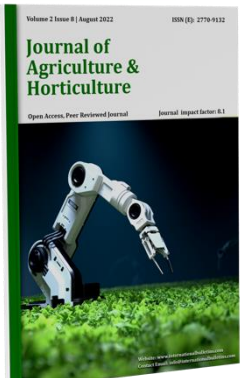

MEASLES DISEASES AND ITS TYPES IN UZBEKISTAN

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Annotation: Measles is a highly contagious infectious disease caused by a virus. Infection can cause serious illness, complications, and even death. This article presents the main issues related to the causative agent, spread and pathogenesis of measles infection, taking into account data on the outbreak of this disease in 2022-2023. The classification of measles, the features of its clinical course in children in the age aspect are presented, the characteristics of clinical forms of the disease with damage to the central nervous system are given, complications of measles are described. The formation of immunity after the disease is shown. The issues related to the differential and laboratory diagnosis of measles infection are outlined, modern approaches to the treatment and specific prevention of measles are presented in detail, and the importance of vaccination within the framework of the National Calendar of Preventive Vaccinations is emphasized. The requirements for anti-epidemic measures in case of a measles outbreak and dispensary monitoring of children who have had measles infection are considered.

Keywords: Epidemiology, virus, pregnancy, contact, complications, seasonality, specific prevention.

Introduction. Measles infects about 10 million people worldwide and causes between 100,000 and 200,000 deaths each year, mainly in children. The figures can change dramatically over a short period of time, depending on the vaccination status of the population. Measles is rare in the United States due to routine vaccination of children, and endemic measles was declared eliminated in the United States in 2000. The Centers for Disease Control and Prevention reported an average of 63 cases per year from 2000 to 2010. Nevertheless, in 2019, the incidence in the United States rose to 1,274 cases, the highest number recorded since 1992. This increase was primarily due to the spread among unvaccinated groups. Parents' refusal to vaccinate is becoming an increasingly common reason for the growth of vaccine-preventable diseases in children. In 2020, amid the global COVID-19 pandemic, only 13 measles cases were reported in the United States. In 2022, 121 cases were registered.

It is estimated that for the period from 2000 to 2022 Measles vaccination, supported by the Measles and Rubella Initiative (currently the Measles and Rubella Partnership) and the GAVI Alliance, has prevented 57 million deaths; most of them have been prevented in the WHO African region and countries supported by the GAVI Alliance. However, if the attention paid to this problem is weakened, the successes achieved at the cost of such efforts can be nullified. Where children are not vaccinated, outbreaks of the disease occur.

Measles is an acute infectious viral disease with a very high level of contagiousness, the causative agent of which is the measles virus. It is characterized by high fever (up to 40.5 C),

inflammation of the mucous membranes of the oral cavity and upper respiratory tract, conjunctivitis and a characteristic spotted papular rash of the skin, general intoxication.

According to the World Health Organization, in 2018, about 140 thousand people died from measles worldwide, most of them children under the age of five. Measles remains one of the prominent causes of child mortality in developing countries. The number of measles cases in the world increased dramatically in 2017. Due to gaps in vaccination coverage, measles outbreaks have been observed in all regions..

Etiology. The causative agent of measles is an RNA virus of the morbillivirus genus of the paramyxovirus family, which has a spherical shape. The virus consists of a nucleocapsid — minus-an RNA strand, three proteins and an outer shell formed by a matrix protein and two surface glycoproteins: one of them is hemagglutinin, the other is a "fusion" protein. The virus remains active in the air and on surfaces for up to 2 hours, it is poorly resistant in the external environment, quickly dies outside the human body from the effects of various chemical and physical factors (irradiation, boiling, treatment with disinfectants). There is a hypothesis about the origin of the measles virus from the bovine plague virus during the emergence of animal husbandry. Despite the instability to the external environment, there are cases of the virus spreading over considerable distances with the flow of air through the ventilation system — in the cold season in one single building. Weakened strains of the measles virus are used to produce a live measles vaccine.

Epidemiology. The success of immunization made it possible to classify measles as "outgoing" infections included in the National Measles Elimination Program (Order No. 192 of the Ministry of Health of the Republic of Uzbekistan dated April 24, 2003), the purpose of which was to eliminate this disease in our country by 2020. The program included several stages: at the first stage, it was planned to achieve widespread stabilization of measles incidence rates at a sporadic level in all regions of the country, at the second — to create conditions for preventing the occurrence of measles cases and complete eradication of measles infection in the Republic of Uzbekistan, at the third (2018-2020) — certification of measles-free territories. However, in 2019-2023, the situation changed dramatically: the incidence of measles in the Republic of Uzbekistan increased. The first cases of the disease were imported from countries such as the United Kingdom, Germany, Italy, France, Finland, Russia, India, Malaysia, and China. According to the WHO Regional Office for Europe and ECDC (European Centre for Disease Prevention and Control), in 2011, more than 31,000 cases of measles were reported in 38 European countries due to viruses of genotypes D4 (more often), D3 and D9.

Mass immunization has affected the age structure of measles incidence, it has led to the "maturation" of measles: currently, adults and children under one year old dominate among the sick (the contingent of the greatest risk of the disease is children 2-7 months old). In the pre-vaccination period, children under one year old from the absence of innate immunity very often get measles and the disease passes in severe form with complications. The study of the immunological structure of the population of the Republic of Uzbekistan in relation to the measles virus showed that, in general, 89.2% of the surveyed have a protective antibody titer. However, the largest proportion of seronegative individuals are children of the second year of life. The reservoirs of infection include organized groups. Thus, the incidence of measles in children under one year old was 13%, kindergartens 1.5%, schools 8.2%, vocational schools and colleges 10.3%. The source of the infection is a person with measles. The transmission

path is airborne. The contagiousness is high (the contagiousness index is 0.97). The patient is contagious at the end of the incubation period, but especially in the catarrhal period and with the appearance of rashes. From the 5th day of the rash, and with the development of complications after 10 days from the moment of rash, the patient is not contagious and is not subject to isolation.

Pathogenesis. When a person is infected, the measles virus exhibits epitheliotropic, lymphotropic and neurotropic properties. The virus enters the human body through the mucous membrane of the upper respiratory tract and then with the blood flow (primary viremia), the virus enters the reticuloendothelial system (lymph nodes) and affects all types of white blood cells. From the 3rd day of the incubation period, typical giant multinucleated Warthin — Finkeldey cells with inclusions in the cytoplasm can be found in lymph nodes, tonsils, and spleen. After multiplying in the lymph nodes, the virus re-enters the bloodstream, repeated (secondary) viremia develops, which is associated with the onset of clinical manifestations of the disease. The measles virus suppresses the activity of the immune system (direct damage to T-lymphocytes is possible), there is a decrease in immunity and, as a result, the development of severe secondary, bacterial complications with predominant localization of processes in the respiratory organs. The virus may also cause temporary vitamin A hypovitaminosis.

The epitheliotropic properties of the virus are realized clinically by an inflammatory reaction in the respiratory tract (measles bronchitis, pneumonia) and the digestive tract (abdominal syndrome, diarrhea). The neurotropic properties of measles virus are clinically associated with the development of infectious toxicosis with the possible occurrence of an encephalic reaction in young children or measles meningoencephalitis in older children and adults. The measles virus can persist in human brain tissue, forming a clinical picture of subacute sclerosing panencephalitis. The lymphotropic properties of the virus in patients are manifested by an increase in lymph nodes (mainly cervical), liver, spleen, and especially damage to immunocompetent cells with the development of immunodeficiency, which predisposes to bacterial complications.

Classification. There are typical and atypical measles. According to the severity, typical measles is divided into mild, moderate and severe. With atypical measles, the main symptoms of the disease are erased or some of them are absent, a change in the duration of individual periods of measles is characteristic: a decrease in the duration of the rash period, the absence of a catarrhal period, a violation of the stages of the rash. Atypical variants also include hypertoxic, hemorrhagic and malignant forms, which are extremely rare.

The clinical picture. The incubation period is from 8 to 17 days. In patients receiving immunoglobulin, blood components, plasma — 21 days. The acute onset is a rise in temperature to 38-40 ° C, dry cough, runny nose, photophobia, sneezing, hoarseness of voice, headache, swelling of the eyelids and redness of the conjunctiva, hyperemia of the pharynx and measles enanthema — red spots on the hard and soft palate. On the 2nd day of the disease, small whitish spots appear on the mucous membrane of the cheeks in the area of the molars, surrounded by a narrow red border: These are the so—called Belsky — Filatov - Koplik spots, which are a pathognomonic symptom of measles. Measles rash (exanthema) appears on the 4th-5th day of the disease, first on the face, neck, behind the ears, the next day on the trunk and on the 3rd day, rashes cover the extensor surfaces of the arms and legs, including the fingers. The rash consists of small papules surrounded by a spot and prone to

fusion (this is its characteristic difference from rubella, in which the rash does not merge). The reverse development of the rash elements begins on the 4th day of the rash: the temperature normalizes, the rash darkens, turns brown, pigmented, flakes (in the same sequence as the rash). Pigmentation persists for one to one and a half weeks. Features of the course of measles in children of the 1st year of life: in the period of prodroma, catarrhal phenomena are poorly expressed, the disease can begin with the appearance of a rash, the stages of rash and the spotted-papular nature of the rash with subsequent pigmentation remain. The Filatov—Koplik symptom may be absent. For young children, the appearance of intestinal dysfunction (frequent loose stools) is characteristic. The course of measles in children of the first year of life is more severe, characterized by more frequent development of early and late complications. Measles can occur in the form of a mitigated (erased) form, which develops in vaccinated children who received immunoglobulin or blood products during the incubation period, proceeds easily, the stage of rashes is disrupted, the incubation period is extended to 21 days. Measles in adults is very rare, most often it affects people who have not received vaccination. In adults, measles disease is usually more severe than in children. Pneumonia and bacterial complications are often observed. Sometimes blindness and significant hearing impairment can result. In patients with HIV, it has a severe course, often ending in death.

Complications. Measles can have a smooth and complicated course. According to the timing of development, there are early complications that occur in the acute catarrhal period and the period of rashes, and late complications caused by secondary infection in the period of pigmentation and convalescence of measles. Early complications are caused directly by the measles virus, the later ones are secondary in nature and are associated with activation of the bacterial flora. Currently, the most common complications of measles are measles croup, laryngotracheitis, otitis media, bronchitis, pneumonia, sinusitis, stomatitis, colitis and enterocolitis, impetigo, furunculosis, which can be both early and late regardless of age. The development of pneumonia is possible in any period of the disease. By their nature, early pneumonia occurs as bronchopneumonia or interstitial pneumonia, characterized by severe course, pronounced symptoms of intoxication, respiratory and heart failure. Late pneumonia is characterized by a deterioration in the child's condition after the 5th day of rashes, an increase in body temperature, the development of respiratory failure, the appearance of physical changes in the lungs in the form of small and medium-bubbly wheezes with radiological signs of focal pneumonia. Pneumonia is most severe in young children. Complications from the central nervous system include serous meningitis, encephalitis, meningoencephalitis, occurring with a frequency of 1:1000 cases of measles and characterized by a severe course with a possible fatal outcome. Less often, panencephalitis is observed, recorded with a frequency of 1:1,000,000.

The damage to the nervous system in measles is caused by perivenous demyelination and destruction of nerve fibers, proliferation of astro- and microglia of the white matter of the brain during the penetration of the measles virus into the central nervous system. In severe forms of measles meningoencephalitis, multiple hemorrhages and degeneration of brain cells develop. In chronic encephalitis and the formation of a slow measles infection in the central nervous system, great importance is attached to immunocomplex disorders with the development of widespread degeneration and gliosis in brain tissue. With measles encephalitis, the most typical syndromes are distinguished: comatose, convulsive, hemiplegic,

akinetic-rigid, psycho-organic, etc. Acute measles encephalitis develops in children of any age with both severe and mild measles on the 3rd-5th day after the rash appears. Against the background of an increase in body temperature to high numbers, general weakness, headache, lethargy, drowsiness appear, which in some cases turns into sopor or coma. Against the background of impaired consciousness, epileptiform seizures of a generalized or local nature, paralysis and paresis of the type of hemiplegia, less often monoplegia, occur. It is possible to develop focal symptoms in the form of hyperkinesis of various types, cerebellar ataxia, nystagmus, diencephalic disorders, damage to cranial nerves, most often facial and visual (decreased vision up to amaurosis), which is reversible. Damage to the spinal cord in the form of myelitis and polyradiculoneuritis is manifested by impaired pelvic organ function, the development of lower paraplegia, conductive sensitivity disorders, trophic disorders. Serous meningitis is characterized by the appearance of headache, meningeal symptoms, vomiting of central origin, and general toxic syndrome against the background of measles. In the cerebrospinal fluid there is moderate pleocytosis (up to 200 • 106 / l) of lymphocytic or mixed genesis, the protein content may be increased. Subacute sclerosing panencephalitis is a slow measles neuroinfection with a long incubation period (up to 8-10 years after measles). The disease develops latently, manifests itself as chronic neuroasthenic syndrome, headache, lethargy, weakness, fatigue. There are changes in the psycho-emotional sphere: memory impairment, less often a decrease in learning ability, disinhibition. Pyramidal and extrapyramidal symptoms gradually join, epileptic seizures and hyperkinesis appear. Panencephalitis is characterized by a progressive course and ends with the development of cachexia, coma, decerebration rigidity, loss of vision due to atrophy of the optic nerves. The diagnosis of measles encephalitis is based on data from an epidemiological history (contact with a measles patient) and clinical symptoms with the corresponding timing of the development of measles rash and neurological disorders in the form of lesions of the brain and spinal cord, meninges and peripheral nerves.

In acute measles encephalitis, electroencephalography is indicated — diffuse changes in bioelectric activity, slow-wave and paroxysmal activity are noted. A magnetic resonance imaging (MRI) scan identifies multiple foci of hyperintensive signal in the brain and spinal cord. Mixed or lymphocytic pleocytosis from 100 to 200 • 106 / l, protein up to 1 g / l is detected in the cerebrospinal fluid. In subacute sclerosing panencephalitis, computed tomography is shown, which determines the atrophy of the brain substance, and MRI shows hyperintensive signals in the white matter of the brain. Moderate pleocytosis is observed in the cerebrospinal fluid with an increase in the amount of protein more than 1 g / l. In the biochemical analysis of blood, hypergammaglobulinemia. In the outcome of measles encephalitis, the development of epilepsy, hyperkinesis, ataxia, and delayed psychomotor development is noted. The mortality rate is 10-30%.

Immunity. The transferred measles forms a strong lifelong immunity, the basis of which is still associated with the humoral link. Specific antibodies in measles (IgM at first) are detected a day after the rash appears in the natural course of the disease, the maximum level is reached on the 7th-10th day of the rash. IgM antibodies can be detected within a month. Their presence indicates an active phase of measles infection caused by either wild or vaccinated measles virus. Almost simultaneously with IgM, IgG antibodies appear, the maximum level of which is determined 2 weeks after the appearance of the rash, then their concentration decreases, but, unlike IgM, they persist for life, confirming the fact of measles or

measles vaccination. Laboratory diagnostics of measles includes various methods — virological, serological, polymerase chain reaction method. As a method of early diagnosis of measles, enzyme immunoassay is used, which allows detecting anticorrosive IgM antibodies from the 5th day of the rash period. Only one serum sample is needed for the reaction. To confirm (exclude) measles in previously vaccinated individuals, to determine virus-specific immunity, IgG antibodies are determined in paired sera of the patient collected from him at intervals of 10-14 days.

Differential diagnosis. Measles should be differentiated from toxic allergic rash, as well as with other exanthemic infections: rubella and diseases caused by enteroviruses, parvovirus B19 and herpes virus type 6. Toxic-allergic skin lesions most often develop in response to the administration of any medications. In this case, the rash appears simultaneously a few minutes or hours after the introduction of the allergen, as a rule, on the entire surface of the body. There is a true polymorphism of rashes: erythema, papules, vesicles, blisters, bullae. With rubella, the rash, as with measles, is spotty-papular, but there is no stage in its appearance. Exanthema is observed mainly on the trunk, extensor surfaces of the limbs, around large joints, to a lesser extent on the face. The general condition suffers little, generalized lymphadenopathy is characteristic, especially the occipital and posterior cervical lymph nodes are enlarged. Enterovirus exanthema is usually combined with other manifestations of enterovirus infection (fever, myalgia, damage to the gastrointestinal tract, etc.) and resembles that of measles, rubella or scarlet fever, capturing the face, trunk, limbs. Characteristic of the Coxsackie virus A (serotypes 5, 10, 16) is the localization of rashes on the hands, feet and in the oral cavity in the form of vesicles up to 3mm in diameter with a corolla of hyperemia. Infectious erythema caused by parvovirus B19 is characterized by the appearance of a rash, mainly on the face, resembling slap marks. Sometimes erythema can spread to the trunk and limbs. In addition, joint lesions and aplastic crises with inhibition of erythroid growth may occur. Sudden exanthema, the etiological factor of which is the herpes virus type 6, is characterized by high fever for 4 days with lytic normalization of body temperature on the 5th day, which is accompanied by the simultaneous appearance of a roseolous (less often spotted papular) rash on the trunk and extremities, to a lesser extent on the face. The elements disappear after a few days without a trace, without pigmentation, sometimes small bran-like peeling is possible on the face. No drugs have been developed for the specific treatment of measles. Treatment of patients can be carried out at home and, first of all, should provide for compliance with the regime, rational nutrition and care. Hospitalization of patients in the box department of an infectious diseases hospital is carried out according to the following indications: severe and complicated course of measles, children from closed groups, children of the first year of life, as well as children from antisocial families. Symptomatic therapy includes antipyretics for fever of 38.5 ° C and above, antihistamines, eye washing with 2% sodium bicarbonate solution followed by instillation of 20% sodium sulfacyl solution. The use of recombinant α-interferons (viferon) in the catarrhal period and the rash period is justified. In case of measles, antihistamines, interferons (viferon) and inhalation therapy (steam inhalations) are indicated, in case of severe croup, glucocorticosteroids (prednisolone 1-2 mg / kg per day intravenously or intramuscularly). Antibacterial therapy is prescribed for severe forms of measles (regardless of the age of the patients), for moderate forms in children before the first year of life and for bacterial complications. Aminopenicillins, macrolides and cephalosporins of the II — III generation are

recommended parenterally in age-related doses. Recombinant interferons, glucocorticoids, neuroprotectors, drugs that improve microcirculation and tissue metabolism are recommended for measles encephalitis. With cerebral edema in the acute period, oncodehydrants, loop diuretics are administered under the control of osmolarity of blood plasma.

Prevention. The most effective way to prevent measles is to vaccinate the population. All children should be vaccinated against measles. The measles vaccine is characterized by safety, effectiveness and low cost. The measles vaccine is administered alone or often in combination with vaccines against mumps, rubella ("MMR II", "PRIORIX"). The KPC vaccine is a combined vaccine against measles, mumps and rubella, which is a mixture of weakened viruses of three diseases, administered by injection. The combined vaccine allows you to stimulate the immune system less painfully than the introduction of three vaccines at the same time, and also faster and more effectively than the introduction of three vaccines at certain intervals. According to the national vaccination calendar of the Republic of Uzbekistan, the first vaccination is given to all children at the age of 12 months and again at the age of 6 years (a dose of 0.5 ml. p / k). Measles vaccination is contraindicated in cases of primary cellular immunity deficiency, during pregnancy and in case of immediate allergic reactions to egg white or neomycin. Persons who have had measles, received 2 doses of the vaccine or have a protective antibody titer (in the passive hemagglutination reaction — 1:10, 1:20) or IgG antibodies in the enzyme immunoassay reaction are considered immune. Anti-epidemic measures in the outbreak should be aimed at preventing the occurrence and spread of measles diseases. The basic requirements for a set of organizational, therapeutic, preventive and sanitary anti-epidemic measures are set out in the sanitary rules "Sanitary norms, rules and hygienic standards of the Republic of Uzbekistan" (07/25/2017 No.0239-07/3).

If the source of infection is registered in a preschool or school, then for a period from the moment the first patient is identified to 21 days from the moment the last patient is identified, children who have not had measles and have not been vaccinated against it are not accepted into the team. Measles patients are hospitalized in the presence of the indications described above for a period until the disappearance of clinical symptoms, but not less than 5 days after the appearance of the rash with mandatory laboratory examination. Convalescents can be admitted to the team after clinical recovery, even if there are secondary cases of infection in the focus. Contact persons in measles foci are examined daily by a doctor or nurse. If there are unvaccinated (or vaccinated once) contact persons who have not had measles, they are medically monitored within 21 days from the moment the first case of the disease is detected in the outbreak, their laboratory examination is carried out at the same time as the patients. In order to prevent the spread of infection in foci, no later than 72 hours from the moment of identification of the first patient, vaccination (revaccination) against measles is carried out for the following categories of contact persons under the age of 35: those who were not ill and not vaccinated earlier; those who were not ill and vaccinated once, if at least 6 months have passed since the vaccination; with unknown infectious and vaccination history; seronegative or having an antibody titer below the protective level. If there are contraindications to vaccination, as well as children under the age of vaccination, normal human immunoglobulin is administered from among the contacts in accordance with the instructions, no later than the 5th day after the first contact with a measles patient. Nonimmune children who are in contact with measles are subject to separation from the 9th to the 17th day (on the 21st day, if

they received immunoglobulin). Children vaccinated against measles are not quarantined if contact occurred no earlier than 21 days after immunization. Dispensary supervision is not required in uncomplicated cases. Children who have suffered from measles encephalitis should be monitored by a neurologist, ophthalmologist, and infectious disease specialist for 2 years with courses of rehabilitation treatment.

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