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COXIELLOSIS (Q-FEVER)

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Etiology, epidemiology of Q fever

The causative agent of the disease is the bacteria of the species *Coxiella burnetii* (Burnet's rickettsia), which belong to the class of gamma-proteobacteria, the order Legionellales, the Coxiellaceae family, the genus *Coxiella* (a microorganism of pathogenicity group II).

Coxiella are gram-negative, obligate, intracellular pathogens that cause disease in a wide range of domestic and wild animal and bird species. In natural foci, the reservoir of coxiella are ixodid and argas ticks, wild small mammals, among domestic animals the main carriers are small and large cattle. *C. burnetii* persists in the stool, urine, and tissues (especially the placenta) of animals, so the infection is easily transmitted through both objects and airborne droplets. The reservoir of *C. burnetii* is maintained in nature through the animal-mite cycle, but arthropods are not involved in infecting humans.

Coxiella are highly invasive, can penetrate the mucous membranes and microtraumas of the skin. The risk group is people who provide veterinary care to sick animals, who are engaged in slaughtering and butchering carcasses. The pathogen exhibits significant survival in the external environment, especially at low temperatures and in a humid environment.

Coxiella have a high virulence for humans: the infectious dose in some cases is less than 10 cells.

Coxiellosis is considered as a multi-organ disease, in which a number of organs and systems are involved in the pathological process. Rickettsia enter the human body through the skin or mucous membranes, while a characteristic feature of Q fever is the absence of any changes at the site of introduction of the pathogen. Then they enter the blood (it has been established that Burnet's rickettsiae multiply mainly in mononuclear phagocytes) and then into the parenchymal organs. Here they multiply and again enter the bloodstream, where they partially die and release the toxin.

The phase of secondary large rickettsemia, or generalization of the process, leads to the emergence of new (additional) foci in the internal organs. The destruction of cells is accompanied by the release of the pathogen into the intercellular space, where one part of the rickettsia dies, and the other gets into new cells or into the blood. The defeat of cells, the release of rickettsiae into the intercellular space with the defeat of new cells, just like in other rickettsiosis, is a multiple process.

In the internal organs, secondary foci of infection are formed, an allergic restructuring of the body is underway. The process continues until the formation of a humoral antibody reaction of sufficient intensity, or, in case of chronicity, coxiella continue to persist in target cells. If immunity is formed slowly, repeated phases of rickettsemia repeat for a long time. A protracted and chronic course of the disease is formed, which leads to allergization of the body and the development of autoimmune processes.

The chronic form of coxiellosis develops with a frequency of 5 to 10% of cases. Most often, patients with the chronic form develop coxiella endocarditis. In 40-45% of patients with immunodeficiency and previous cardiovascular pathology, in particular heart valves or with their prostheses, coxiella endocarditis can manifest itself, bypassing the acute form of the disease.

Clinical classification of Q fever

According to the predominance of the clinical syndrome, the following forms of Q fever are distinguished:

- 1) typical (febrile);
- 2) bronchopneumonic;
- 3) typhoid;
- 4) brucellosis-like;
- 5) nervous.

According to the duration of the course, the forms of the disease are distinguished:

- acute - the duration of the disease is 2- 4 weeks;
- subacute or protracted - the duration of the disease is 1-3 months;



- chronic - from several months to one year or more;
- erased.

Q fever symptoms and syndromes

The incubation period lasts from 2 to 60 days, on average - 19–21 days. The clinical picture in patients with coxiellosis is characterized by pronounced polymorphism.

Almost always (98% of cases), Q fever begins acutely with a headache, tremendous chills, and general malaise. Already in the first hours of the disease, body temperature reaches high numbers (38-40 ° C). Patients complain of muscle pain, pain in the joints and in the eyeballs. Dizziness, nausea, rarely vomiting, nosebleeds are noted. The duration of the febrile period can reach 3 weeks, averaging 15 days.

With a subacute onset of the disease, the disease develops gradually with a feeling of discomfort, mild malaise; sweating, weakness, headache appear, the temperature rises to 37.5–38.5 ° C.

In the absence of specific treatment, fever lasts 8-14 days, in a third of patients - 3-7 days. Within a few days, signs of damage to various organs gradually join, in particular pneumonia (832% of cases). Patients complain of pain and tightness in the chest, cough, often dry, sometimes shortness of breath. Objectively, dullness of percussion sound is noted, with auscultation - hard breathing, dry or wet rales.

The X-ray picture in the lungs does not have any features that make it possible to establish its coxiella origin and distinguish it from lung lesions of another etiology. It has the character of atypical interstitial pneumonia: the transparency of the alveoli decreases, the basal bronchial pattern increases, blackouts appear in the form of separate foci of a rounded shape with blurred contours of various densities. There are cases of dry and exudative pleurisy.

Complete radiological resolution of the process often occurs only 6 months after the onset of the disease. As a rule, the development of pneumonia is associated with the age of patients, the presence of immunodeficiency states and concomitant diseases.

Often in the course of the disease, an exanthema of a polymorphic nature appears: maculopapular or roseolous-papular.

Changes in the cardiovascular system are manifested by the development of bradycardia, hypotension, as well as muffled and even muffled heart sounds, which requires mandatory differential diagnosis with myocarditis of coxiella etiology.

Damage to the hepatobiliary system is manifested by hepatomegaly (100% of cases). In addition, patients may develop specific rickettsial hepatitis.

Damage to the nervous system. All patients with coxiellosis have symptoms of damage to the functions of both the central and peripheral nervous systems of varying severity. One of the leading symptoms is headache. Another important sign of damage to the central nervous system in patients with coxiellosis is insomnia or interrupted (restless) sleep. The defeat of the peripheral nervous system is observed in the form of myalgia, arthralgia. Signs of damage to the autonomic nervous system occur almost constantly: patients complain of general weakness, chills, excessive sweating.

Thus, for practicing physicians, the clinical diagnosis of coxiellosis presents significant difficulties, firstly, due to the rare occurrence, and secondly, due to the polymorphism of clinical symptoms.

Q fever diagnosis

Of great importance for diagnosis is a correctly collected epidemiological history [work in animal husbandry, maintenance and care of large and small cattle, poultry, consumption of raw milk, dairy (cottage cheese, cheese) and meat products that have not undergone sufficient heat treatment].

Laboratory diagnostics

There are no specific changes in the general blood test. More often, a normal or reduced number of leukocytes, lymphocytosis, and a moderate increase in ESR are recorded.

The main role is acquired by methods of special diagnostics. In Russia, these are ELISA and PCR methods. In ELISA, a titer of 1:400 IgM antibodies and 1:200 IgG antibodies is taken as the minimum diagnostic level of antibodies in human blood serum. In the PCR method, *Coxiella burnetii* DNA is determined in the patient's blood [1].

For the purpose of differential diagnosis, the following additional studies may be required:

- serological blood tests in the RSK, ELISA - for differential diagnosis with typhus, viral hepatitis;
- immunogram (with the study of the CEC) in severe and protracted course of Q fever;
- consultations of specialists: a phthisiatrician (with prolonged pneumonia), a cardiologist (if there are symptoms indicating myocarditis or endocarditis), a rheumatologist (if there is pain in the joints, prolonged fever with an increase in C reactive protein, changes in rheumatoid tests).



Instrumental research methods

- X-ray of the lungs, ECG;
- ultrasound examination of the abdominal organs;
- echocardiography.

Vaccine prevention of Q fever

Various versions of the vaccine for the prevention of coxiellosis were developed in Russia, the USA, and Czechoslovakia. Due to the high reactogenicity and insufficient immunological efficacy, these vaccines have not been widely used in practice. Vaccination of people as a means of preventing the disease is currently recommended only for contingents at high risk of infection, i.e. veterinarians, shepherds, slaughterers, engaged in the primary processing of goat down, skins and wool of farm animals.

In the Russian Federation, a live attenuated vaccine based on the M-44 strain (KU fever vaccine M-44 live) is used. Specific prophylaxis for Q fever is permitted from the age of 14 years.

The vaccine is a lyophilizate for the preparation of a suspension for skin scarification application. A single injection of the vaccine is accompanied by the development of specific immunity 3–4 weeks after vaccination. The vaccine is administered once percutaneously by the method of scarification at a dose of 0.05 ml.

Revaccination is carried out with a dose of 0.05 ml not earlier than 1 year after the primary vaccination for persons whose serum does not contain specific complement-fixing antibodies.

The vaccination site (the outer surface of the middle third of the shoulder) is treated with a 70% alcohol solution or ether (the use of other disinfectant solutions is not allowed). After their evaporation with an eye dropper or syringe, 2 drops of the diluted vaccine are applied through the needle at a distance of 30–40 mm. With a sterile scarifier, through each drop of vaccine applied to the skin, three cross-shaped notches 8–10 mm long are made at a distance of 3–4 mm from each other so that the blood appears as small “dewdrops”. The flat side of the scarifier rubs the vaccine into the notches, after which the vaccine should dry for 5–10 minutes.

Subsequent treatment of the vaccination site is not carried out.

The general reaction to the vaccination develops on days 2-3 in some vaccinated and is expressed in a one-day malaise, chills, headache and fever up to 37.5 °C.

A local reaction, characterized by redness and nodular swelling along the incisions, usually develops in at least 90% of those vaccinated. The duration of the local reaction is 3-4 days.

Specialized, including high-tech, medical care is provided by infectious disease doctors with the involvement of the necessary specialist consultants and includes the prevention, diagnosis, treatment of diseases and conditions that require the use of special methods and complex medical technologies, as well as medical rehabilitation.

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