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BRUCELLOSIS: PAST, PRESENT AND FUTURE

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A b s t r a c t: *Aim:* To present an overview and the specificities of the biology and epidemiology, pathogenesis and diagnostics, public health aspects, vaccination and control of brucellosis as a global zoonosis.

Methods: Of the various methods to control brucellosis in animals such as vaccination, hygiene, and test and slaughter of infected animals, widespread vaccination is the most rapid, efficient and effective procedure.

Results: Despite much progress in the control and sometimes eradication of brucellosis in cattle in many countries, the situation with the disease in small ruminants is proving to be much more difficult. Political and socioeconomic problems are deterrents to success. It is a veterinary responsibility to accept the challenge to control animal brucellosis, which will then control the disease in humans. The success of the control effects will be primarily measured by a decrease in human cases.

Conclusion: Effective control of brucellosis requires a long-term commitment from many governmental agencies. Assistance from international animal and human health organizations in resources and expertise is necessary in many developing countries. There are no easy solutions. Research on alternative strategies in vaccines and their usage, diagnostic tests, and treatments should be encouraged.

Key words: animal disease, brucellosis, zoonoses, control/eradication strategies.

Introduction

Brucellosis is endemic in Asia, Sub-Saharan Africa, some countries of Latin America, the Middle East and the Mediterranean and South Eastern Europe Region. The incidence is increasing in several of these. The disease has widespread impacts on human and animal health including socioeconomics.

Brucella are gram-negative coccibacilli, which are classified into species by various techniques such as growth patterns on media and phage susceptibility. There are six “classical” species of the genus *Brucella* (*B. abortus, B. melitensis, B. suis, B. ovis, B. canis,* and *B. neotomae*) [1, 2]. Recently four new *Brucella* species have been recognized and classified (*B. pinnipedialis, B. ceti, B. microti,* and *B. inopinata* [3–6]. Brucella are intracellular parasites where they are largely protected from host defences and chemotherapeutic agents. This characteristic is very important in issues such as the incubation period, relapses, and treatment success.

There are Biblical references to abortions in animals, some of which may have been brucellosis. In 1859, Marston described an illness whose symptoms resembled the disease. The causative agent of brucellosis, *Brucella melitenis*, was identified by Bruce in 1887 in Malta but it was not until 18 years later that a zoonotic relationship was established by Zammit, a Maltese physician. Bang, a Danish veterinarian, isolated *Brucella abortus* from cattle in 1897, and in 1914 Traum isolated *B. suis* from swine. These 3 Brucella species cause nearly all the cases of human infection. *B. melitensis* is responsible for over 90 percent of cases worldwide. It can be argued that there has been little progress in the control of *B. melitensis* worldwide in over a century of efforts [1].

Pathogenesis

The ten currently classified species of the genus Brucella and some of these and biovars have preferential hosts, with *B. melitenis* the least. They vary in pathogenesis and clinical signs and symptoms. The principal effects of brucellosis in livestock are abortion, infertility, decreased milk production and costs of replacement animals, and in humans, medical care and loss of productivity. In cattle, sheep and goats, there may be retained placentae, orchitis and epididymitis.

There are many technical aspects of brucellosis which frustrate control efforts. Perhaps the most serious is the variable incubation period and inability to identify animals which will later become seropositive. Approximately 15 percent of cattle in infected herds may abort before seroconversion. An additional problem is latency. Approximately 5 percent of the progenies of infected dams will retain the infection and become seropositive only after their first parturition. The percentage of latency among sheep and goats in largely unknown.

Diagnosis

The diagnosis of brucellosis may be initiated from either herd/flock surveillance such as the ring test on the milk of dairy cows, serological tests based on Polymerase Chain Reaction (PCR) methods, on specimens collected at slaughterhouses, or diagnostic tests performed on other specimens such as aborted foetuses. Isolation of *Brucella* spp. is still the gold standard for diagnosis. While cultivation of Brucella bacteria is the most conclusive method, facilities and expertise for these procedures are often not available. Accidental laboratory infections are a serious risk. Therefore, serological tests are usually the only diagnostic methods that are performed.

The standard agglutination test (SAT) and buffered agglutination test (BAT-Rose Bengal) are often the first tests on sera and followed by the complement fixation test (CFT) as a confirmatory test on positive sera with agglutination reactions [7]. In some countries the ELISA is used on sera and on pooled milk samples. The latter has superseded the milk ring test in some countries because of easy automation and superiority over the wilk ring test (MRT) in poor quality samples. Research is active on the development of other procedures with special emphasis on simplicity and the differentiation of antibodies from previous vaccination and those of infection. Indirect ELISA tests (iELISAs) and competitive ELISA tests (cELISAs) have been shown to have a high performance value because of high sensitivity and high specificity [8–10]. Use of the complement fixation test presents many difficulties due to lack of standardized reagents and expertise, the complexity of the test, prozones and poor quality sera.

Many papers have reported difficulties in the use of the SAT agglutination test such as delayed results and lack of sensitivity and specificity. These may be from heterospecific antibodies or those from previous vaccination. Therefore, the use of this procedure in animal sera has lessened in favour of more rapid and accurate ones. It is still widely used in tests of human sera. New molecular fingerprinting methods may be used as routine typing methods in the coming years.

There are hundreds of papers on the efficiency and accuracy of serological tests in cattle. However, there is a widespread opinion that the tests are more sensitive and specific when used in cattle than when they are used in sheep and goats.

Public Health

Brucellosis is a true zoonosis and nearly every human case has a direct (contact) or indirect origin. Reduction in the incidence of human brucellosis is largely successful only when veterinary efforts are successful.

The signs and symptoms of brucellosis in humans are well known but diagnosis may be difficult since the syndrome is similar to that of many other diseases. It is a multisystem disease whether acute or chronic. Fever, chills, sweating, headache, malaise, arthralgia, myalgia, weight loss, splenomegaly and diffuse lymphadenopathy may be present. Fever is present in over 90 percent of cases and dairy products are the sources of over 80 percent.

Brucella abortus and *B. melitensis* colonize the udder and are shed in milk. The milking breeds of sheep are very susceptible to *B. melitensis* while western or European breeds are quite resistant. Soft curd cheeses are often consumed from unheated milk. It is estimated that over 85 percent of goat's milk is consumed unpasteurized. Camels become infected from commingling with infected sheep and goats and their milk is often consumed without heating and is a source of human infections. Also, there are several reports of *B. melitensis* infection in large dairy herds. One or more human cases may be the initial evidence of the disease.

Brucellosis is an occupational risk, especially among slaughterhouse and laboratory workers, veterinarians, and livestock caretakers.

While cultures of selected specimens from suspected human cases may be conclusive in the diagnosis, they may be unreliable. The diagnosis is usually made on serological criteria. Tube agglutination, complement fixation, radioimmune assay and ELISA are some of the procedures. The Rose Bengal test, which is widely used in animal sera as a screening test for diagnosis mainly of bovine brucellosis, is simple, sensitive and of low cost [7].

Many treatment regimens have been proposed and studied such as the antibiotics rifampicin, doxycycline, ciprofloxacin and aminoglycocides. A combination of tetracycline and streptomycin has proved to be superior to most others. The primary goals of brucellosis therapy are to alleviate the patient's suffering and the symptoms of the disease, reduce complications and prevent relapses. The currently recommended treatment regimens are based on the recommendations of the World Health Organization in 1986, updated by experts in the field at the Conference for Treatment of Human Brucellosis held in Ioannina 2006 (11–13). Long-term compliance with the recommended regimen is often a problem and relapses of 10 percent or greater are often reported. There appears to be little evidence that Brucella species have developed drug resistance.

While the vaccine strains of *B. abortus* S19 and *B. melitensis* Rev 1 may cause brucellosis in humans if accidentally inoculated, and are sometimes shed in the milk of recently vaccinated animals, this author is not aware of public health risks via ingestion.

No vaccine exists that can be recommended for use in humans.

Control of brucellosis

The justifications for the control of brucellosis are public health and the economics of food production [14]. Losses from the disease in food production include restrictions in commerce, slaughter and replacement of seropositive animals and vaccination costs. It is difficult to measure economic losses due to the disease in humans such as medical costs and reduced productivity. Roth *et al*, 2003, reported an average benefit-cost ratio of 3.2 for society in a scenario of 52 percent reduction from mass vaccination of livestock [15].

Three general methods of control of brucellosis in animals are often given. These are: 1) test and slaughter, 2) hygienic measures and 3) vaccination. These are most effective when they are combined.

Test and slaughter of seropositive animals is usually a part of organized governmental programmes where the goal is eradication. These programmes are preceded by surveys to determine the prevalence in humans and animal species which may be of public health or economic importance. Data from the surveys are used in evaluations of the feasibility of subsequent efforts. Eradication is often the goal but may not be realistic. While much progress has been made in several countries in control or eradication of brucellosis, this progress has largely been with *B. abortus* in cattle. Few countries have eliminated *B. melitensis* if it has become established in small ruminants. An exception is France, which has recently achieved success. Where there is a reduction of brucellosis in livestock, there is a concurrent reduction of brucellosis in humans [15]. Few countries can afford the high costs of test and slaughter. In addition there may be a lack of skilled workers, diagnostic facilities and enforcible legislation. Other negative factors may be nomadism, commingling of flocks, and reservoirs in other species. Compensation for slaughter of animals is often absent, leading to livestock-owner resistance to cooperation.

The purpose of hygienic practices such as isolation of animals which have aborted is to reduce or prevent exposure of susceptibles. Premovement tests at local or international levels are parts of control efforts. These procedures are often difficult to administer and to gain acceptance for. Livestock owners are reluctant to accept controls for long periods, and usually only for emergency diseases. Contamination of areas requiring disinfection is a factor which may have limited impact on reducing exposure. Many studies have shown variables in survival rates of *Brucella spp.*

Vaccination/Immunization

There is wide agreement that vaccination is the most effective and practical method of reducing the incidence of many diseases including brucellosis in livestock. Vaccination against diseases is widely accepted since it is commonly used. The live vaccines *B. abortus* S19 and the *B. melitensis* Rev 1 have proved to be the most effective agents in cattle and in sheep/goats respectively. Strain RB51 has replaced S19 in some countries. There is some controversy about its effectiveness.

S19 and Rev 1 are relatively inexpensive to produce and are highly immunogenic. They may sometimes cause abortions but, in my opinion, this may be practically eliminated by reducing the dose of the vaccines (Table 1). It is necessary to keep the vaccine refrigerated and postvaccinal antibodies may interfere with the interpretation of diagnostic test results. Although immunity may not be complete in some animals, vaccination practically eliminates clinical brucellosis and, in cattle, the herd immunity exceeds 90 percent.

Table 1 – Табела 1

Selected reports on effects of a reduced dose of Rev 1 vaccine on abortion in small ruminants
Селектирани извештаи за ефектите на редуцирана доза Rev 1 вакцина на абортусите кај малите преживари

Authors	**No. Animals**	**Dose**	**Abortions**
Al-Khalaf, S. *et al.* (1992)	350,000	10^7	No increase
Alton, G. (1970)	24	5×10^4	None
Blasco, J. *et al.* (1984)	500	5×10^8	5
Blasco, J. (1997)	> 1 million	10^6	Thousands
Delgado, S. *et al.* (1995)	461	$2.3 \times 10^6 – 3 \times 10^7$	None
Henriques, H. *et al.* (1992)	85	$10^6 – 10^7$	None
Polydorou, K. (1975	90	$10^5 – 10^7$	11
Scharp, D. *et al.* (1999)	1.7 million	5×10^7	Minimal
Zundel, E. (1992)	21	$1–3 \times 10^8$	14

Brucellosis appears to be the only disease in which vaccines are used in non-susceptible animals (sexually immature) and restricted or forbidden in susceptibles. Historically, this is largely because of the diagnostic problem of postvaccinal antibodies. The concept that immunity is directly related to dose of vaccine is not true. Indeed, Parish (1972) has suggested that antibody formation and cell-mediated immunity may be opposing immunogenic processes in adult animals [16]. It is my opinion that we have been "over-vaccinating" and "underimmunizing" with the use of large amounts of antigen (Brucella cells). Field and experimental studies have shown no relationship between levels of postvaccinal antibodies and immunity. It is important that the maximum and minimum doses of brucellosis vaccines have not been established.

The recommendation to restrict Brucella vaccines to young animals is not consistent with epidemiological principles of rapid herd immunity. Diagnostic difficulties from 'whole herd' vaccination can largely be resolved by reducing the dose of vaccine and the use of selected diagnostic tests. Programme control costs are greatly decreased.

Blasco (1997) concluded that *Brucella melitensis* Rev 1 strain is considered the best available for the prophylaxis of brucellosis in small ruminants and that whole flock vaccination is the only feasible alternative to control brucellosis under the extensive management conditions characteristic of many countries [17]. However, he found vaccination of pregnant animals may be followed by abortion. He further concluded that a reduced dose of Rev 1 should not be recommended as an alternative to full standard doses [18]. Administration of the vaccine via the conjunctival route reduced antibody production in young animals [19].

Differences in residual violence and immunogenicity have been demonstrated between the different Rev 1 vaccines produced worldwide and could account for the discrepancies in safety results obtained in mass vaccination trails. Other factors could be breed susceptibility and method of administration [20–24].

Sharp (1999) used a 1/50th dose of Rev 1 in Kuwait and observed a reduced incidence among a large population of sheep and goats [25]. He observed no problems with postvaccinal antibodies and no adverse effects on gestation. This field study followed one by Al-Khalaf (1992) with similar findings and a large reduction of human cases following widespread vaccination of livestock [26].

Reports of the use of Rev 1 in dairy cattle in herds infected with B. melitensis have been somewhat limited. Conclusions differ on the effectiveness of S19. Most studies have reported that Rev 1 is superior to S19 in protection, with no adverse effects.

Brucella vaccines may be administered by a variety of methods and doses. Most studies have been with S19 in cattle. The author compared a reduced (approx 1/25th) dose with a standard dose and found few differences in apparent protection on a herd basis.

There are hundreds of papers on cross-species and reservoir infections of *Brucella spp.* These include many species of wildlife such as bison, hares, elk and swine. In general, these reservoirs have not been a major factor in the control of brucellosis.

In summary, the successful control of brucellosis will depend upon many factors: prevalence, type of animal husbandry, surveillance identification, availability and quality of vaccines, available resources (money, personnel), legal authority, intersectoral cooperation, and many others. Control of human infections depends almost wholly upon control in animals, which is mostly a veterinary responsibility.

Prevalence

It can be debated whether there has been much success in the control of worldwide brucellosis in many decades. Franco (2007) reported that brucellosis remains the most common bacterial zoonosis in the world, with over half a million new cases annually and prevalence rates in some countries exceeding ten cases per 100,000 population [27]. It is a class B bioterrorist agent and underdiagnosed and underreported. There is a re-emergence of the disease in many countries.

Clearly there has been much progress in the control and eradication of *B. abortus* in cattle, with many countries now free of this infection. However, the control of *B. melitensis* has proved to be much more difficult.

Taleski V. *et al*. (2002) reported a very large increase in human and animal brucellosis in Macedonia from 1980–2001 compared with previous years [28]. They concluded that despite implemental measures of test and slaughter, the situation has not changed in many years. Data from many regional countries were included.

Data from OIE/World Annual Health Reports show that among 19 Mediterranean and Middle East countries, there is an increase of reported cases over a 10-year period. Seven out of 19 countries had as much as a 4-fold increase [29]. Pappas, G. *et al*. (2005) concluded that eradication of brucellosis had eluded even the most developed countries and that international travel results in many new cases [30]. They presented a table showing annual reported human cases over an 8-year (1996–2003) period. Few countries reported much successful reduction, with many showing dramatic increases or high prevalences. Corbel (1997) published a list of countries claiming eradication of *B. abortus*, *B. melitensis* and *B. suis* and prevalence of these in other countries. Few statistics were given on prevalence [1].

Future

The title of this presentation includes the word future. After decades of work with this frustrating disease, I have no magical suggestions for its elimination. I am pleased that two concepts that I promote – whole herd vaccination and fewer concerns about postvaccinal antibodies – are advancing. Efforts to develop new vaccines have largely eluded scientists and live whole cell products will surely be the cornerstone products for many years. I would suggest that more studies be performed on oral administration of vaccines. Many aspects would need attention but it could possibly result in more animal immunizations. Clearly, the development of a vaccine for humans has not been successful and I question if this procedure would have much impact on human cases. Control of the disease in animals is by far the most effective.

A more effective treatment, whether prophylactic or in clinical cases, is needed. More studies should be performed on antibiotics targeted at infected cells such as those with carriers such as liposomes.

REFERENCES

1. Corbel M. (1997): Brucellosis: An overview. *Emerg. Inf. Dis.;* 3: 213–21.

2. Moreno E., Cloeckaert A., Moriyon I. (2002): Brucella evolution and taxonomy, *Vet. Microbiol*.; 90: 209–27.

3. Foster G., Osterman BS., Godfroid J., Jacques I., Cloeckaert A. (2007): *Brucella ceti* sp. nov. and *Brucella pinnipedialis* sp. nov. for Brucella strains with cetaceans and seals as their preferred hosts. *Int J Syst Evol Microbiol.;* 57: 2688–93.

4. Scholz HC., Hubalek Z., Sedlácek I., Vergnaud G., Tomaso H., Al Dahouk S. *et al*. (2008): *Brucella microti* sp. nov., isolated from the common vole *Microtus arvalis*. *Int J Syst Evol Microbiol.;* 58: 375–82.

5. Scholz HC., Hubalek Z., Nesvadbova J., Tomaso H., Vergnaud G., Le Flèche P. *et al*. (2008): Isolation of *Brucella microti* from soil. Emerg Infect Dis.; 14: 1316–7.

6. Scholz HC., Hofer E., Vergnaud G., Le Fleche P., Whatmore AM., Al Dahouk S. *et al*. (2009): Isolation of *Brucella microti* from mandibular lymph nodes of red foxes, *Vulpes vulpes*, in lower Austria. *Vector Borne Zoonotic Dis.;* 9:153–6.

7. Greiner M., Verloo D., de Massis F. (2009): Meta-analytical equivalence studies on diagnostic tests for bovine brucellosis allowing assessment of a test against a group of comparative tests. *Prev Vet Med.;* 92: 373–81.

8. Saegerman C., De Waele L., Gilson D., Godfroid J., Thiange P., Michel P. *et al*. (2004): Evaluation of three serum i-ELISAs using monoclonal antibodies and protein G as peroxidase conjugate for the diagnosis of bovine brucellosis. *Vet Microbiol.;* 100: 91–105.

9. Nielsen KH., Kelly L., Gall D., Nicoletti P., Kelly W. (1995): Improved competitive enzyme immunoassay for the diagnosis of bovine brucellosis. *Vet Immunol Immunopathol.;* 46: 285–91.

10. Weynants V., Gilson D., Cloeckaert A., Denoel PA., Tibor A., Thiange P. *et al*. (1996): Characterization of a monoclonal antibody specific for Brucella smooth

lipopolysaccharide and development of a competitive enzyme-linked immunosorbent assay to improve the serological diagnosis of brucellosis. *Clin Diagn Lab Immunol.;* 3: 309–14.

11. Solera J. (2000): Treatment of human brucellosis. *J Med Liban*.; 48: 255–63.

12. Food and Agriculture Organization (FAO) – World Health Organization (WHO). (1986): Expert committee on brucellosis (sixth report). WHO technical report series, no 740. Geneva: World Health Organization: p. 56–7.

13. Ariza J., Bosilkovski M., Cascio A., Colmenero JD., Corbel MJ., Falagas ME. *et al*. (2007): Perspectives for the treatment of brucellosis in the 21st century: the Ioannina recommendations. *PLoS Med.;* 4: e317.

14. Nicoletti P. (1992): The control of brucellosis – a veterinary responsibility. *Saudi Med. J.;* 13: 10–13.

15. Roth F., Zinsstag J., Orkhon D. *et al*. (2003): Human health benefits from livestock vaccination for brucellosis: Case study. *Bull. W. H.O.;* 81: 867–76.

16. Parish C. (1972): The relationship between humoral and cell-mediated immunity. *Transplant. Rev.;* 13: 35–66.

17. Blasco J., Estrada A., Mercadel M. (1984): A note on adult sheep vaccination with reduced dose of *Brucella melitensis* Rev 1. *Ann. Rech. Vet.;* 15: 553–6.

18. Blasco J. (1997): A review of the use of *B. melitensis* Rev 1 vaccine in adult sheep and goats. *Prev. Vet. Med.;* 31: 275–83.

19. Zundel E., Verger J., Grayon M. *et al*. (1992): Conjunctival vaccination of pregnant ewes and goats with *Brucella melitensis* Rev 1 vaccine: Safety and serological response. *Ann. Rech. Vet.;* 23: 177-88.

20. Alton G. (1970): Vaccination of goats with reduced doses of REV 1 *Brucella melitensis* vaccine, *Res. Vet. Sci.;* 11: 54–9.

21. Crowther R., Orphanides A., Polydorou K. (1977): Vaccination of adult sheep with reduced doses of *Brucella melitensis* strain Rev 1: Safety and serological responses. *Trop. An. Hlth Prod.;* 9: 85–91.

22. Delgado S., Carmenes P., Ferndandes M. (1995): Seroprevalences and lack of abortion after vaccination of Churra sheep with reduced doses of Rev 1 *Brucella melitensis* vaccine by subcutaneous or conjunctival routes. *Prev. Vet. Med.;* 23: 153–61.

23. Henriques H., Hueston W., Hoblet K. *et al*. (1992): Field trails evaluating the safety and serologic reactions of reduced-dose *Brucella melitensis* Rev 1 vaccination in adult sheep. *Prev. Vet. Med.;* 13: 205–15.

24. Polydorou K. (1975): Vaccination of sheep with reduced doses of Rev. 1 *Brucella melitensis* vaccine. *Bull. Off. Int. Epiz*.; 43rd Gen. Sess: 1–6.

25. Scharp D., Al-Khalaf S., Muhanna M. *et al*. (1999): Use of mass vaccination with reduced dose of REV 1 vaccine for *Brucella melitensis* control in a population of small ruminants. *Trop. Am. Hlth Prod*. 31: 135–41.

26. Al-Khalaf S., Taha Mohamad., Nicoletti P. (1992): Control of brucellosis in Kuwait by vaccination of cattle, sheep and goats with *Brucella abortus* strain 19 or *Brucella melitensis* Rev 1. *Trop. Anim. Hlth Prod.;* 24: 45–9.

27. Franco M., Milder M., Gilman R. *et al*. (2007): Human brucellosis. *Lancet Infectious Diseases;* 7: 775–86.

28. Taleski V., Zerva L., Kantardjiev T. *et al*. (2002): An overview of the epidemiology and epizootology of brucellosis in selected countries of Central and Southeast Europe. *Vet. Micro.;* 90: 147–55.

29. OIE. (2000–2008): Reported cases of human brucellosis in selected Mediterranean and Middle East Countries. Official Reports; OIE/World Annual Health Reports.

30. Pappas G., Akritidis N., Bosilkovski M. *et al*. (2005): Brucellosis. *N. Engl. J. Med.;* 352: 2325–36.

Р е з и м е

БРУЦЕЛОЗА: МИНАТО, СЕГАШНОСТ И ИДНИНА

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Цел: Да се направи преглед и да се прикажат специфичностите на биологијата, епидемиологијата, патогенезата и дијагностиката, јавно-здравствените аспекти, вакцинацијата и контролата на бруцелозата како глобална зооноза.

Методи: Помеѓу различните методи за контрола на бруцелозата кај животните како вакцинација, хигиена, тестирање и колење на инфицираните животни, широко распространетата вакцинација претставува најбрз, најефикасен и најефективен метод.

Резултати: И покрај големиот напредок во контролата, а понекогаш и во ерадикацијата на бруцелозата кај крупниот добиток во повеќе земји, состојбата со заболувањето кај ситните преживари се покажува дека е многу потешка. Политичките и социоекономските проблеми претставуваат пречка за успехот. Одговорноста за прифаќање на предизвикот за контрола на бруцелозата кај животните припаѓа на ветеринарите, а тоа понатаму би помогнало во контролата на заболувањето кај луѓето. Успехот на ефектите од контролата примарно ќе се мери со намалување на бројот на заболени кај луѓето.

Заклучок: Ефективната контрола на бруцелозата бара долготрајно залагање од страна на многу владини агенции. Поддршката во средства и експертиза од меѓународните организации за здравје на животните и луѓето

е неопходна во многу земји во развој. Не постојат лесни решенија. Потребно е да се охрабруваат истражувањата за алтернативни стратегии за вакцините и нивната употреба, дијагностички тестови и третманот.

Клучни зборови: болест кај животните, бруцелоза, зоонози, стратегии за контрола/ерадикација.

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