Brucellosis and International Travel

Ziad A. Memish and Hanan H. Balkhy

Brucellosis is a zoonotic disease of worldwide distribution that mainly affects persons working with domestic animals and animal products. Despite being controlled in many developed countries, the disease remains endemic in many parts of the world, including Latin America, the Middle East, Spain, parts of Africa, and western Asia. The disease is mainly transmitted to humans through the ingestion of raw milk or non-pasteurized cheese contaminated with one of the four *Brucella* species pathogenic to humans. The clinical presentation can vary from asymptomatic infection with seroconversion to a full-blown clinical picture of fever, night sweats and joint manifestations; rarely, there is hepatic, cardiac, ocular or central nervous system involvement. Since travelers may be affected, travel health physicians need to know the clinical presentation of patients with brucellosis and preventive strategies.

J. A. Martson was the first to describe brucellosis, as "Mediterranean gastric remittent fever", in 1861 from his base in Malta.[1] Sir David Bruce isolated the organism from the spleen.[2] He named it *Micrococcus melitensis*, and later it was renamed *Brucella melitensis* in his honor.

The genus *Brucella* consists of seven species, four of which are pathogenic in humans: *B. melitensis* (goat, sheep, and camel), *B. abortus* (cow), *B. suis* (swine, reindeer, caribou, rodent), and *B. canis* (dog).[3] In most parts of the world, human infection with *B. melitensis* is most common, and may account for up to 90% of all brucellosis cases.[4] The disease is acquired in humans through ingestion of raw milk, cheese or meat, through direct contact with infected animals, or their products of conception,[5] such as placenta and fetus, or through inhalation of infectious aerosols, especially in laboratory personnel, especially when a BSL-3 is not used.[6,7]

Clinical Presentation

Brucellosis is a systemic infection that can involve any organ or organ system of the body, and since many cases go unrecognized, the true incidence of the disease is unknown.[8] The onset may be sudden, over a few days, or gradual, over weeks to months, with nonspecific symptoms including fever, lassitude, malaise, headache, backache, and arthralgia.[9] Sometimes, the manifestations of brucellosis are more pronounced in a specific organ system. The most common local manifestations are: spondylitis, peripheral arthritis (especially of the hip, knee and shoulder) and epididymo-orchitis.[10] Arthritis and joint pain are common and usually migratory in character, affecting mostly the large joints, with unilateral joint involvement being more common among the younger age group. However, monoarticular brucellar septic arthritis is a common presentation in both adults and children.[11–13] Since the organism has a predilection for the reticuloendothelial system, lymph node, hepatic and splenic involvement may be seen.[10] *Brucella* infection of expectant women early in pregnancy may lead to high rates of fetal wastage, up to 40%, while infection later in pregnancy is associated with fewer than 2% of fetal deaths.[14] The term chronic brucellosis has been used in cases where the above-mentioned symptoms persist or recur over a period of 6 months or more. Involvement of the skin is infrequent, but maculopapular rash, nodular lesions and erythema nodosum have been reported.[15] Contact urticaria, "erythema brucellum", has been described after close contact with infected animals, where erythema and itching occur within hours of exposure.[16] Some complications of brucellosis include neurobrucellosis and endocarditis. Both occur in fewer than 2% of cases.[10,17]

Ziad A. Memish, MD, CIC, FRCPC, FACP, FIDSA: Department of Infection Prevention and Control and Department of Medicine, King Abdulaziz Medical City, King Fahad National Guard Hospital, Riyadh, Saudi Arabia; *Hanan H. Balkhy, MD:* Department of Infection Prevention and Control and Department of Pediatrics, King Abdulaziz Medical City, King Fahad National Guard Hospital, Riyadh, Saudi Arabia.

The authors had no financial or other conflicts of interest to disclose.

Reprint requests: *Ziad A. Memish, MD, CIC, FRCPC, FACP, FIDSA,* Chief, Adult Infectious Diseases, Department of Internal Medicine, and Executive Director, Infection Prevention and Control Program, National Guard Health Affairs, King Abdulaziz Medical City, King Fahad National Guard Hospital, PO Box 22490, Riyadh 11426, Saudi Arabia.

J Travel Med 2004; 11:49–55.

Methods of Diagnosis

Prior to ordering appropriate laboratory tests, an index of suspicion needs to be present. If not, cases may go unrecognized for long periods of time. One report describes six high school students from the United States who traveled to Spain and contracted brucellosis.[18] The first patient was diagnosed after more than 2 months of symptoms, during which she was evaluated by three physicians and received several courses of antimicrobials without response; yet the other five cases were diagnosed within a few days of presentation. All six patients had positive blood cultures for *B. melitensis*. In a more recent study, brucella was found to be the third most common infectious disease reported between 1990 and 1998 in the US region bordering Mexico.[19]

The only definitive diagnostic test is isolation of the organism in culture. Where traditional blood culture systems are in use, it may take up to 35 days of incubation before growth is detected. The new third-generation continuous-monitoring blood culture systems have provided an accelerated diagnostic modality.[20,21] The overall positivity from blood culture may vary from 50% to 90%. A better yield is expected early in the disease, with less chance of isolation as the disease progresses.[22]

The serologic test most frequently used in the diagnosis of brucellosis is the serum agglutination test (SAT).[23] The sensitivity and specificity of the SAT test for bacteremic patients are 95.6% and 100%, respectively.[23] A unified significant agglutination titer does not exist; however, most would agree that, in a symptomatic patient in a nonendemic area, a titer of 1 : 160 would be considered positive. In endemic countries, where infections may become chronic or recurrent, a higher titer of 1 : 360 to 1 : 640 is considered positive. A dropping titer with therapy would be more useful than a high titer in making a diagnosis.[24] In some patients, antibodies may not be detected at low serum dilutions. This is known as the prozone phenomenon, where higher dilutions are needed.[25] In other rare situations, blocking antibodies may be found, which also leads to a negative serologic test. If these blocking antibodies are suspected in a patient where a high suspicion of brucellosis is present, one should perform a Coombs test or a specific test for blocking antibodies.[25–27] The Rose Bengal test is a rapid screening test; however, confirmation of a positive test is always needed. Finally, ELISA is suggested to be a more sensitive and rapid way of diagnosing brucellosis, but is much more expensive, especially for hospitals in endemic countries, where the test would be done frequently.[23]

Management

Most patients with acute uncomplicated brucellosis, even when bacteremic, do not need to be hospitalized, and treatment is usually with oral antibiotics.[28] Despite many studies on the medical management of brucellosis over the past two decades, no major changes in the known therapeutic modalities have been recommended (Table 1). There have been a few reports suggesting the superiority of streptomycin–rifampin combination over doxycycline–rifampin specifically when there is bony involvement.[29] However, in general, two principles of brucellosis therapy have emerged from animal and human studies. First, the treatment of brucellosis requires prolonged therapy with at least two agents. Second, chosen agents need to reach adequate intracellular concentrations. In children under 7 years of age and pregnant women, there has been no consensus with regard to the best therapeutic regimen for simple or complicated brucellosis.[14] Surgical management is indicated only in special cases such as drainage of hepatic or splenic abscesses or in the rare case of brucella endocarditis when the infected valve needs to be replaced.

Disease Distribution Worldwide

In Central America, namely, Guatemala, Belice, Honduras, El Salvador, Nicaragua, Costa Rica and Panama, bovines are by far the most relevant natural hosts for *Brucella*. Other hosts do exist, such as swine and dogs (Fig. 1).[30] Herd infection rates have varied over the years, but range from 10% to 25%. El Salvador seems to be the country with the lowest incidence of bovine brucellosis, with a prevalence of 1%, while Guatemala and Costa Rica appear to have the highest prevalence. This may reflect more efficient diagnosis and reporting systems in these countries. A higher prevalence of disease transmission has been noticed among dairy herd farmers, and those farming in the valleys and highland regions of Central America. Disease prevalence among humans in the countries of Central America is thought to be underestimated, despite the demands of the Ministry of Health to report all cases of brucellosis. In Costa Rica, for example, only 156 human cases of brucellosis were reported over an 8-year period, while a survey of a high-risk population of 384 revealed a 45% prevalence rate. This may indicate a high prevalence of brucellosis among animals in the country, where consumption of unpasturized dairy products is common. Epidemiologic data on brucellosis in more commonly visited areas of Central America such as Jamaica and the Bahamas is not available; however, in Jamaica, *B. melitensis* does exist.

In Mexico, brucellosis is one of the most serious bacterial diseases. In the early 1900s, more than 5,000 human cases were reported on a yearly basis. In recent years, a national campaign to eradicate animal brucellosis was led by the Secretariat of Agriculture. Despite this, Mexico continues to see at least 2,000 cases of human brucellosis

Table 1 Choices of Antimicrobial Therapy in *Brucella*-infected Patients

	First-line Therapy	*Second-line Therapy*	*Comments*
Adults	Doxycycline: 100 mg b.i.d. × 4–6 weeks and Streptomycin: 1g IM × 2–3 weeks	Doxycycline: 100 mg b.i.d. × 4–6 weeks and Rifampicin: 600–900 mg × 4–6 weeks or Doxycycline: 100 mg b.i.d. × 4–6 weeks and Gentamicin: 240 mg IM × 5–7 days or Rifampicin: 600–900 mg × 4–6 weeks and Ofloxacin 200 mg b.i.d. × 4–6 weeks	Rifampicin should not be used alone Doxycycline for 6 weeks plus streptomycin for 2 weeks is indicated for bone and joint involvement Triple therapy is recommended for severe infection (CNS and endocarditis)
Pregnancy	Rifampicin: 600–900 mg × 4–6 weeks plus Cotrimoxazole: 800 mg b.i.d. × 4–6 weeks	Cotrimoxazole: 800mg b.i.d. × 4–6 weeks	Tetracycline–doxycycline and streptomycin are contraindicated in pregnancy and breast-feeding mothers
Children	Rifampicin: 10–20 mg/kg/day once a day × 4–6 weeks and Cotrimoxazole: 10 mg/kg/day × 4–6 weeks	Doxycycline: 2–4 mg/kg b.i.d. × 4–6 weeks and Streptomycin: < 25 kg: 40 mg/kg IM single daily dose > 25 kg: adult dose × 3–4 weeks	Rifampicin is to be given before a meal Tetracycline–doxycycline is contraindicated in children under 8 years of age Triple therapy is recommended for severe infections (central nervous system and endocarditis)

per year. All states of Mexico have reported the disease among animals and humans alike. The highest prevalence of brucellosis among tested goats was in the states of Coahuila, Chihuahua, Jalisco, and Zacatecas, and the highest prevalence in bovines was in the states of Chihuahua, Hidalgo, and Guanajuato. The most likely mode of disease transmission in Mexico is known to be the consumption of unpasteurized cow and goat dairy products. More than 35% of cow's milk is consumed unpasteurized, and more than 85% of goat's milk is consumed unpasteurized under poor sanitary conditions.[31]

In most countries of Latin America, brucellosis has been a well-known disease in humans and animals, with *B. abortus* being the most common agent. In Argentina, human brucellosis is more common among the rural population, and is mainly linked to the consumption of fresh and unpasteurized goat cheese. The estimated disease prevalence among cattle in Argentina ranges between 10% and 13%, whereas for caprine brucellosis, it ranges between 20% and 25%.[32]

Brazil, the country with the largest commercial cattle population in the world, reported its first case of human brucellosis in 1993. Since then, most reported cases have been found among abattoir workers and meat processors. It is believed that the number of reported cases is an underestimate, since consumption of fresh cheese is very common.[33]

Finally, in Venezuela, where brucellosis is mainly an infectious occupational hazard, the prevalence among cattle and buffalo was found to average 10%. Large efforts

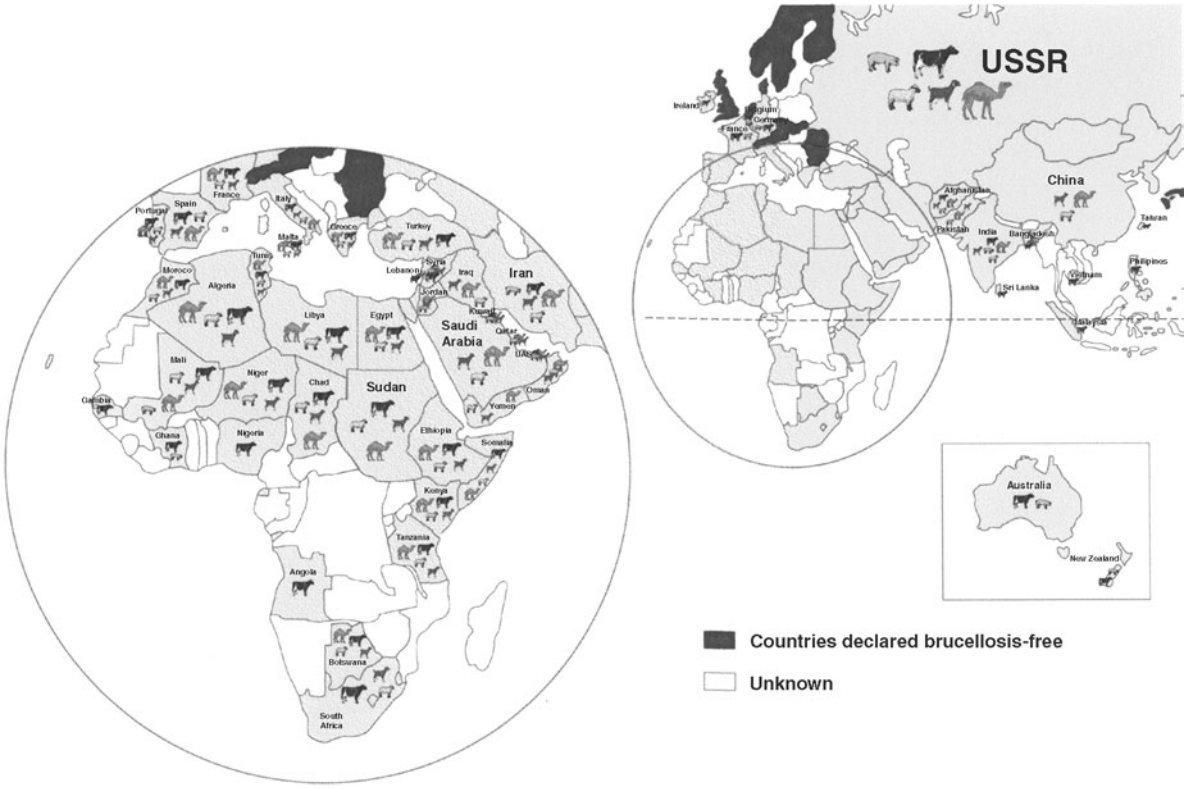

Figure 1 Prominent animal hosts for *Brucella* in North and South America.

are being made to facilitate effective control and eradication.[34]

The Netherlands and England were considered to be free of bovine brucellosis by the turn of the century (Fig. 2).[35] Brucellosis-positive herds were still reported in France, Ireland and Italy, but the incidence has been declining.[35]

In the countries of central and south-eastern Europe, namely Greece, Macedonia, Yugoslavia and Bulgaria, sheep and goats remain a major reservoir of the disease, while cows are less important hosts. In Croatia, brucellosis has also been found in pigs. In most of these countries human disease goes largely unreported, and the true prevalence rates are unknown. It is expected that certain parts of Greece, with the initiation of the brucellosis eradication and control program, will soon be officially declared brucellosis-free. Until then, travelers to Greece and other neighboring countries need to be aware of the possibility of contracting the disease.[36]

In sub-Saharan Africa, the prevalence of brucellosis among animals, mainly cattle, sheep, goats and pigs, is poorly estimated or unknown (Fig. 1). Since the economic status of most of these countries is poor, disease control has been very difficult, making chronic infection and infertility commonplace among the herds. Carcasses and abattoir products provide a continuous supply of the organism to maintain the infectious cycle among animals and humans. Outbreaks of bovine brucellosis in animals have occurred in most sub-Saharan African countries; however, no data are available from Benin, Burundi, Cape Verde, Congo, Equatorial Guinea, Rwanda, or Sierra Leone. In South Africa, more than 300 outbreaks took place each year from 1996 to 2000, with over 5,000 cases reported per year in humans. Most countries of West, East and Central Africa also had outbreaks, but the numbers of cases among animals and humans are less well defined.[37]

In most sub-Saharan countries, the risk is highest among those who fail to boil milk prior to consumption. Beyond the consumers and farmers, abattoir and animal health workers are at high risk of occupational exposure. While bovine, caprine, ovine and porcine brucellosis exist in most sub-Saharan African countries, the true prevalence is either poorly reported or completely unknown.[37]

In the subcontinent of India, brucellosis is prevalent among cattle, sheep, goats, dogs and pigs. Bovine brucellosis is present in almost all parts of India, and seems to be increasing among livestock. Humans are most commonly infected with *B. melitensis*. The disease may be

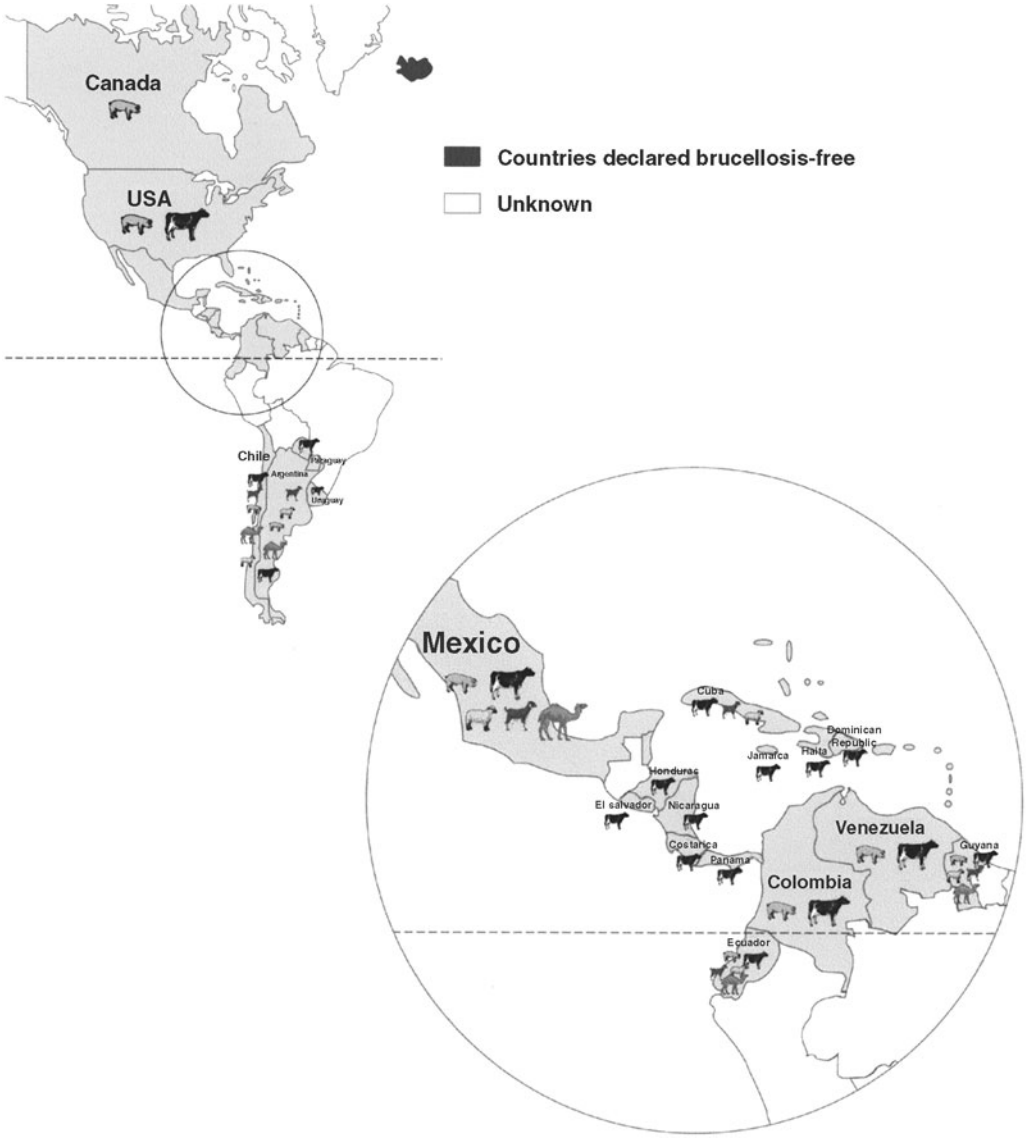

Figure 2 Prominent animal hosts for *Brucella* in Europe, Africa, Asia and Australia.

initially confused with tuberculosis, malaria or typhoid fever, and many cases go unrecognized, undiagnosed or unreported. It is somewhat reassuring, however, that the tradition of consuming unboiled milk, even though it still exists, seems to be declining.[38]

In China, the epidemiology of the disease is classified according to its severity among animals.[39] Areas classified as type 1, also known as severe epidemic regions, include Inner Mongolia, Jilin, Helongiiang, Tibet, Xinjiang, Qinghai Ningxia, and Henan. In type 1 regions, the prevalence of brucellosis among humans is 14%, while infection rates among animals exceed 5%. In type 2 regions, or general epidemic regions, the incidence of human disease is reported to be 6% only, while the prevalence among animals is similar to that in type 1 regions. Type 2 regions include Shandong, Gansu, Hebei, Liaoning, Sichuanand, and Shanxi. Areas of south-eastern China are classified as type 3 or sporadic epidemic regions. In these areas, the incidence among animals is less than 5%, and human cases are reported only sporadically. Between 1991 and 1998, herd outbreaks of brucellosis were most prevalent in the provinces of ShanXi (50 outbreaks) and Hebeixi (28 outbreaks). Even though the overall prevalence of brucellosis in China is increasing, major efforts are being made to reverse this trend and bring the disease under control in animals as well as humans. It is hoped that this can be achieved through the establishment of a national brucellosis surveillance network, quarantine, separation and elimination of infected animals with brucellosis, and vaccination of domestic animals.[39]

Advice for Travelers

Eating is obviously an important experience in any trip. Many travelers are willing to experiment with new foods, drinks and exotic food preparations. Particularly when trying to get "natural" food straight from the farm, they expose themselves to *Brucella*, among many other pathogens.

Travelers need to be educated with regard to the modes of disease transmission, so that they can take care when eating abroad, especially food from street vendors or traditional shops. In the Kingdom of Saudi Arabia, for example, camel's milk may be sold on the main streets and is considered a delicacy. On the premise of increased freshness, the milk is provided frothy and warm from the camel. It is even much easier for campers in the desert to find providers of such kinds of camel or goat milk. In other parts of the Middle East, fresh goat's cheese may be sold in supermarkets. Most local people will use it, fully cooked, to prepare traditional Middle Eastern desserts such as "Kunafa". If such cheeses were purchased and consumed without cooking, there would be a good chance of disease transmission.

Travelers need to be made aware that, first, the brucella organism may persist for several days in milk, until it turns sour, when the acidity kills the organism, and second, that the organism is known to flourish in soft fresh goat or sheep cheese; it may also persist for 4 weeks in ice-cream[40,41] and for several months in butter (Table 2).

Table 2 Studies on *Brucella* Survival Time in Dairy Products

Product	*Species of Brucella*	*Temperature (°C)*	*Survival Time*
Milk	*B. abortus*	71.1	5–15 s
	B. abortus	38	<9 h
	B. abortus	25–37	24 h
	B. abortus	0	18 months
Cream	*B. abortus*	4	6 weeks
	B. melitensis	4	4 weeks
Ice-cream	*B. abortus*	0	30 days
Butter	*B. abortus*	8	142 days
Cheese			
Various	*B. abortus*	–	6–57 days
Various	*B. melitensis*	–	15–100 days
Feta	*B. melitensis*	–	4–16 days
Pecorino	*B. melitensis*	–	<90 days
Roquefort	*B. abortus and B. melitensis*	–	20–60 days
Camembert	*B. abortus*	–	<21 days
Erythrean	*B. melitensis*	–	44 days
Cheddar	*B. abortus*	–	6 months
White	*B. melitensis*	–	1–8 weeks
Whey	*B. abortus*	17–24	<4 days
	B. abortus	5	>6 days

Pasteurization kills the organism, so butter, cheese or ice-cream should be made from pasteurized milk. In many parts of the world, mass education is, by and large, needed;[5] especially where there are strong beliefs that the consumption of raw milk is beneficial and curative for many chronic diseases.

For those travelers who may have contact with live or dead animals, infection may be transmitted via aerosols from infected abattoir products or through direct contact with infected animals, their product of conceptions, such as placenta and fetus, if there are abrasions on the skin. If such contact is unavoidable, the traveler should be advised to adhere to wearing protective gear at the time of animal contact. It should be appreciated, however, that, despite adherence to wearing protective gear, an infection might still occur. The reason for this is that the organism may survive in the soil for several hours despite being exposed to the sun, but for much longer if in the shade. In damp, dung-contaminated soil, as well as in tap water, the organism may survive for several weeks.[40]

Global Disease Control

Since brucellosis is a zoonotic disease, human incidence can only be reduced or controlled by decreasing the incidence of disease in animals. The expansion of the animal industry and the lack of modern animal husbandry in most countries have allowed the rapid movement of animals from one country to another or to different parts of the same country without proper attention being payed to the possibility of disease transmission. Governmental control and eradication programs to eliminate the disease in animals may be expensive and require strong political decision-making.[42] Three control measures in animals have been identified: testing the animals and eliminating those infected, vaccinating all livestock, and, finally, implementing hygienic and control methods to reduce the contact between susceptible animals and those infected.[42] Unfortunately, there have been no published studies comparing the cost–benefit and effectiveness of these three methods. However, two major organizations, the Food and Agriculture Organization (FAO) and the Office International des Epizooties (OIE), have published information on the geographic distribution of the disease among animals (Figs. 1, 2) and the policies necessary for their control.[42]

Acknowledgments

We would like to acknowledge Dr Robert Steffen and Dr Ed Young for their critical review and valuable comments, which improved the quality of the manuscript.

References

1. Martson JA. Report on fever (Malta). Great Britain Army Med Dept Rep 1861; 3:486–521.
2. Bruce D. Note on the discovery of a micro-organism in Malta Fever. Practitioner 1887; 29:161.
3. Ko J, Splitter GA. Molecular host–pathogen interaction in brucellosis: current understanding and future approaches to vaccine development for mice and humans. Clin Microbiol Rev 2003; 16:65–78.
4. Corbel MJ. Brucellosis: an overview. Emerg Infect Dis 1997; 3:213–221.
5. Cooper CW. Risk factors in transmission of brucellosis from animals to humans in Saudi Arabia. Trans R Soc Trop Med Hyg 1992; 86:206–209.
6. Osoba AO, Balkhy H, Memish Z, et al. Diagnostic value of brucella ELISA IgG and IgM in bacteremic and non-bacteremic patients with brucellosis. J Chemother 2001; 13:54–59.
7. Memish Z, Mah MW. Brucellosis in laboratory workers at a Saudi Arabian hospital. Am J Infect Control 2001; 29:48–52.
8. Al Sekait MA. Seroepidemiological survey of brucellosis antibodies in Saudi Arabia. Ann Saudi Med 1999; 19:219–222.
9. Young EJ, Hall WH. Brucellosis. In: Evans AS, Brachman PS, eds. Bacterial infection of humans: epidemiology and control, 3rd edn. New York: Plenum Medical Book Company, 1998:155–167.
10. Colmenero JD, Reguera JM, Martos F, et al. Complications associated with *Brucella melitensis* infection: a study of 530 cases. Medicine (Baltimore) 1996; 75:195–211.
11. Al-Freihi HM, Al Mohaya SA, Almohsen MF, et al. Brucellosis in Saudi Arabia: diverse manifestation of an important cause of pyrexial illness. Ann Saudi Med 1986; 6:95–97.
12. Kiel FW, Khan MY. Brucellosis in Saudi Arabia. Soc Sci Med 1989; 29:999–1001.
13. Shaalan MA, Memish ZA, Mahmoud SA, et al. Brucellosis in children: clinical observations in 115 cases. Int J Infect Dis 2002; 6:182–186.
14. Khan MY, Mah M, Memish ZA. Brucellosis in pregnant women. Clin Infect Dis 2001; 32:1172–1177.
15. Milionis H, Christou L, Elisaf M. Cutaneous manifestations in brucellosis: case report and review of the literature. Infection 2000; 28:124–126.
16. Trunnell TN, Waisman M, Trunnell TL. Contact dermatitis caused by Brucella. Cutis 1985; 35:379–381.
17. Young EJ. Brucella species. In: Mandell GL, Bennett JE, Dolin R, eds. Mandell, Douglas and Bennett's principles and practice of infectious diseases, 4th edn. New York: Churchill Livingstone, 1995:2053–2060.
18. Arnow PM, Smaron M, Ormiste V. Brucellosis in a group of travelers to Spain. JAMA 1984; 251:505–507.
19. Doyle TJ, Bryan RT. Infectious disease morbidity in the US region bordering Mexico, 1990–1998. J Infect Dis 2000; 182:1503–1510.
20. Bannatyne R, Jackson M, Memish Z. Rapid diagnosis of brucella bacteremia by using the BACTEC 9240 system. J Clin Microbiol 1997; 35:2673–2674.
21. Memish Z, Mah MW, Mahmoud S, et al. Brucella bacteremia: clinical and laboratory observations in 160 patients. J Infect 2000; 40:59–63.
22. Yagupsky P. Detection of Brucella in blood cultures. J Clin Microbiol 1999; 37:3437–3442.
23. Memish Z, Almuneef M, Mah MW, et al. Comparison of brucella standard agglutination test with ELISA IgG and IgM in patients with Brucella bacteremia. Diagn Microbiol Infect Dis 2002; 44:129–132.
24. Madkour MM. Brucellosis: overview. In: Madkour MM, ed. Brucellosis, 2nd edn. Berlin, Springer-Verlag, 2001:1–14.
25. Cho HJ, Ingram DG. Mechanisms of prozone formation in agglutination reaction. Can J Microbiol 1972; 18: 449–456.
26. Griffitts JJ. Agglutination and agglutinin-"blocking" property in serums from known cases of brucellosis. Public Health Rep 1947; 62:865–875.
27. Hall WH, Manion RE. Comparison of the Coombs test with other methods for Brucella agglutinins in human serum. J Clin Invest 1953; 32:96–106.
28. Ariza J, Gudiol F, Pallares R, et al. Treatment of human brucellosis with doxycycline plus rifampin or doxycycline plus streptomycin: a randomized, double blind study. Ann Intern Med 1992; 117:25–30.
29. Solera J, Rodriguez-Zapata M, Geijo P, et al. Doxycycline–rifampin versus doxycycline–streptomycin in treatment of human brucellosis due to *Brucella melitensis*. Antimicrob Agents Chemother 1995; 39:2061–2067.
30. Moreno E. Brucellosis in Central America. Vet Microbiol 2002; 90:31–38.
31. Luna-Martinez JE, Mejia-Teran C. Brucellosis in Mexico: current status and trend. Vet Microbiol 2002; 90:19–30.
32. Samartino LE. Brucellosis in Argentina. Vet Microbiol 2002; 90:71–80.
33. Poester FP, Goncalves VS, Lage AP. Brucellosis in Brazil. Vet Microbiol 2002; 90:55–62.
34. Francisco J, Vargas O. Brucellosis in Venezuela. Vet Microbiol 2002; 90:39–44.
35. Godfroid J, Kasbohrer A. Brucellosis in the European Union and Norway at the turn of the twenty-first century. Vet Microbiol 2002; 90:135–145.
36. Taleski V, Zerva L, Kantradjiev T, et al. An overview of the epidemiology and epizootology of brucellosis in selected countries of Central and Southeast Europe. Vet Microbiol 2002; 90:147–155.
37. McDermott JJ, Arimi SM. Brucellosis in sub-Saharan Africa: epidemiology, control and impact. Vet Microbiol 2002; 90:111–134.
38. Renukaradhya GJ, Isloor S, Rajasekhar M. Epidemiology, zoonotic aspects, vaccination and control/eradication of brucellosis in India. Vet Microbiol 2002; 90:183–195.
39. Deqiu S, Donglou X, Jiming Y. Epidemiology and control of brucellosis in China. Vet Microbiol 2002; 90:165–182.
40. European Commission. Brucellosis in sheep and goats (*Brucella Melitensis*). SANCO.C.2/AH/R23/2001. Santa Fe: Scientific Committee on Animal Health and Animal Welfare, 2001.
41. Young EJ. Brucellosis in travelers and *Brucella* that travels. In: Steffen R, Lobel HO, Haworth J, eds. Travel medicine. New York: Springer-Verlag, 1989:375–377.
42. World Health Organization. The development of new improved brucellosis vaccines: report of WHO meeting with the participation of the food and agriculture organization of the United Nations (FAO) and the office international des epizooties (OIE). WHO/EMC/ZDI/98.14. Geneva: WHO, 1997.