MINISTRY OF HEALTH OF UKRAINE
ODESSA NATIONAL MEDICAL UNIVERSITY
Faculty of Medicine
Department of infectious diseases

APPROVED
Vice rector on scientific and pedagogical work
_____ Eduard BURLACHKIVSKYI
01.09.2024

STUDENT'S GUIDELINES FOR SELF-INDIVIDUAL WORK ON STUDY DISCIPLINE

International faculty, course 4
Infectious diseases
Content module 2

Approved:
Meeting of the Department of Infectious Diseases
Odessa National Medical University
Protocol No. 1 of 29.08.2024
Head of the Department of Infectious Diseases _____ Tetiana CHABAN

Teacher(s)
Chaban T.V. PhD. Doctor of Sciences, professor, head of the department.
Associate professors: candidate of medical science Usychenko K.M., Pavlenko O.V., Gerasymenko O.A., N.V. Movlyanova
Assistants: Verba N.V., Bocharov V.M.

Topic: No. 4 "General characteristics of respiratory tract infections"
Goal: Improve students' knowledge of etiology, epidemiology, pathogenesis, clinical manifestations of infectious diseases with an airborne mechanism of transmission, influenza, adenovirus disease, MS infection, rhinovirus infection; to develop professional skills in drawing up an examination plan (laboratory and instrumental), a comprehensive plan for the treatment of the patient and the necessary preventive measures.

Basic concepts: Infectious diseases with an airborne mechanism of transmission, influenza, SARS, parainfluenza, adenovirus disease, MS infection, rhinovirus infection, reovirus infect

PLAN

1. Theoretical questions:

Flu- an acute infectious anthroponous viral disease with an aspiration mechanism of pathogen transmission. It is characterized by short-term fever, intoxication and damage to the respiratory tract. History and distribution.

Etiology. Influenza pathogens belong to the orthomyxavirus family, contain RNA. According to the antigenic structure, the influenza virus is divided into types A, B and C. The human and animal influenza A virus is divided into 13 antigenic subtypes by hemagglutinin (H1-H13) and 10 by neuraminidase (N1-N10). In humans, there are 3 subtypes of antigen H (H1, H2, H3) and 2 subtypes of antigen N (N1, N2), which give combinations. Type A virus has high variability. Two variants of the variability of virus A are known: antigenic drift and antigenic shift. Antigenic drift refers to point mutations in the gene that controls the synthesis of Nagglutinin. Accumulation of these mutations is accompanied by a change in the antigenic properties of hemagglutinin, which causes a partial loss of immunity among the sick. With the antigenic shift, a complete replacement of the subtype of hemagglutinin or neuraminidase, and sometimes both antigens, occurs, which leads to the appearance of fundamentally new antigenic variants of the virus, to which the majority of the population lacks immunity, which is why large epidemics and pandemics occur. The influenza B virus is also heterogeneous in its structure and antigenic properties, but it has greater stability and less virulence. Influenza C virus does not have neuraminidase and is antigenically stable. Influenza viruses are resistant to freezing. Other physical factors and disinfectants quickly inactivate them.

Epidemiology. The only proven source of the causative agent is a person with the flu, who releases the virus into the environment when coughing and sneezing. The patient is especially contagious in the first days of the disease, after the 7th day, the contagiousness rarely persists. Contagious patients with all forms of the disease, including mild and abortive. It is known that influenza A virus infects mammals and birds, it is possible to infect animals from humans and humans from animals. The preservation of the virus in the air environment,

on various objects (dishes, toys) depends on specific conditions and may last several hours, but this factor does not have significant epidemiological significance. Susceptibility to influenza is high. After suffering from influenza A, immunity persists for decades, possibly for life, but it is effective only against the subtype of the virus that caused the disease, so repeated diseases caused by the appearance of new variants of the virus are not uncommon. The duration of immunity for influenza caused by the type B virus is 3-4 years. Epidemic outbreaks of influenza type A are registered every 1-3 years, large epidemics and pandemics after 10-30 years. They occur in November-March (in the northern hemisphere), are explosive in nature, last 1-1.5 months. Epidemics of influenza B have the same seasonality, periodicity of 2-3 years. They are less intense (no more than 20% of the population), last 2.5-3 months. Influenza C virus causes sporadic cases of the disease. Typical clinical manifestations. According to the severity of the course, mild, moderate, severe and very severe (lightning) forms of the disease are distinguished. A typical and atypical course is also distinguished. The incubation period lasts from 15 hours to 3 days. The onset of the disease is acute. The clinical picture is dominated by intoxication and catarrhal-respiratory syndromes. The disease begins with 32 chills, malaise, aches in muscles, bones, joints, feeling broken, headache. The body temperature at the onset of the first painful sensations is subfebrile, but after a few hours it rises to 38-39 ° C, and by the end of the day, or on the 2nd day, it reaches a maximum of 39.5-40 ° C. The duration of the febrile period in uncomplicated cases does not exceed 5-6 days, usually 3-4 days. A two-wave nature of the fever is possible, but the appearance of the second wave is more often associated with the addition of complications. Intoxication is most pronounced on the 2nd-3rd day. The headache intensifies, is localized mainly in the frontal or frontotemporal areas, in the browbones, eyeballs. Dizziness, orthostatic collapse (fainting), vomiting, sleep disturbances, anorexia, thirst are possible. A few hours after the onset of the disease, dryness and itching in the throat and nose, nasal congestion, and photophobia are added. On the 2nd day, scratching in the throat, pain behind the sternum intensifies and a dry, painful cough, hoarseness of voice, abundant serous discharge from the nose appear. Catarrhal phenomena reach their greatest expressiveness on the 3rd-4th day. The cough becomes productive. The sputum is initially mucous, then purulent, nasal secretions also become purulent. Catarrhal phenomena persist until the 7-10th day of the disease. When examined in the first days of the disease, hyperemia and puffiness of the face, injection of scleral vessels attract attention. Pallor of the face in combination with cyanosis of the lips is possible with the development of respiratory failure. There are no rashes on the skin, but the appearance of petechiae in the places of friction of clothes, with a strong cough, hemorrhages in the sclera, eyelids, forehead and neck, which leads to diagnostic errors, is possible. When examining the oropharynx, hyperemia of the soft palate, brackets, back wall of the pharynx, and dryness of the mucous membranes are revealed. Granulation of the back wall of the pharynx, soft palate, brackets, point hemorrhages are possible. By the 3rd-4th day, the

hyperemia decreases, but the marked injection of blood vessels remains. The mucous membrane of the nose is hyperemic, swollen, the nasal passages are narrowed. There may be shortness of breath, harsh breathing during auscultation, isolated dry wheezes. In 33, the majority of patients due to toxic damage to the myocardium have muffled heart sounds, changes on the ECG of a diffuse nature in the form of a decrease in P and T waves, signs of slowing of intracardiac conduction. Heart rate corresponds to body temperature or relative bradycardia is noted. Tachycardia is a prognostically unfavorable symptom, especially in the elderly, as it indicates severe heart damage or the development of other complications. The tongue is coated with a white coating, the stomach is soft, painless (with a strong cough, soreness of the abdominal muscles is possible). Defecation is delayed. The spleen and liver are not enlarged. Diuresis is reduced, proteinuria, cylinduria, and microhematuria may be detected. Damage to the autonomic nervous system is manifested by sweating, lability of the pulse, hyperemia of the skin. Damage to the central nervous system, in addition to headache, insomnia, can be manifested by meningeal syndrome, confusion, delirium. Radicular and neurological pains indicate toxic damage to the peripheral nervous system. During the period of convalescence, the asthenoneurotic syndrome may persist for 5-10 days. A blood test reveals a picture that is characteristic of viral infections: leuko- and neutropenia, relative lymphocytosis. ESR is normal or slowed. A mild form of influenza is characterized by an increase in body temperature within 38 ° C for 2-3 days, mild catarrhal phenomena and intoxication. With a moderately severe form, the body temperature rises within the range of 38 - 40.0 ° C, pronounced intoxication and catarrhal phenomena. The severe form is characterized by the onset of the disease with severe chills and hyperthermia. Symptoms of intoxication with damage to the central nervous system (meningeal syndrome, phenomena of encephalopathy) and the cardiovascular system (tachycardia, pronounced decrease in blood pressure, deafness of heart tones) dominate. Hypertoxic (very severe form) is characterized by the rapid development of respiratory (hemorrhagic pulmonary edema) or cardiovascular failure (collapse, toxic damage to the myocardium), damage to the nervous system. The development of hemorrhagic pulmonary edema is indicated by increasing shortness of breath, pallor and cyanosis of the skin, tachycardia, a drop in blood pressure, and a cough with "rusty" sputum. Breathing during auscultation is hard, weakened, then wet rales of various caliber appear. During the development of NNGM, hemorrhagic encephalitis, disorders of consciousness, convulsions, and meningeal syndrome appear. Death can occur from respiratory arrest. Atypical forms of influenza are rare. At the same time, one of the leading syndromes is missing. So, in the summer, in the inter-epidemic period, the flu can occur without catarrhal phenomena. Intoxication and fever may be absent, and the disease appears to be a catarrhal respiratory syndrome, not different from other SARS. Age features are of significant importance. Influenza is especially severe in children under 1 year of age (pronounced neurotoxicosis, involvement of the lower respiratory tract in the process, frequent

complications). In elderly people, influenza often leads to cardiovascular failure, the development of complications, and exacerbation of chronic diseases. The most common complication of influenza is pneumonia. They can develop against the background of clinical manifestations of influenza and are considered in these cases as primary viral and bacterial. The most common bacterial agents are pneumococcus and staphylococcus. Early pneumonia is accompanied by severe intoxication, often has a destructive nature and is a frequent cause of death, especially in the elderly. Post-influenza bacterial pneumonia develops at the end of the 1st - beginning of the 2nd week of the disease and is more benign. Frequent complications from the ENT organs: sinusitis, otitis, eustachitis, laryngitis (in children) with the phenomenon of stenosis 35 of the larynx (croup), possible acute pyelonephritis or exacerbation of chronic pyelonephritis. Diagnostics. The diagnosis of influenza is established on the basis of a characteristic clinical picture and epidemiological data. Express methods are used for laboratory diagnostics: the fluorescent antibody method, which detects the antigen of the virus in smears-imprints from the mucous membrane of the nasopharynx. Other methods, serological (RSK, RGHA), isolation of virus culture (from blood, nasopharyngeal mucus), are used for retrospective diagnosis. Differential diagnosis is carried out with other SARS, rickettsiosis, typhoid fever, ornithosis, legionellosis, brucellosis, leptospirosis, hemorrhagic fevers, infectious mononucleosis, malaria, neuroinfections, viral hepatitis A (in the pre-jaundice period), measles, pneumonia, sepsis. The main difference between influenza and other SARS is the onset of the disease with fever and intoxication followed by catarrhal respiratory syndrome, dominated by laryngotracheitis. With ARVI, the disease begins with catarrhal phenomena, fever and intoxication appear later, expressed moderately. General principles of treatment and prevention. Patients with the flu are usually treated at home. An indication for hospitalization is a severe and complicated course of the disease, an unfavorable premorbid background. Hyperthermia, disorders of consciousness, convulsions, meningeal syndrome, a pronounced decrease in blood pressure, inadequate body temperature, tachycardia and arrhythmia indicate a severe course of the disease. In case of pneumonia with symptoms of respiratory failure, croup with signs of laryngeal stenosis, a patient with influenza is hospitalized. During treatment at home, bed rest is mandatory during the entire febrile period. Hot spices, fried foods should be excluded from food. Lactic acid products, abundant drinking (tea with honey, raspberries, rosehip decoction, juices, compotes, cranberry juice) are indicated, additionally 36 ascorbic acid is prescribed. Inhalations with menthol, sodium bicarbonate, and eucalyptus are used to combat cough. It is convenient to use aerosols (ingalipt, cameton). The use of chest collections, codeterpin, libexin, bronchicum is shown. Calpol, Coldrex, Fervex, Panadol are used for hyperthermia with intoxication. It is effective when prescribed in the first hours or days of the illness of the antiviral drug "Remantadine", which has a narrow spectrum of action and is active only against human influenza type A viruses. The main contraindications for prescribing rimantadine are: age up to 7 years,

liver and kidney diseases, thyrotoxicosis, pregnancy. The antiviral drug "Tamiflu" (Oseltamivir) is an oral neuraminidase inhibitor of the human influenza virus (all strains of influenza A and B) and the bird flu virus (H5N1). The drug blocks the active zone of the enzyme neuraminidase on the surface of the virus. Due to inhibition of neuraminidase, the influenza virus loses its ability to multiply and infect other cells of the body. Treatment with "Tamiflu" must be started on the 1st or 2nd day of the onset of flu symptoms. The appointment of "Tamiflu" is contraindicated in chronic renal failure, pregnancy, breastfeeding. IFN-α leukocyte or recombinant (Laferon, Roferon A, Intron A and others), which is instilled into both nasal passages, 5 drops every 2 hours; the use of IFN-α in the form of inhalations of 1 million units twice a day is effective. The effect of IFN is based on blocking the receptors of epithelial cells, which prevents their infection with influenza viruses. Anti-influenza immunoglobulin is prescribed for severe forms of influenza in a dose of 3-6 ml 2 times a day until the therapeutic effect is obtained. Passive immunotherapy allows you to bind the flu virus circulating freely in the blood. In the absence of anti-influenza immunoglobulin, it is possible to use normal human immunoglobulin (normal human immunoglobulin ("Biopharma", Ukraine) or "Sandoglobulin" (Switzerland). Pathogenetic therapy of uncomplicated forms of influenza: for the purpose of detoxification: taking a large amount of warm liquid (2.5-3 liters / day); with a severe course of the flu, infusion-detoxification therapy is prescribed with the inclusion of crystalloid and colloid solutions. For the purpose of desensitization: antihistamines (diazolin, tavegil) for 4-5 days. For anti-inflammatory purposes, mefenamic acid is prescribed at 0, 5 g 3 times a day (up to 3 g per day). For the induction of endogenous IFN and stimulation of leukopoiesis, vitamin C is prescribed up to 2 g / day, methyluracil 0.5 3-4 times a day for a course of up to 1 month. In order to reduce the permeability and fragility of capillaries, ascorutin is prescribed (rutin 0.05 g, ascorbic acid 0 .05 g, glucose 0.2 g) 1 pill 3 times a day for 5-7 days. Depending on the nature of complications (brain edema, pulmonary edema, cardiovascular insufficiency, laryngeal stenosis), syndromic therapy is carried out. Antimicrobial drugs are prescribed only for specific indications (addition of bacterial complications or exacerbation of chronic purulent-inflammatory processes). Antibiotics and chemopreparations of a wide spectrum of action are used (semisynthetic penicillins, cephalosporins, fluoroquinolones). The prognosis for influenza is favorable, but fatal consequences are possible in persons with a heavy premorbid background, in children under 1 year of age, with the development of severe pneumonia and lesions of the central nervous system.

Prevention. Patients are isolated at home or in a hospital (from closed groups, dormitories, hotels). During the epidemic, measures are taken to reduce the communication of the population (visits of sick people in hospitals are prohibited, mass holiday events are canceled, school holidays are extended). Workers caring for patients should wear 4-layer gauze masks or respirators. In the premises, ventilation and wet cleaning with a 0.2-0.3% chloramine solution

is necessary. Rimantadine, arbidol, amiksin, alpha-interferon are used for individual prevention. For the purpose of public prevention, vaccination is carried out with inactivated vaccines, the "Vaksigrip" vaccine of the "Pasteur-Marie" company (France) or live influenza vaccines containing weakened A (H1, N1 and H3, N2) and B viruses, which are licensed in Ukraine.

Adenovirus infection- SARS, which is characterized by a predominant lesion of the pharynx, tonsils, conjunctiva, as well as lymphadenopathy and fever. Etiology. Adenoviruses contain double-stranded DNA, are spherical in shape, 70-90 nm in size. The pathogenicity of these viruses is associated with the presence of toxic antigens and the ability to damage the cells in which they replicate. Adenoviruses are persistent in the environment. At room temperature, they remain active for up to 14 days, at 56 ° C they die within 30 minutes. Serovars 1 are most important in human pathology; 3; 4; 5; 7; 8; 12; 14 and 21 adenoviruses.

Epidemiology. The source of the pathogen is sick people and virus carriers. Patients secrete the virus from the separating upper respiratory tract and conjunctiva of the eyes until the 3rd - 7th, sometimes until the 25th day of the disease, with feces for up to 3 weeks, in some cases up to 2 months. The main way of transmission of the pathogen is airborne, food and water are possible, as well as through household items contaminated with the virus. The natural susceptibility of a person is high. After a disease or an asymptomatic infection, species-specific immunity is formed. The disease is registered throughout the year, but the highest incidence is observed in the autumn and winter months.

Typical clinical manifestations. The incubation period lasts from 1 to 14 days, more often 5-7 days. Clinical manifestations of the disease are diverse. Characteristic 40 fever lasting from 2-3 days to 2 weeks, sometimes lasting two minutes. In adults, the temperature reaction is less pronounced, in children the body temperature reaches 39-40°C, but general intoxication is expressed moderately. Most often, the disease proceeds according to the acute respiratory syndrome type. In these cases, nasal congestion, rhinorrhea, pain and dandruff in the throat are observed from the 1st day. During the examination, a picture of acute granulosa pharyngitis is revealed. On the back wall of the pharynx, hyperplastic, brightly hyperemic lymphoid follicles are observed, sometimes with a mucous coating. Tonsils are often involved in the process. They are swollen, moderately hyperplastic, plaques may appear, which are associated with the activation of bacterial flora. A moderate increase in cervical, mandibular, and often other groups of lymph nodes is also characteristic. With severe fever, an increase in the spleen and liver is observed. Laryngitis and tracheitis rarely develop. The most typical form of adenovirus infection is pharyngoconjunctival fever. The latter is characterized by an increase in body temperature, polyadenopathy, and the development of acute conjunctivitis. As a rule, the process is one-sided. The lesion of the second eye develops after 1-5 days. The duration of the disease is up to 2 weeks. Burning, stinging, feeling of a foreign body in the eye are observed. During the examination, swelling of the eyelids and narrowing of the eye slit are noted. The conjunctiva and sclera of

the eyes are sharply hyperemic, hemorrhages in the sclera are possible. The conjunctiva is granular, often a fibrinous film appears on it, which never spreads beyond its borders. Rarely, there is a more severe form of eye damage - keratoconjunctivitis, in which infiltrates form in the subepithelial layer of the cornea, the cornea becomes cloudy, and visual acuity decreases. The process lasts 3-4 weeks and, as a rule, is reversible. Adenovirus infection is often accompanied by dyspeptic disorders in the form of abdominal pain, vomiting, repeated liquid stools without pathological impurities. Of the complications, pneumonia (viral-bacterial, bacterial), sinusitis, and otitis often develop. Changes in the general blood test in adenovirus infection are uncharacteristic. Diagnostics. The diagnosis can be established with the development of a characteristic clinical picture in combination with epidemiological data. Among the laboratory methods of diagnosis, the determination of the virus antigen in swabs-prints from the nose by the immunofluorescence method, as well as the detection of antibodies (RZK and RPGA) are used. Isolation of a virus culture by infecting a culture of epithelial cells with material taken from the nasopharynx or feces is possible, but not used for practical purposes. Parainfluenza is SARS, which is characterized by the development of laryngitis. Etiology. The causative agent of parainfluenza belongs to paramyxoviruses, contains RNA, like the influenza virus has hemagglutinin (H) and neuraminidase (N). In humans, the disease is caused by 4 types of virus (1, 2, 3, 4). The virus is unstable in the environment. At room temperature, it dies after 4 hours. Sensitive to disinfectants. Epidemiology. The source of the pathogen is patients with typical and erased forms of the disease, which are contagious within a week. Infection occurs by airborne droplets. Susceptibility to the disease is high. Typical clinical manifestations. The incubation period lasts from 1 to 7 days. The disease begins gradually. From the 1st day, characteristic dandruff in the throat, hoarseness of the voice, rough barking cough, nasal congestion, rhinorrhea appears later. In adults, the body temperature does not rise or is subfebrile, in children it can be high. General intoxication is expressed weakly or moderately. It is manifested by weakness, muscle pain, headache. Examination reveals mild or moderate hyperemia of the mucous membranes of the oropharynx. The disease lasts up to 2 weeks. Complications usually develop in children in the form of pneumonia, otitis, croup with laryngeal stenosis. Diagnostics. Clinical diagnosis is complicated by similarities with other SARS. A pronounced picture of laryngitis with a satisfactory general condition may allow us to suspect parainfluenza. Among the laboratory tests, detection of the virus antigen in smears from the mucous membrane of the nose using the immunofluorescence method is used. Virological and serological diagnostics have been developed, but they have a retrospective value.

Respiratory syncytial infection (RS infection)- ARVI with predominant damage to the lower respiratory tract.

Etiology. The causative agent - the rhinosyncytial virus belongs to the family of paramyxoviruses, contains RNA, has a cytopathogenic effect, which is manifested by the formation of syncytial areas in the cells of sensitive tissue

structures. Thanks to this property, the pathogen got its name. Epidemiology. The source of the pathogen is patients, sometimes virus carriers. In patients, the virus is released from the nasopharynx 1-2 days before the onset of the disease and by the 3-6th day of the disease. The main way of transmission of the infection is airborne and in close contact with the patient, infection is possible through contaminated hands, underwear, and objects. Susceptibility to the disease is high, immunity is unstable, so repeated diseases are possible. Seasonality is autumn-winter. Typical clinical manifestations. The incubation period lasts from 2 to 6 days. The course of the disease is determined by the age of the patient. In adults and older children, the disease proceeds according to the type of mild respiratory disease. They note malaise, chills, mild headache, dryness and dandruff in the throat, nasal congestion. On the 2nd or 3rd day, slight discharge from the nose appears. The most characteristic are a persistent cough and difficulty breathing. The body temperature is subfebrile, during the examination, hyperemia of the soft palate and palatal arches, less often the back wall of the pharynx, is revealed. An increase in cervical and mandibular lymph nodes is possible. The disease lasts 2-7 days, but a dry cough can last up to 2 weeks.

Diagnostics. The diagnosis can be established with the development of a characteristic clinical picture of bronchitis or bronchiolitis with obstructive syndrome in combination with epidemiological data (group nature of the disease). Among the laboratory methods, immunofluorescence reaction, serological methods (RZK, PH, RPGA, IFA) are used, as well as isolation of virus culture from nasopharyngeal washings.

2. Questions for self-control:

- The place of infectious diseases with an airborne mechanism of transmission in the structure of infectious pathology
- Epidemiological, pathogenetic, clinical features of infectious diseases of the respiratory tract
- To characterize the causative agent of influenza, factors of aggression, different serotypes of the virus and antigenic variants, to define antigenic drift and shift.
- Mechanism of influenza transmission.
- Pathogenesis of influenza and its main clinical symptoms.
- Classification of influenza.
- Describe the main clinical symptoms and name the severity criteria of influenza.
- Name the possible complications of influenza and their diagnostic criteria.
- Consequences of influenza.
- Plan of examination of a patient with influenza.
- Methods of specific diagnosis of influenza.
- Etiotropic therapy of influenza and principles of basic therapy.

- The term and indications for the appointment of antibacterial therapy for influenza.
- Non-specific and specific prevention of influenza.
- Categories of persons to whom vaccination is indicated in the first place.
- Definition of the concepts of ARVI and ARVI. Etiology of SARS.
- Mechanism of vapor transmission of influenza, rhinovirus, respiratory syncytial and adenovirus infections.
- Pathogenesis of SARS and its main clinical symptoms.
- Classification of parainfluenza, rhinovirus, respiratory syncytial and adenovirus infections.
- To characterize the main clinical symptoms and name the severity criteria of SARS.
- Name the possible complications of parainfluenza, rhinovirus, respiratory syncytial and adenovirus infections and their diagnostic criteria.
- Plan of examination of a patient with SARS.
- Methods of specific diagnosis of SARS.
- Etiotropic therapy of SARS and principles of basic therapy.
- The term and indications for the appointment of antibacterial therapy for SARS.
- Non-specific prevention of SARS.

3. Indicative tasks for processing theoretical material.
    - Compile a dictionary of basic concepts on the topic.

4. Practical tasks.

- Create a plan for laboratory and instrumental studies of a patient with influenza and SARS
- Carry out differential diagnosis of influenza and parainfluenza.
- Conduct differential diagnosis of adenovirus infection and MS infection.
- Create a treatment plan for a flu patient.

5. Individual tasks for students of higher education:
   Make an oral report on one of the suggested topics:
    - Characteristics of the main etiotropic agents used to treat influenza, differences between them.
    - A clinical case of influenza (based on the analysis of scientific literature)

6. List of recommended literature:

Main:
1. Infectious diseases: textbook / O.A. Golubovska, M.A. Andreychyn, A.V. Shkurba and others; under the editorship O.A. Golubovska 4th ed., revised. and added K.: VSV "Medicine", 2022. p. 346-358.

Additional:

1. Infectious diseases. Course of lectures: study guide / E.V. Nikitin, K.L. Servetskyi, T.V. Shepherd [and others]. Odesa: ONMedU, 2012. p. 232-249. (Medical student library series).
2. Epidemiology in schemes: study guide / M.D. Chemych, N.G. Malysh, O.M. Chemych, N.I. Ilyina – Vinnytsia: Nova Kniga, 2020. – 256 p.
3. Atlas of infectious diseases / [M.A. Andreychyn, V.S. Kopcha, S.O. Kramarev and others]; under the editorship MA. Andreychyna – 2nd ed., corr. and added – Ternopil: Textbooks and manuals, 2017. – 288 p.
4. Infectious diseases: a textbook: in 2 volumes / edited by V.P. Malyo, M.A. Andreychyna – Lviv: Magnolia 2006, 2018. – Volume 2. - 726 p.
5. Infectious diseases: a textbook: in 2 volumes/ edited by V. P. Malyo, M. A. Andreychyna. – Lviv: Magnolia 2006, 2018. – T. 1. – 652 p.

Electronic information resources:

1. http://moz.gov.ua- Ministry of Health of Ukraine
2. www.ama-assn.org–American Medical Association /American Medical Association
3. www.who.int- World Health Organization
4. www.dec.gov.ua/mtd/home/- State Expert Center of the Ministry of Health of Ukraine
5. http://bma.org.uk– British Medical Association
6. www.gmc-uk.org- General Medical Council (GMC)
7. www.bundesaerztekammer.de– German Medical Association
8. https://library.odmu.edu.ua/catalog/- Electronic catalog

Topic No. 6: "Infectious-toxic shock in the clinic of infectious diseases"

Goal: To improve students' knowledge of pathogenesis, clinical manifestations and emergency care for infectious-toxic shock;

Basic concepts:infectious-toxic shock, bacterial infection, emergency conditions.

Plan

7. Theoretical questions:

Infectious-toxic shock (ITS) is a syndrome, the main manifestation of which is a violation of microcirculation with the development of oxygen debt and multiple organ failure.

Etiology and pathogenesis. It occurs as a complication of various infectious diseases caused by gram-negative and gram-positive bacteria. Rickettsia, spirochetes, fungi and viruses can cause it less often. ITS in infections caused by gram-positive pathogens occurs as a result of the action of exotoxins (peptidoglycan - teichoic acid). In infections caused by gram-negative pathogens, the occurrence of ITS is due to the massive breakdown of bacteria circulating in the blood and the release of endotoxins (lipopolysaccharides) with the formation of immune complexes.

Regardless of the etiological factor, ITS is usually divided into certain stages of development. The classification according to Hardaway is considered the most successful:

1. Reversible shock, which has three stages of development:

1.1 Early reversible shock.

1.2 Late reversible shock.

1.3 Steady reversible shock.

2. Irreversible shock.

Stage 1.1 is characterized by a spasm in the microcirculatory channel and the initial phenomena of hypoxia in the tissues.

Stage 1.2 is characterized by the dilation of the microcirculatory channel and the deposition of blood in it, the increase in cell hypoxia, the beginning of enzymatic metabolism in the cells of the tissues of the most sensitive and vulnerable organs.

At stage 1.3, DIC syndrome develops (up to the level of at least stage 2). As a result of pronounced hypoxia, cells become suppliers of under-oxidized metabolites that spread throughout the body, grossly changing the acid-base state (KOS). There are signs of impaired function of individual organs (multiple organ failure).

At stage 2, the DIC syndrome progresses to a deep level with gross violations of microcirculation and blood coagulation. Pronounced intracellular acidosis leads to disorganization and cell death.

These changes predict the appearance of severe irreversible systemic multiorgan failure. Expansion of necrosis zones and plasmatic generalization precede the impending death of the organism.

The mechanism of impressive action in each type of bacteria is quite individual and is determined by the specific factors of the pathogen's pathogenicity, which actively affect the human body. The most important class of bacterial antigens are

lipopolysaccharides (LPS) of gram-negative bacteria, which form the basis of the so-called endotoxin - the main triggering factor of ITS. Endotoxin diffuses little from the bacterial cell into the environment and is released only after its death. LPS are somatic antigens and exhibit extremely powerful biological activity. The toxic effect of LPS is caused by massive stimulation of the cells of the lymphoreticular system, which leads to the release of a large number of cytokines and other mediators of the systemic inflammatory response and shock. They have the main importance in the appearance of fever, arterial hypotension, tissue damage in ITS. In addition, LPS have a direct cytotoxic and cardiodepressant effect.

Gram-positive bacteria in the vast majority do not contain endotoxin in their membranes, they most often have a liposaccharide capsule and specific antigens, in particular exotoxins. These components of the microbial cell are able to stimulate the production of cytokines, activate alternative pathways of complement, change the activity of macrophages and lymphocytes, so their action is largely associated with humoral factors.

As a result of the activation of various damaging factors, vasodilatation develops, vascular permeability increases, blood cell aggregation is activated and arachidonic acid derivatives, active oxygen radicals, and lysosomal enzymes enter the blood, i.e., a cascade of pathological reactions is triggered, the result of which is a violation of microcirculation, metabolism, damage to blood elements, cells of the endothelium of vessels, increasing the permeability of capillaries.

Against the background of these processes in the microcirculatory channel, there is a decrease in the total peripheral vascular resistance (PVR) and a significant decrease in the volume of perfusion. A spasm of pre- and post-capillaries occurs, short arteriovenous shunts are opened, with the help of which blood is directed past the capillary network from the arterial channel to the venous one. The preload and, accordingly, the afterload decreases, the contractile ability of the myocardium is suppressed. As a compensatory reaction against this background, there is an increase in the production of adrenocorticotropic hormone, cortisol and aldosterone. The release of catecholamines with the development of tachycardia, the effect of antidiuretic hormone, cortisol, and aldosterone, which leads to the retention of Na+ and water, provide some optimization of hemodynamics - preload and afterload temporarily increase slightly, cardiac output, cardiac output,

Interstitial fluid enters the vascular system through the capillary membranes. Deterioration of microcirculation forces the formation of tissue hypoxia. It is the violation of microcirculation and the associated progressive hypoxia of organ tissues that are the main factors contributing to the progression of ITS.

Clinical manifestations: Stage 1.1 ITSH is quite short and is not always clinically evident. Under the action of endotoxin and CVD factors, a hyperdynamic state and peripheral vasodilatation develop. Usually, this stage is manifested by pronounced speech and movement disorders, anxiety, moderately expressed thirst may appear. Vascular tone is preserved, generalized arteriolospasm is most often emphasized, due to which the skin and visible mucous membranes turn pale. The skin is warm to the touch, sometimes slightly moist, occasionally pink. Accelerated pulse, strained, the pulse rate increases slightly with an increase in body temperature. The

filling of the jugular veins is satisfactory. Pupils are narrowed, breathing is deep enough, rhythmic, somewhat accelerated against the background of fever. Most often, at this stage of ITS, the blood pressure level does not decrease or even slightly increases. Heart sounds become loud. The deficit of BCC is compensated by the inflow of blood from the depot, tachycardia, due to which the cardiac output increases. Ventricular systolic and diastolic functions in shock are often depressed, despite high cardiac output. Diuresis decreases, but the time flow of urine is still not less than 40 ml/h. Central venous pressure (CVP) is within the normal range or slightly reduced. There is slight metabolic acidosis, hypercoagulation, and hyperglycemia in the blood.

In most cases, the doctor has the impression of complete well-being and the patient's condition does not cause any concern. This is also reflected in diagnostic considerations - stage 1.1 is almost never present in diagnoses.

Starting from stage 1.2, ITS is characterized by a gradual decrease in cardiac output and MOS, the development of peripheral spasm vessels and functioning of arteriovenous shunts. Blood pressure gradually decreases and tachycardia increases. A decrease in systolic blood pressure (below 70-60 mm Hg) becomes critical, in which renal filtration almost ceases and kidney hypoxia increases significantly. From this moment, the countdown begins, the duration of which determines the possibility of bringing the patient out of shock. The heart sounds are dull or weakened, the pulse is frequent and weak, the jugular veins gradually decrease. Measuring blood pressure in these stages of ITS becomes more and more difficult, CVT decreases significantly. Psychomotor excitement gradually changes to suppression of consciousness. The pallor of the skin increases, it acquires a marble shade, becomes cold and wet, with pronounced peripheral cyanosis - acrocyanosis is emphasized, the face acquires a gray-cyanotic color.

A sharp decrease in PaO2 (below 50 mm Hg) causes hypoxia/hypercapnia. Clear shortness of breath develops, which gradually increases, breathing in the lungs is hard. Pulmonary ventilation can exceed 20 l/min. Such ventilation compensation is insufficient to eliminate tissue acidosis. Diuresis decreases, it becomes below 20 ml/h.

As a result of the deterioration of the DIC syndrome, a different, most often hemorrhagic rash may appear. It is especially expressed in meningococcal sepsis - meningococcemia. The body temperature drops to subfebrile or normal, the patient's condition continues to progressively deteriorate. Tachycardia increases, blood pressure may not be determined. The pulse is so soft and frequent that counting it seems almost impossible. Heart sounds are deaf, sharply weakened. The respiratory rate exceeds 30/min, breathing becomes shallow and ineffective. In the terminal period of ITS, when the pH drops to 7.25 and below, Cheyne-Stokes breathing can be observed. There are signs of the beginning of pulmonary edema - hard breathing, single wet wheezing in the lower parts of the lungs. Gradually, there are more and more wet wheezes, they spread to other areas of the lungs.

Body temperature reaches subnormal level. The symptoms of brain hypoxia deepen, the patient develops a soporotic state, gradually turning into a cerebral coma. Cardiac activity and breathing stop.

Treatment

1. If the patient has cyanosis, low central venous pressure, low blood pressure, it is performedinfusion therapy in a volume of 1000 ml in 2 hours (reopoliklyukin, 5% albumin, saline isotonic solutions). The total volume of liquid per day is 40-50 ml/kg.
2. If the patient has cyanosis, normal or elevated CVT, but low blood pressure
– to connectsympathomimetics: dopamine 5-15 mcg/kg/min, or norepinephrine 0.02 -0.1 μg/kg/min..
3. If the patient has symptoms of peripheral spasm, normal CVT, normal blood pressure - connectvasodilators: nitroglycerin 0.1-0.5 μg/kg/min. If necessary, these drugs can be combined with sympathomimetics.
4. If the patient's skin is pink, BP and CVT are normal, but there is no diuresis - stimulation of diuresisfurosemide 1-5 mg/kg.
5. Prednisolone 10-30 mg/kg per day intravenously, and½ of the daily dose is administered at once, and the second half is administered in different doses every 4-6 hours.
6. Heparin - 100-200 units/kg per day or 0.3-0.6 mlFraxiparin.
7. Contrical 1000-3000 units/kg per day.
8. Broad-spectrum bactericidal antibiotics.
9. Replacement therapy immunoglobulins (sandoglobulin, intraglobin, pentaglobin, normal human immunoglobulin) in a dose of 100 mg/kg per day.

8. Questions for self-control:
   - The concept of intoxication, types of bacterial toxins, their impact on the human body.
   - Stages of the pathogenesis of infectious and toxic shock.
   - Stages of infectious and toxic shock.
   - The main infectious nosologies, which are characterized by the development of infectious-toxic shock.
   - Clinical manifestations of infectious-toxic shock and possible complications.
   - Methods of laboratory-instrumental research, which must be performed in case of suspicion of infectious-toxic shock.
   - Tactics of treatment of patients with infectious-toxic shock.

9. Indicative tasks for processing theoretical material.
   - Compile a dictionary of basic concepts on the topic.

10. Practical tasks.
    - Create a plan for laboratory and instrumental studies of a patient with meningococcemia complicated by ITS.
    - Conduct differential diagnosis of infectious-toxic and cardiogenic shock.
    - to create a treatment plan for a patient with shigellosis complicated by ITS.

11. Individual tasks for students of higher education:
    Make an oral report on one of the suggested topics:

- Characteristics of the main sympathomimetic agents used for the treatment of infectious-toxic shock, differences between them.
- A clinical case of infectious-toxic shock (based on the analysis of scientific literature)

12. List of recommended literature:

Main:

2. Infectious diseases: textbook / O.A. Golubovska, M.A. Andreychyn, A.V. Shkurba and others; under the editorship O.A. Golubovska 4th ed., revised. and added K.: VSV "Medicine", 2022. p. 346-358.

Additional:

6. Infectious diseases. Course of lectures: study guide / E.V. Nikitin, K.L. Servetskyi, T.V. Shepherd [and others]. Odesa: ONMedU, 2012. p. 232-249. (Medical student library series).
7. Epidemiology in schemes: study guide / M.D. Chemych, N.G. Malysh, O.M. Chemych, N.I. Ilyina – Vinnytsia: Nova Kniga, 2020. – 256 p.
8. Atlas of infectious diseases / [M.A. Andreychyn, V.S. Kopcha, S.O. Kramarev and others]; under the editorship MA. Andreychyna – 2nd ed., corr. and added – Ternopil: Textbooks and manuals, 2017. – 288 p.
9. Infectious diseases: a textbook: in 2 volumes / edited by V.P. Malyo, M.A. Andreychyna – Lviv: Magnolia 2006, 2018. – Volume 2. - 726 p.
10. Infectious diseases: a textbook: in 2 volumes/ edited by V. P. Malyo, M. A. Andreychyna. – Lviv: Magnolia 2006, 2018. – T. 1. – 652 p.

Electronic information resources:

9. http://moz.gov.ua- Ministry of Health of Ukraine
10. www.ama-assn.org–American Medical Association /American Medical Association
11. www.who.int- World Health Organization
12. www.dec.gov.ua/mtd/home/- State Expert Center of the Ministry of Health of Ukraine
13. http://bma.org.uk– British Medical Association
14. www.gmc-uk.org- General Medical Council (GMC)
15. www.bundesaerztekammer.de– German Medical Association
16. https://library.odmu.edu.ua/catalog/- Electronic catalog

Topic № 9: Herpesvirus infections

Goal: To form and improve students' knowledge of etiology, epidemiology, pathogenesis, clinical manifestations, diagnosis and treatment of herpesvirus infections.

Basic concepts:herpesvirus infections, DNA-containing viruses, lymphadenopathy, nucleoside and nucleotide antiviral drugs.

Plan:

1. Theoretical questions:

Herpesvirus infections are a group of widespread anthroponotic infectious diseases caused by viruses of the Herpesviridae family, which are characterized by a chronic recurrent course and lifelong persistence of the pathogen in the body. Herpes simplex (Herpes simplex) is an infectious disease caused by HSV 1 or 2 types, with predominant damage to the skin, mucous membranes, central nervous system, and less often internal organs.

Etiology. The causative agent belongs to the family of herpes viruses (Herpes viridae). To date, 8 types of herpesviruses are known: the herpes simplex virus of the 1st (HSV-1, HSV-1) and 2nd (HSV-2, HSV-2) types, the shingles virus (Varicella zoster virus, VZV, HHV-3), Epstein-Barr virus, (Epstein-Barr virus, EBV, HHV-4), cytomegalovirus, CMV (Cytomegalovirus, CMV, HHV-5), herpes virus type 6, VH-6 (Human herpesvirus 6, HHV-6), herpes virus type 7, VH-7 (Human herpesvirus 7, HHV-7), herpes virus type 8, VH-8 (Human herpesvirus 8, HHV-8). HSV types 1 and 2 are DNA-containing viruses.

Epidemiology. Most people are infected with HSV-1 from early childhood. HSV-1 usually causes damage to the mucous membranes of the lips, mouth, and less often the genitals. HSV-2 infection can occur only at the beginning of sexual life. HSV-2 affects the genitals, causing genital herpes. Serologic evidence of HSV-1 infection in humans varies from 56–85% worldwide, and HSV-2 infection from 13–40%. Only about 30% of infected people have clinically significant relapses of HSV infection. The disease is contagious. The main ways of transmission of infection are: household contact, sexual, hemotransfusion, fecal-oral, intrauterine, transplant and airborne.

Pathogenesis. The primary lesion is accompanied by replication of the virus at the site of invasion, and then it exists latently in the cells of the nerve ganglia. In infected individuals, HSV-1 is stored in the trigeminal nerve nodes, HSV-2 in the sacral nerve nodes. Penetration of the virus in the ganglion can be carried out by a hematogenous or neurogenic route. Relapses of the disease can be associated with a decrease in cellular immunity, which occurs under the influence of such factors as trauma, ultraviolet radiation, extreme temperatures, stress, immunosuppression, or hormonal disorders.

Clinical signs. Lesions of the skin and mucous membranes are characterized by rashes on a hyperemic background of grouped blisters (vesicles) with transparent and then cloudy contents. The blisters dry up into crusts, which after rejection do not

leave scars. Predominant localization — on the lips, cheeks, wings of the nose, mucous membrane of the mouth, genitals. Lymphadenopathy is often observed. A characteristic tendency to relapse. Other manifestations of herpetic infection are herpetic eczema, herpetic gingivostomatitis and pharyngotonsillitis, herpetic meningitis, herpetic encephalitis, herpetic eye disease, disseminated herpetic disease.

Diagnostics. The diagnosis is established based on the clinical picture and laboratory diagnostics: cytological research method (Ttsanka test), serological method (ELISA), PCR, cultural diagnostics.

Pharmacotherapy. For the treatment of herpes simplex, the appointment of systemic and local antiviral drugs is recommended. Antiviral drugs for systemic use from the group of nucleosides and nucleotides are used, with the exception of reverse transcriptase inhibitors, namely acyclovir, valacyclovir, famciclovir.

In the case of a primary episode of herpetic infection, acyclovir is used orally at 200 mg 5 r/day or 400 mg 3 r/day for 5–10 days. Valaciclovir 500 mg twice a day for 5–10 days and famciclovir 250 mg 3 times a day for 5 days are also recommended.

In case of recurrence of herpes infection, acyclovir is used internally at 200 mg 5 times a day for 3–5 days; or valacyclovir internally at 500 mg twice a day for 3–5 days; or famciclovir orally 125 mg 3 times a day for 5 days. As an alternative scheme for labial herpes, valacyclovir is used internally at 2000 mg twice a day for 1 day.

For preventive treatment (suppression) of recurrent infections in immunocompetent patients, acyclovir is prescribed internally at 200 mg 4 r/day or 400 mg 2 r/day for 12 months; valacyclovir internally at 500 mg once a day for 12 months; famciclovir orally 250 mg twice a day for 12 months.

For the preventive treatment (suppression) of recurrent infections in patients with immunodeficiency, acyclovir is recommended orally at 200 mg 4 times a day for 12 months, or if necessary, valacyclovir orally at 500 mg 2 times a day for 12 months, or if necessary, famciclovir orally at 500 mg twice a day for 12 months.

2. Questions for self-control:

- Etiology of herpesvirus infections?
- Clinical manifestations of diseases caused by HSV1?
- Clinical manifestations of diseases caused by HSV2?
- Clinical manifestations of diseases caused by VZV?
- Clinical manifestations of diseases caused by EBV?
- Clinical manifestations of diseases caused by CMV?
- Peculiarities of the course of herpesvirus infections in immunodeficient states?
- Methods of laboratory diagnosis of herpesvirus infections?
- Treatment of herpes virus infections?
- Specific prevention of herpes viruses?

3. Tasks for processing theoretical materials.

- Compile a dictionary of basic concepts on the topic.

4. Practical tasks.
   - Perform differential diagnosis of infectious mononucleosis and viral hepatitis A.
   - Make a plan for the laboratory-instrumental examination of a patient suspected of having a generalized form of CMV infection.
   - Make a treatment plan for a patient with recurrent Herpes labialis.

5. Individual tasks for students of higher education:
   Make an oral report on one of the suggested topics:
   - Relevance of herpesvirus infections.
   - Brain lesions in herpesvirus infections.
   - A clinical case of Ramsay-Hunt syndrome (based on an analysis of scientific literature).

6. List of recommended literature:

Main:

1. Infectious diseases: textbook / O.A. Golubovska, M.A. Andreychyn, A.V. Shkurba and others; under the editorship O.A. Golubovska 4th ed., revised. and added K.: VSV "Medicine", 2022. p. 346-358.

Additional:

1. Infectious diseases. Course of lectures: study guide / E.V. Nikitin, K.L. Servetskyi, T.V. Shepherd [and others]. Odesa: ONMedU, 2012. p. 232-249. (Medical student library series).
2. Epidemiology in schemes: study guide / M.D. Chemych, N.G. Malysh, O.M. Chemych, N.I. Ilyina – Vinnytsia: Nova Kniga, 2020. – 256 p.
3. Atlas of infectious diseases / [M.A. Andreychyn, V.S. Kopcha, S.O. Kramarev and others]; under the editorship MA. Andreychyna – 2nd ed., corr. and added – Ternopil: Textbooks and manuals, 2017. – 288 p.
4. Infectious diseases: a textbook: in 2 volumes / edited by V.P. Malyo, M.A. Andreychyna – Lviv: Magnolia 2006, 2018. – Volume 2. - 726 p.
5. Infectious diseases: a textbook: in 2 volumes/ edited by V. P. Malyo, M. A. Andreychyna. – Lviv: Magnolia 2006, 2018. – T. 1. – 652 p.

Electronic information resources:

1. http://moz.gov.ua- Ministry of Health of Ukraine
2. www.ama-assn.org–American Medical Association /American Medical Association
3. www.who.int- World Health Organization
4. www.dec.gov.ua/mtd/home/- State Expert Center of the Ministry of Health of Ukraine
5. http://bma.org.uk– British Medical Association
6. www.gmc-uk.org- General Medical Council (GMC)
7. www.bundesaerztekammer.de– German Medical Association
8. https://library.odmu.edu.ua/catalog/- Electronic catalog