MODERN CONCEPTS AND EPIDEMIOLOGICAL ASPECTS OF BRUCELLOSIS

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Among more than 180 nosological forms of zoonotic infectious diseases, brucellosis remains significant due to the scale of economic damage to livestock and public health. Brucellosis is an infectious, particularly dangerous zoonotic disease caused by bacteria of the genus *Brucella*, which is transmitted from animals to humans and is characterized by a severe and often chronic course [1, 8].

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Brucellosis poses a significant problem for public health worldwide. According to the WHO, more than 500,000 new cases of this disease are registered annually. Brucellosis is typically diagnosed only when a chronic process has developed, with nearly one in four patients experiencing a persistent loss of work capacity. Given that the infection primarily occurs in individuals of working age (20-50 years), the costs associated with disability payments, treatment, and rehabilitation are substantial. Although bacteriological confirmation of brucellosis infection is only reported in 3-10% of cases in practice, the isolation of the causative agent in culture provides absolutely reliable confirmation of the disease diagnosis. Determining the species and biovar of the isolated strain is crucial for epidemiological investigations, as well as for establishing the tactics and scope of necessary epidemic control measures.

The socio-economic significance of the brucellosis problem is determined by the characteristics of this infection, which often leads to chronic forms and frequently results in prolonged loss of work capacity and sometimes disability. The primary affected population is the working-age population, which is linked to both occupational factors and social reasons [18,19].

Brucellosis remains the leading cause of occupational diseases of infectious and parasitic origin. The disease was first described in 1860 by British Army physician J.A. Maraston as "Mediterranean remittent fever" during his time in Malta. The causative

agent of the disease was isolated in 1887 from the spleens of five English soldiers who died from the fever in Malta by D. Bruce, who named the bacteria *Micrococcus melitensis*. Later, the bacterial agent was renamed in his honor, and the disease became known as Malta fever. In 1920, similar bacteria isolated from other animals were classified into a single genus named *Brucella* after D. Bruce, and the disease they caused was termed brucellosis.

The causative agents are aerobic and microaerophilic non-motile gram-negative bacteria of the genus *Brucella*. According to international classification, the genus *Brucella* consists of seven distinct species, which are further divided into several biovars (Table 1). Four representatives are pathogenic to humans: *B. melitensis*, *B. abortus*, *B. suis*, and *B. canis*. *B. melitensis* includes three biovars, with goats and sheep as its main carriers. *B. abortus* has seven biovars, with cattle being the primary host. *B. suis* consists of five biovars, with pigs as the main host; however, the second biovar is also found in rabbits, the fourth in deer, and the fifth in murine rodents. *B. neotomae* has been identified in desert woodrats, *B. ovis* is isolated from sheep, and *B. canis* from dogs. Two new species of *Brucella* have recently been identified: *B. cetaceae* and *B. pinnipediae*, isolated from marine mammals, cetaceans, and pinnipeds [15,16,17].

Brucella species exhibit significant polymorphism: in a single preparation, both cocci and elongated bacilli can be observed. They are facultative intracellular gramnegative coccobacilli, lacking capsules, flagella, spores, and native plasmids. *Brucella* grow slowly; sometimes growth can only be detected in the third or fourth week. When cultured on solid media, two types of colonies are formed: S colonies, which are round, convex, up to 0.5-3 mm in diameter, opaque, smooth, with a pearlescent sheen, and R colonies, which are rough, initially transparent, and then become opaque. R colonies form through dissociation when growth conditions change. *Brucella* are subject to variability and can transition from the S form to R and L forms, the latter being the most variable and likely contributing to the prolonged course and chronicity of the disease. *Brucella* have a lipopolysaccharide outer membrane that is less pyrogenic than that of other gram-negative microorganisms, which accounts for the relatively rare occurrences of high fever in this disease [11,12,13,14].

Brucella is characterized by a significant number of antigens, with the antibody response primarily driven by lipopolysaccharide (LPS). There are two types of LPS: R-LPS from rough or non-smooth colonies of *Brucella* strains, and S-LPS from smooth colonies, which are similar to each other, except for the O strains, where LPS is either absent or present in residual amounts. The S-LPS contains two main antigens: the A antigen (predominantly found in *Br. abortus* and *Br. suis*) and the M antigen (predominantly found in *Br. dolera, salmonellosis, yersiniosis, as well as



E. coli O116, which may account for false-positive reactions in serological tests. The S-LPS in the bacterial cell wall is considered a virulence factor of *Brucella* and plays a role in blocking innate and species-specific immunity in the early stages of infection. It also protects the pathogen from the bactericidal activity of the immune system, inhibits the development of apoptosis in infected cells, and disrupts the infected cell's ability to recognize foreign antigens [8,9,10].

The natural reservoir for *Brucella* in the environment is animals. The main sources of infection for humans are sheep, goats, cattle, and pigs, which are carriers of the three main species of the pathogen (*B. melitensis*, *B. abortus*, *B. suis*). Less commonly, human infections can be caused by *B. canis*, *B. cetaceae*, and *B. pinnipedialis*. The routes of brucellosis transmission are diverse, as *Brucella* is excreted by infected animals through all excretory systems [4,5,6,7]. Transmission of the brucellosis pathogen to humans occurs through contact, alimentary, and less frequently, aerosol routes, and combined transmission routes are possible. Factors transmitting the infection from sick animals to humans include animal-derived raw materials (wool, down, hides), meat and dairy products, contaminated animal care items, feces, and other objects infected with *Brucella*. The role of humans in the transmission of brucellosis infection is not epidemiologically significant. However, there is evidence of the possibility of *Brucella* infection being transmitted from mother to fetus via the placenta, during childbirth, and through breastfeeding. Isolated cases of infection have been reported following blood transfusions, bone marrow transplants, and contamination of medical personnel during cesarean sections. There have also been cases of brucellosis transmission through sexual contact between spouses. In one instance, the husband exhibited clinical manifestations of brucellosisrelated orchiepididymitis, while in another case, *Brucella* DNA was detected in semen [1,2,3].

The contact transmission mechanism plays the largest role in brucellosis outbreaks. The risk of infection is particularly high when assisting animals during childbirth and abortions, especially when manually separating the placenta. Infection can also occur during the processing of meat, hides, wool, and skins from animals infected with brucellosis (workers in the meat processing, leather, and wool industries). In these cases, *Brucella* can enter the human body through the skin. The small size of the infectious agent and its high invasive capacity allow *Brucella* to penetrate intact skin. In contact transmission, the bacteria can also enter through the mucous membranes of the eyes, nose, and oral cavity [4,5,6,7,8,9].

The alimentary route of brucellosis transmission is possible through the consumption of food products derived from infected animals. Raw milk and dairy products (such as feta cheese, cream, sour cream, and koumiss) pose the greatest risk. Cow's milk is responsible for infecting many individuals (especially in urban areas)

who are not professionally involved in animal husbandry. Meat presents significantly less epidemiological danger, as it is typically consumed in a thermally processed form. However, in some cases, undercooked meat and meat products can lead to brucellosis infection. The aerosol route of transmission can occur during shearing sheep, collecting down, cleaning livestock enclosures, processing hides, slaughtering animals, and other production activities associated with the care of infected animals or the handling of products and raw materials obtained from them [10,11,12,13].

The aerosol route of transmission is also possible in bacteriological laboratories during various manipulations involving pure cultures (such as subculturing and centrifugation), which can generate aerosols. Incidence is particularly noted among individuals who have close contact with infected animals (such as shepherds, herders, farm workers—including those in fur farming, veterinary specialists, and dairy workers). In brucellosis outbreaks among livestock, cases are often reported in people of all age groups, from preschool children (including infants) to the elderly. The seasonality of brucellosis incidence in humans is related to agricultural activities, particularly the care of livestock [18,19,20,21].

Particular attention should be paid to the times of calving, lambing, and abortions, as well as to the care of animals during the postpartum period and during sheep shearing and grooming. Human brucellosis caused by caprine and ovine species typically exhibits a spring-summer seasonality. Infections from cattle show a weaker seasonality, which is explained by the prolonged lactation period and the primary transmission through milk and dairy products.

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