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MEASLES IN CHILDREN, ETIOLOGY, PATHOGENESIS, DIFFERENTIAL DIAGNOSIS, PREVENTION

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Abstract
The main issues relating to the etiology, epidemiology and pathogenesis of measles infection are outlined. A classification of measles, features of its clinical course in children in terms of age are presented, characteristics of the clinical forms of the disease with damage to the central nervous system are given, and complications of measles are described. The features of the formation of immunity in measles are shown. Issues related to the laboratory and differential diagnosis of this infection are outlined, modern approaches to the treatment and specific prevention of measles are presented in detail, and the need for vaccination within the framework of the National Preventive Vaccination Calendar is emphasized. The requirements for carrying out anti-epidemic measures in the outbreak of measles and dispensary observation of children who have had measles infection are considered.

Keywords: children, measles, vaccination.

Introduction

Measles is an acute infectious disease of viral etiology, characterized by damage to the respiratory tract and eyes with the development of cyclic exanthema against the background of intoxication syndrome.

Etiology. The causative agent of measles is an RNA virus that belongs to the paramyxovirus family, a genus of measles viruses that includes human measles virus, bovine measles virus, canine distemper virus and subacute sclerosing panencephalitis virus. The latter is capable of long-term persistence in brain cells with the formation of panencephalitis (a variant of chronic measles infection). The antigenic structure of the measles virus is complex. It has a lipoprotein membrane, which ensures adhesion, penetration and reproduction of the virus in sensitive host cells, and a glycoprotein membrane, represented by hemagglutinin (protein H) and hemolysin (F), which induce the formation of specific antibodies - the basis of humoral immunity. Strains of the measles virus isolated in different countries are antigenically identical, which was taken into account when setting the task of eliminating measles. The measles virus is highly contagious, but unstable in the environment; it quickly dies when exposed to sunlight, UV radiation, or when dried.

Pathogenesis. When a person is infected, the measles virus exhibits epitheliotropic, lymphotropic and neurotropic properties. The entry gate for the virus is the mucous membrane of the respiratory tract and, possibly, the conjunctiva of the eyes, where the virus adheres and from where it enters the regional lymph nodes, where it begins to multiply. From the 3-4th day of the incubation period, the virus enters the blood (primary viremia, during which it can be partially neutralized by

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parenteral administration of immunoglobulin) and settles in the lymph nodes, liver, and spleen. A new stage of concentration and intensive reproduction of the virus in these organs begins, as a result of which giant multinucleated cells carrying measles antigen are formed. The multiplied virus again penetrates the blood (secondary viremia) and spreads throughout the body, which corresponds to the onset of the disease. In the capillaries of the mucous membranes and skin, contact between sensitized T cells and cells carrying measles antigen occurs, a delayed-type hypersensitivity reaction, which is clinically manifested by a characteristic rash on the skin and Belsky-Koplik-Filatov spots on the oral mucosa. 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 the 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 the clinical picture of subacute sclerosing panencephalitis. The lymphotropic properties of the virus in patients are manifested by enlargement of the lymph nodes (mainly cervical), liver, spleen, and especially damage to immunocompetent cells with the development of immunodeficiency, which predisposes to the occurrence of bacterial complications.

Classification. There are typical and atypical measles. Based on 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 period of the rash, 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.

Clinical picture. The incubation period for measles is from 9 to 17 days, but can last up to 21–28 days in people who have received immunoglobulin and other blood products. The clinical picture of modern measles in non-immune individuals has not changed [3]. Measles has retained its characteristic clinical symptoms and the stages of the infectious process. As is known, measles occurs cyclically with a successive change of three periods: prodromal (catarrhal), rash and pigmentation period. The first symptoms of the disease often appear on the 13-14th day from the moment of infection. For the catarrhal period, which lasts 3–4 days (with fluctuations from 1 to 6 days), the following are typical: fever, rough dry cough, rhinitis, conjunctivitis with photophobia. Pathognomonic is the appearance on the mucous membranes of the cheeks of rashes in the form of grayish-white dotted spots surrounded by a reddish rim (Belsky-Koplik-Filatov spots), and enanthema on the soft palate, appearing 1-2 days before the rash. In some children, 1-2 days before the period of rash, a prodromal rash is noted - maculopapular, small, pink in color on an unchanged skin background, localized on the face, neck, upper body and disappearing after 8-12 hours. The catarrhal period ends with a decrease in temperature or its complete normalization within 12–24 hours. The period of rash is characterized by a new increase in temperature to 38.6–39.4 ° C, increased symptoms of intoxication, catarrhal phenomena and rash (exanthema). The rash is pink or bright red, tends to merge, is maculopapular in nature, located on an unchanged skin background with moderate humidity. In 30% of children, the rash is hemorrhagic in nature, which does not reflect the severity of the disease. Measles rash typically develops in stages over a period of 3–4 days. Appearing behind the ears, on the forehead, on the back of the nose, within 1 day the rash spreads to the face (cheeks), neck, upper body, and single elements may also appear on other parts

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of the body and arms. On the 2nd day, the rash is localized on the trunk and proximal parts of the upper extremities; on the 3-4th day, the rash spreads to the distal parts of the arms and legs, including the palms and feet. On the 4th-5th day, the period of rashes is replaced by a period of pigmentation - a change in the color of the rash, which becomes brownish-brown. The reverse development of the rash occurs in the same sequence as the rash (head, torso, limbs), which creates a motley picture of a fading purple-cyanotic pigmented rash on the legs. Due to the hemorrhagic nature of the rash, hyperpigmentation remains for a long time, lasting 1.5–2 weeks. In addition, during the period of extinction of the rash, there is peeling in the form of scales and mild itching. By this time, the body temperature will normalize.

Measles in younger children (1–5 years) clinically occurs with severe catarrhal symptoms of the respiratory tract and eyes, with puffiness of the face, swelling of the eyelids, lacrimation, profuse nasal discharge, and a rough cough. In older patients, adolescents and adults with measles, general toxic symptoms dominate: higher fever (up to 39-40°C), headache, perversion of taste and smell, nosebleeds.

Features of the course of measles in children of the 1st year of life: during the prodrome, catarrhal symptoms are mild, the disease can begin with the appearance of a rash, the staged nature of the rash and the maculopapular nature of the rash with subsequent pigmentation remain. The Filatov-Koplik symptom may be absent. Young children are characterized by the appearance of intestinal dysfunction (frequent loose stools). The course of measles in children of the first year of life is more severe and is characterized by a more frequent development of early and late complications. Measles can occur in the form of a mitigated (erased) form, which develops in children who received immunoglobulin at the beginning of the incubation period, or in children of the first year of life who are breastfed (passive maternal immunity). This form is characterized by an increase in the incubation period to 24–28 days, mild or absent catarrhal symptoms, low-grade fever or normal temperature, the absence of Filatov-Koplik spots, the presence of a pale, small, sparse rash with a violation of the stages of the rash.

Differential diagnosis. Measles should be differentiated from a toxic-allergic rash, as well as other exanthemal 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, usually on the entire surface of the body. A true polymorphism of rashes is noted: erythema, papules, vesicles, blisters, bullae. With rubella, the rash, as with measles, is maculopapular, but there is no stage in its appearance. Exanthema is observed mainly on the trunk, extensor surfaces of the limbs, around large joints, and to a lesser extent on the face. The general condition suffers little, generalized lymphadenopathy is characteristic, the occipital and posterior cervical lymph nodes are especially enlarged. Enteroviral exanthema is usually combined with other manifestations of enteroviral infection (fever, myalgia, damage to the gastrointestinal tract, etc.) and resembles that of measles, rubella or scarlet fever, affecting the face, torso, and limbs. Characteristic of the Coxsackie A virus (serotypes 5, 10, 16) is the localization of the rash on the hands, feet and in the oral cavity in the form of vesicles up to 3 mm in diameter with a rim of hyperemia. Erythema infectiosum, caused by parvovirus B19, is characterized by the appearance of a rash, mainly on the face, resembling marks from slaps on the face. Sometimes erythema can spread to the trunk and limbs. In addition, joint damage and aplastic crises with suppression of the erythroid germ may occur. Sudden exanthema, the etiological factor

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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 maculopapular) rash on the trunk and limbs, in to a lesser extent on the face. The elements disappear after a few days without a trace, without pigmentation, sometimes fine pityriasis-like peeling is possible on the face. Treatment of patients can be carried out at home and, first of all, should include adherence to the regimen, proper nutrition and care. Hospitalization of patients in the isolation ward of an infectious diseases hospital is carried out for the following indications: severe and complicated measles, children from closed groups, children in the first year of life, as well as children from asocial families. Symptomatic therapy includes antipyretics for fever of 38.5°C and above, antihistamines, eye washing with a 2% sodium bicarbonate solution followed by instillation of a 20% sodium sulfacyl solution. The use of recombinant α-interferons (Viferon) in the catarrhal period and the period of rash is justified. For measles croup, antihistamines, interferons (Viferon) and inhalation therapy (steam inhalations) are indicated; for 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 patient), for moderate forms in children under the first year of life, and for bacterial complications. In this case, aminopenicillins, macrolides and cephalosporins of the 2nd - 3rd generation parenterally are recommended in age-specific doses. For measles encephalitis, recombinant interferons, glucocorticoids, neuroprotectors, and drugs that improve microcirculation and tissue metabolism are recommended. In case of cerebral edema in the acute period, oncodehydrants and loop diuretics are administered under the control of blood plasma osmolarity.

Prevention. Vaccination against measles is carried out with the domestic live attenuated vaccine L-16 and a divaccine (measles, mumps). The French monovaccine "RUVAX" and combined imported vaccines against measles, rubella, mumps - "MMR II", "PRIORIX" - are also used. Vaccination against measles is contraindicated in cases of primary deficiency of cellular immunity, during pregnancy, and in cases of immediate allergic reactions to egg white or neomycin. Persons who have had measles, received 2 doses of the vaccine, or have a protective titer of antibodies (in the passive hemagglutination reaction - 1:10, 1:20) or IgG antibodies in the enzyme-linked immunosorbent assay reaction are considered immune. If the outbreak of infection is registered in a preschool institution or school, then for the period from the moment the first patient is identified until 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. Patients with measles are hospitalized in the presence of the indications described above for a period until the clinical symptoms disappear, but not less than 5 days from the moment the rash appears with mandatory laboratory examination. Convalescents can be admitted into the team after clinical recovery, even if there are secondary cases of infection in the outbreak. Contact persons in measles outbreaks are examined daily by a doctor or nurse. If among the contact persons there are unvaccinated (or vaccinated once) and have not had measles, medical observation is established for them within 21 days from the moment the first case of the disease is detected in the outbreak, and they are tested in a laboratory at the same time as the sick person. In order to prevent the spread of infection in foci, no later than 72 hours from the moment the first patient is identified, vaccination (re-vaccination) against measles is carried out for the following categories of contact persons under the age of 35 years: those who have not been sick and have not been vaccinated previously; not

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sick and vaccinated once, if at least 6 months have passed since the vaccination; with an 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 vaccination age, contacts are given normal human immunoglobulin in accordance with the instructions, no later than the 5th day from the moment of first contact with a measles patient. Non-immune children exposed to measles are subject to separation from the 9th to the 17th day (to the 21st day if they have received immunoglobulin). Quarantine is not imposed on children vaccinated against measles if the contact occurred no earlier than 21 days after immunization. Clinical observation is not required in uncomplicated cases. Children who have had measles encephalitis are subject to observation by a neurologist, ophthalmologist, or infectious disease specialist for 2 years with courses of rehabilitation treatment.

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