

EPIDEMIOLOGY, DIAGNOSIS, TREATMENT, CONTROL AND ECONOMIC IMPACT OF BRUCELLOSIS

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Abstract

Brucellosis is an infectious disease produced by bacteria of the genus Brucella spp. This disease mainly affects cows, sheep and goats, pigs and dogs. It is a zoonosis in humans it can be transmitted by 4 species of Brucella: B. suis, B. abortus, B. canis and B. melitensis, the latter being the most virulent. In animals the disease has a higher frequency of transmission during birth or abortion this being possible due to the fact that the bacteria colonize in the pregnant uterus. Once in the external environment, bacteria can survive for a long time, especially in wet and cold conditions, thus being able to be ingested by other animals. Colonization of bacteria at the level of the udder causes milk contamination. Male sperm, blood, urine and faeces of sick animals are also sources of contamination. The disease is transmitted to humans through the consumption of unpasteurized or insufficiently pasteurized milk or dairy products, consumption of meat prepared thermally insufficient or by direct contact with the infected animals, bacteria that enter the body through wounds on the skin or mucous membranes. The people most exposed to infection with Brucella spp. are represented by veterinarians, workers in slaughterhouses or farms, microbiologists. Human-to-human transmission of this zoonosis has proven to be extremely rare, but nursing mothers can transmit the infection to their children.

Key words: Brucellosis, Brucella spp., humans, zoonosis.

INTRODUCTION

Bacteria of the genus *Brucella* are small, coccoid or colibacillary bacteria, non-encapsulated and non-sporulated, facultative intracellular, Gram-negative. Regarding cultivation conditions and cultural characteristics, sponges need special environmental conditions to develop. The culture media they prefer are broth, agaul and potato, to which one or more of the following ingredients are added: glycerin 2%, glucose 1% or serum 1-5%. Cultural aspects are different depending on the environment. In the liquid environment, after a few days of incubation, moderate turbidity is observed, gray deposit, sometimes a ring is visible on the surface. On a solid medium, the cultural aspects differ depending on the medium used. On glycerol-glucose agar, the colonies are small, round, opaque and glossy. On glycerinated potato medium, the colonies of *Brucella* appear glossy, yellowish in color, with aging they

become chocolate-brown. In cultures, the bacteria last up to about 2 months. Brucellosis, also called Malta fever or wavy fever, is an anthroozoonosis described for the first time in Malta, in 1861. It is found globally and present in most countries, the incidence being different depending on the number of inhabitants and receptive animals (Qureshi et al., 2023; Şuler et al., 2019).

In Romania, it was identified for the first time in cattle in 1923, followed by pigs in 1934 and rams in 1958. It was diagnosed in humans for the first time in 1939, the 4 transmissible *Brucella* species being *B. suis*, *B. abortus*, *B. canis* and *B. melitensis*, the latter being the most widespread worldwide (Zamri-Saad & Kamarudin, 2016; Díaz Aparicio, 2013).

In animals, the symptoms are different. In cattle, the main symptom is the abortion that occurs in the 6-7 months of gestation, the fetal fluids are cloudy, yellowish in color, placental retention, endometritis, the decrease in volume and the

change in the composition of the milk. In males, epididymitis, testicular enlargement, fever are observed. The incubation period can last between 10 and 239 days, depending on the physiological state of the infected organism (eur-lex.europa.eu; Hull & Schumaker, 2018).

In sheep and goats abortion occurs in the 3-4 months of gestation, placental retention with temporary sterility, mammary glands and nodules in the mammary gland, changes in milk - milk with blood clots and in males epididymitis and reduced fertility (Qureshi et al., 2023; Hull & Schumaker, 2018).

Abortion does not occur in sows, farrowings have time to term, but the viability of the products is reduced, placental retentions and mammitis have a lower frequency, but uterine infections, inflammation of the lymph nodes and arthritis occur instead. In males, inflammation of the testicles can be observed (Qureshi et al., 2023).

In humans, the symptoms of brucellosis are varied, fever being a characteristic symptom. This may be persistent or intermittent, accompanied or not by night sweats. Excessive fatigue and general weakness, muscle and joint pains and swelling that can affect mobility, headache that can vary from mild to severe, constant or intermittent, gastrointestinal symptoms - nausea, vomiting, abdominal pain or diarrhea, and neurological - in more severe forms, severe headaches, confusion, sleep disorders or even depression may appear, they are manifestations that are part of the symptomatology of brucellosis in humans. The average duration of the incubation period is 2 weeks, but it can last between 5 days and several months. *Brucella* are transported in the lymphatic system and can replicate there locally; they can also replicate in other organs such as the liver, spleen, kidneys, breast tissue or joints, causing both localized and systemic infections (Zamri-Saad & Kamarudin, 2016).

MATERIALS AND METHODS

This article was made through a thorough analysis of bibliographic sources from the specialized literature, relevant to the topic addressed, emphasizing the information related to epidemiology, diagnosis, treatment, control and the economic impact of brucellosis.

RESULTS AND DISCUSSIONS

As far as the epidemiology of the disease in animals is concerned, it is predominantly enzootic, the transmission of the infection from one animal to another being carried out mainly directly, through sexual intercourse or indirectly, through water, feed, various species of ticks or other insects hematophagies. The high frequency of spreading in the external environment occurs during parturition or abortion, considering the tropism of *Brucella* for the pregnant uterus. *Brucella* multiply only in the infected organism, having a long resistance in the external environment, which represents a danger for other animals, these being eliminated through the placenta, fetal fluids, abortions, uterine secretions, milk, because *Brucella* also colonizes the udder, urine and the sperm of sick males (Díaz Aparicio, 2013).

Regarding the sensitivity to environmental factors, it was found that at temperatures of 100°C bacteria are destroyed instantly, at 60-65°C between 5 and 15 minutes, in snow or ice they last up to 4 months. In faeces, litter or feed they have a resistance of up to 5 months, in soil or dust up to 10 weeks, in water up to 125 days. It lasts almost 3 months in frozen meat, and 30 days in salted meat. *Brucella* are sensitive to disinfectants such as chloramine, lime chloride, hydrochloric acid, cresol (Díaz Aparicio, 2013). In humans, the transmission of the disease can be done by several ways, namely (Khoshnood et al., 2022):

- Direct contact with infected animals;
- Direct contact with aborted fetuses, fluids or membranes resulting from abortion;
- Direct contact with infected food;
- Consumption of infected food such as raw, unpasteurized or insufficiently pasteurized milk, cheese or curd;
- Exposure to a contaminated environment.

People can become infected through damaged skin or mucous membranes or by inhaling contaminated particles.

The people most exposed to the risk of infection with the *Brucella* bacterium are those who work in the agricultural field, farm workers or animal breeders, veterinarians, workers in slaughterhouses or in laboratories dealing with the diagnosis of brucellosis. It is not transmitted

from human to human (Khoshnood et al., 2022; Głowacka, 2018).

The morbidity of brucellosis is higher in spring and summer, when calving or abortions take place, especially in sheep and goats (Zamri-Saad & Kamarudin, 2016).

Regarding the diagnosis of Brucellosis in animals, it is based on the described symptomatology, corroborating with data related to the livestock - if new animals were introduced, their area of origin in relation to brucellosis cases. For confirmation, blood samples are collected that will undergo laboratory investigations by bacteriological, serological and allergic method (Zamri-Saad & Kamarudin, 2016).

Brucellosis is one of the diseases for which annual serological tests are required (Corbel, 1997):

- for all sheep and goats over 6 months old;
- all rams and rams for reproduction before the breeding season;
- all animals introduced into the farm;
- 5% of the flock of sheep and 5% of the flock of goats existing in non-professional holdings;
- all cattle over 24 months old;
- all breeding bulls and buffaloes.

The tests performed for brucellosis surveillance are the slow agglutination reaction, immunoenzymatic test - ELISA, polymerase chain reaction - PCR, fluorescent evaluation in polarized light - FPA, complement fixation reaction - CFT, the pink Bengal test - RBT, the ring test performed on the milk sample - MRT (Solera, 2000).

In humans, the diagnosis is based on symptoms corroborated with laboratory tests used to detect *Brucella* spp. bacteria, for a definite diagnosis, in blood or other biological samples such as bone marrow, urine, cerebrospinal fluid - CSF, synovial fluid etc. The most used serological tests are the agglutination reaction, the complement fixation reaction and immunoenzymatic. The first two types detect specific antibodies, to confirm the diagnosis it is necessary to demonstrate significantly increased titers, while the immunoenzymatic tests detect IgG and IgM antibodies, necessary to differentiate acute from chronic infection (Solera, 2000).

An epidemiological investigation is also carried out in which it is followed whether the patient had possible contact with infected animals or consumed products contaminated with *Brucella* bacteria (Solera, 2000; Radwan, 1993).

In patients suspected of brucellosis, the differential diagnosis is (Solera, 2000):

- flu;
- leptospirosis;
- malaria;
- meningitis;
- viral hepatitis;
- enteric fever;
- acute epididymitis;
- urinary tract infections.

In animals confirmed with brucellosis, the prognosis is unfavorable both for the infected animal and for the entire farm because they do not undergo treatment. Infected animals are slaughtered and their corpses are destroyed, and the rest of the animals are put under surveillance for 30 days. There is no treatment, the disease is kept under control by vaccination (Alavi & Alavi, 2013).

In patients confirmed with brucellosis, the treatment consists in the administration of antibiotics chosen according to the severity of the disease and the strain of brucellosis involved. The most common antibiotics are doxycycline, rifampicin, streptomycin, trimethoprim-sulfamethoxazole. In addition to these, medicines can be administered to combat fever and joint pain (Akova et al., 1993; Colmenero, 1989).

In brucellosis-free areas, one of the safest methods of preventing the spread of this pathogen is the close supervision of the areas of origin of animals newly introduced to the farm in relation to brucellosis cases. Ideally, they should come from brucellosis-free areas. Also, to control brucellosis, the following measures are required (who.int.2020; Smirnova et al., 2013):

- avoiding contact between sick or suspected disease animals and healthy ones;
- careful supervision of animal movement;
- medical supervision and isolation of animals at the manifestation of any symptom;
- arranging different spaces for pregnant animals;
- proper hygiene on the farm, especially after farrowing;
- the purchase of animals from disease-free areas;
- performing serological tests and quarantine for 60 days before introducing new animals into the herd;
- immunization of farm animals;
- the annual performance of mandatory analyses;
- the prohibition of the purchase of animals from areas with brucellosis;

- straw, garbage or any other objects with which animals infected with *Brucella* spp. came into contact are immediately destroyed, burned or buried after sprinkling with disinfectant;
- disinfection of paddocks, shelters, equipment before introducing other animals;
- means of transport, containers are cleaned and disinfected after transporting animals from an infected herd.

In humans, to control brucellosis, some important measures are necessary, such as (dambovita.dsvsa.ro; Alavi & Alavi, 2013):

- avoiding contact with infected animals or observing minimum protective measures such as wearing gloves, mask and protective equipment;
- rigorous personal hygiene measures such as washing hands and disinfecting surfaces that have come into contact with animals or products from infected animals;
- consumption of safe products, from healthy animals, properly pasteurized milk;
- vaccination against brucellosis of people who work with animals.

In 2021, 165 cases were confirmed in EU member countries, with a global rate of 0.04 per 100,000 inhabitants. Of these, France, Italy, Spain and Greece had the highest number of reported cases, 67% of all confirmations in EU member states. Luxembourg and Cyprus each reported one confirmed case, but the low population in these two countries resulted in relatively high notification rates. In Sweden, all confirmed cases have travel history to countries with brucellosis cases (Ecdc.europa.eu, 2021).

Also, in 2021, the lowest number of cases was reported in February, and the peak was reached

in May-June. Of the total number of confirmations, 61% are for men and 39% for women (Ecdc.europa.eu, 2021).

In Romania, the last outbreak of brucellosis in animals was liquidated in 1959, since then it has remained silent regarding the infection with *Brucella* spp. (Ecdc.europa.eu, 2021).

Brucellosis is a disease with a great economic impact, because the losses it causes can be very high through abortions, morbidity after parturition, the reduction of productions, expenses related to the eradication of the disease, disinfection and surveillance (Akova et al, 1993).

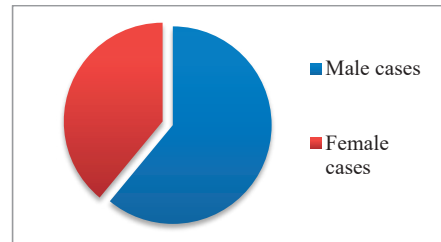


Figure 1. The graph of the percentage difference between the cases reported in men and women (Source: ecdc.europa.eu, 2021)

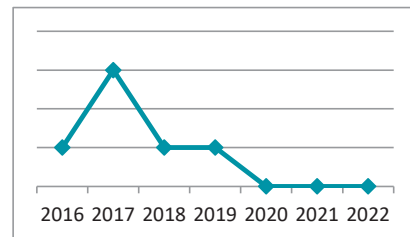


Figure.2. The evolution of human brucellosis cases in Romania (Source:eur-lex.europa.eu, 2016-2022)

Table 1. Number of confirmed brucellosis cases and notification rates per 100 000 population by country and year, EU/EEA, 2017-2021

Country	2017		2018		2019		2020		2021	
	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate
Austria	6	0.07	7	0.08	6	0.07	8	0.09	6	0.07
Belgium	8	0.07	9	0.08	3	0.03	4	0.03	7	0.06
Cyprus	0	0.00	0	0.00	0	0.00	0	0.00	1	0.11
Denmark	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Finland	1	0.02	0	0.00	0	0.00	0	0.00	0	0.00
France	21	0.03	0	0.00	34	0.05	19	0.03	21	0.03
Germany	41	0.05	37	0.04	36	0.04	19	0.02	13	0.02
Greece	94	0.87	97	0.90	65	0.61	30	0.28	24	0.22
Hungary	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Italy	99	0.16	94	0.16	49	0.08	18	0.03	32	0.05
Luxembourg	0	0.00	0	0.00	0	0.00	0	0.00	1	0.16
Netherlands	2	0.01	5	0.03	7	0.04	2	0.01	2	0.01
Poland	2	0.01	0	0.00	2	0.01	0	0.00	1	0.00
Portugal	16	0.16	19	0.18	33	0.32	9	0.09	10	0.10
Romania	3	0.02	1	0.01	1	0.01	0	0.00	0	0.00
Spain	63	0.14	40	0.09	20	0.04	10	NR	25	NR

Source: Ecdc.europa.eu -Country reports; ND: no data reported; NR: no rate calculated

CONCLUSIONS

For free countries, the most important thing is to maintain freedom, especially through strict supervision of the import of animals and their own livestock.

It is one of the most important zoonoses and at the same time one of the most feared occupational diseases.

In animals, brucellosis colonizes the reproductive organs of host animals, causing abortions and sterility. They are shed in urine, milk, placental fluid and other animal fluids.

There is no treatment for brucellosis in animals. Vaccination of cattle, goats and sheep is recommended in enzootic areas with high prevalence rates. Serological or other testing and culling may also be effective in areas of low prevalence.

In cattle, it is caused by *Brucella abortus*, while in goats and sheep by *Brucella melitensis*, this being the main cause of brucellosis in humans.

For humans, the source of infection is represented by sick animals, products from infected animals or the infected environment.

Brucellosis is more common in men than in women, this fact also due to professional exposure to animals. In terms of age, brucellosis is more prevalent in the young population, with 60% of cases in people aged 13-40, 16% in those aged 40-60 and 2.5% in people 60 years and over.

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Ecdc.europa.eu - Brucellosis- Annual Epidemiological Report 2021

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