"MENINGOCOCCAL

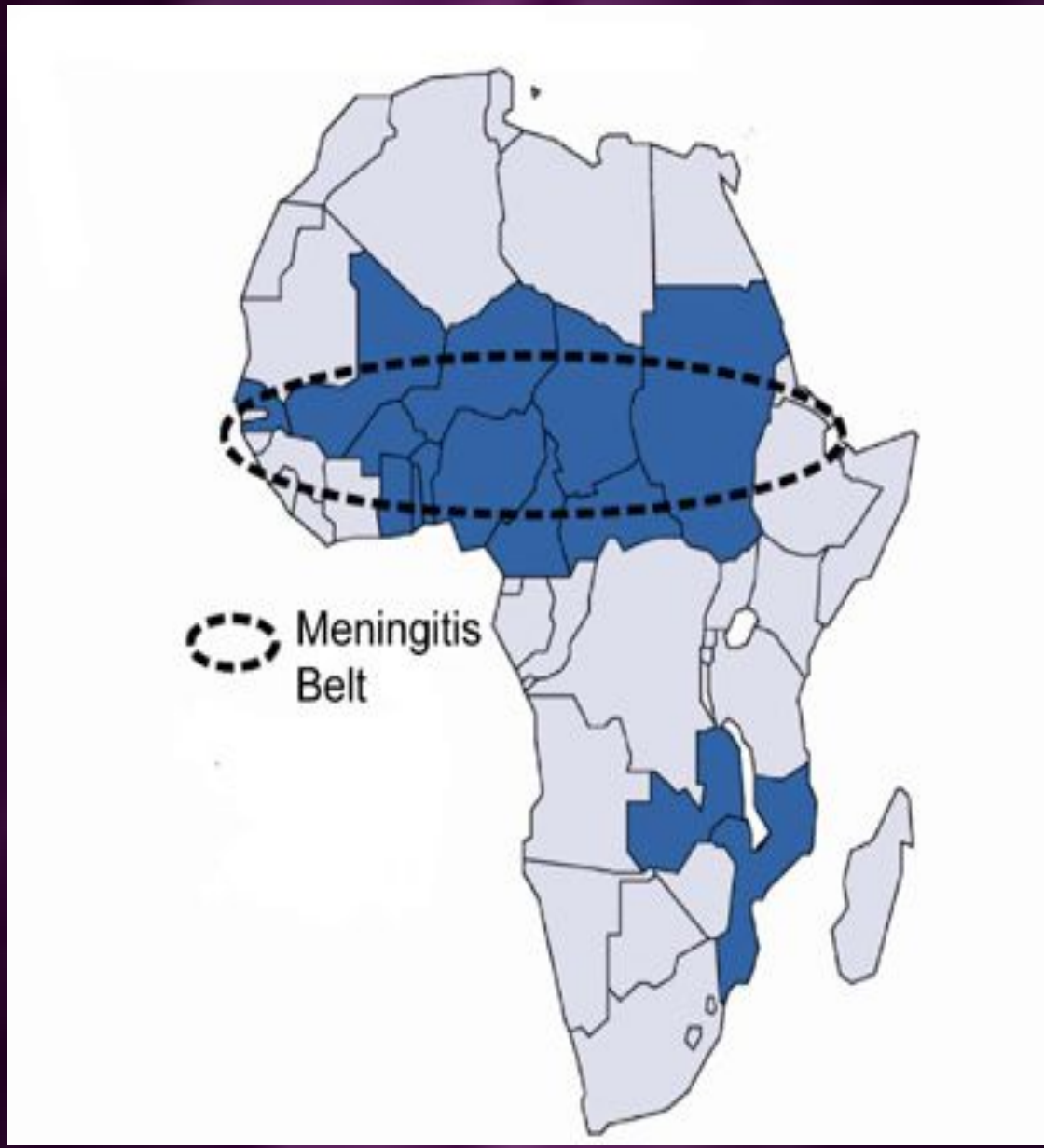
INFECTION"

- **Meningococcal infection**

occurs on the all continents. It is serious problem for public health. It is registered in 170 countries of the world.

- **Meningococcal disease is endemic in India**

The zone lying between 5 and 15 degree N of the equator in tropical Africa is called the "meningitis belt" because of the frequent epidemic waves that have been occurring in that region.



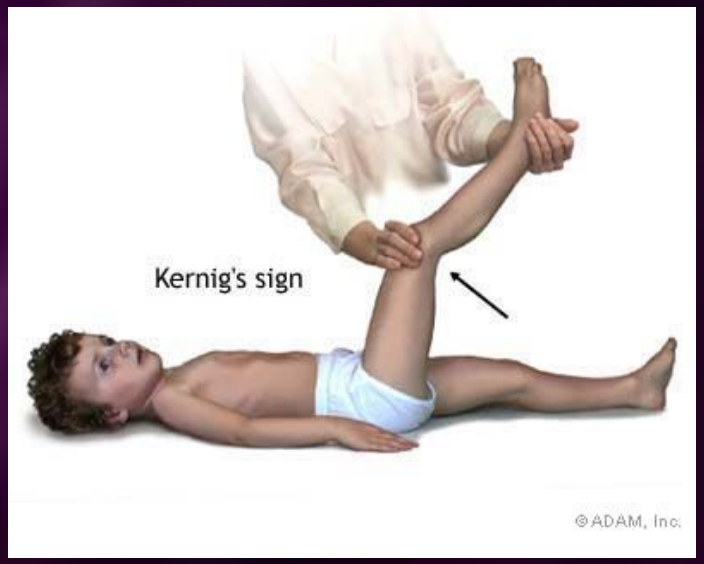
- **Meningococcal infection is an acute infectious disease of the caused by meningococcus Neisseria Meningitidis.**

Meningococcal disease - characterized by fever, intoxication, hemorrhagic rash and purulent inflammation of the arachnoids'membrane

The main clinical syndromes characterize meningococcal infection:

- Intoxication syndrome;
- Hemorrhagic rash

- Meningeal syndrome



- **Waterhause-Fridrechsen syndrome**

Hemorrhages in the adrenal glands and others organs

- **The disease is characterized by damage of the -- mucous membrane of nasopharynx (nasopharingitis);**
- **Generalization of the process in the form of specific septicemia (meningococcemia) and inflammation of the soft cerebral membranes (meningitis).**

The causative agent is Neisseria meningitidis. It is small gramm-negative diplococcus, aerobic, and possesses a polysaccharide capsule, which is the main antigen and determines the serotype of the species.

- **Meningococcus may be seen inside and outside of neutrophils. The main serogroups of the pathogenic organisms are A, B, C, D, W135, X, Y, Z and L.**

- **The serogroupe of a meningococcus is determined by its lipopolysaccharide.**

Serological classification:

- Meningococci are divisible into various serogroups:
- Group A is in most countries, the serogroup associated with epidemic cerebrospinal meningitis. The ability to cause epidemics seems to be associated with certain genetically defined clones;

- Group B meningococci are seen in both epidemic and outbreak situations;
- Group C strains have been associated with epidemics, but more commonly give rise to local outbreaks;
- Serogroup WI35 is occasionally isolated and was associated with a major worldwide outbreak following the pilgrimage to Mecca in 2000 and 2001;
- A few cases due to serogroups X and Y occur;

- **Serogroups Z and 29E (Z') are killed by normal human serum; they rarely cause disease and then only in patients with underlying disease;**

- **Capsule meningococci of serogroups H, I, J, K and L have been described, but not appear to cause disease.**

- Meningococci are very exacting to composition of nutritive mediums.
- Its reproduction may be only in presence of human's protein or animal's protein.
- Due to destruction of the microbe's cell endotoxin is delivered (of lipopolysaccharide origin).
- Exotoxin is no produced.

- The agent of meningococcal infection is characterized by low resistance in the environment.
- Meningococci perish in the temperature 50°C for 5 minutes, in the temperature 100°C - for 30 seconds.
- Meningococci have a little resistance to low temperature.

Epidemiology

- Meningococcal infections occur worldwide and are notifiable in most countries.
- About two-thirds of cases occur in the first 5 years of life.
- The large part of carriers is reveled among adults.
- The morbidity is higher in the towns.

- **The incidence of meningococcal infection is increasing. Acute meningitis causes about 150000 deaths per year.**
- **Epidemic meningitis due to Neisseria *meningitis* (usually group A) is common in a broad belt across sub-Sahara Africa and is also seen in parts of Asia.**
- **In Europe and North America bacterial meningitis is usually sporadic, with B and C strains predominating.**

- Epidemic strains of group A or group B may give rise to a high incidence of disease in sensitive individuals.

- The increase immunity observed with increasing age is likely to be due to asymptomatic infection with avirulent strains, which are carried by 7-20 % of healthy population.

- **The patients with generalized form are more dangerous.**

- **It is proved than they are dangerous for surrounding persons in 6 times than healthy carriers.**

- **However, the main sources of the infection are carriers, because 1200-1800 carriers have occasion to one patients with generalized form of the disease.**

The mechanism of transmission of the infection is air-drop.

The infection is realized in cough, sneezing.

- **In this the narrow contact and sufficient exposition are necessary.**

- **It was proved that the infection is realized on the distance less than 0,5 meter.**

- **In meningococcal infection epidemic process is characterized by seasonal spread.**
- **The morbidity may compose 60-70% from year's morbidity in seasonal rise.**
- **The onset of the seasonal rise is in January in the countries with moderate climate. It achieves of maximum in March – April.**

Pathogenesis

- **In meningococcal infection the entrance gates is mucous membrane of nasopharynx.**
- **It is the place of the primary localization of the agent.**
- **Meningococci cause inflammation of the mucous membrane of the upper respirator tract.**
- **It leads to development of nasopharyngitis**

- **The stages of inculcation on the mucous membrane of nasopharynx and penetration of meningococcus into the blood proceed to entrance of endotoxin into the blood and cerebrospinal fluid.**

- **These stages are realized with help of factors of permeability. It promotes of the resistance of meningococcus to phagocytosis and action of antibodies.**

- **Meningococci are able to break local barriers with help of factors of spread (hyaluronidase).**
- **Capsule protects meningococci from phagocytosis.**
- **Hematogenous way is the principal way of the spread of the agent in the organism (bacteremia, toxinemia).**
- **Only the agent with high virulence and invasive strains may penetrate through hematoencephalic barrier.**
- **The strains of serogroup A have a high invasiveness.**

- **Meningococci penetrate into the blood after break of protective barriers of the mucous membrane of the upper respiratory tract. There is hematogenous dissemination (meningococcemia).**

- **It is accompanied by massive destruction of the agents with liberation of endotoxin.**

- **Meningococcemia and toxinemia lead to damage of endothelium of the vessels. Hemorrhages are observed in the mucous membrane, skin and parenchymatous organs.**

- **It may be septic course of meningococcemia with formation of the secondary metastatic focuses *in* the endocardium, joints, internal mediums of the eyes.**
- **In most of the cases penetration of meningococci in the cerebrospinal fluid and the soft cerebral membranes is fought about by hematogenous ways through the hematoencephalic barrier.**

- Thus, the meningococci enter into subarachnoid space, multiply and course serous-purulent and purulent inflammation of the soft cerebral membranes.
- In severe course of the inflammatory process may lead to involvement of the brain's matter into inflammatory process and development of meningoencephalitis.
- In some cases the process may turn into ependima of the ventricles.

In the pathogenesis of meningococcal infection toxic and allergic components play an important role.

- **Thus, in fulminant forms of meningococcal infection toxic shock develops due to massive destruction of meningococcus and liberation of the considerable quantity of endotoxin.**
- **In toxic shock the development of thrombosis, hemorrhages, necrosis in different organs are observed, even in adrenal glands (Waterhause-Fridrechsen syndrome).**

The severe complication may develop as a result of expressive toxicosis.

- **It is cerebral hypertension, leading frequently to lethal outcome, cerebral coma.**

  This state develops due to syndrome of edema, swelling of the brain with simultaneous violation of out flow of cerebrospinal fluid and its hyperproduction.

- **The increased volume of the brain leads to pressure of brain's matter, its dislocation and wedging of medulla oblongata into the large occipital foramen, pressure of oblong brain, paralysis of the breath and cessation of the cardiovascular activity.**

Clinical manifestation

Classification of the clinical forms of meningococcal infection:

I. Primarily localized forms:

- **a) meningococcal carrier state - in meningococcal carriers the clinical manifestations are absent.**
- **b) acute nasopharyngitis;**
- **c) pneumonia.**

II. Generalized forms:

- a) meningococcemia: typical, acute meningococcal sepsis; chronic;
- b) meningitis; meningoencephalitis;
- c) mixed forms (meningococcemia + meningitis, meningoencephalitis).
- d) rare forms (endocarditis, arthritis, iridocyclitis).

The incubation period is 1-10 days, more frequently 5-7 days.

Meningococcal nasopharyngitis

- The most common complains of the a patients are headache, mainly in the frontal-parietal region, sore throat, dry cough, blocked nose, fatigue, weakness, loss of the appetite, violation of the sleep.
- In the most of the patients body temperature rises up to subfebrile and lasts for not more than 3-7 days.
- The skin is pale, conjunctival vessels and sclera are injected.

Meningococcal nasopharyngitis

- There are hyperemia and edema of the mucous membrane of the nose. In many patients the posterior wall of the pharynx is covered by mucous or mucous - purulent exudation. Inflammatory changes in the nasopharynx can be noticed after 5-7 days, hyperplasion of lymphoid follicles lasts longer.
- In the peripheral blood moderate leukocytosis with neutrophylosis and a shift of leukocytes formula to the left. Nasopharyngitis often precedes to development of generalized forms of the disease.

Meningitis

- It may start after meningococcal nasopharyngitis, but sometimes primary symptoms of the disease arise suddenly.
- In meningitis three symptoms are constantly revealed:

fever,

headache,

vomiting.

- Temperature increases quickly with chill and may reach 40-41° for few hours.
- The patients suffer from severe headache, having diffuse or pulsatory character.
- Headache is very intensive at the night. It increases due to change of the body position, sharp sounds, bright light.
- Vomiting arises without precedent nausea. There is no connection with food and relief after vomiting. It is, as rule, plentiful, by "fountain", repeated. Sometimes, vomiting arises on the peak of headache.

- **The disorders of consciousness occupy the great place in the clinical picture (from sopor till coma).**
- **On objective examination meningeal symptoms stand at the first place.**
- **It is described near 30 meningeal signs. A few meningeal signs are used in practice:**

rigidity of occipital muscles, Kernig's symptom, Brudzinsky's symptom (upper, middle and lower).

- The fulminant course of meningitis with syndrome of brain swelling and edema is the most unfavorable variant.
- There is hypertoxicosis in this form and high percentage of the mortality. The main symptoms are consequence of inclination of the brain into foramen magnum and strangulation of medulla oblongata by tonsils of cerebellum.
- Bradycardia appears. Then it is changed by tachycardia. Arterial pressure may fall catastrophically, but it increases more frequently till high level.
- Tachypnoe arises till 40-60 times/min._Death occurs due to respiratory failure at the first hours of the disease, rarely on 2-3 day or on 5-7 day.

Meningococcemia (meningococcal sepsis).

- The disease is more impetuous, with symptoms of toxicosis and development of the secondary metastatic foci. The onset of the disease is an acute. Body temperature may increase up to 39-41°C.

- The rash appears during the first hours.

  Rash: hemorrhagic, solid, confluent with areas of necrosis. Patients die from the symptoms of acute circulatory failure due to hemorrhage in the adrenal glands.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- Exanthema is more clear, constant and diagnostically valuable sign of meningococcemia.
- Dermal rashes appear in 5-15 hours, sometimes on the second day from the onset of the disease.
- Hemorrhagic rash is more typical (petechias, ecchymosis and purpura). The elements of the rash have incorrect ("star-like") form, dense, coming out over the level of the skin.

- **The deep and extensive hemorrhages may be necrotic. Then it may be formation of deep ulcers. Sometimes deep necrosis is observed on the limbs and also, necrosis of the ear, nose and fingers of the hands and legs. On biopsy meningococci are revealed.**

- **Meningococcal sepsis is combined with meningitis in the majority cases.**

  In 4-10 % of the patients meningococcemia may be without injury of the soft cerebral membranes.

Laboratory diagnostic

Specific methods

- **Bacteriological method**
- **Material for bacteriological examination - a smear of the mucous nasopharynx**
- **blood, cerebrospinal fluid. synovial fluid, skin**
- **latex agglutination and by PCR.**
- **Microscopic method (blood, cerebrospinal fluid - Identification diplococci)**

Nonspecific methods

- **General blood test**
- **clinical analysis of cerebrospinal fluid**
- **coagulagram**

The examination of cerebrospinal fluid (CSF) has the great meaning in diagnostics of meningitis.

On lumbar punction cerebrospinal fluid is

- flows out under high pressure and with frequent drops;
- opalescent in initial stages of the disease;
- Later it is turbid, purulent, sometimes with greenish shade;
- Pleocytosis is high. Pleocytosis achieves till several thousands in 1 mcl.
- Neutrophils leukocytes predominate in cytogram; Neutrophilous compose 60-100 % of the all cells;
- Quantity of protein of cerebrospinal fluid increases.

Treatment

- The therapeutic tactics depends on the clinical forms.
- In the moderate and middle serious course of nasopharyngitis antibacterial remedies are used.
- Peroral antibiotics oxacillin, ampyox, chloramphenicol, erythromycin are administered. The duration of the therapy is 5-7 days and more.

- In the therapy of generalized forms of meningococcal infection used Benzylpenicillin in dosage of 300 000 IU/kg/day.
- In the severe form of meningococcal infection daily dosage may be increased up to 500 000 lU/kg/day.
- Such doses are recommended particularly in meningococcal meningoencephalitis.
- In the presence of ependimatitis or in the signs of the consolidation of the puss the dose of penicillin increases up to 800 000 IU/kg/day.

- Daily dose is injected to the patient every 3 hours. In some cases interval between injections may be increased up to 4 hours. The duration of the antibiotic therapy is decided individually depending on clinical and laboratory data.

- It is necessary to research of a spinal liquid for an estimation of efficiency of antibacterial therapy. If at control research (in 7-10 days of antibacterial therapy) pleocytosis has decreased less than 100 cells in 1 mcl and predominate lymphocytes, antibacterial therapy can be stopped.

- If pleocytosis more than 100 cells in 1 mcl or predominate neutrophyles antibacterial therapy is necessary for continuing. In 3-5 days of therapy it is necessary to investigate a spinal liquid again.

- In meningococcal infection chloramphenicol is highly effective. It is the medicine of the choice in the fulminant meningococcemia. Chloramphenicol is used in dose 50-100 mg/kg 4 times per day. The duration of the treatment of the patients is 6-10 days.

Prophylaxis

- Prophylactic measures, directing on the sources of meningococcal infection include early detection of the patients, sanation of meningococcal carriers, isolation and treatment of the patients. The measures, directing on the rupture of the mechanism of the transmission of the infection, is concluded in disinfection.

- Vaccination