Measles (Rubeola)

Definition

- Measles – acute infectious disease, very contagious, specific to humans, clinically characterized by fever, ocular – nasal and tracheal – bronchial catarrh, specific enanthema (Koplik's spots) followed by a generalized maculopapular eruption.

- Measles - a particularly severe eruptive disease;
- A sick person can infect ~ 18 people;
- In 2016 - 89,780 cases of death predominate children up to 5 years;
- According to WHO, over the last 16 years global measles vaccination has prevented 20.4 million deaths.

- Measles is in the phase of global elimination, but due to the decline of vaccine coverage, it remains one of the essential problems of public health worldwide!

Etiology

- Virus contain *RNA*
- Family - ***Paramyxovridae***
- Group - ***Mixoviridae***
- Virus is very unstable and is soon destroyed outside the human body
- Resists freezing
- Can be isolated from nasopharynx secretion and blood in prodromal period

- Structure of the virus - 6 main proteins, an antigenic type
- In the absence of a major protein, the M polypeptide, the virus becomes defective, developing over time PESS (subacute sclerosing Panencephalitis).
- It is a lymphotropic virus, the targget cells being lymphocytes (T and B), macrophages, platelets and monocytes - temporary immunosuppression, immunodeficiency, anergy.
- Post measles anergy can last from 4 to 6 months.

Epidemiology

- Measles is a disease with universal occurrence, evolving endemoepidemically.
- In the last years, in the countries where the measles vaccination program has been applied to children, its morbidity decreased considerably.
- Measles is recorded there, where the vaccine coverage is small!
- It does not concern the level of economic development, the capacity of the health system, ethnicity, etc.

- Source of infection:

A sick person with typical or atypical forms. There are no carriers of the virus.

- Way of transmission:

Direct (aerogen) - through nasopharyngeal secretions

Indirect - through objects recently contaminated

- Susceptibility: 100%

Stable lifelong postinfectious immunity

Pathogeny

- Measles virus invides the epithelium of the upper respiratory tract, conjunctiva and lymph nodes, where it multiplies, then it is eliminated in the blood;
- Primary viremia;
- Invasion and replication of the virus in lymphoid and reticuloendothelial tissues of internal organs;
- Secondary viremia;
- Immune reactions to the virus in the endotelial cells of dermal capillaries play a substantial role in the development of Koplik's spots and rash;
- Specific antibodies are not detectable before the onset of the rash.

Histological modifications

Essential lesions are found in the:

- ✓ skin
- ✓ nasopharyngeal mucous membranes, bronchi, conjunctiva
- ✓ intestinal tract
- ✓ Multinucleated giant cells (Warthin-Finkeldey) with inclusion bodies in the nucleus and cytoplasm are found in respiratory and lymphoid tissues and are pathognomonic for measles
- ✓ CNS- perivascular infiltration with lymphocytes, giant cells mainly in white substance, oedema, stasis.

Clinical forms

1.According to mode of manifestation:

- **Typical**
- **Atypical:**

✓ *mitigated;*

✓ *bronchial;*

✓ *toxic;*

✓ *haemorrhagic.*

2.According to severity:

- Mild
- Moderate
- Severe

3.According to evolution:

- Noncomplicated
- Complicated

Criteria for severity in measles

General:

- CNS involvement
- Croup syndrome - stenosing laryngotracheitis.
- Obstructive syndrome.

Local:

- 1. The number of eruptive elements and their size.
- 2. Character of eruptions (haemorrhagic, cyanotic).

Clinical pictures

Incubation period – 14 -21 days; **21** days *(in plasma transfusion, γ- globulin at the onset)*

Clinical periods of measles

Prodromal period (catarrhal) – duration 3-4 days;

- malaise;
- increasing fever;
- irritative cough;
- coryza;
- conjunctivitis with lacrimation;
- nasal discharge;
- alterations of the buccal mucosa (enanthema and a diagnostic sign of Koplik's spots).

Koplik's spots are the pathognomonic lesions of the measles:

- ✓ appear 2 days before the onset of rash;
- ✓ are located on the buccal mucosa, alongside the second molars;
- ✓ are 1-2 mm white spots on a bright red background
- ✓ they fade rapidly (in 3 days)
- ✓ Sore throat and gingivitis are another two manifestations of enanthema.

Eruptive period

- a new rise of temperature
- catarrhal sign are in progress
- the appearance of the **rash** on the skin is step-by-step within 3 days:

➢ *1st day - on face, neck, upper part of the chest;*

➢ *2nd day - spreads over the trunk;*

➢ *3rd day - covers the limbs.*

Eruption characteristics

- ✓ Maculopapular elements - red spots, with accentuated edges, confluent;
- ✓ Leave spots of a light-brown pigmentations;
- ✓ Then appears fine branny desquamation.

- ***Convalescence period*** – normalization of clinical signs.

Modified measles

- Is a mild form that occurs in partially immune persons:
- Infants under 6 months of age (the presence of maternally antibody);
- Exposed children who received immune serum, immunoglobulin;
- Rarely, in persons with documented previous measles;

The distinguishing features are: a longer incubation period, minimal prodromal period, atypical appears of the rash, Koplik spots can be absent.

Measles in vaccinated children

- Measles in vaccinated children, which did not form antibodies, typically develops.
- Children with diminished post-vaccine immunity, in case of contamination, develops atypical, mild forms.

Measles in infants

- Up to 6 months it presents atypical aspects as in mitigated measles, in the context of passive immunity transmitted transplacental.

- Newborns from non-immune mothers make typical forms of measles. It frequently develops with severe bacterial complications and increased lethality.

Measles in adults

- Is more severe in adults than in children;
- About 3% of yang adults develop primary viral pneumonia;
- Hepatitis and bronchospasm are more common among adults;
- The rash is more severe and more confluent;
- Bacterial superinfection is more common among adults (sinusitis, otitis, pneumonia).

- In a pregnant woman, measles can lead to spontaneous abortion and stillbirth.
- In immunocompromised patients measles infection evolves as a severe, frequently fatal disease. In these patients, a rash may be absent;

Complications are primary measles (giant-cell) pneumonia, progressive encephalitis beginning weeks or months after initial infection, and (in HIV – infected patients) progression to AIDS.

Complications

Specific:

- ✓ Laryngitis (croup), (Giant-cell)pneumonia,
- ✓ Keratitis,
- ✓ Post infectious encephalomyelitis (PIE) -1/1000 cases of measles,
- ✓ Measles inclusion-body encephalitis (MIBE)-1/10 cases of measles in immunocompromised children,
- ✓ Subacute sclerosing panencephalitis(SSPE)-1/1million cases of measles,

Nonspecific: (bacteria and other virus addition)

- ✓ pneumonia; laryngotracheitis
- ✓ otitis;
- ✓ conjunctivitis;
- ✓ stomatitis (catrrhal,aphthous, ulcerative – necrotic, gangrenous, or noma);

The sequelae in measles

- Intracranial hypertension
- Epileptiform syndrome
- Mental retardation
- Psychic sequelae
- Blindness

Diagnosis:

- Epidemiological anamnesis
- Clinical manifestations
- Laboratory diagnosis:

Non specific laboratory data:

- ✓ Absence of biological inflammatory syndrome.
- ✓ The blood count shows a normal number of leukocytes or leukopenia with lymphomonocytosis.
- ✓ Sometimes increased transaminases, especially in adults.

Etiological diagnosis

- Isolation of measles virus from respiratory secretions is not routinely used in medical practice.
- Serological tests for anti-measles antibodies are the most widely used in medical practice.
- The most used serological tests at present are the ELISA type ones, which can differentiate the IgM type anti-measles antibodies from the IgG type ones.
- The presence of IgM-type anti-measles antibodies signifies recent acute infection and confirms the diagnosis of measles at present.
- The presence of IgG-type anti-measles antibodies shows the existence of a measles immunization acquired in the past, either after the disease or after the measles vaccination.

Differential diagnosis

Prodromal period:

- ARVI (influenza, adenovirus infection, acute rhinopharyngitis, tracheo - bronchitis)
- Enteroviral infection with catarrhal manifestations

Eruption period:

- ✓ Rubella
- ✓ Infectious mononucleosis
- ✓ Enteroviral infection with exanthema
- ✓ Scarlet fever
- ✓ Allergic eruption
- ✓ Toxoplasmosis
- ✓ Kawasaki disease
- ✓ Chickenpox (vericella)
- ✓ Typhoid fever
- ✓ Leptospirosis
- ✓ Brucellosis

TREATMENT

- Patients should be isolated.
- Bed rest.
- The visible mucosa should be systematically cleansed.
- The diet should be nourishing, easily digestible.
- There is no etiological therapy in measles.
- Therapy is symptomatic (antipyretic, analgesic, antitussive).
- In acute post-measles encephalitis, corticosteroid therapy is recommended.
- Antibiotics for bacterial complications.
- Vitamin A.

Criteria for the discharge of patients with measles from the hospital.

- Clinical healing (improvement), no earlier than the 5th day after the onset of exanthema;
- In the case of pneumonia - not earlier than on the 10th day after the onset of the rash;
- In encephalitis, meningoencephalitis - not earlier than 21 days.

Post-hospital surveillance of measles patients with CNS involvement (encephalitis, meningoencephalitis).

- It will be performed by the family doctor and the neurologist.
- Duration - 2 years.
- Frequency - year I - once at 3 months, year II - once at 6 months.
- Surveillance character: clinical and paraclinical examination (neurosonography, cranial ultrasound, electroencephalography) as needed.

- In the first 6 months after discharge, it is not allowed to be in the sun, jumping, performing sports.
- Vaccinations are allowed in measles after the patient has healed.
- In case of neurological complications - after consultation of the neuropediatric doctor and not earlier than 6 months.
- Note: measles develops immunosuppression (risk of bacterial and viral overgrowth), need for surveillance after 2-3 weeks by the family doctor.

Measles prophylaxis

- **Nonspecific prophylaxis**, which consists in isolating the patient with measles for 5 days from the onset of the rash and clinical supervision of contacts.
- **Specific prophylaxis:**

✓ ***Passive immunization*** of measles contacts, which consists of the administration of standard immunoglobulins, currently less used, being reserved for unvaccinated contacts, who risk developing severe forms of the disease: immunocompromised children, children with many associated pathologies, infants under 6 months, pregnant women. Administration should be performed within the first 3 days of infectious contact.

- Passive immunization provides short-term protection (30 days).The protection provided by passive immunization will not always prevent the onset of the disease, but if it does occur, it will be in a milder form (mitigated measles).

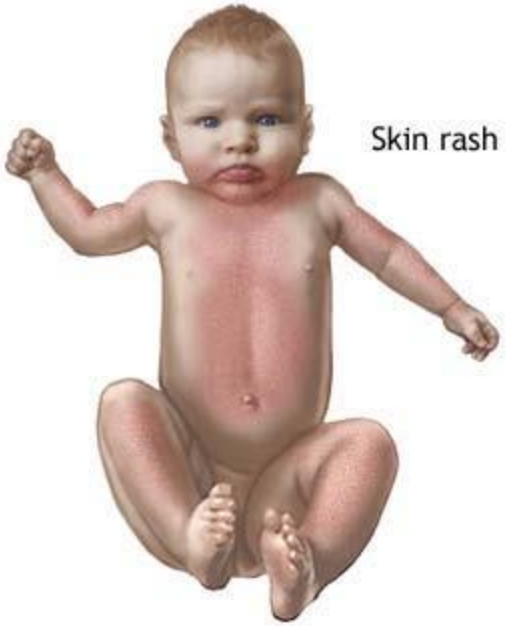
- **Active immunization through measles vaccination.** The measles vaccine is a live attenuated virus vaccine that provides 90-95% post-vaccination protection.
- Currently, the national vaccination program in the Republic of Moldova uses the trivalent measles-mumps-rubella vaccine (MMR), all 3 valences containing live attenuated virus.
- Current MMR vaccination schedule

MMR-vaccine (Measles-Mumps-Rubella)

- *First dose* – 12 months,
- *Second dose* - 6 -7 years,
- *Third dose* - 15-16 years.

Being a live attenuated virus vaccine, the measles vaccine is contraindicated in pregnancy and in the immunocompromised.

Rubella (German measles)



Rubella is an acute illness characterized by:

- Fever
- Rash
- Limphadenopathy
- Other possible manifestations

Etiology

- ✓ Rubella virus a member of the:
- ✓ Togaviridae family
- ✓ Rubivirus genus
- ✓ Composed of capsid of RNA and a lipoprotein envelope
- ✓ Doesn't have antigenic variations.
- ✓ It is sensible to low temperatures.

Epidemiology
Acquired Rubella

Rubella is typically a childhood disease seen predominantly in the 5-14 year age group;

- Peak incidence in the spring;
- Epidemic and sporadic character;
- Source of infection − sick person and newborns with congenital rubella who eliminate the virus through nasopharyngeal secretions, feces and urine up to 1-3years afterbbirth.

The route of transmission:

- Is mostly airborne, through nasopharyngeal secretions
- Indirectly through objects recently contaminated
- Transplacental (congenital rubella).

Pathogenesis

- Viruses attachment and replication in the mucosa of the upper respiratory tract;
- Primary viremia - (spreading to local lymph node causing their hypertrophy and the stimulation of the formation of young leukocytes and plasma cells) multiplies and disseminates again (secondary viremia);
- Secondary viremia - the virus reaches:

- the liver and spleen;

- the lungs (causing interstitial lesions);

- there occur inflammatory phenomena, responsible for the onset of encephalitis, during theillness stage o the disease or the virus may persist in a latent state with the occurrence of SSPE, in time;

- the skin (causing damage to the capillary endothelium, with the extravasation of pericapilary elements, wich explains the emergence of maculopapular rash; the joints (the virus has been identified in the synovial fluid.

Clinical manifestations

Postnatal rubella (acquired rubella)

- **The Incubation stage lasts:** 14 - 21 days (the disease is often clinically inapparent).
- **The Prodromal period** (2-3 days) – shorter than of measles.
- the insidious onset, with malaise, fever (which mai be absent), minimum respiratory catarrhal simptoms and generalised swelling of the lymph nodes;
- Polyadenopathy (pathognomic symptom) with the swelling of suboccipital, retroauricular, latero- cervical, submandibular and other, bilateral. lymph nodes sensitive to touch, well defined, nonadherent to the deep areas.
- Widespread nodal involvement occurs 4-10 days before the rash and persist 2-6 weeks (the first and the lasts clinical manifestation of the disease).

The illness stage (eruptive) takes 3-5 days.

The exantema appears in one spurt, starts on the face and then spreds quickly, covers the whole body in a cranio-caudal direction and disappears within hours or maximum one day („comes and goes quickly”.

The eruption is:

- maculopapular, pinc,
- with areas of normal skin,
- disappears when pressed,
- are more abundant on the face, trunk,
- discrete, with no tendency to coalesce,
- disappear in 1- 2 days without a trace.

- In adults, fever, catarrhal manifestations and exanthema are stronger expressed.

Diagnosis

- Epidemiological date
- Clinical symptoms

Nonspecific laboratory data:

- ✓ Absence of biological inflammatory syndrome.
- ✓ The blood count shows a normal number of leukocytes or leukopenia with lymphomonocytosis.
- ✓ Plasmacytosis and hyperbasophilia (Turck cells).
- ✓ Thrombocytopenia sometimes severe, this is a complication of rubella.

Etiologic diagnosis

- Isolation of rubella virus from respiratory secretions is not routinely used in medical practice.
- The most used serological tests at present are the ELISA type ones, which can differentiate the IgM type anti-rubella antibodies from the IgG type ones.
- The presence of IgM-type anti-rubella antibodies signifies recent acute infection and confirms the diagnosis of rubella at present.
- The presence of IgG-type anti-rubella antibodies shows the existence of a rubella immunization acquired in the past, either after the disease or after the vaccination.

Differential diagnosis

Measles, scarlet fever, enteroviruses, adenoviruses, infection by B 19 parvovirus, infectious mononucleosis, allergic eruptions, CMV infection, tuberculosis toxoplasmosis, leukemia, etc..

Complications

- Trombocytopenic purpura,
- Rubella arthritis, polyarthritis
- Encephalitis, encephalomyelitis
- Guillain-Barre syndrom, etc..

Treatment

- **Hygienic-dietary therapy:**

✓ Rest, during the febrile and eruptive stage.

- **Symptomatic:**

✓ Antipyretic, anti-inflammatory: paracetamol, ibuprofen,

- **Pathogenic:** it s usually reserved for severe forms of the disease, complicated with meningoencephalitis:

✓ Admission to intensive care units;

✓ Oxygen therapy;

✓ Corticotherapy: dexamethasone;

✓ Diuretics (mannitol, etc..);

✓ Anticonvulsants (diazepam, etc..).

Congenital Rubella Syndrome

- The rubella virus is part of the **TORCH** group of congenital infectious.
- The malformation risk approaches 100% when the infection happens during the first month of pregnancy and decreases to 20% in the fourth month.

Pathogeny

- During acute rubella virus infection, viremia occurs, during which it can cross the placenta to the fetus, thus causing the infection of the conception product with rubella virus, which determines a series of fetal changes:

✓ inhibition of cellular mitosis, with inhibition of cell growth and slowing of organ growth;

✓ angiopathic lesions with fetal vasculitis and / or placental vasculitis, which may cause tissue damage;

✓ inhibition of fibroblasts, with inhibition of fetal growth;

✓ chromosomal alterations, which lead to malformations.

All of these changes will lead to spontaneous abortion or stillbirth.

- If the maternal rubella infection occurs in the first trimester of pregnancy, the teratogenic risk is maximum (70% -100%) and rubella embryopathy will occur, and if the infection occurs after the 20th week of pregnancy, the fetus will present with congenital rubella.

- **Rubella embryopathy (Gregg malformative syndrome)** - consists of a multitude of fetal malformations:

➢ ocular (cataract, iridocyclitis)

➢ auditive (vestibular disturbance, deafness)

➢ cardiovascular (pulmonary artery stenosis, coarctation of aorta, etc.)

➢ neurological lesions (microcephaly, encephalitis, etc.)

➢ hematological (thrombocytopenic purpura, hemolytic anemia)

➢ digestive

➢ metabolic and of growth

➢ genito-urinary

Usually, the child with rubella embryopathy has malformations incompatible with life.

Progressive congenital rubella

- Progressive congenital rubella is described when the infection occurs after the end of organogenesis and consists of a chronic disseminated infection of the fetus, with a lethality of 20%.
- The newborn is born with chronic disseminated rubella infection and is contagious for a long time (6 months-1 year), due to persistent viral replication and prolonged elimination through biological fluids.
- Although there are no malformations, the organs have impaired functionality, describing multivisceral disorders: myocarditis, interstitial pneumonia, meningoencephalitis, bone lesions, etc .. There are also a number of late manifestations:

➢ diabetes is present in 40% of those who survive a congenital rubella.

➢ PESS-like progressive encephalopathy.

Diagnosis

- Epidemiological date
- Clinical symptoms

Laboratory diagnosis: demonstration of rubella antibodies of the IgM tipe in infants is diagnostic of congenital rubella.

IgM antibodies do not cross the placenta, so their presence indicates that they must have been synthesized by the infant, in uterus in response to the presence of rubella infection transmitted transplacental from the mother.

Placental biopsy may show the presence of rubella antigen.

Differential diagnosis

Includes other congenital infections:

- ✓ Toxoplasmosis
- ✓ CMV and herpes simplex virus infection
- ✓ Syphilis

Rubella, Measles prophylaxis

- MMR-vaccine (Measles-Mumps-Rubella)
- Scheme: 12-months, 6-7 years, 15-16 years

To eliminate rubella and congenital rubella syndrom, it is necessary to immunize women of childbearing age, as well as all school – age children.

Rubella syndrome