Historical perspective of brucellosis: a microbiological and epidemiological overview

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SUMMARY

The historical process of brucellosis extends back to humankind’s first contact with animals. Although brucellosis is a sporadic disease observed in animals in certain regions of the world, it is an important disease in humans that can affect many organs and systems due to the consumption of contaminated milk or milk products. Studies have shown that the presence of Brucella dates back to 60 million years ago. In 450 BC, Hippocrates described a disease similar to brucellosis. Since Hippocrates’ time, brucellosis has been characterized by fever. Our aim is to investigate selfless work undertaken by scientists on the epidemiology, diagnosis and clinical findings of brucellosis until today, and to gain a historical perspective about the disease that is as old as human history, still has importance today, causes economic losses in treated animals and harms human health.

Keywords: brucellosis, historical perspectives.

INTRODUCTION

Brucellosis, which is primarily an animal disease, is a zoonosis that is transmitted to humans from infected animals’ meat, milk, urine, body fluids, and pregnancy material, as well as from milk products prepared by infected milk [1, 2]. Brucellosis is an infection seen all over the world, especially in the Mediterranean countries, the Arabian Peninsula, India, Mexico, and Central and North America. In developed countries, the infection has been eradicated from animals, but developing countries still have significant morbidity [1-3]. Brucella species cause mild or asymptomatic diseases in animals, which are their natural hosts. Eritriol, located in animals’ breasts, uterus, placenta, and epididymis, is a growth factor for these bacteria. For this reason, Brucella can lead to abortion and sterility in animals. Due to absence of eritriol in the human placenta, the abortion risk due to brucellosis is not higher than the abortion risk that may occur due to other infectious diseases [2, 3]. The disease is generally transmitted to humans by eating cheese, made from raw milk, and milk products such as cream and butter. Brucella can protect their vitality for 1-2 months in fresh cheese, 4 months in butter, 1 month in ice cream, and 6 months in cream. Therefore, brucellosis is not transmitted in cheese aged for at least three months. Brucella cannot live in yogurt [2, 3]. The disease may also be transmitted by eating animals’ reticuloendotelial organs, such as the spleen and liver, without proper cooking. In addition, it may be transmitted by way of infected secretions coming into contact with skin cracks, conjunctiva, or the inhalation of dust in stables. Therefore, breeders, veterinarians, laboratory workers, and abattoir workers are occupational risk groups for the disease’s dairy form [2, 4, 5].

The history of the disease extends back to people’s first contact with animals. Studies have demonstrated that the presence of brucellosis in humans and animals is ancient. Moreno et al. reported the presence of Brucella abortus and Brucella melitensis in double-hoofed animals around twenty million years ago in their study. The study also suggested...
that seals, otters, and wild rodents may have become natural hosts for *Brucella suis* in the process of evolution [6]. We do not know exactly when people first encountered this disease. However, the disease’s historical process, which is as old as human history, extends to people’s first contact with animals. Thus, the assumption of the presence of *Brucella* infections in the earliest periods of human history is not wrong. Archaeological and anthropological studies confirm our opinion. Views performed on a human skeleton (*Australopithecus africanus*) in South Africa from 2.4-2.8 million years ago shows that lytic bone lesions detected in the lumbar vertebrae (L4-L5) overlap with brucellosis radiologically, macroscopically, and microscopically (Figure 1) [7].

Bone lesions that are typical of brucellosis have been found in anthropologic studies performed in adult skeletons found in the ruins of an old Roman city destroyed by a volcanic eruption in 79 AD; additionally, the presence of cocci-like forms, morphologically similar to *Brucella*, were found in an embedded carbonized cheese analysis performed with an electron microscope (Figure 2) [8].

Studies have demonstrated that, in ancient times, fresh cheese and other milk products were often part of the regional diets for communities living in Albania and other countries surrounding the Mediterranean basin [9]. People living in these communities might have lived in contact with contaminated milk products and infected animals. Capasso showed a correlation between milk products and brucellosis in his research, which was performed in the ancient city of Herculaneum [10]. The presence of *Brucella spp.* was clearly shown by morphological, and molecular analyses done on skeletons found in Albania (ancient Butrint) (Figure 3) [9].

In the middle of the 17th century, George Cleghorn (1716-1789) identified cases of recurrent febrile seizures in Minorca while on duty [11]. As a surgeon in the British army, Cleghorn served in Minorca between the years 1736-1749, and collected data about the most common diseases on the island while treating not only British troops but also the local community [12].

Manuel Rodríguez Caramazana (1765-1836), a surgeon in the Spanish army, was appointed as

Figure 1 - Human skeleton in South Africa from 2.4-2.8 million years ago shows the lytic bone lesions detected in the lumbar vertebrae (L4-L5).
chief surgical clinician at Minorca Military Hospital in 1802. In 1803, he clearly described Malta fever and distributed an eight-page brochure about this title in Minorca. This brochure was not met favorably by the authorities, due to its recommendation of stringent measures to protect people from the disease [11].

Brucellosis was first described by Jeffery Allen Marston (Figure 4) in 1860. As a surgical assistant in the Royal Academy of Medicine in the UK, Marston was the first to define brucellosis; he wrote his findings in detail and defined the disease as “gastric remittent fever” [13]. Marston wrote to the medical department in the same year, but the report was only published in 1863. Although Marston did not know the exact form of the causative agent of the disease, he made a distinctive definition from other Mediterranean fevers [11-14].

Several years before Marston’s disease, Florence Nightingale (Figure 5), the founder of modern nursing (1820-1910), also caught brucellosis during the Crimean War [15-16]. During the war years, she worked in hospitals in Istanbul (Üsküdar) and Crimea (Balaclava) and provided im-
important services. She became sick while stationed in Crimea in 1855, and her high fever and severe symptoms confined her to bed. In the following weeks, the typical symptoms of brucellosis (undulant fever) appeared. Nightingale felt better in the morning, yet her situation became much worse in the afternoon. Doctors at the time believed that the situation was induced by her fatigue and psychological situation. In the 20th century, scientists who examined her life have concluded that she had chronic brucellosis.

She was probably infected in a hospital in Uskudar (Figure 6).

After returning from Crimea, Florence Nightingale suffered many of the symptoms related to...
chronic brucellosis. She had five major attacks during the course of the disease, which were probably the usual symptoms of bacteremic episodes. The attack in 1861 was contained the specific symptoms of brucellosis. In 1863, she had severe spinal pain, caused by spondilitis, which continued until her death. Nightingale spent the last six years of her life bedridden [17].

In 1887, the Scottish physician Sir David Bruce (1855-1931) identified the first disease factor (Figure 7). He isolated gram-negative coccobacili, which were termed *Micrococcus* due to being small, from the spleens of five British soldiers, who died of a fever in Malta. Due to the disease being seen for the first time in Malta, the organisms’ name is derived from the word “melita,” meaning Malta in Latin (*Micrococcus melitensis*) [12].

In 1895, the Danish veterinarian Bernard Lauritz Frederik Bang (Figure 8) isolated microorganisms, called *Bacillus abortus*, from cattle giving birth as low factors of cattle placenta, fetus, and uterine wall secretions [2].

Figure 7 - Sir David Bruce. Discoverer of *Brucella melitensis* (Brucellosis).

Figure 8 - Danish veterinarian Bernard Lauritz Frederik Bang.

Figure 9 - Members of the Mediterranean Fever Commission. Photograph circa 1907. Standing: Dr Themi Zammit, Capt Crawford Kennedy, Major J G McNaught. Front row seated: Major J C Weir, Dr J W H Eyre, Col D Bruce, Maj T McCulloch, Staff Surgeon E A Clayton.
In 1897, Wright and Smith explained that brucellosis was a zoonotic disease, after detecting specific antibodies of *Brucella melitensis* in human and animal serum agglutination tests. The diagnosis of the disease using the serum agglutination test, which is currently used, was carried out for the first time here [18]. The Mediterranean Fever Commission was established in 1904. Between 1904 and 1907, several reports were published on the epidemiology, bacteriology, and pathology of brucellosis (Figure 9) [19].

In 1905, Themistocles Zammit (1864-1935) isolated *B. melitensis* from goat’s milk and urine; he explained that goats hosted *B. melitensis* and that people intake it from raw milk and milk products. He showed the presence of the bacteria in infected goat’s milk, urine, and blood to prove this hypothesis by doing experiments and epidemiological studies. Then, he developed the test used by other investigators [20].

At the time, the Maltese distributed milk directly from goats at the door, and they consumed raw milk. According to a rumor, there were modern villas in front and single-story farmhouses just behind them along the narrow coastal strip in a region known as Medine. Goats and cattle were usually fed on farms; the goats and cows were then herded in front of the luxury villas, stopping in front of each house, where freshly milked milk was then drunk (Figure 10).

Zammit discovered that goats were reservoirs of brucellosis, so he enabled a rapid decline in infection and death among military personnel by preventing the use of unpasteurized goat’s milk. The sale of milk at the door was banned after determining that humans caught disease from raw goat’s milk. Milk vendors protested and held banners describing their victimization throughout Malta by going on strike in 1906 (15 May to 1 June). During this period, milk came from canned milk imports from the UK. During this period, as a result of strikes by milk workers, people became aware of the potential harm and did not return to their old habits [19].

Jacob Traum detected *Brucella suis* from prematurely born piglets’ livers, stomachs, and kidneys in the state of Indiana in the United States in 1914 [19-21].

In 1918, the American bacteriologist Alice Evans (Figure 11) showed that Malta fever and Bang disease had highly homologous factors with each other. She explained that the three factors observed in goats, pigs and cattle only had antigenic differences, but no morphological, cultural, or biochemical differences. A short time later, Evans stated that they were in the same genus, after comparing the two diseases’ morphological, cultural, and biochemical properties; in memory of Sir David Bruce, it was called the *Brucella* genus [1]. Evans offered evidence that raw cow’s milk...
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was a factor of brucellosis in humans. She found that *B. melitensis* in people and *B. abortus* in cows were associated with undulant fever [22]. During this work, Evans also became infected. Despite taking every precaution while doing her research, she became infected; *Brucella* were isolated from her blood in 1922. The possible modes of transmission were expected to be from the respiratory tract. Although her disease was associated with remission and relapse, it sometimes affected her health very negatively. In 1927, she was elected as president of the Society of American Bacteriologist (American Society for Microbiology, ASM); however, she was bedridden due to her relapsed brucellosis and could not attend the society’s meeting. In 1943, Evans developed a hypersensitivity to the *Brucella* antigen and could no longer work with live cell cultures. However, as a patient with chronic brucellosis, she shared valuable information from her own experiences. Thus, the evidence related to chronic brucellosis was identified in the first half of the 20th century [22-24].

In 1924, *B. abortus* infections in humans were reported by Orpen in England. In Puerto Rico, similar studies were conducted by Morales-Otero. In 1953, *Brucella ovis* in sheep was described by Van Drimmelen. In 1957, *Brucella neotoma* was isolated from a wood tick in the state of Utah, in the United States, by Stoenn and Blackman [22]. In 1968 *Brucella canis* was isolated in beagle dogs by Carmichael and Bruner. Although *B. canis* normally outbreaks in hunting dogs, it was found in a female patient in 1977 [1-22]. In 1994, British and American researchers, independently of each other, isolated previously unknown *Brucella* organisms from mammals’ carcasses and California dolphins in the Scottish coast. They isolated differential metabolic profiles, paint, and phage sensitivities; identical sensitivities were found in what was named *B. maris* [25]. Ewalt, Ross, and colleagues isolated two new *Brucella* species from whales, dolphins and seals called *Brucella pinnipediae* and *Brucella ceteae* [26, 27]. Marine mammals are contaminated from damaged skin, direct contact with mucous membranes, ingesting other infected marine mammals, and infected mother’s fetal tissue and milk [28]. As experimentally demonstrated in cattle, *Brucella* species can also infect terrestrial mammal species [29]. Information about the transmission of brucellosis from marine mammals to humans is available in the literature. Among laboratory workers, transmission has been reported to occur after occupational exposure. In another case, infection was reported in a patient with spinal osteomyelitis in New Zealand [30-31]. Finally, in 2008, *Brucella microti* was isolated from field mice in Central Europe and the mandibular lymph nodes of a wild red fox by Scholz et al. This species has not been shown to cause disease in humans but is a potential risk, especially for hunters [32].

In these aforementioned studies, the isolation of *Brucella* from different animals and humans by researchers has elucidated the epidemiology of *Brucella*, which is an anthropozoonosis, and sheds light on the present studies.

In our country, the first studies to determine *Brucella*’s factors began with the isolation of *B. melitensis* in a soldier, who was treated at the Kuleli Military Hospital (Figure 12) by Doctor Hüsamettin Kural (Figure 13) and Mahmut Sami Akalın in 1905. In our country, the first isolation in cattle was reported by Zühtü Berke in 1931-32. *B. melitensis* in sheep was first detected in 1944 by Aktan and Köylüoğlu at the Bandırma Merinos farm [33]. In Turkey, *Brucella* were detected with serological methods in humans and animals by Golem in 1943 [34]. *B. canis* factor in dogs was determined serologically by İstanbulluoğlu et al. in 1983. In Turkey, the most comprehensive study on

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*Figure 11 - American bacteriologist Alice Evans.*
the epidemiology of brucellosis in humans was made by Çetin et al. between 1984–1987, with the help of The Scientific and Technological Research Council of Turkey (TUBITAK) [35]. The historical names of brucellosis include “undulant fever”, “Bang’s disease”, “Gibraltar disease”, “Mediterranean fever”, Malta fever”, “Constantinople fever” and “Crete fever”. When the disease was first detected in the island of Malta, the disease was named “Malta fever” or “Mediterranean fever.” Due to the typical fever trace in the disease’s clinical course, the disease was called “undulant fever”. In Turkey, due to B. melitensis contamination from sheep to humans, the disease is called “sheep disease”; due to disease transmission from animals to humans, it is called “cost disease” or “cheese disease”; however, the most commonly used name is brucellosis [2, 3].

CONCLUSION

Although brucellosis historically goes back to people’s first contact with animals, it is still an endemic, zoonotic infectious disease in many countries today. Studies have shown evidence that brucellosis occurred in animals 60 million years ago and in humans nearly 3 million years ago. The present anthropological, morphological, and molecular studies provide evidence related to the presence of the disease in Mediterranean countries during the first century AD and the 13th and 14th centuries. Some scientists who have engaged in research related to the disease were infected during their studies and gave important information about brucellosis by explaining their clinical condition or isolating the disease factor from their blood. At the same time, they have contributed to science by developing tests to diagnose the disease. Additionally, epidemio-
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logical studies of the disease and the discovery of new species have provided us with valuable information that sheds light. We commemorate all of them here.

From a historical perspective, brucellosis was detected first in domestic mammals, then it was detected in wild mammals, and finally in marine mammal species.

Although limited publications about bird species that are not affected by the disease are available, we believe that detailed research, especially about birds of prey that feed on meat and birds fed with parasites from animals, are needed [36]. We should be conducting studies with the support of technological facilities, since scientists who study this disease have limited opportunities. Public health experts, veterinarians, infectious disease specialists, and microbiologists have serious duties regarding this issue.

Our aim was to highlight the scientists’ selfless work on the epidemiology, diagnosis, and clinical findings of brucellosis until today, as well as to collect a historical perspective about a disease that is as old as human history and still has importance today, since it causes economic losses through animal and human health. We hope that these efforts have shown guidance in acting against Brucella.

REFERENCES


[34] Wright A.E., Smith F. On the application of the serum test to the differential diagnosis of typhoid fever and Malta fever. Lancet. 1, 656-659,1897.


