tests (p24+ ELISA, ELI, MEIA/ ELFA/ECLIA): includes Architect, Duo, Combo/Combi etc		●	●
1st/2nd/3rd generation antigen only tests (ELISA, ELI, MEIA/ELFA/ ECLIA): includes TriDot etc			●
Rapid tests: finger prick and oral swab test are antibody only: includes OraQuick.			●
Western blot tests look for antibodies to specific HIV proteins. They confirm a positive HIV antibody test result.			●
* Viral genetic material			

Fig. 5. Average time after exposure to detect HIV antigens and antibodies



The pool of human lymphocytes possesses specific glycoproteins of their surface that play an important role in the cells activity and function CD-4 positive lymphocytes are the primary target of HIV infection, and the CD-4 receptor is the primary binding site of HIV. Throughout the course of chronic HIV infection the number of CD-4 lymphocytes is depleted and the loss of these cells is associated with development of the characteristic opportunistic infection and malignancies of AIDS. Thus the measurement of CD-4 positive lymphocytes is one of the most impotent determinates for clinically staging the disease status of HIV infected patients. In

uninfected controls normal values for the CD-4/CD-8 ratio are 2.0 to 1.0. Normal values for CD-4 counts are generally 500 to 1,000 cells/mL^3 in adults.

Differential diagnosis. The differential diagnosis of the acute retroviral syndrome includes a number of other illnesses: infectious mononucleosis; other viral infections such as influenza, measles, rubella, and herpes simplex; and secondary syphilis. Evaluation of patients presenting with an illness consistent with acute retroviral infection should include a careful history to elicit risks for HIV infection, laboratory tests to rule out mononucleosis and syphilis, HIV antibody and antigen tests, and complete blood counts and differential. Sequential HIV antibody tests may need to be performed over several months to confirm the diagnosis.

The differential diagnosis of persistent generalized lymphadenopathy (PGL) includes HIV infection and a wide variety of other processes that are associated with generalized lymphadenopathy: sarcoid, secondary syphilis, and Hodgkin's disease, for example. In patients with HIV infection, lymphadenopathy may also be caused by mycobacterial infections, KS, and lymphoma. In patients with clinical findings suggesting opportunistic disease, needle aspiration of lymph nodes may help establish a specific diagnosis. Examination of aspirates with cytologic, acid-fast, and Gram stains is valuable in identifying infection or malignancy. If a specific diagnosis is not determined after staining and culture of node aspirates, then lymph node biopsy is indicated. Aspiration of lymph nodes in patients with PGL usually reveals benign cells. Biopsy specimens show follicular hyperplasia, with the normal architecture distorted by greatly expanded germinal centers composed of B lymphocytes. It is now known that active viral replication is occurring in these follicular cells and dendritic cells, although the patient may appear well clinically.Most patients with PGL require no invasive evaluation and can be managed expectantly for the occurrence of other AIDS-related manifestations.

A limited differential diagnosis of isolated thrombocytopenia in an HIV-infected person includes drug-induced thrombocytopenia, particularly in heroin addicts and alcoholics, consumptive thrombocytopenia, or splenic sequestration. Some patients with thrombocytopenia may also present with leukopenia or anemia. The presence of constitutional symptoms and pancytopenia suggests an opportunistic infection, particularly disseminated mycobacterial or fungal infection, or a lymphoma.

Treatment. Basic therapy consists of indication of antiviral agents. There are used preparations, that inhibit the return transcriptasa of the virus: azydotymidin (AzT), didanosin (ddi), zalcytobyn (ddc), stavodin (d4T), lamivudin, abacavir (ABC), nevirapapin (NVP).

Till now monotherapy AZT (retrovir, zidovudin) was used. The preparations are prescribed 0.2 gm 3 times per day constantly or courses, duration is not less than 3 months. Treatment will be carried out under the control of the general blood analysis with 2 times per one month during the first 2 months and subsequently once per month. In a stage of preAIDS (secondary diseases) AZT is necessary to indicate till disappearance of a clinical symptomatology. If the clinical picture is not better zidovudin is indicated only for that patient in which blood concentration are less than 500 cells in 1 mkL. With such treatment it is possible to prolong patients life, the number of resistant viruses to a preparation however is marked. So, monotherapy AZT is recommended only for prophylaxis of infection of fetus from mother.

Among new means with other mechanism of action a specific inhibitor of proteases krixivan is used, which is effective concerning resistant to AZT populations of a virus 0.8 gm every 8 hour. Preparations of a choice may be rotonavir, nelfinavir, sacvinar-SGC, amprenavir.

Recently it is proved, that efficiency of treatment essentially can be increased using a combination of two or three antiviral preparations. Therefore monotherapy was changed for polytherapy. The most frequently combination of two inhibitors of virus return transcriptasa (stavudin + didanosin, stavudin + lamivudin, zidovudin+didanosin, zidovudin + lamivudin, zidovudin+abacavir) and one inhibitor of a protease is used. At patients with high risk of disease progress (viraemia over 1 million copies/mL), and also in urgent cases the two inhibitors of proteases and 1-2 inhibitors of virus return transcriptasa are used.

Efficiency of specific treatment is controlled by monitoring with following criteria: 1) level HIV RNA in plasma; 2) quantity of T-lymphocytes CD4; 3) a clinical condition of the patient; 4) morphology and biochemistry of a blood (for detection of undersirable effects of an organism). Level HIV RNA in plasma is researched after 4-8 and 12-16 weeks from the beginning of treatment and subsequently each 3-4 months. The major condition of successful antiretrovirus therapy is its usage during all life of the patient, however it is interfered by a high toxicity of preparations and the complications connected with them. Complete treatment of patients with

AIDS remains an unsolved problem. Last combination is considered the most effective, but also it does not cure patients with AIDS.

It is not less important preventive treatment of secondary diseases at AIDS. Against pneumocystic pneumonias the basic agent is bactrim. For initial prophylaxis of this disease bactrim is indicated 1 tablet during 3 days each week. At occurrence of pneumonia daily reception of preparation is prescribed. In case of an intolerance of bactrim it is possible to indicate dapsone or primachin in a combination with clindamicin. At presence of herpetic infections indicate acyclovir.

Against criptococus and other funguses amphotericinum is used, against bacteria - the appropriate antibiotic. At Kaposi's sarcoma freezing of eruption elements by liquid nitrogen, irradiation, chemotherapy is indicated. The immunotherapy of AIDS is at developing stage.

Prophylaxis. The most effective method for preventing mother-to-child transmission (PMTCT) of HIV is by initiating HIV-positive pregnant women on antiretroviral therapy (ART) as early as possible. ART decreases viral levels in the mother’s bloodstream, thus reducing the risk that she will transmit the infection to her infant. ART should also be administered to a child before and after birth; treatment will help a baby’s body resist infection.

Globally, an estimated 82% of pregnant or breastfeeding women living with HIV were receiving antiretroviral medicines to prevent transmission of HIV to their children in 2018.

Planning of the lesson

Table 5

n/n	The main stages of a lesson, their contents	The methods of control	Methodical equipment	Time in % from total time of a lesson
1	**2**	**3**	**4**	**5**
				10-20 %
1	Organization stage			
2	Purposes of a lesson		Relevance of the Theme. Tutorial goals of a lesson	1-3min
3	Basic knowledge and skills control	Control questions	The list of control questions	10-15 min
	1.Etiology, epidemiology, classification of disease	Test-control (first grade)	Tests of the first level	
	2. Manifestations in connection with pathogenesis	Methods of the second grade: Individual questioning in oral and writing form. Standard task's solution. Second grade test-control	Questions Clinical cases (tests of the second grade) Theory tasks for writing answers. Second grade tests	
	3. Treatment	Methods of the third grade: 1. Solution of complicated tasks. 2.Third grade test-control	Third grade questions and tasks Third grade tests	
	4. Prevention			

Continuing **Table 5**

1	2	3	4	5
				70-80 %
1	Professional skills formation	Patients with studied disease and similar diseases, patient's histories, medical cases.		
	To master the skills of: a) Diagnosis b)Laboratory confirmation c) Treatment	Laboratory data of the patients, antibacterial drugs and drugs for supportive care		
	Independent work with patients	Patients, patient's histories, medical cases.		
	Differential diagnosis	Drawing schemes of pathogenesis and clinical course of disease; making up a differential diagnosis table and list of prescriptions for intensive care.		
				10 %
	Teacher's control, recommendations, the task for the next lesson		10-15 min	

Tasks and assignments for self-assessment

Questions for self-control:

1. Infectious agent of AIDS, its biological properties.
2. Epidemiology of AIDS, contingents of the promoted risk of AIDS infection.
3. Mechanisms and ways of contamination.
4. Pathogenesis of AIDS.
5. Basic periods of AIDS development, their clinical symptoms.
6. Manifestation of AIDS in children.
7. Epidemiological and clinical criteria of diagnosis.
8. Laboratory diagnosis.
9. Principles of medical treatment.
10. Prophylaxis of AIDS.

Tests for self-control:

1. Criteria for classification of HIV infection by WHO, approved by the Ministry of Health of Ukraine (2006) for use in our country:

   A. clinical manifestations
   B. viral load in the blood
   C. the number of CD4 lymphocytes in the blood
   D. G. duration of the disease more than 5 years
   E. All of the above are correct except for item G.

2. HIV positive is dangerous as a source of infection:

   A. from the first day after infection
   B. a few weeks after infection and throughout life
   C. only during the clinical manifestation of the disease
   D. throughout life after a period of acute HIV infection.
   E. only in the chronic phase of the disease

3. The clinical signs of HIV infection are:

   A. fungal lesions of the tonsils
   B. causative diarrhea within 2 weeks
   C. micropoliadenopathy for 3 weeks

D. persistent fever for 1 month or longer

E. all answers are correct

4. The leading factors for HIV infection are:

A. Blood transfusion and its preparations

B. Kisses

C. Sex, including homosexuality in men

D. fecal-oral in the presence of relevant HIV-associated infectious diseases

E. Transmissive, especially in Africa

5. Etiotropic treatment of HIV infection is carried out by:

A. antiretroviral monotherapy:

B. antiretroviral therapy with several drugs

C. combined antibiotic therapy with a wide range of drugs

A. D, sulmetoprim in combination with immunomodulators

D. a combination of 2 antiretroviral agents with laser blood irradiation.

6. Complaints of the patient with pneumocystis pneumonia:

A. chills with fever, weakness. Dry cough, shortness of breath

B. cough with a large amount of serous purulent sputum

C. complaints are absent in the majority of patients

D. cough in the absence of radiological changes

E. cough with bloody sputum

7. The acute stage of HIV infection is most often manifested by:

A. generalized form of candidiasis

B. mononucleoside syndrome

C. Cachexia

D. total immunodeficiency

E. diarrhea

8. AIDS-related infections include:

A. recurrent erysipelas

B. typhus

A. C.Malaria

C. disseminated histoplasmosis

D. pneumoconiosis

9. Source of the causative agent of HIV infection:

A. Rodents

B. Wild animals

C. Pets

D. Man

A. E.Human monkeys

10. HIV infection is:

A. Anthroponosis, the sensitivity of the human body to this disease depends on race

B. zoanthroponosis, 100% sensitivity of the human body to this disease

C. anthroponosis, sensitivity depends on the presence of a mutation of the gene CCR5

D. anthroponosis, sensitivity depends on the antigens of the histocompatibility complex HLA

E. zooanthroponosis, the most sensitive are black people

Test answers

1	2	3	4	5	6	7	8	9	10
E	B	D	C	B	A	B	D	D	B

TASK 1

Patient T, 10 years old was admitted to the infectious hospital with complaints of fever to 37.3 C for 2 months, a general weakness. Over the last 6 months weight loss by 7kg.

Objective status: Normal skin, palpable small peripheral lymph nodes. Pulse 84 beats / min, rhythmic, blood pressure 110/70 mm Hg Heart tones are muted, vesicular breathing is above the lungs. The abdomen is a soft, painless, hepatolyenial syndrome. Dysuric disorders were not detected. There is no meningeal syndrome. In the general analysis of blood: leukocytes - $3{,}2x10^9$/L.

What is the most likely diagnosis? Which laboratory tests for diagnosis are informative?

TASK 2

Patient K, 14 years old, was admitted to the infectious hospital with complaints of fever up to 38 C, general weakness, pain in the rectum, rare faeces 4-5 times a day with a mixture of

mucus and blood, some hoarseness of voice. Over the past 6 months, weight loss of 11 kg, and diarrhea, pain in the rectum and fever lasted more than 2 months.

In the objective status, attention was paid to micropoliadenopathy, white gentle plaques in the oropharynx, hepatolyenial syndrome. In EGFD: candidiasis esophagitis.

Rectromanoscopy: on the background of minor hyperemia of the mucous membrane of the lower third of the rectum ulcers up to 0.5 cm in diameter. In the general blood test - leukopenia, lymphopenia.

What is the most likely diagnosis? Which laboratory tests for diagnosis are informative?

TASK 3

Having a 28-year-old woman suffering from HIV. There were no women's consultations at the dispensary. There was no specific therapy during pregnancy. Pregnancy and childbirth passed without complications. She gave birth to a baby weighing 3.2 kg without signs of pathology.

What is the doctor's tactics for the patient and her child? What is a child screening plan? What is the child's treatment plan?

Aids and material tools: Charts “HIV”, “AIDS”, “HIV/AIDS

Student’s practical activities:

I. To perform the diagnosis:

1. Ask complaints, anamnesis and life history.
2. Examine the patients, find clinical features of disease
3. Make diagnose due to clinical and laboratory dates.

II Provide the treatment of HIV/AIDS and prevention of diseases that may be complicated by croup syndrome.

Students must know :

1. Etiology, epidemiology and pathogenesis of HIV/AIDS.
2. Clinical diagnostic features of HIV/AIDS.
3. Laboratory data in patient with HIV/AIDS.
4. Differential diagnosis of HIV/AIDS in children.
5. Main treatment of HIV/AIDS.
6. Prevention of HIV/AIDS.

Student should be able to

1. Separate anamnesis data, which told us about risk factors of HIV/AIDS.
2. Find diagnostic clinical criterions of HIV/AIDS during examination of patients.
3. To perform differential diagnosis among diseases which have the same clinical features.
4. To learn main tendentions of the HIV/AIDS treatment.
5. To perform prevention of HIV/AIDS.

References:

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Planning of the lesson

Table 1

References:

5. Kramarev B. B. Pediatric infectious diseases / B. B. Kramarev, O. B. Nadraga. – Kyiv, 2015. – 238 c.
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