

# **MENINGOCOCCAL INFECTION (MI) IN CHILDREN**

- Meningococcal infection (MI) is an acute infectious disease caused by meningococcus that is transmitted through the air by drops and is characterized by various clinical forms from rhinopharyngitis to generalized (invasive) forms: purulent meningitis, meningoenzephalitis, meningococemia, being affected and other organs.
- Meningococcal infection (MI) ranks 1st in the group of infections with nervous system damage (neuroinfections) in children.
- It is characterized by the periodicity of epidemic outbreaks.

- MI is spread all over the world.
- It occurs sporadically annually with a higher incidence in winter and spring.
- Large epidemics break out at intervals of 8-30 years, mainly affecting children's communities.
- The overall lethality in invasive MI is estimated at 10-12%.
- Nosocomial infections with meningococcus are possible.

# Etiology

- The causative agent of (MI) is *Neisseria meningitides* - diplococcus, gram-negative and placed outside the cells, but also inside the cells.
- it is very unstable in the external medium
- it is sensitive to antibiotics like as penicillin, chloramphenicol, cephalosporine gen. III;
- optimal temperature is 36-37°C;
- There has been established 12 serotypes of meningococci (according to antigenic structure: A, B, C, D, E, X, Y, Z, 135W, etc.). Type A is associated with epidemic outbreaks of the disease, types B and C cause sporadic cases of the disease.

# Epidemiology

## The sources of infection:

- sick persons with nasopharyngitis;
- patients with generalized forms;
- carriers of meningococcus.

## Ways of transmission:

- aerial-droplet route;
- indirect route – through infected objects (rarely);
- transplacental route (described by some authors).
- High contagiousness.

## Susceptibility:

- is maximal at children (70-80%);
- 50% - at small children till the age of 5 years;
- 20-40% at infants;
- extremely rare – at newborns;
- 50% of newborns are immune to meningococcal infections, and after 6 months develop a maximal susceptibility.

## Immunity:

- Is specific for the group of causative agent.

# Pathogenesis:

- **The portal of the infection entry** is the nasopharyngeal mucosa.
- nasopharyngeal (adaptation of meningococci, carriage, nasopharyngitis);
- lymph-haematological infection generalisation (meningococemia);
- dissemination of meningococci to different organs and systems, meningitis, meningoencephalomyelitis, myocarditis, arthritis, pneumonia, etc.
- sequels.

# Pathological anatomy

- **Death in children occurs from the following causes:**
- fulminating meningococemia with toxic shock;
- acute cerebral oedema;
- meningoencephalitis;
- meningitis and ependymatits, others.
- **In fulminating meningococemia** develop multiple vascular lesions (thrombosis and extravasates), haemorrhages in organs and tissues, on skin (typical eruptions).
- **In adrenal glands** – atrophy of cortex, necrosis.
- In first hours of the disease, if the child dies, at necropsy it can be seen that meninges of the brain are congested and with serous fluid. **Later, in 3-5 days**, there is a swelling of **meninges**, and a purulent fluid covers the brain – a “**purulent cap**”. Acute oedema of the brain can cause protrusion of the cerebellar tonsil into the great foramen and compression of cerebral trunk. On cerebellar tonsils may be seen ditch of strangulation.
- In all organs are present degenerative changes.

# Classification of the clinical forms (by Pokrovsky V.I.):

- **I. Local forms:**

- Carrier of meningococci
- Meningococcal nasopharyngitis

- **II. Generalized forms:**

- Meningococcemia
- Meningitis, meningoenzephalitis
- Meningitis and meningococcemia (mixte forms)

- **III. Rare forms:**

- Meningococcal endocarditis
- Meningococcal arthritis (poliarthritis)
- Meningococcal iridocyclitis
- Meningococcal pneumonia



# Meningococcal nasopharyngitis

Is the most common clinical form of the meningococcal infection.

## **Onset:**

- **sudden;**
- **fever;**
- **headache;**
- **sometimes vomiting;**
- **painful swallowing;**
- **dry cough;**
- **rhinitis.**

## **Examination:**

- **hyperaemia of the pharynx and hyperplasia of lymphoid follicles**
- **sometimes labial's or nasal herpes**
- **Fever persists 1-3 days.**
- **Duration of the disease is 5-7 days.**
- **In 5-12% cases id a mild and moderate severity of the disease course,**
- **Blood test:**
- **leucocytosis;**
- **neutrophilosis with a shift to the left;**
- **the ESR is increased.**
- **Bacterioscopy shows meningococci within and out of cells.**

# Meningococcal meningitis

- **Onset could be:**
- Acute, violent and usually at a healthy child
- the temperature (39-40°C)
- strong headache
- severe vomiting
- clonic and tonic convulsions
- hyperaesthesia of the skin
- coma
- menyngeal signs and CSF changes.

# Menyngeal signs:

- Rigidity of the occipital muscles (develops early and is persistent)
- Kernig's sign
- Brudzinsky's sign (superior, medium and inferior) that are not so manifested according to the severity of the disease.
- There are possible disturbances of the consciousness till coma.
- If the patient is found late, he may have the syndrome of muscular contraction, that lead to a specific posture of the patient:
  - the head is in a hyperextension to the back and the occipital part is near to the spinal cord;
  - another typical position – the child is lying on his side with the head tossed back and legs flexed to the abdomen and arms are hold between knees.
- The child is pale, hyperaemia of the face, injection of the sclera, red dermographism. It is quiet common the lip and nasal herpes. Osteo-tendinous reflexes are exaggerated, abdominal reflexes are decreased or absent.

# Features peculiar to meningitis in infants

## **Onset of the disease:**

- Restlessness
- Respiratory symptoms
- Fever,
- Convulsions
- Vomiting, diarrhea and refusal to suckle
- Hyperesthesia
- Loudly crying
- Meningeal symptoms are often mild or absent
- Tension and protrusion of the unossified anterior fontanelle are apparent at the beginning of the disease

# Meningitis in the newborn

- ✓ In newborn meningococcal meningitis is rare, manifesting atypically with: fever, convulsions, tremor of the limbs, agitation, cyanosis, constipation.
- ✓ Meningeal signs are not determined (physiological rigidity present).
- ✓ The diagnosis is based on examination of the cerebrospinal fluid.
- ✓ Mortality remains high among the newborns and infants less than three months old

## **Cerebral spinal fluid:**

- flows under increased pressure;
- turbid (as diluted milk);
- purulent;
- cytosis is thousands of cells per  $\text{mm}^3$ , with a marked neutrophilosis;
- a considerable protein content
- sugar content is lowered;
- chlorides are also lower.

## **Blood:**

- manifest leucocytosis;
- neutrophilosis with a shift to the left;
- the ESR is considerably increased.

# MI, meningoencephalitis

Meningoencephalitis occurs in young children.

From the first days, the symptoms of nevrax damage appear and predominate:

- ✓ disturbances of consciousness
- ✓ convulsions
- ✓ paresis, paralysis of cranial nerves
- ✓ Meningeal signs are less expressed
- ✓ Poor prognosis
- ✓ Consequences:
  - sequels (paresis, paralysis, epileptic seizures, mental retardation, etc.)
  - evolution to death

# MI, meningitis and ependymatits

Is found in children up to 1 year. Ependymatits occurs in the first days of meningitis, but may occur later in the case of delayed diagnosis and antimicrobial treatment. Evolving with severe signs of meningoencephalitis:

- ✓ generalized convulsions
- ✓ generalized muscular rigidity
- ✓ opisthotonus
- ✓ urination and involuntary stool
- ✓ cachexy
- ✓ coma

Specific position of the patient:

- ✓ **in hyperextension**
- ✓ **legs are crossed at the level of shanks**
- ✓ **arms are extended with tightened fists**
- ✓ poor prognosis



# **Meningococemia (meningococcal septicaemia)**

It presents a generalized clinical form in which is a complex affection, not just of the skin but also of different organs and systems (lungs, kidneys, adrenal glands, joints, eyes, etc.).

## **The onset is violent with:**

- fever
- chill
- muscular pain
- joint pain
- psychic agitation or apathy
- **typical haemorrhagic eruption appears on the skin at 1-2 day.**

Characteristics of eruption: different size and shape - from petechial to ecchymosis, of a dark red colour, irregular limits (star-like), dense, slightly prominent, frequent with superficial or deep necrosis.

- **Preferred place** – lower limbs and buttocks where they are abundant, less on upper top and upper limbs. If they appear on the mucosa it is a sign of a poor prognosis.
- In severe cases – necrosis of the skin, fingers, nose, ears.

- **At infants** meningococemia has an onset with macular eruptions, maculo-papulous eruptions, being mixed up with rubella, rubeola, allergic rash, scarlet fever.

# **Fulminant meningococemia. (Purpura Fulminans)**

Has a sudden turbulent onset with high fever, chill, confluent hemorrhagic eruption, ecchymosis, necrosis. It is perhaps the most rapidly lethal form of septic shock experienced by humans.

**Waterhouse –Friderichsen syndrom, a dramatic example of DIC-** induced microthrombosis, hemorrhage, and tissue injury. Rapidly septic shock develops (caused by bacteria and their endotoxin) with following clinical signs:

- pale skin;
- cyanosis;
- tachycardia;
- blood hypotension;
- agitation;
- coma;
- Disseminate Intravascular Coagulation Syndrome (DICS)

# Septic shock I degree (compensate)

**General condition of the patient is severe;**

- the child is conscious;
- the skin is pale, dry, warm, hemorrhagic eruption with “star-like” on legs, buttocks;
- hyperhidrosis;
- fever – 38-40°C;
- tachycardia;
- increased respiratory rate;
- BP normal or easily increased;
- urine elimination is normal;
- (DIC) - blood hypercoagulation PHASE .

## Septic shock II degree (subcompensate)

general condition of the patient extremely severe;

- skin is very pale, cyanosis, hemorrhagic eruption with central necrosis on legs, buttocks, trunk, mucosa;
- fever – 39-40°C;
- tachycardia, weak pulse, heart beats are attenuated;
- BP – decreased with 50% in comparison versus normal;
- oliguria;
- adynamia, obnubilation;
- (DIC) - phase blood hypo coagulation.

## **Septic shock III degree (decompensate)**

- general condition extremely severe;
- temperature is subnormale, cyanosis, blood stases like “cadaver spots”, large haemorrhages and deep skin necrosis, multiple also on mucosa;
- extremities are cold;
- weak pulse or is not detectable;
- tachycardia - bradycardia;
- increased respiratory rate then decreased;
- BP- decreased a lot or is not detectable
- convulsions, strabismus;
- sopor, coma;
- anurya;
- (DIC) - blood coagulopathy because of the absence of all coagulation factors.

## Septic shock IV degree (decompensate)

- The patient is in an agonic phase.
- unconsciousness;
- reflexes are absent;
- muscular atony;
- pupils are enlarged;
- cerebral and lung oedema;
- diffuse haemorrhages



# MI, acute cerebral oedema

- high fever;
- disturbances of consciousness – obtundation, sopor, coma;
- clonic and tonic convulsions, generalized convulsions;
- meningeal signs are manifest;
- signs of focal cerebral lesions;
- increased respiratory rate, then decreased respiratory rate, then respiratory stop;
- tachycardia, then bradycardia.

# Cerebral hypotension syndrome (cerebral collapse) in MI.

- more frequent develop at infants who manifest vomiting, diarrhea, high fever;
- general condition deteriorates in a short time;
- clinical features are:
  - ✓ disturbances of consciousness;
  - ✓ convulsions;
  - ✓ hypotonia;
  - ✓ menyngeal signs often are weak or absent;
  - ✓ manifest dehydration symptoms;
  - ✓ CSF flows weakly with rare drops.

## **Meningococcal infection – complications and sequels:**

- acute renal insufficiency;
- acute lung oedema;
- pneumonia;
- deep skin necrosis;
- hydrocephalus (pyocephalus);
- subdural exsudate;
- ependymatitis;
- paresis, paralysis;
- cerebral hypertension syndrome;
- epileptiform syndrome;
- deeply retarded mental development.

# Meningococcal meningitis should be differentiated by :

- purulent meningitis caused by pneumococci, Haemophilus influenzae, staphylococci, enterobacteria, etc;
- serous meningitis (with clear CSF);
- meningismus;
- meningitis in tuberculosis;
- neurotoxicosis in influenza, acute viral respiratory infections;
- acute intestinal infections;
- brain tumours;
- pneumonia.

# **Meningococccemia should be differentiated by:**

- measles, rubeola, scarlet fever;
- allergic eruption at children;
- haemorrhagic eruption (purpura Shonlein-Genoch, Verligof);
- thrombocytopenia;
- septicaemia caused by other agents.

## **Signs of unfavorable prognosis in meningococemia:**

- young age (especially up to 18 months);
- the surface of the skin covered by hemorrhagic eruptions or cyanotic plaques more than 15% of the body surface;
- the existence of a significant or lasting collapse (more than 1 hour);
- alteration of consciousness;
- general blood test: leukopenia, thrombocytopenia.

# Diagnosis

- Clinical findings.
- Epidemiological history.
- Etiological diagnosis is confirmed by following laboratory examinations:
  - bacteriology (CSF, blood, nasopharyngeal secretions) (meningococci grow best on Mueller-Hinton or chocolate blood agar);
  - bacterioscopy (CSF, gross blood drop, skin eruption);
  - immunology :
    - Latex agglutination reaction;
    - Immunophoresis.
    - PCR.

# **Emergency in meningococcal infection at children**

- **Septic shock**
- **Acute cerebral edema**



# Treatment

- Treatment should be started urgently at the prehospital stage and continued during transportation.
- Patients are treated in infectious disease hospitals, in intensive care units.

# Antibacterial therapy

- **antibiotic treatment and duration depends on the clinical form, the evolution of the disease and the laboratory results especially of the cerebrospinal fluid in case of meningitis.**
- most commonly in the treatment of generalized forms are used parenterally:
  - Penicillin G,
  - Chloramphenicol,
  - Cefotaxim ,
  - Ceftriaxone,
  - Meropenem

- The treatment with antibiotics is over, when:
  - general condition is improving;
  - body temperature has been normal at least 3-4 days;
  - CSF – lymphocyte pleocytosis under  $100 \text{ cells} \cdot 10^6/\text{l}$ , glucose is normal, level of proteins is normal.

- **In meningococcal rhinopharyngitis,** treatment includes Ampicillin 50-100 mg / kg / 24 hours 5 days, or Azithromycin 5 mg / kg once daily 3 days, antipyretics, fluids.
- After 3 days of stopping antibiotic therapy, culture of nasopharyngeal secretions will be performed on meningococcus.

# Pathogenetic treatment

- dehydration;
- corticosteroids;
- aniconvulsivants;
- antipyretics;
- cardiac stimulants;
- inhibitors of proteolysis;
- vitamins;
- oxygen.

## **SURVEILLANCE OF PATIENTS WITH GENERALIZED**

**MI** after discharge will be performed by the family doctor and the neurologist or neuropsychiatrist.

- Duration not less than 2-3 years.
- Frequency: year 1 - once every 3 months, years 2-3 - once every 6 months.
- The character of medical supervision: clinical and paraclinical examination (neurosonography, cranial ultrasound, electroencephalography) if necessary.
- In the first 3 months after discharge, avoid: sun exposure, sports.

## **PROPHYLAXIS.**

Meningococcal infection is a disease with compulsory hospitalization.

**Specific prophylaxis** with meningococcal vaccines is not widely performed in all countries. It requires vaccination of people, including children, who leave for countries with an increased incidence of MI (1,2). The existing meningococcal vaccines at the current stage are:

- Bivalent (serogroups A and C) and tetravalent (serogroups A, C, Y, W135) unconjugated polysaccharide vaccines effective in children after 2 years of age.
- Monovalent (serogroup C) and tetravalent (serogroups A, C, W135, Y) conjugated polysaccharide vaccines with the name Nimenrix, which can be given to children from 6 weeks of age.
- Meningococcal vaccines against serogroup B (Bexsero for children from 2 months of age and Trumenda - after the age of 10 years).

## **Nonspecific prophylaxis.**

- Persons who have been in contact with the sick person and in children's communities are monitored for 10 days, examined bacteriologically twice at intervals of 3 and 7 days (in family outbreaks once given).
- Meningococcal carriers are treated the same as patients with meningococcal rhinopharyngitis, antibiotics should be administered as early as possible (first 24-48 hours).
- Bacteriological control is exercised after 3 days.
- In case of repeated isolation of meningococci, a second course of antibiotics with erythromycin or azithromycin 5 mg / kg one dose per day for 3 days (3) is indicated.